



## Research Article

# Factors Associated with Cardiorespiratory Fitness in a Swiss Working Population

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**Background.** Good cardiorespiratory fitness (high  $VO_{2max}$ ) has beneficial effects on morbidity and mortality. Therefore, a tool to estimate  $VO_{2max}$  in daily clinical practice is of great value for preventing chronic diseases in healthy adults. This study aimed at exploring the cardiometabolic profile in a representative Swiss working population. Based on these insights, a regression model was derived revealing factors associated with  $VO_{2max}$ . **Methods.** Cross-sectional data of 337 healthy and full-time employed adults recruited in the Basel region, Switzerland, were collected. Anthropometric measurements to compute body mass index (BMI) and waist circumference (WC) were performed. A 20-meter shuttle run test was conducted to determine individual  $VO_{2max}$ . Heart rate (HR) was measured at rest, during maximal exertion, and two minutes after exercise. Systolic (SBP) and diastolic blood pressure (DBP) were assessed at rest and after exercise. A multiple linear regression model was built to identify a set of nonexercise predictor variables of  $VO_{2max}$ . **Results.** Complete data of 303 individuals (63% male) aged 18 to 61 years (mean  $33 \pm 12$  years) were considered for analysis. The regression model (adjusted  $R^2 = 0.647$ ,  $SE = 5.3$ ) identified sex ( $\beta = -0.699$ ,  $p < 0.001$ ), WC ( $\beta = -0.403$ ,  $p < 0.001$ ), difference of maximal to resting HR ( $\beta = 0.234$ ,  $p < 0.001$ ), smoking ( $\beta = -0.171$ ,  $p < 0.001$ ), and age ( $\beta = -0.131$ ,  $p < 0.01$ ) as the most important factors associated with  $VO_{2max}$ , while BMI, SBP, and DBP did not contribute to the regression model. **Conclusions.** This study introduced a simple model to evaluate  $VO_{2max}$  based on nonexercise parameters as part of daily clinical routine without needing a time-consuming, cost-intensive, and physically demanding direct assessment of  $VO_{2max}$ . Knowledge about  $VO_{2max}$  may help identifying individuals at increased cardiovascular risk and may provide the basis for health counselling and tailoring preventive measures.

## 1. Introduction

Physical inactivity is rising on a global scale, thus yielding dramatic consequences for the general health of the population and representing a huge burden to the healthcare systems [1]. According to the World Health Organization (WHO), inactive individuals have higher levels of body fat and are at higher risk for cardiovascular (CV) disease compared to regularly active persons [1]. Physical inactivity is estimated to be the fourth leading risk factor for mortality worldwide [1]. Nevertheless, previous studies indicated that cardiorespiratory fitness measured as maximal oxygen uptake ( $VO_{2max}$ ) is more closely correlated with CV risk factors than

physical activity [2].  $VO_{2max}$ , defined as the maximum rate at which oxygen can be utilized by the body during maximal exertion, is usually given in ml of consumed oxygen per kg of body weight per min and values range from  $<20$  ml/kg/min in inactive adults to 70-94 ml/kg/min in athletes [3]. Factors affecting  $VO_{2max}$  include oxygen diffusion capacity of the lungs, cardiac output, oxygen transport capacity of the blood, capillary density of the muscles, and muscular mitochondria mass [3].  $VO_{2max}$  further depends on sex, age, genetics, body fat, medical conditions, and smoking [4-6]. Obesity was also found to correlate with lower maximal oxygen uptake and poorer cardiorespiratory fitness [7]. Longitudinal studies indicated that a low  $VO_{2max}$  is an independent and strong

predictor of various diseases, such as stroke, hypertension, and metabolic syndrome [8, 9]. On the other hand,  $\text{VO}_{2\text{max}}$  values above 30 ml/kg/min correlate with a reduced relative risk of mortality [10].

The gold standard for measuring  $\text{VO}_{2\text{max}}$  is spiroergometry—a direct measurement of oxygen uptake during maximal exertion, usually by using a cycle ergometer or treadmill [11]. However, spiroergometry is time-consuming, requiring special equipment and skilled personnel [12]. In addition, the availability of appropriate infrastructure is limited, particularly in primary care settings. For this reason, alternative methods have been developed to estimate  $\text{VO}_{2\text{max}}$  on a large scale within the population [12]. These methods include submaximal exercise testing as well as mathematical models not requiring exercise at all [13–15]. However, most of the prediction models were developed for specific patient groups and are not cross-validated in larger populations.

Therefore, the present study aimed at exploring parameters reflecting metabolic and CV profile in a representative Swiss working population in order to identify a set of nonexercise variables associated with  $\text{VO}_{2\text{max}}$ . The goal was to develop a simple model for daily clinical routine not requiring time-consuming, cost-intensive, and physically demanding direct assessment of  $\text{VO}_{2\text{max}}$ . Knowledge about  $\text{VO}_{2\text{max}}$  may help identifying individuals at increased CV risk and may provide the basis for health counselling and tailoring preventive measures. Early detection of increased CV risk might have a great impact on risk reduction, well-being, and work productivity in the general population.

## 2. Materials and Methods

**2.1. Study Design.** This cross-sectional analysis is based on data from a previous study by Brighenti-Zogg et al. [16], which enrolled healthy and full-time employed ( $\geq 80\%$  full-time equivalent) individuals aged 18 to 65 years from various small and medium sized companies of the Basel region, Switzerland. Details on study design and recruitment are published elsewhere [16]. Exclusion criteria were missing informed consent, insufficient knowledge of the German language, movement restrictions, and diseases and accidents within the last three months that affected productivity at the workplace. The study was approved by the local ethics committee for northwest and central Switzerland (EKBB: 260/12) on December 21, 2012.

