RESEARCH ARTICLE

Cardio-Respiratory Reference Data in 4631 Healthy Men and Women 20-90 Years: The HUNT 3 Fitness Study

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Abstract

Purpose: To provide a large reference material on key cardio-respiratory variables in a healthy population of Norwegian men and women aged 20–90 years.

Methods: Sub maximal and peak levels of cardio-respiratory variables were measured using cardiopulmonary exercise testing during treadmill running.

Results: The highest peak ventilation among men (141.9 ± 24.5 L·min⁻¹) and women (92.0 ± 16.5 L·min⁻¹) was observed in the youngest age group (20–29 years, sex differences p < 0.001) with an average 7% reduction per decade. The highest tidal volumes were observed in the 30–39 and 40–49 year age groups among men (2.94 ± 0.46 L) and women (2.06 ± 0.32 L) (sex differences p < 0.001), with a subsequent average 6% reduction per decade. Ventilatory threshold and respiratory compensation point were observed at approximately 77% and 87% of peak oxygen uptake (VO₂peak) among men and women, respectively. The best ventilatory efficiency (EqVCO₂Than) was observed in the youngest age group (20–29 years) in both men (26.2 ± 2.8) and women (27.5 ± 2.7) (sex differences p < 0.001) with an average 3% deterioration in ventilatory efficiency per decade.

Conclusion: This is the largest European reference material of cardio-respiratory variables in healthy men and women aged 20–90 years, establishing normal values for, and associations between key cardio-respiratory parameters. This will be useful in clinical decision making when evaluating cardiopulmonary health in similar populations.
Introduction

Cardiopulmonary exercise testing (CPET) is an underutilized clinical procedure [1], despite several published recommendations by international health organizations [2–5]. It is a good tool for evaluating mechanisms and limitations of exercise tolerance [6], and for the assessment of cardiopulmonary health [1]. Consequently, CPET is a valuable tool in clinical decision making [2]. There are numerous large studies establishing spirometry reference values [7–14]. However, studies containing a combination of principal cardio- respiratory variables, such as ventilation (V̇E), tidal volume (V̇T), breathing frequency (fB), oxygen uptake (VO2), expired carbon dioxide (VCO2) and ventilatory efficiency (EqVCO2) are limited. Previous research have included only a few of these key variables, are limited to selected age groups and fitness levels, or small populations e.g. [15–25]. The aim of this study was to establish a large reference material on submaximal and maximal cardiopulmonary variables in healthy men and women aged 20–90 years.

Methods

Participants

The HUNT 3 fitness study is the third wave of the Nord-Trøndelag Health Studies (ntnu.edu/hunt). Data were collected between October 2006 and June 2008. The entire population >20 years of age (n=94194) were invited to participate, 54% (n=50821) accepted. Eligible candidates had to be free from cardiovascular disease, respiratory symptoms, cancer, and the use of blood pressure medication. Based upon self-reported information, 30513 candidates presented as suitable for VO2max testing. Out of these, 12609 candidates resided in the 3 municipals selected for VO2max testing, and 5633 of them volunteered to participate. Subsequent the primary inclusion the medical interview excluded an additional 390 candidates not meeting medical inclusion criteria, leaving 5243 candidates. 4631 candidates completed a VO2peak test. These 3 locations were chosen due to geographical location to minimize travel distance for participants. We experienced technical difficulties with Cortex MetaMax II, and during service at Cortex data was lost, thus, total sample sizes on tidal volume (V̇T) and breathing frequency (fB) was n=3667.

Ethics statement

The study was approved by the Regional committee for medical research ethics (2012/1672/REK nord), the Norwegian Data Inspectorate and the National Directorate of Health, and is in compliance with the Helsinki declaration. Written informed consent was obtained from all participants.
Cardio Pulmonary Exercise Test (CPET)

An individualized graded protocol [26] was used for measuring cardio-respiratory variables (Cortex MetaMax II, Cortex, Leipzig, Germany). Before starting the testing procedure several MetaMax II apparatus were tested against Douglas-bag and iron lung (Cortex, Leipzig, Germany) and those finally used found reliable and valid [27]. Speed and angle of the test treadmills were calibrated prior to testing. The MetaMax II was calibrated prior to the first test each day using a standard two-point gas calibration procedure. The calibration included measurements of ambient air and a gas mix of known content (15.03% O2 and 4.98% CO2 in N2), a calibration of the Triple-V volume transducer with a calibrated 3 L syringe (Calibration syringe D, SensorMedics, CareFusion, San Diego, CA, USA), and barometric pressure control. Volume calibration was performed every third test and the two-point gas calibration every fifth. Before each test the ambient room air was checked. Heart rate was measured by radio telemetry (Polar S610i, Polar Electro Oy, Kempele, Finland). Body mass was measured using the weighing scale Model DS-102 (Arctic Heating AS, Nøtterøy, Norway). Participants had a treadmill familiarization phase of 8–10 minutes during warm-up. They were instructed to avoid grabbing the handrails if not absolutely necessary. The individualized warm-up workload determined the initial speed/angle on the subsequent treadmill test. Candidates used a face mask (Hans Rudolph, Germany) of appropriate size linked to the MetaMax II. When participant maintained a stable oxygen uptake >30seconds, velocity (0.5–1.0 kmh-1) or inclination (1–2%) was increased. Increased workload was if possible obtained with increased speed and keeping a fixed slope angle of the treadmill. If a participant was unable to increase speed, the angle was increased. Tests were ended when candidates reached volitional exhaustion (e.g. shortness of breath and leg fatigue). VO2max was considered achieved if subjects reached a VO2 plateau that remained stable even with increased work load [28], i.e. VO2 did not increase more than 2 mL·kg⁻¹·min⁻¹ despite increased work load, and R≥1.05. Since 12.6% of the subjects failed to reach VO2max we used the expression VO2peak. Measurements were done at 3 different workloads, 2 submaximal and peak. Level 1: The individual initial workload was determined during warm-up, and stable VO2 and heart rate were reached after 3 minutes. Level 2: Treadmill gradient was increased by 2% or speed increased 1 km·h⁻¹, with steady state obtained after 2–3 minutes. Peak workload is described above.

Ventilatory anaerobic threshold (VThan) and respiratory compensation point (RCP)

The transition point from aerobic to anaerobic metabolism denotes VThan [29]. With increasing workload aerobic metabolism alone cannot provide the energy required, and energy production must increasingly depend upon anaerobic metabolism [30]. RCP marks the respiratory compensation for metabolic acidosis, beneath which VE is strongly linked to VCO2, whereas above VE increases faster.
relative to VCO₂ [31], hence, onset of hyperventilation [32]. Both VT \( V_{\text{T,than}} \) and RCP were established by the V-slope method [31].

