



Maximal aerobic capacity in ageing subjects: actual measurements *versus* predicted values

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ABSTRACT We evaluated the impact of selection of reference values on the categorisation of measured maximal oxygen consumption ($V'O_{2peak}$) as “normal” or “abnormal” in an ageing population.

We compared measured $V'O_{2peak}$ with predicted values and the lower limit of normal (LLN) calculated with five equations. 99 (58 males and 41 females) disease-free subjects aged ≥ 70 years completed an incremental maximal exercise test on a cycle ergometer.

Mean $V'O_{2peak}$ was $1.88 \text{ L}\cdot\text{min}^{-1}$ in men and $1.26 \text{ L}\cdot\text{min}^{-1}$ in women. $V'O_{2peak}$ ranged from 89% to 108% of predicted in men, and from 88% to 164% of predicted in women, depending on the reference equation used. The proportion of subjects below the LLN ranged from 5% to 14% in men and 0–22% in women, depending on the reference equation. The LLN was lacking in one study, and was unsuitable for women in another. Most LLNs ranged between 53% and 73% of predicted. Therefore, choosing an 80% cut-off leads to overestimation of the proportion of “abnormal” subjects.

To conclude, the proportion of subjects aged ≥ 70 years with a “low” $V'O_{2peak}$ differs markedly according to the chosen reference equations. In clinical practice, it is still relevant to test a sample of healthy volunteers and select the reference equations that better characterise this sample.



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As $V'O_{2peak}$ % pred differs markedly with the reference value, reference equation choice is critical in the elderly <http://ow.ly/YsXHD>



Introduction

Measuring the maximal oxygen consumption ($\dot{V}O_{2\max}$) during an incremental test provides relevant information on risk or prognosis of various diseases [1–3]. In addition, precisely assessing the subject's functional capacity allows tailoring of rehabilitation programmes. Such programmes are increasingly offered to ageing subjects [4, 5]. Proper interpretation of the measured $\dot{V}O_{2\max}$ requires its comparison with well-selected reference values. The use of some equations has been recommended in international guidelines [6, 7]. However, most of these equations have been elaborated from small series, and include subjects under the age of 71 [8] or 74 years [9–11]. As a result, these validated reference equations provide predicted values for the elderly that are largely extrapolated from the models established by these authors. Other authors provide specific reference values for healthy ageing men and women [12–14], but only one study [12] has been referenced in guidelines [6]. In addition, earlier reference values published in the 1970s and 1980s [8–10] may no longer be adapted to the current ageing population, which, with respect to previous ones, has a different history and lifestyle, and increased longevity. Consequently, it may be justified to use reference values derived from studies that include contemporary population samples. In view of this, recent studies have been published [15–17]. These well-designed studies are population-based and provide predicted $\dot{V}O_{2\max}$ values over a wide range of ages.

Taking into account the disparities between the studies discussed above, we hypothesised that predicted $\dot{V}O_{2\max}$ values for older people may vary significantly according to the selected reference equation. Therefore, to evaluate the impact of selection of reference values on the categorisation of $\dot{V}O_{2\max}$ as “normal” or “abnormal”, we compared the measured maximal oxygen consumption ($\dot{V}O_{2\text{peak}}$) on a cycle ergometer in 99 healthy Caucasian subjects aged ≥ 70 years with the predicted $\dot{V}O_{2\max}$ provided by five different studies. We calculated the differences between the measured $\dot{V}O_{2\text{peak}}$ and the predicted $\dot{V}O_{2\max}$, and also examined relationships between the measured $\dot{V}O_{2\text{peak}}$ and the lower limit of normal (LLN).

Materials and methods

Design, subjects and exercise tests

This study was approved by the Ethics Committees of the Medical, Dentistry and Pharmacy Faculties (University of Strasbourg, Strasbourg, France) and of the Strasbourg Hospital, Strasbourg, France (administration number: 2013/26). Table 1 provides the reference equations/predicted values and LLNs we used in this study. To compare predicted $\dot{V}O_{2\max}$ values to measured $\dot{V}O_{2\text{peak}}$, 99 healthy subjects referred by their general practitioner before participating in an exercising programme offered by their medical insurance or before joining sports clubs or associations between January 2009 and December 2012 were included. All subjects lived in the department of Bas-Rhin, in Alsace, France. Subjects were free of chronic diseases, but mild and controlled hypertension or dyslipidaemia, tobacco consumption or overweight were not exclusion criteria [8, 10–13]. An activity questionnaire (adapted from [18]) was filled out by each participant. A maximal symptom-limited incremental exercise test was performed using an electrically braked cycle ergometer (Ergoselect 200P; Ergoline, Bitz, Germany) following recommendations [6]. Oxygen uptake ($\dot{V}O_2$) was measured using a breath-by-breath method (Ultima Cardio2; MedGraphics, Milan, Italy). We measured $\dot{V}O_{2\text{peak}}$ since, as expected, a $\dot{V}O_2$ plateau was not achieved by all subjects [12, 13]. The exercise test was considered maximal if it was symptom-limited with overall fatigue (Borg scale rating 9–10, on a 0–10 scale) and inability to maintain the pedalling rate >60 rpm [7].

