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Oxygen Uptake Efficiency Slope in Healthy Children

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The objective of this study was to investigate the characteristics of the submaximal Oxygen Uptake Efficiency Slope (OUES) in a healthy pediatric population. Bicycle ergometry exercise tests with gas-analyses were performed in 46 healthy children aged 7–17 years. Maximal OUES, submaximal OUES, $\dot{V}O_2$peak, $V_E$peak, and ventilatory threshold (VT) were determined. The submaximal OUES correlated highly with $\dot{V}O_2$peak, $V_E$peak, and VT. Strong correlations were found with basic anthropometric variables. The submaximal OUES could provide an objective, independent measure of cardiorespiratory function in children, reflecting efficiency of ventilation. We recommend expressing OUES values relative to Body Surface Area (BSA) or Fat Free Mass (FFM).

Exercise testing is currently widely used in clinical practice to assess the response to exercise in both patients and healthy individuals. Maximal oxygen uptake ($\dot{V}O_2$max), the highest rate at which an individual can consume oxygen during exercise, is widely recognized as the single best measure of person's aerobic fitness (26). $\dot{V}O_2$max requires maximal effort and leveling-off (plateau) of oxygen uptake, despite continuing exercise and increasing workload. Therefore, its application is mainly limited to healthy adult subjects who can fulfill these requirements (18). In pediatric populations, a true plateau in oxygen uptake is seldom attained (21,25). Since several authors (2,3,25) have shown that a true plateau is not essential for defining the highest oxygen uptake in children, it gradually became more usual to use the rate of oxygen uptake occurring at peak exercise ($\dot{V}O_2$peak; 4, 18). However, the measurement of these parameters can be strongly influenced by the patients' motivation, the selected exercise protocol, and the experience of the tester (1,7,18,28). Furthermore, exhaustive incremental tests for determining the $\dot{V}O_2$peak in pediatric populations generally do not mimic activity levels of their daily life. Therefore, exercise performance at submaximal exercise might be more representative in pediatric populations, especially in children with a chronic condition.

Baba et al. (5) introduced the Oxygen Uptake Efficiency Slope (OUES) in an attempt to develop an objective and effort-independent submaximal measure

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of cardiopulmonary reserve. Their approach involves deriving the slope of the semilog plot of minute ventilation (V_E) versus oxygen uptake ($\dot{V}O_2$). As such, the OUES provides an estimation of the efficiency of ventilation with respect to $\dot{V}O_2$, with steeper slopes indicating a larger ventilatory efficiency. Physiologically, the OUES is based on: (i) the development of metabolic acidosis, which is controlled by the distribution of blood to the skeletal muscles; and (ii) the physiological dead space, which is affected by the perfusion to the lungs (5,7). The OUES was initially applied in a cohort of healthy children and children with heart disease (7), however the OUES has also been frequently investigated in healthy adults, adolescents, and patient populations later on (19).

To our knowledge, merely five studies (5,6,11,22) examined the properties of the OUES in children and adolescents. All the aforementioned studies included healthy children while the study of Baba et al. (5) also included children with heart disease. To verify the assumption that the OUES is independent of exercise duration (effort), both maximal and submaximal values of OUES were calculated in four of these studies (5,11,21,22). Two studies (5,11) described that the submaximal OUES was slightly, however significantly, lower compared with the maximal OUES. One study (21) described higher submaximal OUES values, whereas a fourth study (22) did not describe any effects of exercise duration on the OUES.

In general, strong correlations were reported between the maximal OUES and $\dot{V}O_2$max (r = .94) and $\dot{V}O_2$peak (r = .77, r = .91, r = .92; 11, 21, 22). Only two studies (5,11) assessed also the aforementioned correlations for the submaximal OUES and reported a correlation with $\dot{V}O_2$max of r = .95 in healthy children and children with heart disease, and r = .59 in overweight adolescents, respectively.

The OUES appears to be significantly higher in boys compared with girls (2335 ± 875 versus 1730 ± 580; and 2254 ± 735 versus 1943 ± 497; 21, 22) and correlates significantly with basic anthropometric parameters, including age (r = .83, r = .76), height (r = .88, r = .84), body mass (r = .78, r = .85), Body Mass Index (BMI; r = .48, r = .57), Body Surface Area (BSA; r = .86), and Fat Free Mass (FFM; r = .86, r = .84); with $p < .001$ for all coefficients; 21, 22). However, these characteristics were only examined for the maximal OUES and not for the submaximal OUES.

