CHEST Online Supplement

Normative Cardiopulmonary Exercise Test Responses at the Ventilatory Threshold in Canadian Adults 40 to 80 Years of Age

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e-Appendix 1

Detailed eligibility criteria

Specific exclusion criteria for the current study were: 1) cigarette smoking history of >5 pack years; 2) self-reported chronic bronchitis, chronic obstructive pulmonary disease, diabetes, angina or myocardial infarction (participants who self-reported systemic hypertension with no other cardiovascular disease were not excluded); 3) abnormal pulmonary function at rest, defined as a forced expiratory volume in 1-sec (FEV_1), forced vital capacity (FVC) or diffusing capacity of the lungs for carbon monoxide less than the lower limit of normal or a total lung capacity less than 80% predicted, using recommended reference values (references[15-17] in main manuscript) and/or evidence of reversible airflow obstruction (i.e., increase in FEV_1 or FVC >12% and >200 mL 10-15 min after administration of 200-400 mcg albuterol or equivalent) ; 4) not achieving a symptom or physiological limitation to CPET, which was defined as meeting one or more of the criteria of: a respiratory exchange ratio ≥1, an intensity rating of breathing/leg discomfort of ≥5 on the 0-10 modified Borg scale or a peak heart rate no less than 10 beats·min^{-1} of the age-predicted maximum of 220-age; or 5) an abnormal CPET response determined by the supervising physician.

Inspiratory capacity derived parameters

Inspiratory capacity (IC) derived parameters included:

- Inspiratory reserve volume (IRV) = IC assessed at peak exercise minus the concomitant 30-sec averaged tidal volume [V_T]);

- End-expiratory lung volume (EELV) = total lung capacity (TLC) assessed with body plethysmography at rest minus IC;

- End-inspiratory lung volume (EILV) = TLC assessed with body plethysmography at rest minus IRV.

IC maneuvers were visually inspected and adjusted to the level of a stable EELV, if required. This approach assumed TLC did not change during exercise in healthy adults (Stubbing et al. *J Appl Physiol Respir Environ Exerc Physiol*. 1980;49(3):506-10. doi: 10.1152/jappl.1980.49.3.506).

Ventilatory threshold (Tvent) identification

The Tvent was identified using two established and commonly used non-invasive methods during incremental CPET, the V-Slope (see references[22-26] of main manuscript) and Dual Criterion (see reference[27] of main manuscript). The V-slope method identifies Tvent as the point at which the rate of CO_2 production ($V'CO_2$) accelerates beyond the rate of oxygen consumption ($V'O_2$), without hyperventilation. Identifying Tvent using the V-slope method requires plotting $V'CO_2$ against $V'O_2$ and evaluating the point of inflection. The Dual Criterion method involves simultaneous evaluation of the ventilatory equivalent for O_2 ($V'_E/V'O_2$) and ventilatory equivalent for CO_2 ($V'_E/V'CO_2$); Tvent is identified as the point at which there is a systematic increase in $V'_E/V'O_2$ without a simultaneous increase in $V'_E/V'CO_2$. For accurate identification of Tvent, clinical CPET guidelines recommend using both V-slope and Dual Criterion methods. Two independent raters (OE, FN) first identified $V'O_2$ at Tvent using the V-slope method with data averaged in 10-sec epochs. This value was cross-referenced with the Dual Criterion method, making manual adjustments if necessary.

e-Table 1 Health characteristics and peak rate of oxygen consumption (V'O$_{2peak}$) responses for participants included in the current study (n=96) compared to those excluded (n=46) due to cardiopulmonary exercise testing data inaccessible for analyses

Participant characteristic	Participants of current study *n=96*	Participants from excluded sites *n=46*	*p=**
Age (years)	63 (9)	62 (9)	0.620
Sex (male n=, %)	47 (49%)	16 (35%)	0.158
Height (cm)	168.0 (9.0)	164.0 (9.8)	0.017
Body mass (kg)	76.2 (14.0)	70.2 (13.7)	0.017
BMI (kg·m^{-2})	27.0 (4.2)	26.2 (4.6)	0.320
FEV$_1$ (L)	2.95 (0.71)	2.80 (0.72)	0.228
FEV$_1$ (%predicted)	104 (14)	105 (13)	0.642
FVC (L)	3.80 (0.91)	3.53 (0.89)	0.095
FVC (%predicted)	104 (14)	104 (13)	0.966
TLC (%predicted)	102 (12)	109 (13)	0.003
D$_L$CO (%predicted)	112 (19)	130 (19)	<0.001
Cigarette Pack Years	0.64 (1.40)	0.18 (0.89)	0.021
Cigarette smoking status, n= (%)			0.004
Never	71 (74%)	44 (96%)	
Former	25 (26%)	2 (4%)	
MVPA (hours·week^{-1})	2.7 (2.5)	2.3 (1.8)	0.267
V'O$_{2peak}$ (mL·kg·min^{-1})	26.7 (7.3)	21.7 (8.2)	0.001
V'O$_{2peak}$ (%predicted)[#]	108 (23)	88 (22)	<0.001

*unpaired t-test for continuous variables; chi-squared test for categorical variables
[##]Predicted using reference equations by Lewthwaite et al. [11]
Results presented as mean (SD) unless otherwise indicated

BMI, body mass index; D$_L$CO, carbon monoxide diffusing capacity of the lungs; FEV$_1$, forced expiratory volume in 1-sec; FVC, forced vital capacity; MVPA, moderate-to-vigorous intensity physical activity assessed by self-report with the Community Healthy Activities Models Program for Seniors questionnaire [20]; TLC, total lung capacity

e-Table 2 Rate of O$_2$ consumption (V'O$_2$) during symptom-limited incremental cardiopulmonary cycle exercise testing at the ventilatory threshold (Tvent) identified by two blinded and independent raters using a combination of V-slope and Dual Criterion detection methods.

