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Authors' Reply

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We thank Saynor and colleagues for their comments [1] to our
Statement on Exercise Testing in Cystic Fibrosis [2]. Saynor et al.
[1] suggest an alternative to the Godfrey protocol for cycle ergome-
try as best practice. The Godfrey protocol uses 1-min step incre-
ments to maximal exertion, with the steps adjusted to complete the
test in 8–12 min. Saynor et al. [1] suggest an exercise test protocol
instead which consists of two parts: a ramp increase in exercise
intensity by 10–25 W/min to volitional fatigue and – after 5 min
of active recovery and 10 min of rest – a constant work rate test at
110% of peak power to verify oxygen uptake at peak exercise [3].
They further state that our proposed indicators of a peak patient
effort may not allow determining peak oxygen uptake ($\text{VO}_{2\text{peak}}$).

It is important to remember why exercise testing is being rec-
ommended. Exercise testing is performed to determine functional
capacity and the sources of exercise limitation, to provide guidance
and counselling for physical activity, physical interventions and/
or to prognosticate. To accomplish this, the results from a Godfrey
protocol symptom-limited exercise test provide us with the infor-

mation to answer these important questions. We fully agree with
Saynor et al. [1] that any cardiopulmonary exercise test protocol
should produce valid and reliable results. However, to be recom-
mended for clinical practice, the test protocol also needs to be fea-
sible. Adding a second verification test puts more burden on the
patient and the exercise testing facility, which has to be well justi-
fied.

The protocol suggested by Saynor et al. [1] has been used in a
relatively small ($n = 14$) group of children and adolescents with
cystic fibrosis and mild to moderate lung disease in a research set-
ting so far [3]. Data on adults or patients with advanced pulmonary
disease are missing. In contrast, the Godfrey protocol has been
used both for clinical and research purposes in large groups of pa-
tients all over the world. For our statement, the following criteria
for selecting an exercise testing protocol have been applied: 'The
exercise testing protocol should be as universally applicable as pos-
sible to allow follow-up of patients over time, facilitate compar-
isons between centers and enable analyses of large databases in the
future, e.g. patient registries. Thus, the protocol should be valid for
testing young and older as well as severely impaired and very fit
patients, and suitable to address the clinical indications for an ex-
ercise test in CF' [2] (page 5).

The main argument of Saynor et al. [1] is that their complex
protocol [3, 4] elicits, only in three patients, a higher VO_2 than a
ramp test alone in some patients. However, in their publications,
the authors failed to report individual peak heart rate, peak respi-
ratory exchange ratio, etc. during their ramp test, so that it remains
unclear how many tests would have been rejected based on the
criteria of a maximum effort proposed in our statement [2]. In
other words: it might well be that the incremental tests reported by
Saynor et al. [3], which resulted in much lower peak VO_2 values
than the following constant workload tests in a few patients, would
have been invalid ('no maximal effort') according to the criteria
defined in our Statement. In the case of a non-maximal effort, we
recommend to consider repeating the test rather than using the
data [2, see flow chart there, page 13]. If this approach had been
taken by Saynor et al. [4] to select only valid ramp tests, possibly
the reproducibility of $\text{VO}_{2\text{peak}}$ determined during such tasks would
have improved. Indeed, data from the Children's Health and Ex-
ercise Research Centre in Exeter – the same institution as Saynor
et al. – show high reproducibility of $\text{VO}_{2\text{peak}}$ measurements ob-
tained during an incremental cycle test in children without a su-
pramaximal validation [5]. The coefficient of variation of the typ-
ical error (4.1%) was even lower in this latter study [5] compared
to the value (9.3%) reported in the study by Saynor et al. [4], which
included a supramaximal validation. Perhaps a secondary analysis
of the data collected by Saynor et al. [4] with exclusion of ramp tests
without a maximal effort could provide more insight.

The concept of using secondary criteria to validate a maximal
effort during an incremental cycling task as recommended in our
Statement does not seem to be fully appreciated by Saynor et al.
[1]. As clearly described in our Statement, criteria are used *follow-*

ing an incremental test to volitional fatigue to substantiate a maximal effort. Since there is large interindividual variation in peak values of heart rate, respiratory exchange ratio (RER), etc., the approach taken by Saynor et al. [1] to look at VO_2 at a given heart rate or RER *during* an incremental test to find out that the VO_2 is lower than at peak exercise is not surprising and no valid argument against our approach.

Validity of a cardiopulmonary exercise test not only requires a valid measure of $\text{VO}_{2\text{ peak}}$ but is further substantiated by its association with important clinical outcomes, such as prognosis, quality of life or exacerbations. Interestingly, the respective relationships have been shown in all respective publications cited by Saynor et al. [1] using an incremental exercise test without a supra-maximal constant load verification test.

With respect to total exercise time when using the Godfrey protocol with the selection of work rate increments based on patients' height and FEV_1 as suggested in our Statement, we did never observe exercise times less than 6 min if the effort was maximal. Even when using the equation developed by Hulzebos et al. [6] to calculate work rate increments for an incremental cycle test in children and adolescents, exercise time varied between 7 and 16 min. Nevertheless, the publication has been acknowledged in our Statement [2].

Our Statement on Exercise Testing in Cystic Fibrosis will be reviewed and likely revised in 2020. In that revision, the existing evidence for using an additional supramaximal verification test in the assessment of $\text{VO}_{2\text{ peak}}$ will be assessed and the information integrated in the document.

References

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