**2.2. Study Procedures and Measurements.** After providing written informed consent, participants underwent measurements of body height, weight, and WC during the study visit. Body weight was performed on volunteers in light clothing without shoes by a medical scale (model Seca 877, load capacity: 200 kg, Seca AG, Reinach, Switzerland) with an accuracy of 0.1 kg. Body height was assessed without shoes by a medical measuring stick (model Seca 217, measurement range: 20 to 205 cm, Seca AG, Reinach, Switzerland) to the nearest mm. The measurement of WC was determined midway between the lowest rib and the iliac crest using a medical measuring tape (model Prym, length: 150 cm, Germany) with a precision of 0.1 cm. Abdominal obesity was defined as  $>94$  cm in

men and  $>80$  cm in women [17]. Measurements of height and weight were used to calculate BMI ( $\text{BMI} = \text{weight} / \text{height}^2$ ). Participants with a BMI of  $\geq 30$  kg/m<sup>2</sup> were classified as obese [18]. Furthermore, personal and job-related factors were recorded by a generic questionnaire including age, sex, nationality, smoking status, profession, daily working hours, medication, current illnesses, and accidents. Then, participants had to perform a 20-meter shuttle run in order to measure  $\text{VO}_{2\text{max}}$  [19]. They were briefed to run forth and back between two lines with a distance of 20 meters according to audio signals. Starting speed was 8.5 km/h and every minute speed was increased by 0.5 km/h. Once the participant could no longer keep the pace ( $>3$  meter away from the 20-meter line), the test was terminated. The number of reached stages and shuttles was used to estimate  $\text{VO}_{2\text{max}}$  [12].  $\text{VO}_{2\text{max}}$  values were subdivided based on percentiles in order to classify participants into three fitness level groups (i)  $<25$ th percentile ( $<P25$ ), (ii) 25th–75th percentile ( $P25$ – $75$ ), and (iii)  $>75$ th percentile ( $>P75$ ). Heart rate (HR) was recorded before (resting HR), during (maximal HR), and two minutes after the exercise test (recovery HR) using a wrist-worn polar watch (model Polar RS300X sd, Polar Electro Oy, Kempele, Finland). The difference of maximal to resting HR, respectively, of maximal to recovery HR was calculated. In addition, age-predicted maximal HR was determined using the validated formula ‘ $208 - (0.7 \times \text{age})$ ’ by Tanaka et al. [20], which has been described as more accurate than the most common formula ‘ $220 - \text{age}$ ’ [21]. Systolic (SBP) and diastolic blood pressure (DBP) were measured in a standardized way according to the 2013 European Society of Hypertension (ESH) guidelines [22] using an automated BP device for use at the upper arm (Omron M6W, Omron Healthcare Co., Kyoto, Japan). One measurement each was taken at rest and during recovery (two minutes after the test). The double product was calculated as HR multiplied by SBP at rest. Following the study visit, daily physical activity was recorded with the Sense Wear Mini armband (BodyMedia Inc., Pittsburgh, PA, USA) on seven consecutive days (23 hours per day). As recommended by the WHO, participants were classified into groups with sufficient and insufficient activity levels based on the cut-off  $\geq 30$  minutes of moderate-to-vigorous physical activity (MVPA) per day [1].

**2.3. Statistical Analysis.** Statistical analysis was performed using SPSS Statistics (Version 22.0, IBM, Switzerland). Data are presented as mean and standard deviation (SD). Normal distribution of data was evaluated with the Shapiro-Wilk test. Differences between fitness level groups were analysed using One-Way Analysis of Variance (ANOVA) or Kruskal-Wallis test, if appropriate. Categorical data were analysed using the Chi-Square test. Bivariate correlations between measured and estimated values of  $\text{VO}_{2\text{max}}$  as well as maximal HR were calculated using Spearman’s rho (one-sided). In order to identify the most important factors associated with  $\text{VO}_{2\text{max}}$ , a forward-stepwise multiple linear regression analysis was performed including age, sex, smoking status, metabolic parameters (BMI, WC), vital signs (HR, SBP, DBP, double product), and physical activity level (MVPA) as independent variables based on previous research. Validity

TABLE 1: Characteristics of study participants.

