



# RESPIRATORY MUSCLE DYSFUNCTION IN CHRONIC DISEASE STATES:

## CLINICAL IMPORTANCE AND IMPLICATIONS FOR CARDIOPULMONARY REHABILITATION

**ISCVPR ANNUAL MEETING**  
INDIANAPOLIS, IN  
THURSDAY APRIL 25<sup>TH</sup>, 2024

# SESSION LEARNING OBJECTIVES

**Learning objective 1:** Compare different techniques used to assess respiratory muscle function and understand the metrics used to define respiratory muscle dysfunction.

**Learning objective 2:** Identify the prevalence and clinical importance of respiratory muscle dysfunction in different cardiopulmonary disease states.

**Learning objective 3:** Evaluate the potential role for specific respiratory muscle training as a rehabilitative strategy in patients undertaking phase II cardiopulmonary rehabilitation.

**Learning objective 4:** Recognize the practical considerations for including respiratory muscle function assessment and specific inspiratory muscle training in the phase II cardiopulmonary rehabilitation setting.



# **INSPIRATORY MUSCLE WEAKNESS & DYSFUNCTION:**

## **CLINICAL SIGNIFICANCE & HOW TO MEASURE IT**

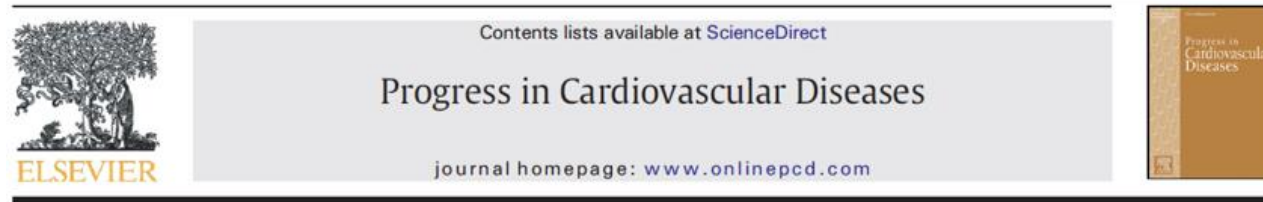
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DEPARTMENT OF CARDIOVASCULAR MEDICINE  
MAYO CLINIC FLORIDA



# NO DISCLOSURES

# WHAT IF I SAID...

THE ASSESSMENT OF INSPIRATORY MUSCLE FUNCTION SHOULD BE STANDARD IN ALL PATIENTS ENROLLED IN PHASE II CR OR PR.



Inspiratory muscle weakness in cardiovascular diseases: Implications for cardiac rehabilitation



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Editorial

## **Respiratory Muscle Weakness in Patients with Heart Failure: Time to Make It a Standard Clinical Marker and a Need for Novel Therapeutic Interventions?**

BRYAN J. TAYLOR, PHD, AND T. SCOTT BOWEN, PHD

*Leeds, UK*

# LEARNING OBJECTIVES

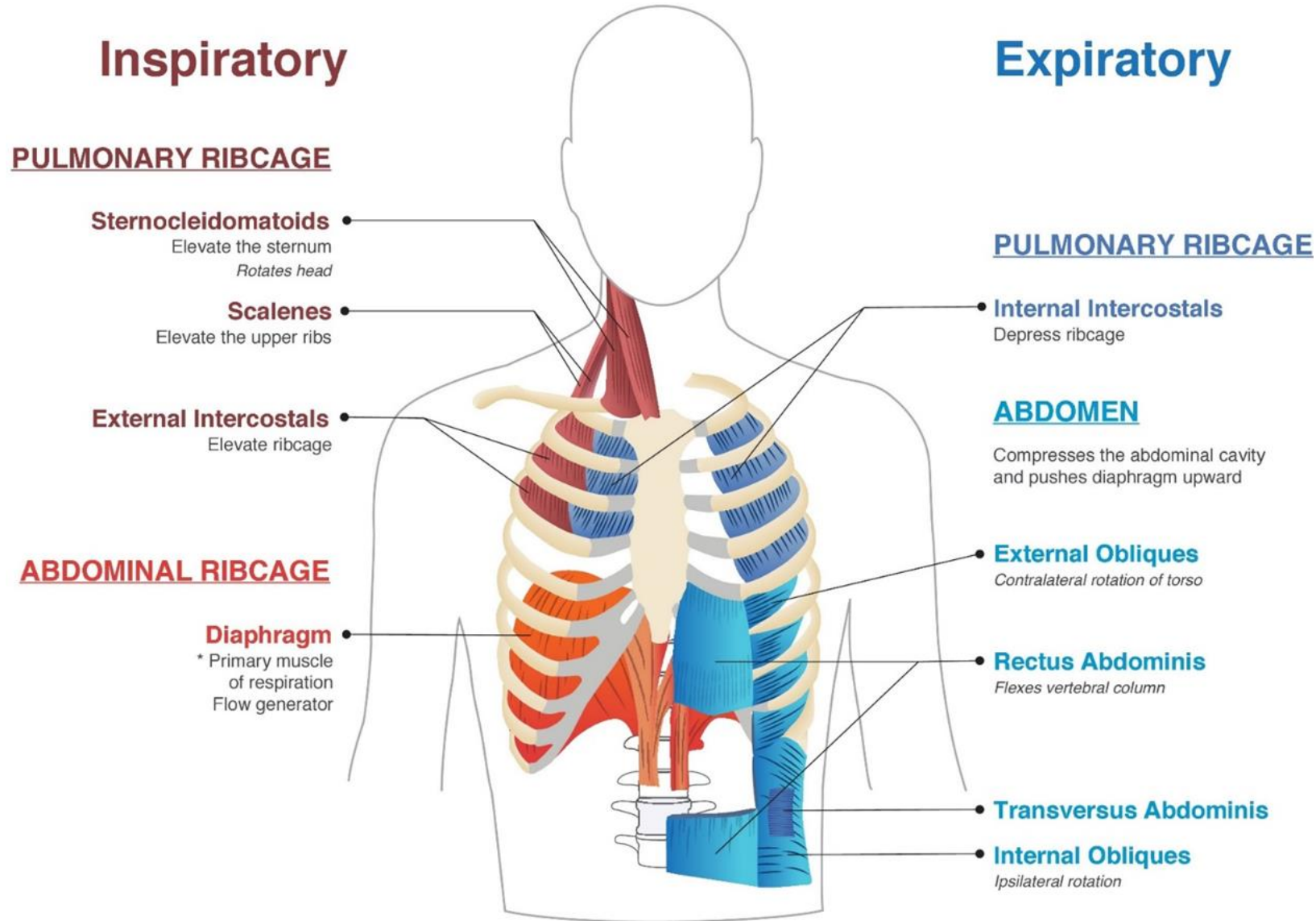
**Learning objective 1:** Identify the key muscles of breathing; understand their basic structure and function.

**Learning objective 2:** Define respiratory muscle dysfunction and weakness. Identify the clinical importance of inspiratory muscle dysfunction in different cardiopulmonary disease states.

**Learning objective 3:** Compare different techniques used to assess inspiratory muscle function and understand the metrics used to define respiratory muscle dysfunction.

# 1 THE RESPIRATORY MUSCLES

# THE RESPIRATORY MUSCLES







# 2

# INSPIRATORY MUSCLE WEAKNESS & DYSFUNCTION

# WEAKNESS & DYSFUNCTION

ANY PROCESS THAT INTERFERES WITH DIAPHRAGMATIC INNERVATION, CONTRACTILE MUSCLE FUNCTION, OR MECHANICAL COUPLING TO THE CHEST WALL.



## **Aging, sarcopenia**

General muscle atrophy, fiber type shift (II → I), contractile protein wasting



## **Paralysis & elevation**

Unilateral or bilateral; neurologic or trauma (phrenic nerve)



## **Accelerated in CHF, COPD, etc.**

Increased oxidative stress, increased proteolysis



## **Diaphragm weakness, dysfunction**

Decreased muscle mass, contractility (*thickening*), excursion (*motility*)



## **Lung hyperinflation**

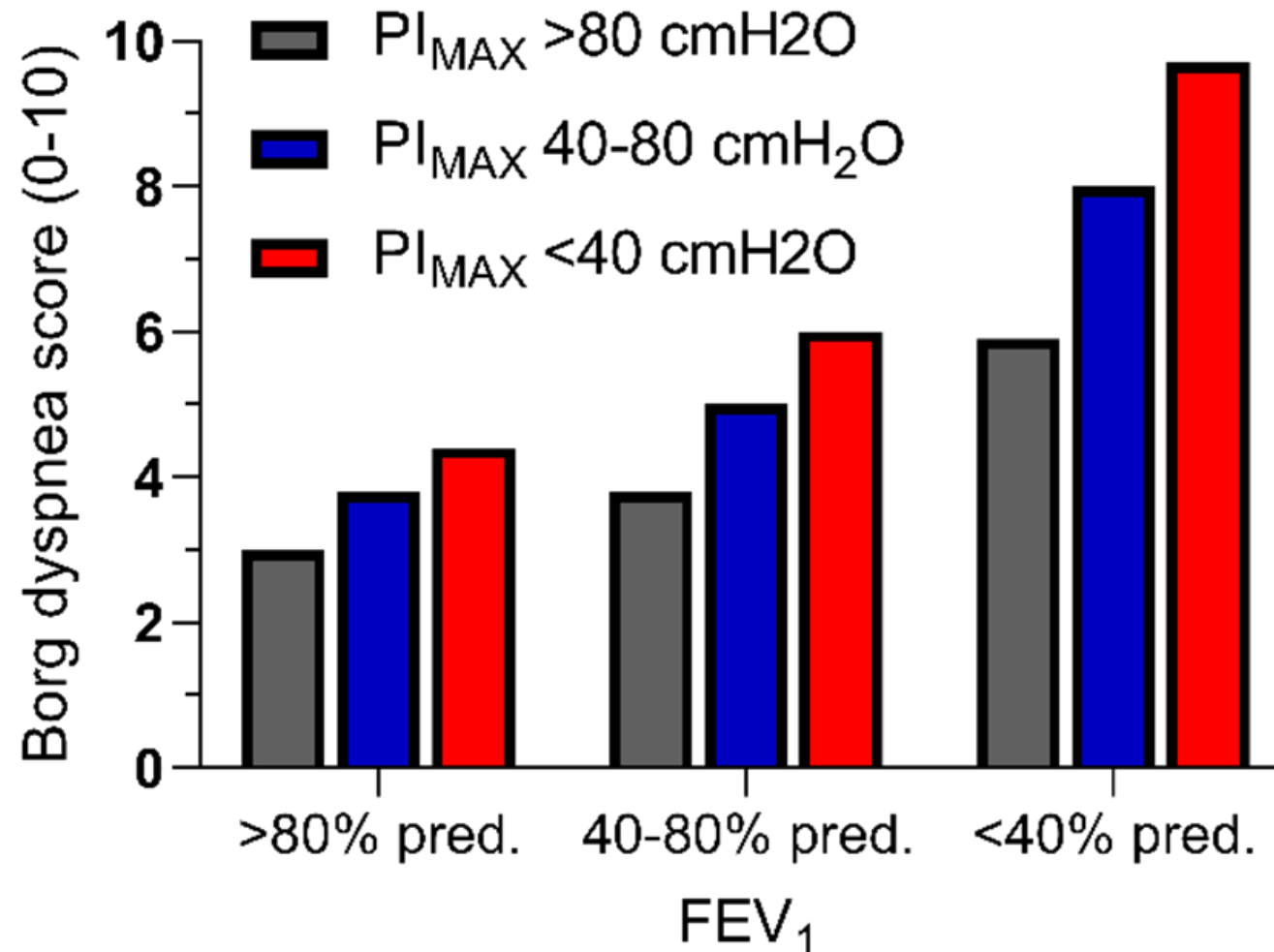
Mechanical weakening of the diaphragm (e.g., COPD)