**Ventilatory efficiency**

We calculated the ventilatory equivalent EqVO₂ \( (V_{E} \cdot VO_{2}^{-1}) \) and EqVCO₂ \( (V_{E} \cdot VCO_{2}^{-1}) \) at VO₂peak and VT \( V_{\text{T,than}} \). The ventilatory equivalents describe the fraction of minute ventilation \( (V_{E}) \) to oxygen uptake \( (VO_{2}) \), or to expired carbon dioxide \( (VCO_{2}) \).

**Statistical analysis**

Parametric analysis was used and QQ-plots supported the assumption of normally distributed data. Data are presented as arithmetic mean ± standard deviation. Analysis of variance (Anova) was used to determine differences between age groups. If a significant F-ratio was achieved, post hoc evaluations were completed using Bonferroni tests. An Independent-Samples T-test was used for establishing level of significance between sexes. Linear regression and curve linear regression, with 95% confidence interval, were used to test associations between cardiorespiratory parameters. Multiple linear regressions were used to generate prediction models. All statistical tests were two-sided. SPSS 20.0 (Statistical package for Social Sciences, Chicago; Illinois, USA), and GraphPad Prism 4.01 (GraphPad Software, San Diego, California, USA) were used to analyze data. Correlations were done using data from Level 1, Level 2 and peak as described above. A p-value of <0.05 was considered statistically significant.

**Results**

Descriptive characteristics for men and women are presented in Table 1.

**Peak ventilation (\( V_{\text{E,peak}} \)) and tidal volume (\( V_{\text{T,peak}} \))**

Women had a 34% (p<0.001) lower \( V_{\text{E,peak}} \) than men. \( V_{\text{E,peak}} \) was similar and highest in the two youngest age groups (20–29 and 30–39 years) in both men and women. In women \( V_{\text{E,peak}} \) became 8% (p<0.01) lower per decade from age 30–39 up to 60–69 years. Compared to men aged 20–39 years, men aged 40–49 years had 3.5% (p<0.05) lower \( V_{\text{E,peak}} \), whereupon it decreased by 9% (p<0.001) per decade up to those aged 60–69 years. For both sexes we observed an average 16% (p<0.001) lower \( V_{\text{E,peak}} \) between the 2 most senior age groups (60–69 vs. +70 years) (Table 2).

Women had approximately 32% (p<0.001) lower \( V_{\text{T,peak}} \) than men. For both sexes the highest \( V_{\text{T,peak}} \) was found among those aged 30–49 years, despite no differences in stature compared to the youngest age groups. In both sexes we observed an average 4% (p<0.05) and 11% (p<0.001) drop in \( V_{\text{T,peak}} \) per decade in age groups 40–69 years, and between the 2 most senior age groups, respectively.
Table 1. Descriptive data for men and women in the HUNT 3 fitness study.

|                        | Men            | Women           |
|------------------------|----------------|-----------------|
| Age (yr.)              | 48.9 ± 13.5    | 48.0 ± 13.7     |
| Anthropometrical data  |                |                 |
| Height (cm)            | 179.2 ± 6.5    | 165.9 ± 5.9     |
| Weight (kg)            | 85.6 ± 11.5    | 69.8 ± 11.2     |
| BMI (kg·m⁻²)           | 26.6 ± 3.2     | 25.4 ± 3.9      |
| Smoking status         |                |                 |
| Never smoked/Quit smoking (%) | 50.9/27.5 | 49.1/27.4       |
| Daily smoker/Occasional smoker (%) | 10.1/11.5 | 13.1/10.4       |

Data are presented as arithmetic mean ± SD. BMI: bod mass index.

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The highest breathing frequency ($f_B$) in both men and women, 50 ± 9 breaths·min⁻¹ and 47 ± 7 breaths·min⁻¹, respectively, was found in the youngest age group (20–29 years), with an average 5% (p<0.05) decrease per subsequent decade (Table 2).

Stratified by height an 11% (p<0.01) rise in $V_{E\text{peak}}$ and $V_{T\text{peak}}$ was observed per 10 cm increased height, in both sexes (Table 3).

Carbon dioxide ($VCO_2$) elimination

Women displayed roughly 34% (p<0.001) lower $VCO_2\text{peak}$ than men. Stratified by age the highest $VCO_2\text{peak}$ was found in the youngest age groups. No significant differences in $VCO_2\text{peak}$ were observed neither for men nor women between age groups 20–29 and 30–39 years, whereupon an approximate 6% (p<0.001) and 5% (p<0.001) decrease was observed between age groups 30–39 vs. 40–49 years, respectively. In subsequent age groups exponential reductions were observed, ending with an average 18% (p<0.001) lower peak $VCO_2$ in the most senior age group compared with men and women aged 60–69 years (Table 2).

Ventilatory anaerobic threshold ($V_{Than}$)

