

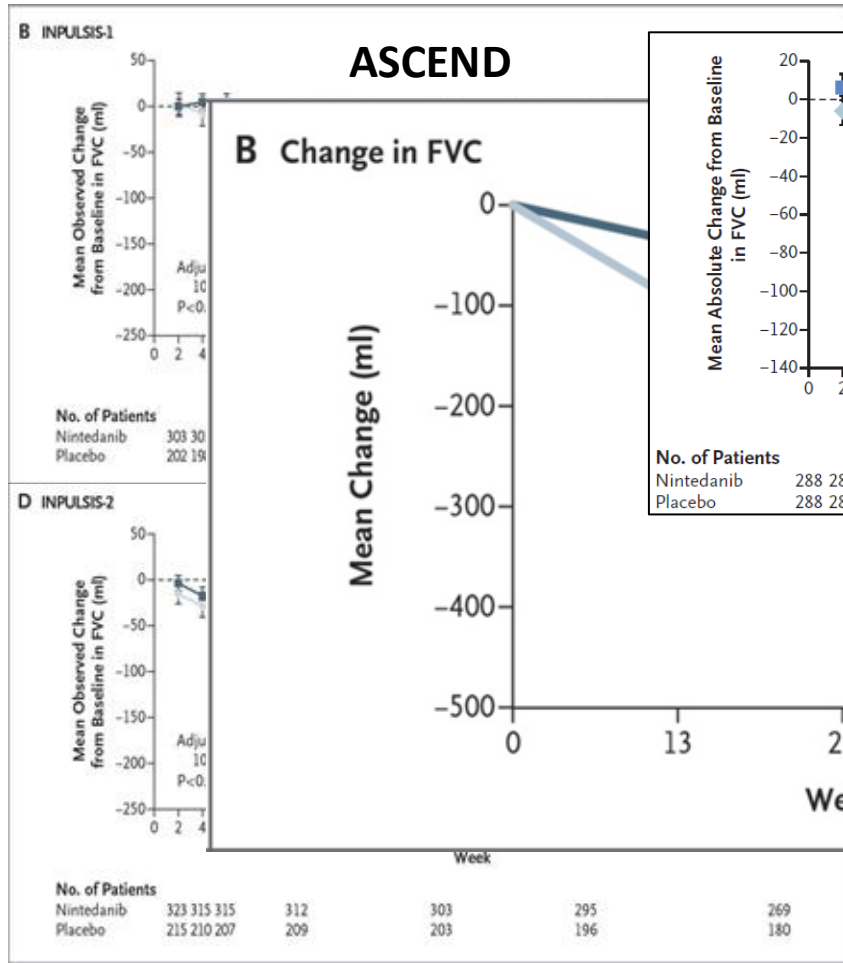
More Than Meds: Nonpharmacologic Treatments for ILD

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MGH Interstitial Lung Disease Program

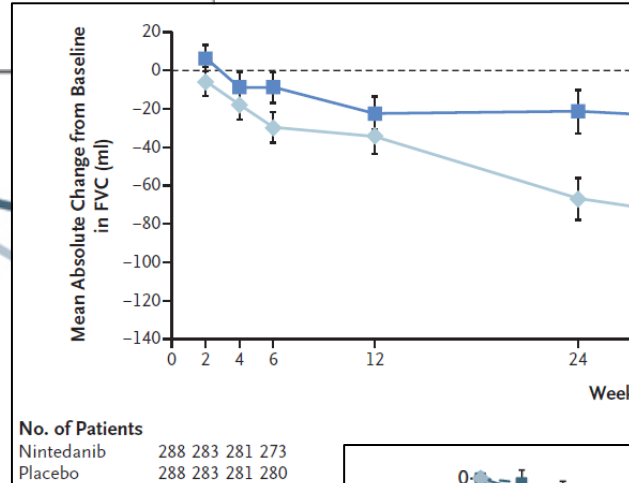
Pharmacologic Treatment for ILD

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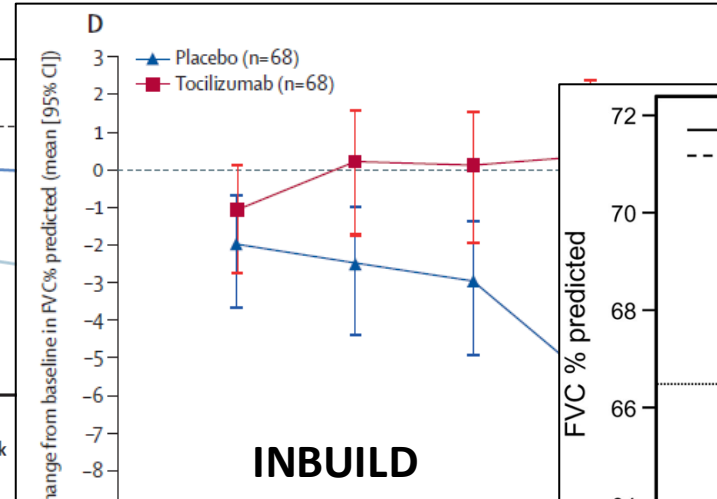


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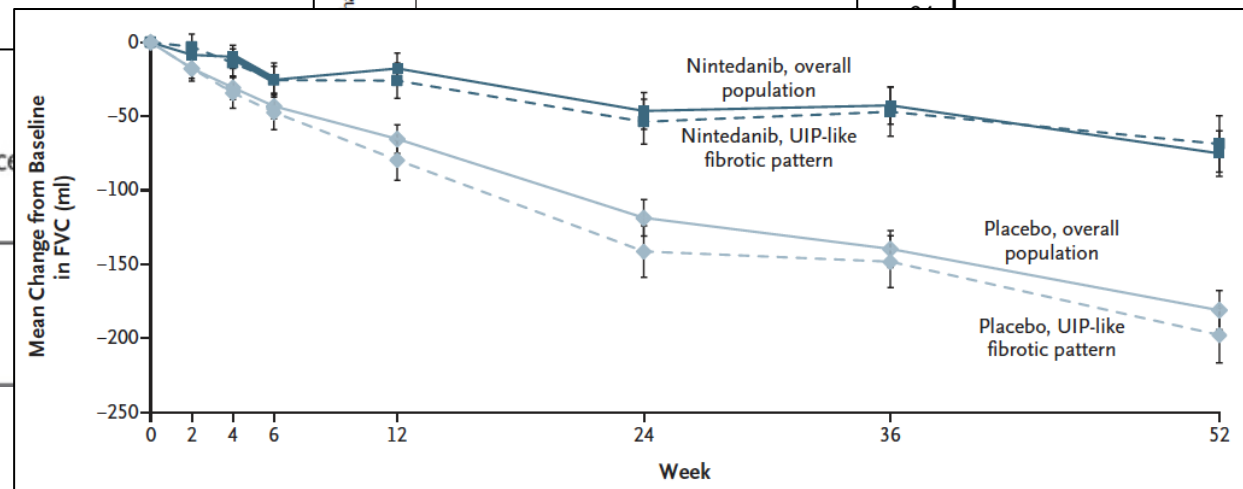
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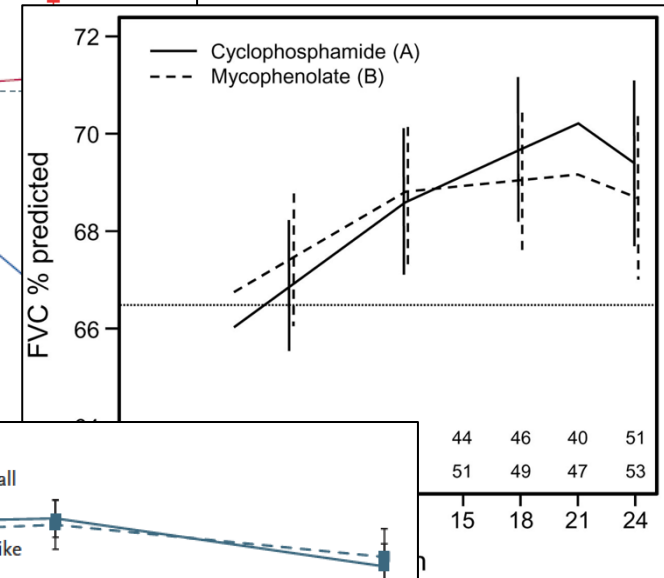
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SLS II