# **WHAT IS THE CLINICAL SIGNIFICANCE OF INSPIRATORY MUSCLE WEAKNESS & DYSFUNCTION?**

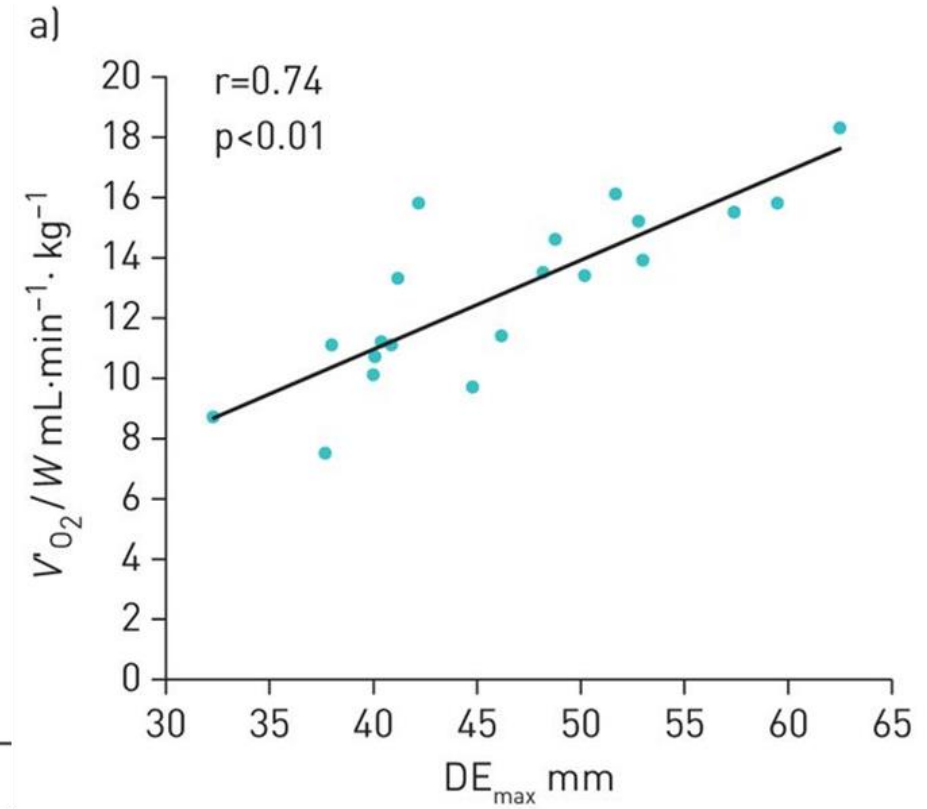
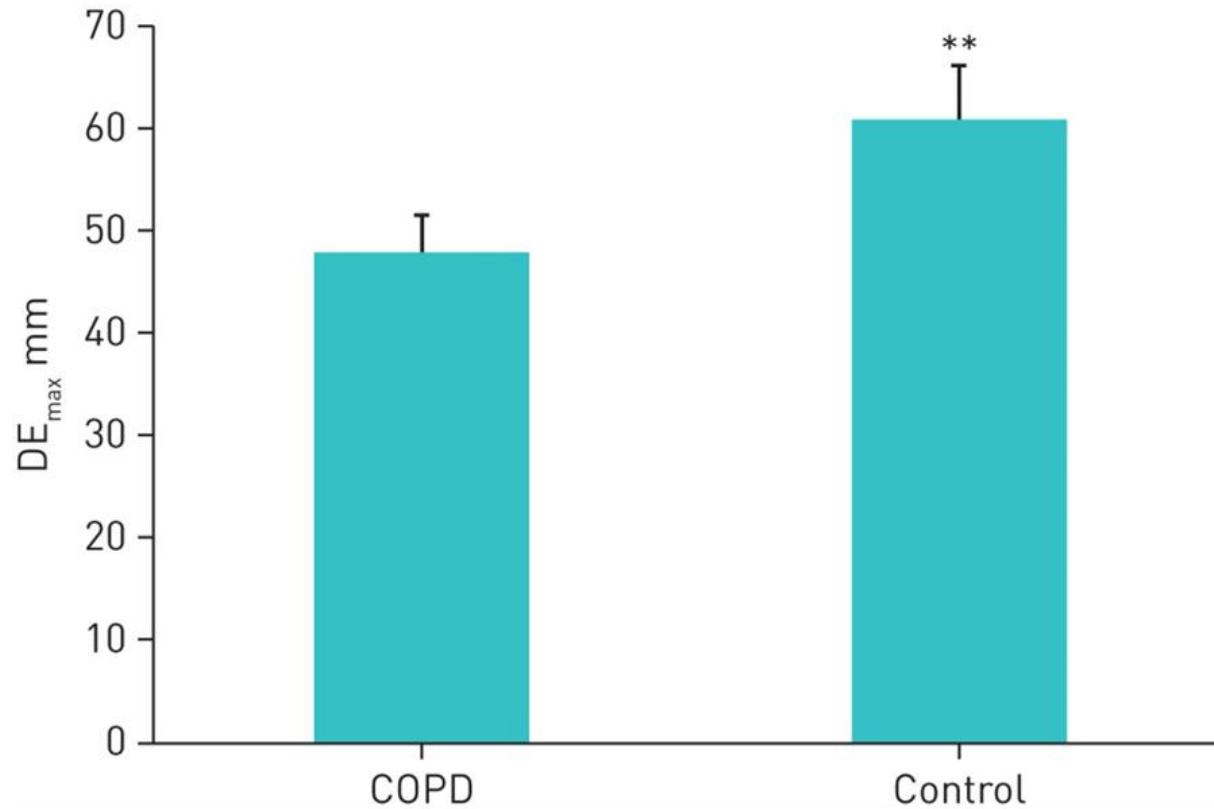
# WEAKNESS & DYSFUNCTION: CLINICAL SIGNIFICANCE

## GREATER BREATHLESSNESS DURING EXERCISE WITH LOWER INSPIRATORY MUSCLE STRENGTH



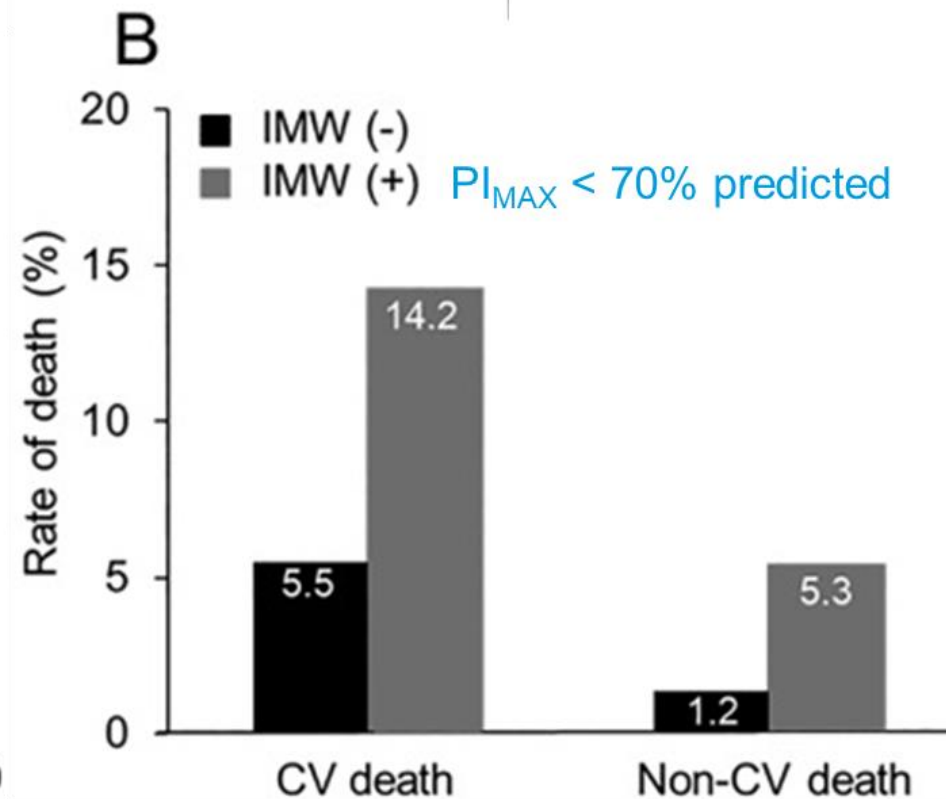
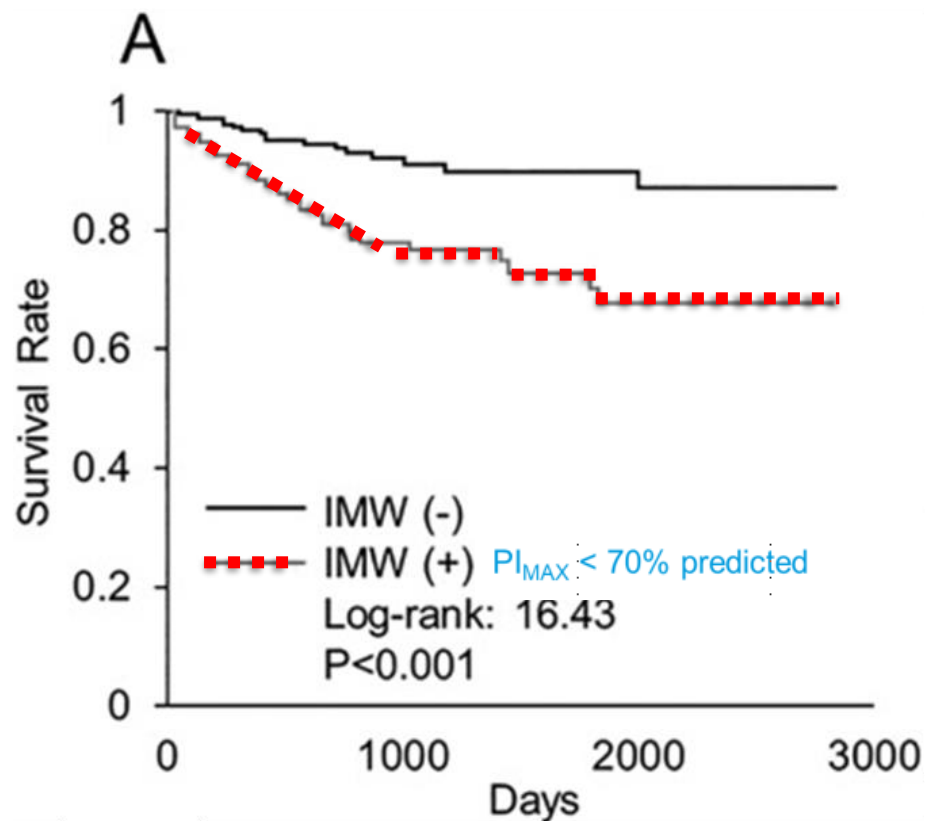
# WEAKNESS & DYSFUNCTION: CLINICAL SIGNIFICANCE

## REDUCED DIAPHRAGM MOTILITY RELATED TO DECREASED EXERCISE CAPACITY IN COPD



# WEAKNESS & DYSFUNCTION: CLINICAL SIGNIFICANCE

## INSPIRATORY MUSCLE WEAKNESS INCREASES RISK OF DEATH IN HEART FAILURE WITH REDUCED EJECTION FRACTION

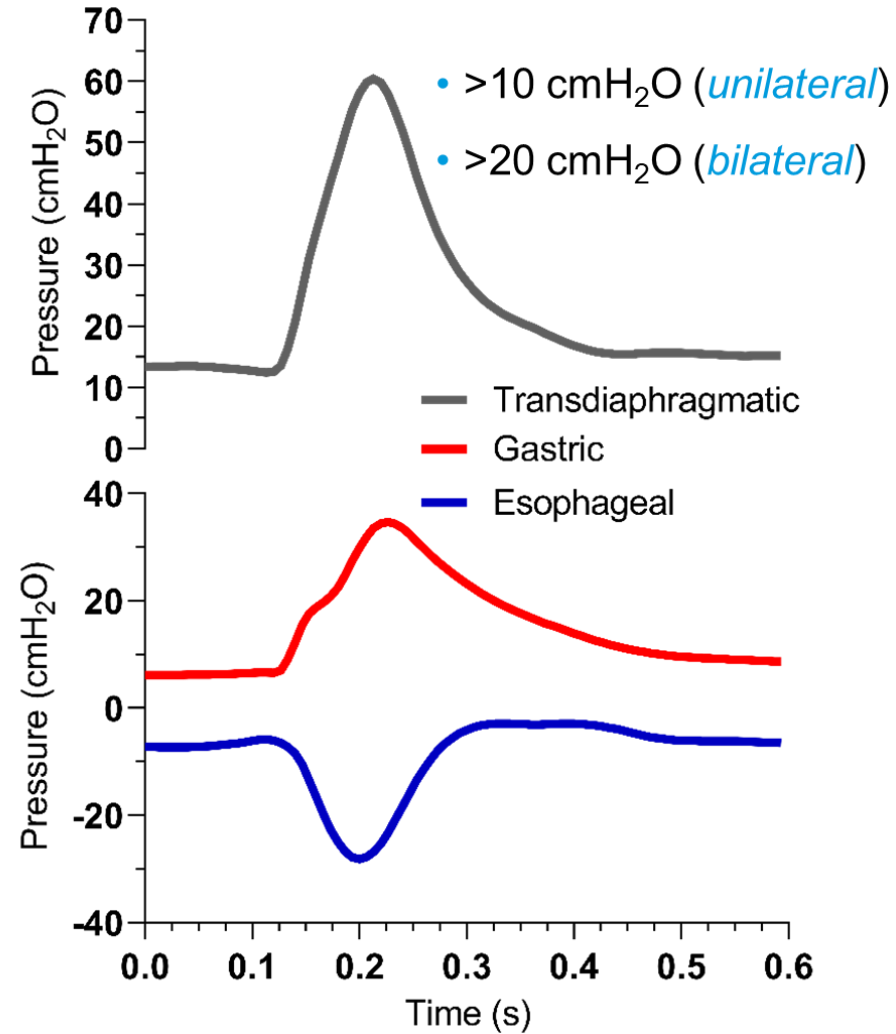


43% of HFrEF had IMW; median follow-up = 1.8 years

# 3

**HOW DO WE ASSESS  
INSPIRATORY MUSCLE  
FUNCTION, WHAT IS  
NORMAL?**

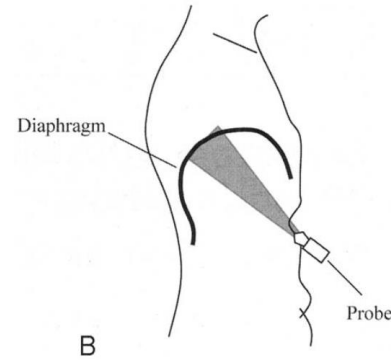
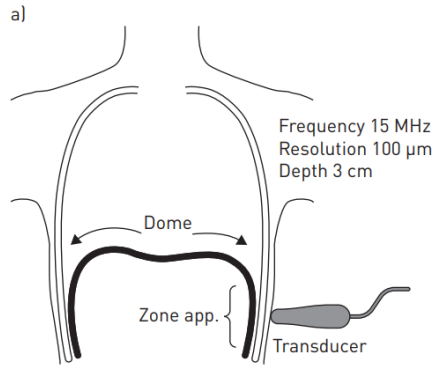
# ASSESSING THE DIAPHRAGM EVOKED DIAPHRAGM TWITCH PRESSURE