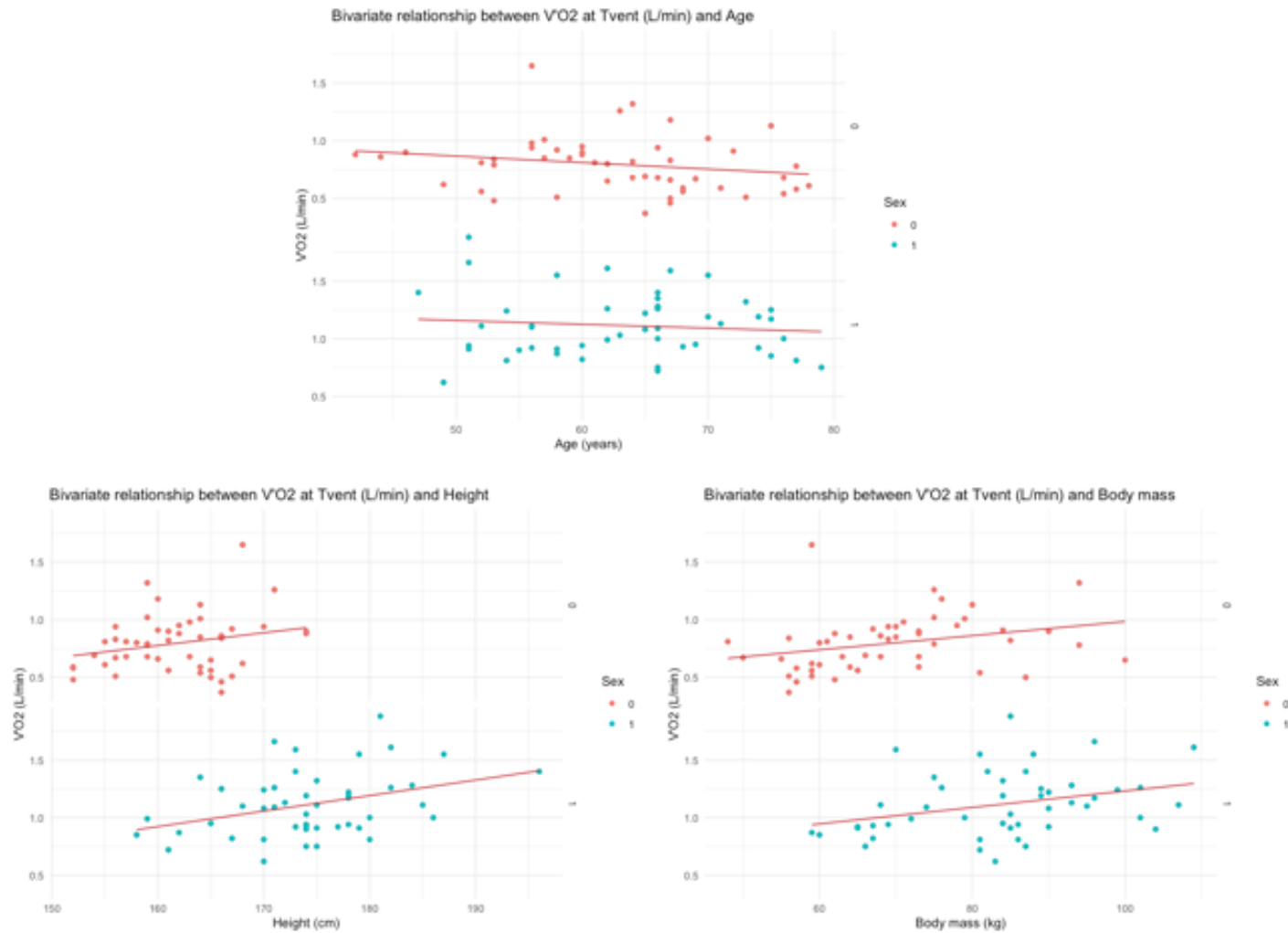|	Rater 1	Rater 2	Absolute (L·min^{-1}) mean difference (Rater 1-Rater 2)	Relative (%) mean difference (Rater 1-Rater 2)
V'O$_2$ (L·min^{-1}), mean± SD [min-max]	0.94 ± 0.31 [0.36 – 1.95]	0.96 ± 0.31 [0.38 – 1.81]	0.06 ± 0.05 [-0.18 – 0.14]	6 ± 6 [-23 – 25]

e-Figure 1 (a-j): Bivariate relationships between explanatory variables and physiological responses during symptom-limited incremental cardiopulmonary cycle exercise testing at the ventilatory threshold (Tvent) in Canadian adults aged 40-80 years.