The highest $V_{Than}$ was observed in the youngest age groups. No statistical differences in $V_{Than}$ was observed between the 3 youngest age groups (20–49 years) among both sexes, whereupon we observed an approximate 10% (p<0.001) lower $V_{Than}$ per decade. $V_{Than}$ was obtained at 75.2 ± 10.7 and 76.7 ± 9.4% of $VO_2\text{peak}$ for men and women (20–29 years), respectively, which corresponds to approximately 88 ± 7% of peak heart rate ($f_{c\text{peak}}$), with no major differences between age groups (Table 4).
| Table 2. Physiological cardio-respiratory variables in the HUNT 3 Fitness study stratified by intensity levels, sex and age groups. |
|---------------------------------------------------------------|
| **Level 1 (≤V_{than})** | **Level 2 (≤RCP)** | **Peak** |
| **Men** | **Women** | **Men** | **Women** | **Men** | **Women** |
| **Workload (Watts)** | 99.2 ± 24.2 | 68.6 ± 19.0 | 115.1 ± 24.8 | 81.7 ± 19.9 | 177.2 ± 37.0 | 119.0 ± 25.0 |
| f_{peak} (beats min^{-1}) | 149 ± 19 | 153 ± 19 | 160 ± 18 | 180 ± 16 | 179 ± 15 |
| %f_{peak} | 78.8 ± 8.0 | 83.3 ± 7.5 | 85.6 ± 7.3 | 89.6 ± 6.5 |
| %VO_{2peak} | 67.5 ± 11.2 | 72.4 ± 10.6 | 74.9 ± 10.7 | 79.8 ± 9.9 |
| f_{a} (1-min^{-1}) | 26 ± 5 | 28 ± 5 | 30 ± 6 | 31 ± 6 | 44 ± 8 | 42 ± 8 |
| V_{E} (L-min^{-1}) | 60.8 ± 14.6 | 45.1 ± 10.7 | 73.7 ± 19.6 | 54.6 ± 14.2 | 123.7 ± 25.7 | 81.8 ± 17.6 |
| V_{T} (V_{E}\cdot f_{a}^{-1}) | 2.32 ± 0.46 | 1.61 ± 0.32 | 2.51 ± 0.47 | 1.76 ± 0.33 | 2.84 ± 0.49 | 1.94 ± 0.33 |
| V_{CO2} (L-min^{-1}) | 2.14 ± 0.50 | 1.54 ± 0.36 | 2.54 ± 0.58 | 1.82 ± 0.41 | 4.22 ± 0.92 | 2.76 ± 0.62 |
| V_{O2} (L-min^{-1}) | 2.46 ± 0.56 | 1.77 ± 0.38 | 2.78 ± 0.61 | 1.98 ± 0.42 | 3.74 ± 0.76 | 2.47 ± 0.51 |
| R (CO_{2}-VO_{2}^{-1}) | 0.89 ± 0.06 | 0.88 ± 0.06 | 0.94 ± 0.08 | 0.95 ± 0.08 | 1.12 ± 0.07 | 1.11 ± 0.08 |
| BMI | 26.6 ± 3.2 | 25.4 ± 3.9 |
| **20–29 years** | | | | | | |
| **Men** | **Women** | **Men** | **Women** | **Men** | **Women** |
| Workload (Watts) | 109.5 ± 24.0 | 78.1 ± 15.0 | 125.5 ± 22.9 | 90.9 ± 13.3 | 197.2 ± 40.2 | 126.3 ± 24.4 |
| f_{a} (beats-min^{-1}) | 158 ± 20 | 164 ± 20 | 172 ± 14 | 176 ± 16 | 196 ± 11 | 194 ± 9 |
| %f_{peak} | 80.8 ± 8.8 | 85.0 ± 8.3 | 87.8 ± 5.4 | 0.7 ± 6.5 |
| %VO_{2peak} | 64.5 ± 12.5 | 68.3 ± 10.9 | 73.1 ± 10.7 | 6.3 ± 9.6 |
| f_{a} (1-min^{-1}) | 29 ± 6 | 30 ± 5 | 32 ± 6 | 34 ± 7 | 50 ± 9 | 47 ± 7 |
| V_{E} (L-min^{-1}) | 61.3 ± 15.7 | 45.4 ± 10.8 | 75.1 ± 19.3 | 57.9 ± 15.9 | 141.9 ± 24.5 | 92.0 ± 16.5 |
| V_{T} (V_{E}\cdot f_{a}^{-1}) | 2.14 ± 0.41 | 1.53 ± 0.31 | 2.39 ± 0.46 | 1.73 ± 0.31 | 2.84 ± 0.52 | 1.91 ± 0.31 |
| V_{CO2} (L-min^{-1}) | 2.31 ± 0.60 | 1.62 ± 0.39 | 2.87 ± 0.66 | 1.98 ± 0.40 | 4.94 ± 0.87 | 3.17 ± 0.57 |
| V_{O2} (L-min^{-1}) | 2.72 ± 0.67 | 1.92 ± 0.42 | 3.16 ± 0.72 | 2.20 ± 0.41 | 4.30 ± 0.73 | 2.77 ± 0.47 |
| R (CO_{2}-VO_{2}^{-1}) | 0.90 ± 0.06 | 0.89 ± 0.06 | 0.96 ± 0.05 | 0.97 ± 0.08 | 1.15 ± 0.06 | 1.14 ± 0.06 |
| BMI | 24.2 ± 3.1 | 23.9 ± 3.9 |
| **30–39 years** | | | | | | |
| **Men** | **Women** | **Men** | **Women** | **Men** | **Women** |
| Workload (Watts) | 109.3 ± 21.9 | 76.7 ± 16.9 | 123.1 ± 22.0 | 90.9 ± 19.3 | 196.8 ± 32.6 | 127.4 ± 23.9 |
| f_{a} (beats-min^{-1}) | 149 ± 17 | 157 ± 17 | 163 ± 16 | 169 ± 16 | 190 ± 9 | 188 ± 11 |
| %f_{peak} | 78.9 ± 7.4 | 83.3 ± 6.9 | 86.0 ± 6.4 | 90.3 ± 5.8 |
| %VO_{2peak} | 62.1 ± 10.1 | 69.1 ± 10.1 | 71.0 ± 10.1 | 78.1 ± 9.9 |
| f_{a} (1-min^{-1}) | 26 ± 5 | 29 ± 5 | 30 ± 7 | 32 ± 6 | 47 ± 8 | 45 ± 7 |
| V_{E} (L-min^{-1}) | 61.7 ± 15.3 | 47.3 ± 12.2 | 76.4 ± 20.1 | 58.6 ± 15.3 | 136.8 ± 21.5 | 91.5 ± 15.5 |
| V_{T} (V_{E}\cdot f_{a}^{-1}) | 2.36 ± 0.45 | 1.66 ± 0.35 | 2.56 ± 0.45 | 1.82 ± 0.35 | 2.94 ± 0.46 | 2.06 ± 0.32 |
| V_{CO2} (L-min^{-1}) | 2.31 ± 0.53 | 1.66 ± 0.40 | 2.75 ± 0.54 | 1.98 ± 0.42 | 4.82 ± 0.75 | 3.13 ± 0.57 |
| V_{O2} (L-min^{-1}) | 2.63 ± 0.52 | 1.91 ± 0.40 | 2.98 ± 0.52 | 2.16 ± 0.44 | 4.20 ± 0.65 | 2.74 ± 0.50 |
| R (CO_{2}-VO_{2}^{-1}) | 0.89 ± 0.06 | 0.88 ± 0.06 | 0.95 ± 0.08 | 0.96 ± 0.08 | 1.14 ± 0.06 | 1.14 ± 0.06 |
| BMI | 27.3 ± 3.5 | 25.2 ± 4.0 |
| **40–49 years** | | | | | | |
| **Men** | **Women** | **Men** | **Women** | **Men** | **Women** |
| Workload (Watts) | 106.2 ± 21.5 | 74.2 ± 15.1 | 123.0 ± 21.8 | 87.7 ± 16.0 | 187.5 ± 32.9 | 124.2 ± 22.5 |
| f_{a} (beats-min^{-1}) | 144 ± 18 | 151 ± 16 | 157 ± 18 | 163 ± 15 | 183 ± 12 | 182 ± 11 |
| %f_{peak} | 78.6 ± 7.7 | 83.1 ± 7.1 | 85.7 ± 7.3 | 90.0 ± 6.0 |
| Workload (Watts) | %VO₂peak | f_b (1-min⁻¹) | V_e (L-min⁻¹) | V_T (V_e-f_b) | VCO₂ (L-min⁻¹) | VO₂ (L-min⁻¹) | R (CO₂-VO₂⁻) | BMI | %VO₂peak | f_b (1-min⁻¹) | V_e (L-min⁻¹) | V_T (V_e-f_b) | VCO₂ (L-min⁻¹) | VO₂ (L-min⁻¹) | R (CO₂-VO₂⁻) | BMI |
|----------------|------------|----------------|---------------|--------------|----------------|---------------|----------------|-----|------------|----------------|---------------|--------------|----------------|----------------|---------------|----------------|-----|
| 50–59 years    |            |                |               |              |                |               |                |     |           |                |               |              |                |                |               |                |     |
| (n=246)        | (n=267)    | (n=227)        | (n=230)       | (n=441)      | (n=444)        |               |                |     |           |                |               |              |                |                |               |                |     |
| Workload (Watts) |            |                |               |              |                |               |                |     |           |                |               |              |                |                |               |                |     |
| Men            | Women      | Men            | Women         | Men          | Women         |                |                |     |           |                |               |              |                |                |               |                |     |
| 60–69 years    |            |                |               |              |                |               |                |     |           |                |               |              |                |                |               |                |     |
| (n=203)        | (n=167)    | (n=186)        | (n=144)       | (n=313)      | (n=284)       |               |                |     |           |                |               |              |                |                |               |                |     |
| Workload (Watts) |            |                |               |              |                |               |                |     |           |                |               |              |                |                |               |                |     |
| Men            | Women      | Men            | Women         | Men          | Women         |                |                |     |           |                |               |              |                |                |               |                |     |
| +70 years      |            |                |               |              |                |               |                |     |           |                |               |              |                |                |               |                |     |
| (n=66)         | (n=60)     | (n=60)         | (n=52)        | (n=103)      | (n=99)        |               |                |     |           |                |               |              |                |                |               |                |     |
| Workload (Watts) |            |                |               |              |                |               |                |     |           |                |               |              |                |                |               |                |     |
| Men            | Women      | Men            | Women         | Men          | Women         |                |                |     |           |                |               |              |                |                |               |                |     |
Respiratory compensation point (RCP)