# ASSESSING THE DIAPHRAGM

## ULTRASOUND IMAGING



End-expiratory thickness

➤ LLN 0.15 cm

Thickening fraction

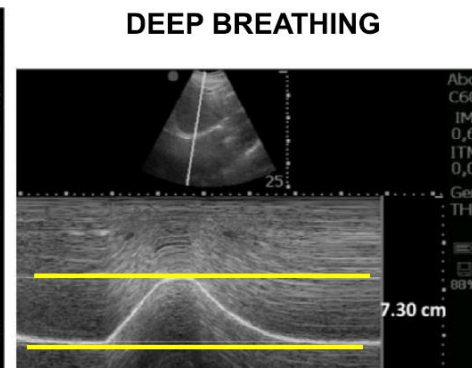
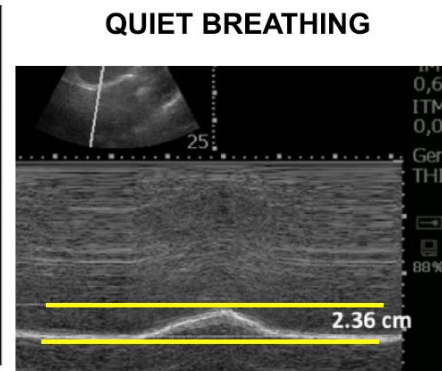
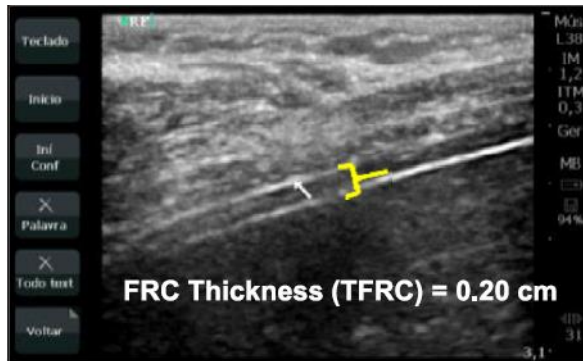
➤ LLN 20-30%

➤ Frequently >100%

Excursion (*deep breath*)

➤ LLN 3.6 cm (female)

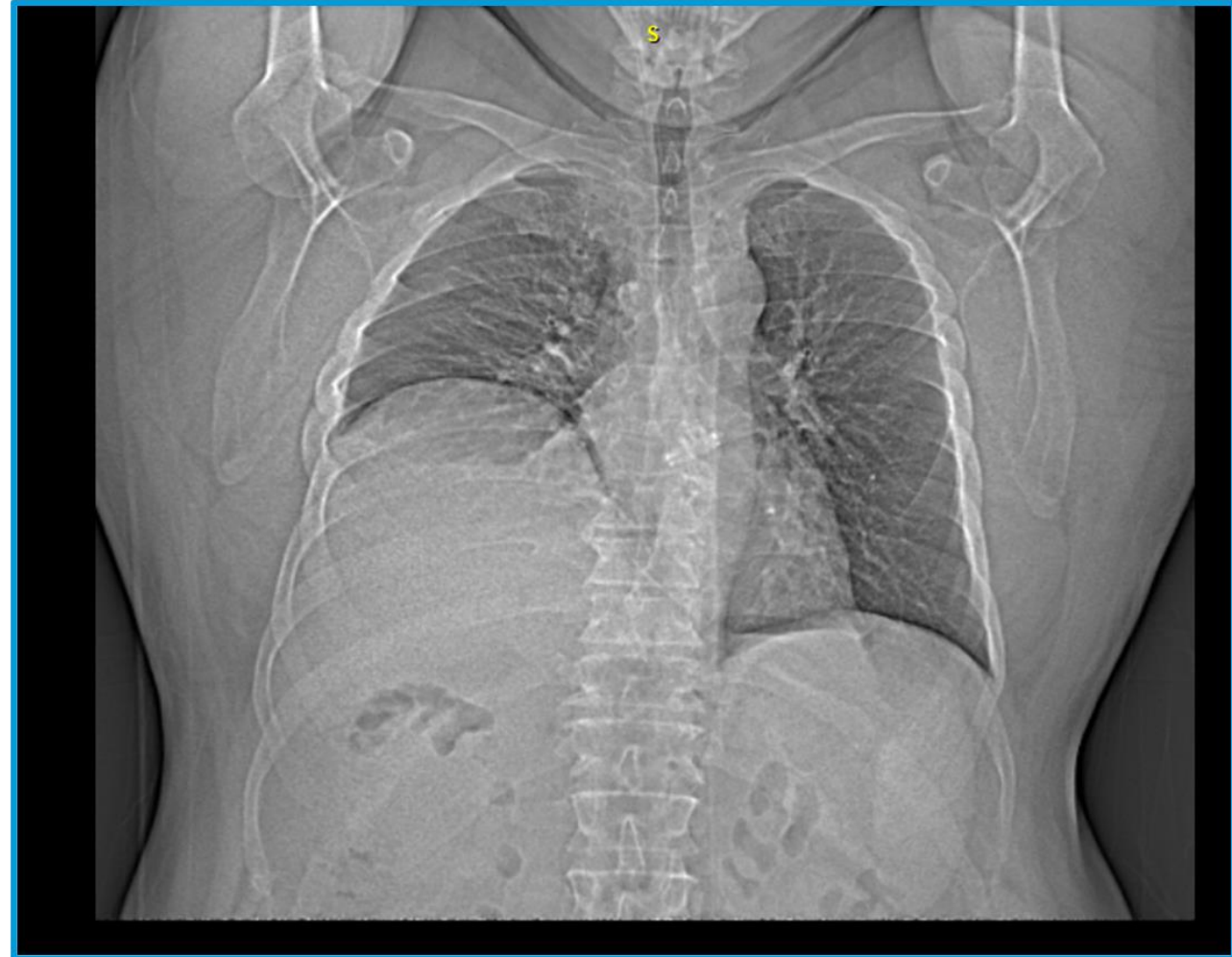
➤ LLN 4.7 cm (male)



# ASSESSING THE DIAPHRAGM

## CHEST CT OR X-RAY

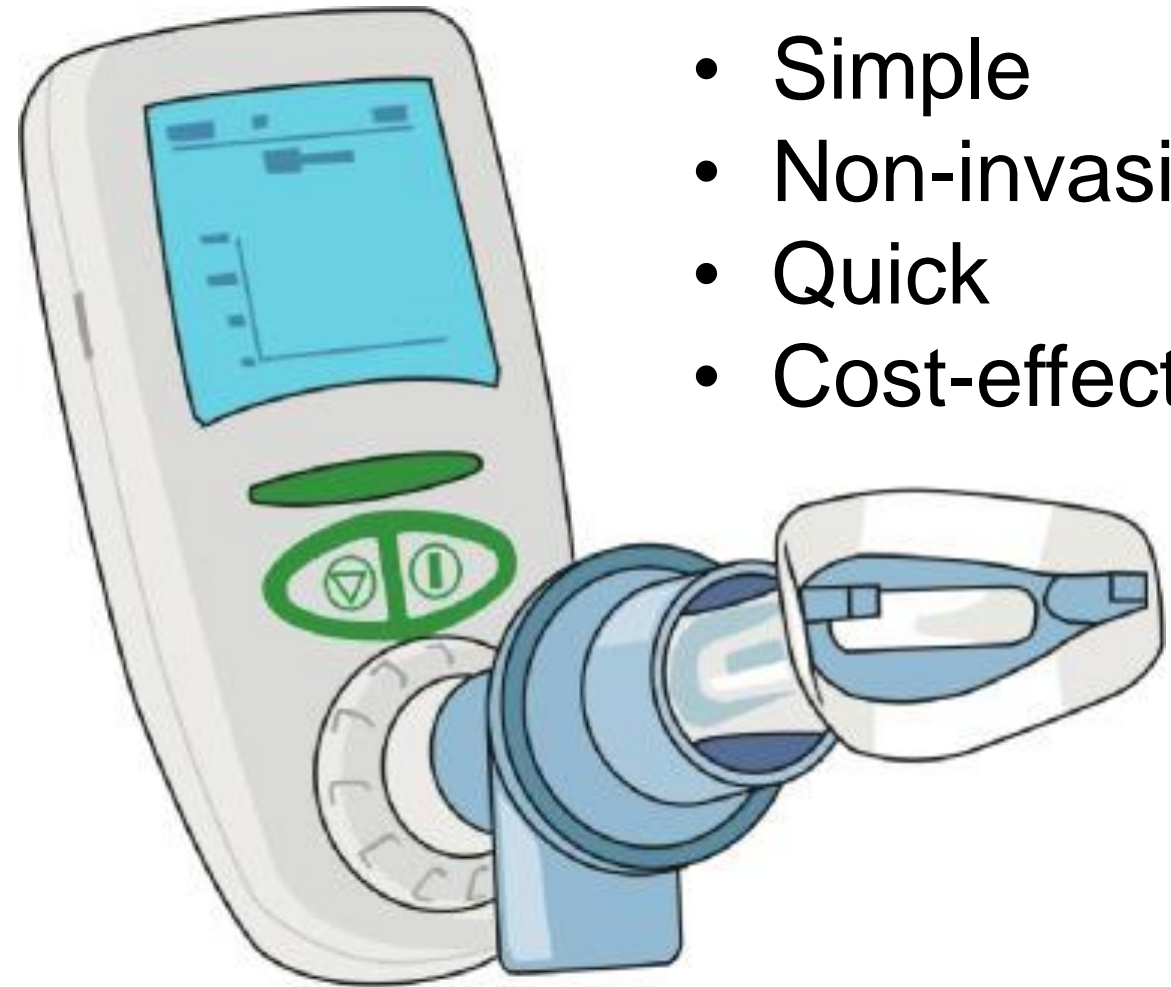
- ✓ **Neuropathic**  
Disease states that cause nerve damage or demyelination of phrenic nerve
- ✓ **Inflammatory**  
Secondary to viral and potentially some bacterial infections; noninfectious inflammatory causes also noted (e.g., sarcoidosis)
- ✓ **Idiopathic**  
Cause considered unknown; ~20% of cases
- ✓ **Traumatic**  
Cardiothoracic surgery; freezing injury due to necessary cooling; direct trauma (e.g., CABG)



Unilateral elevation of right hemidiaphragm >2 cm higher than left

INVASIVE, COSTLY, TIME-CONSUMING,  
REQUIRES EXPERT TRAINING &  
COMPLICATED ANALYSIS; *NOT WELL  
SUITED TO ROUTINE ASSESSMENT IN CR &  
PR...*







# ASSESSING THE DIAPHRAGM MAXIMAL INSPIRATORY PRESSURE



- Simple
- Non-invasive
- Quick
- Cost-effective

# MAXIMAL INSPIRATORY PRESSURE

## PRACTICAL CONSIDERATIONS

-  **Volitional**  
Patient encouragement required
-  **Posture**  
Seated, upright, no 'holding on'
-  **Length-tension relationship**  
Typically recommended MIP is measured at RV
-  **Practice & warm-up**  
Learn correct technique; warm-up improves reliability
-  **'Sustained' effort**  
MIP recorded as highest over 1 s (maintain for ~3-4 s)
-  **Acceptable reproducibility**  
Highest value from 3 efforts that vary by  $\leq 10\%$

# MAXIMAL INSPIRATORY PRESSURE

## PRACTICAL CONSIDERATIONS; WHAT IS NORMAL?

### CAUTION WHEN USING PREDICTIVE EQUATIONS WHEN CONSIDERING WHAT IS NORMAL

*RODRIGUES ET AL., CHEST, 152 (2017); 32-39...*

- PREVALENCE OF WEAKNESS RANGED FROM 33.4 TO 66.9% (6 EQNS)
- THE CHOICE OF MIP REFERENCE VALUES STRONGLY IMPACTS ON THE PREVALENCE OF WEAKNESS

# MAXIMAL INSPIRATORY PRESSURE

## PRACTICAL CONSIDERATIONS; WHAT IS NORMAL?

Age, y	MEN		WOMEN	
	Studies/sample size	MIP, cmH <sub>2</sub> O (95% CI)	Studies/sample size	MIP, cmH <sub>2</sub> O (95% CI)
18-29	6/96	128 (116-140)	6/92	97 (89-105)
30-39	6/69	129 (119-139)	6/66	89 (85-94)
40-49	6/72	117 (105-129)	6/71	93 (78-107)
50-59	5/61	108 (99-118)	5/60	78 (75-85)
60-69	5/65	93 (85-101)	5/66	75 (67-83)
70-83	5/63	76 (66-86)	5/59	65 (58-73)

# MAXIMAL INSPIRATORY PRESSURE

## PRACTICAL CONSIDERATIONS; WHAT IS NORMAL?

Age (yrs)	P <sub>I</sub> max (cmH <sub>2</sub> O)	
	Men*	Women <sup>+</sup>
< 40	63	58
40-60	55	50
61-80	47	43
> 80	42	38

MIP of  $\geq 80$  cmH<sub>2</sub>O (*males*) or  $\geq 70$  cmH<sub>2</sub>O (*females*) thought to exclude clinically significant inspiratory muscle weakness



# INTERIM SUMMARY

- Inspiratory muscle weakness & dysfunction is associated with dyspnea, exercise intolerance, & prognosis in CVD and chronic lung disease
- Maximal inspiratory pressure is the most viable method for standard assessment of inspiratory muscle function in CR & PR



# INSPIRATORY MUSCLE WEAKNESS IN CR/PR: PREVALENCE AND REHABILITATIVE STRATEGIES

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# DISCLOSURES

- No disclosures

# OVERVIEW

- Prevalence of inspiratory muscle weakness in CR and PR populations?
- Impact of exercise-based CR and PR on inspiratory muscle function
- Addition of inspiratory muscle training on inspiratory muscle function in the CR/PR setting
- Practical guidance for inspiratory muscle training in the CR/PR setting

**1**

# **PREVALENCE OF INSPIRATORY MUSCLE WEAKNESS**

# **WHAT IS THE PREVALENCE OF INSPIRATORY MUSCLE WEAKNESS IN CR & PR?**

# INSPIRATORY MUSCLE WEAKNESS IN CR & PR

Study	Population	N=	Measure (vs CTL)	Prevalence
Hamazaki, 2020	HFrEF	445		MIP <70% pred; ~43%
Hamazaki, 2020	HFpEF	578		MIP <70% pred; ~39%
Miyagi, 2018	HFr/pEF	77	Ultrasound; dia. thickness @ TLC	<4.0 mm; ~44%
Meyer, 2001	HFrEF	244	MIP: 77 ± 34 vs. 107 ± 38 cmH <sub>2</sub> O	
Fernandes, 2018	HTxp	23	MIP; 60 ± 30 cmH <sub>2</sub> O (~48-55% pred)	

**Inspiratory muscle weakness is associated with all-cause and CV mortality in HFrEF and HFpEF.**

# INSPIRATORY MUSCLE WEAKNESS IN CR & PR

Study	Population	N=	Measure (vs CTL)	Prevalence
Stein, 2009	CABG	20	MIP; $65 \pm 16$ cmH <sub>2</sub> O (60% pred.)	
Morsch, 2009	CABG	108	MIP; $66 \pm 29$ cmH <sub>2</sub> O	
Palaniswamy, 2010	Valve	20	MIP: $51 \pm 10$ cmH <sub>2</sub> O (~49% pred.)	

