



## AATD 2024

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Marburg/Schönau a.K./Salzburg

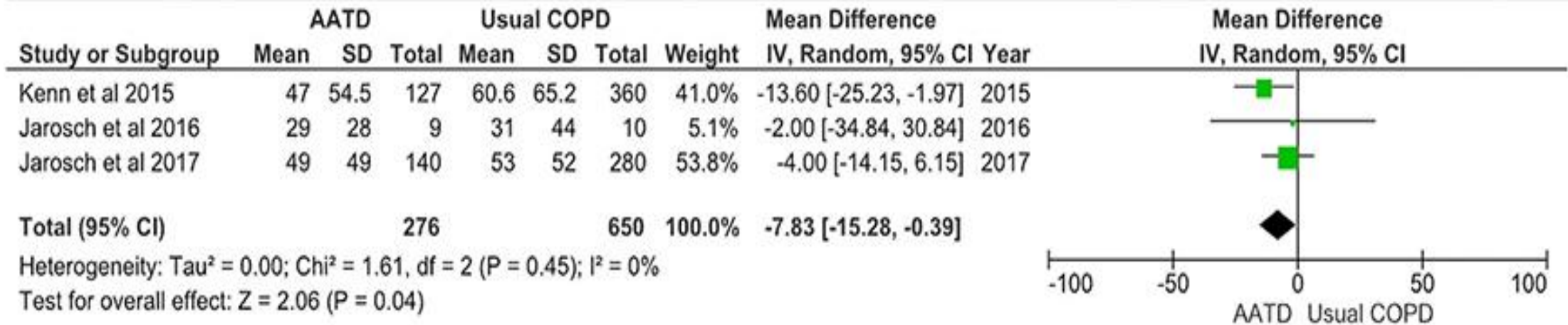
# Conflicts of interest

senTEC

GRIFOLS




**Figure 2. Forest Plot of the 6-Minute Walk Test**



AATD=alpha-1 antitrypsin deficiency; COPD=chronic obstructive pulmonary disease; SD=standard deviation; CI=confidence interval

		High-intensity training (HIT)	Moderate-intensity training (MIT)
<b>Endurance training</b>	Duration per session	Week 1: 18-24 min. Week 2: 30 min. Week 3: 36 min. (30 sec. intervals)	Week 1: 15-20 min. Week 2: 25 Week 3: 30 (continuously)
	Intensity	100%PWR	60-70% PWR
	Frequency	5-6x/ week	5-6x/ week
	Tool	Cycling ergometer	Cycling ergometer
	Adjustment	Increase when Borg score $\leq 3$ on a 10-point scale, reduction when Borg score $\geq 7$ pts.	Increase when Borg score $\leq 3$ on a 10-point scale, reduction when Borg score $\geq 7$ pts.
<b>Strength training</b>	Volume	3 sets à 8 repetitions	3 sets à 20 repetitions
	Intensity	aiming for local muscular failure after 8 repetitions	aiming for local muscular failure after 20 repetitions
	Frequency	5-6 x/ week	5-6 x/ week
	Tool	Machine training	Machine training
<b>Squat training</b>	Surface	Whole-body vibration platform (side-alternating, peak-to-peak displacement 4-5 mm)	Floor
	Volume	4x 2 min. à 24-26Hz	4x 2 min.
	Frequency	3x/ week	3x/ week

# High-intensity vs. moderate-intensity

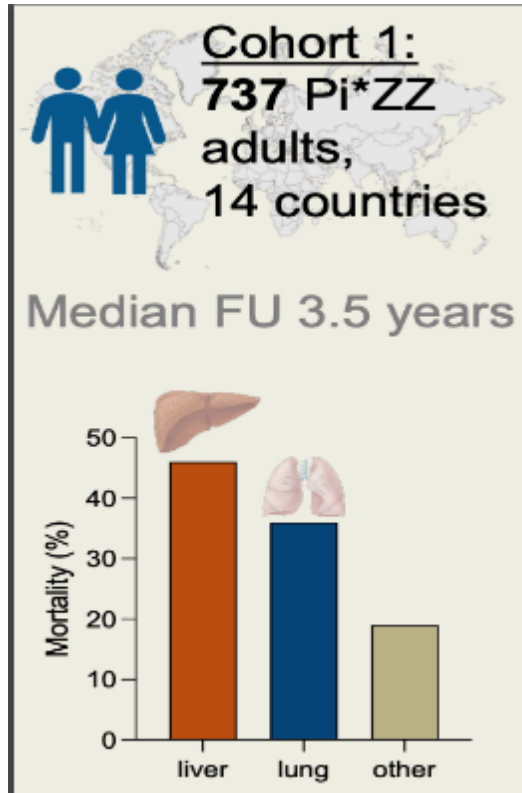
		HIT	MIT
<b>Endurance</b>	Duration	18-36 Min. (30 sec. intervals)	15-30 min. (continuously)
	 Intensity	100%PWR	60-70% PWR
	Frequency	5-6x/ week	5-6x/ week
<b>Strength</b>	Volume	3 sets à 8 repetitions	3 sets à 20 repetitions
	Intensity	provoking local muscular fatigue	provoking local muscular fatigue
	Frequency	5-6 x/ week	5-6 x/ week