a) Bivariate relationships between explanatory variables and O_2 pulse during symptom-limited incremental cardiopulmonary cycle exercise testing at the ventilatory threshold (Tvent) in Canadian females (closed blue circles; n=49) and males (closed red circles; n=47) aged 40-80 years.
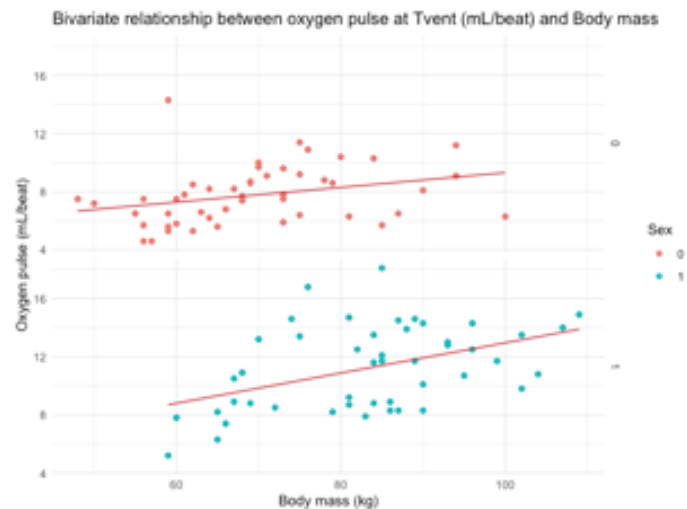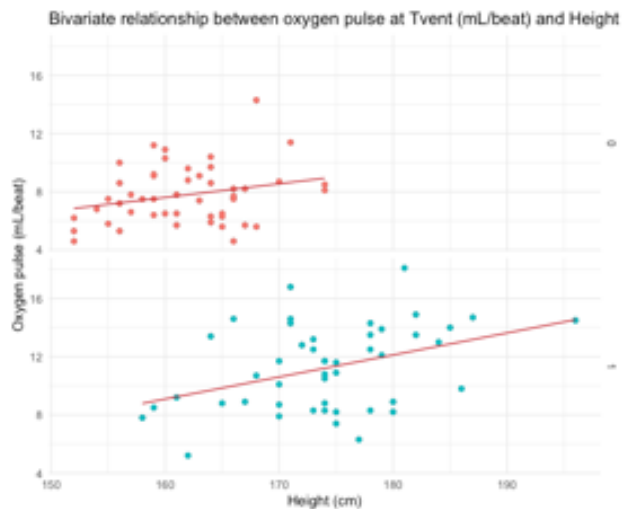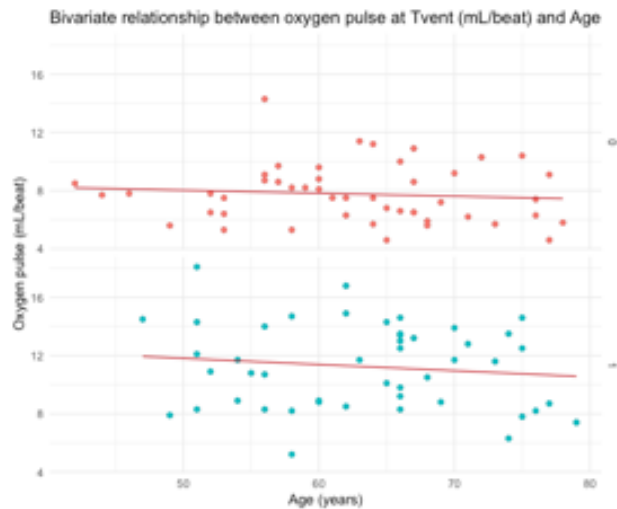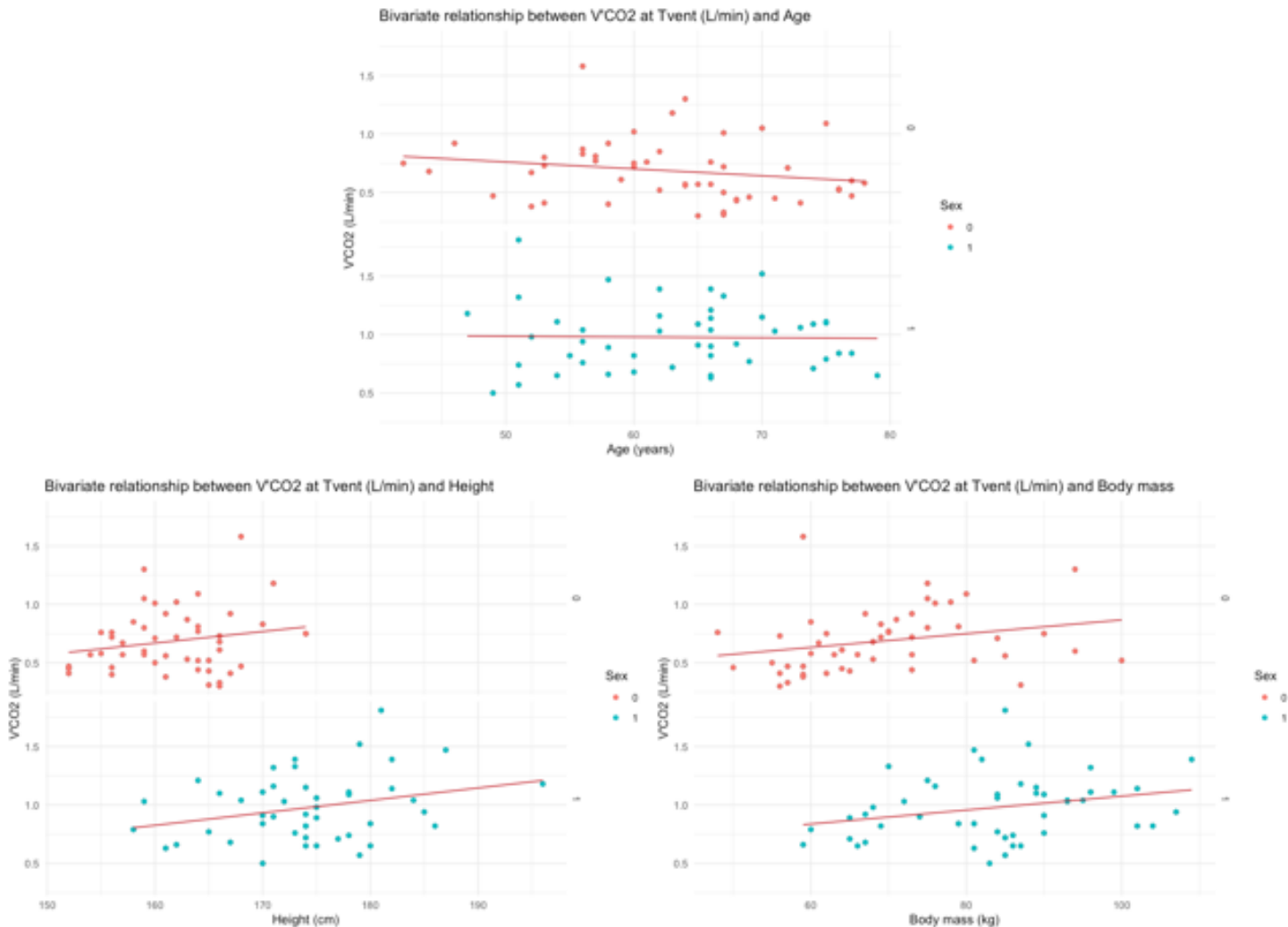
b) Bivariate relationships between explanatory variables and the rate of oxygen consumption (V'O₂) during symptom-limited incremental cardiopulmonary cycle exercise testing at the ventilatory threshold (Tvent) in Canadian females (closed blue circles; n=49) and males (closed red circles; n=47) aged 40-80 years.
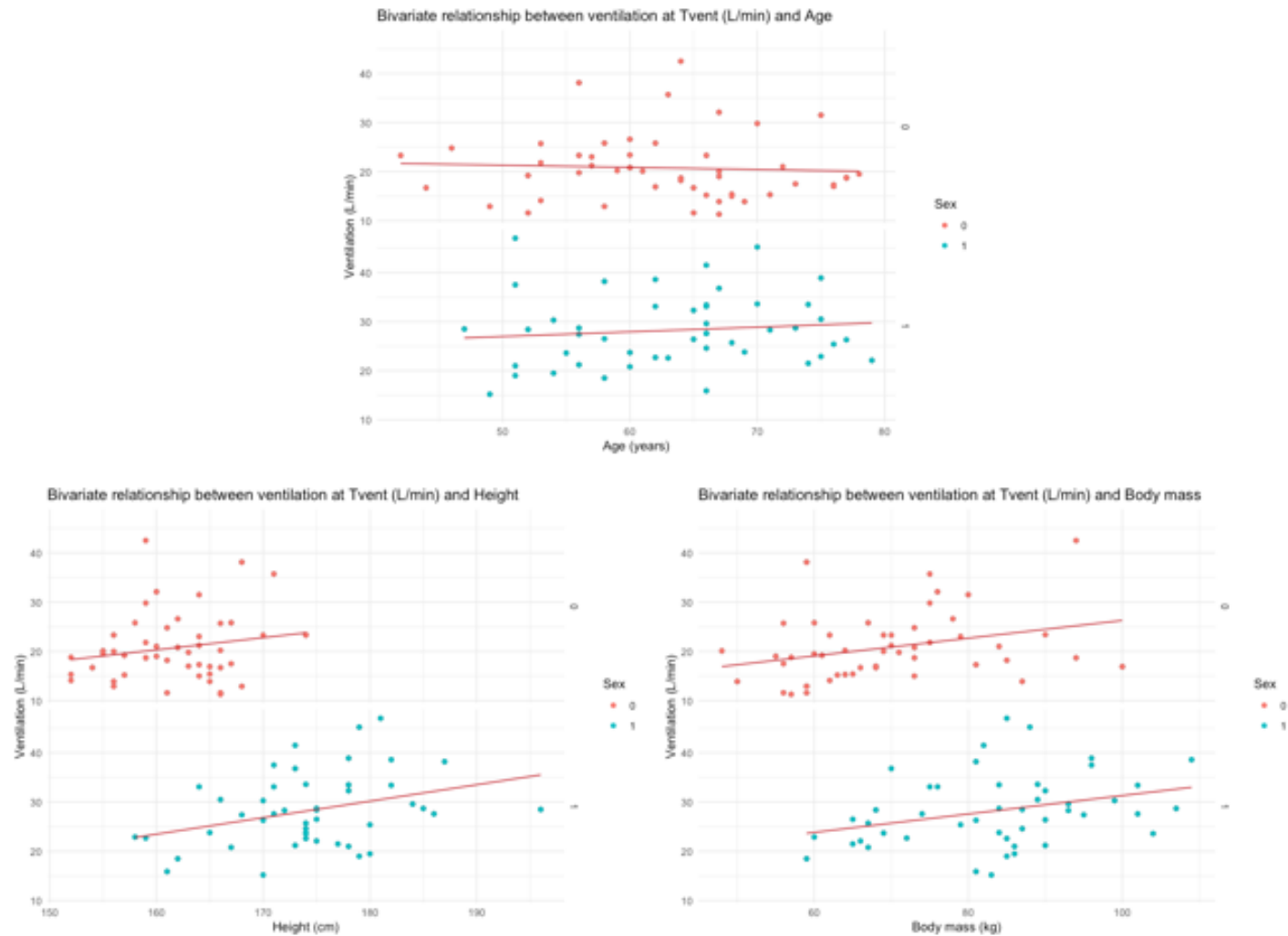

