Using exercise to evaluate dyspnea and impaired functional capacity

Mike Stickland, PhD

Professor
Pulmonary Division
Faculty of Medicine
U of Alberta

Scientific Director
Respiratory Health
Strategic Clinical
Network
Alberta Health Services

Director
G.F. MacDonald
Centre for
Lung Health

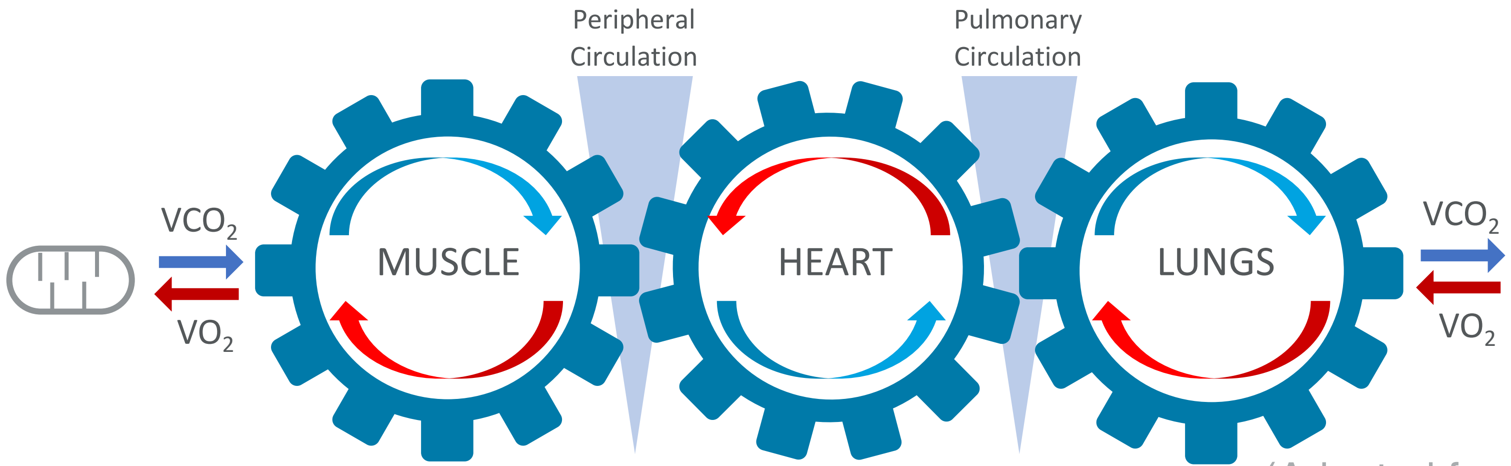
Overview

1. Exercise Physiology 101
2. Field Walking Tests – 6MWD & ISWT
3. Exercise challenge testing

   Exercise-induced bronchoconstriction
4. Cardiopulmonary exercise testing

   Determination of unexplained dyspnea

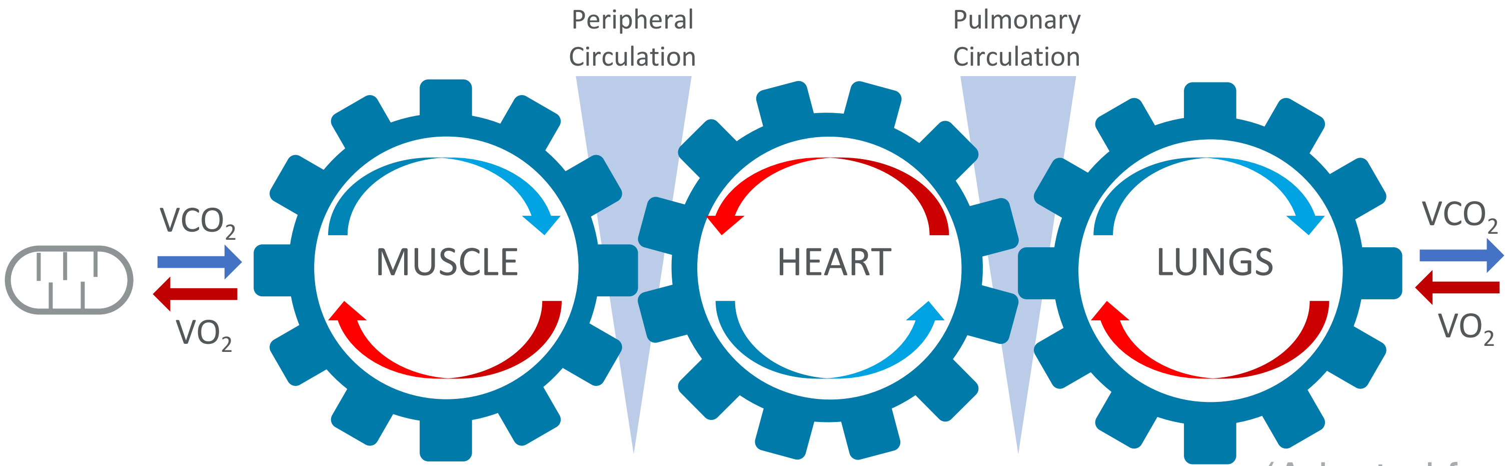
Cardiorespiratory Response to Exercise



(Adapted from Wasserman et al.)

(Dr. P.D. Wagner)

Cardiorespiratory Response to Exercise



(Adapted from Wasserman et al.)

$$VO_2 = (HR \times SV) \times (CaO_2 - CvO_2)$$

Exercise as a stress on ventilation

$$PACO_2 \sim \frac{\dot{V}CO_2}{\text{Alveolar Ventilation}}$$

$$PAO_2 \sim \frac{\text{Alveolar Ventilation}}{\dot{V}O_2}$$

$PACO_2$ = Alveolar PCO_2

PAO_2 = Alveolar PO_2

$$PETCO_2 \sim \frac{\dot{V}CO_2}{\text{Alveolar Ventilation}}$$

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$PETCO_2$ = Alveolar PCO_2

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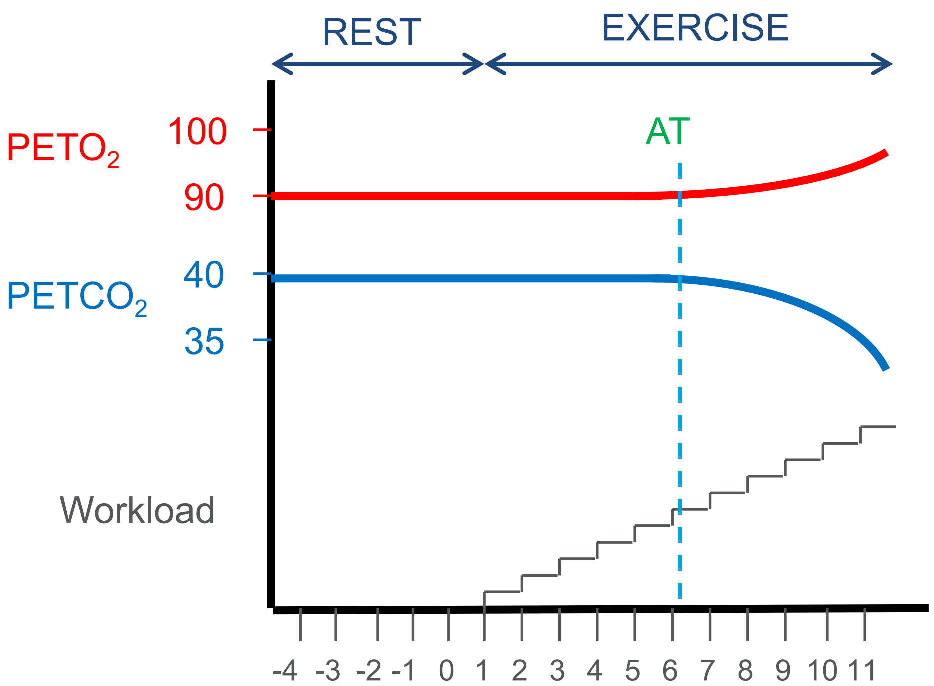