Pharmacologic Treatment for ILD

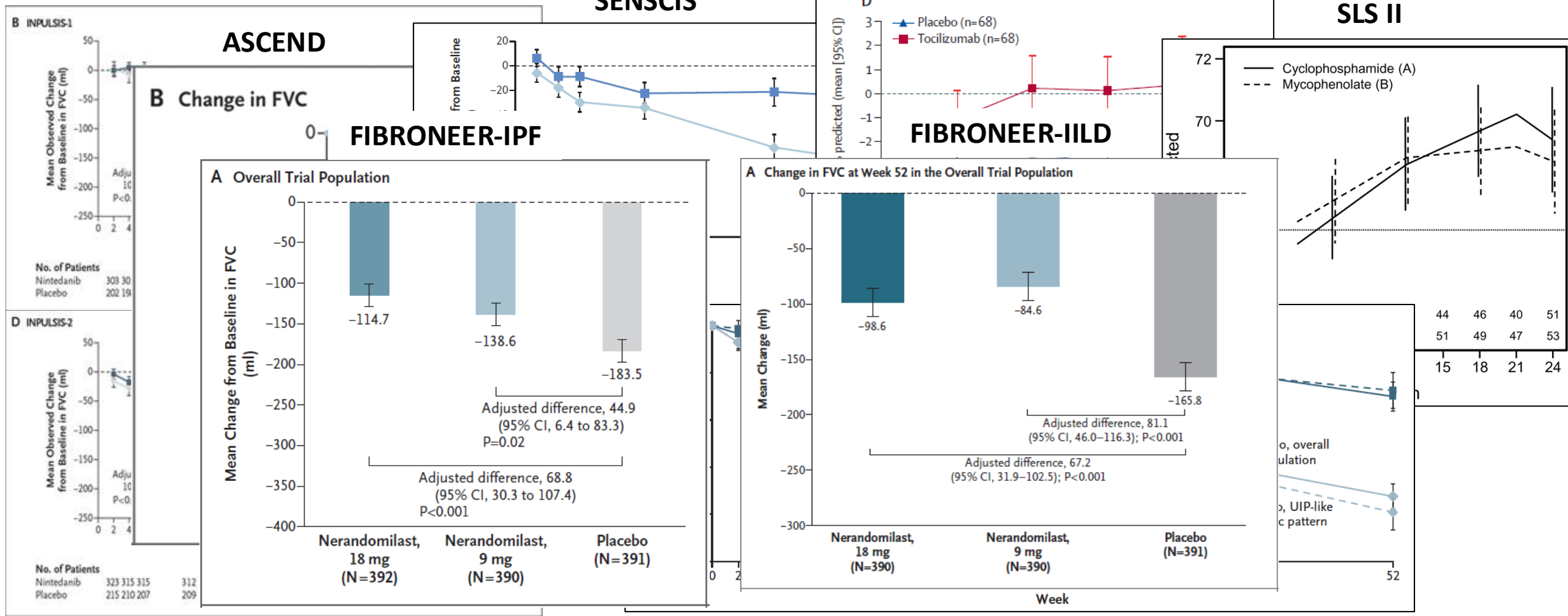
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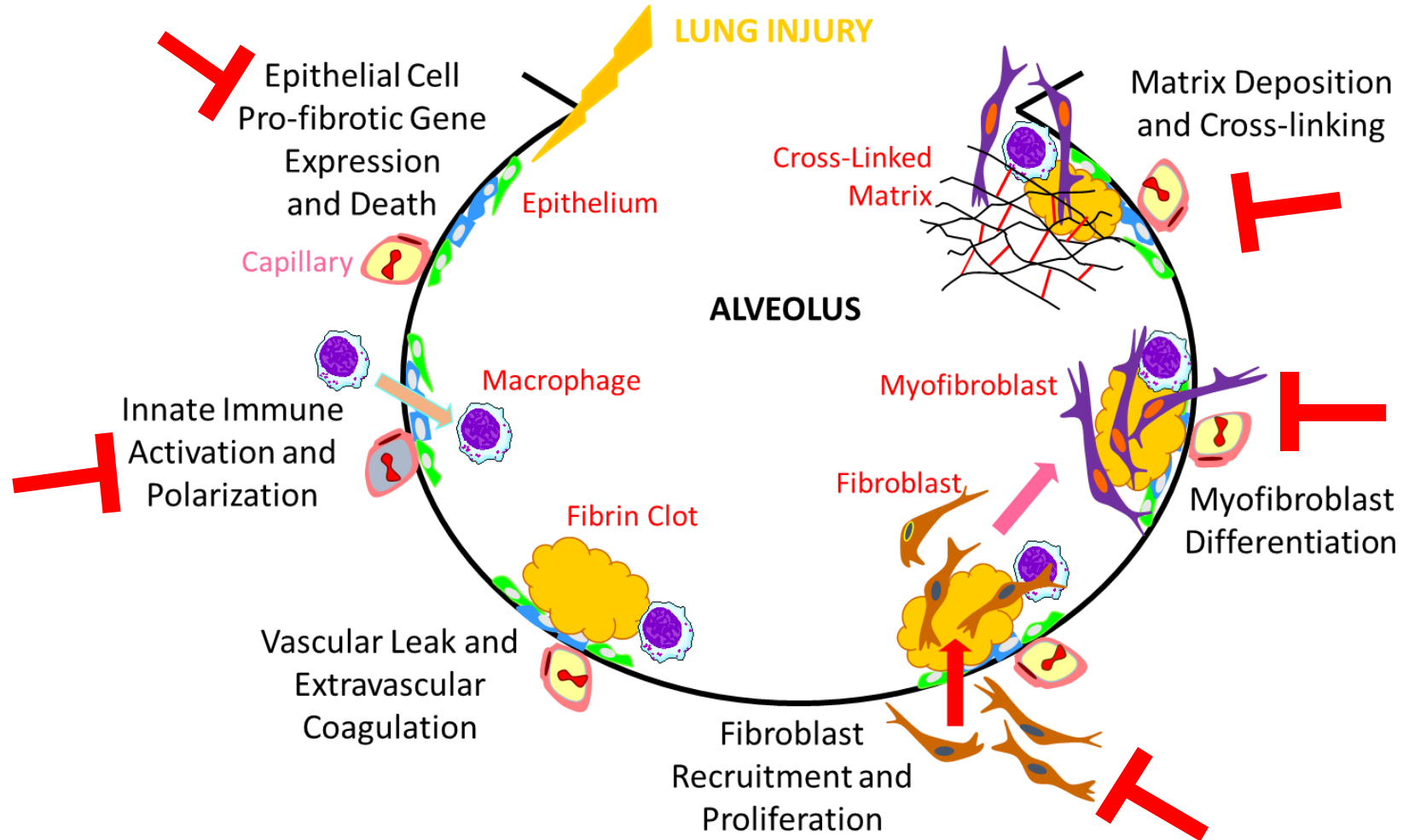
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SLS II