The highest RCP was observed in the youngest age groups with roughly the same decline rate per decade as observed for $V_{\text{Than}}$ (Table 4).

Ventilatory efficiency at $VO_{2\text{peak}}$ and at $V_{\text{Than}}$

$EqVO_{2\text{peak}}$ were similar between sexes and age groups. $EqVCO_{2\text{peak}}$ was on average 1.2% ($p<0.05$) higher in women than in men. In men aged 20–59 years no differences were observed between subsequent age groups, upon which we observed a 4.4% ($p<0.001$) higher $EqVCO_{2\text{peak}}$ for men aged 60–69 years compared to those aged 50–59 years. No differences were shown between the two oldest male age groups. In women we observed no differences in $EqVCO_{2\text{peak}}$ between subsequent age groups throughout all decades. Comparing the youngest and oldest age groups an 8% ($p<0.001$) higher $EqVCO_{2\text{peak}}$ was observed in the oldest age group, in both men and women (Table 5).

$EqVO_{2\text{Than}}$ was on average 3% ($p<0.001$) higher in women than in men. $EqVO_{2\text{Than}}$ was similar and lowest in the two youngest male age groups (20–29 and 30–39 years). We observed a 5.2% ($p<0.05$) higher $EqVO_{2\text{Than}}$ for men aged 40–49 years compared to those aged 30–39 years, with no differences between the subsequently older male age groups (40–49 through +70 years). In women no differences were observed between subsequent age groups throughout all decades. When comparing the youngest and oldest age groups a 12% ($p<0.05$) higher $EqVO_{2\text{Than}}$ was observed in the oldest age group, among both men and women (Table 5).

$EqVCO_{2\text{Than}}$ was on average 2.5% ($p<0.001$) higher in women compared to men. $EqVCO_{2\text{Than}}$ was alike and lowest in the two youngest male age groups (20–29 and 30–39 years), whereas a 4.9% ($p<0.01$) higher $EqVCO_{2\text{Than}}$ was observed in men 40–49 years compared to the 30–39 years group. No differences were found between men aged 40–49 years and 50–59 years, whereupon an average 5.3% ($p<0.05$) higher $EqVCO_{2\text{Than}}$ was observed per decade between the three oldest male age groups. In women aged 20–69 years no differences in $EqVCO_{2\text{Than}}$ was observed between subsequent age groups, upon which a 5.4% ($p<0.05$)

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Table 2. Cont.

|                  | Level 1 ($<V_{\text{Than}}$) | Level 2 ($<RCP$) | Peak       |
|------------------|------------------------------|------------------|------------|
|                  | Men                          | Women            | Men        | Women            | Men        | Women            |
| $VCO_2$ (L·min$^{-1}$) | 1.64 ± 0.43                  | 1.19 ± 0.25      | 1.92 ± 0.50 | 1.38 ± 0.32      | 2.90 ± 0.67 | 1.89 ± 0.42      |
| $VO_2$ (L·min$^{-1}$)   | 1.91 ± 0.44                  | 1.39 ± 0.29      | 2.14 ± 0.50 | 1.52 ± 0.32      | 2.71 ± 0.56 | 1.80 ± 0.36      |
| $R$ ($CO_2/VO_2$)        | 0.88 ± 0.06                  | 0.88 ± 0.06      | 0.92 ± 0.06 | 0.93 ± 0.08      | 1.06 ± 0.08 | 1.04 ± 0.07      |
| BMI                  | 26.0 ± 2.7                   | 26.2 ± 3.9       |            |                  |            |                  |

Data are presented as arithmetic mean ± SD. Workload: treadmill exercise load, fc: cardiac frequency, fB: breathing frequency, VE: minute ventilation, VT: tidal volume, $VCO_2$: expired carbon dioxide, $VO_2$: oxygen uptake, $R$: respiratory exchange ratio, BMI: body mass index, $V_{\text{Than}}$: ventilatory anaerobic threshold, $RCP$: respiratory compensation point.

