WS03.6

Referral pathway to the genetics service for families of paediatric patients newly diagnosed with cystic fibrosis

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Objectives: A discussion about the inherited nature of cystic fibrosis (CF) is important when disclosing the diagnosis to parents. Reproductive options exist for couples where both individuals are known to be carriers of a variant in the cystic fibrosis transmembrane regulator gene. In order to facilitate these reproductive choices, all parents of children newly diagnosed with CF should be offered a referral to clinical genetics service. We audited our current practice with resulting recommendations.
Methods: All patients with a diagnosis of CF who were born in the last five years and are under the care of our regional CF centre were identified. Notes were reviewed for these patients, and their elder siblings where applicable, to establish referral practice to clinical genetics. Notes were also reviewed by the regional genetics service to establish if families had accessed the service via another route.
Results: 31 patients were identified, 6 of these patients had older siblings. 13 of the 31 patients had a positive family history of CF. Out of the 31 families, 8 were referred to clinical genetics, but only 5 of these referrals were because of the history of CF (16%). This is falling well below the standard of 100%, however the reason for this is not clear as to whether it was lack of discussion from the clinical team or lack of uptake by the family.
Conclusion: Ascertaining why so few referrals are made will be important in order to gain further understanding and allow better support to families. Enhancing access to clinical genetics will enable families to have reproductive choice. As there is no dedicated information to offer families, we have introduced a parent information leaflet to facilitate discussions and to clarify the role of clinical genetics in family planning for our region. This leaflet will be offered to all families at diagnosis and again at a later stage.

Workshop 4 – Improvements in understanding how physical activity and exercise impact cystic fibrosis

WS04.1

A comparison of subjective verses objective measures for assessing physical activity in cystic fibrosis: a systematic review

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Objectives: Physical activity (PA) is a key component in the management of cystic fibrosis (CF). Accurate assessment of PA is required to guide clinical practice in assessing PA levels, implementing, and assessing treatment plans, and in the evaluation of effective interventions designed to increase PA. This study aimed to identify if there is a correlation between subjective (self-reporting e.g., questionnaires) and objective (direct measures e.g., accelerometry) measures of PA in CF in order to determine if these outcomes are interchangeable in clinical practice.
Methods: Relevant electronic databases were searched, and studies were only included if they compared at least one subjective measure to an objective measure in a CF population. Quality and risk of bias of all included studies was assessed with a modified Downs and Black checklist.
Results: An initial search identified 622 studies, of which five were included in this review. Within the studies, correlation between subjective and objective measures was inconsistent with some studies identifying agreement between the measures and others finding no relationship. Critical appraisal of results using a modified Downs and Black checklist indicated that included studies varied between low and good quality.
Conclusion: The results indicate that there are inconsistencies between subjective and objective measurements of PA in the CF population. Subjective measurements were not consistent at measuring different intensities of PA. This suggests that the subjective PA measurement may significantly impact on the observed levels of PA. More studies are needed to rely solely on the use of PA questionnaires in CF. This review identifies the need for further research to determine valid, reliable, and accurate measurements of PA in people with CF. This will be important in order to evaluate PA levels, determine the effectiveness of PA interventions and establish relationships between PA and health outcomes.

WS04.2

To investigate which physical factors influence the cardiorespiratory fitness in paediatric patients with cystic fibrosis who have no ventilatory limitation during exercise (ventilatory reserve ≥15%)