Additional ILD therapies on the horizon?



Beyond FVC and survival – morbidity in ILD

- Dyspnea
- Exercise limitation / Fatigue
- Cough
- Anxiety and mood disturbances
- Quality of Life (QOL)

Treatment of IPF and other ILDs has to focus on limiting morbidity and improving QOL as much as it does on prolonging survival!

- Pulmonary rehab
- Supplemental O2
- Cough management



IPF Treatment Guidelines

Pharmacologic Therapy	Recommendation		
	For (✓) /Against (X)	Strength	Evidence quality
Anticoagulation (warfarin)	X	Strong	Low
Azathioprine + prednisone + N-acetylcysteine	X	Strong	Low
Imatinib	X	Strong	Moderate
Selective endothelin receptor antagonists	X	Strong	Low
Dual endothelin receptor antagonists	X	Conditional	Moderate
Antipulmonary hypertension therapy	X	Conditional	Very low
N-acetylcysteine monotherapy	X	Conditional	Low
Phosphodiesterase-5 inhibitor (sildenafil)	X	Conditional	Moderate
Anti-reflux therapy	X	Conditional	Very low
Pulmonary rehabilitation	✓	Conditional	Low
Supplemental oxygen	✓	Strong	Very low
Lung transplantation	✓	Strong	Low
Nintedanib	✓	Conditional	Moderate
Pirfenidone	✓	Conditional	Moderate

Pulmonary rehab improves functional capacity and reduces symptoms in ILD

Retrospective analysis 402 patients with ILD (50% IPF)

- 80% on O₂, mean FVC 54%

	Admission	Discharge	Change	p-value
Lung function parameters[#]				
PO ₂ mmHg	61 ± 1	63 ± 1	2 ± 1	0.012
PCO ₂ mmHg	39 ± 0	40 ± 0	1 ± 0	0.002
VC % pred	54 ± 1	55 ± 1	1 ± 0	0.002
TLC % pred	65 ± 1	65 ± 1	0 ± 0	0.322
FEV ₁ % pred	55 ± 1	56 ± 1	1 ± 0	<0.001
6MWT and dyspnoea rating[*]				
6MWD m	308 ± 6	354 ± 6	46 ± 3	<0.001
Dyspnoea-free walk distance m	291 ± 7	343 ± 7	52 ± 4	<0.001
VAS (before exertion)	3.2 ± 0.1	3.3 ± 0.1	0.1 ± 0.1	0.572
VAS (after exertion)	6.5 ± 0.1	6.3 ± 0.1	-0.2 ± 0.1	0.176
Health status (SF-36)⁺				
Physical functioning	24 ± 1	29 ± 1	5 ± 1	<0.001
Bodily pain	60 ± 2	66 ± 2	7 ± 2	<0.001
Physical role functioning	12 ± 2	17 ± 2	5 ± 2	0.009
General health perceptions	29 ± 1	33 ± 1	4 ± 1	<0.001
Vitality	32 ± 1	45 ± 1	13 ± 1	<0.001
Social role functioning	52 ± 2	63 ± 2	11 ± 2	<0.001
Emotional role functioning	49 ± 3	56 ± 3	7 ± 3	0.029
General mental health	58 ± 1	67 ± 1	9 ± 1	<0.001
Physical summary score	31 ± 1	37 ± 1	6 ± 1	<0.001
Mental summary score	47 ± 1	57 ± 1	10 ± 1	<0.001

Pulmonary rehab improves functional capacity and reduces symptoms in ILD

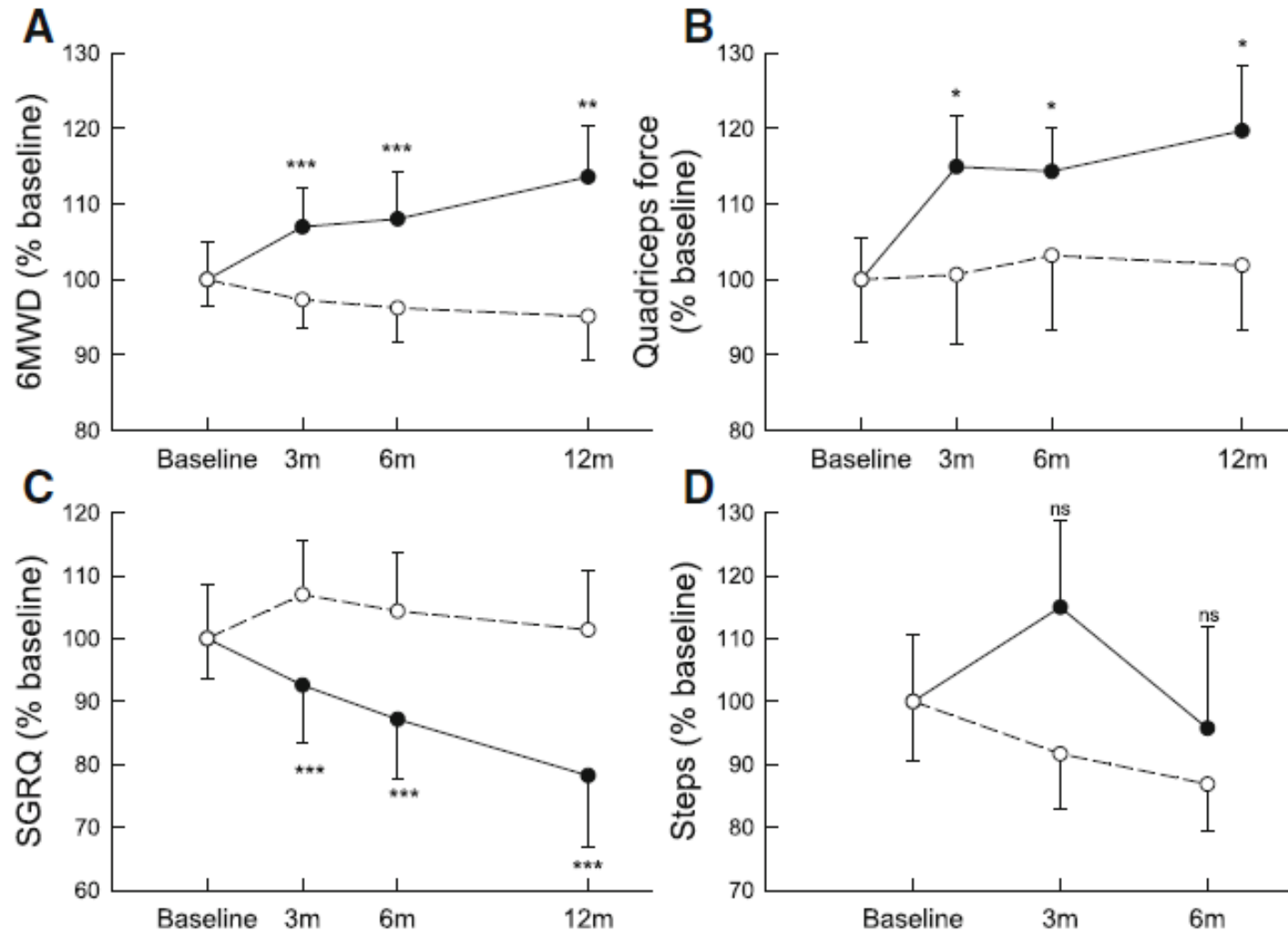
Prospective study of 41 patients with ILD (63% IPF)