Since the original rationale of the OUES was to provide a submaximal measure of cardiorespiratory function, which could be used as a possible substitute for or an addition to $\dot{V}O_2$peak or $\dot{V}O_2$max in populations unable to perform maximal exercise, it would be appropriate to examine submaximal OUES characteristics. Therefore, the aim of our current study was to investigate the properties of the submaximal OUES in a healthy pediatric population.

Material and Methods

Participants

Forty-six children and adolescents (27 boys and 19 girls; aged 7–17 years) participated in this study. These subjects included family members of our hospital staff and children living in the neighborhood of the hospital. All children were in good health, without chronic diseases, and were not on medications which might affect their exercise capacity. Informed consent was obtained from the parents and/or from the children themselves if they were ≥12 years of age. The study protocol was approved by the Medical Ethics Committee of the University Medical Center Utrecht, the Netherlands.

Anthropometric Measures

The participants' body mass and height were determined using respectively an electronic scale and a stadiometer, respectively. BMI was calculated as body mass (kg)/height $(m)^2$. BSA was calculated using the equation of Haycock et al. (17): BSA $(m^2) = 0.024265 \cdot Ht^{0.3964} \cdot Wt^{0.5378}$, where Ht represents height in cm and Wt is body mass in kg. This equation is validated in infants, children, and adults (17). Subcutaneous fat distribution was measured from skin fold measurement (mm) using Harpender skin fold calipers. The measurements were taken at four sites (at the right side of the body); triceps, biceps, subscapular, and supra-iliacal according to Deurenberg et al. (10). The sum of the four skin folds (å4SF) was used to estimate the body density by means of the equations by Deurenberg et al. (10) derived from anthropometric data of Dutch children aged 7–20 years. Percentage body fat and subsequent FFM were estimated using a modification of the Siri equation proposed by Weststrate and Deurenberg (37).

Exercise Testing

Cardiopulmonary exercise tests were performed using an electronically braked cycle ergometer (Lode Corrival, Lode BV, Groningen, the Netherlands). The test started with one minute of unloaded cycling before the application of resistance to the ergometer. Subsequently, workload was increased with a constant increment of 10, 15 or 20 Watts every minute according to the Godfrey protocol (16). This protocol continued until the patient stopped because of voluntary exhaustion, despite strong verbal encouragement of the test-leader. Heart rate (HR) was measured continuously during the maximal exercise test by using a heart rate monitor (Polar, Kempele, Finland).

Analysis of Expired Gas

During the exercise tests, subjects breathed through a facemask (Hans Rudolph Inc, Kansas City, MO) connected to a calibrated respiratory gas analysis system (Jaeger Oxycon Champion, Cardinal Health, Houten, the Netherlands). Expired gas passed through a flowmeter (Triple V volume transducer), oxygen (O_2) analyzer, and a carbon dioxide (CO_2) analyzer. The flowmeter and gas analyzers were connected to a computer, which calculated breath-by-breath V_E, $\dot{V}O_2$, carbon dioxide output (VCO_2), and the Respiratory Exchange Ratio (RER) from conventional equations. Output from the gas analyses was averaged at 10 s-intervals and stored in an Excel file for the off-line calculation of the OUES. Maximal effort was defined when at least one of the following criteria was met: HR > 180 beats per minute or RER > 1.0. $\dot{V}O_2$peak and peak ventilation ($V_E$peak) were determined as the average $\dot{V}O_2$ and V_E value over the last 30 s during the maximal exercise test. The ventilatory threshold (VT) was determined as the level of $\dot{V}O_2$ at which the linear relation between VCO_2 and $\dot{V}O_2$ disappeared, according to the V-slope method. The OUES was determined by plotting $\dot{V}O_2$ (mL·min^{-1}) against the logarithm of V_E (L·min^{-1}) and calculating the slope of this linear relation through single regression analysis.

In accordance with the original equation introduced by Baba et al. (5): ($\dot{V}O_2$ = a log V_E + b), this slope 'a' represents the OUES. For submaximal OUES determination, only data up to VT were included in the analyses. Data from the first minute of exercise were excluded because of the often very irregular breathing pattern at the onset of exercise (36). Relative values for the exercise parameters were calculated by dividing the absolute values by body mass, FFM or BSA. Several studies reported good reproducibility of OUES in healthy participants (4,32).