Bivariate relationship between V'O2 at Tvent (L/min) and Age

Bivariate relationship between V'O2 at Tvent (L/min) and Height

Bivariate relationship between V'O2 at Tvent (L/min) and Body mass

c) Bivariate relationships between explanatory variables and the rate of CO_2 production (V'CO_2) during symptom-limited incremental cardiopulmonary cycle exercise testing at the ventilatory threshold (Tvent) in Canadian females (closed blue circles; n=49) and males (closed red circles; n=47) aged 40-80 years.
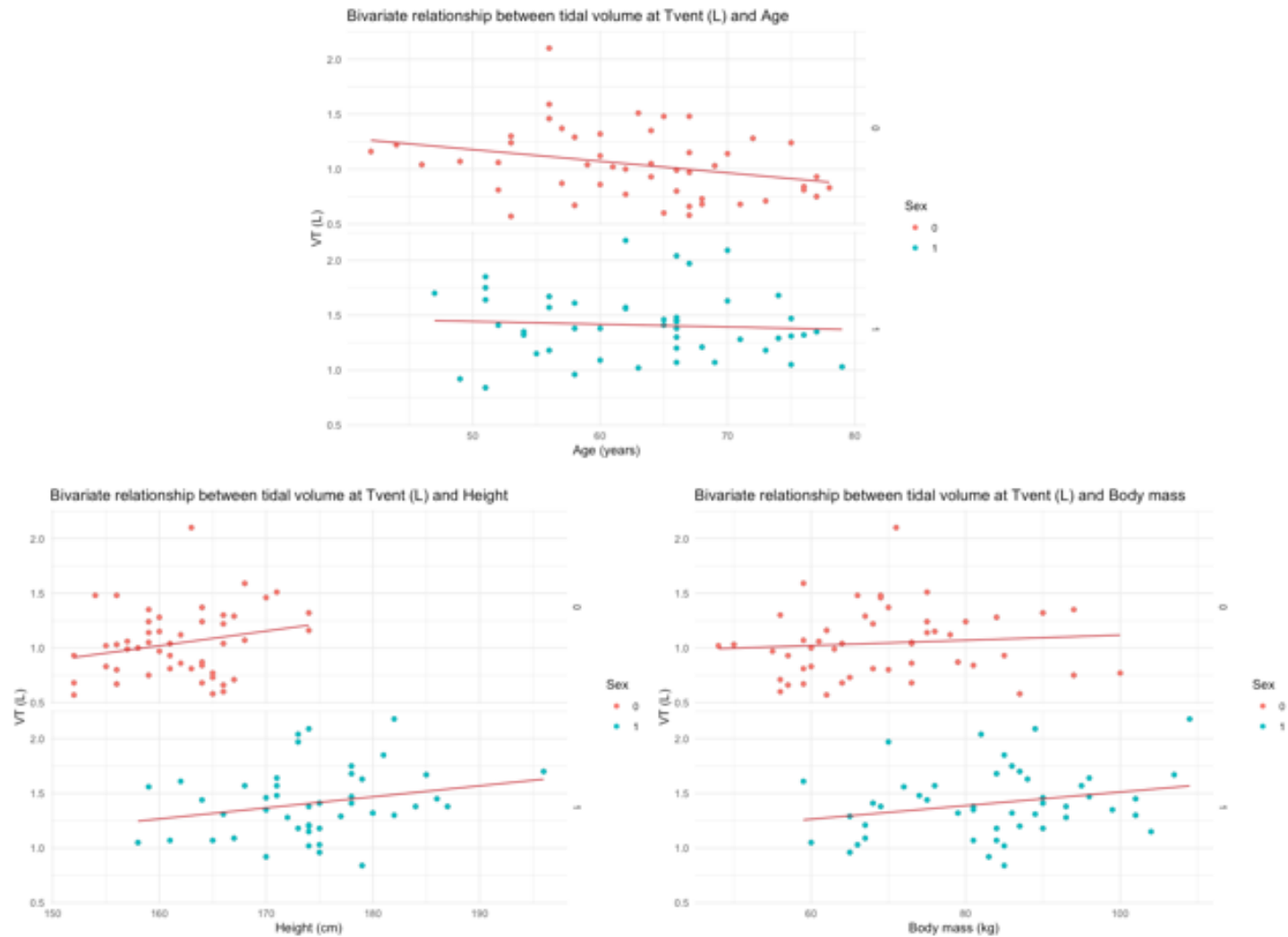
d) Bivariate relationships between explanatory variables and minute ventilation during symptom-limited incremental cardiopulmonary cycle exercise testing at the ventilatory threshold (Tvent) in Canadian females (closed blue circles; n=49) and males (closed red circles; n=47) aged 40-80 years.
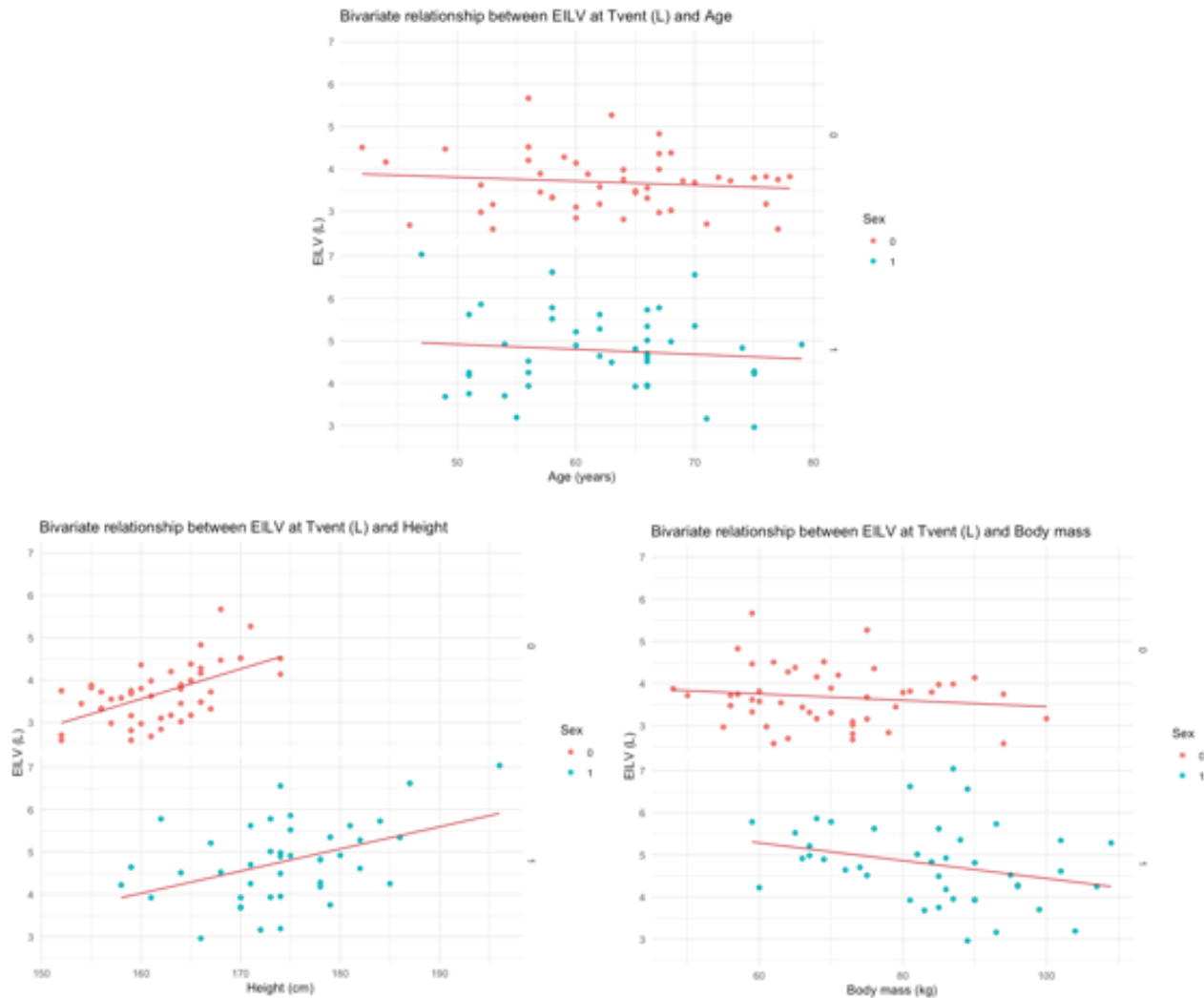
e) Bivariate relationships between explanatory variables and tidal volume (V_T) during symptom-limited incremental cardiopulmonary cycle exercise testing at the ventilatory threshold (Tvent) in Canadian females (closed blue circles; n=49) and males (closed red circles; n=47) aged 40-80 years.