**The values above are pre-surgery. CABG and heart valve surgeries are associated with a ~17-36% reduction in inspiratory muscle strength and can persist for several weeks to months.**



# INSPIRATORY MUSCLE WEAKNESS IN CR & PR

Study	Population	N=	Measure (vs CTL)	Prevalence
Kofod, 2019	COPD	97	MIP: 63 vs. 76 cmH <sub>2</sub> O	MIP <50% pred; ~10% MIP <60 cmH <sub>2</sub> O; ~40%
Basso-Vanelli, 2016	COPD	25	MIP: 64 ± 17 cmH <sub>2</sub> O (67% pred.)	

**Evidence that inspiratory muscle weakness in COPD is associated with hyperinflation and contributes to hypercapnia, dyspnea, and exercise intolerance in these patients.**

# 2 REHABILITATIVE STUDIES

# **CAN EXERCISE TRAINING IN THE CR/PR SETTING IMPROVE INSPIRATORY MUSCLE FUNCTION?**

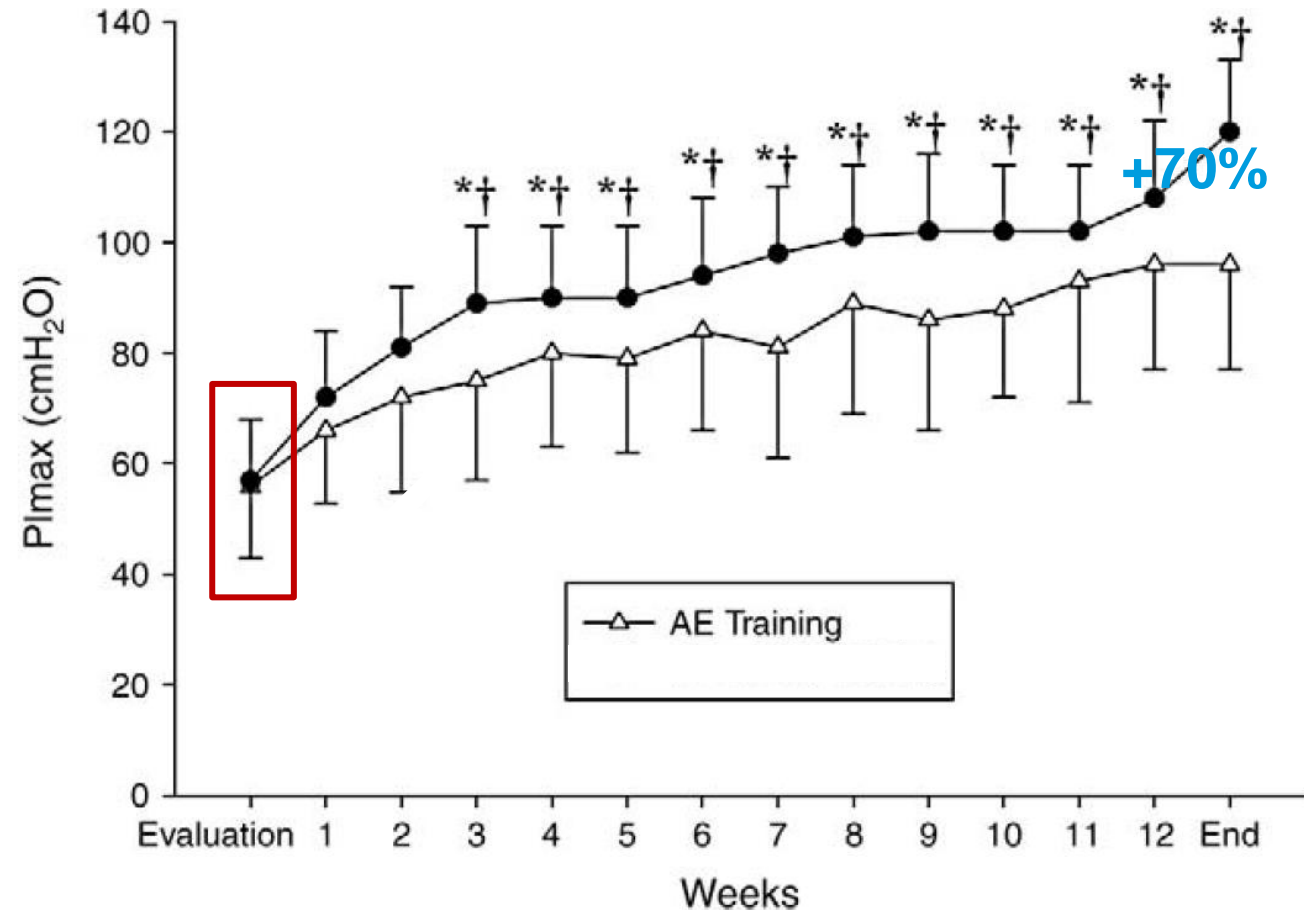
# AEROBIC TRAINING

## AEROBIC EXERCISE IN HFREF

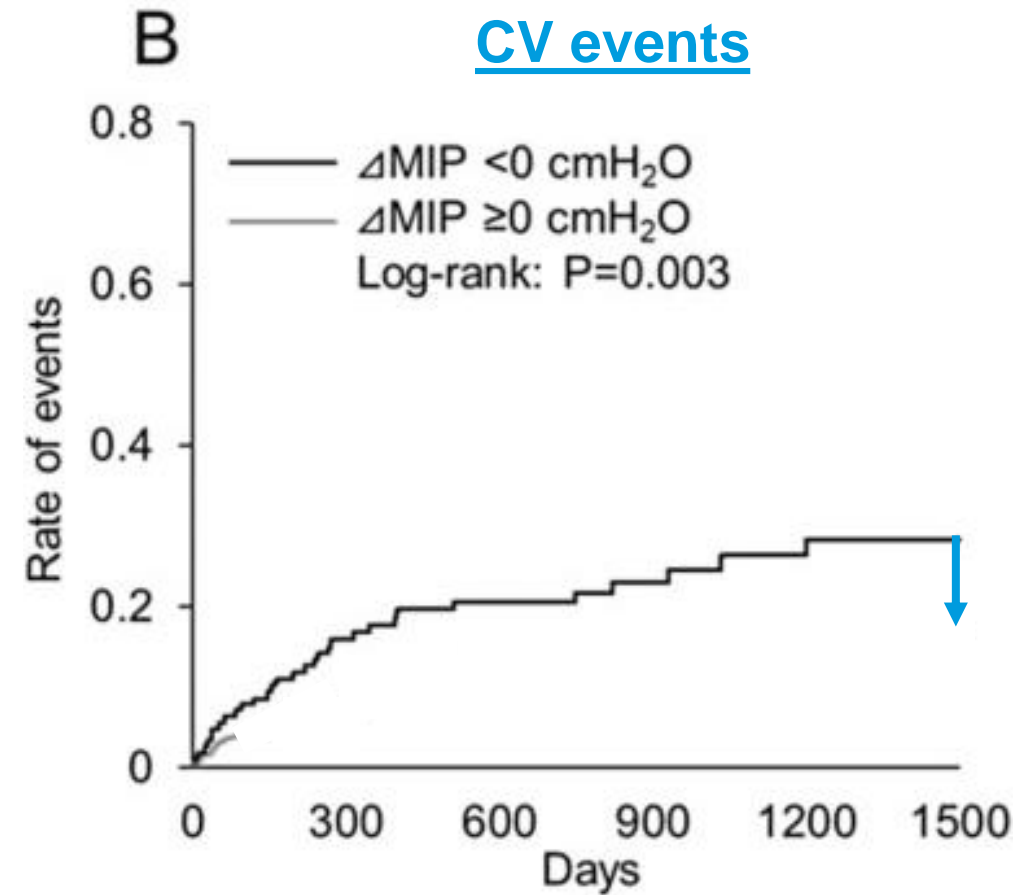
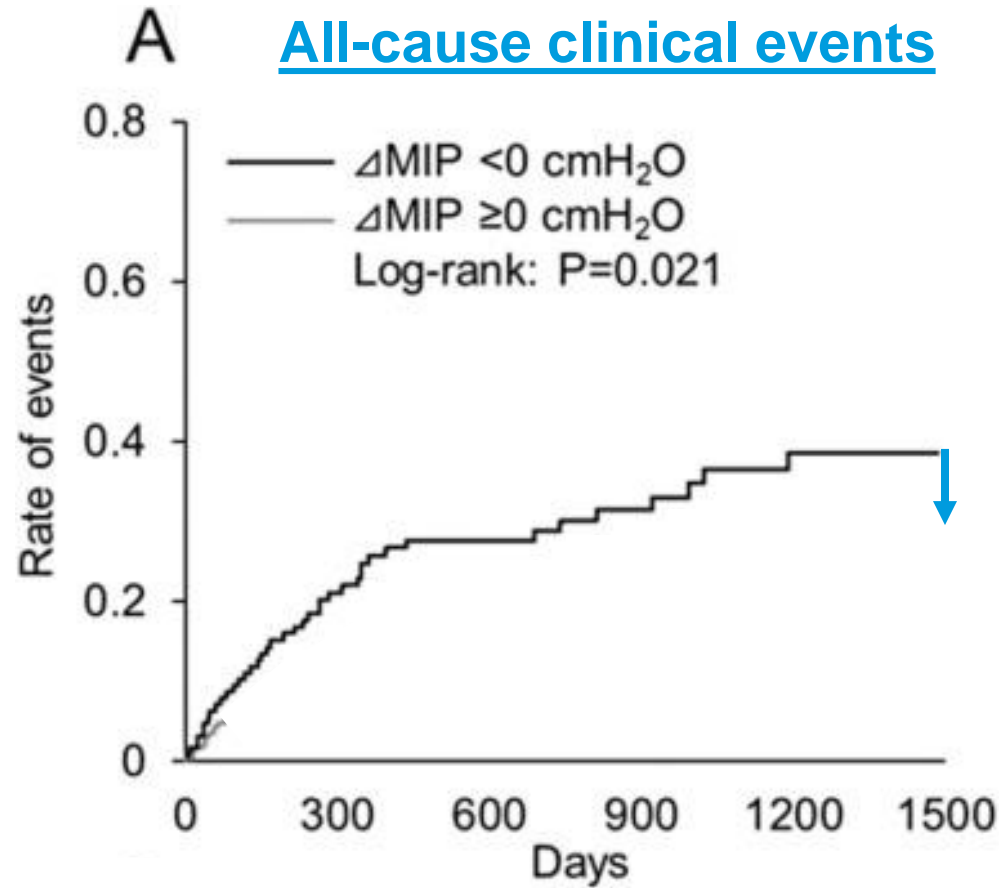
### Supervised exercise training

- 3 times per week for 12 weeks
- Target intensity was heart rate at first ventilatory threshold
- Duration was 20 min and progressed to 45 min

Other studies have reported a smaller MIP increase (~15%) with baseline MIP likely significantly contributing to the degree of MIP improvement