Statistical Analysis

All data were analyzed using the Statistical Package for the Social Sciences (version 15.0; SPSS Inc., Chicago, IL). Data are presented as mean values ± *SD* (*SD*) and corresponding ranges. Differences between boys and girls were examined using the independent-sample T-test for the anthropometric variables and the Mann-Whitney test for the exercise parameters. A Wilcoxon signed ranks test was used to determine whether the submaximal OUES differed significantly from the maximal OUES. Spearman correlation coefficients were calculated to examine the relationships between the different exercise parameters and between the submaximal OUES and basic anthropometric variables. Significance was set a priori at the .05 level.

Results

Participant characteristics are depicted in Table 1. No significant differences were found between boys and girls regarding age, height, BSA, and FFM; whereas body mass, BMI, the Σ4SF, body density, and BF% were significantly lower in boys compared with girls.

Table 1 Population Characteristics

	Boys (*n* = 27) Mean ± *SD*. Range		Girls (*n* = 19) Mean ± *SD*. Range		
Age (years)	11.8 ± 2.2	(7.9–16.8)	12.9 ± 2.6	(8.4–16.5)	
Height (m)	1.54 ± 0.15	(1.29–1.91)	1.59 ± 0.12	(1.39–1.79)	
Body mass (kg)	41.5 ± 12.0	(24.1–66.5)	49.4 ± 14.3	(28.2–81.7)	*
BMI (kg·m^{-2})	17.0 ± 2.0	(13.8–21.3)	19.0 ± 3.0	(14.6–25.5)	**
BSA (m^2)	1.32 ± 0.25	(0.92–1.86)	1.47 ± 0.27	(1.03–2.02)	
Σ4SF (mm)	28.87 ± 9.55	(19.67–65.17)	40.59 ± 14.27	(22.17–71.67)	**
Body density (kg·L^{-1})	1.05 ± 0.01	(1.03–1.06)	1.04 ± 0.01	(1.03–1.06)	**
BF (%)	16.04 ± 3.18	(12.01–26.43)	20.94 ± 4.21	(14.41–28.66)	***
FFM (kg)	35.02 ± 10.14	(20.78–56.31)	38.87 ± 10.22	(24.14–59.74)	

Abbreviations: BMI = body mass index; BSA = body surface area; Σ 4SF = sum of the four skin folds; BF = percentage of body fat; FFM = fat free mass; * $p<.05$, ** $p<.01$, *** $p<.001$

All maximal cardiopulmonary exercise tests were completed without adverse effects, such as dizziness, fainting, or vomiting. Results are presented in Table 2. During the interpretation of the exercise tests, the VT could not be properly be determined in one subject. The average submaximal OUES of the entire population was 2200.5 ± 693.6, with values varying over a wide range (1062.6–4120.5; Figure 1). After adjusting for the anthropometric variables height (1383.8 ± 342.9; range: 764.5–2527.9), body mass (49.5 ± 9.9; range: 34.4–82.7), BMI (122.1 ±30.2; range 66.4–219.8), FFM (60.6 ± 10.7; range 39.7–97.0), or BSA (1569.9 ± 306.7; range 974.9–2747.0), the variation within submaximal OUES values was reduced.

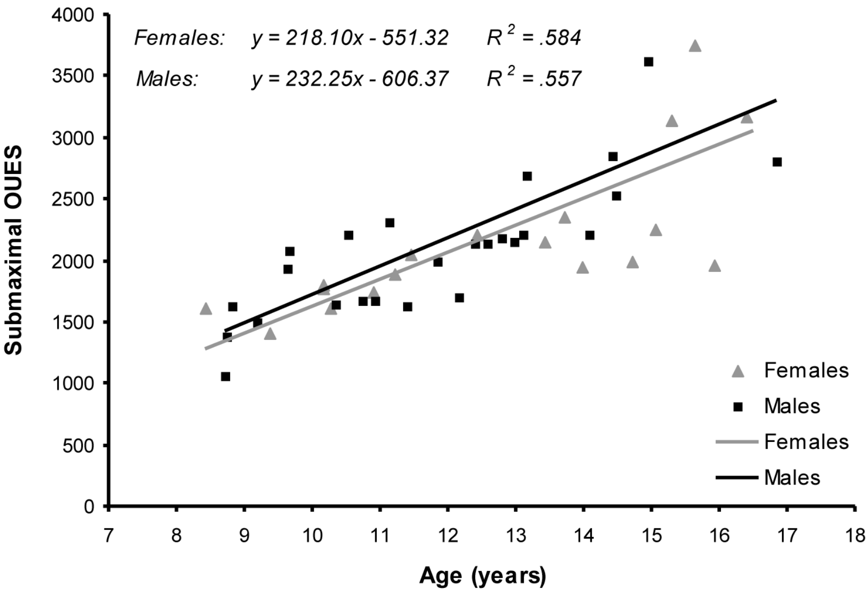

Figure 1 — Age-related changes in OUES.