Bivariate relationship between tidal volume at Tvent (L) and Age

Bivariate relationship between tidal volume at Tvent (L) and Height

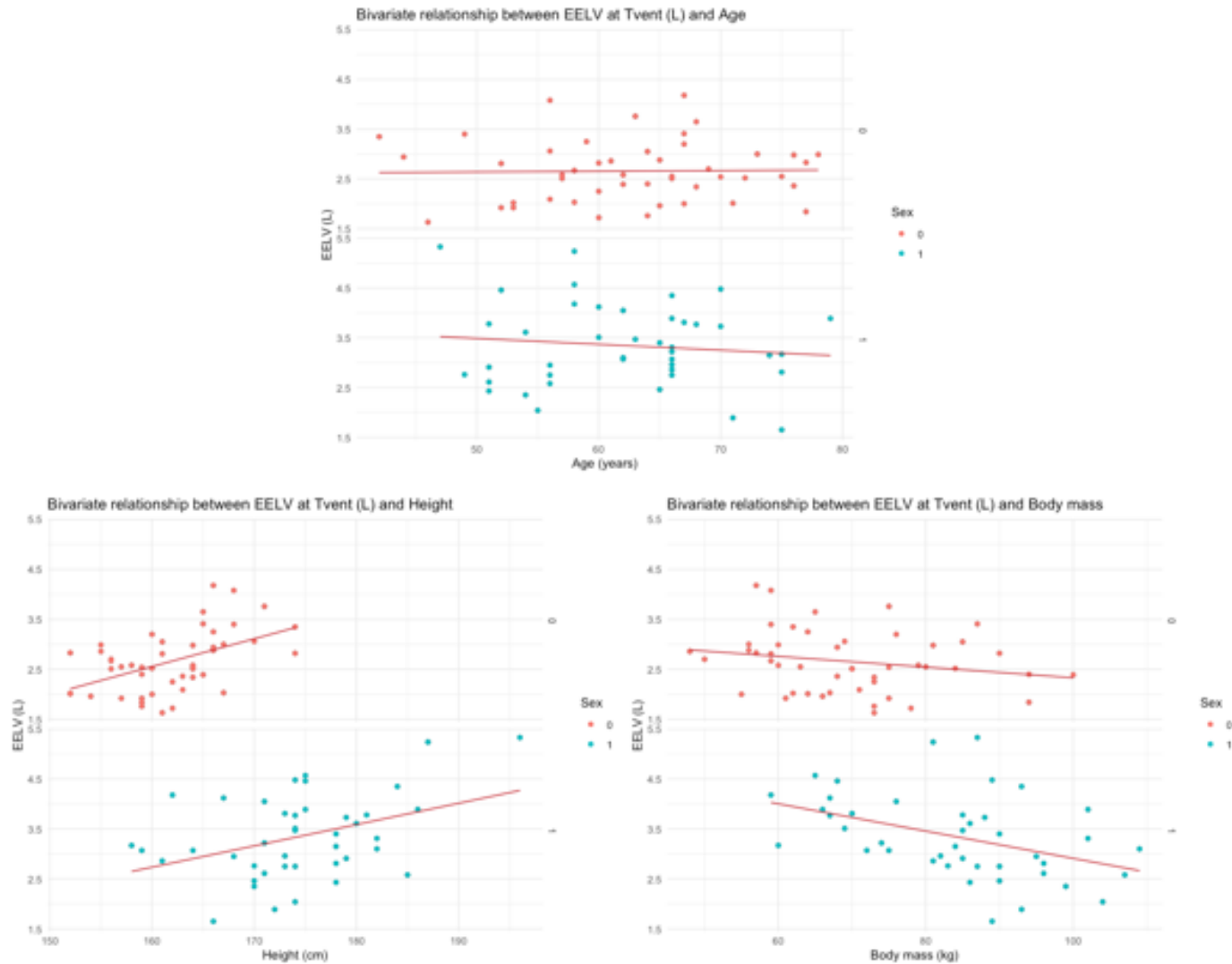Bivariate relationship between tidal volume at Tvent (L) and Body mass