Data analysis

Results are expressed as mean \pm SD or proportions. Predicted $\dot{V}O_{2\max}$ was calculated using five different sets of reference equations, by WASSERMAN *et al.* [11], JONES *et al.* [8], BLACKIE *et al.* [12], HAKOLA *et al.* [13] and KOCH *et al.* [17]. To compare measured $\dot{V}O_{2\text{peak}}$ with predicted $\dot{V}O_{2\max}$, we calculated the mean difference ($\dot{V}O_{2\text{peak}}$ minus predicted $\dot{V}O_{2\max}$), and the 90% confidence interval of the differences for each predicted equation. Only one author provided equations to calculate the fifth percentile, used as LLN [17]. For the other studies, we determined LLN as mean -2 SD. Since no standard deviation was available in the publication by WASSERMAN *et al.* [11], no LLN could be calculated. The percentage of subjects with values below the LLN of $\dot{V}O_{2\max}$ was calculated for each equation. $\dot{V}O_{2\text{peak}}$ was compared according to the grade of physical activity using a two-way ANOVA.

Results

Table 1 provides the reference equations we used [8, 11–13, 17], as well as the characteristics of the population samples selected by the authors to elaborate these equations. Predicted $\dot{V}O_{2\max}$ and LLN ($\text{L}\cdot\text{min}^{-1}$) have been calculated for an illustrative individual (72 years-old; man: 80 kg and 172 cm; woman: 67 kg and 160 cm) using each equation.

The characteristics of our subjects are presented in table 2. 58 men and 41 women were included. All subjects were Caucasian, and had normal spirometry and echocardiography. 83% of men and 63% of

TABLE 1 Equations used for calculation of predicted maximal oxygen consumption ($\dot{V}O_{2\max}$)

First author [ref.], year	Characteristics of the population samples	Prediction equations for $\dot{V}O_{2\max}$ [#]
WASSERMAN [11], 1999	The published equations were modified from: HANSEN <i>et al.</i> [10] 77 males, 34–74 years Asbestos exposed workers with normal cardiorespiratory function, California, USA BRUCE <i>et al.</i> [9] 138 males, 157 females, 29–73 years General population, Washington, USA	Men $(50.72 - [0.372 \times \text{Age}]) \times \text{Weight}$ (units of mL·min ⁻¹) Example [¶] : predicted value: 1.92 L·min ⁻¹ ; no LLN can be calculated Women $(22.78 - [0.17 \times \text{Age}]) \times (\text{Weight} + 43)$ (units of mL·min ⁻¹) Example [¶] : predicted value: 1.16 L·min ⁻¹ ; no LLN can be calculated
JONES [8], 1985	50 males, 50 females, 15–71 years Subjects recruited by advertising from the local university and general population, Ontario, Canada	$(0.046 \times \text{Height}) - [0.021 \times \text{Age}] - [0.62 \times \text{Sex}] - 4.31$ (units of L·min ⁻¹) Sex: male=0; female=1 Men Example [¶] : predicted: 2.09 L·min ⁻¹ ; LLN: 1.14 (55% pred) Women Example [¶] : predicted: 0.92 L·min ⁻¹ ; LLN: 0.15 (16% pred)
BLACKIE [12], 1989	81 males, 47 females, 55–80 years Subjects recruited locally by advertising from hospital and community centres, British Columbia, Canada	Men $(0.0142 \times \text{Height}) - [0.0494 \times \text{Age}] + [0.00257 \times \text{Weight}] + 3.015$ (units of L·min ⁻¹) Example [¶] : predicted: 2.11 L·min ⁻¹ ; LLN: 1.25 (60% pred) Women $(0.0142 \times \text{Height}) - [0.0115 \times \text{Age}] + [0.00974 \times \text{Weight}] - 0.651$ (units of L·min ⁻¹) Example [¶] : predicted: 1.45 L·min ⁻¹ ; LLN: 0.90 (62% pred)
KOCH [17], 2009	Disease-free subjects, 253 males, 281 females, 25–80 years Representative sample selected from the population registration offices in Pomerania, Germany	$47.7565 - [0.988 \times \text{Age}] - [0.2356 \times \text{Age}^2] - [8.8697 \times \text{Sex}] + [2.3597 \times \text{BMI}] - [2.0308 \times \text{Age} \times \text{BMI}] - [3.7405 \times \text{Sex} \times \text{BMI}] + [0.2512 \times \text{Age} \times \text{Sex}] + [1.3797 \times \text{Age} \times \text{Sex} \times \text{BMI}]$ (units of L·kg ⁻¹ ·min ⁻¹) With: Age >65 years=5; Sex male=1, female=2; BMI ≤25 kg·m ⁻² =0, BMI >25 kg·m ⁻² =1 Men Example [¶] : predicted: 1.97 L·min ⁻¹ ; LLN: 1.43 (73% pred) Women Example [¶] : predicted: 1.35 L·min ⁻¹ ; LLN: 1.13 (84% pred)
HAKOLA [13], 2011	Nondiseased subjects, 117 males, 112 females, 57–78 years Subjects randomly selected from the town of Kuopio, Finland	Men $4.846 - [0.039 \times \text{Age}]$ (units of L·min ⁻¹) Example [¶] : predicted: 1.91 L·min ⁻¹ ; LLN: 1.12 (59% pred) Women $3.475 - [0.031 \times \text{Age}]$ (units of L·min ⁻¹) Example [¶] : predicted: 1.32 L·min ⁻¹ ; LLN: 0.70 (53% pred)

