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Data Availability Statement: Due to ethical restrictions involving patient consent, third party data used from the HUNT Study in research projects will when reasonably requested by others be made available on request to the HUNT Data Access Committee (hunt@medisin.ntnu.no). The HUNT data access information (available here: http://www.ntnu. edu/hunt/data) describes in detail the policy regarding data availability.

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# Predicting VO<sub>2peak</sub> from Submaximal- and Peak Exercise Models: The HUNT 3 Fitness Study, Norway

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## Abstract

## Purpose

Peak oxygen uptake (VO<sub>2peak</sub>) is seldom assessed in health care settings although being inversely linked to cardiovascular risk and all-cause mortality. The aim of this study was to develop  $VO_{2peak}$  prediction models for men and women based on directly measured  $VO_{2peak}$  from a large healthy population

## Methods

VO<sub>2peak</sub> prediction models based on submaximal- and peak performance treadmill work were derived from multiple regression analysis. 4637 healthy men and women aged 20–90 years were included. Data splitting was used to generate validation and cross-validation samples.

## Results

The accuracy for the peak performance models were 10.5% (SEE =  $4.63 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ) and 11.5% (SEE =  $4.11 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ) for men and women, respectively, with 75% and 72% of the variance explained. For the submaximal performance models accuracy were 14.1% (SEE =  $6.24 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ) and 14.4% (SEE =  $5.17 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ) for men and women, respectively, with 55% and 56% of the variance explained. The validation and cross-validation samples displayed SEE and variance explained in agreement with the total sample. Cross-classification between measured and predicted VO<sub>2peak</sub> accurately classified 91% of the participants within the correct or nearest quintile of measured VO<sub>2peak</sub>.

## Conclusion

Judicious use of the exercise prediction models presented in this study offers valuable information in providing a fairly accurate assessment of VO<sub>2peak</sub>, which may be beneficial for risk stratification in health care settings.



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## Introduction

Peak oxygen uptake (VO<sub>2peak</sub>) is widely referred to as cardiorespiratory fitness (CRF) [1], and is inversely linked to cardiovascular disease, hypertension, certain cancers, metabolic syndrome [2,3], and all-cause mortality [4]. At present there is no consensus identifying a precise threshold of cardiorespiratory fitness to be associated with increased cardiovascular risks. However, values below 8 METs and 6 METSs in healthy men and women, respectively, are linked with higher all-cause mortality and adverse cardiovascular effects [4]. Additionally, data suggest that MET levels > 9 and > 7 (vs. lower MET levels) among men and women, respectively, is associated with a mortality risk reduction of  $\geq$  50% over an average 8 years follow-up [5]. Despite being an essential health indicator, VO<sub>2peak</sub> is rarely assessed in health care settings [5,6], likely because direct gas analysis measurements of VO<sub>2peak</sub> is expensive, necessitate the use of advanced equipment, and trained personnel [2]. However, reliable and valid prediction models should be considered as several studies have shown that either directly measured or estimated VO<sub>2peak</sub> enhance CVD-mortality prediction beyond traditional risk factors [7,8].

Although a maximal test is considered a safe practice, complications and adverse effects occur, normally linked to underlying disease [9]. Consequently, health care personnel should monitor when testing individuals at high risk.

There exist several VO<sub>2peak</sub> prediction models in the literature. Common limitations in these models are the use of uniform age samples [10–12], only one-gender represented [13–17], as well as models being based on subjects with homogenous cardiorespiratory fitness levels [10,12,13,15,18]. Hence, they yield fair VO<sub>2peak</sub> predictions only in subjects similar to those used in generating the model [2,19].

Therefore, the aim of the present study was to develop  $VO_{2peak}$  prediction models from both submaximal- and peak treadmill performance, on the basis of data from a large healthy population of both men and women 20–90 years, with a great diversity in measured  $VO_{2peak}$ . If these models show fair predictive accuracy they will provide a safe and feasible method for estimating  $VO_{2peak}$  for a wide variety of people.

## Methods

## Study sample

In 2006–2008, the total population above 20 years of age in Nord-Trøndelag county, in Norway, were invited to the third wave of the HUNT study (HUNT 3). Out of a total population of 94194, 54% accepted the invitation (n = 50821). A sub-study (The HUNT Fitness Study) invited healthy subjects (without cardiovascular disease, cancer, pulmonary disease and use of blood pressure medication) in three pre-selected municipalities within the county, to perform treadmill testing with direct measurement of maximal oxygen uptake ( $VO_{2max}$ ). Out of 12609 potential eligible participants, 5633 appeared, and 1003 failed to complete the cardiopulmonary exercise test (CPET), withdrew or were excluded for medical reasons detected during medical interview. 4637 participants completed the exercise testing.

## Ethics statement

The study was approved by REK- Regional Committees for Medical and Health Research Ethics (2013/1788/REK nord), the Norwegian Data Inspectorate and the National Directorate of Health. The study was conducted in conformity with the Declaration of Helsinki and all participants signed a document of informed consent.

## Exercise test procedures

A 10-minute warm-up was implemented with workload individualized to induce some sweat, moderately augmented heart rate and breathing, but devoid of exhaustion. Subsequent the warm-up subjects entered the treadmill used for testing (DK7830; DK City, Taichung, Taiwan) and were equipped with a heart rate monitor (Polar S610 or RS400; Polar, Kempele, Finland) and face mask (Hans Rudolph; Shawnee, KS). Subjects were instructed to avoid handrail grasp. Cardiorespiratory variables were measured continuously using ergospirometry (MetaMax II; Cortex Biophysik GmbH, Leipzip, Germany) connected to computer software (Cortex Meta-Soft, version 1.11.5). A graded individualized treadmill protocol, starting with the warm-up workload, was used with subjects walking or running at gradually increased speed and/or inclination. Treadmill speed was increased  $(0.5-1.0 \text{ km}\cdot\text{h}^{-1})$  when VO<sub>2</sub> uptake measurements remained stable > 30 s, keeping a fixed inclination if possible. Test was terminated when subject reached volitional exhaustion (e.g. leg fatigue and shortness of breath), preferably within 8-12 minutes (Table 1). VO<sub>2max</sub> was taken as the mean of the three successive highest 10-s  $VO_2$  values and defined by a leveling off of  $VO_2$  (<2 mL·kg<sup>-1</sup>·min<sup>-1</sup> change over the span of these successive measurements) despite increasing speed and/or inclination, in combination with a respiratory exchange ratio (R) above 1.05 and subjective volitional exhaustion (e.g. leg fatigue and shortness of breath). Since a total of 17.6% of the subjects failed to reach all the criteria, the term VO<sub>2peak</sub> was used. During the incremental test most subjects had their steady-state  $VO_2$  measured at one (n = 2827) or two (n = 2576) submaximal levels. At the first submaximal level (VO<sub>2</sub> < ventilatory anaerobic threshold (established by V-slope)) steady-state VO2 was attained from each subject after 3 minutes. Measurements at this level were used to develop the submaximal models. At each level, as well as at peak performance, treadmill-velocity and inclination in addition to heart rate were also registered. Velocities in the range 5.9-8.0  $\text{km}\cdot\text{h}^{-1}$  typically represents the transition from walking to running, with individual variation attributed differences in e.g. stride length, leg length and body-size [20-22]. Test velocities used in development of the VO2peak prediction models suggest that most participants (92%) walked during the first submaximal measurement, whereas approximately 80% were running during peak measurements. An average of 87% of all participants used 10% treadmill inclination during both the first submaximal and the peak measurements. For development of the submaximal performance models peak heart rates ( $HR_{peak}$ ) were predicted from age in two gender specific linear regression models based on the HUNT 3 fitness data (men: HR<sub>peak</sub> = 215.336–0.73 x age,

#### Table 1. Test protocol for using the VO<sub>2peak</sub> prediction models derived from treadmill work.

Submaximal performance model*	Peak performance model**
Warm-up: 10-minutes with individualized work heart rate and breathing, but devoid of exhaust	load that induces some sweat, moderately increased stion. Do not grab handrails if not necessary***.
Continue for 3 minutes on the established warm-up workload	Use warm-up settings (velocity and inclination) as initia workload for the 3 first minutes. Then increase velocity (0.5–1.0 km·h <sup>-1</sup> ) or inclination*** approximately every minute.(Anticipated test duration: 8–12 minutes)
Record HR <sub>submax</sub> , velocity and inclination after 3 minutes and use for prediction	Record velocity and inclination subsequent last workload endured > 30 seconds and use for prediction
	Walk for 5 minutes at a low workload to reduce heart rate and allow removal of accumulated lactate.
	Submaximal performance model* Warm-up: 10-minutes with individualized work heart rate and breathing, but devoid of exhaus Continue for 3 minutes on the established warm-up workload Record HR <sub>submax</sub> , velocity and inclination after 3 minutes and use for prediction

\*Approximately 92% walked during the submaximal measurements

\*\*Approximately 80% ran during peak measurements; anticipated test duration 8-12 minutes

\*\*\*87% used 10% inclination as fixed slope angle during both submaximal and peak tests

 $R^2 = 0.40$ , SEE = 12.25 and women:  $HR_{peak} = 2$  12.497–0.702 x age,  $R^2 = 0.40$ , SEE = 11.71) and integrated into the fraction peak heart rate variable (Fraction peakHR:  $HR_{submax}/215.336$ –0.73 x age (men);  $HR_{submax}/212.497$ –0.702 x age (women)). All tests were performed by trained personnel and test equipment were routinely calibrated with volume ventilation calibrated every third test and gas calibrated every fifth test. Height was measured in centimeters with one decimal, and weight in kilograms with one decimal by internally standardized procedures.