Variables	Total (n = 303) Mean ( $\pm$ SD) or n (%)	Male (n = 190) Mean ( $\pm$ SD) or n (%)	Female (n = 113) Mean ( $\pm$ SD) or n (%)
Age [yrs]	33 (12)	33 (13)	35 (12)
Current smokers	64 (21%)	46 (24%)	18 (16%)
BMI [kg/m <sup>2</sup> ]	24 (3)	25 (3.2)	23 (4)
Normal	187 (62%)	106 (56%)	81 (72%)
Overweight [ $\geq 25$ kg/m <sup>2</sup> ]	95 (32%)	67 (35%)	28 (25%)
Obesity [ $\geq 30$ kg/m <sup>2</sup> ]	21 (7%)	17 (9%)	4 (4%)
WC [cm]	86 (11)	89 (10)	80 (11)
Normal	200 (66%)	139 (74%)	61 (53%)
Abdominal obesity [m >94 cm, f >80 cm]	102 (34%)	50 (27%)	52 (46%)
Heart rate [bpm]			
HR <sub>rest</sub> [bpm]	72 (13)	70 (13)	74 (13)
HR <sub>max</sub> [bpm]	183 (15)	187 (14)	178 (15)
HR <sub>recovery</sub> [bpm]	106 (15)	108 (14)	102 (16)
Blood pressure [mmHg]			
SBP <sub>rest</sub> [mmHg]	136 (15)	140 (12)	128 (18)
SBP <sub>recov</sub> [mmHg]	164 (19)	171 (17)	152 (16)
DBP <sub>rest</sub> [mmHg]	82 (10)	82 (9)	80 (10)
DBP <sub>recov</sub> [mmHg]	84 (10)	84 (10)	83 (9)
Normal BP [ $< 140/90$ mmHg]	173 (57%)	86 (45%)	87 (77%)
Increased SBP [ $\geq 140$ mmHg]	76 (25%)	64 (34%)	12 (11%)
Increased DBP [ $\geq 90$ mmHg]	9 (3%)	8 (4%)	1 (1%)
Increased SBP and DBP [ $\geq 140/90$ mmHg]	45 (15%)	32 (17%)	13 (12%)
BP lowering drug therapy	10 (3%)	7 (4%)	3 (3%)
VO <sub>2max</sub> [ml/kg/min]	40 (10)	45 (8)	33 (7)
<P25	71 (23%)	13 (7%)	58 (51%)
P25-75	155 (51%)	10 (55%)	50 (44%)
>P75	77 (25%)	72 (38%)	5 (4%)
Daily MVPA [min/d]	121 (96)	144 (106)	83 (61)
Insufficient [ $< 30$ min/d]	37 (13%)	16 (9%)	21 (20%)
Sufficient [ $\geq 30$ min/d]	242 (87%)	157 (91%)	85 (80%)

BMI, body mass index; BP, blood pressure; BPM, beats per minute; DBP, diastolic blood pressure; HR, heart rate; MVPA, moderate-to-vigorous physical activity; <P25, unfit group; P25-75, middle group; >P75, fittest group; SBP, systolic blood pressure; SD, standard deviation; VO<sub>2max</sub>, maximal oxygen uptake; WC, waist circumference.

of the regression model was proved by checking essential assumptions (i.e., multicollinearity of independent variables, homoscedasticity, independence, and normality of errors). Statistical significance was set at the 5%-level.

### 3. Results

Complete datasets were available from 303 participants. Two-thirds (n = 190, 62.7%) were male and mean age was 33.5  $\pm$  12.0 years, ranging from 18 to 61 years. Most of the participants (77.9%) were younger than 45 years. The majority were Swiss (72.9%), 23.1% European, and 4.0% other nationalities. Further characteristics are summarized in Table 1.

Mean VO<sub>2max</sub> was significantly higher in men compared to women (p < 0.001). The fittest group showed a mean of

52.7  $\pm$  3.7 ml/kg/min, the middle group a mean of 40.1  $\pm$  4.3 ml/kg/min, and the unfit group a mean of 27.8  $\pm$  3.1 ml/kg/min. Sex differences were evident across all fitness level groups (p < 0.05). Subjects in the fittest group (27.6  $\pm$  8.4 years) were significantly younger than those in the middle (33.8  $\pm$  12.0 years) and unfit group (38.1  $\pm$  14.4 years) (p < 0.001). Mean BMI was significantly higher in men than in women (p < 0.001). While 6.9% of the participants were obese, 33.8% presented with abdominal obesity with a significant difference between men and women (p < 0.001). Individuals in the fittest group showed a trend towards lower BMI and WC than those in the middle and unfit group.

HR at rest was significantly higher in women compared to men (p < 0.05), respectively, in the unfit (78  $\pm$  13 bpm) compared to the middle (71  $\pm$  12 bpm) and fittest group (67

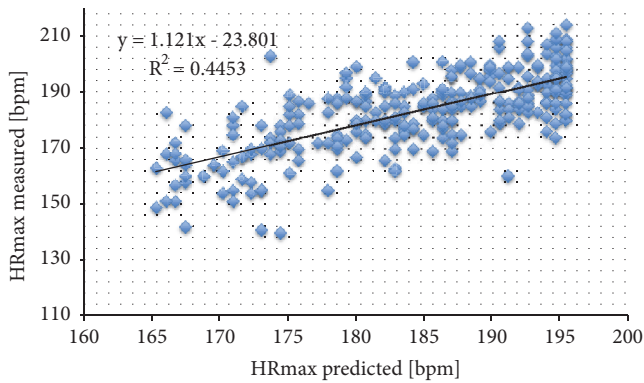


FIGURE 1: Scatterplot illustrating the correlation between  $HR_{\max}$  measured during the 20-meter shuttle run test (Y-axis) and  $HR_{\max}$  predicted using the formula of Tanaka et al. [20] (x-axis).  $HR_{\max}$ : maximal heart rate.

$\pm 13$  bpm) ( $p < 0.001$ ). In contrast, higher HR was observed in men at maximal exertion ( $p < 0.001$ ) and during recovery ( $p < 0.01$ ). Maximal HR was highest in the fittest group ( $191 \pm 10$  bpm) and lowest in the unfit group ( $174 \pm 17$  bpm) ( $p < 0.001$ ). Mean age-predicted maximal HR ( $185 \pm 9$  bpm) [23] and measured maximal HR ( $183 \pm 15$  bpm) were strongly correlated ( $r = 0.699$ ,  $p < 0.001$ ), which is illustrated in Figure 1. Resting SBP was significantly higher in men than in women ( $p < 0.001$ ), respectively, in the fittest compared to the unfit group ( $139 \pm 12$  vs.  $129 \pm 14$  mmHg,  $p < 0.001$ ). However, when stratified for sex, SBP did no longer differ between fitness level groups. SBP during recovery was also higher in the fittest ( $170 \pm 16.7$  mmHg) compared to the middle ( $164 \pm 18.7$  mmHg) and unfit group ( $156 \pm 18.6$  mmHg) ( $p < 0.01$ ). DBP at rest and during recovery did not differ between the three fitness level groups. The double product was lower in the fittest compared to the unfit group, although not statistically significant.