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higher EqVCO\textsubscript{2 Than} was observed in the oldest age group compared to those 60–69 years. Comparing the youngest and the oldest age groups showed a 16% (p<0.001) higher EqVCO\textsubscript{2 Than} in the oldest group, in both men and women (Table 5).

EqVCO\textsubscript{2 Than}, among the 3 oldest age groups, stratified by fitness quartiles

In those aged 50–59 years there was a 7.2% (p<0.05) and 8.2% (p<0.001) increase between the most fit (Q\textsubscript{1}) and least fit (Q\textsubscript{4}), men and women, respectively. The middle (60–69 years) and the most senior groups (+70 years) had increases of 13.4% (p<0.001; men) vs. 13.1% (p<0.001; women), and 16.4% (p<0.01; men) with no significant differences among women, between the fittest (Q\textsubscript{1}) and least fit (Q\textsubscript{4}), respectively (Table 6).
Estimating key cardio pulmonary parameters from non-exercise prediction models

Prediction equations for $V_{\text{Epeak}}$, $VCO_2\text{peak}$ and $V_{\text{Than}}$ were derived from non-exercise variables, including weight, height, age and sex. Weight and age proved negligible in predicting $VT_{\text{peak}}$, as did weight and height in predicting $EqVCO_2V_{\text{Than}}$ and $EqVO_2V_{\text{Than}}$, hence these variables were excluded from the respective models. For all models gender should be substituted with 1 or 2 for men and women, respectively. The final regression models are presented in table 7. Non-exercise prediction models for VO$_2\text{peak}$ are previously published from the HUNT 3 fitness material [33].

Association between $EqVCO_2V_{\text{Than}}$ and age

Figure 1 displays the relationship between $EqVCO_2V_{\text{Than}}$ and age, with relative low, but statistical strong correlations $r=0.27$ ($p<0.0001$) and $r=0.18$ ($p<0.001$) among men and women, respectively.

Table 4. Cardiorespiratory variables in the HUNT 3 Fitness study stratified by sex, age groups.

|                | N   | VO$_{2\text{peak}}$ (L·min$^{-1}$) | VO$_{2\text{peak}}$ (mL·kg·min$^{-1}$) | $V_{\text{Than}}$ (L·min$^{-1}$) | $V_{\text{Than}}$ (%VO$_{2\text{peak}}$) | RCP (L·min$^{-1}$) | RCP (%VO$_{2\text{peak}}$) |
|----------------|-----|-----------------------------------|----------------------------------------|---------------------------------|-------------------------------|------------------|------------------|
| **All**        |     |                                   |                                        |                                 |                               |                  |                  |
| Men            | 1050| 3.74 ± 0.76                       | 44.2 ± 9.3                             | 2.83 ± 0.67                     | 76.4 ± 10.4                   | 3.24 ± 0.71     | 86.4 ± 10.9     |
| Women          | 1013| 2.47 ± 0.51                       | 35.8 ± 7.7                             | 1.90 ± 0.43                     | 77.6 ± 9.7                    | 2.21 ± 0.50     | 89.2 ± 10.4     |
| **20–29 years**|     |                                   |                                        |                                 |                               |                  |                  |
| Men            | 101 | 4.30 ± 0.73                       | 54.0 ± 8.8                             | 3.20 ± 0.75                     | 75.2 ± 10.7                   | 3.59 ± 0.69     | 85.6 ± 10.3     |
| Women          | 92  | 2.77 ± 0.47                       | 42.8 ± 7.6                             | 2.08 ± 0.44                     | 76.7 ± 9.4                    | 2.48 ± 0.43     | 90.9 ± 8.3      |
| **30–39 years**|     |                                   |                                        |                                 |                               |                  |                  |
| Men            | 172 | 4.20 ± 0.65                       | 48.6 ± 7.9                             | 3.17 ± 0.62                     | 75.6 ± 10.3                   | 3.57 ± 0.65     | 85.4 ± 10.5     |
| Women          | 203 | 2.74 ± 0.50                       | 39.6 ± 7.0                             | 2.07 ± 0.45                     | 75.6 ± 9.8                    | 2.44 ± 0.52     | 88.9 ± 12.3     |
| **40–49 years**|     |                                   |                                        |                                 |                               |                  |                  |
| Men            | 264 | 4.00 ± 0.62                       | 46.6 ± 8.0                             | 3.04 ± 0.63                     | 76.6 ± 11.0                   | 3.44 ± 0.67     | 85.5 ± 11.0     |
| Women          | 249 | 2.62 ± 0.44                       | 37.8 ± 7.0                             | 2.02 ± 0.40                     | 77.6 ± 9.7                    | 2.36 ± 0.45     | 88.5 ± 9.9      |
| **50–59 years**|     |                                   |                                        |                                 |                               |                  |                  |
| Men            | 267 | 3.61 ± 0.60                       | 41.9 ± 7.6                             | 2.71 ± 0.53                     | 76.2 ± 10.1                   | 3.19 ± 0.62     | 86.9 ± 11.4     |
| Women          | 259 | 2.35 ± 0.38                       | 33.7 ± 5.7                             | 1.82 ± 0.36                     | 78.2 ± 9.4                    | 2.12 ± 0.42     | 89.1 ± 11.2     |
| **60–69 years**|     |                                   |                                        |                                 |                               |                  |                  |
| Men            | 182 | 3.23 ± 0.57                       | 38.4 ± 6.9                             | 2.48 ± 0.49                     | 77.5 ± 10.1                   | 2.85 ± 0.54     | 88.4 ± 10.8     |
| Women          | 152 | 2.14 ± 0.36                       | 30.5 ± 5.1                             | 1.68 ± 0.34                     | 78.9 ± 9.3                    | 1.94 ± 0.34     | 90.8 ± 8.2      |
| **70+ years**  |     |                                   |                                        |                                 |                               |                  |                  |
| Men            | 64  | 2.71 ± 0.56                       | 34.2 ± 7.1                             | 2.05 ± 0.48                     | 77.4 ± 9.8                    | 2.37 ± 0.49     | 87.4 ± 9.6      |
| Women          | 58  | 1.80 ± 0.36                       | 26.8 ± 5.1                             | 1.44 ± 0.33                     | 79.8 ± 10.7                   | 1.59 ± 0.33     | 87.3 ± 10.1     |

Data are presented as arithmetic mean ± SD. VO$_2\text{peak}$: peak oxygen uptake, VThan: Ventilatory anaerobic threshold, RCP: respiratory compensation point.