	HIT group (n=12)			MIT group (n=13)			Between-group difference	
	Base- line	3 weeks	Difference	Base- line	3 weeks	Difference	Mean difference (95%CI)	P-value
<b>Exercise capacity</b>								
6MWD, m	395±120	418±115	<b>37 ± 43*</b>	424±68	457±78	<b>32 ± 28**</b>	5.0 (-26.2 to 36.2)	ns
Time to desaturate (SpO <sub>2</sub> <90%) during 6MWD, sec	113±57	139±53	22.3±51.8	104±47	108±54	4.5±28.5	17.8 (-33.6 to 69.1)	ns
ESWT, sec	464±452	521±436	57.3±154	411±322	520±330	108.9±339.9	51.6 (-170.1 to 273.3)	ns
ESWT, m	618±743	686±742	28.3±110.0	533±426	655±423	121.5±470	93.2 (-194.5 to 380.9)	ns
1STST, n	20±10	26±13	<b>5.6±4.9**</b>	24±9	30±11	<b>5.6±4.5***</b>	0 (-4.0 to 4.0)	ns
5STST, sec	11.6±4.7	9.3±3.2	-2.3±-1.9	11.7±5.7	9.8±4.2	<b>-1.9±2.0**</b>	0.4 (-2.1 to 2.9)	ns
Quadriceps strength, N	298±129	355±166	49.0±52.9	285±135	349±114	54.7±65.4	5.6 (-45.7 to 57.0)	ns

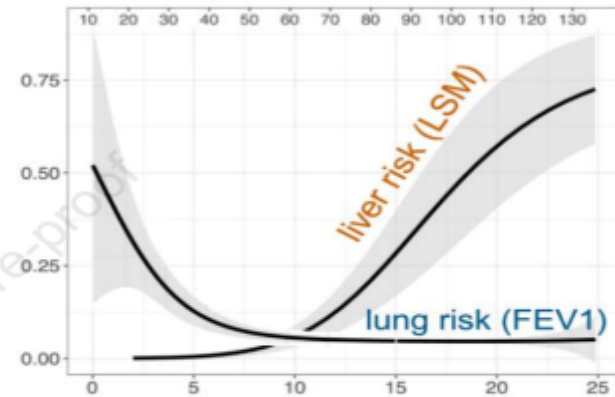
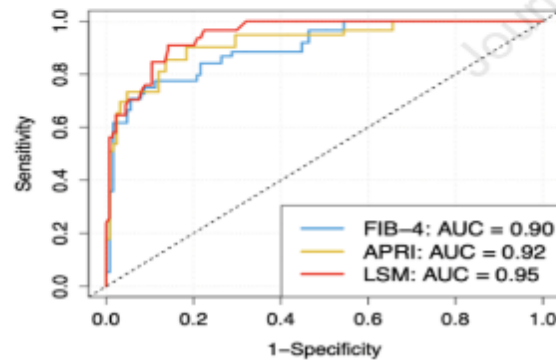
No between-group differences!

6MWD, 6-minute walking distance; ESWT, endurance shuttle walk test; HIT, high-intensity training; MIT, moderate-intensity training; ns, non-significant; STST, sit-to-stand test.  
Jarosch I, et al, Respiration. 2014; In press.