- Moderate disease (FVC 74.5%, DLCO 45.5%)
- Standardized PR course (24 sessions)

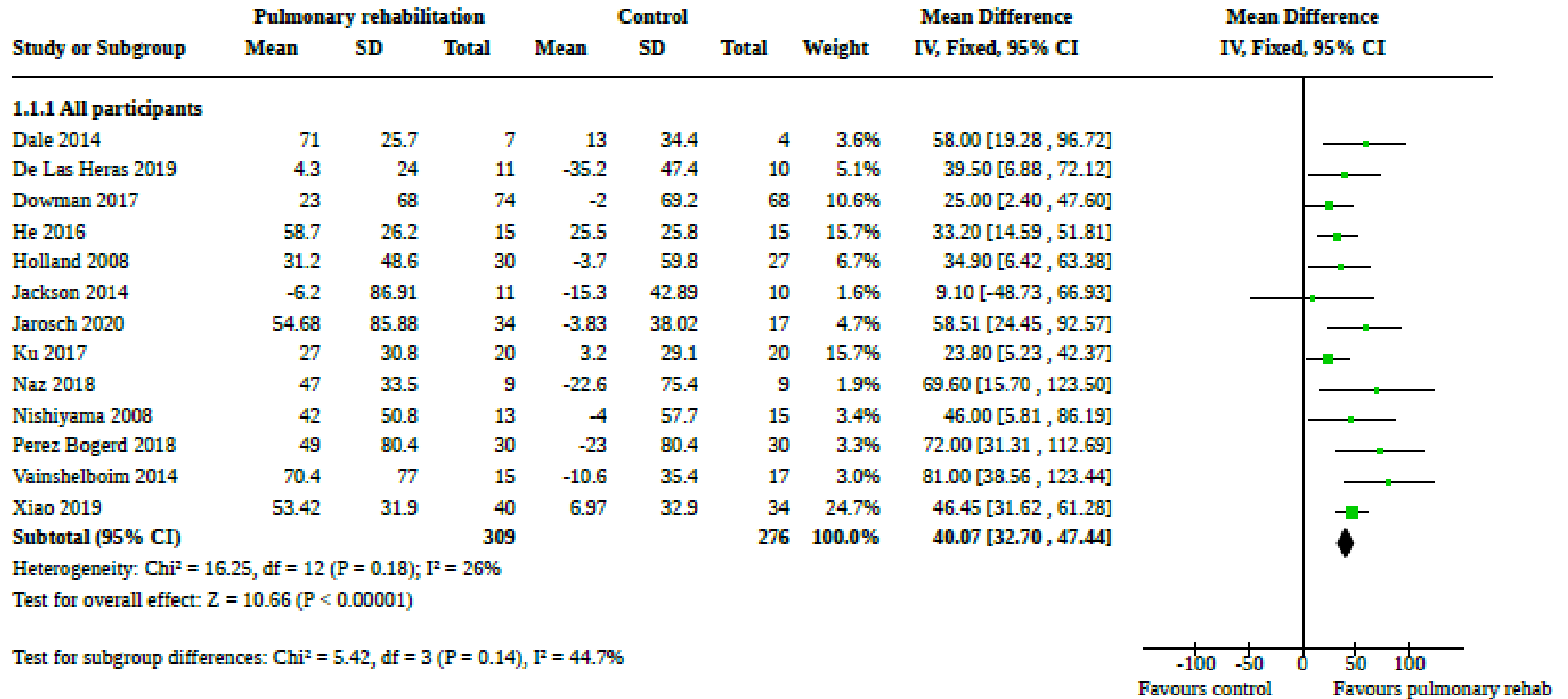
Table 2 Outcome measures with absolute and relative change following PR

Outcomes	n	Before PR	Post PR	Absolute change	Relative change (%)	p
MRC	40	2.8 ± 0.8	1.7 ± 1.1	- 1.1 ± 0.8	-40.8 ± 35	<.001
SGRQ (Total)	39	50.6 ± 13.9	38.5 ± 13.7	- 12.1 ± 11.1	-23.3 ± 19	<.001
SGRQ (Activity)	39	67.6 ± 14	58.9 ± 19.6	- 8.8 ± 17.6	-12.5 ± 24.7	0.009
SGRQ (Impact)	39	43.7 ± 19.1	29.9 ± 15.9	- 13.7 ± 14.6	-29.9 ± 41.5	<.001
SGRQ (Symptoms)	39	40.4 ± 20.9	26.7 ± 20.8	- 17 ± 19.8	-36 ± 22.1	<.001
6MWD (m)	39	376.8 ± 94.6	430.9 ± 96.4	54.1 ± 55.4	16.7 ± 37.8	<.001
Dyspnea 6MWD (Borg Scale)	39	5.2 ± 2.3	3.8 ± 2.2	-1.4 ± 2.1	-23.4 ± 40.1	.015
Leg fatigue 6MWD (Borg Scale)	39	3.5 ± 2.7	2 ± 2.2	-1.6 ± 1.5	-48.1 ± 71.5	.006
Cycle dyspnea ^a (Borg scale)	40	6.1 ± 2	4.2 ± 2.7	- 1.8 ± 1.9	-33 ± 35.1	<.001
Cycle leg fatigue ^a (Borg scale)	40	5.9 ± 2.1	3.7 ± 2.7	- 2.2 ± 2	-39.5 ± 106	<.001
Cycle endurance time (min)	40	7.7 ± 3.8	12.5 ± 8.4	4.8 ± 6.9	66 ± 108.1	<.001
Cycle endurance power (watt)	40	57.5 ± 23.7	88.2 ± 57.1	31 ± 53.5	63.4 ± 33.9	.003