Exercise tests were performed using cycle ergometers. LLN: lower limit of normal; BMI: body mass index. #: for all equations, age is in years, height in cm and weight in kg; ¶: Predicted $\dot{V}O_{2\max}$ and LLN (L·min⁻¹) have been calculated for an illustrative individual (72 years-old; male: 80 kg and 172 cm; female: 67 kg and 160 cm).

women had a body mass index >25 kg·m⁻². 63% of males and 22% of females were current or former-smokers. Most subjects (53% of men and 66% of women) reported moderate physical activity, while 19 males and females reported intense physical activity. These physical activities included heavy gardening and yard work, yoga and gymnastic/fitness, walking/hiking, cycling, swimming, and cross-country skiing. The 19 (19%) subjects who reported intense physical activity practiced at least two sports. The more intense the activity level the higher the $\dot{V}O_{2\text{peak}}$ ($p < 0.05$). $\dot{V}O_{2\text{peak}}$ was 23.05 ± 5.47 mL·min⁻¹·kg⁻¹ in men and 18.94 ± 4 mL·min⁻¹·kg⁻¹ in women, and maximal workload was 127 ± 37 W (1.57 W·kg⁻¹) in men and 84 ± 18 W (1.27 W·kg⁻¹) in women. Oxygen saturation monitored by pulse oximetry remained stable throughout the exercise test. Maximal heart rate, ventilation, respiratory exchange ratio and respiratory equivalents were not different in men and women.

Table 3 provides means and 90% confidence intervals of the differences between measured and predicted $\dot{V}O_2$ values. Figure 1 illustrates the measured $\dot{V}O_{2\text{peak}}$ in our subjects and the normal values calculated with the five equations for an 80 kg and 172 cm man, and a 67 kg and 160 cm woman. Table 3 shows that mean $\dot{V}O_{2\text{peak}}$ ranged from 89% and 108% of predicted, and mean (measured–predicted) differences ranged from –250 mL to +150 mL in men, according to the reference values used. In women, mean