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Table 5. Ventilatory equivalents at peak exercise and at ventilatory anaerobic threshold in the HUNT 3 fitness study.

| Age Group |       | Men         |       | Women        |
|-----------|-------|-------------|-------|--------------|
|           |       | (n=207)     |       | (n=246)      |
| 20–29 years | EqVO2peak (Vepeak:VO2peak⁻¹) | 33.2±4.1 |       | 33.5±5.0     |
|           | EqVCO2peak (Vepeak:VCO2peak⁻¹) | 29.0±3.3 |       | 29.3±4.0     |
| 30–39 years | EqVO2peak (Vepeak:VO2peak⁻¹) | (n=69)   |       | (n=75)       |
|           | EqVCO2peak (Vepeak:VCO2peak⁻¹) | 25.0±2.9 |       | 26.9±4.2     |
|           | EqVO2peak (Vepeak:VO2peak⁻¹) | (n=342)  |       | (n=417)      |
|           | EqVCO2peak (Vepeak:VCO2peak⁻¹) | 26.7±2.4 |       | 28.5±3.6     |
| 40–49 years | EqVO2peak (Vepeak:VO2peak⁻¹) | (n=593)  |       | (n=604)      |
|           | EqVCO2peak (Vepeak:VCO2peak⁻¹) | 33.2±4.4 |       | 33.8±4.6     |
|           | EqVO2peak (Vepeak:VO2peak⁻¹) | (n=265)  |       | (n=259)      |
|           | EqVCO2peak (Vepeak:VCO2peak⁻¹) | 29.3±3.6 |       | 29.9±3.8     |
|           | EqVO2peak (Vepeak:VO2peak⁻¹) | (n=579)  |       | (n=592)      |
|           | EqVCO2peak (Vepeak:VCO2peak⁻¹) | 26.6±3.9 |       | 27.0±3.5     |
|           | EqVO2peak (Vepeak:VO2peak⁻¹) | (n=401)  |       | (n=373)      |
|           | EqVCO2peak (Vepeak:VCO2peak⁻¹) | 33.9±5.3 |       | 33.0±5.0     |
| 50–59 years | EqVO2peak (Vepeak:VO2peak⁻¹) | (n=241)  |       | (n=245)      |
|           | EqVCO2peak (Vepeak:VCO2peak⁻¹) | 30.8±4.5 |       | 30.6±4.5     |
|           | EqVO2peak (Vepeak:VO2peak⁻¹) | (n=203)  |       | (n=158)      |
|           | EqVCO2peak (Vepeak:VCO2peak⁻¹) | 27.5±4.1 |       | 27.4±3.6     |
|           | EqVO2peak (Vepeak:VO2peak⁻¹) | (n=137)  |       | (n=134)      |
|           | EqVCO2peak (Vepeak:VCO2peak⁻¹) | 31.6±4.5 |       | 31.4±7.8     |
| 60–69 years | EqVO2peak (Vepeak:VO2peak⁻¹) | (n=69)   |       | (n=56)       |
|           | EqVCO2peak (Vepeak:VCO2peak⁻¹) | 28.6±3.9 |       | 28.5±3.9     |
|           | EqVO2peak (Vepeak:VO2peak⁻¹) | (n=137)  |       | (n=134)      |
|           | EqVCO2peak (Vepeak:VCO2peak⁻¹) | 31.3±4.0 |       | 31.0±3.0     |

Data are presented as arithmetic mean ± SD. EqVO2 and EqVCO2: ventilatory efficiency.

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Associations between $V_E$ and $VCO_2$

*Figure 2* show the relationship between $V_E$ and $VCO_2$ from start of test until $V_{Than}$, with strong correlations (men: $r=0.94$; women: $r=0.93$).

**Discussion**

This is the largest European cardio-respiratory reference material in healthy men and women aged 20–90 years. Previous papers mostly present smaller, selected age groups [15, 18, 34–40], or only male populations [23, 25, 41]. Hence, this study will serve as a useful addition to previous research.

**Sex and age group differences in peak ventilation ($V_{Epeak}$) and tidal volume ($V_{Tpeak}$)**

In this study women had approximately 34% and 32% lower $V_{Epeak}$ and $V_{Tpeak}$, respectively, and a 4% lower peak $f_{Bpeak}$ than men. This is in agreement with other population-based studies on $V_{Epeak}$ [39, 42–44], $V_{Tpeak}$ and $f_{Bpeak}$ [22, 45], and as expected as women have smaller lung size and dynamic lung function volumes than men, also after adjusting for differences in stature [46]. We observed 6–30% higher $V_{Epeak}$ among men and women compared to that seen in Brazilian [42] (n=3992), American [43] (n=988) and French [44] (n=150) populations, as well as in small sample size studies [22, 45, 47, 48]. Yet, a Norwegian study [49] (n=759) displays $V_{Epeaks}$ fairly consistent with ours. Hence, there might be population differences, which highlight the need of reference data in different populations.

Lower $V_{Epeak}$ with increasing age is consistent with findings in Brazilian [42] (n=3992), Israeli [23] (male =1424), Canadian [39] (n=100), [25] (male =816) and French [44] (n=150) studies, and in line with an age attenuation in dynamic lung function largely attributed to decreased elastic recoil [50, 51].

In this study the highest $V_{Tpeak}$ was observed among the 30–49 year groups, in both men and women, with a decrease in subsequent age groups. These findings are unexpected, since the highest $V_T$ should be in the youngest age group, with deterioration between subsequently older age groups [50, 51]. Our findings could be explained by the relative low sample size in the youngest age group. Contrary to us a Canadian [39] (n=100) and Israeli [23] (n=1424) study presented their highest $V_{Tpeak}$ in the youngest age groups (15–25 yrs). Interestingly, while the Canadian study displayed the same male average $V_{Tpeak}$ as us, they have significantly lower $V_{Epeak}$, signaling a necessarily lower $f_{Bpeak}$ (not displayed).