Table 2 presents the results of the forward-stepwise multiple linear regression analysis with  $VO_{2\max}$  as dependent variable. The overall fit of the regression model was high explaining 64.7% of variance (standard error (SE) = 5.3) in  $VO_{2\max}$ . In decreasing order, sex, WC, difference of maximal to resting HR, smoking, and age were the most important factors associated with  $VO_{2\max}$ . In contrast, BMI, SBP, DBP, difference of maximal to recovery HR, double product, MVPA, and daily working hours did not contribute significantly to the regression model and were therefore excluded. The strong and highly significant correlation ( $r = 0.805$ ,  $p < 0.001$ ) between  $VO_{2\max}$  determined by the 20-meter shuttle run test and  $VO_{2\max}$  estimated using the developed regression equation is depicted in Figure 2.

Based on these results, the following regression equation for estimating  $VO_{2\max}$  was derived:

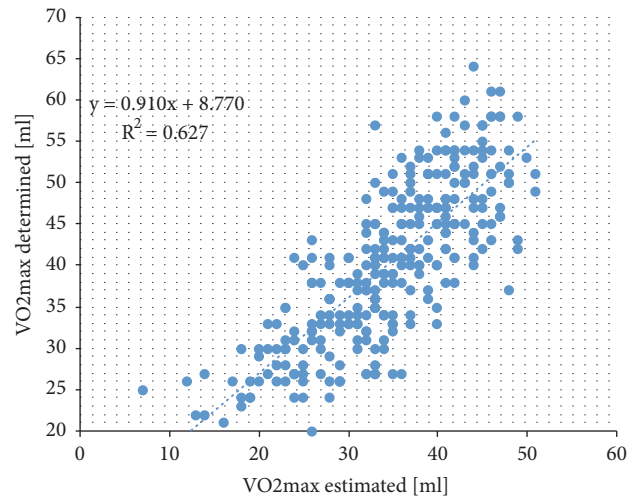
$$VO_{2\max} [\text{ml/kg/min}] = 77.947 - (13.374 \times \text{sex; men} = 1, \text{ women} = 2) - (0.338 \times \text{waist circumference}) + (0.121 \times HR_{\max} - \text{to-}HR_{\text{rest}}) - (3.938 \times \text{smoking; never smoker} = 1, \text{ current smoker} = 3) - (0.098 \times \text{age}).$$


FIGURE 2: Scatterplot depicting the correlation between  $VO_{2\max}$  determined by the 20-meter shuttle run test [12] (y-axis) and  $VO_{2\max}$  estimated using the developed regression equation (x-axis).  $VO_{2\max}$ : maximal oxygen uptake.

*Example 1.* A 20-year-old male nonsmoker with a normal WC of 80 cm and a low resting HR of 50 bpm would have the following  $VO_{2\max}$ , when calculating maximal HR using the formula of Tanaka et al. ( $208 - (0.7 \times 20) = 194$ ):

$$77.947 - (13.374 \times 1) - (0.338 \times 80) + (0.121 \times 194) - (3.938 \times 1) - (0.098 \times 20) = 49.1 \text{ ml/kg/min}$$

*Example 2.* A 50-year-old male smoker with a high-risk WC of 100 cm and a high resting HR of 80 bpm would have the following  $VO_{2\max}$ , when calculating maximal HR using the formula of Tanaka et al. ( $208 - (0.7 \times 50) = 173$ ):

$$77.947 - (13.374 \times 1) - (0.338 \times 100) + (0.121 \times 93) - (3.938 \times 3) - (0.098 \times 50) = 25.3 \text{ ml/kg/min}$$

While Example 1 representing a young and healthy male individual achieved a  $VO_{2\max}$  close to the mean of the fittest group,  $VO_{2\max}$  of Example 2 with a high-risk metabolic and CV profile was below the mean of the unfit group.

## 4. Discussion

The key finding of this cross-sectional analysis including data from 303 healthy Swiss employees was that participants in the fittest group were younger, had a lower BMI and WC, a higher difference of maximal to resting HR, a lower double product ( $HR \times SBP$ ), and were more physically active. Multiple linear regression analysis identified sex, WC, difference of maximal to resting HR, smoking, and age as the most important factors associated with cardiorespiratory fitness ( $VO_{2\max}$ ), while SBP and DBP did not correlate with  $VO_{2\max}$ .

*4.1. Metabolic and Cardiovascular Profile.* BMI defined obesity was found in 9% of male and 4% of female participants. These rates are lower than those reported in the Swiss menuCH survey in 2015 [24]. The difference may be explained by the fact that our study included relatively young



TABLE 2: Forward-stepwise multiple linear regression analysis with  $VO_{2max}$  as dependent variable.

Model: Adjusted $R^2 = 0.647$	B	SE B	$\beta$	p-value
<i>Constant</i>	77.947	5.322		<0.001
Sex [male vs. female]	-13.374	0.852	-0.699	<0.001
WC	-0.338	0.037	-0.403	<0.001
$HR_{max}$ -to- $HR_{rest}$	0.121	0.022	0.234	<0.001
Smoking status [never vs. yes]	-3.938	0.857	-0.171	<0.001
Age [yrs]	-0.098	0.032	-0.131	0.002

B, unstandardized regression coefficient;  $\beta$ , standardized beta coefficient;  $HR_{max}$ -to- $HR_{rest}$ , difference of maximal to resting heart rate; SE, standard error;  $VO_{2max}$ , maximal oxygen uptake; WC, waist circumference.