## Statistical analysis

Descriptive statistics are given as mean and standard deviation for men and women, respectively. Potential variables were chosen on the basis of correlation with measured VO<sub>2peak</sub> in previous literature, and entered subsequently in a hierarchical linear regression model. All the retained variables (Treadmill inclination and velocity, weight, age and Fraction HR<sub>peak</sub>) made a considerable influence on total model fit. The models were checked for normality and homoscedasticity of residuals and these assumptions were satisfied. All models presented in this paper were derived from the total sample. Internal cross-validation was checked by data-splitting procedures, i.e. SPSS randomly selected approximately 50% of all cases, here denoted validation sample, with the remaining cases denoted cross-validation sample. In these subsets linear regression analysis were performed on the validation sample and applied to predict VO<sub>2peak</sub> in both the validation- and the cross-validation samples. Model fit was evaluated by squared multiple regression coefficients  $(R^2)$  and standard errors of the estimate (SEE).  $R^2$  and R<sup>2</sup> adjusted increased similarly for each new independent variable added to the models. R<sup>2</sup> and  $R^2$  adjusted were either identical or differed in the third decimal place, showing that both had almost identical impact on the outcome variable. As a result  $R^2$  was chosen throughout this paper. To be able to compare the model precision to models derived from external samples we also calculated the % SEE which refers to the percentage of the measured mean VO<sub>2peak</sub> within which the estimates generally fall. In the total sample, as well as subgroups of age, VO<sub>2peak</sub> and treadmill velocity, we calculated constant error (CE) and total error (TE) for the model. CE represents the mean difference between measured and predicted values ( $\Sigma$  (measured-predicted)/n), while TE represents the squared mean differences ( $\sqrt{\Sigma}$  (measured-predicted)<sup>2</sup>/n). Pearson correlation and variance explained between measured and predicted VO<sub>2peak</sub> were used to examine potential shrinkage between validation and cross-validation samples. Further internal validation was done by cross-classifying subjects into quintiles of measured and predicted VO<sub>2peak</sub>. Measures of rank correlation and agreement were tested by use of Kendall 'Tau and Cohens' Kappa statistics. Two-sided Paired Samples T-test was used to establish differences between measured and predicted VO<sub>2peak</sub>. Statistical analyses were performed with SPSS 20.0 (Statistical package for social sciences, Chicago, IL, USA).

## Results

Descriptive characteristics are presented in <u>Table 2</u>. Descriptive data in the validation and cross-validation samples were equally distributed (<u>Table 3</u>). Additional descriptive data of the HUNT 3 fitness population are displayed in a previous study [23].

## Predicting VO<sub>2peak</sub> from peak treadmill performance

Peak treadmill inclination and velocity accounted for most of the variance explained by the  $VO_{2peak}$  prediction model (men:  $R^2 = 0.72$ , p<0.001; women:  $R^2 = 0.68$ , p<0.001), with velocity being the paramount factor. Modest influence were seen from weight and age, and the total explained variance for the peak performance prediction model was  $R^2 = 0.75$  (p<0.001) in men and  $R^2 = 0.72$  (p<0.001) in women. Including resting heart rate and peak heart rate into

	All	Men	Women
	(n = 4637)	(n = 2266)	(n = 2371)
Age (yr.)	49 ± 14	50 ± 14	49 ± 14
Physical data			
Height (cm)	172.0 ± 9.1	179.2 ± 6.5	165.7 ± 6.0
Weight (kg)	77.4 ± 13.9	85.6 ± 11.6	70.1 ± 11.6
Physiological data			
VO <sub>2peak</sub> (L⋅min <sup>-1</sup> )	3.10 ± 0.91	3.75 ± 0.76	2.47 ± 0.50
VO <sub>2peak</sub> (mL·kg <sup>-1</sup> ·min <sup>-1</sup> )	40.0 ± 9.5	44.3 ± 9.3	35.9 ± 7.8
$R (VCO_2 \cdot VO_2^{-1})$	1.12 ± 0.07	1.13 ± 0.07	1.12 ± 0.07
HR <sub>peak</sub> (beats⋅min <sup>-1</sup> )	179 ± 15	180 ± 16	179 ± 15
RHR (beats·min <sup>-1</sup> )	59 ± 10	58 ± 9	61 ± 10

#### Table 2. Descriptive data: The HUNT 3 fitness study.

Data are presented as arithmetic mean ± SD. VO<sub>2peak</sub>: peak oxygen uptake; HR<sub>peak</sub>: peak heart rate; RHR: resting heart rate.

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the model did not contribute considerable changes in R<sup>2</sup> and SEE and were thus excluded from the models. A strong correlation was demonstrated between the predicted- and measured  $VO_{2peak}$  (men: r = 0.87; women: r = 0.85) (Fig 1). Two gender specific  $VO_{2peak}$  prediction equations were derived from multiple linear regression using the total sample, male:  $VO_{2peak} = 24.24 + (0.599 \text{ x treadmill inclination in \%}) + (3.197 \text{ x treadmill velocity in km} \cdot h^{-1}) - (0.122 \text{ x body weight in kilos}) - (0.126 \text{ x age in years}); women: <math>VO_{2peak} = 17.21 + (0.582 \text{ x treadmill inclination in percent}) + (3.317 \text{ x treadmill velocity in km} \cdot h^{-1}) - (0.116 \text{ x weight in kilos}) - (0.099 \text{ x age in years}) (Tables 4, 5 and 6).$ 

## Cross-validation of the peak performance prediction model

The Coefficient of determination ( $R^2$ ) remained stable between the total sample (0.75 and 0.72) and the validation sample (0.76 and 0.72) among both men and women, respectively (Tables 5 and 7), thus suggesting an internally robust prediction model. Also, there were non-significant differences between measured and predicted VO<sub>2peak</sub>, and we display CE values close to zero,

#### Table 3. Descriptive data for the male and female validation and cross-validation sample: The HUNT 3 fitness study.

	Validatio	n sample	Cross-valida	ation sample
	Men	Women	Men	Women
	(n = 1105)	(n = 1199)	(n = 1161)	(n = 1172)
Age (yr.)	50 ± 14	49 ± 14	50 ± 14	49 ± 14
Physical data				
Height (cm)	179.1 ± 6.5	165.6 ± 6.1	179.2 ± 6.5	165.8 ± 5.9
Weight (kg)	85.4 ± 11.7	69.8 ± 11.1	85.7 ± 11.5	70.5 ± 12.0
Physiological data				
VO <sub>2peak</sub> (L⋅min <sup>-1</sup> )	3.75 ± 0.77	2.47 ± 0.51	3.75 ± 0.75	2.48 ± 0.50
VO <sub>2peak</sub> (mL·kg <sup>-1</sup> ·min <sup>-1</sup> )	44.4 ± 9.3	36.0 ± 7.9	44.3 ± 9.2	35.9 ± 7.6
$R(VCO_2 \cdot VO_2^{-1})$	1.13 ± 0.07	$1.12 \pm 0.08$	1.13 ± 0.07	1.12 ± 0.07
HR <sub>peak</sub> (beats⋅min <sup>-1</sup> )	180 ± 16	178 ± 15	180 ± 16	180 ± 15
RHR (beats·min <sup>-1</sup> )	58 ± 9	61 ± 10	58 ± 10	61 ± 10

Data are presented as arithmetic mean ± SD. VO<sub>2peak</sub>: peak oxygen uptake; HR<sub>peak</sub>: peak heart rate; RHR: resting heart rate.