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Objectives: [1] To investigate the cardiorespiratory fitness (CRF) levels in paediatric patients with cystic fibrosis (CF) who are not ventilatory limited (ventilatory reserve ≥15%) during exercise; [2] to assess which physical factors predict CRF best.
Methods: A cross-sectional study design was used in 8–18 year-old patients. Cardiopulmonary exercise testing was used to determine maximum oxygen uptake related to body weight as a measure of CRF. Non-fit patients were defined when CRF was less than 82% predicted. Physical predictors used in this study were body mass index, z-score, *P. aeruginosa* lung infection, impaired glucose tolerance (IGT) including CF-related diabetes (CFRD), CF-related liver disease (CFRLD), pulmonary function ($ppFEV_1$), sweat chloride concentration, and self-reported physical activity (PA). Backward LR logistic regression analysis was used.
Results: 60 patients (51.7% male) with a median age of 15.3 years (25–75th percentile 12.9–17.0 years) and mean $ppFEV_1$ 88.5% (±16.9) participated. Mean CRF was 81.4% ± 12.4. Thirty-three patients (55.0%) were classified as non-fit. The final model that fitted low CRF best, included IGT ($p = 0.085$; $Exp(B) = 6.770$) and *P. aeruginosa* lung infection ($p = 0.095$; $Exp(B) = 3.945$). This model was able to explain between 26.7% and 35.6% of variance.
Conclusions: CRF is reduced in a large part of our current paediatric population. Glucose intolerance and *P. aeruginosa* lung infection seem important physical predictors for CRF in paediatric patients with CF. Maintaining and improvement of CRF, combined with early detection and prevention of glucose intolerance and *P. aeruginosa* colonisation remain, even in the current decade a very important aspect in the lifelong treatment of paediatric patients with CF.

WS04.3

Lung function as a determinant of the evolution of exercise capacity over a three-year follow-up period in patients with cystic fibrosis

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Objective: Patients with cystic fibrosis (CF) develop with intolerance to exercise as disease progresses and its main associated factors have been little explored. Thus, the objective of this study was to evaluate the influence of clinical and demographic variables on the evolution of exercise capacity over a three-year follow-up period.
Methods: This is a prospective cohort. Patients with a diagnosis of CF, aged ≥6 years, who underwent two cardiopulmonary exercise tests (CPET) and two lung function tests (spirometry), with an interval of three years, were included. Anthropometry (body mass index - BMI), lung function (FEV_1 and FVC - % of predicted) and CPET variables (peak oxygen consumption – VO_2peak - $mL.Kg^{-1}.min^{-1}$) were collected in both years 1 and 3. The use of antibiotics (ATB) was also recorded. For statistical purposes, Pearson

correlation, paired Student's *t*-test and a multiple linear regression model were used. The study was approved by the University's Research Ethics Committee.
Results: Eighteen patients (72.2% male), mean age 17.6 ± 6.7 years, were included. Progression over the 3 years indicated changes in FEV_1 (88.2 ± 16.8 × 78.1 ± 22.2), FVC (95.1 ± 13.9 × 86.2 ± 19.3), and no significant differences for BMI (21.1 ± 3.6 × 21.4 ± 3.6) and VO_2peak (40.5 ± 8.6 × 38.7 ± 10.0), although 50% of patients presented decreased VO_2peak from year 1 to 3. An average of 63.6 days of ATB use was demonstrated. Moderate correlations were found between the delta (Δ = year 3-year 1) of VO_2peak with ΔFEV_1 (r = 0.64, $p = 0.004$) and ΔFVC (r = 0.62, $p = 0.006$). In the multiple linear regression analysis, age, sex, chronic colonisation by *Pseudomonas aeruginosa*, BMI, lung function and use of ATB were included. The only significant variable to predict the progression of VO_2peak was the ΔFEV_1 ($r^2 = 0.51$, $p = 0.001$).
Conclusion: Lung function was the main determinant in the evolution of exercise capacity over a period of three years in patients with CF.

WS04.4
Exercise testing and training in German cystic fibrosis centres – temporal trends from 2001 to 2019

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Objective: In 2001, 87% of 63 German cystic fibrosis (CF) centres responding to a survey regarded physical exercise as at least very important and 61% advised their patients to be physically active. Exercise testing was viewed as somewhat important by 77% of centres. The objective of this study was to assess changes in caregiver's attitude towards exercise testing and training over 18 years.
Methods: The identical questionnaire used for the survey in 2001 was sent to specialised CF centres and inpatient rehabilitation institutions in Germany, Austria and Switzerland in 2019.
Results: 59 centres caring for 6,198 patients and 4 inpatient rehabilitation centres completed the survey in 2019. The importance of physical activity was rated significantly higher in 2019 than in 2001, with 95% of respondents marking at least very important. There was no change in the rating of importance of exercise testing (rated at least somewhat important by 82% in 2019 vs. 77% in 2001). In 2019, all centres provided advice to their patients to be active. The availability of equipment for full cardiopulmonary exercise testing (CPET) increased from 56% of centres in 2001 to 73% of centres in 2019.
Conclusion: Compared to an identical survey 18 years ago, caregivers in specialised CF centres and inpatient rehabilitation units rated the importance of physical activity as significantly higher. The attributed importance of formal exercise testing was unchanged over time, while the number of CPET facilities increased from 2001 to 2019.