f) Bivariate relationships between explanatory variables and inspiratory capacity (IC) during symptom-limited incremental cardiopulmonary cycle exercise testing at the ventilatory threshold (Tvent) in Canadian females (closed blue circles; n=49) and males (closed red circles; n=47) aged 40-80 years.
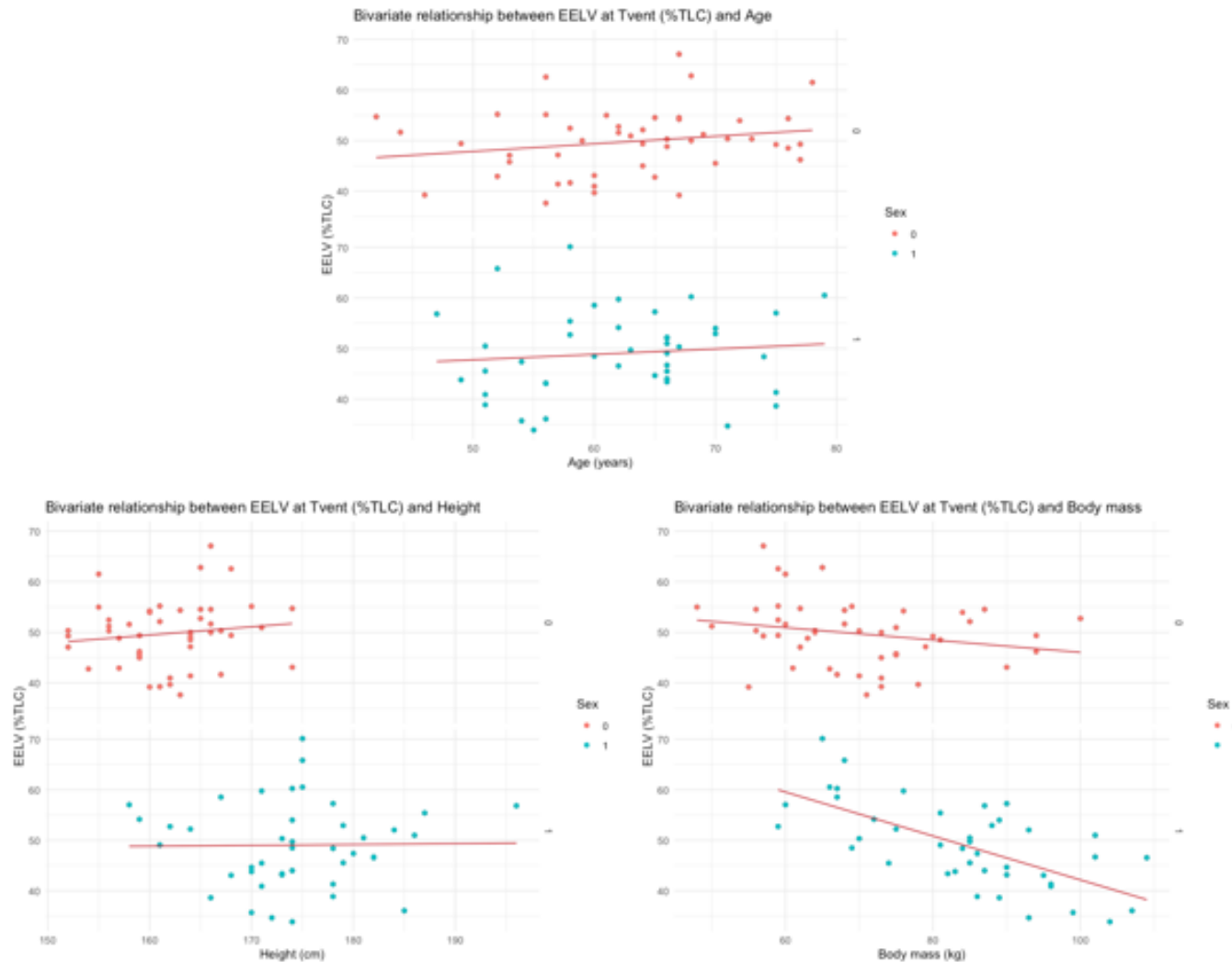

Bivariate relationship between IC at Tvent (L) and Age

Bivariate relationship between IC at Tvent (L) and Height

Bivariate relationship between IC at Tvent (L) and Body mass

g) Bivariate relationships between explanatory variables and end-inspiratory lung volume (EILV) during symptom-limited incremental cardiopulmonary cycle exercise testing at the ventilatory threshold (Tvent) in Canadian females (closed blue circles; n=49) and males (closed red circles; n=47) aged 40-80 years.

h) Bivariate relationships between explanatory variables and end-expiratory lung volume (EELV) during symptom-limited incremental cardiopulmonary cycle exercise testing at the ventilatory threshold (Tvent) in Canadian females (closed blue circles; n=49) and males (closed red circles; n=47) aged 40-80 years.

i) Bivariate relationships between explanatory variables and end-expiratory lung volume (EELV) expressed as a percentage of total lung capacity (TLC) during symptom-limited incremental cardiopulmonary cycle exercise testing at the ventilatory threshold (Tvent) in Canadian females (closed blue circles; n=49) and males (closed red circles; n=47) aged 40-80 years.