The submaximal OUES did not differ significantly from the maximal OUES (p = .296), even when the OUES values were expressed relative to body mass (p = .413), BSA (p = .370), or FFM (p = .579). A Bland-Altman plot of the maximal OUES versus the submaximal OUES is shown in Figure 2. Furthermore, a strong correlation was observed between both parameters (r = .92). The submaximal OUES showed a high correlation with $\dot{V}O_2$peak (r = .88), $V_E$peak (r = .73), and VT (r = .85); with $p < .01$ for all coefficients. However, when normalized for body mass, the correlations with $\dot{V}O_2$peak and $V_E$peak declined (r = .60 and r = .51, respectively; $p < .01$). Similarly, lower correlations were found when normalized for BSA (r = .67 and r = .45, respectively) or FFM (r = .49 and r = .39, respectively); with $p < .01$ for all coefficients. No significant gender differences were found for the absolute values of all studied exercise parameters (data not shown). However, when expressed relative to body mass, BSA or FFM, both $\dot{V}O_2$peak and $V_E$peak

Table 2 Population Exercise Parameters

	Boys (n = 27) Mean ± SD	Range	Girls (n = 19) Mean ± SD	Range	
HR_{peak} (beats·min^{-1})	192.6 ± 7.9	(181–206)	193.7 ± 6.8	(180–212)	
RER_{peak}	1.15 ± 0.06	(1.02–1.28)	1.16 ± 0.08	(1.01–1.29)	
VT (mL·min^{-1})[a]	1533.6 ± 468.3	(830.0–2712.0)	1425.4 ± 498.5	(936.0–2767.0)	
$\dot{V}O_2$peak (mL·min^{-1})	2188.0 ± 671.4	(1150.0–3590.0)	2176.8 ± 807.8	(1230.0–4140.0)	
$\dot{V}O_2$peak/kg (mL·min^{-1}·kg^{-1})	52.9 ± 6.7	(40.3–63.3)	43.6 ± 5.5	(33.6–55.6)	***
$\dot{V}O_2$peak/BSA (mL·min^{-1}·m^{-2})	1633.0 ± 248.3	(1128.6–2086.7)	1449.3 ± 276.1	(1138.9–2102.7)	*
$\dot{V}O_2$peak/FFM (mL·min^{-1}·kg^{-1})	62.85 ± 7.26	(49.42–74.49)	55.75 ± 6.78	(46.67–71.31)	**
$V_E$peak (L·min^{-1})	77.7 ± 25.1	(45.2–149.5)	76.1 ± 28.2	(44.6–144.3)	
$V_E$peak/kg (L·min^{-1}·kg^{-1})	1.88 ± 0.28	(1.42–2.40)	1.55 ± 0.32	(0.82–2.06)	**
$V_E$peak/BSA (L·min^{-1}·m^{-2})	58.1 ± 9.6	(41.7–80.4)	51.2 ± 11.8	(28.6–78.0)	*
$V_E$peak/FFM (L·min^{-1}·kg^{-1})	2.25 ± 0.29	(1.68–2.76)	1.96 ± 0.40	(1.15–2.64)	*
Maximal OUES	2185.2 ± 676.2	(849.0–3521.5)	2237.0 ± 759.5	(1236.1–3777.1)	
Maximal OUES/kg	52.9 ± 8.6	(35.2–70.7)	45.2 ± 6.1	(37.3–59.9)	**
Maximal OUES/BSA	1632.2 ± 294.3	(922.9–2347.7)	1496.3 ± 261.3	(1144.5–1998.5)	
Maximal OUES/FFM	62.71 ± 9.67	(40.85–82.86)	57.51 ± 7.13	(47.32–71.08)	*
Submaximal OUES[a]	2156.8 ± 668.6	(1062.6–4120.5)	2260.3 ± 740.6	(1405.2–4074.5)	
Submaximal OUES/kg[a]	51.8 ± 10.3	(34.4–82.7)	46.3 ± 8.5	(36.0–62.9)	
Submaximal OUES/BSA[a]	1602.9 ± 323.8	(974.9–2747.0)	1524.6 ± 283.9	(1202.0–2202.4)	
Submaximal OUES/FFM[a]	61.70 ± 11.80	(39.71–96.95)	59.15 ± 9.14	(46.19–74.69)	

Abbreviations: BSA = body surface area; FFM = fat free mass; HR = heart rate; OUES = oxygen uptake efficiency slope; RER = respiratory exchange ratio; VT = ventilatory threshold; V_E = minute ventilation; $\dot{V}O_2$ = oxygen uptake. [a] VT was not determinable in one boy, so in this case n = 26 for the boys. * p<.05, ** p<.01, *** p<.001.