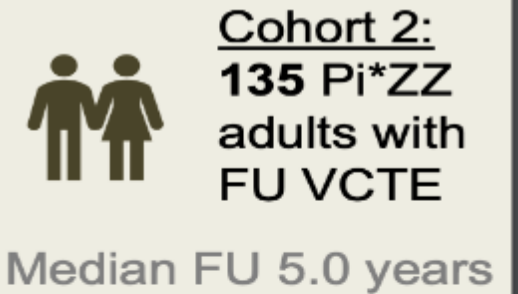


→ **NITs accurately predict hepatic endpoints in AATD (e.g., AUC LSM 0.95).**

→ Lung surrogates are less predictive for pulmonary endpoints (e.g., AUC FEV1 0.76).

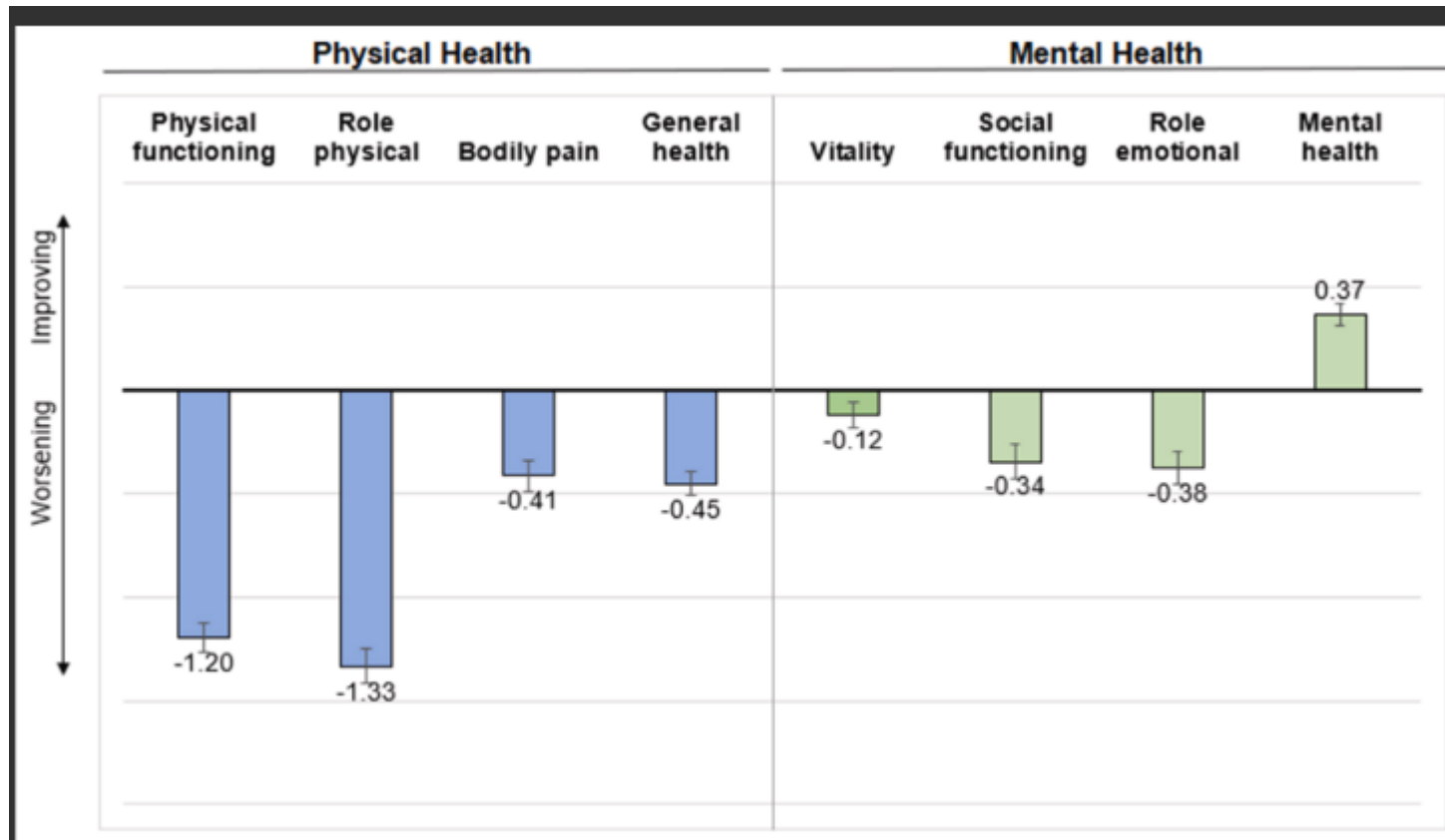


→ **Comparison of liver and lung surrogates facilitates patient management.**



→ Fibrosis progression rare + primarily in those with preexisting risks.