# AEROBIC TRAINING



**Any CR-induced increase in MIP is associated with lower rates of all-cause and CV events in HFrEF**

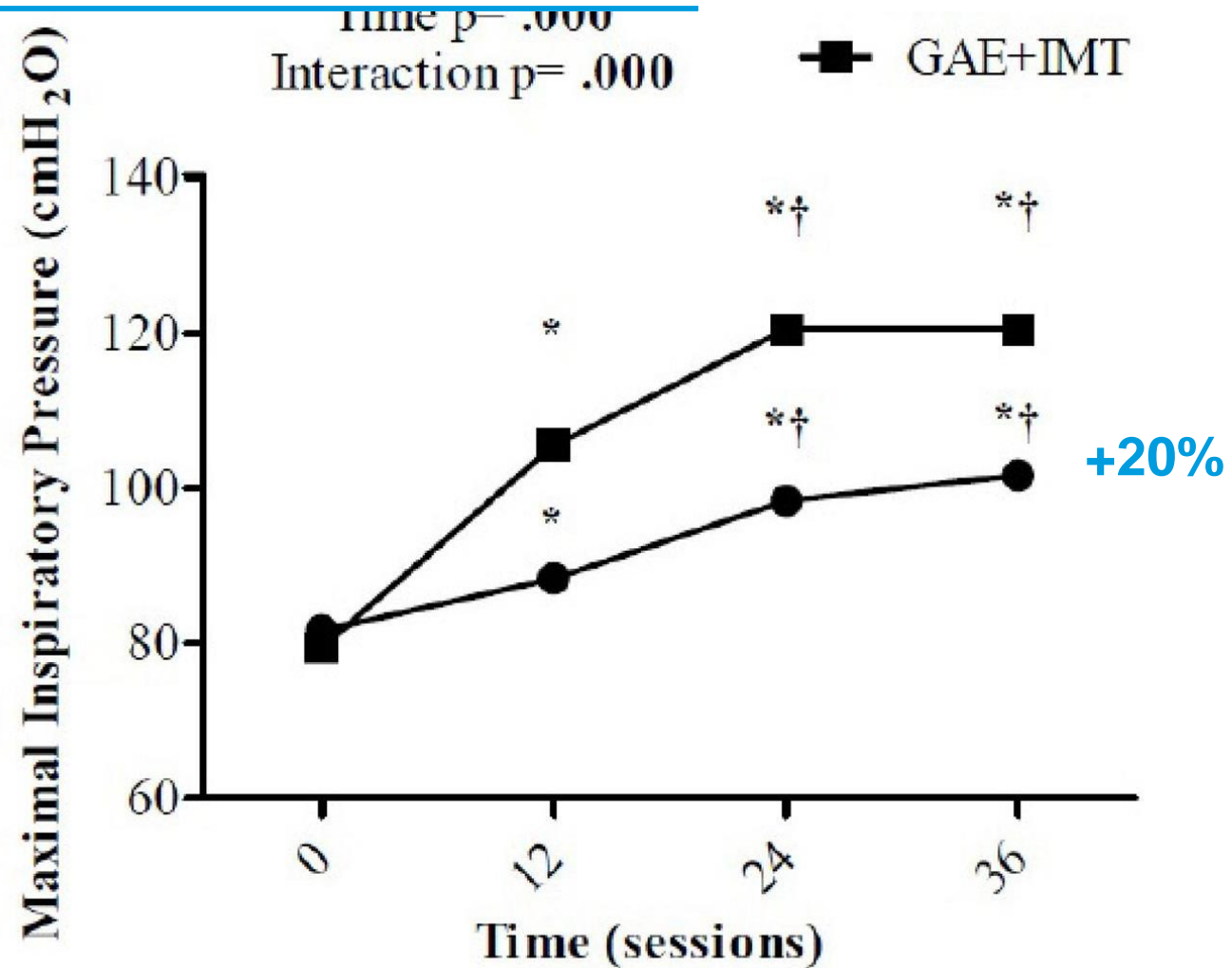
# AEROBIC TRAINING

## AEROBIC EXERCISE FOLLOWING CABG SURGERY

### Supervised exercise training

- 3 times per week for 12 weeks
- Target intensity was 50% to 80% heart rate reserve (progressive increase)
- Duration was 40 min

Other studies have reported no MIP improvement in response to CR following CABG surgery, but the patients in these studies have had higher MIP values at CR entry



# AEROBIC TRAINING

## AEROBIC EXERCISE FOLLOWING CABG SURGERY

Taken together, these findings provide evidence that exercise training in the CR setting elicits improvements in MIP in HFrEF and following CABG with those patients exhibiting inspiratory muscle weakness likely exhibiting the greatest increases in inspiratory muscle function.

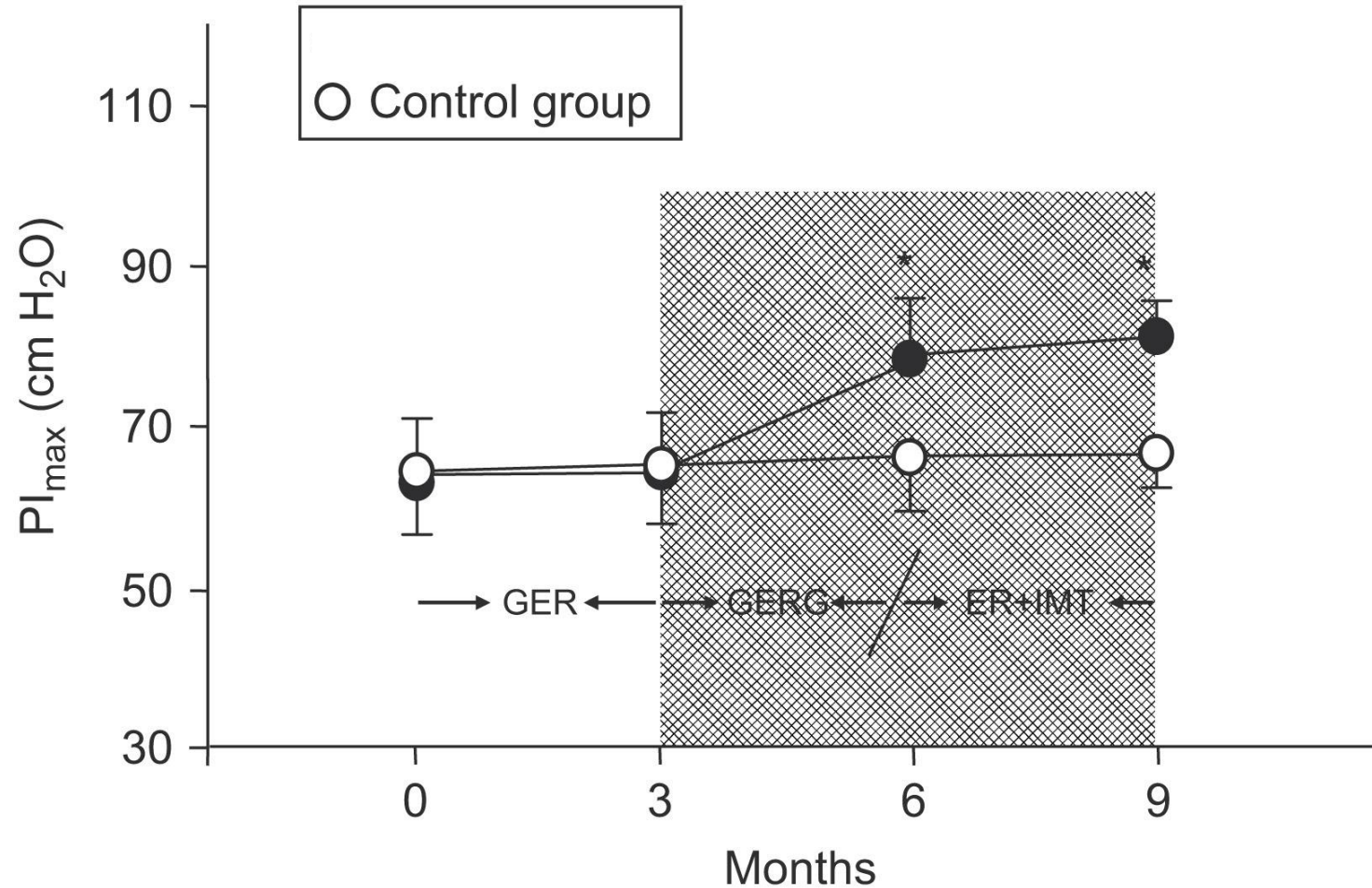
# AEROBIC TRAINING

## AEROBIC EXERCISE IN COPD

Supervised PR program

- 3 times per week for 12 weeks
- General exercise reconditioning program
- Duration was 1.5 hours including endurance exercise and strength training

**These findings are consistent with other studies finding minimal increases in MIP with PR in patients with COPD**





# **EFFECT OF EXERCISE TRAINING & INSPIRATORY MUSCLE TRAINING (IMT) ON INSPIRATORY MUSCLE FUNCTION AND EXERCISE CAPACITY**