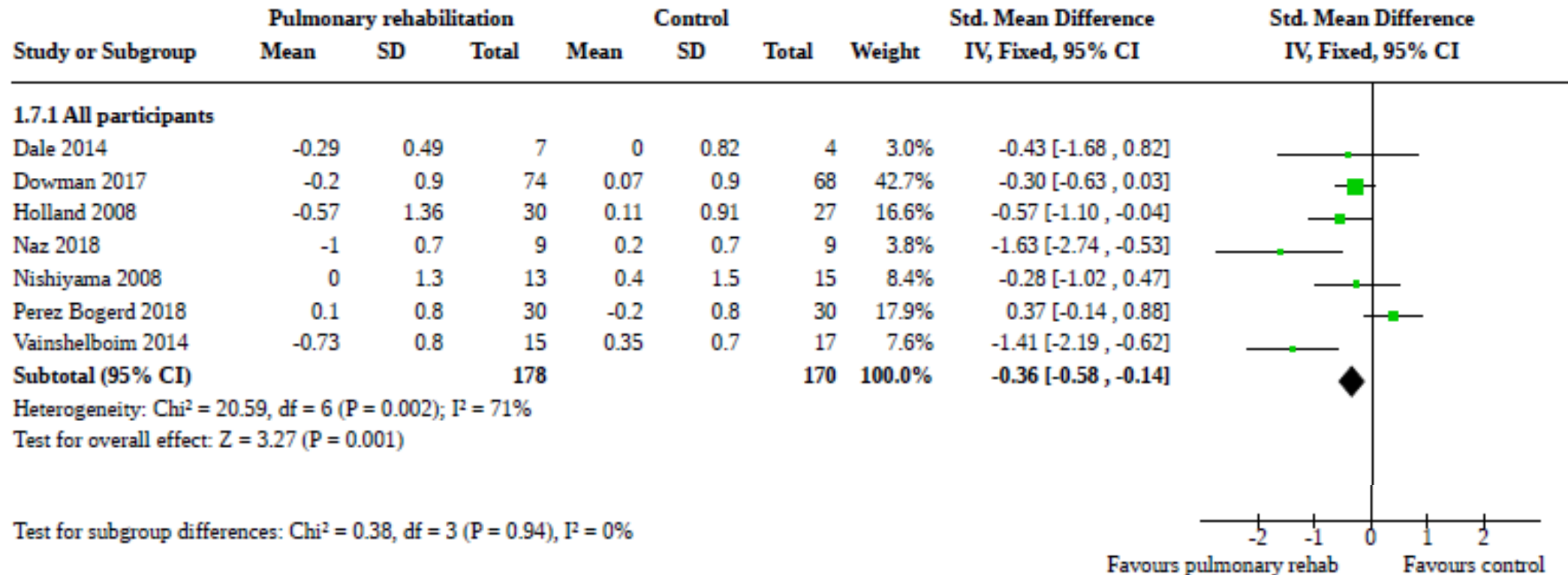
Beneficial Effects of Pulmonary Rehab in ILD Persist at 12 Months