Gastroenterology

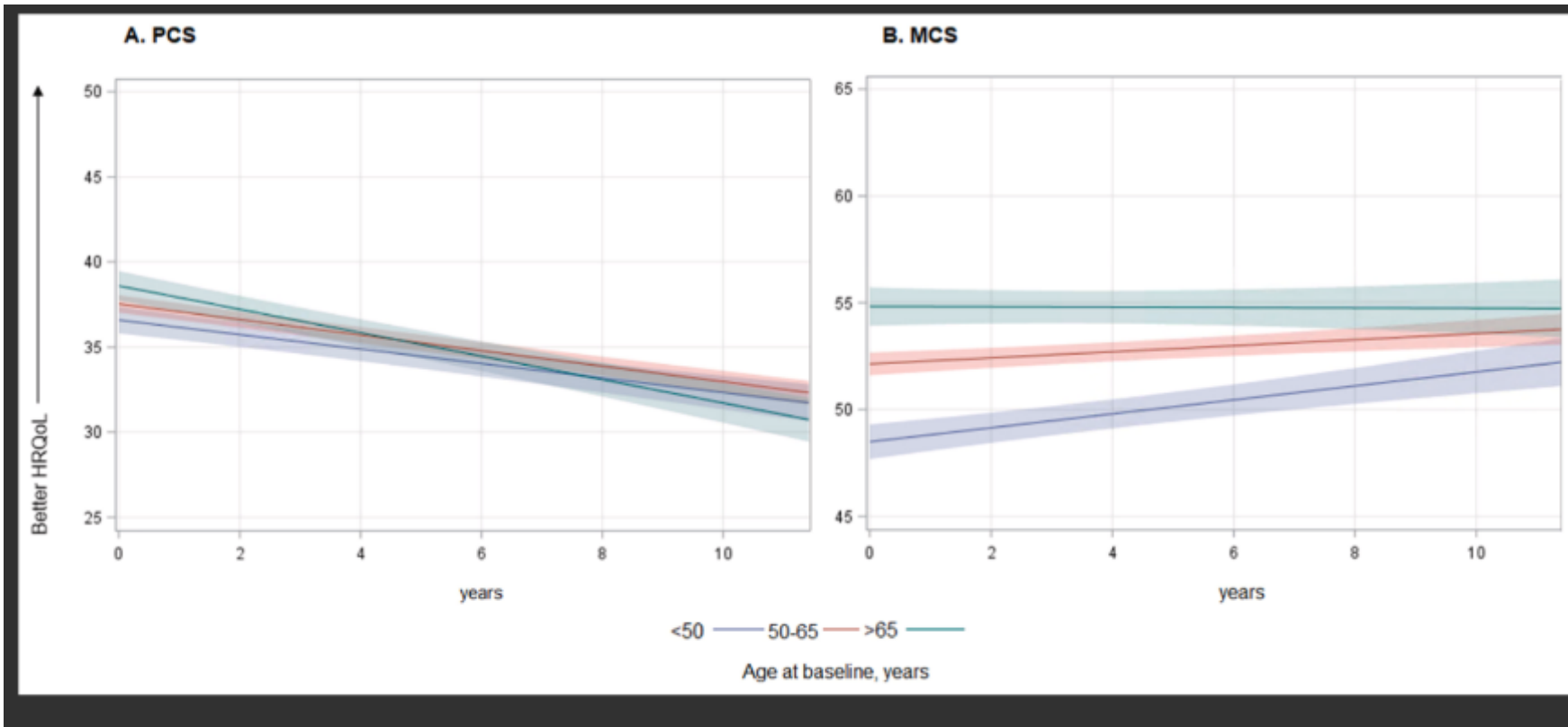


**Fig. 3. Annual change in SF-36 scale score means.**

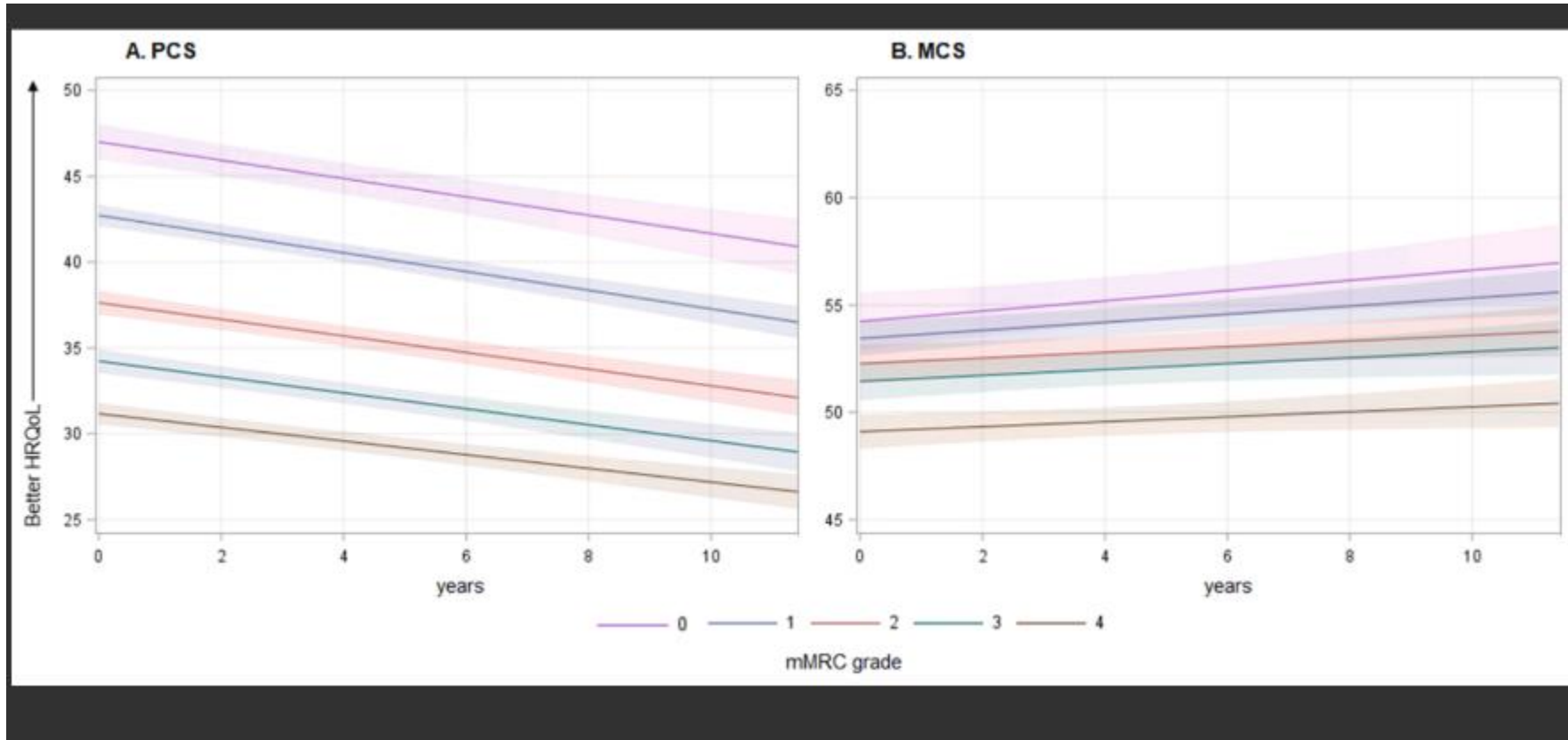
Note: SF-36 scale scores range from 0 to 100, with higher scores indicating better health.

Chioate et al Respir Med  
 . 2024 Oct 14:234:107838.





**Fig. 4. Longitudinal trajectories of SF-36 summary scores by age at baseline.**  
 PCS-Physical Component Summary; MCS-Mental Component Summary; norm-based, mean = 50 (SD = 10) in the general US population.  
 PCS slopes: <50: 0.4252/year; 50–65: 0.4561/year; >65: 0.6882/year. (p-value for interaction age\*time = 0.0016).  
 MCS slopes: <50: 0.32663/year; 50–65: 0.14193/year; >65: 0.00787/year. (p-value for interaction age\*time = 0.0012).  
 Note: shaded areas indicate 95 % confidence intervals.