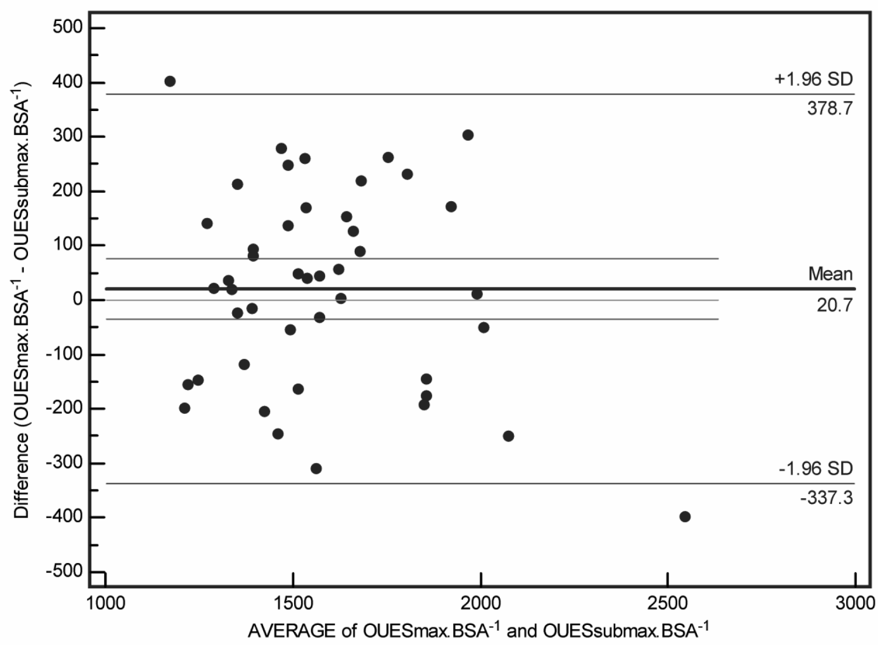

Figure 2 — Bland-Altman plot of maximal OUES·BSA^{-1} and submaximal OUES·BSA^{-1} showing the bias (difference in mean) and limits of agreement.

were significantly higher in boys compared with girls, whereas adjustment of the submaximal OUES did not result in gender differences. High correlations were found between the submaximal OUES and basic anthropometric variables, including height (r = .82), BSA (r = .77), age (r = .82), body mass (r = .75), FFM (r = .84) and BMI (r = .53); with p < .01 for all coefficients. The submaximal OUES appeared to linearly increase with age, as is shown in Figure 1.

Discussion

This study describes submaximal OUES characteristics in a healthy pediatric population, aged 7–17 years. The main findings indicate that the OUES in healthy children (i) is independent of exercise intensity, (ii) correlates highly with other exercise parameters (such as $\dot{V}O_2$peak, $V_E$peak, VT), and (iii) shows a linear increase with age during childhood and into adolescence. However, our results also illustrate that the OUES is considerably influenced by anthropometric variables and that its values show large interindividual variation.

The submaximal OUES values found in our population are in line with earlier studies of children with corresponding ages (11,21,22); despite the fact that those two studies used a treadmill rather than a cycle ergometer to perform the maximal exercise tests. The strong correlation between the submaximal OUES and $\dot{V}O_2$peak also is in line with the results of Baba et al. (5) who reported a very strong correlation between the submaximal OUES and $\dot{V}O_2max$ ($r = .95$). The submaximal OUES did not significantly differ from the maximal OUES in this current study, which confirms the results of Marinov et al. (22). Other studies, however, found submaximal OUES values to be slightly, but significantly, higher (21) or lower (5,11) compared with maximal OUES values. Large interindividual differences in OUES values might be responsible for these inconsistent findings among the abovementioned studies. Although previous studies reported the OUES to be significantly higher in boys compared with girls, our current study suggest that although boys generally achieve higher peak values in both $\dot{V}O_2$ and V_E, their ventilatory efficiency (OUES) does not differ significantly from girls.