Excluded variables: body mass index, systolic and diastolic blood pressure, double product, difference of maximal to recovery heart rate, moderate-to-vigorous physical activity, and daily working hours.

and healthy individuals. However, based on WC, one-third of the participants presented with abdominal obesity. WC provides a more reliable measure for obesity than BMI, as it is not confounded by muscle mass [25]. Moreover, it is more accurate in predicting morbidity and mortality by reflecting fat distribution and given the fact that intra-abdominal fat is the most metabolically active, CV risk [23, 26]. Despite this advantage, the measurement of WC may be challenging [27].

Resting HR was higher in women compared to men, which is in line with physiological literature. Since heart volume and muscle mass are both lower in women, less volume generates a smaller stroke volume (SV) and a higher HR is needed for the same cardiac output and oxygen supply to the body (Cardiac output = HR x SV). In contrast, maximal HR was found to be higher in men. Female's higher body fat content may explain this finding [28], as their maximal oxygen uptake normalized by body weight per heartbeat is lower than in men. A woman therefore reaches earlier maximal HR that in turn relates to lower work performance. In agreement with data from the Swiss Federal Statistical Office in 2012, a quarter of the participants presented with increased SBP [29]. Interestingly, a higher rate was revealed in males compared to females (34% vs. 11%). The Swiss Federal Statistical Office confirmed that until the age of 65 years, men tend to have higher rates of increased BP than women [29].

The present study showed that 87% of the participants met the current recommendations on physical activity of at least 30 minutes MPA per day, clearly exceeding the findings of the Swiss Health Survey 2012 (72%) [30]. An explanation could be that in our study physical activity was measured objectively 23 hours a day, whereas the Swiss Health Survey used a self-report questionnaire, which only assessed physical activity during leisure-time.

**4.2. Associations of Metabolic and Cardiovascular Factors with  $VO_{2max}$ .** This study detected a mean  $VO_{2max}$  of 40 ml/kg/min with a highly significant difference between men and women (45 ml/kg/min vs. 33 ml/kg/min). Compared to reference values for healthy nonathletes ranging from 30 to 50 ml/kg/min, the study subjects were found to be on an average level with regard to cardiorespiratory fitness [3].

Participants in the fittest group were significantly younger compared to subjects in the unfit group. A decline in  $VO_{2max}$

with age is well known with a linear 10%-decrease per decade (1% per year in men, 0.8% per year in women) after the age of 25 years [31, 32].  $VO_{2max}$  is determined by cardiac output and arteriovenous oxygen difference, with the former probably being the driving factor for this decline. Reasons for a reduction in cardiac output with age include a notable decline in maximal HR [20] and a decrease in SV of about 10-20% compared to values at young age caused by increased peripheral resistance from reduced elasticity of the arteries and arterioles [33]. As expected, participants in the fittest group had a lower BMI and WC than those in the unfit group. This is consistent with previous findings and points to the impact of body fat on oxygen uptake and cardiorespiratory dynamics [7].

Several studies demonstrated that the likelihood of developing hypertension is lower in physically active compared to inactive individuals [34]. In contrast, this study showed a higher SBP in the fittest compared to the unfit group. A possible explanation is that mostly men were in the fittest group, who typically had a higher SBP than women. Indeed, this relationship did not substantiate when adjusted for sex. A study examining CV health in 3.000 men over a period of 16 years revealed that high HR at rest correlated with lower cardiorespiratory fitness, higher BP, higher levels of circulating blood fats, and higher body weight [35]. Our data underscore these findings, since the fittest group had a significantly lower resting HR compared to the unfit group. In addition, the fittest group showed a significantly higher increase in HR during exercise and a greater decline during recovery, indicating a substantially reduced CV risk compared to the unfit group [36]. This is further supported by the finding that the double product was lower in the fittest group. Previous studies detected a strong association between the double product and CV mortality, thereby emphasizing its prognostic value [37].

**4.3. Regression Model to Estimate  $VO_{2max}$ .**  $VO_{2max}$  is a well-established measure for cardiorespiratory fitness and closely linked to all-cause mortality [10]. Despite its clinical relevance, methods for direct assessment remain time-consuming and difficult to perform in primary care [12]. This study revealed that  $VO_{2max}$  is primarily influenced by sex, WC, difference of maximal to resting HR, smoking, and

age. The resulting regression model based on these readily available nonexercise variables proved accurate in estimating  $VO_{2max}$  in a healthy working population when compared to values determined by the 20-meter shuttle run test.