$$PETCO_2 \sim \frac{\dot{V}CO_2}{\text{Alveolar Ventilation}}$$

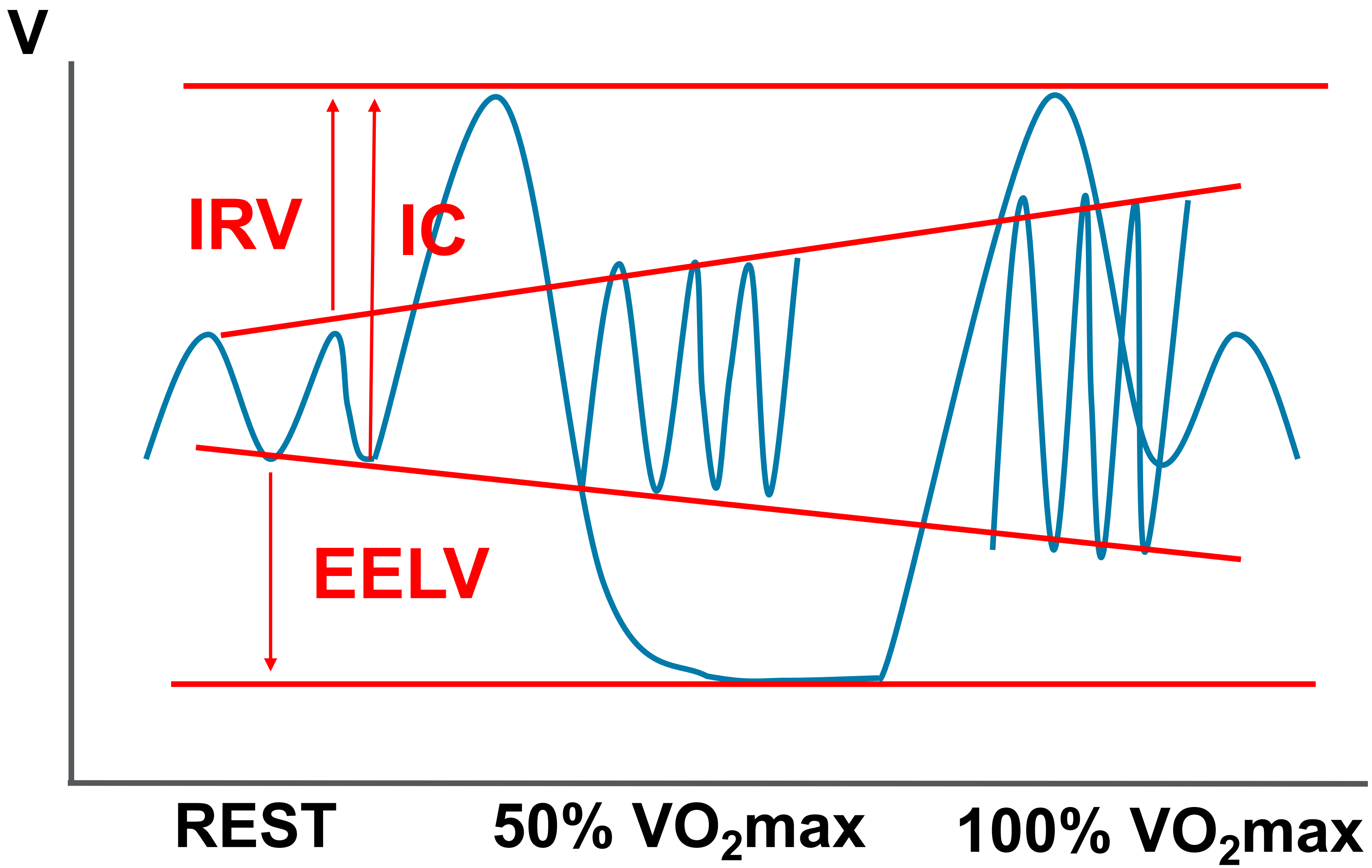
$$PETO_2 \sim \frac{\text{Alveolar Ventilation}}{\dot{V}O_2}$$

$PETCO_2$ = Alveolar PCO_2

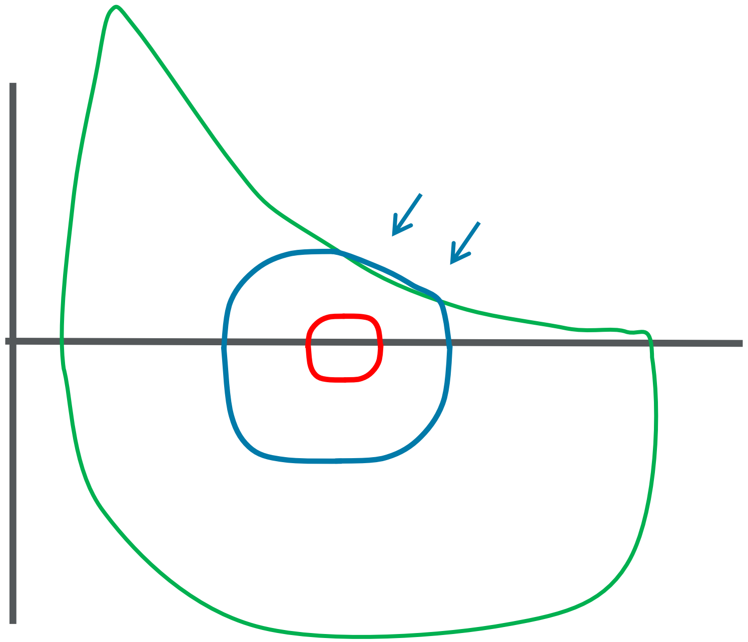
$PETO_2$ = Alveolar PO_2

In order to exercise you have to be able to ventilate!

Lung Volumes During Exercise



Expiratory Flow Limitation:

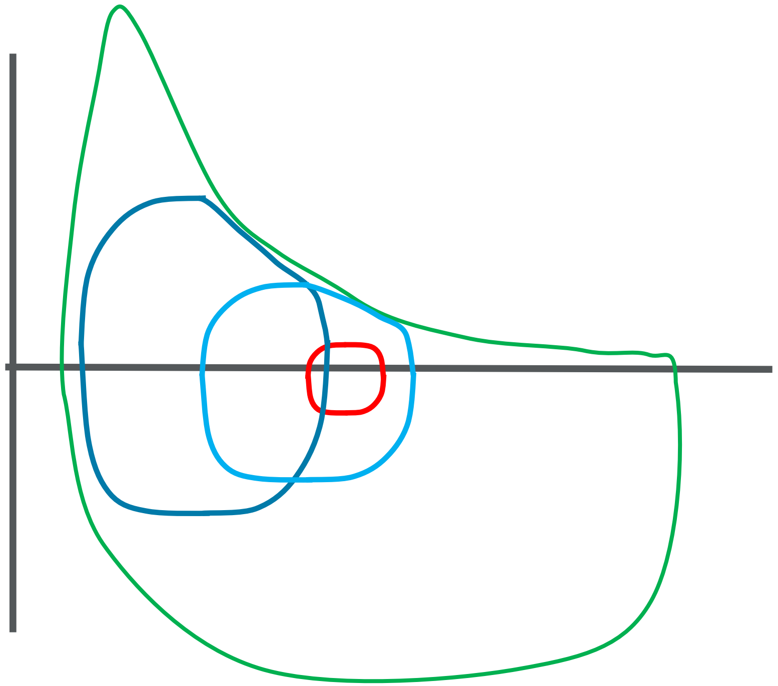


Promotes:

1. Increased work of breathing
2. Increased sensations of dyspnea
3. Dynamic hyperinflation

(Calverley & Koulouris, Eur Respir J 2005; O'Donnell & Laveneziana Eur Respir J 2006)

EFL & Dynamic Hyperinflation:



↓ IC

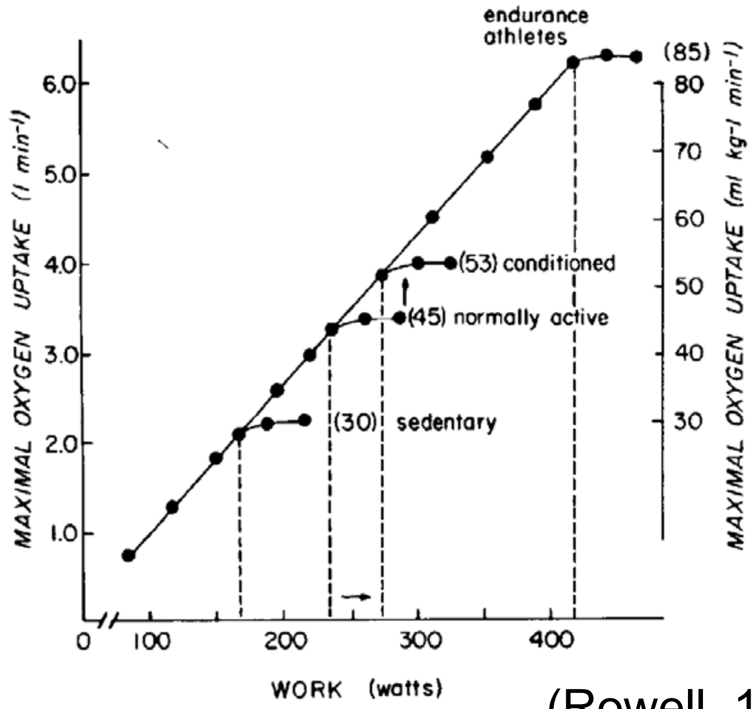
↓ IRV

Promotes:

1. Increased elastic work of breathing
2. Functional inspiratory muscle weakness by shortening diaphragm
3. Reduced ability of tidal volume to expand appropriately
4. Hypoventilation

(O'Donnell & Laveneziana Eur Respir J 2006)