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in the total sample (- 0.03 and 0.02), validation sample (- 0.03 and - 0.03) and cross-validation sample (- 0.21 and - 0.04) in both men and women, respectively (Tables <u>8-10</u>), signifying a valid prediction of the mean VO<sub>2peak</sub> without systematical over- or under prediction, respectively. Our prediction models continue to be stable when stratified into subgroups of age and treadmill velocity (non-significant differences between measured and predicted VO<sub>2peak</sub>). However, when divided into VO<sub>2peak</sub> subgroups the least fit participants (<35 mL·kg<sup>-1</sup>·min<sup>-1</sup> for men and <30 mL·kg<sup>-1</sup>·min<sup>-1</sup> for women) tended to be overestimated (men: p<0.001; women: p<0.001), and the most fit participants (>50 mL·kg<sup>-1</sup>·min<sup>-1</sup> for men and >40 mL·kg<sup>-1</sup>·min<sup>-1</sup> for women) tended to be underestimated (men: p<0.001; women: p<0.001).



		Men		Women				
	β	Standardized β	Pearson Correlation	β	Standardized β	Pearson Correlation		
Intercept	24.24			17.21				
Inclination	0.599	0.084	-0.260	0.582	0.130	-0.286		
Velocity	3.197	0.729	0.842	3.317	0.717	0.818		
Weight	-0.122	-0.152	-0.346	-0.116	-0.168	-0.410		
Age	-0.126	-0.185	-0.572	-0.099	-0.175	-0.574		
R	0.866			0.848				
R <sup>2</sup>	0.750			0.719				
SEE	4.63			4.11				

#### Table 4. Multiple linear regression coefficients for predicting $VO_{2peak}$ (mL·kg<sup>-1</sup>·min<sup>-1</sup>) from peak measurements in total sample.

R: multiple regression coefficient; R<sup>2</sup>: coefficient of determination; SEE: standard error of estimate, Inclination (%), Velocity (km·h<sup>-1</sup>), Weight (kg), Age (yr.).

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This is in agreement with the validation and cross-validation samples. The least fit men and women showed CE values of – 3.50 and – 2.60 vs. most fit 2.73 and 2.81, respectively, with corresponding TE values of 5.01 and 4.35 vs. 5.27 and 4.80, with similar tendencies in validation and cross-validation samples. In the medium fit participants (VO<sub>2peak</sub> between 35 and 50 mL·kg<sup>-1</sup>·min<sup>-1</sup> for men and between 30 and 40 mL·kg<sup>-1</sup>·min<sup>-1</sup> for women) the model appears to predict VO<sub>2peak</sub> fairly well (men: p<0.05; women: p<0.001), with CE values in men and women of – 0.28 and – 0.37, respectively. The same tendencies are shown in the validation and cross-validation samples (Tables <u>8–10</u>). Pearson correlation showed minimal shrinkage between validation- sample (men: r = 0.870, R<sup>2</sup> = 0.757, p < 0.01; women: r = 0.846, R<sup>2</sup> = 0.716, p < 0.01) and cross-validation sample (men: r = 0.863, R<sup>2</sup> = 0.745, p = 0.01; women: r = 0.850, R<sup>2</sup> = 0.723, p < 0.01). Thus, the entire sample was used in development of the models.

# Cross-classification of participants in the peak performance prediction model

The models managed to categorize participants fairly accurately into the correct measured  $VO_{2peak}$  group when cross-classifying participants into quintiles of measured and predicted  $VO_{2peak}$  (Table 11). In total, 75.3% and 77.6% of the men and women, predicted to be in the lowest quintile, were classified correctly into the lowest measured quintile, respectively, while 95.4% and 96.7% were correctly classified within the correct or closest measured quintile.



		Men							Women				
	R	R <sup>2</sup>	ΔR <sup>2</sup>	р	SEE	%SEE	R	R <sup>2</sup>	ΔR <sup>2</sup>	р	SEE	%SEE	
Inclination	0.26	0.07	_		8.94	20.2	0.29	0.08	_		7.43	20.7	
Inclination, Velocity	0.85	0.72	0.65	<0.001	4.94	11.2	0.83	0.68	0.60	<0.001	4.38	12.2	
Inclination, Velocity, Weight	0.85	0.73	0.01	<0.001	4.83	10.9	0.84	0.70	0.02	<0.001	4.25	11.8	
Inclination, Velocity, Weight, Age	0.87	0.75	0.02	<0.001	4.63	10.5	0.85	0.72	0.02	<0.001	4.11	11.5	

R: multiple regression coefficient; R<sup>2</sup>: coefficient of determination; SEE: standard error of estimate; p: level of significance, Inclination (%), Velocity (km·h<sup>-1</sup>), Weight (kg), Age (yr.).

	Table 6. VO	<sub>peak</sub> prediction models based on p	beak (P) and submaximal (S) treadm	ill performance in men and women.
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Equations	Velocity (Range)	Inclination (Range)	R <sup>2</sup>	SEE (%)
Men				
VO <sub>2peak</sub> (P) = 24.24 + (0.599 x inclination) + (3.197 x velocity)–(0.122 x weight)–(0.126 x age)	9.6 ± 2.1 (3.5– 17.0)	10.3 ± 1.3 (0–15)	0.75	10.5
VO <sub>2peak</sub> (S) = 35.25 + (1.276 x inclination) + (6.402 x velocity)–(0.196 x weight)–(27.615 x test heart rate/215.336–0.73 x age)	5.6 ± 1.0 (2.5– 12.0)	9.7 ± 1.3 (0–10)	0.55	14.1
Women				
VO <sub>2peak</sub> (P) = 17.21 + (0.582 x inclination) + (3.317 x velocity)–(0.116 x weight)–(0.099 x age)	7.6 ± 1.7 (2.5– 14.0)	10.7 ± 1.7 (0–16)	0.72	11.5
VO <sub>2peak</sub> (S) = 23.77 + (1.205 x inclination) + (6.051 x velocity)–(0.16 x weight)–(20.671 x test heart rate/212.497–0.702 x age)	5.0 ± 0.8 (2.0– 8.0)	9.3 ± 1.8 (0–15)	0.56	14.4

VO<sub>2peak</sub>: peak oxygen uptake, velocity (km·h<sup>-1</sup>) and inclination (%) are presented as arithmetic mean ± SD, Range (minimum-maximum), age (yr.), weight (kg), R<sup>2</sup>: coefficient of determination, SEE: standard error of estimate.

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77.4% and 78.0% of the men and women, predicted to be in the highest quintile, were correctly classified into the highest measured quintile, respectively, with 95.8% and 95.9% being classified correctly into one of the two highest quintiles (Table 11). The rank correlation between measured and predicted quintiles were 0.74 and 0.70 in men and women, respectively, while measure of agreement by Kappa statistic was 0.45 in men and 0.41 in women.

## Predicting VO<sub>2peak</sub> from submaximal treadmill performance

Treadmill inclination and velocity accounted for the major part of the explained variance in predicting VO<sub>2peak</sub> (men:  $R^2 = 0.40$ , p<0.001; women:  $R^2 = 0.43$ , p<0.001), with velocity being the most important variable (men:  $R^2 = 0.35$ , p<0.001; women:  $R^2 = 0.34$ , p<0.001). Weight (men:  $R^2 = 0.06$ , p<0.001; women:  $R^2 = 0.34$ , p<0.001). Weight (men:  $R^2 = 0.06$ , p<0.001) and fraction peakHR (HR<sub>submax</sub> and age, men:  $R^2 = 0.09$ , p<0.001; women:  $R^2 = 0.06$ , p<0.001) accounted for a lesser but considerable part of the total variance (men:  $R^2 = 0.55$ , p<0.001; women:  $R^2 = 0.56$ , p<0.001). Resting heart rate yielded negligible changes in  $R^2$  and SEE and hence excluded from the prediction model. A high correlation (r = 0.75) was observed between predicted- and measured VO<sub>2peak</sub> among men and women (Fig 1). The final regression models derived from total sample were  $35.25 + (1.276 \text{ x treadmill inclination in \%}) + (6.402 \text{ x velocity in km·h<sup>-1</sup>})-(0.196 \text{ x weight in kilos})-(27.615 \text{ x HR}_{submax}/215.336-0.73 \text{ x age in years}) for men and <math>23.77 + (1.205 \text{ x treadmill inclination in \%}) + (6.051 \text{ x velocity in km·h<sup>-1</sup>})-(0.160 \text{ x weight in kilos})-(20.671 \text{ x HR}_{submax}/212.497-0.702 \text{ x age in years}) for women (Tables <u>6, 12</u> and <u>13</u>).$ 

## Table 7. Multiple linear regression analysis for predicting VO<sub>2peak</sub> (mL·kg<sup>-1</sup>·min<sup>-1</sup>) from peak measurements in men and women, validation samples: The HUNT 3 fitness study.