The present findings are in line with previous studies indicating that female sex is a strong negative predictor of  $VO_{2max}$  and associated with 10-15% lower levels than in males [38, 39]. Women not only have a smaller SV, but also a lower hemoglobin concentration [38]. Thus, less oxygen is transported per liter of SV. Another reason is that men have more mitochondria due to the higher muscle mass, which in turn results in higher oxygen metabolism [3]. However, the sex difference in this study (13 ml/kg/min) was substantially larger than in similar regression equations developed in adolescents (~5-7 ml/min/kg) [40, 41]. It could be hypothesized that differences in  $VO_{2max}$  between sexes are more pronounced in adults, when growth is completed. Our results also highlight a significant association of  $VO_{2max}$  with WC, which particularly in men has been described to be stronger than with BMI [42]. Several studies confirmed the inverse relationship of abdominal obesity with cardiorespiratory fitness [14, 42]. Furthermore, the present findings are consistent with Uth et al. [43] showing a highly significant correlation between  $VO_{2max}$  and the ratio of maximal to resting HR. This can partly be explained by exercise-induced lowering of resting HR while increasing maximal HR, which in turn results in a higher  $VO_{2max}$ . By adjusting for age in the regression model, the fact that people in the fittest group were younger and would have a higher maximal HR due to their age was controlled. The negative association of  $VO_{2max}$  with smoking is again in line with previous research [5]. A trial found higher HR as well as lower  $VO_{2max}$  and anaerobic threshold in smokers, possibly due to reduced oxygen availability for the exercising muscles [44]. Moreover, age was regarded as one of the most important factors associated with  $VO_{2max}$  based on results from a maximal graded exercise test in adults aged 18 to 65 years [15]. The present results similarly point to age as a negative determinant of  $VO_{2max}$ , although the effect was only 0.1 ml/kg/min decrease per year, which is less than seen in the literature (~0.3-0.5 ml/kg/min per year) [31, 32]. This discrepancy may be explained by the fact that the age effect is partly represented in the difference of maximal to resting HR, which has not been included as independent variable in other regression equations. In this study, physical activity did not appear to independently determine  $VO_{2max}$ , which is supported by McMurray et al. indicating that cardiorespiratory fitness is more closely associated with the risk of CV disease than physical activity [2]. Surprisingly, neither SPB nor DBP correlated significantly with  $VO_{2max}$ . This is in contrast to a prior study that showed a negative association between BP and  $VO_{2max}$  in normal weight persons [44].

**4.4. Implications for Clinical Practice.** Previous studies convincingly demonstrated that good cardiorespiratory fitness has beneficial effects on morbidity and mortality. High  $VO_{2max}$  reduces the risk of various diseases such as stroke, ischemic heart disease, hypertension, type 2 diabetes, and metabolic syndrome. Therefore, the design of a tool to

estimate  $VO_{2max}$  is of pivotal importance for preventing CV and other diseases in healthy adults. Furthermore, it is evident that such tools are of little value unless they become implemented in daily clinical routine. Thus, the development of a regression model that is simple in use, solely includes readily available parameters, and does not require any specific measurement, equipment, or infrastructure is highly needed. The model derived in this study provides the potential for use in computer applications to support clinical decisions. The given examples elucidate how  $VO_{2max}$  is influenced by the individual metabolic and CV profile. Consequently, the formula contributes to further increase the accessibility to CV risk assessment and personalized advice on preventive measures.

**4.5. Strengths and Limitations.** This study included a wide range of healthy employees, providing data from a typical cross-section of the Swiss working population. Moreover, the data on mean  $VO_{2max}$  as well as  $VO_{2max}$  values stratified for sex are comparable with data from a population-based study in US employees [15].

Several limitations of the study must be taken into consideration when interpreting the results. *First*, the 20-meter shuttle run test was used to determine  $VO_{2max}$  rather than spiroergometry, which is the gold standard for direct measurement of  $VO_{2max}$  [11]. However, spiroergometry depends on trained staff and is labor-intensive and time-consuming and therefore not feasible for evaluating large populations [12]. A recent study verified that the 20-meter shuttle run test was accurate in predicting  $VO_{2max}$  in healthy adults, as the results showed a strong and highly significant correlation between the number of achieved shuttles and directly measured  $VO_{2max}$  [45]. *Second*, the regression model for estimating  $VO_{2max}$  developed in this study may have limited generalizability, given that it was based on healthy younger adults in Switzerland. Thus, future research should focus on other populations in order to refine the model, e.g., elderly or diseased people. Nevertheless, the different age groups included here accurately reflect the distribution of the Swiss working population, where preventive measures may be most effective for maintaining health and work productivity. *Third*, it remains uncertain if individuals with great interest in health issues and fitness were more willing to participate in the study than others, thereby resulting in a possible selection bias. A lack of motivation among the low fit individuals may also have influenced the results, as they might have terminated the 20-meter shuttle run test earlier resulting in lower maximal HR and  $VO_{2max}$ . *Fourth*, only one BP measurement was performed at rest and during recovery, respectively, whereas the 2013 ESH guidelines suggest at least two measurements [22]. This may have led to a lack of relationship between  $VO_{2max}$  and BP. *Fifth*, the present study was cross-sectional in nature, which provided a snapshot of the relation between cardiometabolic factors and  $VO_{2max}$ . However, cause-effect relationships are difficult to ascertain. To overcome this limitation in future, longitudinal studies are required.

## 5. Conclusions

This study introduced a simple model for estimating  $VO_{2max}$  based on nonexercise parameters without needing a time-consuming, cost-intensive, and physically demanding direct assessment of  $VO_{2max}$ . Thus, the study enabled a new way to efficiently and effectively evaluate  $VO_{2max}$  as part of daily clinical routine. However, determining an individual's  $VO_{2max}$  is not only intended to estimate cardiorespiratory fitness, but also to identify future health risks associated with a low  $VO_{2max}$ .

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

David Miedinger was employed at Suva at the time of conducting the study until September 2017, but did not have any financial conflicts of interest. The other authors declare that they have no conflicts of interest.

## Authors' Contributions

Sara Kind and Stefanie Brighenti-Zogg contributed equally to this manuscript.