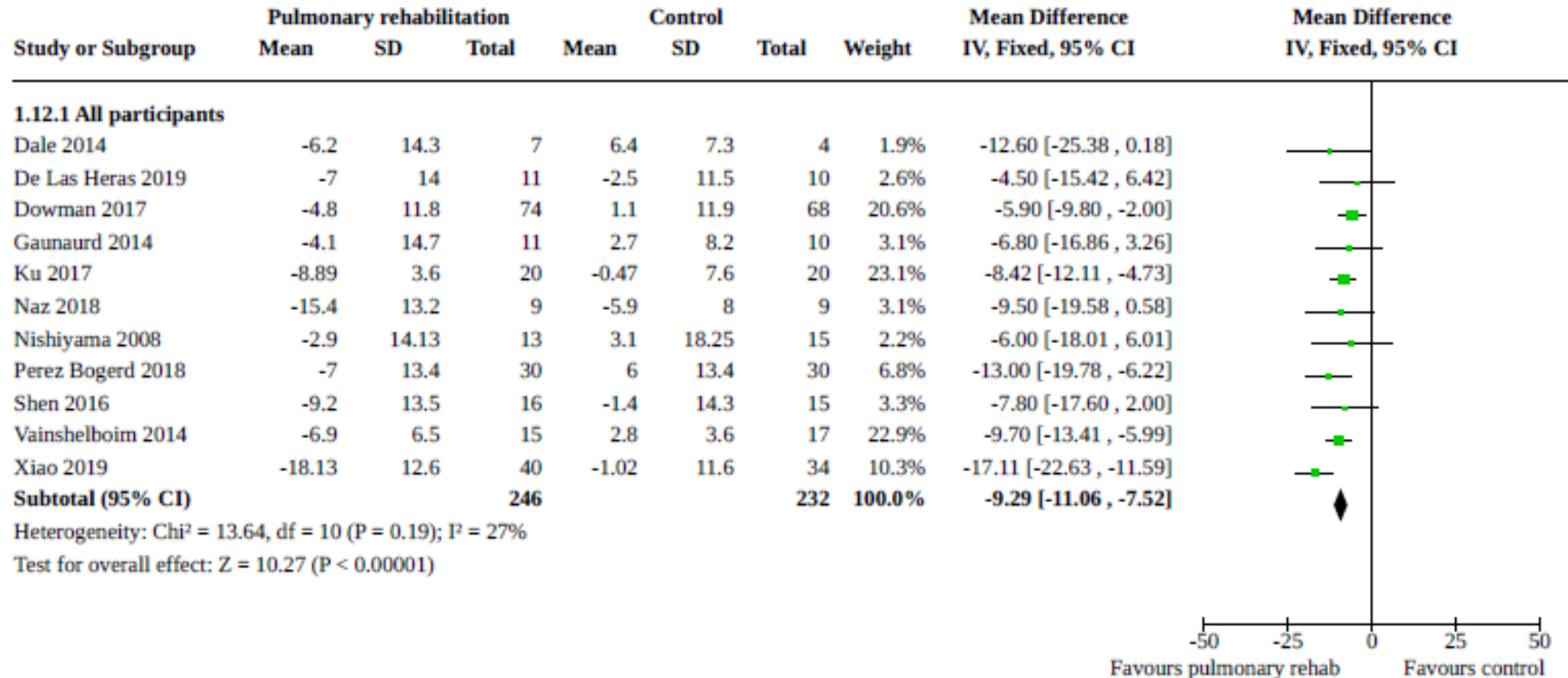
Pulmonary Rehab Improves 6MWD in ILD



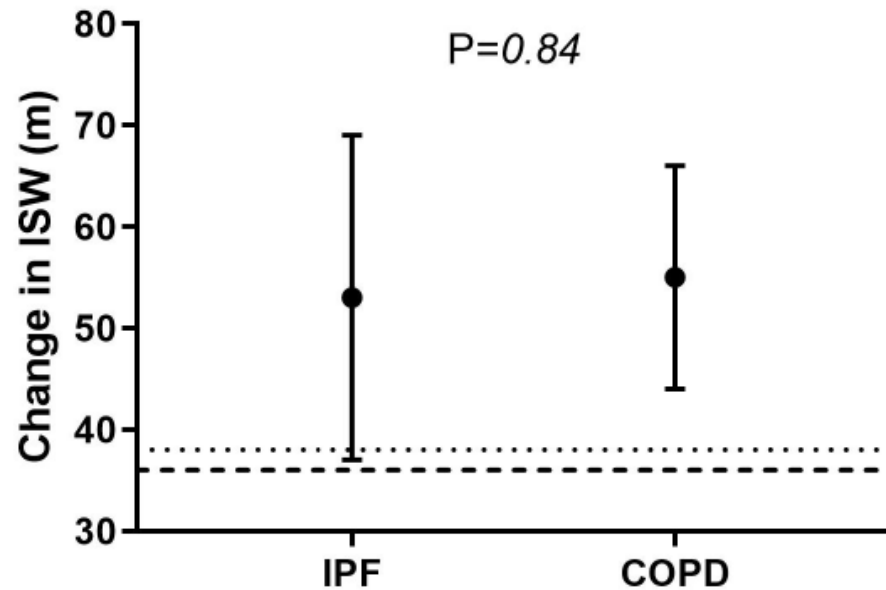
Pulmonary Rehab Improves Dyspnea in ILD



Pulmonary Rehab Improves QOL in ILD



PR has Similar Benefits in IPF and COPD



Variables	Within group response to PR				Between group difference in response to PR	
	IPF (n=113)		COPD (n=103)		Between group difference	p
	Mean (95 % CI)	p*	Mean (95 % CI)	p*	Mean (95 % CI)	p
Δ ISW (metres)	53 (37 to 69)	<0.001	55 (44 to 66)	<0.001	2 (-18 to 22)	0.84
Δ MRC	-0.7 (-0.8 to -0.5)	<0.001	-0.7 (-0.9 to -0.6)	<0.001	0.0 (-0.2 to 0.3)	0.36
Δ CRQ Dyspnoea	4.0 (2.9 to 5.1)	<0.001	5.0 (3.7 to 6.2)	<0.001	1.0 (-0.7 to 2.6)	0.25
Δ CRQ Fatigue	1.9 (1.0 to 2.8)	<0.001	2.2 (1.3 to 3.1)	<0.001	0.3 (-0.9 to 1.5)	0.62
Δ CRQ Emotional Function	2.3 (1.0 to 3.5)	<0.01	3.3 (2.0 to 4.7)	<0.001	1.1 (-0.7 to 2.9)	0.24
Δ CRQ Mastery	1.4 (0.6 to 2.2)	<0.001	2.2 (1.3 to 3.1)	<0.001	0.8 (-0.4 to 1.94)	0.19
Δ CRQ Total	9.6 (6.5 to 12.6)	<0.001	12.7 (9.2 to 16.2)	<0.001	3.2 (-1.4 to 7.7)	0.18

Hypoxemia and Supplemental O2 in ILD

59 y.o. F

- FVC 96%
- DLCO 62%

	Effort #1	Effort #2
Exercise state	Rest	6min walk
Suppl O2 Flow (L/ min)	0	0
Exercise distance (m)		449
SpO2 site	Finger	Finger
SpO2 (%)	97	97
Heart rate (freq/ min)	89	118

55 y.o. M

- FVC 45%
- DLCO 32%

	Effort #1	Effort #2	Effort #3	Effort #4	Effort #5
Exercise state	Rest	Hall walk	Hall walk	Hall walk	Hall walk
Suppl O2 Flow (L/ min)	0	0	2	4	5
Exercise distance (m)		502	120	120	120
SpO2 site	Finger	Finger	Finger	Finger	Finger
SpO2 (%)	96	73	84	88	90
Heart rate (freq/ min)	90	132	112	119	119

69 y.o. M

- FVC 71%
- DLCO 41%

	Effort #1	Effort #2	Effort #3
Exercise state	Rest	Hall walk	Hall walk
Suppl O2 Flow (L/ min)	0	0	3
Exercise distance (m)			600
SpO2 site	Finger	Finger	Finger
SpO2 (%)	97	87	91
Heart rate (freq/ min)	74	110	112

Would he benefit from O2?

Does he need O2?

How much O2?



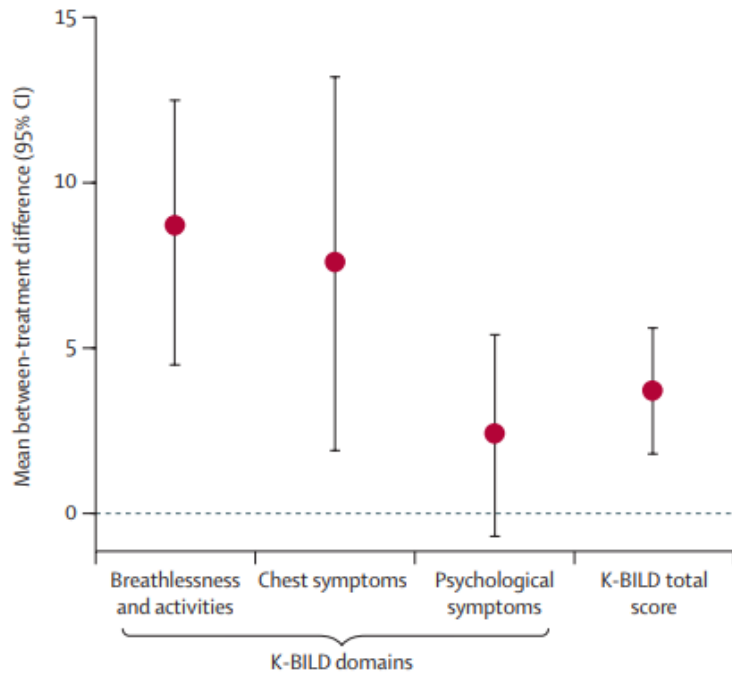
Supplemental O2 in ILD

- 2011 International Consensus Guidelines on IPF:
 - Strong recommendation (*weak evidence*) for LTOT in IPF patients with resting hypoxemia (SpO2 <89%; based on data from COPD)
 - *No recommendation* for or against LTOT for isolated exertional hypoxemia
- LOTT Study: supplemental O2 for COPD with exertional hypoxemia or mild resting hypoxemia (NEJM 2016)
 - No difference in long term outcomes, symptoms, or exercise capacity!
- Bell et al. *Eur Resp Rev.* 2017:
 - Meta-analysis of 12 studies of O2 supplementation in ILD (n = 4185 total)
 - LTOT (>12h/day) and “short-term” (e.g. exertional) O2 administration
 - No clear effects on dyspnea during exercise, variable effects on exercise capacity (6MWD, cycle endurance time)