		,	Validatio	n sample m	nen		Validation sample women						
	R	R <sup>2</sup>	ΔR <sup>2</sup>	р	SEE	%SEE	R	R <sup>2</sup>	ΔR <sup>2</sup>	р	SEE	%SEE	
Inclination	0.23	0.05	_		9.09	20.5	0.26	0.07	_		7.62	21.2	
Inclination, Velocity	0.85	0.73	0.68	< 0.001	4.88	11.0	0.83	0.68	0.62	< 0.001	4.45	12.4	
Inclination, Velocity, Weight	0.86	0.74	0.01	<0.001	4.78	10.8	0.84	0.70	0.02	<0.001	4.33	12.0	
Inclination, Velocity, Weight, Age	0.87	0.76	0.02	<0.001	4.61	10.4	0.85	0.72	0.02	<0.001	4.21	11.7	

R: multiple regression coefficient; R<sup>2</sup>: coefficient of determination; SEE: standard error of estimate; p: level of significance, Inclination (%), Velocity (km·h<sup>-1</sup>), Weight (kg), Age (yr.).



		М	en				Women					
	Measured VO <sub>2peak</sub>	Predicted VO <sub>2peak</sub>	CE	% SEE	% TE	N (%)	Measured VO <sub>2peak</sub>	Predicted VO <sub>2peak</sub>	CE	% SEE	% TE	N (%)
Age (yr.)												
<40	50.9 ± 8.5	51.1 ± 7.2	-0.25	9.0	9.0	550 (24.4)	41.0 ± 7.4	41.1 ± 6.0	-0.09	10.5	10.5	664 (28.0)
40-60	44.1 ± 8.1	44.0 ± 6.6	0.10	10.4	10.4	1231 (54.4)	35.6 ± 6.8	35.6 ± 5.2	0.06	11.4	11.4	1249 (52.8)
>60	37.3 ± 7.4	37.4 ± 5.7	-0.09	12.6	12.6	479 (21.2)	29.4 ± 5.4	29.4 ± 4.3	0.06	13.0	13.4	455 (19.2)
VO <sub>2peak</sub>												
<35(<30)	31.2 ± 3.2	34.7 ± 4.1	-3.50	8.6	16.1	388 (17.2)	26.4 ± 2.8	29.0 ± 4.0	-2.60	8.9	16.5	547 (23.1)
35-50 (30-40)	42.8 ± 4.2	43.0 ± 5.2	-0.28	7.7	9.7	1266 (56.0)	34.9 ± 2.9	35.2 ± 4.0	-0.37	7.0	10.1	1154 (48.7)
>50(>40)	56.0 ± 5.0	53.3 ± 5.6	2.73	6.8	9.4	607 (26.8)	45.6 ± 4.8	42.8 ± 5.0	2.81	7.7	10.5	668 (28.2)
Velocity												
<7	31.9 ± 5.3	32.1 ± 3.2	-0.17	13.1	13.1	209 (9.3)	29.3 ± 4.7	$29.2 \pm 3.4$	0.15	12.4	12.5	757 (31.9)
7-10	41.0 ± 6.2	41.0 ± 4.0	0.05	11.2	11.2	1260 (55.7)	37.9 ± 5.9	38.0 ± 3.9	-0.10	11.3	11.3	1459 (61.6)
>10	52.9 ± 6.7	53.0 ± 4.8	-0.11	9.1	9.1	792 (35.0)	50.1 ± 5.4	49.6 ± 3.2	0.47	8.9	8.9	153 (6.5)
Total	44.3 ± 9.3	44.3 ± 8.0	-0.03	10.5	10.5	2261	35.9 ± 7.8	35.9 ± 6.6	0.02	11.5	11.5	2369

#### Table 8. Measured vs. Predicted VO<sub>2peak</sub>, from peak measurements, in the total sample: The HUNT 3 fitness study.

 $VO_{2peak}$  were categorized into 3 groups from measured  $VO_{2peak}$ ; <35, 35–50, >50 (mL kg<sup>-1</sup> min<sup>-1</sup>) and <30, 30–40, >40 (mL kg<sup>-1</sup> min<sup>-1</sup>) were cutoff values for men and women, respectively; velocity: treadmill velocity (km h<sup>-1</sup>).

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## Cross-validation of the submaximal performance prediction model

 $R^2$  was stable between the total sample (0.55 and 0.56) and validation sample (0.54 and 0.56) in men and women, respectively (Tables 13 and 14), indicating a strong prediction model. Furthermore, there were non-significant differences between the measured and predicted VO<sub>2peak</sub>, and CE was close to zero in the total sample (-0.14 and -0.12), validation sample (-0.27 and - 0.03) and cross-validation sample (- 0.09 and - 0.11), among both men and women, respectively (Tables 15-17), thus suggesting a valid estimation of mean VO<sub>2peak</sub>. The submaximal prediction models are less stable when stratified into subgroups of age, VO<sub>2peak</sub> and treadmill velocity groups. There was a tendency towards underestimating VO<sub>2peak</sub> (p<0.001 and p<0.001, with CE 3.03 and 1.46 among men and women, respectively, TE 6.78 and 5.63) in the youngest subjects (<40 years), with a subsequent overestimation (p<0.001 and p<0.001, with CE-2.88 and -1.70 among men and women, respectively, TE 6.42 and 4.86) in the oldest subjects (>60 years), whereas VO<sub>2peak</sub> was predicted fairly well (non-significant difference and p<0.01, with CE-0.41 and -0.58 among men and women, respectively, TE 5.90 and 5.02) in middle age group (40-60 years). In the VO<sub>2peak</sub> subgroups there was an apparent overestimation (p<0.001 and p<0.001, with CE- 5.82 and - 4.37 among men and women, respectively, TE 8.04 and 6.12) in the least fit groups ( $<35 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  for men and  $<30 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ for women), with a succeeding underestimation (p<0.001 and p<0.001, with CE 5.30 and 4.10 among men and women, respectively, TE 7.41 and 5.94) in the most fit group (>50 mL·kg<sup>-1</sup>·min<sup>-1</sup> for men and >40 mL·kg<sup>-1</sup>·min<sup>-1</sup> for women). However, the submaximal models



		Validatio	n sample	;				Cross-valida	tion san	nple		
	Measured VO <sub>2peak</sub>	Predicted VO <sub>2peak</sub>	CE	% SEE	% TE	N (%)	Measured VO <sub>2peak</sub>	Predicted VO <sub>2peak</sub>	CE	% SEE	% TE	N (%)
Age (yr.)												
<40	50.9 ± 8.6	51.2 ± 7.2	-0.34	8.6	8.6	274 (24.8)	50.8 ± 8.4	51.2 ± 7.8	-0.43	9.3	9.5	276 (23.8)
40-60	43.9 ± 8.0	43.8 ± 6.6	0.14	10.4	10.4	610 (55.4)	44.3 ± 8.3	44.5 ± 6.9	-0.17	10.5	10.5	621 (53.6)
>60	37.4 ± 8.1	37.5 ± 6.2	-0.07	13.2	13.2	218 (19.8)	37.3 ± 6.8	37.4 ± 5.7	-0.10	12.1	12.2	261 (22.6)
VO <sub>2peak</sub>												
<35	31.0 ± 3.4	34.5 ± 4.3	-3.54	8.5	16.0	189 (17.2)	31.4 ± 3.0	34.6 ± 4.1	-3.20	8.5	15.7	199 (17.2)
35-50	42.9 ± 4.3	43.1 ± 5.2	-0.26	7.8	9.8	616 (55.8)	42.7 ± 4.1	43.1 ± 5.4	-0.40	7.6	10.1	650 (56.1)
>50	56.0 ± 5.0	53.3 ± 5.7	2.70	6.5	9.2	297 (27.0)	56.0 ± 5.0	53.9 ± 5.7	2.10	7.1	9.3	310 (26.7)
Velocity												
<7	31.0 ± 5.8	31.4 ± 3.5	-0.44	15.0	15.0	93 (8.4)	32.7 ± 4.8	32.2 ± 3.0	0.54	11.3	11.3	116 (10.0)
7-10	40.9 ± 6.2	40.9 ± 4.0	0.11	11.4	11.4	621 (56.4)	41.0 ± 6.2	41.0 ± 4.1	0.04	11.0	11.0	639 (55.1)
>10	53.0 ± 6.5	53.1 ± 4.7	- 0.14	8.4	8.4	388 (35.2)	52.8 ± 7.0	53.6 ± 5.0	-0.82	9.7	9.8	404 (34.9)
Total	44.4 ± 9.3	44.4 ± 8.1	-0.03	10.4	10.4	1102	44.3 ± 9.2	44.5 ± 8.3	-0.21	10.5	10.5	1159

#### Table 9. Cross-validation of Measured vs. Predicted VO<sub>2peak</sub>, from peak measurements, in men: The HUNT 3 fitness study.

