initiated on insulin therapy, and then censored from analyses. Fifteen PwCF were treated with a CF transmembrane conductance regulator modulator during the study (4 on elexacaftor/tezacaftor/ivacaftor). At baseline, LBMI (15.8 kg/m^2, range 13.7–23.7 kg/m^2 vs 15.5 kg/m^2, range 12.6–24.2 kg/m^2; $p = 0.7$), ALBMI (6.9 kg/m^2, range 5.4–10.3 kg/m^2 vs 6.8 kg/m^2, range 5.3–11.5 kg/m^2; $p = 0.7$), and FMI (6.4 kg/m^2, range 3.1–12.3 kg/m^2 vs 7.5 kg/m^2, range 3.2–12.8 kg/m^2; $p = 0.5$) did not differ between PwCF and HCs. Over the study period, LBMI ($p = 0.8$), ALBMI ($p = 0.2$), and FMI ($p = 0.1$) did not change in the study population. LBMI accrual, adjusted for sex and baseline age, was similar for PwCF and HCs ($p = 0.6$), as was ALMBI accrual ($p = 0.5$). Similarly, no group differences in FMI accrual were found ($p = 0.3$). Further adjustment for BMI did not result in group differences in indices. In male and female PwCF, LBMI over time was not associated with increasing FBG ($p = 0.8$), OGTT 1-hour glucose ($p = 0.9$), or OGTT 2-hour glucose ($p = 0.9$). ALBMI and FMI accrual were not associated with FBG or OGTT 1- or 2-hour glucose, either ($P > 0.1$ for all). Use of a CFTR modulator was not associated with changes in LBMI, ALBMI, or FMI in PwCF ($P > 0.1$ for all).

Conclusions: Over a 2-year period, body composition in PwCF remained stable and was comparable with body composition of individuals without CF. This small CF cohort also demonstrated a lack of association between body composition and early glucose intolerance or CFTR modulator therapy. With overall advances in CF care and better lung function and nutritional status, a subgroup of PwCF may be less vulnerable to the traditional nutritional decline with glucose intolerance and may experience no additional gain in LBM with CFTR modulator use.

Acknowledgements: This work was supported by Public Health Service research grants National Institute of Diabetes and Digestive and Kidney Diseases K23 DK107937 (to S.S.) and UL1 TR001878 (University of Pennsylvania Centers for Human Phenomic Science).

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Promise: Glucose excursion and insulin secretion after 12 to 18 months of highly effective modulator therapy

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Background: Clinical observations, case series, and registry data revealed greater glucose tolerance, better insulin secretion, and fewer cystic fibrosis (CF)-related diabetes (CFRD) diagnoses with ivacaftor. Inspired by these data, this study was designed to test the effect of clinically prescribed elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) on glucose intolerance and insulin secretion and sensitivity.

Methods: Three-hour 10-sample oral glucose tolerance tests (OGTTs) were performed at baseline and 12 to 18 months at 10 designated endocrine substudy centers of *pROMISE,* a 56-center prospective, observational study of ELX/TEZ/IVA in people with CF aged 12 and older with at least one *F508del* mutation. Rapid-acting insulin was withheld for the subset treated with insulin. Glucose tolerance (GT) was defined as: normal (NGT), early glucose intolerance (EGI; 60 minutes at ≥155 mg/dL then 120 minutes at <140 mg/dL), impaired glucose tolerance (IGT; 120 minutes at ≥140 mg/dL then <200 mg/dL, CFRD (120 minutes at ≥200 mg/dL), and hypoglycemia (≤65 mg/dL). Incremental area under the curve ($iAUC_{30}$) for glucose tolerance, glycosylated hemoglobin (HbA1C), OGTT glucose (0, 60, 120 minutes), insulin sensitivity, and 0- to 30-minute glucose and insulin secretory rates (ISRs) were compared at baseline and follow-up using mixed-effects ordinal or linear models (fixed effect: visit; random effect: subject) and to further test for relationships with age, body mass index (BMI) Z-score, and percentage predicted forced expiratory volume in 1 second (FEV_1pp).