**Fig. 5.** Longitudinal trajectories SF-36 summary scores by baseline mMRC.

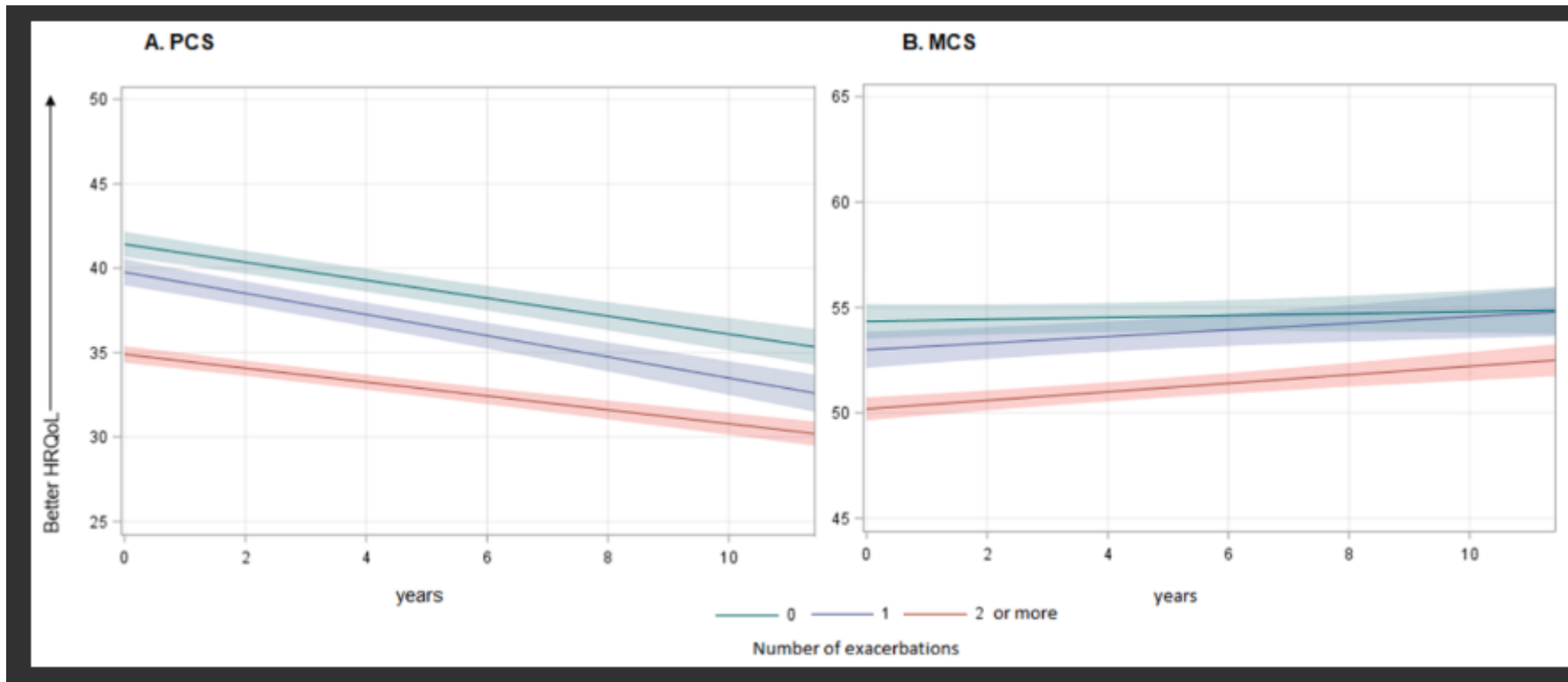
PCS-Physical Component Summary; MCS-Mental Component Summary; norm-based, mean = 50 (SD = 10) in the general US population.

PCS slopes: mMRC grade 0: 0.5337/year; grade 1: 0.54497/year; grade 2: 0.48406/year; grade 3: 0.4638/year.

grade 4: 0.3986/year; (p-value for interaction mMRC\*time = 0.3153).

MCS slopes: mMRC grade 0: 0.2383/year; grade 1: 0.18874/year; grade 2: 0.1317/year; grade 3: 0.1371/year; grade 4: 0.1156/year; (p-value for interaction mMRC\*time = 0.7827).

Note: shaded areas indicate 95 % confidence intervals.



