Letter to the Editor: Prediction of peak oxygen uptake using the modified shuttle test –

2 **Methodological concerns and implications for clinical practice.**

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9 To the Editor

10 We note with interest the paper by Vendrusculo *et al* (1) and their attempt to predict the peak

11 oxygen uptake (V̇O2peak) using the modified shuttle test (MST) in children and adolescents with

12 cystic fibrosis (CF). The authors conclude "that it is possible to predict VO2peak using the MST"

13 (page 6). However, the issue is not whether one variable can predict another variable, but it is

14 the accuracy and error of the prediction that is of most importance. Therefore, we have serious

15 concerns about the conclusions based on this data set regarding: 1) the variation and error in

16 the model at an individual level; 2) the development of the regression model; and 3) the

17 measurement of the criterion variable.

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19 Firstly, there is a high level of variation and error in the estimate, such that on any given test,

20 the variation around an individual measure is ~ 8 mL.kg-1.min-1, which seems unacceptable

21 given the likely change from exercise or other interventions. We support the authors in their

22 rationale for assessing exercise capacity, given its association with mortality (2), however if

23 such a prediction were genuinely applied in a clinical setting, it could have serious

24 consequences regarding treatment options, which may be unnecessary and unethical (e.g.

25 referral for lung transplant).

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27 Secondly, in developing the model, it is noteworthy that the presented prediction equation has

28 failed to account for several independent factors that may influence V̇O2peak, such as age, sex

29 and lung function. The authors state in their methodology that they have utilised a multiple

30 linear regression to derive the equation, but provide no account of the type of model used nor

31 explain how variables were considered and selected. If no additional factors have been

included, this should be confirmed by authors. This apparent failure to control for such factors is further surprising given the significant correlations reported between FEV1 and both MST distance (r = 0.62, p = 0.001) and V̇O2peak (r = 0.47, p = 0.02). Importantly, the authors fail to use an independent validation group for its prediction equations. Prediction equations are influenced by a low sample size (n = 24), which is heterogeneous in its clinical characteristics (i.e. FEV1 = 76.4 ± 23.8%Predicted) and therefore will inflate the r value. The work needed validation on another sample before any conclusions surrounding its ability to predict V̇O2peak could be made.

Lastly, a reliance upon primary (plateau in V̇O2) and secondary (i.e. RPE, HRmax, RER) criteria to determine a maximal effort has been previously advocated to establish the validity of the criterion measurement i.e., V̇Opeak. However, the authors fail to report how many participants displayed a plateau in V̇O2, and the use of secondary criteria is inherently flawed (3), particularly in a paediatric cohort. As a result, supramaximal verification bouts should be considered during cardiopulmonary exercise testing (CPET) to ensure confidence that a 'true' maximal value has been achieved (4). Unfortunately, no such verification testing has been undertaken in the present study to confirm the maximality of patients' efforts. As an example, it appears that the maximum V̇E value is very low and published data from our own Centre (5), as well as further unpublished data on 37 patients with a similar age (age range 8-20 years; mean 14.7 ±3.4 y) as Vendrusculo *et al.*, found a mean V̇Epeak of 90 ± 38.8 L.min-1, a value in stark contrast to the reported 47 ± 15 L.min-1. This contrast of maximum V̇E values is further compromised as our values were obtained on a cycle ergometer, whilst Vendrusculo *et al.* were on a treadmill, which should on average attain higher values than cycle ergometry tests.

Consequently, if participants in this study have not achieved a maximal effort during their CPET, then the accuracy of the prediction equation developed is further brought into doubt.

In summary, whilst the rationale for this study is well intentioned, we respectfully interpret the findings of this study differently. Firstly, the error in the prediction is likely too large for clinical decision making. Secondly, without external validation of the model, its utility has to be questioned. And thirdly, having used invalid procedures to determine the criterion measure, the precision of the V̇Opeak values cannot be verified. In light of these concerns, we would

63 advocate that CF centres continue to use CPET, and where this is not feasible nor possible, use
64 distance walked during the MST as a discrete result, and to not estimate V̇O2peak using the
65 presented equation.
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