The strong correlations between the submaximal OUES and various basic anthropometric variables in this study reflect changes in ventilatory efficiency during childhood and into adolescence, and are in line with to those found for the maximal OUES in earlier studies (21,22). During maturation, with the associated changes in length, body mass, and body composition, absolute peak values of both V_E and $\dot{V}O_2$ will also change making it reasonable that it will affect the OUES as well.

Maximal indices such as $\dot{V}O_2peak$ are known to be strongly influenced by changes in body size. Therefore, $\dot{V}O_2peak$ is often expressed in relation to body mass. Although this does not fully compensate the influence of body size on $\dot{V}O_2peak$ (20). The study of Marinov & Kostianev (21) showed that normalizing $\dot{V}O_2peak$ by dividing it by BSA compensates for the differences between various weight groups. Therefore, OUES during childhood should be interpreted with caution, which is in line with the current study results which indicate that the submaximal OUES in children is considerably influenced by anthropometric variables. Adjusting its values for body size seems appropriate, especially in childhood. Previous studies have expressed OUES relative to body mass, FFM, and BSA. Our current study results indicate that FFM will reduce the overall variability to the greatest extent, followed by BSA, and hence adjustment of submaximal OUES values for BSA or FFM in children seems recommended. Moreover, from a physiological perspective, FFM provides the best indication of $\dot{V}O_2peak$ (as a direct relation is assumed between muscle mass and its capacity to consume oxygen for energy metabolism) (13,29,34), whereas BSA is supposed to provide a more precise indication of body volume compared with merely height or body mass (12,23).

This present study has some limitations such as the relatively small and heterogeneous population, which could be responsible for the large interindividual variation and skewed distributions. During data exploration five individuals were detected as outliers. All deviated on the top side of the box plot, indicating that they had a significantly higher aerobic capacity than the rest of the group. Profound investigation revealed that these subjects were significantly older than the other participants (15.45 ± 1.12 versus 11.83 ± 2.25 years respectively; $p < .001$), participated regularly (>3 $hr \cdot week^{-1}$) in endurance sports, and showed significantly higher $\dot{V}O_2peak$ values. As a result of their physical activity patterns, these subjects might be highly trained and therefore may not be representative for a normal pediatric population. Elimination of the outliers resulted in a decrease in overall distribution of OUES values. However, it might be a first indication of the responsiveness of the OUES with exercise training in children.

Furthermore, appropriate cut-off values should be used for submaximal OUES determination. However, at present it remains unclear which endpoint approach is most useful to simulate submaximal effort (approaches based on RER, VT, heart rate reserve, or a percentage of exercise duration or $\dot{V}O_2$max; 19). In the current study, VT was used as a cut-off value for submaximal OUES determination, although VT cannot always be determined and its values depend on the method used for detection (27). Shimizu et al. showed that the V-slope method had consistently good agreement among observers (with intraclass correlations ranging from .85 to .98) and was least affected by the used exercise protocol. Furthermore, the study of Wasserman (35) identified this method as the most practical method. Since the submaximal OUES is derived from multiple data points up to VT and the OUES appears to be effort-independent (15,22,24,31), the exact endpoints will nonetheless not have influenced OUES values to a great extent.

There is a need for adequate reference values for the OUES in (healthy) children. Appropriate reference values should be generated with respect to age, gender, race, and other relevant factors such as maturation and anthropometrics. To our knowledge, influences of puberty on the OUES have not been investigated. Since puberty could lead to significant changes in body composition, muscle strength, $V_E$max, ventilatory equivalent, and physical activity patterns, it might also influence ventilatory efficiency (OUES). Future studies should address these variables.

Furthermore, it is currently unknown whether the submaximal OUES is able to differentiate between healthy children and children with a (chronic) disease. Previous findings suggest that OUES has discriminative value in adults (7,8,18,30,31), however further research is required to assess its discriminative properties in different pediatric populations.

The responsiveness of the OUES to physical training is another issue that has not been addressed in pediatric populations. Results from adult studies suggest the OUES to increase following physical training in cardiac patients (9,14,33). The OUES is useful to evaluate progression in exercise capacity, given that an increase in OUES suggests that a similar oxygen uptake is achieved with lower ventilatory cost (increase in efficiency; 9, 14, 33). Several authors even state that the OUES is more stable and robust than the maximal parameter $\dot{V}O_2$peak, since peak work load attained during a symptom-limited exercise test can be influenced by multiple factors (14,18,31). However, large interindividual variation may limit the usefulness of OUES in clinical practice. To the best of our knowledge, none of the studies in the current literature on OUES investigated the practical application of OUES by correlating OUES values in children with their running speeds or other practical test criteria. However, children with higher $\dot{V}O_2$peak values, indicating better endurance performance, show higher OUES values than children with lower values of $\dot{V}O_2$peak. The responsiveness and the practical application of the OUES in pediatric populations remains subject of further research.