Exercise as a stress on gas exchange



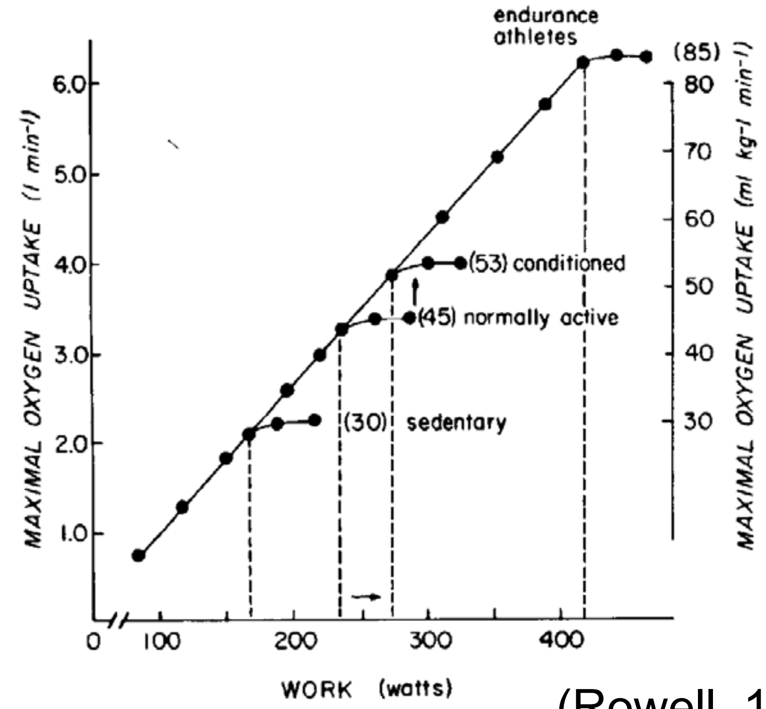
(Rowell, 1993)

$$VO_2 = (HR \times SV) \times (CaO_2 - CvO_2)$$

$$DLO_2 = \frac{\dot{V}O_2}{AaDO_2}$$

$(PAO_2 - PaO_2)$

Exercise as a stress on gas exchange



(Rowell, 1993)

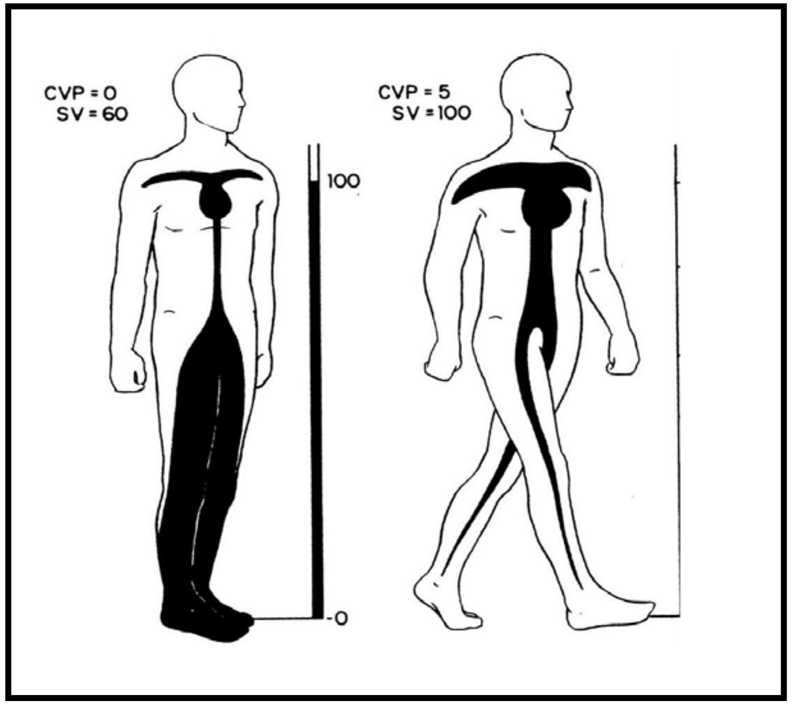
$$VO_2 = (HR \times SV) \times (CaO_2 - CvO_2)$$

$$DLO_2 = \frac{\uparrow \dot{V}O_2}{\uparrow AaDO_2}$$

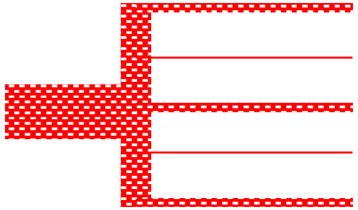
$(PAO_2 - PaO_2)$

$$\uparrow AaDO_2 \rightarrow \downarrow PaO_2$$

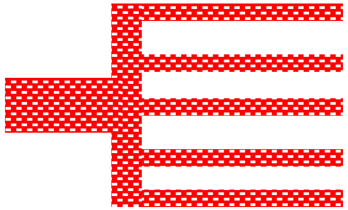
$$AaDO_2 \; (PAO_2 - PaO_2) = \frac{\uparrow \dot{V}O_2}{\uparrow DLO_2}$$



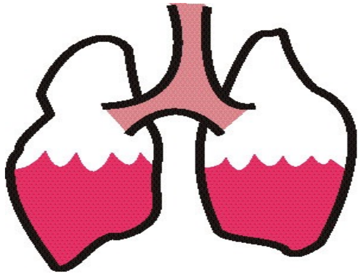
Rest



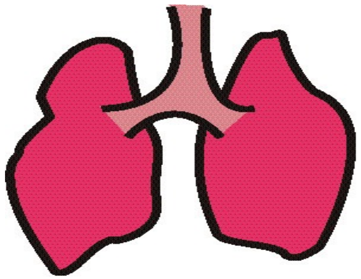
Exercise



Cap Blood Vol



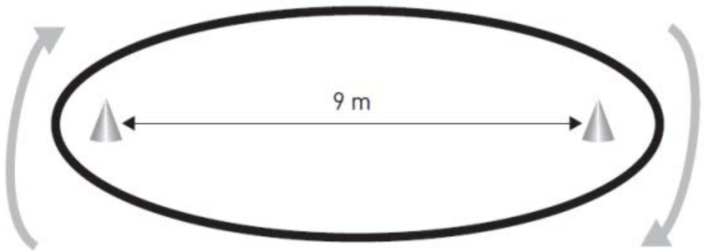
Cap Blood Vol



Field Walking Tests

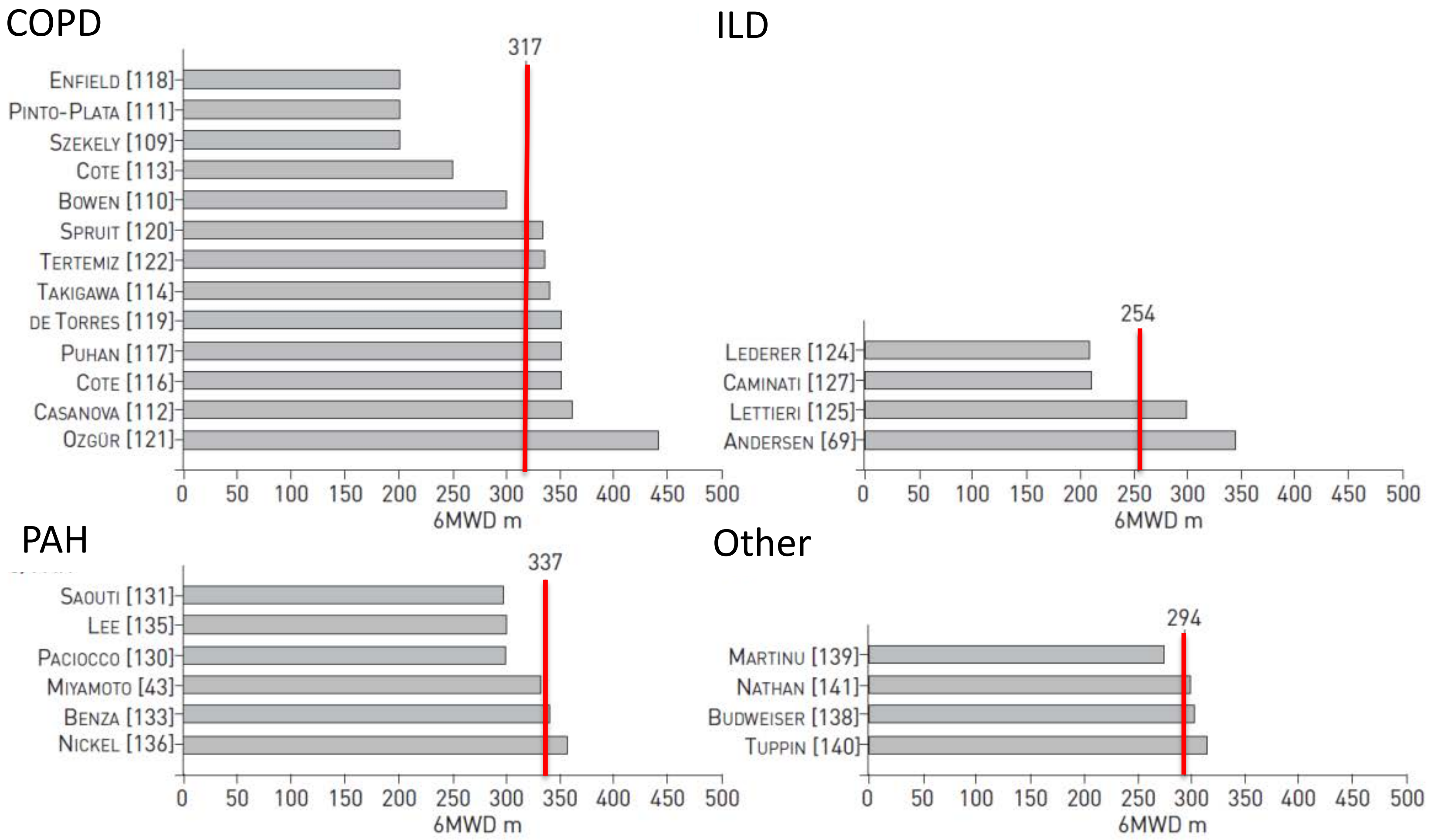
6min Walk Test

Incremental Shuttle Walk



(Holland et at. ERS/ATS Task Force, ERJ 2014)