Table 1 (abstract 15):
Baseline and 12- to 18-month demographic, glucose, and insulin data

N=65; 32M/33F	Baseline Mean (95% CI)	12-18 mo post-ETI Mean (95% CI)	p-value
BMI-Z	0.02 (-0.22-*0.26)	0.27 (0.05-0.49)	<0.001
FEV1%-predicted	82.9 (77.4-88.5)	95.7 (90.5-100.9)	<0.001
HbA1C, %	5.83 (5.64-6.01)	5.53 (5.39-5.68)	<0.001
No insulin treatment (n=53)	5.57 (5.48-5.67)	5.33 (5.24-5.42)	<0.001
NGT/EGI/IGT/CFRD	8/22/23/12	8/29/17/11	0.22
Hypoglycemia *(5 had abbreviated OGTT)*	15/60	23/60	0.059
Fasting glucose, mg/dL *No basal insulin treatment (n=58)*	94 (92-96)	91 (89-93)	0.019
60-min glucose, mg/dL	200 (189-211)	201 (188-214)	0.82
120-min glucose, mg/dL	158 (141-175)	150 (132-167)	0.17
$iAUC_{30}$Glucose, (mg/dL)/min (n=51)	942 (855-1029)	957 (842-1071)	0.46
$iAUC_{30}$ISR, (pmol/L)/min (n=51)	2164 (1873-2454)	2269 (1965-2572)	0.38
$iAUC_{30}$ISR : $iAUC_{30}$Glucose, mU/mg (n=51)	0.043 (0.036-0.05)	0.045 (0.038-0.052)	0.63
SI (μU/mL)/min	8.48 (6.36-10.6)	7.37 (6.11-8.66)	0.37

Results: Baseline and follow-up OGTTs were available in 65 of 69 participants (33F/32M, median age 18.3, range 12–51.9); 13 were treated with insulin. Percentage HbA1C and fasting glucose improved, but no differences in glucose tolerance were found (Table 1); 17 or 57 participants with abnormal glucose tolerance improved, and nine of 41 without CFRD worsened; hypoglycemia rates and 60- and 120-minute glucose were not different. For the 51 participants for whom complete data were available, no differences in $iAUC_{30}$glucose, $iAUC_{30}$ISR, $iAUC_{30}$ISR: $iAUC_{30}$glucose, or insulin sensitivity were found. These results persisted after adjustment for age, BMI, FEV_1pp, and CFRD history, and although CFRD was associated with lower $iAUC_{30}$ISR:$iAUC_{30}$glucose, no interaction between CFRD and visit was found.
Conclusions: In these preliminary analyses, OGTT-related glucose excursion and insulin secretion did not improve with 12 to 18 months of clinically prescribed ELX/TEZ/IVA, despite modest decreases in HbA1C, although HbA1C better reflects longer-term glycemia. The effects of longer ELX/TEZ/IVA treatment on insulin secretion and glucose tolerance remain to be determined.
Acknowledgements: This work was supported by the Cystic Fibrosis Foundation (PROMISE-OB-18) and the National Institutes of Health (UL1 TR001878 [University of Pennsylvania Center for Human Phenomic Science] and P30 DK19525 [University of Pennsylvania Diabetes Research Center]).

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Provider education for sexual and reproductive health for adolescents with cystic fibrosis

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Background: Adolescents with cystic fibrosis (CF) are sexually active at the same rate as their healthy peers and have general and disease-specific educational needs regarding sexual and reproductive health. CF care team providers recognize the importance of discussing sexual and reproductive health, but many lack knowledge, comfort, and time to address these topics with adolescents. Providing a clinical practice guideline and education to increase provider confidence in addressing sexual and reproductive health is an important step to implement regular discussions in routine CF clinic visits.
Methods: A quality-improvement project was implemented in the CF clinic in the Intermountain West to increase provider's knowledge and self-efficacy in discussing sexual and reproductive health with adolescents. Provider surveys were reviewed to identify specific educational needs, and previous guidelines were adapted. The clinical practice guideline included information on disease-specific and general sexual and reproductive health topics and a timeline for discussion. The educational module included general tips regarding sexual and reproductive health, mnemonics to assist in discussion, scripting to introduce confidential time during a visit, providing inclusive care, and a clinic-specific referral list. A postintervention survey was sent to care team providers to determine their intent to change practice and to obtain feedback regarding the guideline and education.
Results: Postintervention surveys were sent to nine CF care team members, and the response rate was 22.2% (n = 2). Providers intended to change their practice and implement regular sexual and reproductive health into clinic visits. Providers found the mnemonics and information regarding inclusive care most helpful in increasing their self-efficacy in providing sexual and reproductive health education. Time continues to be the greatest barrier to implementing the guidelines and techniques.
Conclusions: Providers found the guideline and education helpful in increasing their self-efficacy in conversations with adolescents regarding sexual and reproductive health. Further quality improvement work is needed to apply these guidelines to clinical practice and monitor implementation of regular discussion with adolescents in routine visits.