Supplemental O2 in ILD

AmbOx Study: 84 patients with fibrotic ILD and isolated exertional hypoxemia

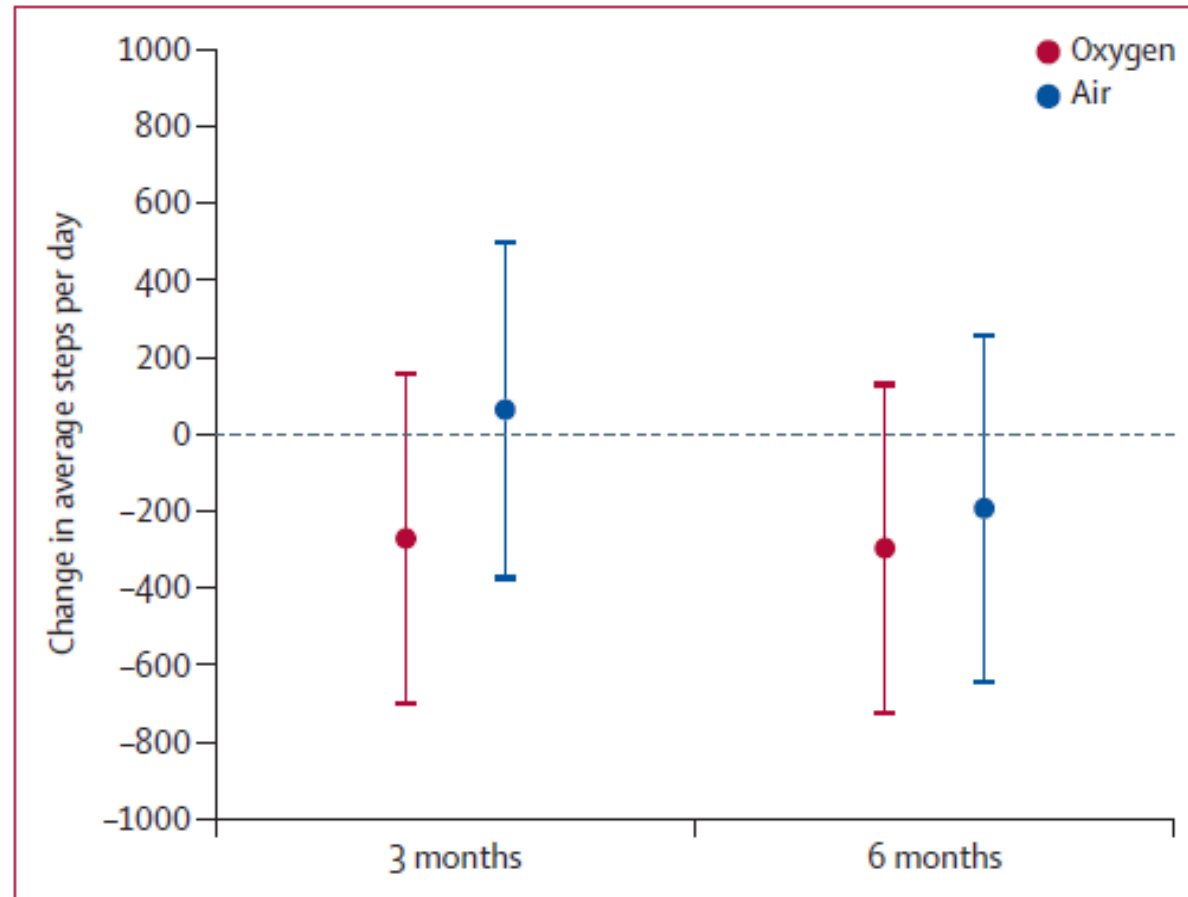


Outcome	Oxygen	Placebo Air	Difference	P value
SpO2 at end of test	90.6 (5.7)	84.7 (4.7)	5.9 (4.8 to 7.0)	<0.0001
Minimum SpO2	88.9 (4.3)	82.9 (4.4)	5.9 (4.8 to 7.1)	<0.0001
Distance walked, m	373.2 (89.9)	354.7 (97.8)	18.5 (10.9 to 26.1)	0.001
Heart rate at end of test	99.9 (14.3)	102 (18.3)	-2.2 (-4.9 to 0.6)	0.12
Maximum heart rate	104.4 (13.8)	108.9 (15)	-4.5 (-6.2 to -2.8)	0.01
SpO2 recovery time, s	117 (101)	217.7 (124)	-101 (-129 to -73)	<0.0001
Heart rate recovery time	163.7 (138.7)	191.9 (145.3)	-28.2 (-67.9 to 11.5)	0.06
Borg dyspnea score	2.1 (0.7 to 3.4)	3.0 (2.0 to 5.1)	-1.6 (-2.1 to -1.1)	<0.0001
Borg fatigue score	0.0 (0.0 to 1.4)	0.1 (0.0 to 2.6)	-0.4 (-1.1 to -0.2)	<0.0001
Borg dyspnea score recovery time, s	112 (72 to 164)	171 (114 to 229)	-49 (-99 to -1)	0.0008
Borg fatigue score recovery time, s	0 (0 to 82)	0 (0 to 174)	-14 (-64 to -0.5)	<0.0001

Data in table are expressed as mean (standard deviation) for first 7 rows and as median (interquartile range) for Borg score data;
K-BILD= King's Brief Interstitial Lung Disease questionnaire. Visca D et al. *Lancet Respir Med.* 2018;6:759-770.

Supplemental O2 in ILD

PFOX Study: O2 vs. sham for fILD with isolated exertional hypoxemia



Barriers to O2 use in ILD

Physiologically, the ideal scenario is $SpO_2 \geq 90\%$ at all times

➤ This is not realistic!

Physical/Mechanical Barriers	Psychological/Social Barriers
Equipment weight and size	Dependency
Tank duration/battery life	Emotionally constrained
Flow rate	Appearance of weakness, illness, vulnerability
Continuous vs. pulsed flow	Stigma (self-inflicted problem?)
Severity of hypoxemia	
Physically constrained	



Pragmatic Approach to O2 in ILD

Scenario	Treatment Approach
Resting SpO2 <89%	- Strong recommendation for O2
Mild exertional hypoxemia (SpO2min 86-88%)	- Self-monitoring SpO2 - Trial of O2 based on symptoms - PR-guided O2
Mod-severe exertional hypoxemia (SpO2min ≤85%)	- Recommend O2 with self-monitoring

2020 ATS Guidelines on home O2

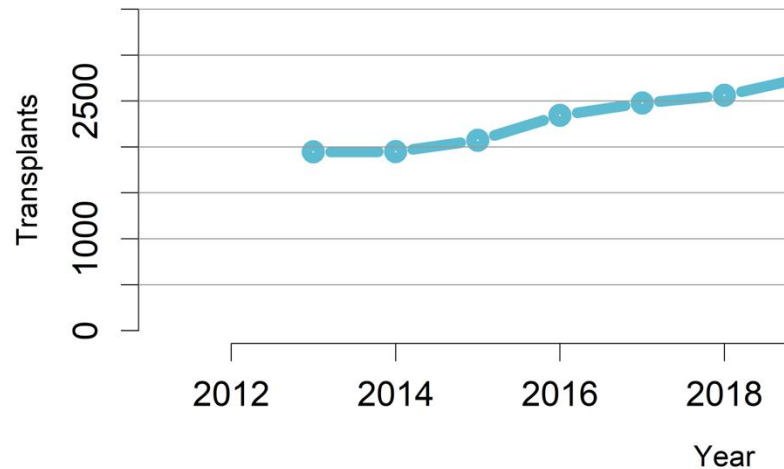
- *Strong* recommendation for O2 Rx for severe resting hypoxemia (very low quality evidence)
- *Conditional* recommendation for O2 Rx for severe exertional hypoxemia (low quality evidence)

- Spot-check self-monitoring SpO2 is very helpful!
 - Rest vs. usual activities (room-to-room, stairs, etc.) vs. formal exercise
- Goal SpO2 has to be individualized and based on many factors
 - Symptoms, SpO2min and recovery time
 - Feasibility: maximum flow rate vs. tank size/battery life
 - May be a moving target as disease changes over time
 - Some is better than none!