6min Walk Distance Threshold for Survival



(Singh et at. ERS/ATS Task Force, ERJ 2014)

6min Walk Distance vs. 2yr Survival in COPD

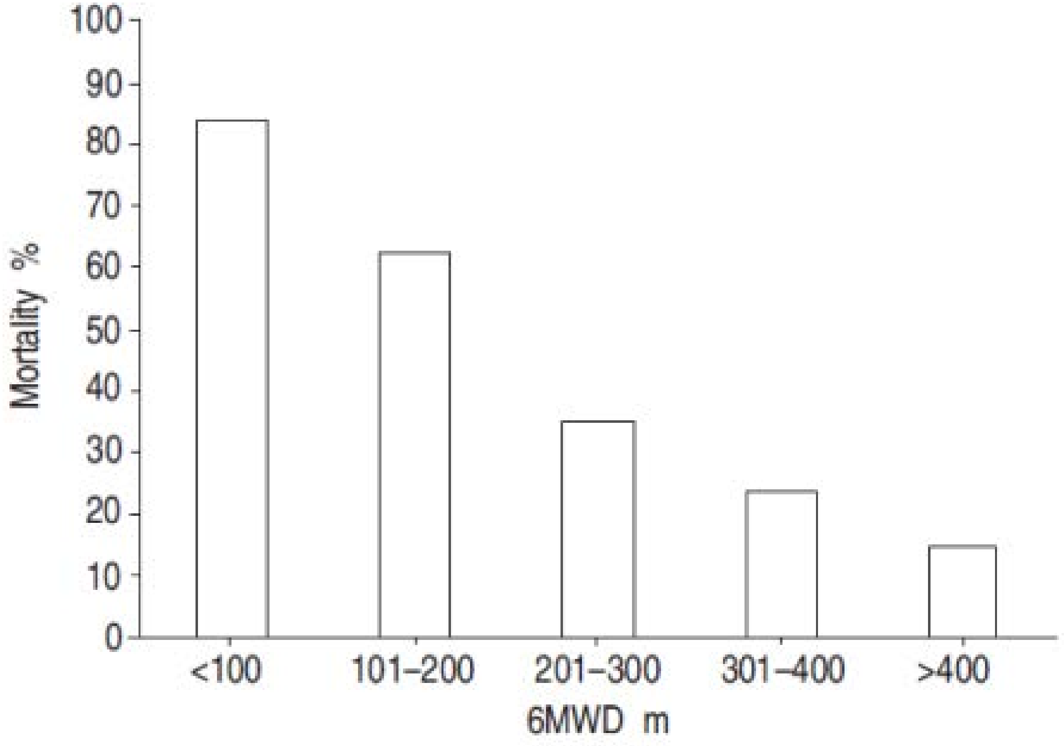


Fig. 3. – Mortality progressively decreases as the 6-min walking distance (6MWD) increases. For distances <100 m, n=19; for 101–200 m, n=61; for 201–300 m, n=57; for 301–400 m, n=46; and for >400 m, n=15.

(Pinto-Plata et al. ERJ 2004)

Equipment Required for Field Tests

- At least one chair positioned at one end of the walking course
- A validated scale to measure dyspnea and subjective fatigue (Borg 10pt)
- Sphygmomanometer for blood pressure measurement
- Pulse oximeter
- Stopwatch
- Pre-measured marks along the track/corridor
- Access to oxygen and telephone in case of an emergency
- An emergency plan
- Portable supplemental O_2 if required by patient to perform test
- Reporting sheet and pen

- 6MWT: minimum 30m track
- ISWT: 10m track

(Holland et at. ERS/ATS Task Force, ERJ 2014)

6min Walk & Incremental Shuttle Walk Test – *The Good*

- Both a valid and reliable measure of exercise capacity
- Both correlated w/ VO_{2peak}, Dyspnea, HRQOL
- Both show good responsiveness to treatment (medications, rehab etc)
- Both can identify exertional hypoxemia (nadir SpO_2)
- Both appear safe w/ few significant adverse events
- 6MWD MCID: 25-33m, ISW MCID: 47.5m (in COPD)
- ISW provides maximal intensity/speed which can facilitate Ex prescription similar to CPET

6min Walk & Incremental Shuttle Walk Test – The *not-so-good*

- 6MWD: *self-paced* & very sensitive to variations in methodology, including use of encouragement & track layout
  - Ensure standard language
- Both demonstrate learning effect (min 2 tests & take best)
- Both elicit a peak oxygen uptake VO_{2peak} that is similar to that during a cardiopulmonary exercise test (CPET)
  - As a result, the contraindications and precautions for field testing should be consistent with those used for a CPET
- 6MWD: Not ideal to objectively evaluate dyspnea (not a standardized stimulus)

Exercise Challenge Testing

- Used to identify exercise-induced bronchoconstriction

Cardiopulmonary exercise test ≠ Exercise challenge test

Practice Parameter

Pathogenesis, prevalence, diagnosis, and management of exercise-induced bronchoconstriction: a practice parameter

(Weiler et al. Annals of Allergy, Asthma & Immunology, 2010)

Exercise-induced bronchoconstriction (EIB): transient narrowing of the lower airway following exercise in the presence or absence of clinically recognized asthma

Exercise-induced asthma (EIA): should not be used b/c it implies incorrectly that exercise *causes* rather than *exacerbates/triggers* asthma

Bronchial hyperresponsiveness (BHR): increased sensitivity to an agent and is expressed as the dose/concentration that reduced FEV_1

Mechanism of EIB:

Exercise → dehydration → ↑ airway osmolarity → release inflammatory mediators (prostaglandins, leukotrienes and histamine) → ***bronchoconstriction***.

(Rundell et al., 2008)

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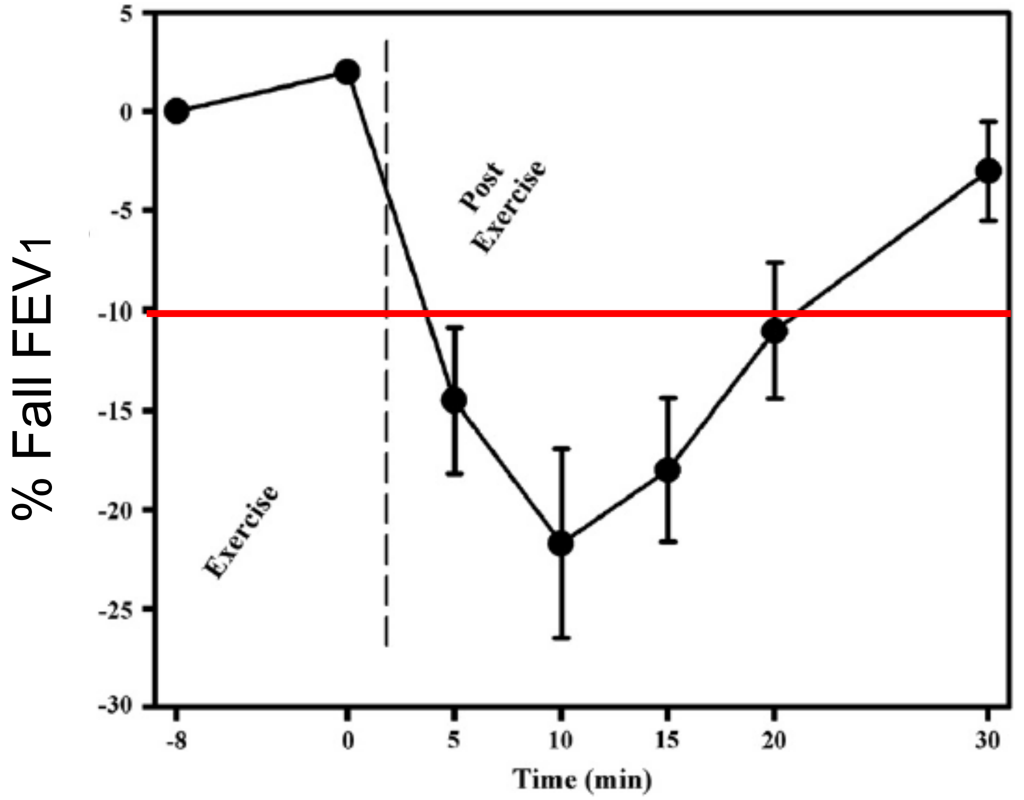
Exercise → dehydration → ↑ airway osmolarity → release inflammatory mediators (prostaglandins, leukotrienes and histamine) → ***bronchoconstriction***.