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## References

- [1] World Health Organization, "Global recommendations on physical activity for health," 2010, [http://apps.who.int/iris/bitstream/10665/44399/1/9789241599979\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/44399/1/9789241599979_eng.pdf).
- [2] R. G. McMurray, B. E. Ainsworth, J. S. Harrell, T. R. Griggs, and O. D. Williams, "Is physical activity or aerobic power more influential on reducing cardiovascular disease risk factors?" *Medicine & Science in Sports & Exercise*, vol. 30, no. 10, pp. 1521–1529, 1998.
- [3] W. L. Kenney, J. H. Wilmore, and D. L. Costill, "Adaptions to aerobic and anaerobic training," in *Physiology of Sport and Exercise*, pp. 261–291, Human Kinetics, Champaign, Ill, USA, 6th edition, 2015.
- [4] T. Zhang, C. F. Zhang, F. Jin et al., "Association between genetic factor and physical performance," *Yi Chuan*, vol. 26, pp. 219–226, 2004.
- [5] R. R. Suminski, L. T. Wier, W. Poston et al., "The effect of habitual smoking on measured and predicted  $VO_{2max}$ ," *Journal of Physical Activity & Health*, vol. 6, no. 5, pp. 667–673, 2009.
- [6] T. Hirai, Y. Kusaka, N. Suganuma, A. Seo, and Y. Tobita, "Work form affects maximum oxygen uptake for one year in workers," *Industrial Health*, vol. 49, no. 3, pp. 321–327, 2011.
- [7] S. Green, E. O'Connor, C. Kiely, D. O'Shea, and M. Egaña, "Effect of obesity on oxygen uptake and cardiovascular dynamics during whole-body and leg exercise in adult males and females," *Physiological Reports*, vol. 6, Article ID e13705, 2018.
- [8] S. P. Hooker, X. Sui, N. Colabianchi et al., "Cardiorespiratory fitness as a predictor of fatal and nonfatal stroke in asymptomatic women and men," *Stroke*, vol. 39, no. 11, pp. 2950–2957, 2008.
- [9] M. J. LaMonte, C. E. Barlow, R. Jurca, J. B. Kampert, T. S. Church, and S. N. Blair, "Cardiorespiratory fitness is inversely associated with the incidence of metabolic syndrome," *Circulation*, vol. 112, no. 4, pp. 505–512, 2005.
- [10] M. J. Castillo-Garzón, J. R. Ruiz, F. B. Ortega, and Á. Gutiérrez, "Anti-aging therapy through fitness enhancement," *Clinical Interventions in Aging*, vol. 1, no. 3, pp. 213–220, 2006.
- [11] K. Wasserman, "Diagnosing cardiovascular and lung pathophysiology from exercise gas exchange," *CHEST*, vol. 112, no. 4, pp. 1091–1101, 1997.
- [12] R. Ramsbottom, J. Brewer, and C. Williams, "A progressive shuttle run test to estimate maximal oxygen uptake," *British Journal of Sports Medicine*, vol. 22, no. 4, pp. 141–144, 1988.
- [13] E. L. Fox, "A simple, accurate technique for predicting maximal aerobic power," *Journal of Applied Physiology*, vol. 35, no. 6, pp. 914–916, 1973.
- [14] L. T. Wier, A. S. Jackson, G. W. Ayers, and B. Arenare, "Nonexercise models for estimating  $VO_{2max}$  with waist girth, percent fat, or BMI," *Medicine & Science in Sports & Exercise*, vol. 38, no. 3, pp. 555–561, 2006.
- [15] D. I. Bradshaw, J. D. George, A. Hyde et al., "An accurate  $VO_{2max}$  nonexercise regression model for 18–65-year-old adults," *Research Quarterly for Exercise and Sport*, vol. 76, no. 4, pp. 426–432, 2005.
- [16] S. Brighenti-Zogg, J. Mundwiler, U. Schüpbach et al., "Physical workload and work capacity across occupational groups," *PLoS ONE*, vol. 11, no. 5, Article ID e0154073, 2016.
- [17] World Health Organization, *Waist Circumference and Waist-Hip-Ratio; Report of a WHO Expert Consultation*, Geneva, Switzerland, 2008, [http://apps.who.int/iris/bitstream/handle/10665/44583/9789241501491\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/handle/10665/44583/9789241501491_eng.pdf?ua=1).
- [18] World Health Organization, *Obesity and Overweight*, Geneva, Switzerland, 2015, <http://www.who.int/mediacentre/factsheets/fs311/en/>.
- [19] L. A. Léger, D. Mercier, C. Gadoury, and J. Lambert, "The multistage 20 metre shuttle run test for aerobic fitness," *Journal of Sports Sciences*, vol. 6, no. 2, pp. 93–101, 1988.
- [20] H. Tanaka, K. D. Monahan, and D. R. Seals, "Age-predicted maximal heart rate revisited," *Journal of the American College of Cardiology*, vol. 37, no. 1, pp. 153–156, 2001.
- [21] P. O. Astrand and I. Ryhming, "A nomogram for calculation of aerobic capacity (physical fitness) from pulse rate during sub-maximal work," *Journal of Applied Physiology*, vol. 7, no. 2, pp. 218–221, 1954.