Bivariate relationship between EELV at Tvent (%TLC) and Age

Bivariate relationship between EELV at Tvent (%TLC) and Height

Bivariate relationship between EELV at Tvent (%TLC) and Body mass

j) Correlation matrices for explanatory variables and CPET responses at the ventilatory threshold during symptom-limited incremental cardiopulmonary cycle exercise testing at the ventilatory threshold (Tvent) in Canadian females (a) and males (b) aged 40-80 years


a) Females (n=49)
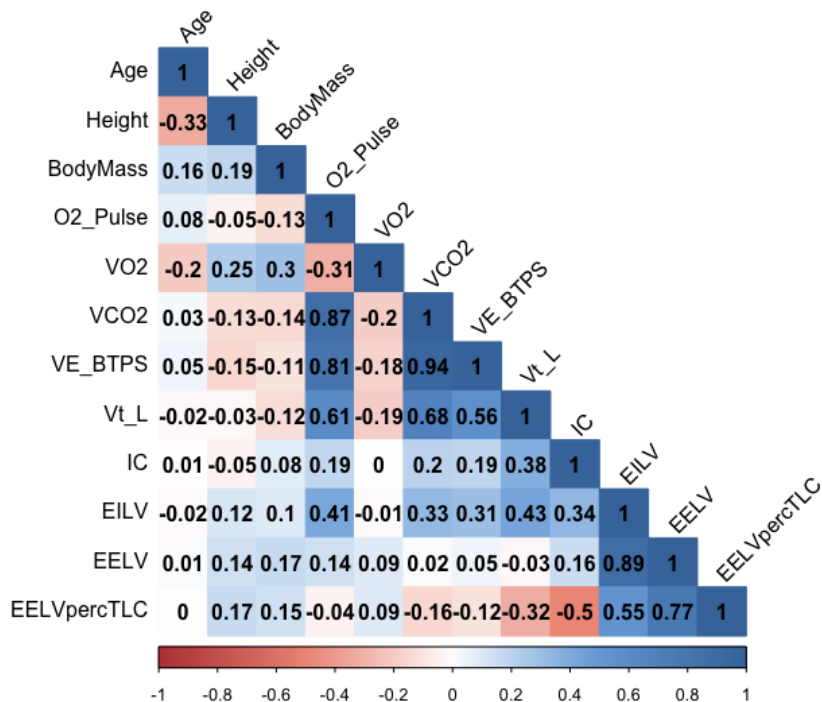
b) Males (n=47)
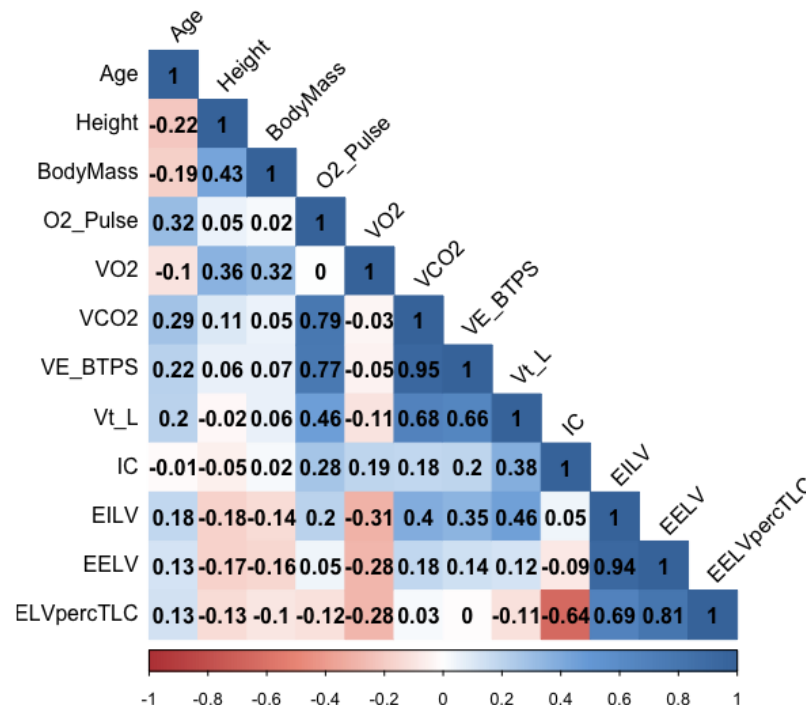
EELV, end-expiratory lung volume; EELVpercTLC, EELV as percentage of total lung capacity; EILV, end-inspiratory lung volume; IC, inspiratory capacity; O2_Pulse, oxygen pulse; VCO2, rate of carbon dioxide production; VE, minute ventilation; VO2, rate of oxygen consumption; Vt_L, tidal volume.

e-Figure 2: Age distribution of males (n=47) and females (n=49) from the Canadian Cohort Obstructive Lung Disease study that were included in the current study