Impairment in Spirometry post-exercise:



(Rundell et al., 2008)

Exercise Challenge Protocol:

- Pulmonary medication withdrawn (8hr SABA, 48hr LABA)
- No vigorous exercise 4 hours before
- HR should reach 80-90% of max ***within 4min of exercise***
- Target HR should be ***maintained*** for 4-6 minutes
- Relative humidity (RH) <50% (compressed air)
- Air temperature 20-25° C
- Use of noseclip etc. to force mouth breathing
- Measure spirometry up to 15-20 minutes post ECT
- EIB: ≥ 10% fall in FEV_1

(Am J Respir Crit Care Med 161: 309-329, 2000)

- Only 11% of published research in EIB follow ATS criteria

(Stickland et al. J Aller Clin Immun, 2010)

Can alternatives to exercise be used to diagnose EIB?

1. Eucapnic hyperpnea

- Poor sensitivity (25-90%) and specificity (0-71%)

2. Mannitol

- Small number of studies (n=3), and modest sensitivity (58-96%) and specificity (65-78%)

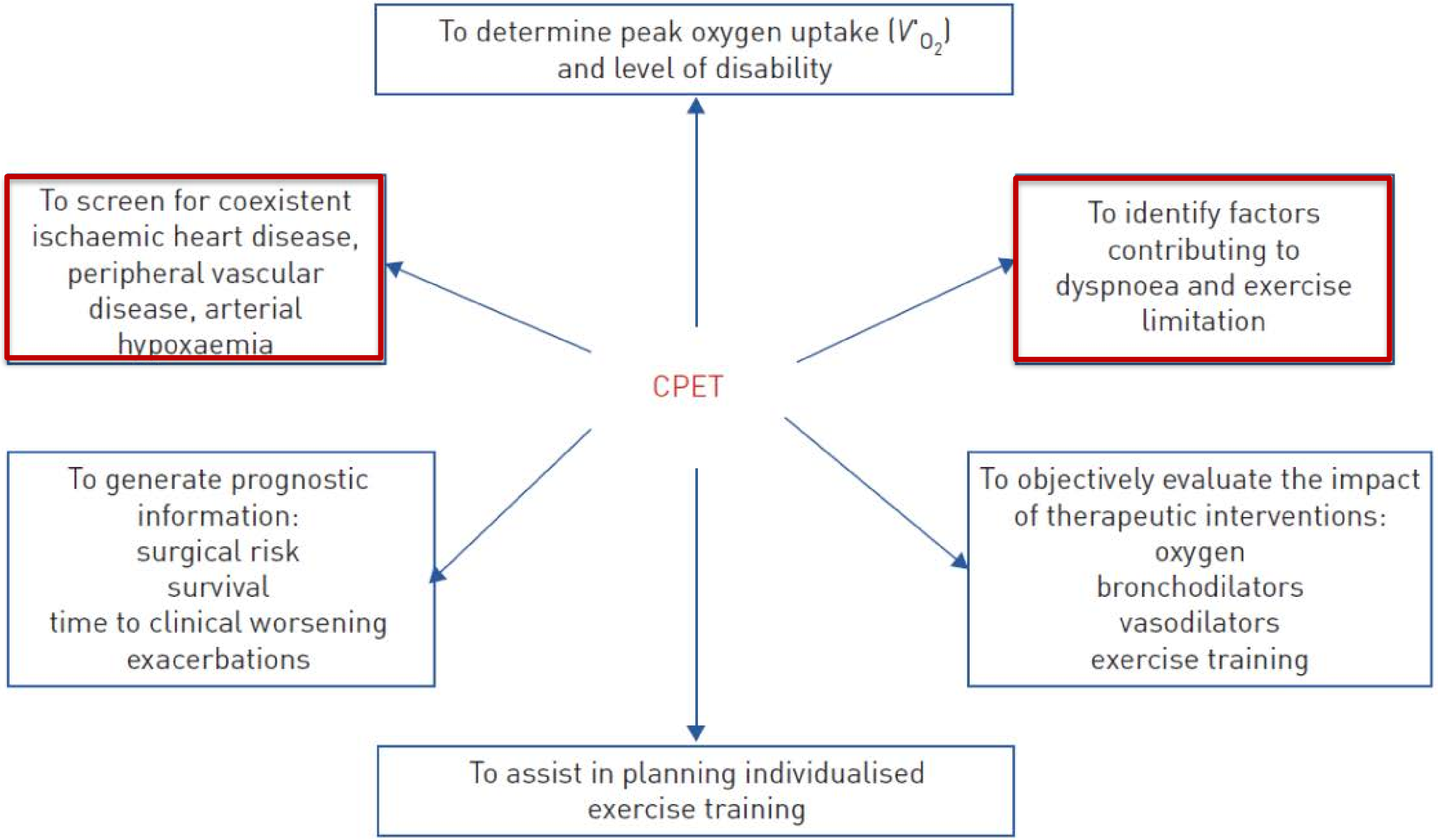
3. Methacholine

- Different pathway (indirect challenge)
- Poor sensitivity/specificity

None **of these appropriate alternatives to exercise challenge testing**

(Stickland et al. Ann Allergy Asthma Immunol, 2011)

Purpose of Cardiopulmonary Exercise Testing



Laveneziana et al. Eur Respir Rev 2021

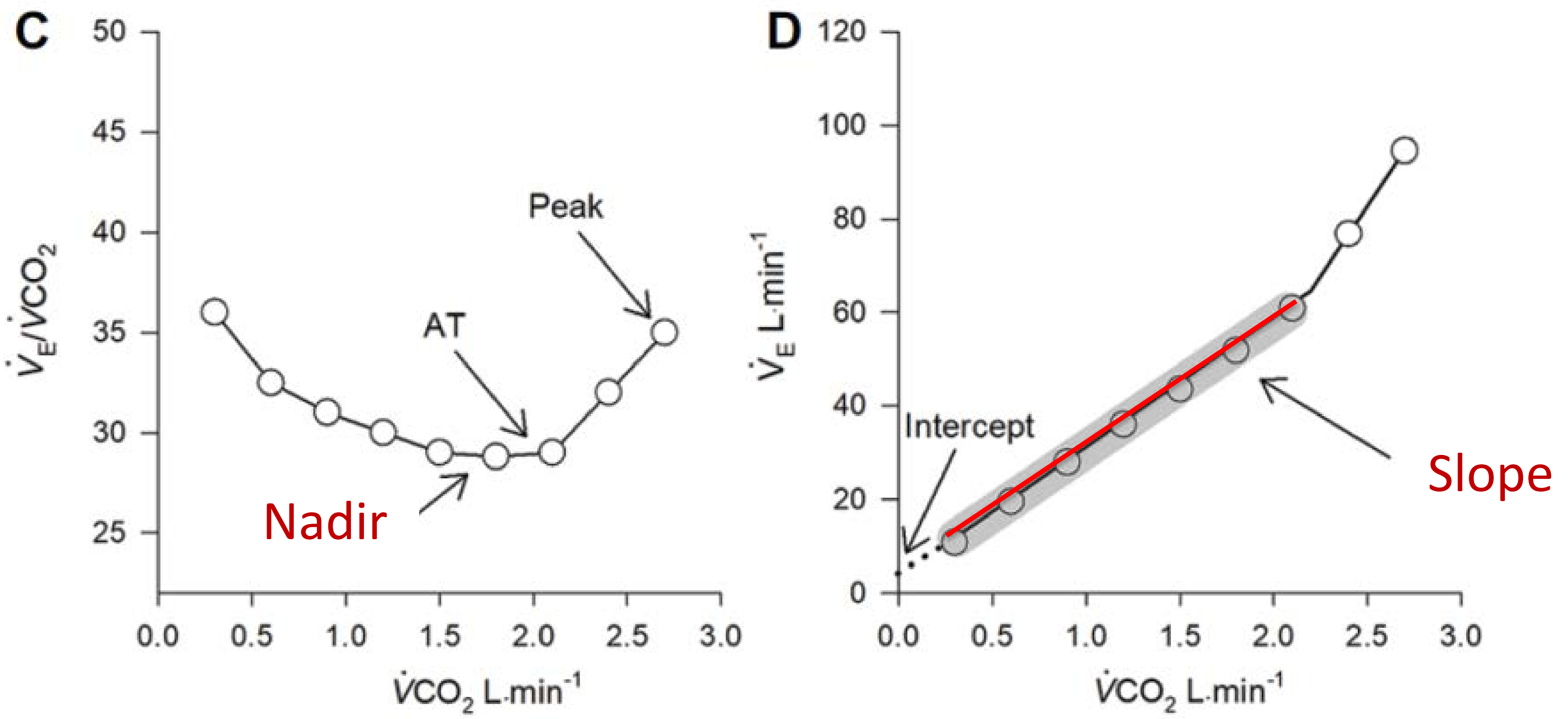
Using Cardiopulmonary Exercise Testing to Understand Dyspnea and Exercise Intolerance in Respiratory Disease

Check for updates

Michael K. Stickland, PhD; J. Alberto Neder, MD; Jordan A. Guenette, PhD; Denis E. O'Donnell, MD; and Dennis Jensen, PhD

CHEST 2022; 161(6):1505-1516

Ventilatory Efficiency
(Is ventilation appropriate for metabolic demand?)