**Association between $V_T$ and $V_E$ below and above $V_{Than}$**

On the initial sub maximal workloads the $V_T$ vs. $V_E$ slope displays a steeper gradient than towards test termination. This is to be expected, since it is well established that $V_T$ increases steeper than $f_B$ below $V_{Than}$, whereas $f_B$ mostly accounts for the increase in $V_E$ at workloads above $V_{Than}$ [47, 52].
Sex and age group differences in VThan and RCP

We observed VThan at an average 77% of VO2peak, in both sexes, and in line with other studies (n=204–3992) [24, 40, 42, 53, 54] minor sex differences. Previous studies report VThan at significantly lower fractions (49–70% of VO2peak) [23, 24, 40, 42, 53, 54], or more consistent to that observed by us [25, 55, 56]. Differences are most likely caused by use of different methods and analyzing

### Table 6. Ventilatory efficiency and oxygen uptake presented in fitness quartiles: The HUNT 3 fitness study.

|          | Men                                                                 | Women                                                                 |
|----------|----------------------------------------------------------------------|----------------------------------------------------------------------|
|          | VEVThan×VCO2Than⁻¹ | VO2peak (mL·kg⁻¹·min⁻¹) | VEVThan×VCO2Than⁻¹ | VO2peak (mL·kg·min⁻¹) |
| 50–59 years | (n=241) |                                                                      | (n=242) |                                                                      |
|          | Q1     | 27.6±3.8                                                               | 51.8±4.3 | 28.2±2.8                                                               | 41.3±2.9 |
|          | Q2     | 27.5±2.9                                                               | 44.0±2.9 | 28.1±2.8                                                               | 35.1±1.3 |
|          | Q3     | 28.5±3.0                                                               | 39.2±1.5 | 29.1±2.5                                                               | 31.5±1.1 |
|          | Q4     | 29.6±4.4                                                               | 32.6±3.0 | 30.5±3.5                                                               | 26.8±2.4 |
| 60–69 years | (n=202) |                                                                      | (n=158) |                                                                      |
|          | Q1     | 28.4±2.6                                                               | 47.6±4.1 | 28.2±2.9                                                               | 37.1±3.0 |
|          | Q2     | 29.5±3.7                                                               | 40.2±1.4 | 29.5±3.0                                                               | 32.1±0.9 |
|          | Q3     | 29.5±3.8                                                               | 35.5±1.2 | 28.7±2.7                                                               | 28.7±1.0 |
|          | Q4     | 32.2±5.5                                                               | 30.3±3.0 | 31.9±3.9                                                               | 24.2±2.4 |
| +70 years | (n=69)  |                                                                      | (n=56)  |                                                                      |
|          | Q1     | 29.2±3.8                                                               | 43.5±4.4 | 30.1±3.0                                                               | 33.4±3.7 |
|          | Q2     | 31.0±3.1                                                               | 35.9±1.4 | 30.8±2.6                                                               | 27.9±0.9 |
|          | Q3     | 30.7±3.6                                                               | 31.4±1.4 | 30.9±2.3                                                               | 24.8±0.8 |
|          | Q4     | 34.0±4.2                                                               | 25.6±2.5 | 32.7±3.4                                                               | 20.8±2.0 |

Data are presented as arithmetic mean ± SD. VEVThan×VCO2Than⁻¹: ventilatory efficiency at ventilatory anaerobic threshold. Q1-4: quartiles of ventilatory efficiency and oxygen uptake.

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### Table 7. Multiple linear regression models for predicting key cardio respiratory variables from non-exercise variables: The HUNT 3 fitness study.

| Equations | R² | SEE |
|-----------|----|-----|
| V_{Peak} (L·min⁻¹) = 16.843 + (0.178 x weight) + (0.876 x height) − (0.762 x age) − (28.171 x gender) | 0.67 | 17.5 |
| VCO_{2Peak} (L·min⁻¹) = 1.264 + (0.012 x weight) + (0.025 x height) − (0.031 x age) − (0.981 x gender) | 0.70 | 0.59 |
| V_{Than} (L·min⁻¹ of VO2) = (0.01 x weight) + (0.016 x height) − (0.017 x age) − (0.581 x gender) +0.514 | 0.59 | 0.47 |
| V_{Tpeak} (L) = (0.032 x height) − (0.468 x gender) −2.379 | 0.64 | 0.37 |
| EqVCO_{2Than} =23.897 + (0.072 x age) + (0.826 x gender) | 0.08 | 3.47 |
| EqVO_{2Than} =23.148 + (0.050 x age) + (0.808 x gender) | 0.04 | 3.91 |

V_{Peak}: peak ventilation, VCO₂: peak expiration of carbon dioxide, VThan: ventilatory anaerobic threshold, VTpeak: peak tidal volume, EqVCO₂Than and EqVO₂Than: ventilatory efficiency at ventilatory anaerobic threshold, R²: coefficient of variation, SEE: standard error of the estimate.

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approaches applied in the different studies, which makes direct comparisons difficult [23, 25, 42, 55, 56].

In this study $V_{\text{Than}}$ was observed at $\approx 75\%$ in the youngest age groups and at $\approx 80\%$ of $\text{VO}_{2\text{peak}}$ in the oldest age groups, in both men and women, with significant differences ($p < 0.05$) between the youngest and the 60–69 year age group. Age related increase in $V_{\text{Than}}$ (as percent of $\text{VO}_{2\text{peak}}$) is reported in previous studies as well [23–25, 42, 44, 53, 54, 57]. This is to be expected since $V_{\text{Than}}$ (L·min$^{-1}$) declines at a slower rate than $\text{VO}_{2\text{peak}}$ (L·min$^{-1}$) with increasing age [58, 59], and consequently occurs at a higher percent of $\text{VO}_{2\text{max/peak}}$ [60]. This is suggested to be, at least partly, due to changes in skeletal muscle composition associated with increasing age, with the selective loss of type II fibers and therefore a relative increase in type I fibers [61]. Contrary to this Lenti and colleagues [34] report a decrease in percent $V_{\text{Than}}$ in a trained senior group ($n=16$), compared to their young trained, whereas the untrained groups are consistent with our findings ($n=16$). The small sample size taken into account, their data must be interpreted with caution.

Figure 1. Correlations between $\text{EqVCO}_{2\text{Than}}$ (ventilatory efficiency at ventilator anaerobic threshold) and age groups: The HUNT 3 fitness study.
RCP was observed at 86% and 90% of VO2peak, among men and women, respectively. This is consistent with the findings of several other studies \cite{18,35,37}. However, direct comparisons are difficult due to their small sample sizes (n=9–22) and the use of different measuring methods.

Ventilatory efficiency stratified by sex

In line with previous studies \cite{17,22} we observed similar EqVO2peak in men and women. Wasserman \cite{52} suggests that EqVCO2 should be determined at VThan or between VThan and RCP as V_e is least variable in this range. Our submaximal level 2 measurements are close to VThan and we observed slightly higher (p<0.001)
EqVCO_{2V_{Than}} in women than men, hence indicating less efficient ventilation in women. These observations are in agreement with previous studies [19, 20, 62]. Women’s lower ventilatory efficiency might be explained by differences in ventilatory stimuli (e.g. [H^+], [K^+]), metaboreceptors, and central command [63, 64].