WS04.5
Exercise testing using supramaximal verification in cystic fibrosis

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Objectives: Annual exercise testing is recommended for all patients with cystic fibrosis (CF) above 10 years of age. Cardiopulmonary exercise testing (CPET) is the gold-standard technique, although the explicit protocol to be used remains equivocal. Recently, supramaximal verification testing (Smax), a secondary exercise bout at 110% of peak power achieved during a prior incremental bout to volitional exhaustion, is recommended to verify attainment of a true maximal oxygen uptake (VO_{2max}). Use of Smax in CF is possible but sparsely utilised, and therefore the aim of this study is to establish the attainment of a "maximal" test between the incremental bout and its subsequent verification bout for this protocol.
Methods: Annual exercise test data was reviewed to ascertain agreement between incremental and Smax data in a cohort of $n = 88$ patients with CF. A difference ≤10% in VO_2 between phases was utilised to verify attainment of VO_{2max}. Descriptive statistics, Pearson's correlations and Bland-Altman analyses, and associated limits of agreements (LoA) were utilised.
Results: A total of $n = 77$ patients were identified as performing Smax protocols ($n = 11$ did not perform Smax due to clinical time restraints). A total of 56/77 patients had VO_{2max} verified (i.e. change between incremental and Smax was ≤10%). Mean VO_2 from incremental and Smax phases were 1.81 ± 0.16 and 1.90 ± 0.68 $L.min^{-1}$ respectively, and were significantly correlated ($r = 0.97$, $p < 0.01$). The mean difference was 0.09 ± 0.17 $L.min^{-1}$. This equated to 5.1 ± 9.4% (LoA = −13.7–23.9%).
Conclusions: The majority of patients who perform Smax verification as part of an annual CPET have their true VO_{2max} verified, changing by only ~5% between incremental and Smax phases. However, a small number of patients do not and clinicians may have to consider a repeat test or be reliant on secondary verification criteria to ascertain whether a VO_{2max} has occurred.

WS04.6
Effects of a partially supervised conditioning program in cystic fibrosis: an international multi-centre, randomised controlled trial (ACTIVATE-CF)

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Objectives: The aim of the trial ACTIVATE-CF was to evaluate a 12-month partially supervised exercise intervention along with regular motivation and feedback in cystic fibrosis (CF). The primary endpoint was change in FEV_1 at 6 months. Secondary endpoints included physical activity (PA) and fitness, time to first exacerbation, quality of life, levels of anxiety, depression and stress, and control of blood sugar.
Methods: 117 of intended 296 relatively inactive patients with CF aged ≥12 years recruited by 27 centres in 8 countries were randomised to a control (CG, n = 57) or an intervention (IG, n = 60) group. IG consented to add 3 hours of intense PA per week to baseline activity, while CG was asked to keep PA level constant. Data were analysed using mixed linear models with multiple imputation of missing data (intention to treat).
Results: In contrast to our hypothesis, CG had significantly improved FEV_1 over IG by 2.70%pred (95%-CI: 0.13 to 5.26; p = 0.04) after 6 months of intervention. After 12 months, change in FEV_1 in the IG was non-significantly higher than in CG by 1.87%pred. (95%-CI: −1.00 to 4.74; p = 0.20). IG reported increased vigorous PA vs baseline at each study visit which was significantly higher than in the CG (1.7 to 2.4 hours/week). The intervention led to a higher peak workrate at both time points - 6 and 12 months - assessed during intervention, more aerobic steps (≥60 steps/min over ≥10 minutes) and a significantly higher peak oxygen uptake at 12 months. There was no effect of the intervention on time to first exacerbation, quality of life, anxiety, depression, stress, or glucose tolerance.
Conclusion: Despite not reaching statistical power, ACTIVATE-CF is the largest exercise intervention trial to date. A partially supervised exercise program including motivation/feedback demonstrated increased intense PA and aerobic fitness – with effects carried over for the subsequent 6 months – but did not show effects on primary outcome FEV1.