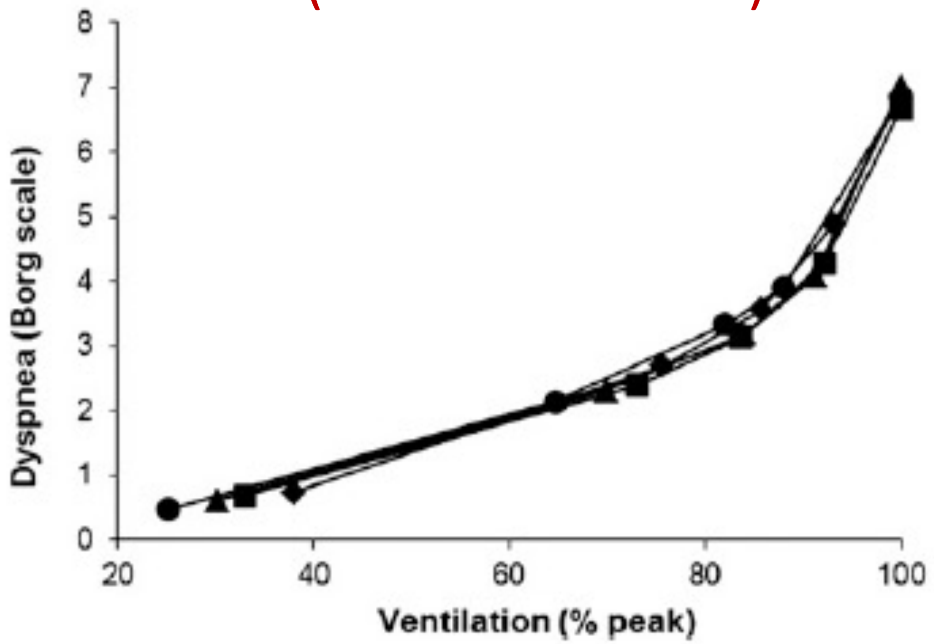


- Prediction equations available for both nadir & slope

(Phillips, Collins & Stickland, Frontiers Phys 2020)

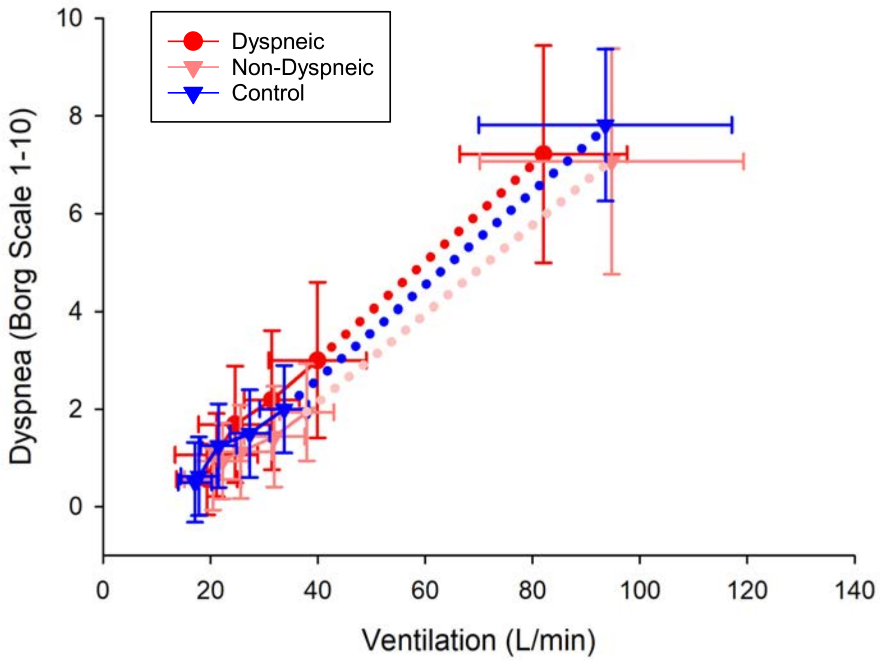
Dyspnea / Ventilation

COPD
(across severities)



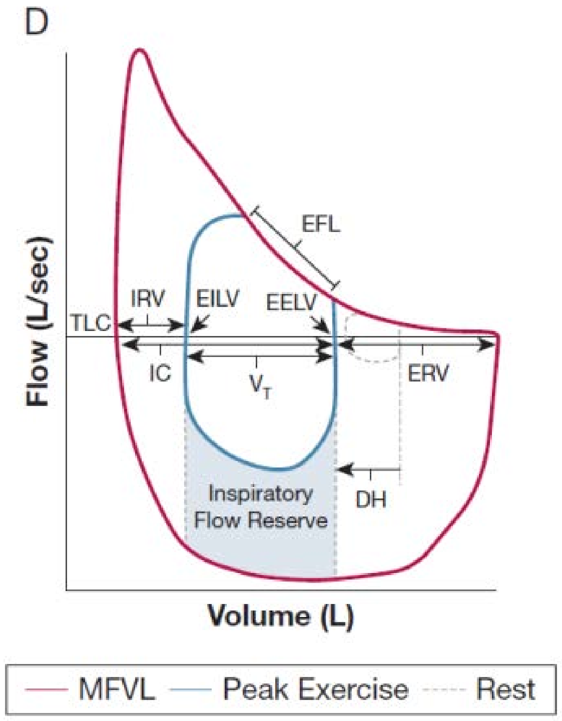
O'Donnell et al. CHEST 141(3):753–762, 2012

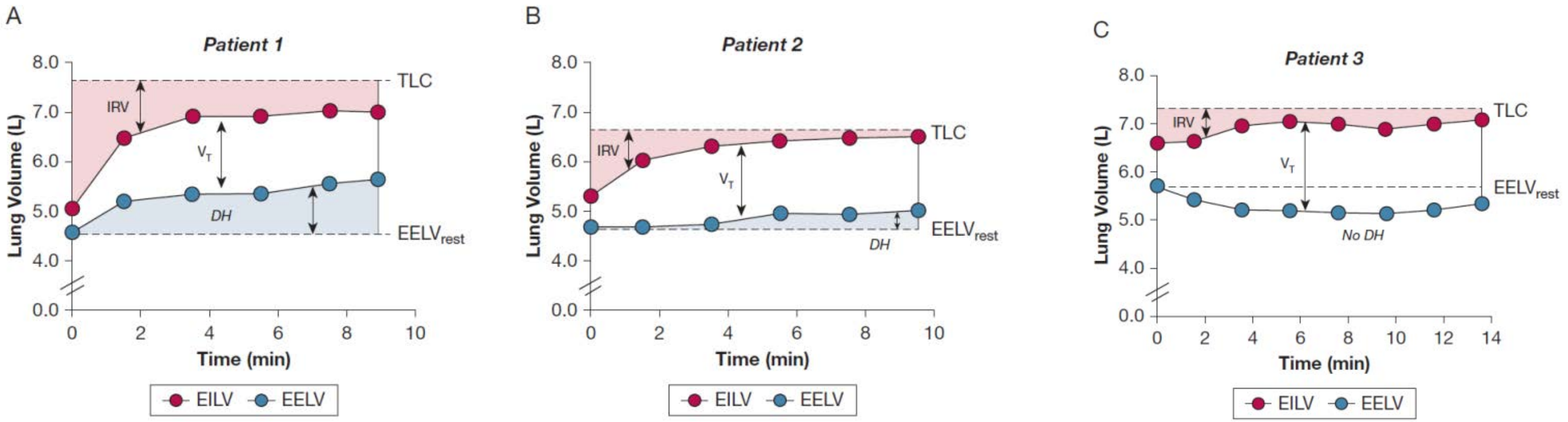
COVID



(Beaudry et al. Front Phys, 2022)

Operating Lung Volumes During Exercise (Is there hyperinflation?)

