

## **Reference values of cardiopulmonary exercise test parameters in the contemporary paediatric population**

### **Short title: Paediatric CPET parameters Z-scores**

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**Supplementary Table 1. Criteria from the ATS/ACCP statement on high-quality CPET assessment**

| Criteria                            | Description                                                                                                                                                           | Current study |
|-------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| <i>Population characteristics</i>   |                                                                                                                                                                       |               |
| (1) Subjects are community based    | The subjects studied preferably be community bases rather than hospital based.                                                                                        | No            |
| (2) Physical activity               | Level of physical activity is reported.                                                                                                                               | No            |
| (3) Racial groups                   | No exclusion of different racial groups.                                                                                                                              | Yes           |
| (4) Smokers                         | Exclusion of smokers in the sample studied.                                                                                                                           | Yes           |
| (5) Definition of confidence limits | No lack of definition of de confidence limits for individual or specified characteristics. (Include age, sex, and anthropomorphic considerations).                    | Yes           |
| <i>Sample size</i>                  |                                                                                                                                                                       |               |
| (6) Number of subjects tested       | The number of subjects tested is sufficiently equal or larger than the appropriately powered sample size, with a uniform distribution of subjects for sex and groups. | Yes           |
| <i>Randomization</i>                |                                                                                                                                                                       |               |
| (7) Randomization was applied       | The study design includes a randomization process to avoid the potential bias seen when more physically active subjects volunteer for the study.                      | No            |
| <i>Design:</i>                      |                                                                                                                                                                       |               |

|                       |                            |     |
|-----------------------|----------------------------|-----|
| (8) Prospective study | A prospective study design | Yes |
|-----------------------|----------------------------|-----|

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*Quality assurance of equipment and methodologies*

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|---------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| (9) Quality control was applied | Quality was achieved using recommendations contained in the ATS/ACCP guidelines and the CPET protocols in accordance with recommendations specified in the ATS/ACCP guidelines | Yes |
|---------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|

|                                               |                                                         |     |
|-----------------------------------------------|---------------------------------------------------------|-----|
| (10) Exercise testing protocol and procedures | Exercise testing protocol and procedures are described. | Yes |
|-----------------------------------------------|---------------------------------------------------------|-----|

|                                                               |                                                                                                                                                            |     |
|---------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| (11) Results are obtained by either breath-by-breath analysis | Results are obtained by either breath-by-breath analysis or mixing chamber treated in accordance with recommendation contained in the ATS/ACCP guidelines. | Yes |
|---------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|

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*Treatment of data*

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|-------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| (12) CPET result in interval averaged and the peak value reported | CPET result in interval averaged, preferably every 30–60 s (to avoid the noise of shorter interval), and the peak value reported represents the mean of the last-completed stage or of all the data collected during the final stage, but preferably for no less than 30 s. | Yes |
|-------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|

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*Validation*

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|                                        |                                                                                                      |     |
|----------------------------------------|------------------------------------------------------------------------------------------------------|-----|
| (13) Reference equations are validated | Reference equations are validated in population other than those used to generate the existing data. | Yes |
|----------------------------------------|------------------------------------------------------------------------------------------------------|-----|

Statistical treatment of data:

(14) The function that most accurately describes the distribution of the data are used. For example, describes the distribution of the data are curvilinear (power) functions may more accurately describe the distribution of the data. Yes used. Furthermore, the precision of the individual and population predicted values are reported

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Legend: ATS, American Thoracic Society, ACCP, American College of Chest Physicians.