References

1. Andreacci, J.L., L.M. LeMura, S.L. Cohen, E.A. Urbansky, S.A. Chelland, and S.P. Von Duvillard. The effects of frequency of encouragement on performance during maximal exercise testing. *J Sports Sci.* 20:345–352, 2002.
2. Armstrong, N., J. Welsman, and R. Winsley. Is peak VO2 a maximal index of children's aerobic fitness? *Int. J. Sports Med.* 17:356–359, 1996.

3. Astrand, P.O. *Experimental studies of physical work capacity in relation to sex and age*. Copenhagen: Munksgaard, 1952.
4. Baba, R., N. Kubo, Y. Morotome, and S. Iwagaki. Reproducibility of the oxygen uptake efficiency slope in normal healthy subjects. *J Sports Med Phys Fitness.* 39:202–206, 1999a.
5. Baba, R., M. Nagashima, M. Goto, et al. Oxygen uptake efficiency slope: a new index of cardiorespiratory functional reserve derived from the relation between oxygen uptake and minute ventilation during incremental exercise. *J. Am. Coll. Cardiol.* 28:1567–1572, 1996.
6. Baba, R., M. Nagashima, Y. Nagano, M. Ikoma, and K. Nishibata. Role of the oxygen uptake efficiency slope in evaluating exercise tolerance. *Arch. Dis. Child.* 81:73–75, 1999b.
7. Baba, R., K. Tsuyuki, Y. Kimura, et al. Oxygen uptake efficiency slope as a useful measure of cardiorespiratory functional reserve in adult cardiac patients. *Eur. J. Appl. Physiol. Occup. Physiol.* 80:397–401, 1999c.
8. Davies, L.C., R. Wensel, P. Georgiadou, et al. Enhanced prognostic value from cardiopulmonary exercise testing in chronic heart failure by non-linear analysis: oxygen uptake efficiency slope. *Eur. Heart J.* 27:684–690, 2006.
9. Defoor, J., D. Schepers, T. Reybrouck, R. Fagard, and L. Vanhees. Oxygen uptake efficiency slope in coronary artery disease: clinical use and response to training. *Int. J. Sports Med.* 27:730–737, 2006.
10. Deurenberg, P., K. van der Kooy, and J.G. Hautvast. The assessment of the body composition in the elderly by densitometry, anthropometry and bioelectrical impedance. *Basic Life Sci.* 55:391–393, 1990.
11. Drinkard, B., M.D. Roberts, L.M. Ranzenhofer, et al. Oxygen-uptake efficiency slope as a determinant of fitness in overweight adolescents. *Med. Sci. Sports Exerc.* 39:1811–1816, 2007.
12. Dunnill, M.S. Postnatal Growth of the lung. *Thorax.* 17:329–333, 1962.
13. Fleg, J.L., and E.G. Lakatta. Role of muscle loss in the age-associated reduction in VO2 max. *J. Appl. Physiol.* 65:1147–1151, 1988.
14. Gademan, M.G., C.A. Swenne, H.F. Verwey, et al. Exercise training increases oxygen uptake efficiency slope in chronic heart failure. *Eur. J. Cardiovasc. Prev. Rehabil.* 15:140–144, 2008.
15. Giardini, A., S. Specchia, G. Gargiulo, D. Sangiorgi, and F.M. Picchio. Accuracy of oxygen uptake efficiency slope in adults with congenital heart disease. *Int. J. Cardiol.* 133:74–79, 2009.
16. Godfrey, S. *Exercise testing in children*. London: W.B. Saunders Company Ltd, 1974.
17. Haycock, G.B., G.J. Schwartz, and D.H. Wisotsky. Geometric method for measuring body surface area: a height-weight formula validated in infants, children, and adults. *J. Pediatr.* 93:62–66, 1978.
18. Hollenberg, M., and I.B. Tager. Oxygen uptake efficiency slope: an index of exercise performance and cardiopulmonary reserve requiring only submaximal exercise. *J. Am. Coll. Cardiol.* 36:194–201, 2000.
19. Hulzebos, H.J., M. Akkerman, M. Van Brussel, P.J.M. Helders, and T. Takken. The Oxygen Uptake Efficiency Slope (OUES) in children: a narrative review? *Proceedings of XXV Pediatric Work Physiology Meeting, Le Touquet Paris Plage, France.*, 2009.
20. Loftin, M., M. Sothern, L. Trosclair, A. O'Hanlon, J. Miller, and J. Udall. Scaling VO(2) peak in obese and non-obese girls. *Obes. Res.* 9:290–296, 2001.
21. Marinov, B., and S. Kostianev. Exercise performance and oxygen uptake efficiency slope in obese children performing standardized exercise. *Acta Physiol. Pharmacol. Bulg.* 27:59–64, 2003.
22. Marinov, B., S. Mandadzhieva, and S. Kostianev. Oxygen-uptake efficiency slope in healthy 7- to 18-year-old children. *Pediatr. Exerc. Sci.* 19:159–170, 2007.