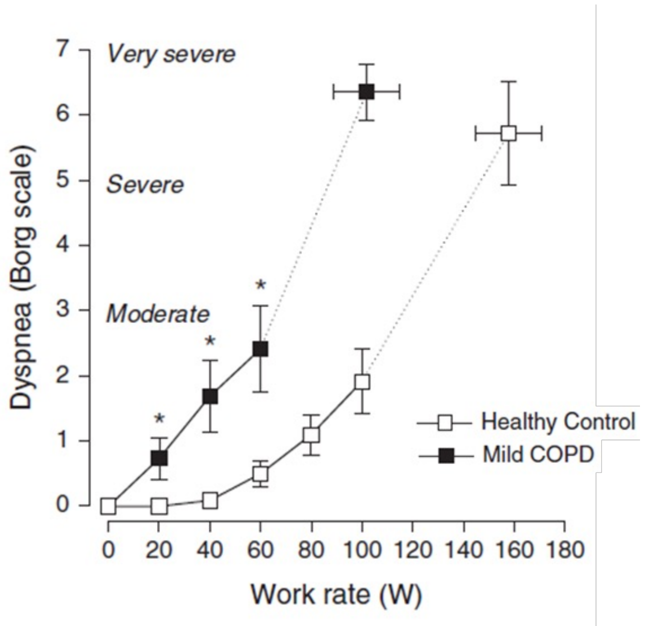




(Stickland et al. Chest, 2022)

Operating Lung Volumes During Exercise (Is there hyperinflation?)

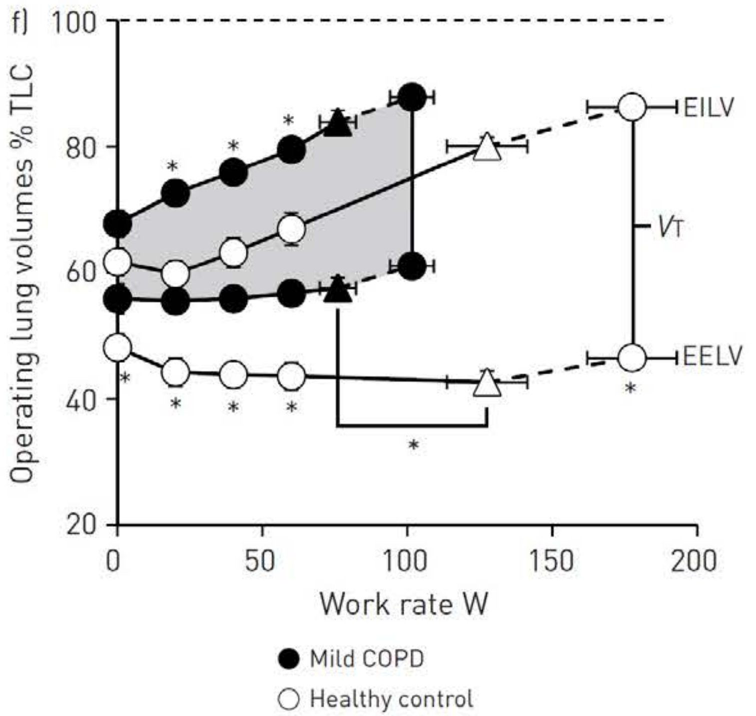
↑ Dyspnea



FEV1/FVC: 0.61,
FEV1: 94% pred,
Resting DLCO: 78% pred

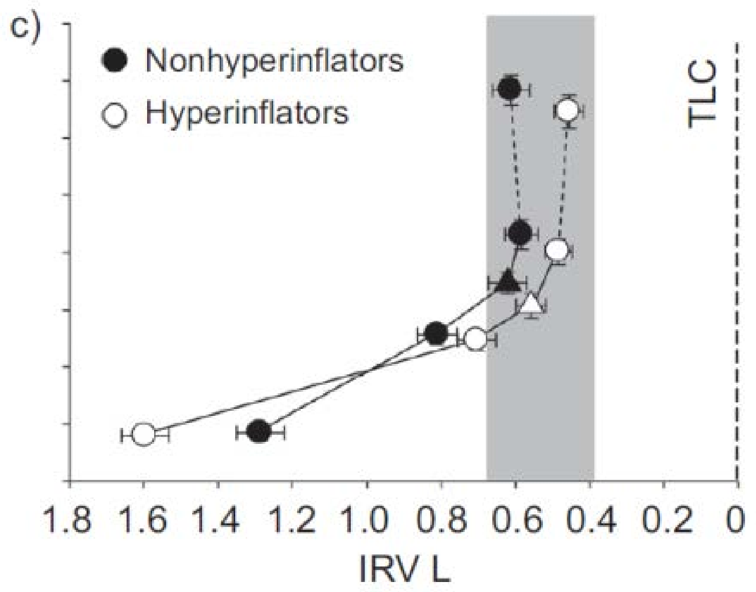
(Elbehairy et al 2015. AJRCCM)

↑ Ventilatory constraint



(Guenette et al 2014. ERJ)

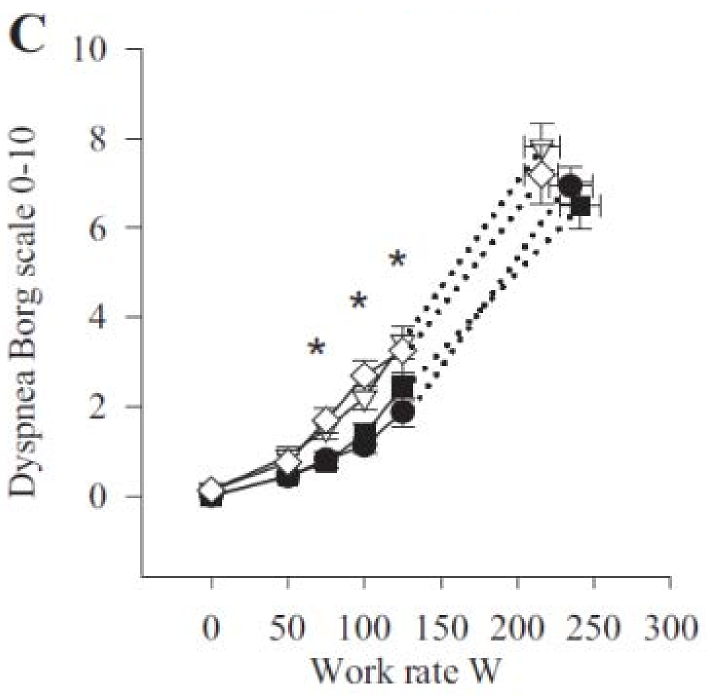
↓ IRV → ↑ Dyspnea



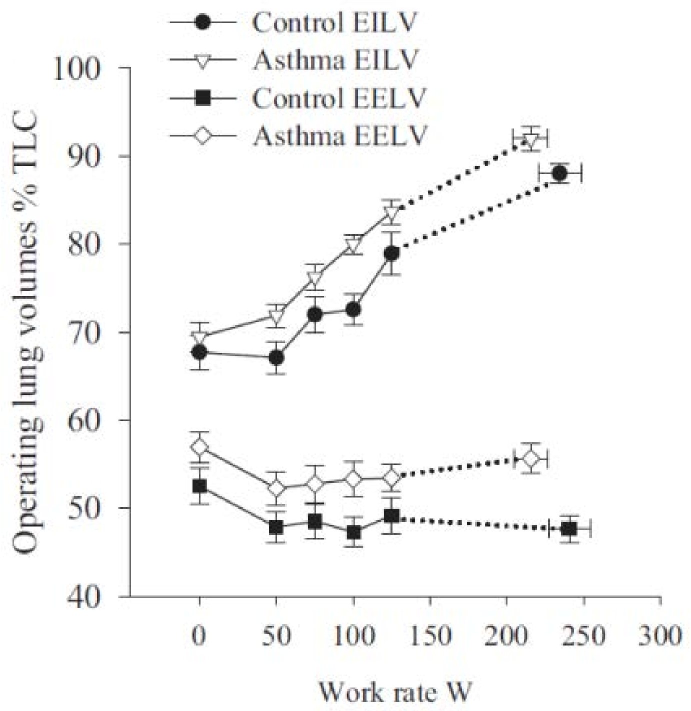
(Guenette et al 2012 ERJ)