a) Females
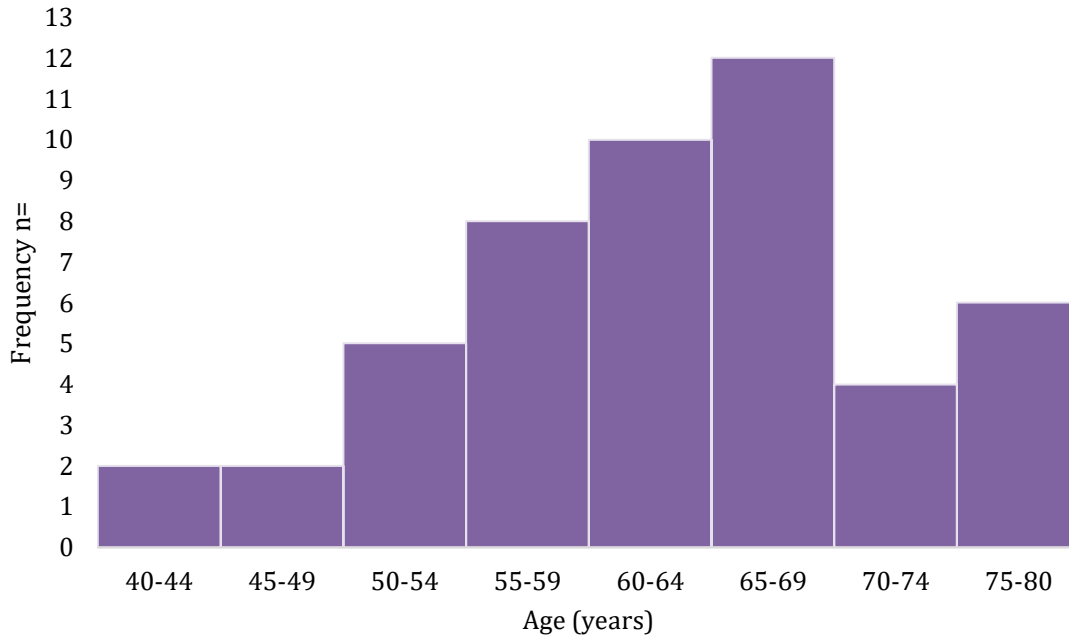
b) Males
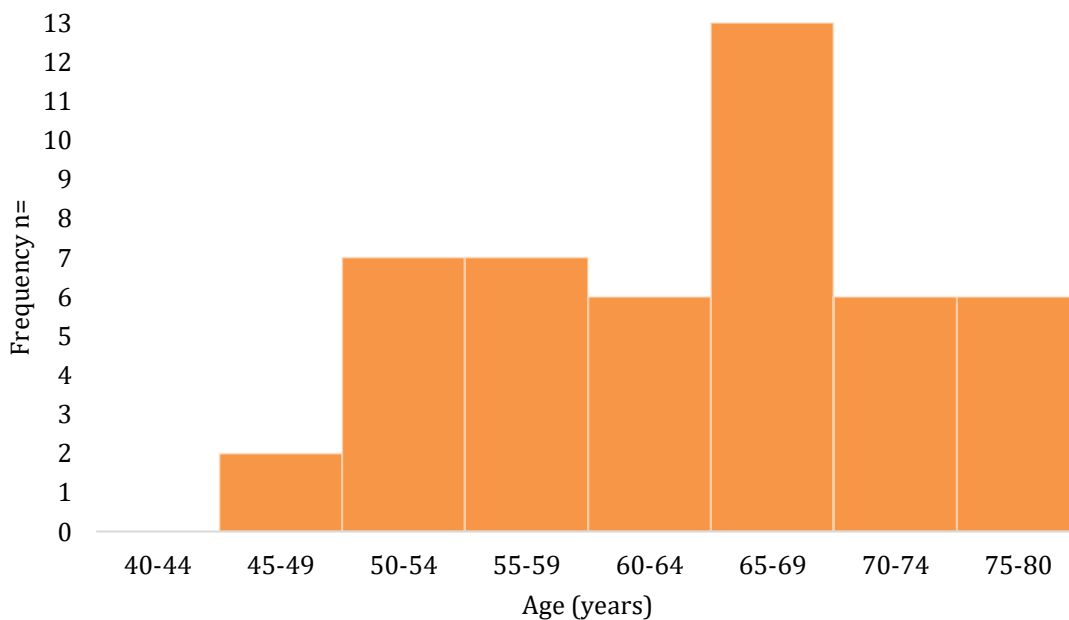
e-Figure 3: Comparison between the measured rate of O₂ consumption (V'O₂) at the ventilatory threshold during incremental cycle cardiopulmonary cycle exercise testing, and the V'O₂ predicted using the newly developed prediction models (Lewthwaite et al.) and prediction models from Jones et al. (1985) (*see reference[10] of main manuscript*) and the Study of Health in Pomerania (SHIP) cohort (Koch et al. 2009, *see reference[38] of main manuscript*).
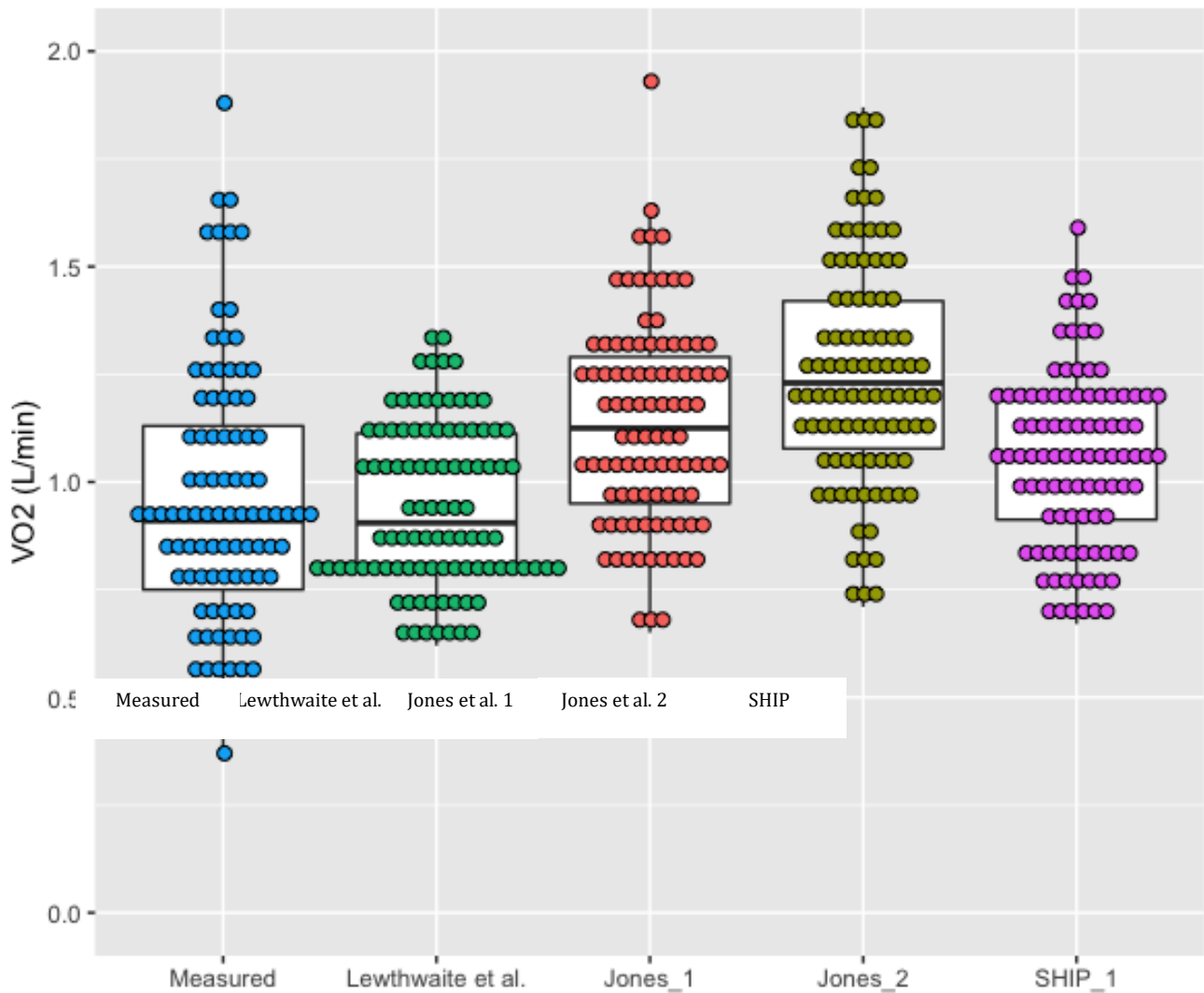
Key: Jones et al. 1 reference equations are based on participant height and age, while Jones et al. 2 reference equations additionally include participant body mass.

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