**Supplementary Table 2. Best R<sup>2</sup> according to CPET and anthropometric parameters.**

| CPET parameters       |                                                   | Sex        | Type of model*         | Best R <sup>2</sup>     |                         |                         |                   |
|-----------------------|---------------------------------------------------|------------|------------------------|-------------------------|-------------------------|-------------------------|-------------------|
|                       |                                                   |            |                        | Age                     | Height                  | Weight                  | BMI               |
| Maximal parameters    | HR <sub>max</sub> ( <i>bpm</i> )                  | All gender | Without transformation | <0.05                   |                         |                         |                   |
|                       | RER <sub>max</sub>                                | Girls      | Without transformation | <b>0.14<sup>a</sup></b> | 0.12 <sup>c</sup>       | 0.07 <sup>c</sup>       | 0.00 <sup>c</sup> |
|                       |                                                   | Boys       | Log-Log                | 0.13 <sup>a</sup>       | <b>0.14<sup>c</sup></b> | 0.07 <sup>c</sup>       | 0.01 <sup>c</sup> |
|                       | Workload <sub>max</sub> ( <i>Watt</i> )           | Girls      | Log-Log                | 0.51 <sup>a</sup>       | <b>0.58<sup>a</sup></b> | 0.49 <sup>c</sup>       | 0.20 <sup>c</sup> |
|                       |                                                   | Boys       | Log-Log                | 0.65 <sup>a</sup>       | <b>0.75<sup>a</sup></b> | 0.55 <sup>c</sup>       | 0.22 <sup>c</sup> |
|                       | O <sub>2</sub> pulse <sub>max</sub> ( <i>mL</i> ) | Girls      | Log-Log                | 0.49 <sup>a</sup>       | 0.62 <sup>a</sup>       | <b>0.64<sup>c</sup></b> | 0.33 <sup>c</sup> |
|                       |                                                   | Boys       | Log-Log                | 0.64 <sup>c</sup>       | <b>0.76<sup>a</sup></b> | 0.66 <sup>c</sup>       | 0.33 <sup>c</sup> |
|                       | VAT ( <i>mL/min</i> )                             | Girls      | Log-Log                | 0.36 <sup>a</sup>       | 0.44 <sup>a</sup>       | <b>0.53<sup>c</sup></b> | 0.32 <sup>c</sup> |
|                       |                                                   | Boys       | Log-Log                | 0.54 <sup>c</sup>       | <b>0.66<sup>a</sup></b> | 0.63 <sup>c</sup>       | 0.33 <sup>c</sup> |
|                       | VE/VCO <sub>2</sub> slope                         | Girls      | Log-Log                | <b>0.06<sup>a</sup></b> | 0.06 <sup>a</sup>       | 0.06 <sup>c</sup>       | 0.02 <sup>c</sup> |
| Submaximal parameters |                                                   | Boys       | Log-Log                | <b>0.19<sup>a</sup></b> | 0.17 <sup>c</sup>       | 0.12 <sup>c</sup>       | 0.4 <sup>c</sup>  |
|                       | OUES                                              | Girls      | Log-Log                | 0.40 <sup>a</sup>       | 0.50 <sup>a</sup>       | <b>0.55<sup>c</sup></b> | 0.31 <sup>c</sup> |
|                       |                                                   | Boys       | Log-Log                | 0.57 <sup>b</sup>       | <b>0.67<sup>a</sup></b> | 0.61 <sup>c</sup>       | 0.28 <sup>c</sup> |
|                       |                                                   |            |                        |                         |                         |                         |                   |

|                        |                          |            |                        |                   |                         |                         |                   |
|------------------------|--------------------------|------------|------------------------|-------------------|-------------------------|-------------------------|-------------------|
| Ventilatory parameters | VT <sub>max</sub> (L)    | Girls      | Log-Log                | 0.61 <sup>a</sup> | <b>0.71<sup>a</sup></b> | 0.58 <sup>c</sup>       | 0.22 <sup>c</sup> |
|                        |                          | Boys       | Log-Log                | 0.66 <sup>c</sup> | <b>0.78<sup>a</sup></b> | 0.63 <sup>c</sup>       | 0.28 <sup>c</sup> |
|                        | RR <sub>max</sub> (/min) | Girls      | Without transformation | 0.04 <sup>a</sup> | <b>0.05<sup>a</sup></b> | 0.04 <sup>a</sup>       | 0.02 <sup>a</sup> |
|                        |                          | Boys       | Log-Log                | 0.06 <sup>a</sup> | 0.05 <sup>a</sup>       | <b>0.07<sup>a</sup></b> | 0.05 <sup>a</sup> |
|                        | Breathing reserve (%)    | Girls      | Without transformation |                   | <0.05                   |                         |                   |
|                        |                          | Boys       | Without transformation |                   | <0.05                   |                         |                   |
|                        | VEqCO <sub>2max</sub>    | All gender | Log-Log                |                   | <0.05                   |                         |                   |
|                        | VEqO <sub>2max</sub>     | Girls      | Log-Log                |                   | <0.05                   |                         |                   |
|                        |                          | Boys       | Log-Log                |                   | <0.05                   |                         |                   |

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Legends: CPET, cardio-pulmonary exercise test; HR<sub>max</sub>, maximum heart rate; O<sub>2</sub> pulse<sub>max</sub>, maximum oxygen pulse; OUES, oxygen uptake efficiency slope; RER<sub>max</sub>, maximum respiratory exchange ratio; RR<sub>max</sub>, maximum respiratory rate; VAT, ventilatory anaerobic threshold; VEqCO<sub>2max</sub>, maximum ventilatory equivalent for CO<sub>2</sub>; VEqO<sub>2max</sub>, maximum ventilatory equivalent for O<sub>2</sub>; VT<sub>max</sub>, maximum tidal volume. For each anthropometric predictor and each CPET parameter, only the R<sup>2</sup> of the best statistical model is presented among the following models: <sup>a</sup> linear model; <sup>b</sup> quadratic model; and <sup>c</sup> polynomial model. For each CPET parameter, the best anthropometric predictor's R<sup>2</sup> is marked in bold.