23. Petrini, M.F., M.S. Phillips, and D.A. Walsh. Pulmonary tissue volume and blood flow as functions of body surface area and age. *Lung.* 166:47–63, 1988.
24. Pogliaghi, S., E. Dussin, C. Tarperi, A. Cevese, and F. Schena. Calculation of oxygen uptake efficiency slope based on heart rate reserve end-points in healthy elderly subjects. *Eur. J. Appl. Physiol.* 101:691–696, 2007.
25. Rowland, T.W. Does peak VO2 reflect VO2max in children?: evidence from supramaximal testing. *Med. Sci. Sports Exerc.* 25:689–693, 1993.
26. Shephard, R.J., C. Allen, A.J. Benade, et al. The maximum oxygen intake. An international reference standard of cardiorespiratory fitness. *Bull. World Health Organ.* 38:757–764, 1968.
27. Shimizu, M., J. Myers, N. Buchanan, et al. The ventilatory threshold: method, protocol, and evaluator agreement. *Am. Heart J.* 122:509–516, 1991.
28. St Clair Gibson, A., M.I. Lambert, J.A. Hawley, S.A. Broomhead, and T.D. Noakes. Measurement of maximal oxygen uptake from two different laboratory protocols in runners and squash players. *Med. Sci. Sports Exerc.* 31:1226–1229, 1999.
29. Toth, M.J., M.I. Goran, P.A. Ades, D.B. Howard, and E.T. Poehlman. Examination of data normalization procedures for expressing peak VO2 data. *J. Appl. Physiol.* 75:2288–2292, 1993.
30. Van de Veire, N.R., C. Van Laethem, J. Philippe, et al. VE/VCO2 slope and oxygen uptake efficiency slope in patients with coronary artery disease and intermediate peakVO2. *Eur. J. Cardiovasc. Prev. Rehabil.* 13:916–923, 2006.
31. Van Laethem, C., J. Bartunek, M. Goethals, P. Nellens, E. Andries, and M. Vander-Heyden. Oxygen uptake efficiency slope, a new submaximal parameter in evaluating exercise capacity in chronic heart failure patients. *Am. Heart J.* 149:175–180, 2005.
32. Van Laethem, C., J. De Sutter, W. Peersman, and P. Calders. Intratest reliability and test-retest reproducibility of the oxygen uptake efficiency in healthy participants. *Eur. J. Cardiovasc. Prev. Rehabil.* 16:493–489, 2009.
33. Van Laethem, C., N. Van De Veire, B. Backer, et al. Response of the oxygen uptake efficiency slope to exercise training in patients with chronic heart failure. *Eur. J. Heart Fail.* 9:625–629, 2007.
34. Vanderburgh, P.M., and F.I. Katch. Ratio scaling of VO2max penalizes women with larger percent body fat, not lean body mass. *Med. Sci. Sports Exerc.* 28:1204–1208, 1996.
35. Wasserman, K. Anaerobic threshold and cardiovascular function. *Monaldi Arch. Chest Dis.* 58:1–5, 2002.
36. Wasserman, K., J.E. Hansen, D.Y. Sue, R. Casaburi, and W. B.J. *Prinicples of Exercise Testing and Interpretation: Including Pathophysiology and Clinical Interpretation*. Philadephia: Lippincott Williams & Wilkins, 1999.
37. Weststrate, J.A., and P. Deurenberg. Body composition in children: proposal for a method for calculating body fat percentage from total body density or skinfold-thickness measurements. *Am. J. Clin. Nutr.* 50:1104–1115, 1989.