TABLE 2 Subjects' characteristics, spirometry and exercise test results

	Men	Women
Subjects n	58	41
Age years	73.6±4.0	73.2±2.7
Weight kg	81.3±13.3	67.7±11.5
Height cm	172.2±0.1	159.5±0.1
Body mass index kg·m⁻²	28.0±3.6	26.2±3.6
Current smokers	5 (8.6)	0 (0)
Former smokers	32 (55.0)	9 (21.9)
Intense physical activity	13 (22.4)	6 (14.6)
Moderate physical activity	31 (53.4)	27 (65.8)
Sedentary	14 (24.2)	8 (19.6)
FVC L	3.7±0.7	2.8±0.6
FVC % predicted	101.7±20.1	122.8±25.4
FEV₁ L	2.7±0.6	2.2±0.4
FEV₁ % pred	99.6±22.8	117.1±21.6
FEV₁/FVC %	74.1±8.9	78.7±6.3
Oxygen uptake at rest L·min⁻¹	0.30±0.07	0.23±0.06
Heart rate at rest beats·min⁻¹	76±12	77±13
Ventilation at rest L	11.52±2.61	8.42±1.64
Maximal oxygen uptake L·min⁻¹	1.88±0.41	1.26±0.24
mL·min⁻¹·kg⁻¹	23.05±5.47	18.94±4.00
Maximal workload W	127.33±36.66	84.20±18.29
Maximal heart rate beats·min⁻¹	142±21	137±18
% pred[#]	87.2±13.0	85.8±10.6
Maximal ventilation L	72.77±18.31	49.50±13.22
% pred[#]	77.6±17.4	68.0±16.7
Maximal V_E/V_{CO₂}	34.19±4.63	34.83±5.66
Maximal V_E/V_{O₂}	38.38±7.37	39.40±6.91
Maximal respiratory exchange ratio	1.14±0.10	1.15±0.07

Data are presented as mean±SD or n (%), unless otherwise stated. The exercise test was performed on an electrically-braked cycle ergometer. FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 s; V_E: minute ventilation; V_{CO₂}: carbon dioxide output; V_{O₂}: oxygen uptake. #: predicted maximal ventilation was calculated as the subject's FEV₁×35; predicted maximal heart rate was calculated as 210–0.65×(age) [7].

V_{O₂peak} ranged from 88% and 164% of predicted, and mean (measured–predicted) differences ranged from –190 mL to +350 mL. The proportion of men below the LLN ranged from 5% to 14%, and the proportion of women ranged from 0% to 22%. The dispersion of the (measured–predicted) differences (reflected by the bounds of the 90% CI; table 2) was wider using the equation of JONES *et al.* [8] for women, because of the huge dispersion of the predicted values using this equation (0.14–1.54 L·min⁻¹). In addition, these predicted values for women were very low.

Discussion

In this study, we expressed the measured V_{O₂peak} of 99 disease-free, ≥70 year-old subjects as the percentage of the reference values calculated using five different reference equations. Mean V_{O₂peak} ranged from 89% to 108% of predicted in men, and from 88% to 164% in women, depending on the reference equation used. In addition, we found that the proportion of subjects showing V_{O₂peak} below the LLN ranged from 5% to 14% in men and 0% to 22% in women, depending on the reference equation.

This study has three main limitations. First, the maximal exercise tests were performed on a cycle ergometer. Thus, the results cannot be extrapolated to V_{O₂max} measured on a treadmill. Secondly, not all available reference equations were tested. Thirdly, the characteristics of our sample subjects can be a subject of discussion.

Numerous reference equations or normal values have been published for V_{O₂max}, which do or do not include older people. We did not perform a comprehensive review of these equations, but aimed to show that V_{O₂peak} expressed as per cent predicted as well as proportions of subjects with “low” V_{O₂peak} differ markedly according to the equation used. Among the five studies we selected, the studies by JONES *et al.* [8], WASSERMAN *et al.* [11] and BLACKIE *et al.* [12] were regarded by the 1997 European Respiratory Society task force [6] to fulfil the minimum requirements to be used in the clinical setting. The 2003 American Thoracic Society/American College of Chest Physicians committee [7] concluded that, even if not optimal, the

TABLE 3 Comparison of measured maximal oxygen consumption ($V'O_{2,peak}$) versus predicted maximal oxygen consumption ($V'O_{2,max}$) according to prediction equations from five studies

Sample	Prediction equation	$V'O_{2,peak}$ % predicted	$V'O_{2,peak}$ minus $V'O_{2,max}$ L·min ⁻¹	Subjects with $V'O_{2,peak}$ <LLN [#]
58 disease-free men, >70 years old	WASSERMAN <i>et al.</i> [11]	108±23	0.15 (−0.50–0.79)	
	JONES <i>et al.</i> [8]	92±20	−0.18 (−0.87–0.52)	3 (5)
	BLACKIE <i>et al.</i> [12]	93±21	−0.16 (−0.85–0.54)	4 (7)
	KOCH <i>et al.</i> [17]	89±20	−0.25 (−0.95–0.45)	8 (14)
	HAKOLA <i>et al.</i> [13]	103±24	0.04 (−0.65–0.74)	3 (5)
41 disease-free women, >70 years old	WASSERMAN <i>et al.</i> [11]	117±20	0.19 (−0.17–0.55)	
	JONES <i>et al.</i> [8]	164±103	0.35 (−0.19–0.88)	0 (0)
	BLACKIE <i>et al.</i> [12]	88±16	−0.19 (−0.59–0.22)	0 (0)
	KOCH <i>et al.</i> [17]	90±17	−0.15 (−0.59–0.28)	9 (22)
	HAKOLA <i>et al.</i> [13]	98±18	−0.03 (−0.41–0.35)	0 (0)