EPIDEMIOLOGY & POPULATION-BASED RESEARCH

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Fetal impact of cystic fibrosis transmembrane conductance regulator modulator use during assisted and natural reproduction and partner pregnancy in men with cystic fibrosis

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Background: Increasing availability of highly effective cystic fibrosis (CF) transmembrane conductance regulator (CFTR) modulator therapy (HEMT) has improved the quality of life and long-term prognosis for many people with CF. Thus, more people with CF are considering parenthood. Almost all men with CF (MwCF) are infertile because of congenital bilateral absence of the vas deferens (CBAVD). Based on CF animal models, CBAVD occurs early in gestation and is unlikely to be reversible using HEMT, but assisted reproductive techniques (ARTs) can enable MwCF to father children using the sperm in their testes. Animal reproductive models suggest no HEMT teratogenicity, and the amount of exposure of the fetus to HEMT via absorption of seminal fluid through the vaginal wall is predicted to be negligible, although to ensure no sperm exposure to HEMT, the life span of sperm would require MwCF to discontinue CFTR modulators for approximately 3 months before ART. Because abrupt discontinuation of CFTR modulators may result in health decline, MwCF and their providers must consider all potential risks. There are no published data in MwCF regarding use of HEMT during conception and partner pregnancy.
Methods: Beginning in August 2021, CF center staff in the United States, United Kingdom, and Australia completed a two-page anonymous questionnaire regarding MwCF who used CFTR modulators during ART (sperm retrieval and in vitro fertilization) or natural conception with subsequent partner pregnancy.
Results: Providers have submitted 34 surveys for MwCF on CFTR modulators whose partner became pregnant after use of ART (n = 32) or natural conception (n = 2). The median age of the sample was 32 (range 24–43). Fifteen were homozygous for F508del, median percentage predicted forced expiratory volume in 1 second was 76% (range (22–111%), and median body mass index was 24 kg/m^2 (range 18.5–32.1). Twenty-three were taking elexacaftor/tezacaftor/ivacaftor. The median time that MwCF were taking CFTR modulators before partner conception was 18 months (range 0–82). One newly diagnosed man initiated HEMT after sperm retrieval. Four MwCF stopped CFTR modulators before sperm retrieval, one of whom experienced pulmonary decline. None of the 19 MwCF whose condom use during pregnancy was known used condoms. Fetal complications in partners of MwCF included three first-trimester miscarriages, two* COVID, two breech presentation, two* vaginal bleeding, and one vasa previa. None of the complications were deemed definitively related to use of CFTR modulators. One MwCF experienced testicular infection after sperm retrieval#. Postpartum complications included three# infants with hypoxemia requiring neonatal intensive care unit stay, three maternal blood loss, one forceps delivery, and one caesarean section. No congenital anomalies were reported for any infant. (*/# overlap).
Conclusions: Use of CFTR modulator therapy during partner conception and pregnancy in 34 MwCF has not resulted in higher-than-expected miscarriage rates or congenital anomalies. Providers should consider the risk to the health of MwCF combined with the lack of teratogenicity in animal reproductive models and limited safety data in the human fetus before discontinuing CFTR modulators before ART or natural partner conception. Survey collection is ongoing; results will be updated for presentation.
Acknowledgements: Funded by the Asher Family Fund.