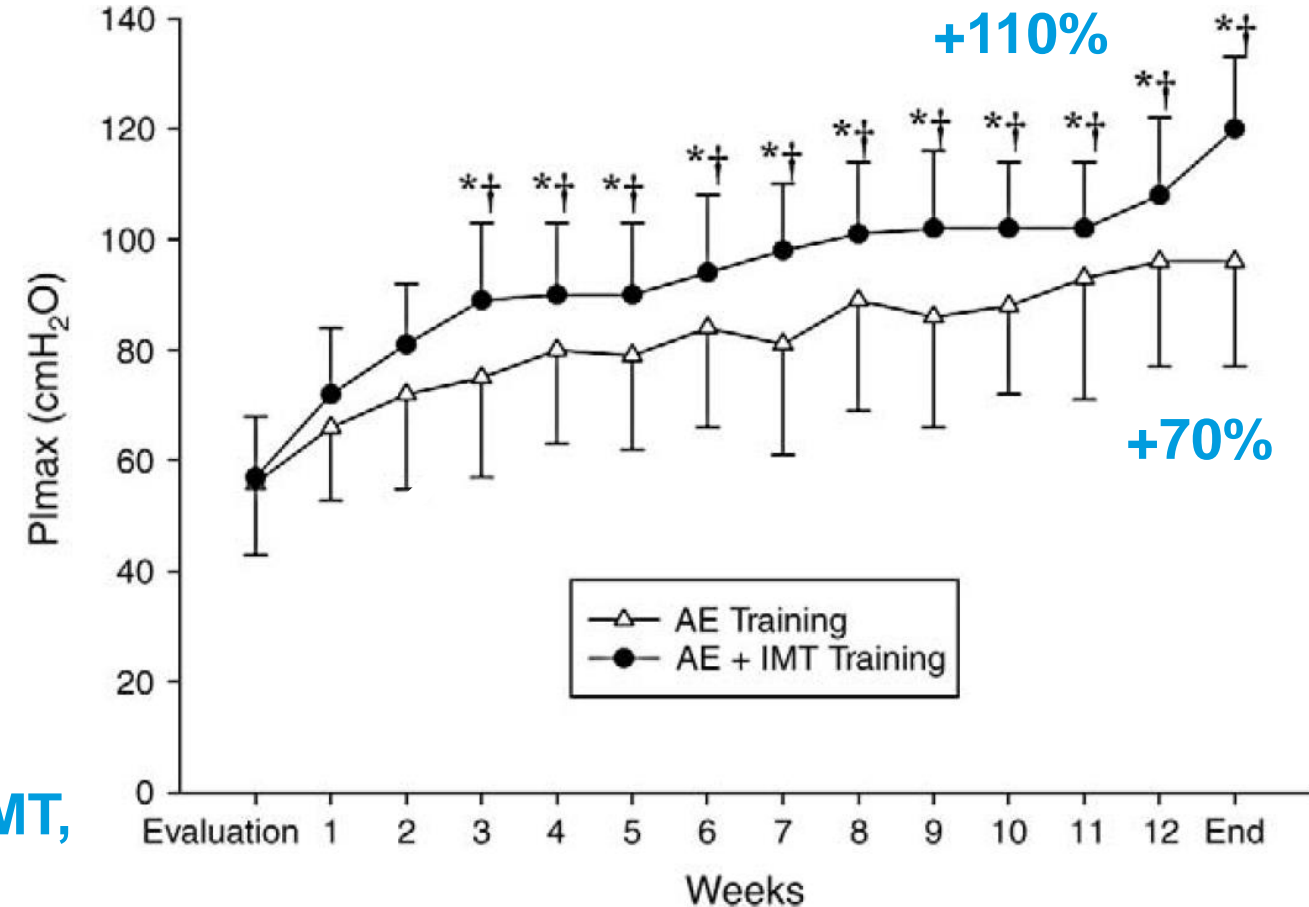
# AEROBIC/INSPIRATORY MUSCLE TRAINING

## AEROBIC EXERCISE VS. AEROBIC EXERCISE PLUS IMT IN HFREF

### Inspiratory muscle training

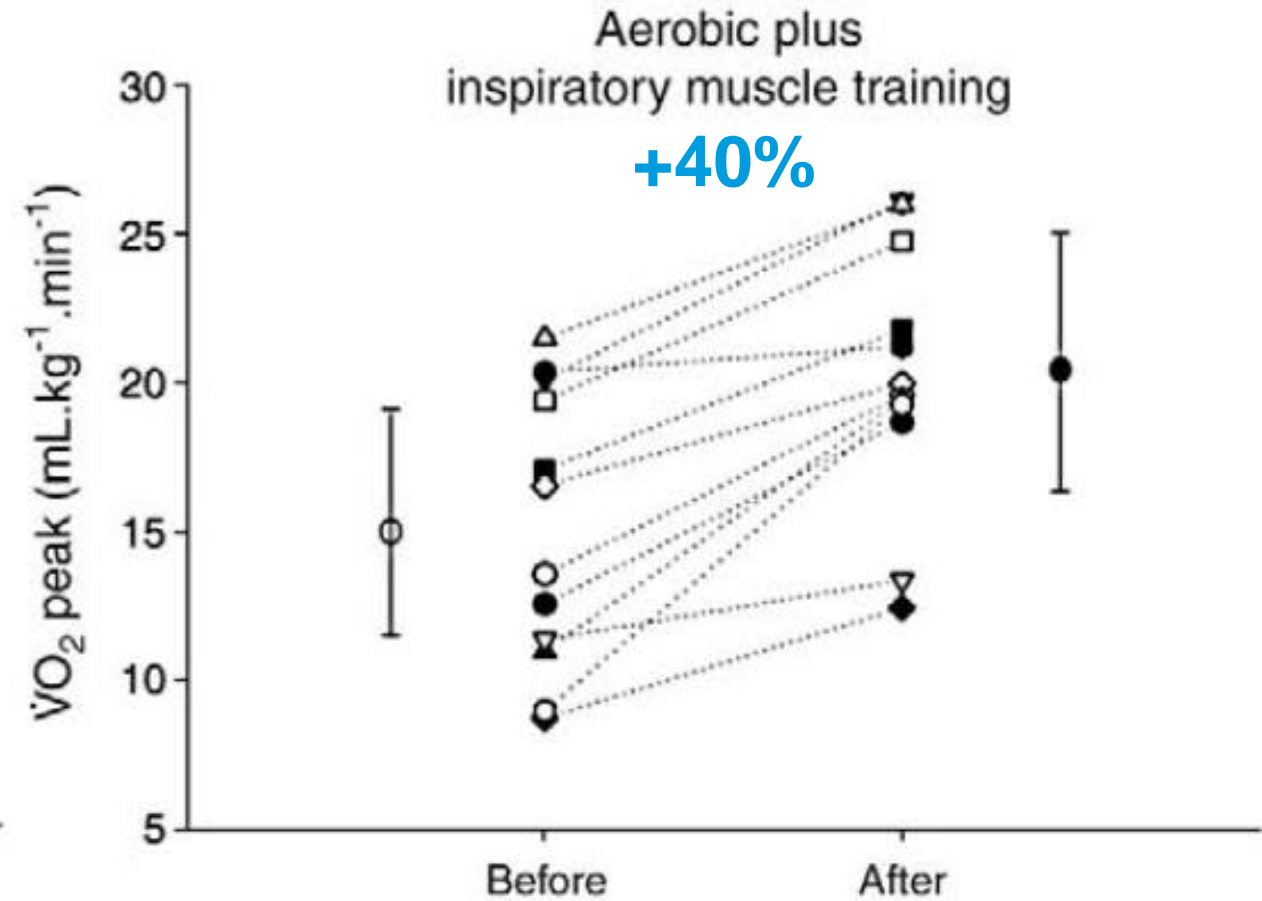
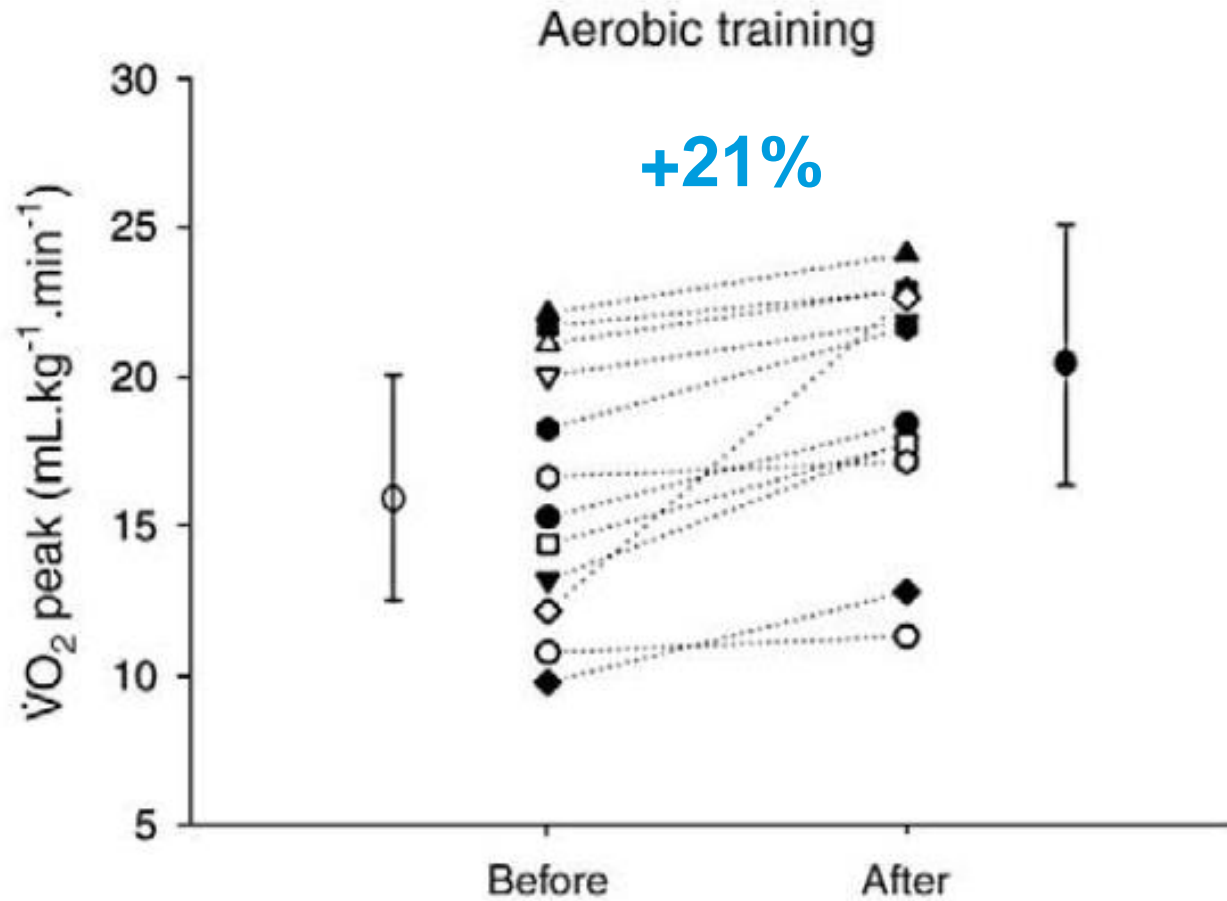
- 7 days per week for 12 weeks (1 session supervised and 6 sessions at home)
- 30% of MIP
- Duration was 30 min per session

Other studies in HFrEF without inspiratory muscle weakness have found no additional benefit in inspiratory muscle strength with IMT, but these patients did exhibit greater improvements in quality of life and dyspnea than exercise training alone.



# AEROBIC/INSPIRATORY MUSCLE TRAINING

AEROBIC EXERCISE VS. AEROBIC EXERCISE PLUS IMT IN HFREF

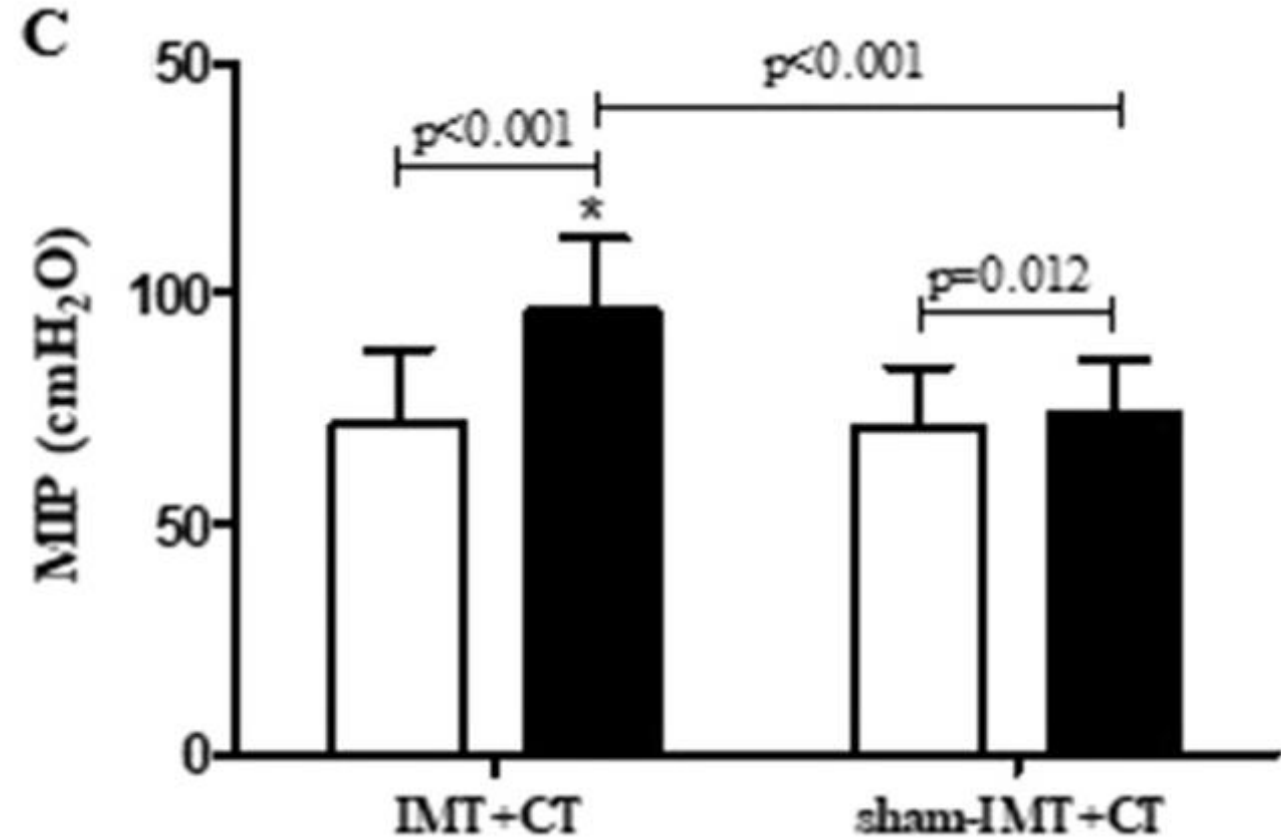


# AEROBIC/INSPIRATORY MUSCLE TRAINING

## AEROBIC EXERCISE VS. AEROBIC EXERCISE PLUS IMT FOLLOWING CABG SURGERY

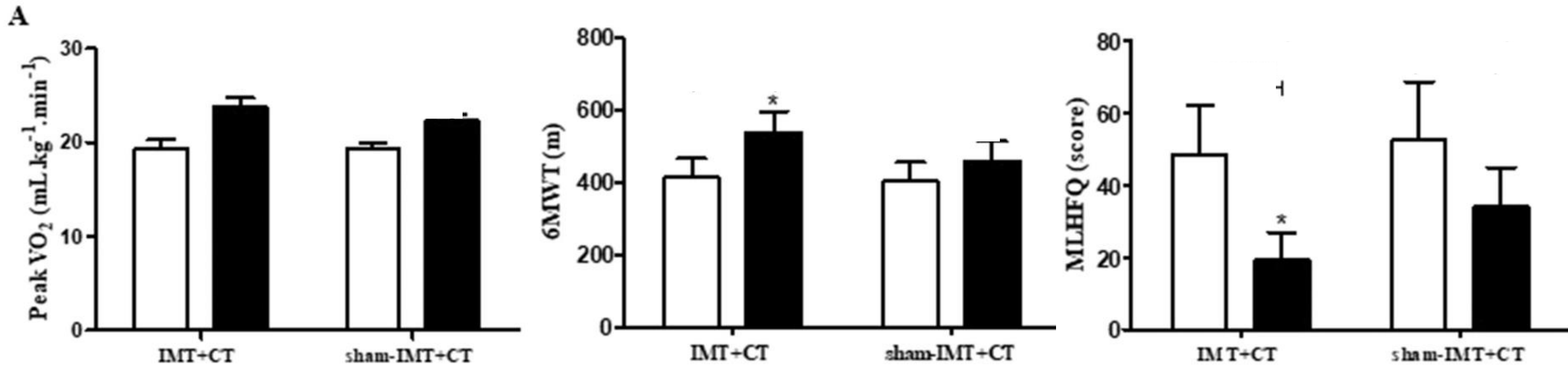
### Inspiratory muscle training

- 2 days per week for 12 weeks
- 50% to 80% of MIP (progressive increase from week 1 to week 8)
- 5 sets of 10 repetitions with 1 min of rest between each set



# AEROBIC/INSPIRATORY MUSCLE TRAINING

## AEROBIC EXERCISE VS. AEROBIC EXERCISE PLUS IMT FOLLOWING CABG SURGERY

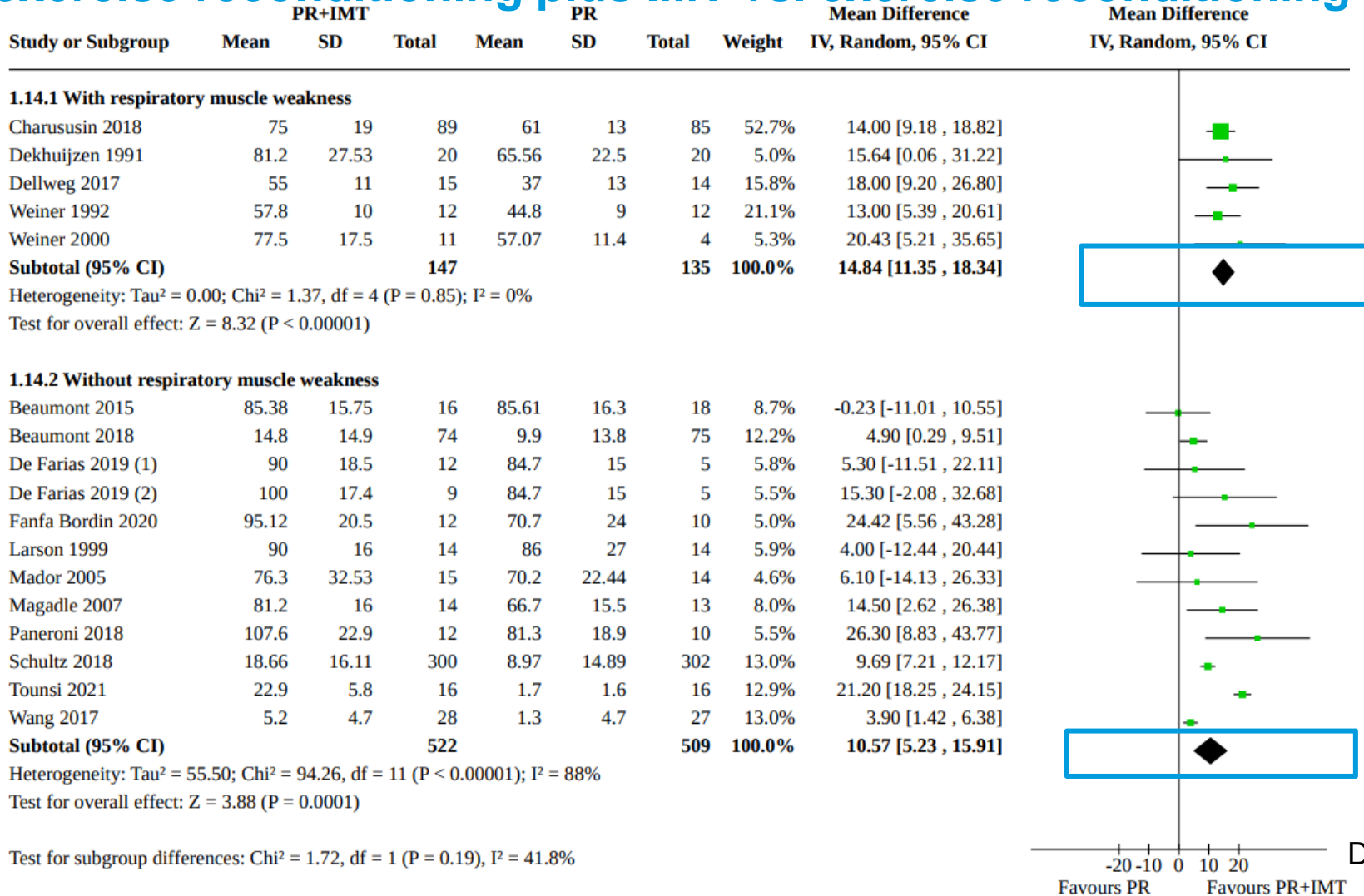


Aerobic training in the CR setting combined with IMT resulted in greater improvements in VO<sub>2</sub> peak, 6-minute walk, and quality of life following CABG surgery.