VO<sub>2peak</sub> were categorized into 3 groups from measured VO<sub>2peak</sub>; <35, 35–50, >50 (mL kg<sup>-1</sup> min<sup>-1</sup>) were cutoff values for men; velocity: treadmill velocity (km h<sup>-1</sup>).

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predicted VO<sub>2peak</sub> fairly well (p<0.001 and p<0.001, with CE– 0.79 and– 0.53 among men and women, respectively, TE 4.83 and 4.07) in the medium fit subjects (VO<sub>2peak</sub> in the range of 35– 50 mL·kg<sup>-1</sup>·min<sup>-1</sup> for men and between 30 and 40 mL·kg<sup>-1</sup>·min<sup>-1</sup> for women). All velocity groups predicted VO<sub>2peak</sub> fairly well, with no significant differences between measured and predicted VO<sub>2peak</sub> (<5 km·h<sup>-1</sup>: CE– 0.44 and– 0.49 among men and women, respectively, and TE 5.80 and 4.80; 5–6 km·h<sup>-1</sup>: CE– 0.35 and– 0.24, TE 6.24 and 5.28; > 6 km·h<sup>-1</sup>: CE– 0.36 and– 0.91, with TE 6.54 and 6.96). Findings in the total sample are in agreement with the overall tendencies in the validation and cross-validation samples (Tables <u>15–17</u>). Pearson correlation showed minor shrinkage between validation- sample (men: r = 0.733, R<sup>2</sup> = 0.537, p < 0.01; women: r = 0.749, R<sup>2</sup> = 0.561, p < 0.01) and cross-validation sample (men: r = 0.755, R<sup>2</sup> = 0.570, p = 0.01; women: r = 0.743, R<sup>2</sup> = 0.552, p < 0.01). Hence, the entire sample was utilized in development of the models.

# Cross-classification of participants in the submaximal performance prediction model

Cross-classification of predicted (from submaximal performance) and measured VO<sub>2peak</sub> achieved a fairly accurate placing of subjects into the correct VO<sub>2peak</sub> quintile (<u>Table 18</u>). In total, 62.0% and 50.3% of the men and women were predicted appropriately into the lowest measured quintile, respectively, with an increase to 91.3% and 80.9% within the closest



		Validatio	n sample	)				Cross-valida	tion san	nple		
	Measured VO <sub>2peak</sub>	Predicted VO <sub>2peak</sub>	CE	% SEE	% TE	N (%)	Measured VO <sub>2peak</sub>	Predicted VO <sub>2peak</sub>	CE	% SEE	% TE	N (%)
Age (yr.)												
<40	41.2 ± 7.4	41.5 ± 5.9	-0.27	10.9	10.9	337 (28.1)	40.7 ± 7.4	40.7 ± 6.1	0.03	10.1	10.1	327 (28.0)
40-60	35.8 ± 6.8	35.6 ± 5.0	0.18	11.5	11.6	628 (52.4)	35.5 ± 6.7	35.6 ± 5.4	-0.16	11.2	12.2	621 (53.1)
>60	$29.0 \pm 5.4$	29.2 ± 4.6	-0.23	13.3	13.6	233 (19.5)	$29.9 \pm 5.4$	29.7 ± 4.2	0.23	13.2	13.3	222 (18.9)
VO <sub>2peak</sub>												
<30	26.2 ± 2.7	28.8 ± 4.1	-2.60	8.8	16.8	279 (23.3)	26.6 ± 2.8	29.2 ± 4.0	-2.60	8.9	16.3	268 (22.9)
30-40	34.9 ± 2.9	35.3 ± 4.0	-0.44	7.1	10.1	575 (48.0)	34.8 ± 2.9	35.2 ± 4.1	-0.37	7.0	10.2	579 (49.5)
>40)	45.7 ± 4.8	43.0 ± 4.9	2.73	8.2	10.9	344 (28.7)	45.5 ± 4.7	42.8 ± 5.3	2.69	6.9	9.9	324 (27.6)
Velocity												
<7	29.2 ± 4.8	29.1 ± 3.6	0.07	12.6	12.8	392 (32.7)	29.4 ± 4.6	29.2 ± 3.4	0.22	12.1	12.3	365 (31.2)
7-10	38.2 ± 6.1	38.2 ± 3.9	-0.02	11.4	11.4	725 (60.5)	37.6 ± 5.7	37.8 ± 4.0	-0.26	11.2	11.2	734 (62.6)
>10	49.1 ± 5.7	49.5 ± 3.0	-0.38	9.7	9.7	81 (6.8)	51.3 ± 4.8	50.3 ± 3.5	0.99	7.5	7.8	72 (6.2)
Total	36.0 ± 7.9	36.0 ± 6.7	-0.03	11.7	11.7	1198	35.9 ± 7.6	35.9 ± 6.6	-0.04	11.2	11.2	1171

### Table 10. Cross-validation of Measured vs. Predicted VO<sub>2peak</sub>, from peak measurements, in women: The HUNT 3 fitness study.

 $VO_{2peak}$  were categorized into 3 groups from measured  $VO_{2peak}$ ; <30, 30–40, >40 (mL kg<sup>-1</sup> min<sup>-1</sup>) were cutoff values for women; velocity: treadmill velocity (km h<sup>-1</sup>).

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#### Table 11. Cross-tabulation between measured and predicted VO<sub>2peak</sub> quintiles from peak performance for men and women.

			M	en					Woi	men			
			Measure	d VO <sub>2peak</sub>			Measured VO <sub>2peak</sub>						
Predicted	Q <sub>1</sub>	Q <sub>2</sub>	Q <sub>3</sub>	Q <sub>4</sub>	Q <sub>5</sub>	Total	Q1	Q <sub>2</sub>	Q <sub>3</sub>	Q <sub>4</sub>	Q <sub>5</sub>	Total	
VO <sub>2peak</sub>													
Q <sub>1</sub>	259	69	14	2	0	344	256	63	10	1	0	330	
	75.3%	20.1%	4.1%	0.6%	0%	100%	77.6%	19.1%	3.0%	0.3%	0%	100%	
Q <sub>2</sub>	169	232	108	30	3	542	158	216	134	30	5	543	
	31.2%	42.8%	19.9%	5.5%	0.6%	100%	29.1%	39.8%	24.7%	5.5%	0.9%	100%	
$Q_3$	19	132	206	123	22	502	53	152	208	127	29	569	
	3.8%	26.3%	41.0%	24.5%	4.4%	100%	9.3%	26.7%	36.6%	22.3%	5.1%	100%	
$Q_4$	4	18	110	221	108	461	6	40	109	246	135	536	
	0.9%	3.9%	23.9%	47.9%	23.4%	100%	1.1%	7.5%	20.3%	45.9%	25.2%	100%	
$Q_5$	0	2	15	76	319	412	1	2	13	70	305	391	
	0%	0.5%	3.6%	18.4%	77.4%	100%	0.3%	0.5%	3.3%	17.9%	78.0%	100%	
Total	451	453	453	452	452	2261	474	473	474	474	474	2369	

 $Q_{1-5}$ , quintile cut-off values for measured and predicted  $VO_{2peak}$ . Men: <36.0, 36.0–41.5, 41.6–46.5, 46.6–52.0, >52.0 (measured quintiles); and <37.1, 37.1–41.6, 41.7–46.0, 46.1–51.3, >51.3 (predicted quintiles). Women: <29.1, 29.1–33.3, 33.4–37.3, 37.4–42.1, <42.1 (measured quintiles), and <30.5, 30.5–33.8, 33.9–37.1, 37.2–41.2, >41.2 (predicted quintiles). Kendall's Tau statistic: 0.74 for men and 0.70 for women. Cohen Kappa statistic: 0.45 in men and 0.41 in women.