Data are presented as mean±SD, mean difference (90% CI) or n (%). LLN: lower limit of normal.
#: WASSERMAN *et al.* [11] did not provide LLN.

reference values of JONES *et al.* [8] and WASSERMAN *et al.* [11] should continue to be used clinically. We tested these equations on subjects aged ≥ 70 years, whose demand for exercise testing and rehabilitation is growing. However, the validity of the predicted $V'O_{2,max}$ values may be questioned for this age group. Indeed, the oldest subjects in the studies by JONES *et al.* [8] and WASSERMAN *et al.* [11] were only 71 and 74 years old, respectively. As a result, predicted values for people aged >70 years people are mainly extrapolated from their linear models. Since the $V'O_{2,max}$ /age relationship has been found to be nonlinear in some studies [16, 17, 19] using these equations may lead to improper reference values. We also studied two equations derived from “ageing” populations. The studies by HAKOLA *et al.* [13] and BLACKIE *et al.* [12] included 15 and 36 subjects aged >70 years, which is not that high. We eventually selected the equation from KOCH *et al.* [17], elaborated from one of the largest published population-based series. It included 25 subjects aged >65 years [17]. When using this equation, the predicted $V'O_{2,max}$ for a given subject with stable weight and height doesn't vary beyond age 65 years, since age is not a continuous variable. It is interesting to note that WASSERMAN *et al.* [11] and KOCH *et al.* [17] took into account the effect of obesity or overweight on $V'O_{2,max}$, whereas height and weight were not included in the equation used by HAKOLA *et al.* [13].

The selection of our subjects needs to be further discussed. First, a lack of disease or risk factors beyond the age of 70 years is uncommon. Our subjects were free of chronic diseases and had normal echocardiography and spirometry. However, we included, as did other authors, subjects who strictly speaking could not to be considered as “healthy”. Smokers or ex-smokers [12, 13, 15, 17] or overweight subjects [11, 13, 15, 17] were not excluded from most studies. KOCH *et al.* [17] showed that arterial hypertension and/or beta blocker treatment did not have a significant influence on $V'O_{2,max}$, and these were not regarded as exclusion criteria. We recorded normal end-exercise cardiorespiratory values for this age group [20], in both men and women. Compared with younger subjects, it has been demonstrated that maximal $V'O_2$, carbon dioxide output ($V'CO_2$), heart rate, ventilation and end-tidal carbon dioxide tension

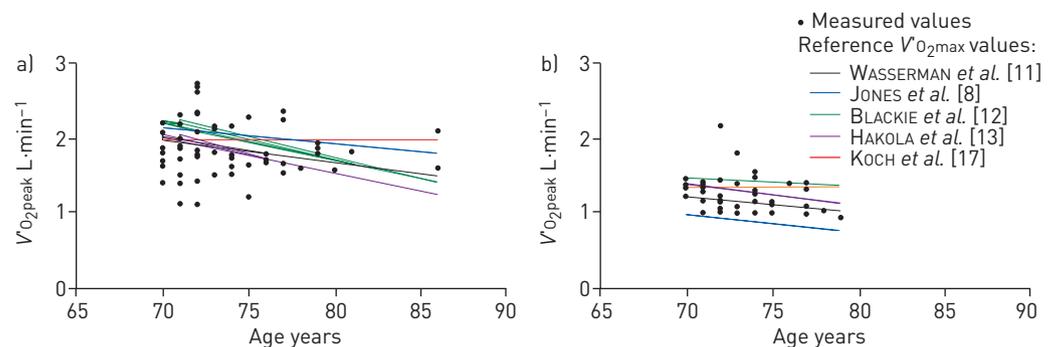


FIGURE 1 Measured maximal oxygen consumption ($V'O_{2,peak}$) in a) 58 men and b) 41 women, aged >70 years and free of chronic diseases. Predicted maximal oxygen consumption ($V'O_{2,max}$) reference values and their changes with age were calculated using reference equations by WASSERMAN *et al.* [11], JONES *et al.* [8], BLACKIE *et al.* [12], HAKOLA *et al.* [13] and KOCH *et al.* [17] for an illustrative individual (male: 80 kg and 172 cm; female: 67 kg and 160 cm; mean heights and weights in our study).