# AEROBIC/INSPIRATORY MUSCLE TRAINING

## AEROBIC EXERCISE VS. AEROBIC EXERCISE PLUS IMT IN COPD

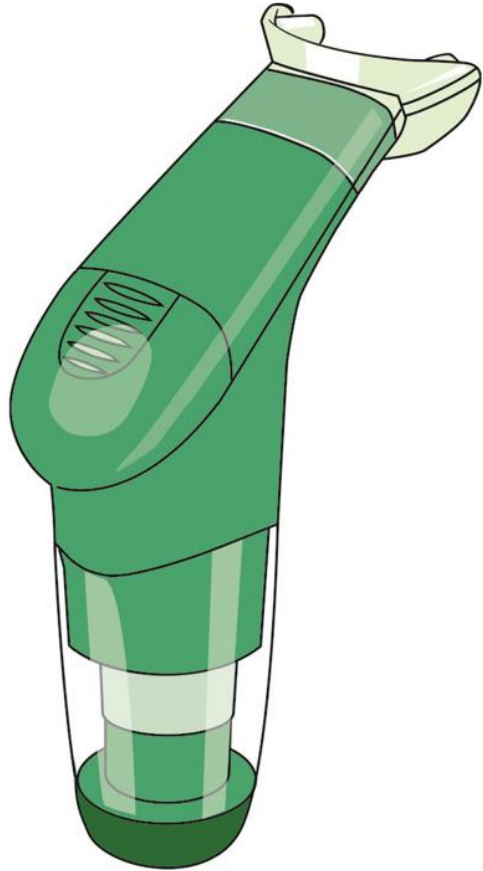
### Effect of exercise reconditioning plus IMT vs. exercise reconditioning alone on MIP



# 3 PRACTICAL GUIDANCE

# INSPIRATORY MUSCLE TRAINING

## PRACTICAL GUIDANCE



### Adjunct therapy

Inspiratory muscle function, breathlessness, exercise capacity (?)



### Three primary modalities

Hyperpnea, 'fixed' resistive loading, pressure threshold loading\*\*



### Consider baseline MIP

Intervention most effective in those with existing inspiratory muscle weakness (MIP <60 cmH<sub>2</sub>O)



# OPTIMAL IMT PRESCRIPTION?

## 'Standard'

- 2 × 30 dynamic efforts
- 6-to-7 days per week
- 4-to-10+ weeks
- ~50% of MIP
- Progression
  - Periodically increase load such that completion of 30 breaths approximates limit of inspiratory muscle tolerance

## 'High-intensity'

- 2-min loaded inspirations, 1-min recovery
- Repeat 7 times
- 3-to-5 days per week
- ~8 weeks
- Start 'low' (~20-30% MIP)
- Progress to ~70% by 3<sup>rd</sup> or 4<sup>th</sup> session; further increase load such that final 2 min of session 'only just' completed

# INSPIRATORY MUSCLE TRAINING

## PRACTICAL GUIDANCE

**TABLE 1** Benefits and evidence levels of pulmonary rehabilitation outcomes in chronic obstructive pulmonary disease (COPD)

Benefits	Evidence
Improves exercise capacity	A
Reduces the perceived intensity of breathlessness	A
Improves health-related quality of life	A
Reduces the number of hospitalisations and hospital days	A
Reduces anxiety and depression associated with COPD	A
Strength and endurance training of the upper limbs improves arm function	B
Benefits extend well beyond the immediate period of training	B
Improves survival	C
<b>Respiratory muscle training can be beneficial, especially when combined with general exercise training</b>	C

Category A: randomised controlled trials, rich body of data; Category B: randomised controlled trials, limited body of data; Category C: nonrandomised trials or observational studies. Reproduced from [3] with permission from the publisher.



### Consider baseline MIP

Intervention (**ExT and/or IMT**) most effective in those with existing inspiratory muscle weakness (MIP <60 cmH<sub>2</sub>O)

# INTERIM SUMMARY (PART II)

- Inspiratory muscle weakness is prevalent in heart failure and COPD.
- The prevalence of inspiratory muscle weakness in patients with other indications to CR (e.g., stable angina) is needed.
- Exercise-based CR and PR with/without IMT may improve inspiratory muscle function, physiological responses, and clinical outcomes.
- Evidence suggests that patients with inspiratory muscle weakness may exhibit the most benefit from exercise-based CR and PR with/without IMT.



# CASE PRESENTATION: DIAPHRAGM DYSFUNCTION AFTER AORTIC VALVE REPLACEMENT

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# PHASE II CR FOLLOWING AVR: CASE PATIENT

## 54-YEAR-OLD MALE



### History

- Hypertension
- Hyperlipidemia
- Sleep apnea
- CA calcification
- Bicuspid aortic valve, severe stenosis



### Medications

- Atorvastatin
- Metoprolol Succinate
- Warfarin
- Amlodipine
- Lisinopril
- Chlorthalidone
- Famotidine



### Procedure

Mechanical aortic valve replacement via right mini thoracotomy



### Phase II CR

25 total sessions over 15 weeks with 5 week 'break' due to work & family commitments

# PHASE II CR FOLLOWING AVR: CASE PATIENT

## 54-YEAR-OLD MALE

	Rest	6MWT
Weight, lbs	288	
BMI, kg/m <sup>2</sup>	35.1	
Heart rate, bpm	75	90
BP, mmHg	156/64	198/84
SpO <sub>2</sub> , %	97	95
RPE		9
Distance, ft		1,402
Speed, mph		2.6
METS		3
ECG	NSR, no ectopy	NSR, no ectopy

# CLINICAL COURSE

- Complaints of dyspnea after surgery, thought to be related to post-op deconditioning
- Pt was able to complete 30 min of seated aerobic exercise during his rehab sessions with minimal complaints of dyspnea
- Dyspnea worsened during resistance training
- Coached patient in proper breathing technique during resistance training without any symptom improvement

# PHASE II CR FOLLOWING AVR: CASE PATIENT

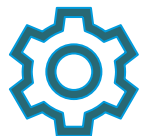
## 54-YEAR-OLD MALE

- Patient was absent from rehab for 5 weeks due to family/work commitments
- Returned with persistent/worsening dyspnea, especially during resistance exercise prompted review of medical history with emphasis on the patients' pulmonary history
- Multifactorial breathlessness in setting of obesity, weight gain, post-operative deconditioning
- Weight gain after CR 'break' (296 lbs, +8 lbs)



# PHASE II CR FOLLOWING AVR: CASE PATIENT

54-YEAR-OLD MALE



**Iatrogenic right  
hemidiaphragm  
paralysis &  
elevation**

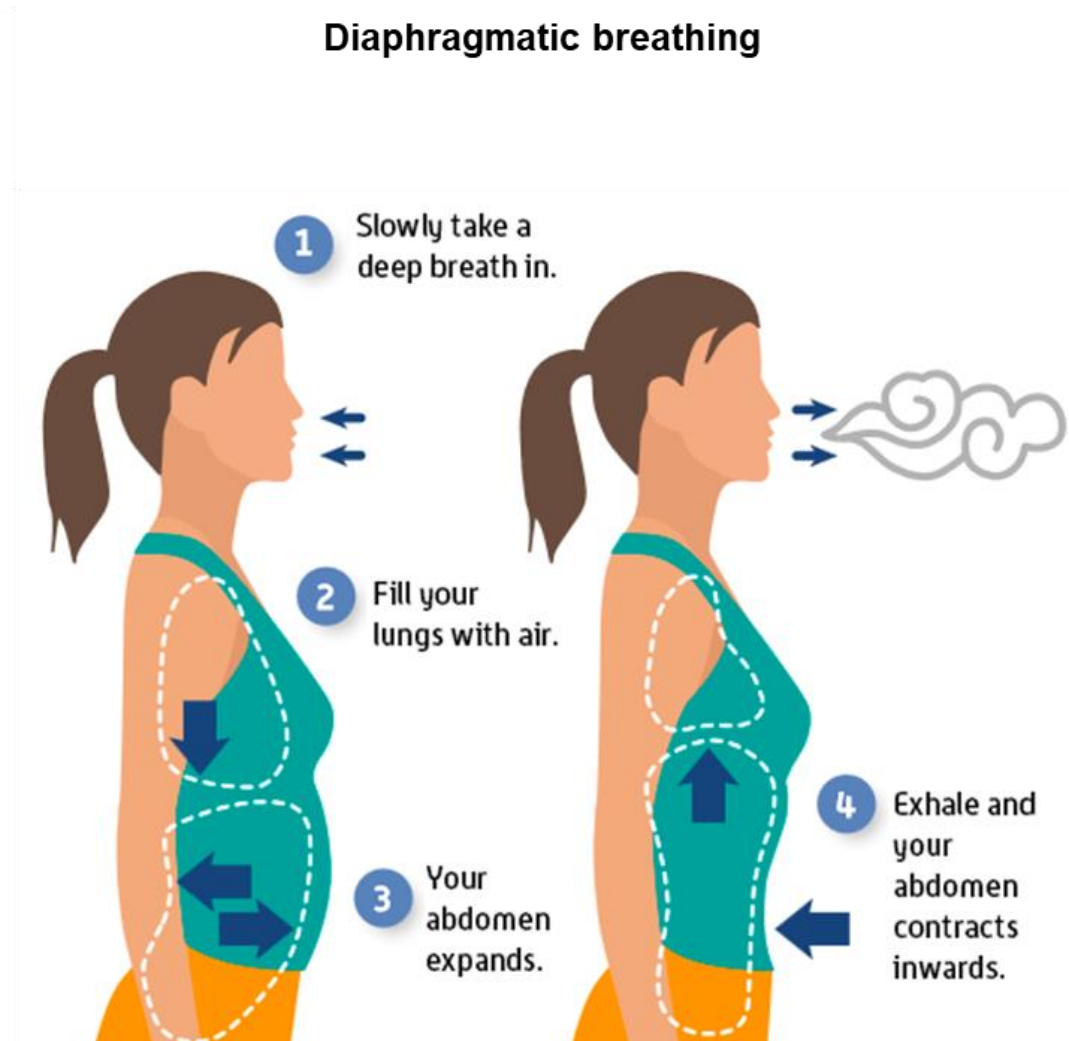
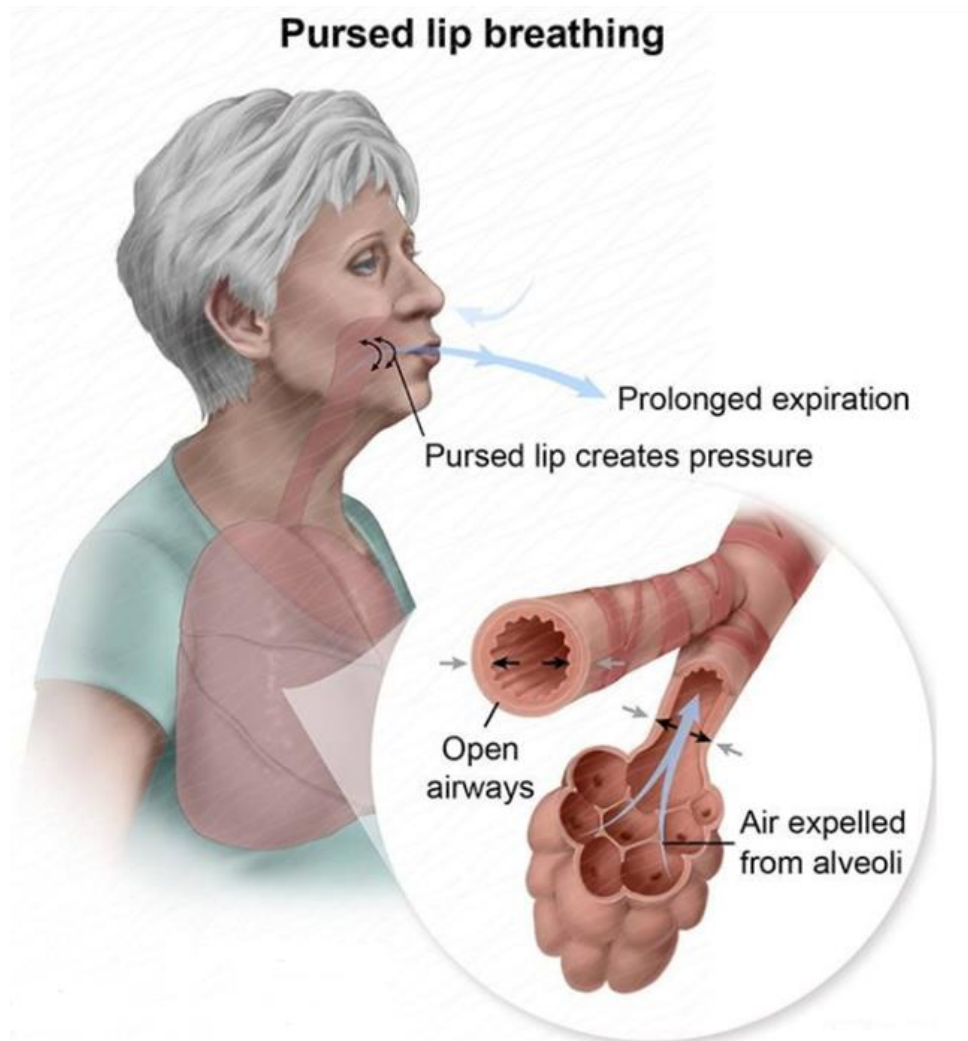
Injury to the  
phrenic nerve  
during cardiac  
surgery