		Men		Women					
	β	Standardized β	Pearson Correlation	β	Standardized β	Pearson Correlation			
Intercept	35.25			23.77					
Inclination	1.276	0.200	0.233	1.205	0.307	0.300			
Velocity	6.402	0.662	0.612	6.051	0.606	0.612			
Weight	-0.196	-0.240	-0.346	-0.160	-0.228	-0.410			
Fraction HR <sub>peak</sub>	-27.615	-0.280	-0.014	-20.671	-0.253	-0.040			
R	0.744			0.746					
R <sup>2</sup>	0.554			0.557					
SEE	6.24			5.17					

### Table 12. Multiple linear regression coefficients for predicting VO<sub>2peak</sub> (mL·kg<sup>-1</sup>·min<sup>-1</sup>) from submaximal measurements in total sample.

Fraction HR<sub>peak</sub>: fraction of peak heart rate; R: multiple regression coefficient; R<sup>2</sup>: coefficient of determination; SEE: standard error of estimate, Inclination (%), Velocity (km·h<sup>-1</sup>), Weight (kg).

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measured quintiles. A total of 59.0% and 72.5% of the men and women, in the highest predicted quintile, were correctly categorized into the highest measured quintile, respectively, increasing to 84.9% and 89.0% within one of the two highest quintiles (<u>Table 18</u>). The rank correlation between measured and predicted quintiles were 0.61 and 0.60 in men and women, respectively, while measure of agreement by Kappa statistic was 0.30 in men and 0.28 in women.

## Discussion

The exercise-based prediction models generated in this study accurately placed approximately 91% of the low- and high-fit participants within the correct or nearest quintile of measured  $VO_{2peak}$  and predicted  $VO_{2peak}$  with fair precision using both the peak performance and submaximal models.

## Accuracy of the VO<sub>2peak</sub> prediction models

The peak performance models displayed accuracy (SEE) of 10.5% ( $R^2 = 0.75$ ) and 11.5% ( $R^2 = 0.72$ ), in men and women, respectively. This is better than some previous research reporting accuracy in the range 13.3–16.6% [14,24], and also less accurate or equal to that reported by yet others (4.5–11.4%) [10–13,15,18,25]. Better prediction accuracy in other models may partly be attributed their homogeneous fitness level in sample subjects [10,12,13,15,18] and/or narrow age range [10–12]. Validating other models using HUNT 3 data is difficult given the use of

				Men			Women						
	R	R <sup>2</sup>	ΔR <sup>2</sup>	р	SEE	%SEE	R	R <sup>2</sup>	ΔR <sup>2</sup>	р	SEE	%SEE	
Inclination	0.23	0.05			9.00	20.3	0.30	0.09	_	_	7.34	20.4	
Inclination, Velocity	0.63	0.40	0.35	<0.001	7.16	16.2	0.66	0.43	0.34	<0.001	5.81	16.2	
Inclination, Velocity, Weight	0.68	0.46	0.06	<0.001	6.77	15.3	0.70	0.49	0.06	<0.001	5.48	15.2	
Inclination, Velocity, Weight, Fraction HR <sub>peak</sub>	0.74	0.55	0.09	<0.001	6.24	14.1	0.75	0.56	0.06	<0.001	5.17	14.4	

Fraction HR<sub>peak</sub>: fraction of peak heart rate; R: multiple regression coefficient; R<sup>2</sup>: coefficient of determination; SEE: standard error of estimate; p: level of significance, Inclination (%), Velocity (km·h<sup>-1</sup>), Weight (kg).

Table 14. Multiple linear regression analysis for predicting VO<sub>2peak</sub> from submaximal measurements in men and women from validation samples: The HUNT 3 fitness study.

		Valida	tion san	nple men			Validation sample women						
	R	R <sup>2</sup>	ΔR <sup>2</sup>	р	SEE	%SEE	R	R <sup>2</sup>	ΔR <sup>2</sup>	р	SEE	%SEE	
Inclination	0.25	0.06		—	8.78	19.8	0.31	0.10	_	_	7.33	20.4	
Inclination, Velocity	0.62	0.38	0.32	<0.001	7.13	16.1	0.66	0.44	0.34	<0.001	5.75	16.0	
Inclination, Velocity, Weight	0.67	0.45	0.07	<0.001	6.75	15.2	0.71	0.50	0.06	<0.001	5.44	15.1	
Inclination, Velocity, Weight, Fraction HR <sub>peak</sub>	0.73	0.54	0.09	<0.001	6.21	14.0	0.75	0.56	0.06	<0.001	5.21	14.5	

Fraction HR<sub>peak</sub>: fraction of peak heart rate; R: multiple regression coefficient; R<sup>2</sup>: coefficient of determination; SEE: standard error of estimate; p: level of significance, Inclination (%), Velocity (km·h<sup>-1</sup>), Weight (kg).

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different independent variables, e.g. watts on cycle ergometer [13,18,25] or 20m-shutle run [10–12]. Although the ACSM running model [20] used, similar to us, speed and gradient, it is developed from steady-state submaximal aerobic exercise, and can be used exclusively in predicting VO<sub>2</sub> during steady-state submaximal work. Hence, it will overestimate VO<sub>2</sub> for peak exercise since contribution from anaerobic metabolism is significant [20], which was confirmed in a previous validation study [24]. However, we were able to validate a model by Uth and colleagues [15] using heart rate ratio (HR<sub>peak</sub>/resting heart rate) as predictor variable for

Table 15. I	Measured vs. Predicted VO <sub>2peal</sub>	, from submaximal measurements	, in the total sample:	The HUNT 3 fitness study.
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		M	en				Women						
	Measured VO <sub>2peak</sub>	Predicted VO <sub>2peak</sub>	CE	% SEE	% TE	N (%)	Measured VO <sub>2peak</sub>	Predicted VO <sub>2peak</sub>	CE	% SEE	% TE	N (%)	
Age (yr.)													
<40	50.8 ± 8.5	47.8 ± 7.0	3.22	11.4	13.4	291 (21.9)	41.0 ± 7.4	$39.5 \pm 5.4$	1.46	13.0	13.7	371 (27.1)	
40-60	44.1 ± 8.1	44.6 ± 6.2	-0.41	13.4	13.4	726 (54.5)	35.6 ± 6.8	$36.3 \pm 4.9$	-0.58	14.0	14.1	717 (52.4)	
>60	$37.3 \pm 7.4$	40.2 ± 6.4	-2.88	15.1	17.2	315 (23.6)	29.4 ± 5.4	31.1 ± 5.0	-1.68	14.3	16.5	281 (20.5)	
VO <sub>2peak</sub>													
<35(<30)	31.2 ± 3.2	37.0 ± 5.6	-5.82	9.4	25.8	218 (16.4)	26.4 ± 2.8	30.8 ± 4.9	-4.25	9.3	23.2	308 (22.5)	
35-50 (30- 40)	42.8 ± 4.2	43.5 ± 5.0	-0.79	8.8	11.3	749 (56.2)	34.9 ± 2.9	35.4 ± 4.2	-0.53	7.5	11.7	667 (48.7)	
>50 (>40)	56.0 ± 5.0	50.7 ± 5.7	5.34	7.7	13.2	366 (27.4)	45.6 ± 4.8	41.5 ± 4.1	4.21	8.8	13.0	394 (28.8)	
Velocity													
<5	$35.4 \pm 6.5$	36.0 ± 5.0	-0.44	15.4	16.4	216 (16.2)	31.0 ± 5.6	31.5 ± 4.4	-0.49	15.0	15.5	535 (39.1)	
5-6	43.9 ± 7.9	44.2 ± 4.4	-0.35	14.2	14.2	911 (68.3)	38.3 ± 6.9	38.5 ± 4.1	-0.24	13.7	13.8	787 (57.5)	
>6	52.9 ± 8.0	53.2 ± 5.6	-0.36	12.2	12.4	206 (15.5)	46.7 ± 7.6	47.6 ± 3.7	-0.91	14.9	14.9	47 (3.4)	
Total	44.3 ± 9.3	44.4 ± 6.9	-0.14	14.1	14.1	1333	35.9 ± 7.8	36.1 ± 5.8	-0.12	14.4	14.4	1369	

 $VO_{2peak}$  were categorized into 3 groups from measured  $VO_{2peak}$ ; <35, 35–50, >50 (mL kg<sup>-1</sup> min<sup>-1</sup>) and <30, 30–40, >40 (mL kg<sup>-1</sup> min<sup>-1</sup>) were cutoff values for men and women, respectively; velocity: treadmill velocity (km h<sup>-1</sup>).