**Supplementary Table 3. Distribution of CPET parameter values in children of normal weight.**

| CPET parameters       |                                                   | Sex   | N   | 5 <sup>th</sup> percentile | Median | 95 <sup>th</sup> percentile |
|-----------------------|---------------------------------------------------|-------|-----|----------------------------|--------|-----------------------------|
| Maximal parameters    | VO <sub>2max</sub> ( <i>mL/Kg/min</i> )           | Girls | 299 | 29.3                       | 37.9   | 49.8                        |
|                       |                                                   | Boys  | 340 | 36.1                       | 46.5   | 56.7                        |
|                       | HR <sub>max</sub> ( <i>bpm</i> )                  | All   | 639 | 173                        | 189    | 203                         |
|                       | RER <sub>max</sub>                                | Girls | 299 | 1.01                       | 1.17   | 1.35                        |
|                       |                                                   | Boys  | 340 | 1.00                       | 1.15   | 1.31                        |
|                       | Workload <sub>max</sub> ( <i>Watts</i> )          | Girls | 270 | 75                         | 125    | 200                         |
|                       |                                                   | Boys  | 300 | 80                         | 140    | 250                         |
|                       | O <sub>2</sub> pulse <sub>max</sub> ( <i>mL</i> ) | Girls | 299 | 5.4                        | 8.4    | 11.9                        |
|                       |                                                   | Boys  | 340 | 6.0                        | 9.5    | 16.8                        |
| Submaximal parameters | VAT ( <i>mL/Kg/min</i> )                          | Girls | 299 | 19.0                       | 26.3   | 37.8                        |
|                       |                                                   | Boys  | 340 | 24.2                       | 32.5   | 42.3                        |
|                       | %-predicted VAT (%)                               | All   | 639 | 55.3                       | 70.5   | 83.7                        |
|                       | VE/VCO <sub>2</sub> slope                         | All   | 639 | 24                         | 30     | 37.6                        |

|                        |                                    |       |     |      |      |      |
|------------------------|------------------------------------|-------|-----|------|------|------|
| Ventilatory parameters | OUES <sub>kg</sub>                 | Girls | 197 | 28.9 | 40.3 | 55.0 |
|                        |                                    | Boys  | 242 | 38.9 | 49.5 | 63.8 |
|                        | VT <sub>max</sub> ( <i>mL/Kg</i> ) | Girls | 299 | 22.9 | 29.5 | 38.9 |
|                        |                                    | Boys  | 340 | 24.3 | 33.4 | 43.0 |
|                        | RR <sub>max</sub> ( <i>/min</i> )  | Girls | 296 | 34.4 | 49.1 | 67.3 |
|                        |                                    | Boys  | 333 | 36.0 | 51.0 | 69.4 |
|                        | Breathing reserve (%)              | Girls | 299 | 0.3  | 29.0 | 53.0 |
|                        |                                    | Boys  | 339 | 0.0  | 24.0 | 47.0 |
|                        | VEqCO <sub>2max</sub>              | All   | 639 | 25.2 | 31.0 | 37.8 |
|                        | VEqO <sub>2max</sub>               | Girls | 299 | 28.4 | 36.9 | 47.0 |
|                        |                                    | Boys  | 340 | 27.2 | 34.7 | 45.3 |

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Legends: HR<sub>max</sub>, maximum heart rate; O<sub>2</sub> pulse<sub>max</sub>, maximum oxygen pulse; OUES, oxygen uptake efficiency slope; OUES<sub>kg</sub>, weight-normalized value of OUES; RER<sub>max</sub>, maximum respiratory exchange ratio; RR<sub>max</sub>, maximum respiratory rate; VAT, ventilatory anaerobic threshold; %-predicted VAT, VAT expressed as a percentage of the predicted VO<sub>2max</sub>; VEqCO<sub>2max</sub>, maximum ventilatory equivalent for CO<sub>2</sub>; VEqO<sub>2max</sub>, maximum ventilatory equivalent for O<sub>2</sub>; VT<sub>max</sub>, maximum tidal volume.