# HOW DID WE MANAGE THE PATIENT IN CR?

# PHASE II CR FOLLOWING AVR: CASE PATIENT

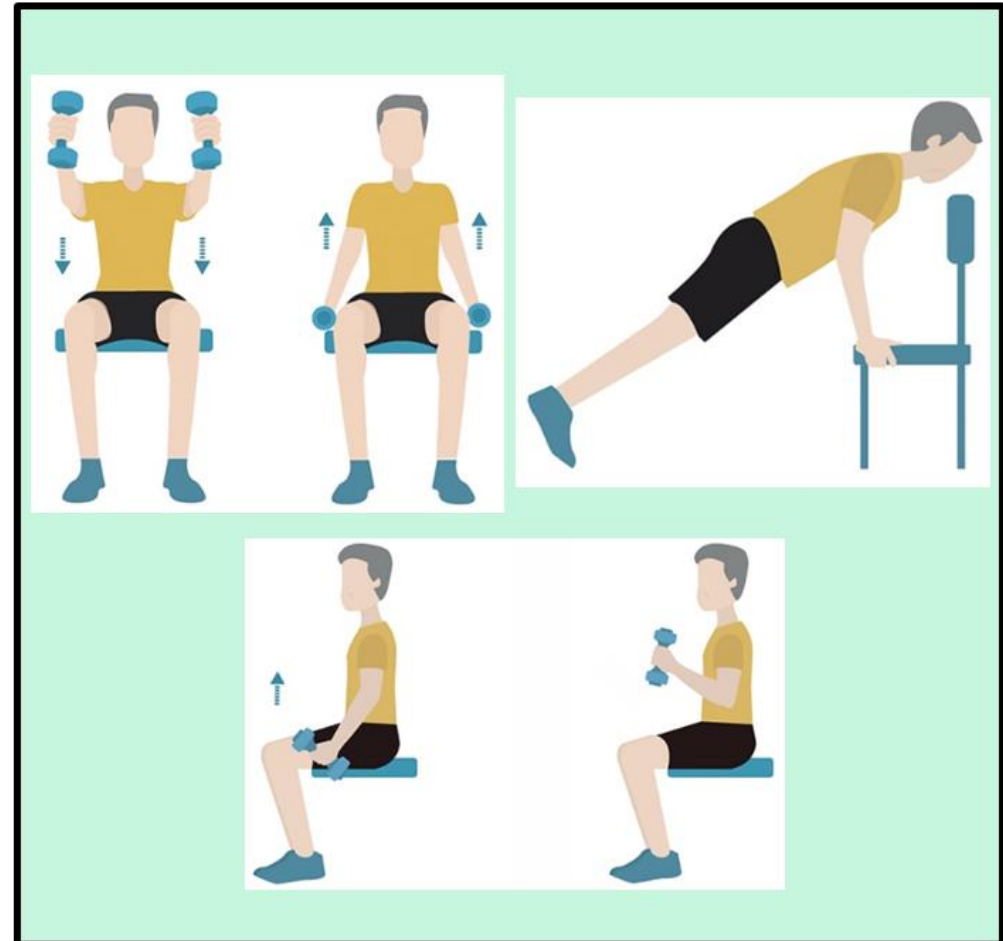
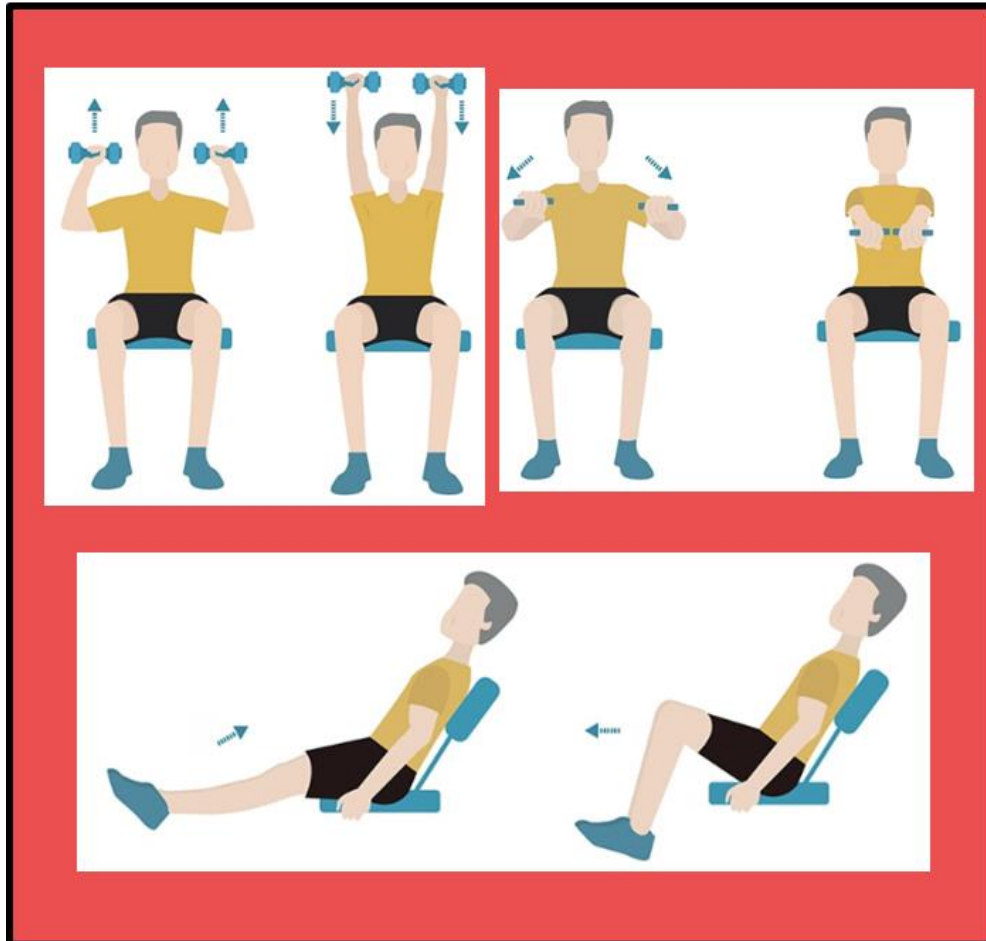
## 54-YEAR-OLD MALE



# PHASE II CR FOLLOWING AVR: CASE PATIENT

## 54-YEAR-OLD MALE

Modification of resistance exercise training plan.



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<b>23 total sessions over 15 weeks</b>	<b>Before CR (rest)</b>	<b>After CR (rest)</b>	<b>Δ</b>
Weight, lbs	288	292	+4
BMI, kg/m <sup>2</sup>	35.1	35.5	+0.4
Heart rate, bpm	75	82	
<b>BP, mmHg</b>	<b>156/64</b>	<b>122/60</b>	<b>-34/4</b>
SpO <sub>2</sub> , %	97	96	
ECG	NSR, no ectopy	NSR, no ectopy	

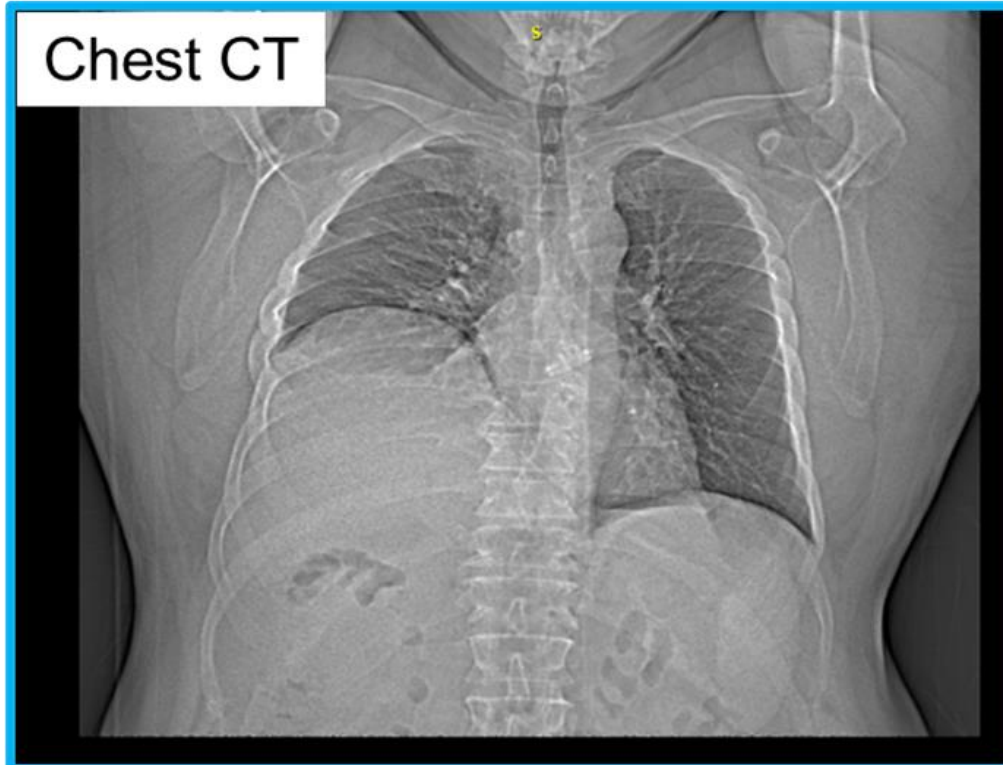
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## 54-YEAR-OLD MALE

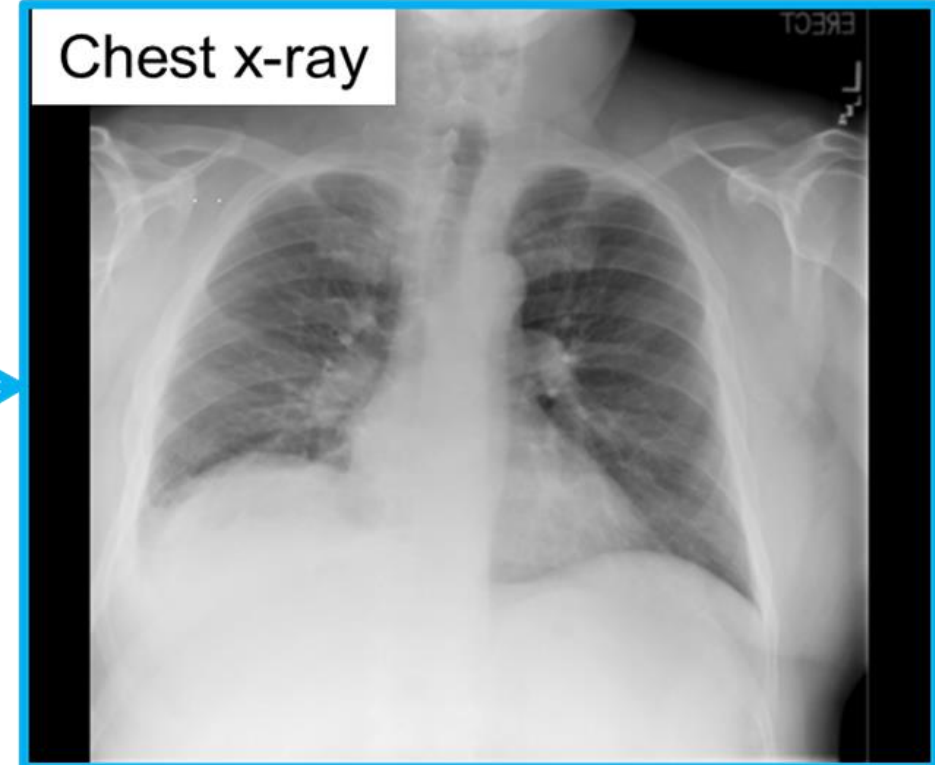
23 total sessions over 15 weeks	Before CR (6MWT)	After CR (6MWT)	Δ
Heart rate, bpm	90	109	
BP, mmHg	198/84	148/66	
SpO <sub>2</sub> , %	95	98	
RPE	9	15	
Distance, ft	1,402	1,620	+218
Speed, mph	2.6	3.1	+0.5
METS	3	3.3	+0.3
ECG	NSR, no ectopy	NSR, no ectopy	

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## 54-YEAR-OLD MALE



Iatrogenic right hemidiaphragm  
paralysis and elevation



Adhesions between right  
hemidiaphragm & lower lobe freed; right  
hemidiaphragm lowered 2 rib spaces

# QUESTIONS & ANSWERS