		Validatio	n sample	)			Cross-validation sample						
	Measured VO <sub>2peak</sub>	Predicted VO <sub>2peak</sub>	CE	% SEE	% TE	N (%)	Measured VO <sub>2peak</sub>	Predicted VO <sub>2peak</sub>	CE	% SEE	% TE	N (%)	
Age (yr.)													
<40	50.9 ± 8.2	47.9 ± 6.7	3.14	10.7	12.5	142 (21.6)	50.7 ± 8.8	47.5 ± 6.9	3.44	12.4	14.0	150 (22.1)	
40-60	43.9 ± 8.1	44.9 ± 5.9	-1.03	14.0	14.0	362 (55.5)	44.3 ± 8.1	45.0 ± 5.9	-0.62	12.7	12.7	364 (53.5)	
>60	37.8 ± 7.1	40.7 ± 6.5	-2.86	13.7	16.0	149 (22.9)	36.9 ± 7.7	40.2 ± 6.1	-2.97	16.4	18.6	166 (24.4)	
VO <sub>2peak</sub>													
<35	31.4 ± 3.1	37.4 ± 5.4	-5.94	9.0	25.4	102 (15.6)	31.0 ± 3.2	37.2 ± 5.6	-6.32	9.9	27.2	116 (17.1)	
35-50	42.8 ± 4.1	43.8 ± 4.8	-0.93	8.9	11.4	374 (57.3)	42.7 ± 4.3	43.5 ± 4.7	-0.81	8.7	10.7	375 (55.1)	
>50	55.8 ± 5.1	50.5 ± 5.6	5.41	7.5	13.2	177 (27.1)	56.2 ± 4.9	50.4 ± 5.2	5.69	7.9	13.4	189 (27.8)	
Velocity													
<5	$36.0 \pm 6.7$	37.1 ± 4.9	-0.86	14.4	16.3	97 (14.9)	34.9 ± 6.3	36.2 ± 5.0	-1.14	15.5	16.7	119 (17.5)	
5-6	43.8 ± 7.9	44.2 ± 4.5	-0.37	14.0	14.0	456 (69.8)	43.9 ± 7.9	44.4 ± 4.1	-0.42	14.4	14.5	455 (66.9)	
>6	52.8 ± 8.0	54.0 ± 5.6	-1.14	12.6	12.7	100 (15.3)	52.9 ± 8.2	53.9 ± 5.5	-1.01	11.9	12.1	106 (15.6)	
Total	44.3 ± 9.1	44.6 ± 6.7	-0.27	14.0	14.0	653	44.3 ± 9.5	44.4 ± 6.7	-0.09	14.2	14.2	680	

#### Table 16. Cross-validation of Measured vs. Predicted VO<sub>2peak</sub>, from submaximal measurements in men: The HUNT 3 fitness study.

VO<sub>2peak</sub> were categorized into 3 groups from measured VO<sub>2peak</sub>; <35, 35–50, >50 (mL kg<sup>-1</sup> min<sup>-1</sup>) and <30, 30–40, >40 (mL kg<sup>-1</sup> min<sup>-1</sup>) were cutoff values for men and women, respectively; velocity: treadmill velocity (km h<sup>-1</sup>).

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 $VO_{2max}$ . The Uth model, derived from 46 well-trained men, presented a SEE of 4.5%. This accuracy was considerably lower when validated using HUNT 3 data (18% and 19% SEE in men and women, respectively), which is supported by Esco and colleagues [14] who also observed a substantial reduction in accuracy (SEE of 16.6%), using 109 healthy men to validate the Uth model. This underscores the importance of similar gender, age and physical fitness between the subjects using the model and the subjects used in developing the model to assure best possible accuracy [2,19].

Submaximal VO<sub>2peak</sub> prediction models are generally outperformed on accuracy by models derived from peak workload[26], which is also the case in this study presenting accuracies (SEE) of 14.1% ( $R^2 = 0.55$ ) and 14.4% ( $R^2 = 0.56$ ), in men and women, respectively. Moreover, non-exercise based prediction models derived from HUNT 3 fitness data [27] yielded a somewhat better accuracy (12.8% and 14.3% in men and women, respectively) than the present submaximal models, while the present peak models had better accuracy. Previous research reported prediction error in the range 7.3–20.9% [2,16,28–36]. The bench-mark Åstrand-Ryhming nomogram [37] reported accuracy of approximately 10%, which was confirmed when validated by Cink & Thomas [38]. Both Åstrand and Cink observed minor differences between measured and predicted  $VO_{2peak}$ . However, both used small groups of physically fit college students for their calculations. Validating the Åstrand-Rhyming nomogram using untrained sedentary subjects [39] showed a 26.5% systematic underestimation of  $VO_{2max}$ . Several peak [13,18,25] and submaximal models [16,29–31,34,35] used cycle ergometer to measure



		Validation	n sample	e			Cross-validation sample						
	Measured VO <sub>2peak</sub>	Predicted VO <sub>2peak</sub>	CE	% SEE	% TE	N (%)	Measured VO <sub>2peak</sub>	Predicted VO <sub>2peak</sub>	CE	% SEE	% TE	N (%)	
Age (yr.)													
<40	41.1 ± 7.3	39.5 ± 5.1	1.68	13.1	14.0	187 (27.4)	40.8 ± 7.5	39.7 ± 5.5	1.16	12.8	13.3	184 (26.8)	
40-60	35.5 ± 6.7	36.3 ± 4.9	-0.67	13.8	13.9	346 (50.6)	35.8 ± 6.8	36.4 ± 4.8	-0.48	14.3	14.4	371 (54.1)	
>60	29.3 ± 5.7	30.7 ± 5.0	-1.37	15.1	17.0	150 (22.0)	29.7 ± 5.1	31.6 ± 5.0	-1.82	13.8	15.8	131 (19.1)	
VO <sub>2peak</sub>													
<30)	26.3 ± 2.8	30.6 ± 4.9	-4.23	9.5	23.7	164 (24.0)	26.5 ± 2.7	31.1 ± 4.9	-4.41	8.9	22.9	144 (21.0)	
30-40	34.9 ± 2.8	35.4 ± 4.2	-0.43	7.3	11.5	320 (46.9)	34.8 ± 2.9	35.5 ± 4.1	-0.77	7.6	11.9	347 (50.6)	
>40	45.6 ± 4.8	41.5 ± 4.0	4.08	8.9	12.9	199 (29.1)	45.6 ± 4.7	41.6 ± 4.1	4.24	8.7	13.0	195 (28.4)	
Velocity													
<5	30.8 ± 5.5	31.4 ± 4.4	-0.56	15.3	16.0	273 (40.0)	31.3 ± 5.7	31.7 ± 4.2	-0.38	14.6	14.8	262 (38.2)	
5-6	38.3 ± 6.7	38.5 ± 4.2	-0.16	13.6	13.8	386 (56.5)	38.3 ± 7.0	38.7 ± 3.9	-0.39	13.7	13.8	401 (58.4)	
>6	47.1 ± 7.9	47.0 ± 4.1	0.19	13.5	14.2	24 (3.5)	46.3 ± 7.4	48.5 ± 3.2	-2.10	15.4	15.6	23 (3.4)	
Total	35.9 ± 7.8	36.0 ± 5.9	-0.03	14.5	14.5	683	36.1 ± 7.7	36.3 ± 5.7	-0.11	14.2	14.3	686	

#### Table 17. Cross-validation of Measured vs. Predicted VO<sub>2peak</sub>, from submaximal measurements in women: The HUNT 3 fitness study.

 $VO_{2peak}$  were categorized into 3 groups from measured  $VO_{2peak}$ ; <35, 35–50, >50 (mL kg<sup>-1</sup> min<sup>-1</sup>) and <30, 30–40, >40 (mL kg<sup>-1</sup> min<sup>-1</sup>) were cutoff values for men and women, respectively; velocity: treadmill velocity (km h<sup>-1</sup>).

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 $VO_{2peak/max}$ , however, compelling evidence points to a 6–15% lower  $VO_{2peak}$  compared to that obtained when running [40–44].

## Cross-validation of VO<sub>2peak</sub> prediction models

Randomly splitting data into validation and cross-validation samples established good stability throughout all models, suggesting minor shrinkage in accuracy if used on other similar populations. Moreover, data splitting will minimize potential over fitting that might deteriorate the external validity of the models [45].

For the peak performance models, error estimates are fairly stable across subgroups of both age and treadmill velocity. Conversely, in the  $VO_{2peak}$  subgroups we observed a trend of systematic under- and overestimation of the predicted values in the high- and low-fit participants, respectively. This is consistent with previous findings [12,46,47].