Ventilatory efficiency at V_{Than} stratified by age groups
We observed deterioration in ventilatory efficiency, both in EqVO_{2V_{Than}} (p<0.05) and EqVCO_{2V_{Than}} (p<0.001), between the youngest and oldest age groups. This is in agreement with the findings of other studies (n=69–474) [19, 20, 57, 62]. It is presently uncertain which factors are responsible for diminished ventilatory efficiency during exercise with increasing age [65]. Clearly, increased dead space might be a major contributing factor, as well as the lung’s mechanical limitation to airflow, which deteriorate as the lung loses elastic recoil with increasing age [66]. In women evidence points to decreased leg muscle strength as a contributing factor [65]. Other suggestions are factors linked to muscle afferent excitability as a result of fiber type shifts [67], and neuromuscular alterations with growing age [68].

EqVCO_{2V_{Than}} stratified by fitness quartiles
Individuals in the three oldest age groups (50–59, 60–69, +70 years) in the present study are more likely to be referred to clinical exercise testing than younger age groups, and have been studied in more depth than other age groups when it comes to EqVCO_{2V_{Than}}. Interestingly, among individuals in these age groups approximately 25% had EqVCO_{2V_{Than}} higher than 30. EqVCO_{2V_{Than}} <30 is considered normal with a possible increase among older age groups [1]. In these age groups we observed minor differences in EqVCO_{2V_{Than}} between those that were among the three first quartiles of fitness (VO_{2peak} quartiles), whereupon we observed a significant drop in ventilatory efficiency (hence, an increase in EqVCO_{2V_{Than}}) in those categorized as being least fit (Q_4) in both sexes and all three age groups. All fitness quartiles in the oldest age group (+70 years), and the least fit quartiles in the two younger age groups (50–59, 60–69 years) had EqVCO_{2V_{Than}} ≈>30, which could be caused by high dead space ventilation due to diminished alveoli perfusion [19]. More importantly, diminished ventilatory efficiency can reflect disease severity and prognosis in several patient groups including chronic obstructive pulmonary disease, pulmonary arterial hypertension, hypertrophic cardiomyopathy and interstitial lung disease [1, 15], and are displayed in the range 41–60 in more severe cases of congestive heart failure [15]. Although we cannot totally exclude the possibility of unknown diseases in some of our participants, the self-report and medical interview, adhering to our inclusion criteria, provides a healthy population. Therefore seen in context of our sample size our findings may represent normal ventilatory efficiency values for the oldest age groups and least fit population.
Non-exercise prediction models for key cardio-respiratory variables

There is a plethora of $VO_{2\text{peak}}$ prediction models. However, models on other key cardio-respiratory variables are less abundant. The accuracy of previously published models on $VO_{2\text{peak}}$ from the HUNT 3 fitness data (Men: 12.8%, Women: 14.3%) \cite{33} is in fair agreement with previous large sample studies (Jurca 2005). Smaller sample studies \cite{69–71} with uniform populations \cite{72,73} show accuracies in the range ±7–17%. Also $V_{\text{Than}}$ accuracy (±19.9%) is approximately the same compared to 7 previous small-scale studies \cite{40}. Our precision of $V_{\text{Epeak}}$ prediction (±17.2%) is in agreement with a large study of males \cite{23}, contrasted by a small study \cite{39} showing 28% accuracy. However, it was hard to compare our $V_{\text{Tpeak}}$ accuracy (±15.5%) with others \cite{23}, since key data was not presented. The 12.1% accuracy in predicting $EqVCO_{2\text{VThan}}$ was similar to a small sample study \cite{62}. Our prediction models will provide a rough estimation of these key variables, regardless of gender and age. Moreover, the models use non-exercise variables that are easy to measure, thus making these models easy to use in both clinical settings and for recreational athletes.

Association between ventilatory efficiency and workload

The slope of the ventilatory equivalent for oxygen ($EqVO_{2\cdot W^{-1}}$) increases with rising workload (w), which demonstrates reduced ventilatory efficiency as the workload increases. This is supported by two former case studies \cite{30,52}. More interestingly the $EqVCO_{2\cdot W^{-1}}$ displays a gradient close to zero, which indicates a constant ventilatory efficiency throughout the incremental workload, and is in fair agreement with Wasserman and colleagues \cite{52}, yet, contradicted by another study \cite{30} that presents an increase in $EqVCO_{2}$ as the workload approaches peak. However, it is noteworthy that these studies are based on single case observations, and thus difficult to compare with our findings.

Strengths and limitations

The large sample size, inclusion of men and women, wide age distribution and cardio-respiratory measurements up to the true $VO_{2\text{max}}$ makes this study robust. The lack of spirometry data limits the assessment of ventilatory parameters. Also this study may be subject to bias due to self-selection caused by the low participation rate. However, almost all those invited to the current Fitness study from the large HUNT study agreed to participate in the fitness test. Due to limited capacity at the test sites resulting in long waiting lines, some potential participants chose to withdraw their participation from the study. Those who finally participated in the study could thus be healthier than those who quit or declined participation. However, a comparison of the participants in the fitness study with a healthy sample of the total HUNT population (i.e. free from cardiovascular or pulmonary diseases, cancer, or sarcoidosis) confirmed that the fitness participants did not considerably differ from other healthy HUNT participants \cite{26}. 
Conclusions

The selection of key cardio-respiratory variables combined with an age and sex stratified large sample size makes this material unique. The inconsistencies between this and earlier research, and the scarce availability of large sample size materials support the usefulness of a large reference material as presented in this study. The HUNT 3 Fitness study presents the largest European reference material of cardio-respiratory variables in healthy men and women aged 20–90 years. Our material establishes normal values for, and associations between, as well as providing prediction models for these key cardio-respiratory parameters.

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Author Contributions

Conceived and designed the experiments: UW. Performed the experiments: UW. Analyzed the data: HL SS UW. Contributed reagents/materials/analysis tools: HL SS UW. Wrote the paper: HL SS UW. Contributed substantially to design, analysis and interpretation of data, final approval of manuscript and was accountable for all aspects of the work: HL SS UW. Drafted manuscript: HL. Critical revision of manuscript for important intellectual content: SS UW. Conception and acquisition of work: UW.

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