significantly decline with age, whereas minute ventilation (V_E)/ $V'CO_2$ and $V_E/V'O_2$ slightly increase, and respiratory exchange ratio and end-tidal oxygen tension do not change significantly [20]. Secondly, our selection of subjects was inherently biased as no formal random selection from a large population was used. Our subjects were referred before joining sports clubs or exercise programmes, lived in Alsace, and were part of our routine clinical practice. Thirdly, comparison of our maximal $V'O_2$, ventilation and heart rate values to recently published values [15, 16] may suggest that the efforts of some of our subjects may have been submaximal. These observations are of course of relevance. However, our purpose was not to provide normal values for French older people, but to use $V'O_{2peak}$ results obtained routinely, in “healthy” subjects, to compare actual to predicted $V'O_{2max}$.

This study led to some findings that could guide the selection of reference equations for ageing people. In men, predicted $V'O_{2max}$ were not very different from one another and fitted with our subjects' measured $V'O_{2peak}$, whatever the reference equation. In women, predicted values were more widely distributed than in men. The studies by JONES *et al.* [8] and WASSERMAN *et al.* [11] provided the lowest predicted $V'O_{2max}$ values. In our opinion, the equation of JONES *et al.* [8] provides unsuitable predicted $V'O_{2max}$ for ageing women, as our mean $V'O_{2peak}$ value corresponded to 164% of predicted. Predicted values for women calculated using the equations of BLACKIE *et al.* [11], KOCH *et al.* [17] and HAKOLA *et al.* [13] were reasonably close to each other and fit our population. Interestingly, predicted $V'O_{2max}$ values provided by two recent studies are very high compared with those we selected [15, 16]. For instance, the predicted $V'O_{2max}$ is 2.81 L·min⁻¹ for men aged >70 years and 1.85 L·min⁻¹ for women aged >70 years in the study by LOE *et al.* [16]. The subjects were tested on a treadmill and not on a cycle, and the use of a treadmill usually results in 10–15% higher $V'O_{2max}$ [21]. However, after application of the corrective factor, these predicted $V'O_{2max}$ remain higher than the previous ones, raising the question of a secular trend.

The main finding of this study is that LLN differed a lot from one study to another. As a result, depending on the selected reference equation, 5–14% of men and 0–22% of women were categorised as “abnormal”. We showed that the LLN of JONES *et al.* [8] for women were very low and seem unsuitable for clinical practice, whatever the studied female population. The data of WASSERMAN *et al.* [11] did not allow calculation of the LLN. In such a case, a <80% of predicted cut-off is frequently used in practice to define “abnormality”. As shown in table 1, we found that after excluding the extremes, LLN ranged between 53% and 73% of the predicted value in both men and women. This demonstrates that the choice of an 80% cut-off leads to overestimate the proportion of “abnormal” older subjects and should not be used. Again, we found that the LLN was more widely distributed in women (16–84% of predicted) than in men (55–73% of predicted) (table 1). Altogether, these results provide evidence that LLN needs to be well characterised in published studies and applied in clinical practice. In addition, the wide range of LLN recorded in the literature should prompt additional studies in women.

The heterogeneity of the reference values we examined can be partly explained by technical reasons (*e.g.* exercise protocol and type of gas exchange analyser) and partly by methodological issues (*e.g.* sample size, criteria for subject selection and maximal effort, and treatment of data). However, the main factor is probably the characteristics of the reference population from which the sample is drawn. Obviously, reference equations cannot be used irrespective of the population from which a subject comes. Guidelines recommend testing a sample of healthy volunteers and selecting the reference values that better characterise this sample [7], emphasising the importance of matching reference values to the population base. Based on the current analysis, this recommendation still appears worthy of consideration.

To conclude, this study stresses the importance of the selection of $V'O_{2max}$ reference equations, especially for older subjects, and offers clinicians some information to guide their choice. However, an alternative approach to the difficult issue of subjects' categorisation as “normal” or not would be to evaluate mortality risk or prognosis associated with $V'O_{2max}$ results, which would be particularly relevant in ageing subjects. Indeed, the question of how healthy older people should be to be regarded as “normal” today is a matter of debate.

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