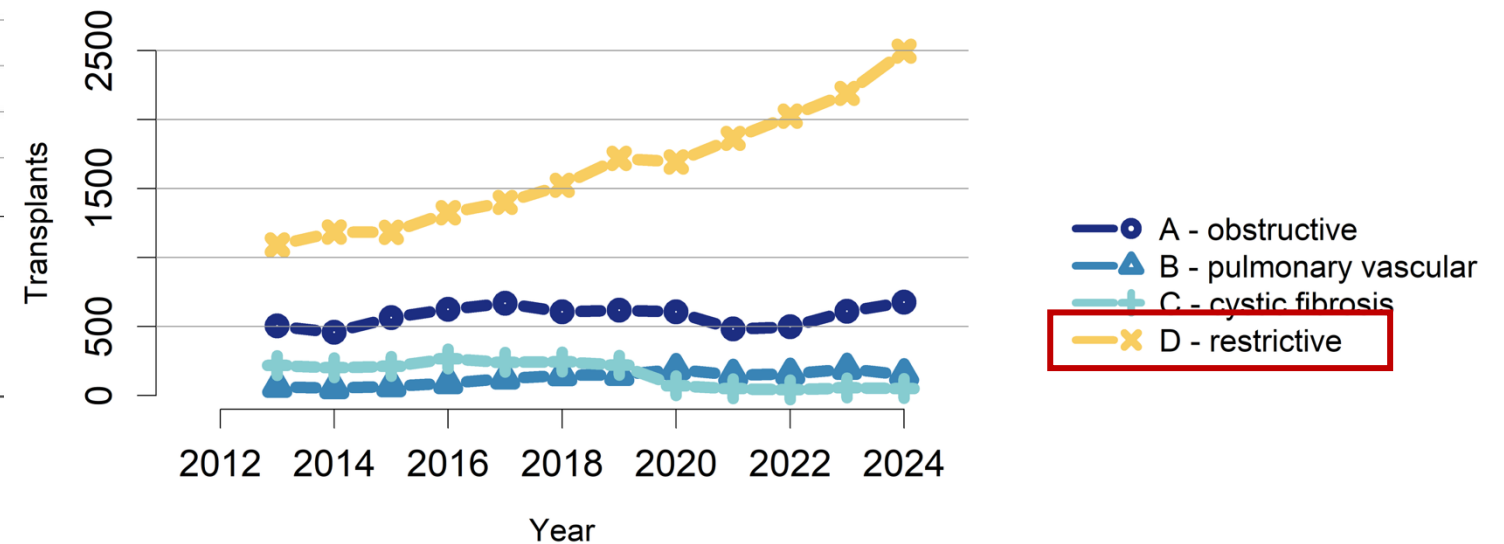
ILD is the Leading Indication for Lung Transplant in the U.S.

Figure LU 34: Overall lung transplants



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Figure LU 41: Adult lung transplants by diagnosis group

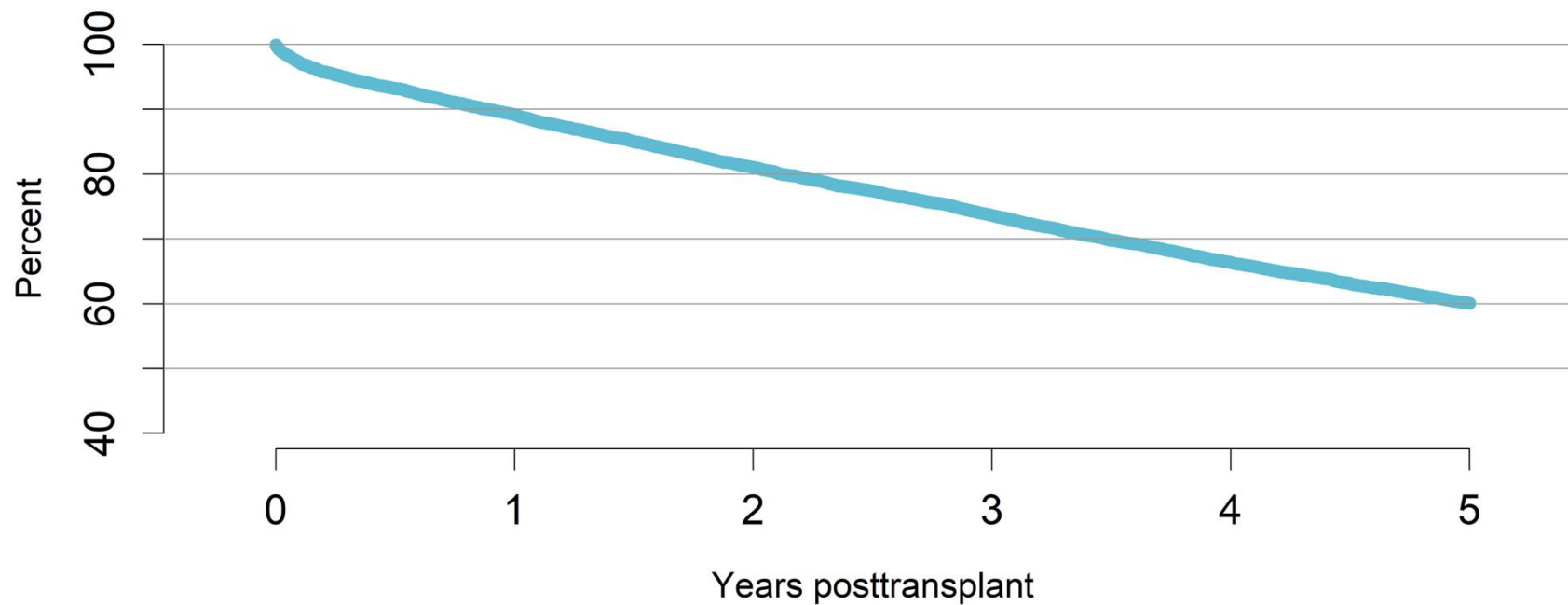


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Survival after Lung Transplantation

Figure LU 49: Patient survival among adult lung transplant recipients, 2017-2019



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Summary/Overview of ILD Management