- [22] G. Parati, G. Stergiou, E. O'Brien et al., "European society of hypertension practice guidelines for ambulatory blood pressure monitoring," *Journal of Hypertension*, vol. 32, pp. 1359–1366, 2014.
- [23] A. J. Flint, K. M. Rexrode, F. B. Hu et al., "Body mass index, waist circumference, and risk of coronary heart disease: A prospective study among men and women," *Obesity Research & Clinical Practice*, vol. 4, no. 3, pp. e171–e181, 2010.
- [24] M. Bochud, A. Chatelan, and J. M. Blanco, "Anthropometric characteristics and indicators of eating and physical activity behaviors in the Swiss adult population - results from menuCH 2014-2015," Report on behalf of the Swiss Federal Office of Public Health and the Food Safety and Veterinary Office, 2018, <https://menuch.iumsp.ch/index.php/catalog/4/download/58>.
- [25] A. M. Prentice and S. A. Jebb, "Beyond body mass index," *Obesity Reviews*, vol. 2, no. 3, pp. 141–147, 2001.
- [26] H. Hauner, P. Bramlage, C. Lösch et al., "Prevalence of obesity in primary care using different anthropometric measures - Results of the German metabolic and cardiovascular risk project (GEMCAS)," *BMC Public Health*, vol. 8, article no 282, 2008.
- [27] P. Sebo, S. Beer-Borst, D. M. Haller, and P. A. Bovier, "Reliability of doctors' anthropometric measurements to detect obesity," *Preventive Medicine*, vol. 47, no. 4, pp. 389–393, 2008.
- [28] S. M. Camhi, G. A. Bray, C. Bouchard et al., "The relationship of waist circumference and BMI to visceral, subcutaneous, and total body fat: sex and race differences," *Obesity*, vol. 19, no. 2, pp. 402–408, 2011.
- [29] Swiss Federal Statistical Office, "Persons with hypertension," 2018, <https://www.bfs.admin.ch/bfs/de/home/statistiken/gesundheit/gesundheitszustand/krankheiten/herz-kreislauf-erkrankungen.assetdetail.4103618.html>.
- [30] Swiss Federal Statistical Office, "Physical Activity," 2018, <https://www.bfs.admin.ch/bfs/de/home/statistiken/gesundheit/determinanten/koerperliche-aktivitaet.html>.
- [31] A. S. Jackson, E. F. Beard, L. T. Wier et al., "Changes in aerobic power of men, ages 25-70-Yr," *Medicine & Science in Sports & Exercise*, vol. 27, pp. 113–120, 1995.
- [32] A. S. Jackson, L. T. Wier, G. W. Ayers et al., "Changes in aerobic power of women, ages 20-64 yr," *Medicine & Science in Sports & Exercise*, vol. 28, pp. 884–891, 1996.
- [33] W. L. Kenney, J. H. Wilmore, and D. L. Costill, "Aging in sport and exercise," in *Physiology of Sport and Exercise*, pp. 457–479, Human Kinetics, Champaign, Ill, USA, 6th edition, 2015.
- [34] E. D. Parker, K. H. Schmitz, D. R. Jacobs, D. R. Dengel, and P. J. Schreiner, "Physical activity in young adults and incident hypertension over 15 years of follow-up: the CARDIA study," *American Journal of Public Health*, vol. 97, no. 4, pp. 703–709, 2007.
- [35] M. T. Jensen, P. Suadicani, H. O. Hein, and F. Gyntelberg, "Elevated resting heart rate, physical fitness and all-cause mortality: a 16-year follow-up in the Copenhagen Male Study," *Heart*, vol. 99, no. 12, pp. 882–887, 2013.
- [36] C. R. Cole, E. H. Blackstone, F. J. Pashkow, C. E. Snader, and M. S. Lauer, "Heart rate recovery immediately after exercise as a predictor of mortality," *The New England Journal of Medicine*, vol. 341, no. 18, pp. 1351–1357, 1999.
- [37] A. H. Sadrzadeh Rafie, F. E. Dewey, G. W. Sungar et al., "Age and double product (systolic blood pressure x heart rate) reserve-adjusted modification of the Duke Treadmill Score nomogram in men," *American Journal of Cardiology*, vol. 102, no. 10, pp. 1407–1412, 2008.
- [38] K. Cureton, P. Bishop, P. Hutchinson, H. Newland, S. Vickery, and L. Zwiren, "Sex difference in maximal oxygen uptake," *European Journal of Applied Physiology*, vol. 54, no. 6, pp. 656–660, 1986.
- [39] S. Maldonado-Martín, I. Mujika, and S. Padilla, "Physiological variables to use in the gender comparison in highly trained runners," *The Journal of Sports Medicine and Physical Fitness*, vol. 44, no. 1, pp. 8–14, 2004.
- [40] A. Barnett, L. Y. Chan, and L. C. Bruce, "A preliminary study of the 20-m multistage shuttle run as a predictor of peak VO<sub>2</sub> in Hong Kong Chinese students," *Pediatric Exercise Science*, vol. 5, no. 1, pp. 42–50, 1993.
- [41] M. T. Mahar, G. J. Welk, D. A. Rowe, D. J. Crotts, and K. L. McIver, "Development and validation of a regression model to estimate VO<sub>2</sub>peak from PACER 20-m shuttle run performance," *Journal of Physical Activity & Health*, vol. 3, no. s2, pp. S34–S46, 2006.
- [42] S. S. Dagan, S. Segev, I. Novikov, and R. Dankner, "Waist circumference vs body mass index in association with cardiorespiratory fitness in healthy men and women: a cross sectional analysis of 403 subjects," *Nutrition Journal*, vol. 12, article no 12, 2013.
- [43] N. Uth, H. Sorensen, K. Overgaard et al., "Estimation of VO<sub>2</sub>max from the ratio between HR<sub>max</sub> and HR<sub>rest</sub> - the Heart rate ratio method," *European Journal of Applied Physiology*, vol. 93, no. 4, pp. 508–509, 2005.
- [44] J. Y. Shin and C. H. Ha, "Relationships between blood pressure and health and fitness-related variables in obese women," *Journal of Physical Therapy Science*, vol. 28, no. 10, pp. 2933–2937, 2016.
- [45] G. P. Paradisis, E. Zacharogiannis, D. Mandila, A. Smirtiotou, P. Argeitaki, and C. B. Cooke, "Multi-stage 20-m shuttle run fitness test, maximal oxygen uptake and velocity at maximal oxygen uptake," *Journal of Human Kinetics*, vol. 41, no. 1, pp. 81–87, 2014.