Similarly for the submaximal models, error estimates are reasonably stable across the treadmill velocity subgroups, whereas across the age subgroups there is a tendency towards under- and overestimating  $VO_{2peak}$  in the youngest and oldest, respectively. For the  $VO_{2peak}$  subgroups an even greater tendency towards under- and over estimation in the high- and low-fit participants, respectively, is observed compared to the peak performance models. Wier and colleagues [26] argue that the underestimation of the fittest participants is of less importance from a public health perspective, since a high level of fitness is not associated with adverse health outcomes. However, it highlights the necessity of using models derived from aerobically



			M	en					Wo	men				
			Measure	d VO <sub>2peak</sub>			Measured VO <sub>2peak</sub>							
Predicted	<b>Q</b> <sub>1</sub>	Q <sub>2</sub>	Q <sub>3</sub>	$Q_4$	$Q_5$	Total	<b>Q</b> <sub>1</sub>	Q <sub>2</sub>	Q <sub>3</sub>	$Q_4$	$Q_5$	Total		
VO <sub>2peak</sub>														
<b>Q</b> 1	127	60	16	2	0	205	171	104	49	15	1	340		
	62.0%	29.3%	7.8%	1.0%	0%	100%	50.3%	30.6%	14.4%	4.4%	0.3%	100%		
Q <sub>2</sub>	71	74	48	23	5	221	63	102	88	48	11	312		
	32.1%	33.5%	21.7%	10.4%	2.3%	100%	20.2%	32.7%	28.2%	15.4%	3.5%	100%		
$Q_3$	39	81	75	61	11	267	23	52	79	97	38	289		
	14.6%	30.3%	28.1%	22.8%	4.1%	100%	8.0%	18.0%	27.3%	33.6%	13.1%	100%		
$Q_4$	18	44	84	111	51	308	6	16	38	82	86	228		
	5.8%	14.3%	27.3%	36.0%	16.6%	100%	2.6%	7.0%	16.7%	36.0%	37.7%	100%		
$Q_5$	3	13	34	86	196	332	1	5	16	33	145	200		
	0.9%	3.9%	10.2%	25.6%	59.0%	100%	0.5%	2.5%	8.0%	16.5%	72.5%	100%		
Total	258	272	257	283	263	1333	264	279	270	275	281	1369		

#### Table 18. Cross-tabulation between measured and predicted VO<sub>2peak</sub> quintiles from submaximal performance in men and women.

 $Q_{1-5}$ , quintiles cut-off values of measured and predicted  $VO_{2peak}$ . Men: <36.0, 36.0–41.5, 41.6–46.5, 46.6–52.0, >52.0 (measured quintiles); and <39.0, 39.0–42.9, 43.0–46.0, 46.1–49.5, >49.5 (predicted quintiles). Women: <29.1, 29.1–33.3, 33.4–37.3, 37.4–42.1, <42.1 (measured quintiles), and <31.4, 31.4–34.8, 34.9–37.5, 37.6–40.7, >40.7 (predicted quintiles). Kendall Tau statistic: 0.61 for men and 0.60 for women. Cohen Kappa statistics: 0.30 for men and 0.28 for women.

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fit subjects to obtain high predictive accuracy and stability for a well-trained population. Such models are previously developed [12,15,18], while models with high predictive accuracy for low-fit populations are scarce. The models inability to accurately identify fitness level in the low-fit subjects represent a potential concern, since low aerobic fitness is associated with increased prevalence of chronic disease as well as a higher mortality risk, e.g. cardiovascular disease and metabolic syndrome [3,4,48]. However, cross-classification accurately predicted approximately 91% of participants, in both sexes, within the nearest quintile of measured  $VO_{2peak}$ .

There are several factors that might contribute to the systematic over- and underestimation of  $VO_{2peak}$ , as well as to the attenuation of prediction accuracy. The statistical rationale is that our models are based on linear regression, where the distribution assumptions smooth out extreme observations compared to the grand mean, and may therefore under predict high observations and conversely over predict low observations (regression-to-the-mean phenomenon).

For the submaximal performance models there are additional plausible factors. Genetics account for an additional source of prediction inaccuracy as maximal heart rate is heterogeneous, with significant variations in a population [1]. Based on HUNT 3 fitness data, our group recently reported a standard deviation on measured maximal heart rate of  $\pm 14$  beats·min<sup>-1</sup> [23]. Consequently, imbedding fraction of maximal/peak heart rate as a separate equation in the model weakens the accuracy of the VO<sub>2peak</sub> prediction [1]. Furthermore, since the models are based on linear predictions the best trained are underestimated, and could be so because they have a good movement economy, conversely an overestimation of the least fit, attributed poor movement economy. These additional possible explanations are supported by the considerably higher over- and under estimation of VO<sub>2peak</sub> in the submaximal performance models compared to the peak performance models. Moreover if a person using the prediction

equation has a better movement economy than that of the subjects in the HUNT 3 fitness study, he or she will be overestimated using the submaximal model, and conversely underestimated with poor movement economy. The person will have a better or worse aerobic capacity, influenced by movement economy, not by  $VO_{2peak}$ .

## The independent variables influence on VO<sub>2peak</sub>

Calculating standardized  $\beta$  weights, for the models based on peak performance, revealed velocity as the key determinant of VO<sub>2peak</sub>, followed by age and weight, among both sexes. Not surprisingly inclination had the least impact on VO<sub>2peak</sub>, since approximately 87% of the subjects tested on 10% treadmill inclination in the peak performance models.

Likewise for the submaximal models velocity was paramount in determining  $VO_{2peak}$  among both sexes. In men importance of succeeding determinants of  $VO_{2peak}$  were fraction  $HR_{peak}$  (consisting of age and work heart rate), weight and inclination. For women this was altered to inclination, fraction of  $HR_{peak}$  and weight. Inclination being more potent in women may be related to a larger diversity in running inclination. Explained variances in the submaximal models were 55% and 56% in men and women, respectively, which yields better predictive capabilities than some (31–51%) [17,31,34], and yet worse than other previous models (60–83%) [2,16,28,29,32,33,35].

## Strengths and Limitations

The large sample size, including both men and women, and wide age range makes this study robust. Our direct test to volitional exhaustion to measure VO<sub>2peak</sub> by ventilatory gas analysis is preferable compared to indirect estimates when making prediction equations from population studies, since direct measurements display higher correlations as well as lower standard error of estimate [5]. The low participation rate may contribute to bias caused by self-selection. Still, 5633 (45%) of those invited to the present Fitness study from the total HUNT population volunteered for the cardiopulmonary exercise test. Out of these 5633, 1003 candidates withdrew, did not complete the CPET or were excluded for medical reasons, leaving 4631 (37%) completed tests. Some potential candidates declined participation due to long waiting lines caused by limited capacity at test sites. Consequently, it is possible that those who finally partook could be healthier than those who withdrew from testing. However, comparing the Fitness study participants to a healthy sample from the total HUNT population (i.e. free from pulmonary- and cardiovascular diseases, sarcoidosis or cancer) established that there were no considerable differences between the two [3]. However, the consistent overestimation of the least fit candidates associated with the highest health risks is more precarious. This should be taken into account when applying the models.

The models inability to accurately identify fitness level in the low-fit subjects represent a potential concern, since low aerobic fitness is associated with increased prevalence of chronic disease as well as a higher mortality risk, e.g. cardiovascular disease and metabolic syndrome

## **Practical implications**

In a health care setting the models good ability to detect subjects with low  $VO_{2peak}$  is paramount to classify persons in need of physical activity and lifestyle intervention. Cross-classification of participants into quintiles of measured and predicted  $VO_{2peak}$  demonstrate the models reasonable ability to classify participants appropriately. More importantly, both the use of peak- and submaximal performance models are considered a generally safe practice on high-risk cardiovascular disease patients [49]. Our models are derived from a large population

of both men and women, with a wide heterogeneity in fitness levels as well as covering a large age span (20–90 years). This provides a high degree of applicability for widespread use.

## Conclusions

The  $VO_{2peak}$  prediction models presented in this study are inexpensive and uncomplicated to utilize, thus a convenient option for both recreational athletes as well as in health care settings. Judicious and appropriate use of these predictive models will offer valuable information in providing a fairly accurate estimate of peak oxygen uptake, which is beneficial for establishing cardiorespiratory fitness, and with potentially improved risk stratification.

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## **Author Contributions**

Conceived and designed the experiments: UW. Performed the experiments: UW BMN. Analyzed the data: HL BMN UW. Contributed reagents/materials/analysis tools: HL BMN UW. Wrote the paper: HL BMN UW. Drafting of manuscript or revising it critically for important intellectual content: HL BMN UW. Final approval of the version to be published: HL BMN UW.

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