Asthma

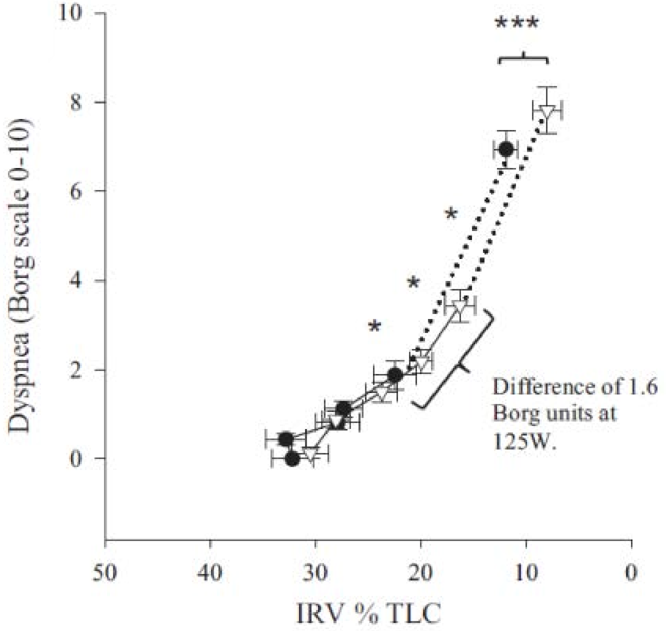
↑ Dyspnea



↑ Ventilatory constraint



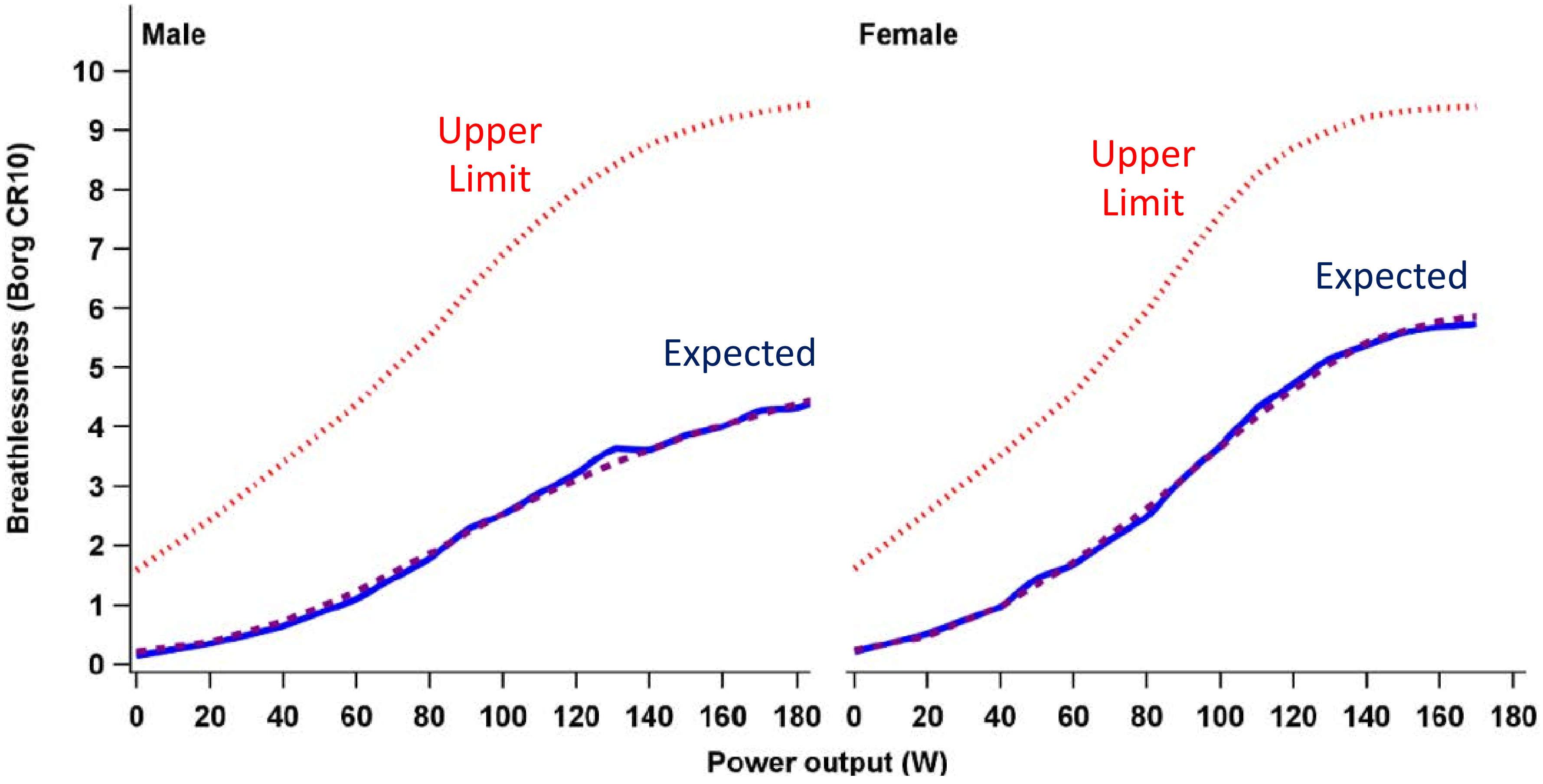
↓ IRV → ↑ Dyspnea



Age: 25 ± 4yrs
Post BD FEV_1: 101%pred

(Moore et al JAP, 2018)

Determining abnormal dyspnea response w/ CPET



- Ref equations based on sex, age & BMI
- Prediction equations for power output, VE, VO_2

(Ekstrom Annals of ATS, In-Press)

Key drivers of dyspnea that can be evaluated w/ CPET

- Exercise tolerance (VO_{2peak})
- Hypoxemia (SpO_2)
- Exagerated ventilatory response to exercise (VE/VCO_2)
- Altered lung mechanics (Reduced IRV or IC)
- Hypoventilation ($PaCO_2$)

Summary

- 6MWD & ISWT good to evaluate exercise tolerance
  - Because of no standardization of stimulus, not ideal to evaluate dyspnea
- Exercise challenge the gold standard (and only) way to identify EIB
- CPET gold standard to evaluate mechanisms of exertional dyspnea

Thank You

TABLE 5 Standardised instructions for the 6-min walk test

The aim of this test is to walk as far as possible for 6 minutes. You will walk along this hallway between the markers, as many times as you can in 6 minutes.

I will let you know as each minute goes past, and then at 6 minutes I will ask you to stop where you are. 6 minutes is a long time to walk, so you will be exerting yourself. You are permitted to slow down, to stop, and to rest as necessary, but please resume walking as soon as you are able.

Remember that the objective is to walk AS FAR AS POSSIBLE for 6 minutes, but don't run or jog.

Do you have any questions?

TABLE 6 Standardised encouragement for the 6-min walk test

1 min	You are doing well. You have 5 minutes to go.
2 min	Keep up the good work. You have 4 minutes to go.
3 min	You are doing well. You are halfway.
4 min	Keep up the good work. You have only 2 minutes left.
5 min	You are doing well. You have only 1 minute to go.
6 min	Please stop where you are.
If the patient stops during the test, every 30 s once S_{pO_2} is ⩾85%	Please resume walking whenever you feel able.

S_{pO_2}: arterial oxygen saturation measured by pulse oximetry.

TABLE 4 Absolute and relative contraindications for field walking tests

Absolute	Relative
Acute myocardial infarction (3–5 days)	Left main coronary stenosis or its equivalent
Unstable angina	Moderate stenotic valvular heart disease
Uncontrolled arrhythmias causing symptoms or haemodynamic compromise	Severe untreated arterial hypertension at rest (200 mmHg systolic, 120 mmHg diastolic)
Syncope	Tachyarrhythmias or bradyarrhythmias
Active endocarditis	High-degree atrioventricular block
Acute myocarditis or pericarditis	Hypertrophic cardiomyopathy
Symptomatic severe aortic stenosis	Significant pulmonary hypertension
Uncontrolled heart failure	Advanced or complicated pregnancy
Acute pulmonary embolus or pulmonary infarction	Electrolyte abnormalities
Thrombosis of lower extremities	Orthopaedic impairment that prevents walking
Suspected dissecting aneurysm	
Uncontrolled asthma	
Pulmonary oedema	
Room air S_{pO_2} at rest $\leqslant$85%#	
Acute respiratory failure	
Acute noncardiopulmonary disorder that may affect exercise performance or be aggravated by exercise (*i.e.* infection, renal failure, thyrotoxicosis)	
Mental impairment leading to inability to cooperate	

S_{pO_2}: arterial oxygen saturation measured by pulse oximetry. #: exercise patient with supplemental oxygen. Reproduced from [108] with permission from the publisher.

TABLE 7 Incremental and endurance shuttle walk test instructions

Incremental shuttle walk test instructions
The object of the progressive shuttle walking test is to walk as long as possible, there and back along the 10-metre course, keeping to the speed indicated by the bleeps on the audio recording. You will hear these bleeps at regular intervals.
You should walk at a steady pace, aiming to turn around the cone at one end of the course when you hear the first bleep, and at the other end when you hear the next. At first, your walking speed will be very slow, but you will need to speed up at the end of each minute. Your aim should be to follow the set rhythm for as long as you can. Each single bleep signals the end of a shuttle and each triple bleep signals an increase in walking speed. You should stop walking only when you become too breathless to maintain the required speed or can no longer keep up with the set pace.
The test is maximal and progressive. In other words, it is easier at the start and harder at the end. The walking speed for the first minute is very slow. You have 20 seconds to complete each 10-metre shuttle, so don't go too fast. The test will start in 15 seconds, so get ready at the start now. Level one starts with a triple bleep after the 4-second countdown.
Endurance shuttle walk test instructions
Walking test level (1 to 16). The instructions below are repeated for all 16 levels.
The walking speed for the first 2 minutes is fairly slow, so don't go too fast. The test will start in 10 seconds so get ready at the start now. The test starts with a triple bleep after a 4-second countdown.
At the next triple bleep increase your walking speed.