**Fig. 6.** Longitudinal trajectories of SF-36 summary scores by exacerbation frequency in the past year at baseline.

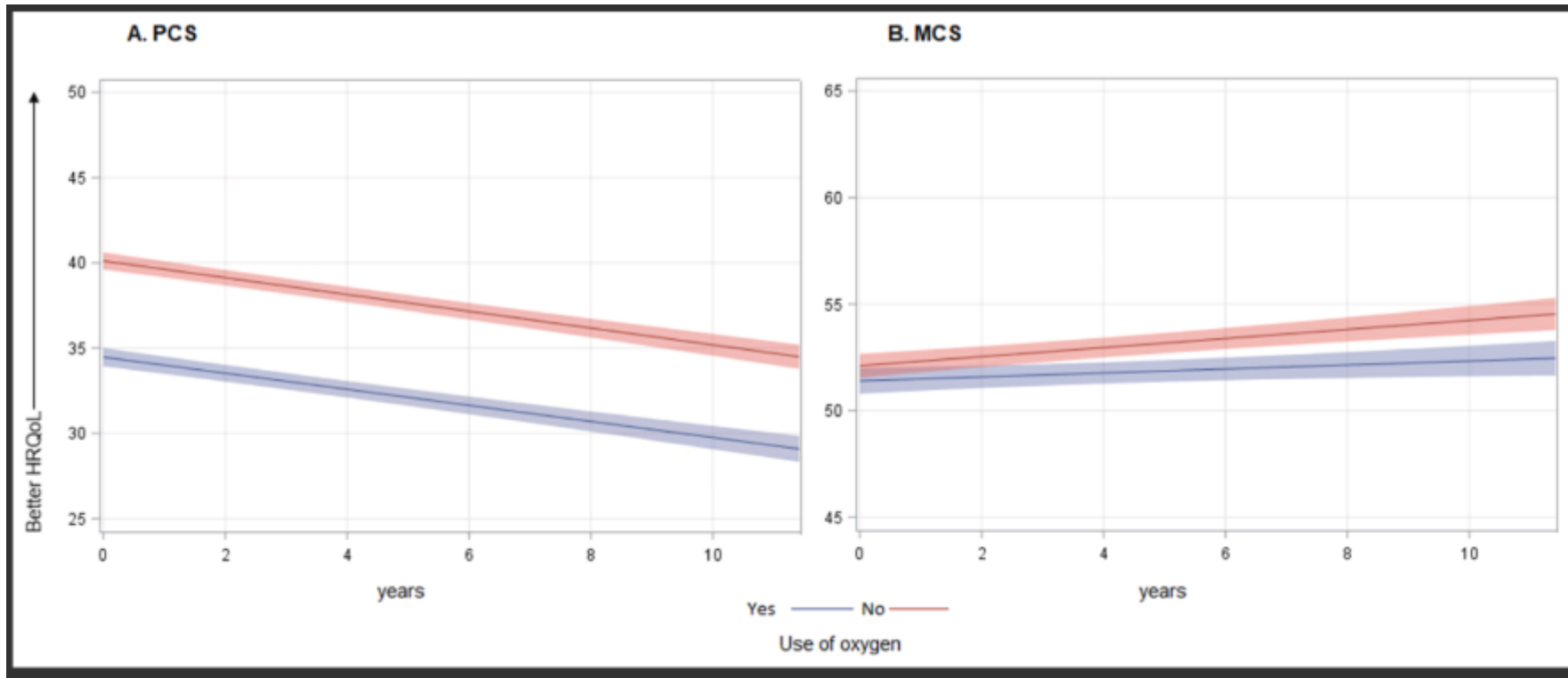
PCS-Physical Component Summary; MCS-Mental Component Summary; norm-based, mean = 50 (SD = 10) in the general US population.

PCS slopes: frequency of exacerbations in the past year: 0: 0.5323/year; 1: 0.62712/year; grade 2 or more: 0.4107/year; (p-value for interaction frequency of exacerbations+time = 0.0019).

MCS slopes: frequency of exacerbations in the past year: 0: 0.04619/year; 1: 0.15669/year; grade 2 or more: 0.20229/year; (p-value for interaction frequency of exacerbations+time = 0.0939).

Note: shaded areas indicate 95 %

Chioate et al Respir Med  
 . 2024 Oct 14:234:107838.



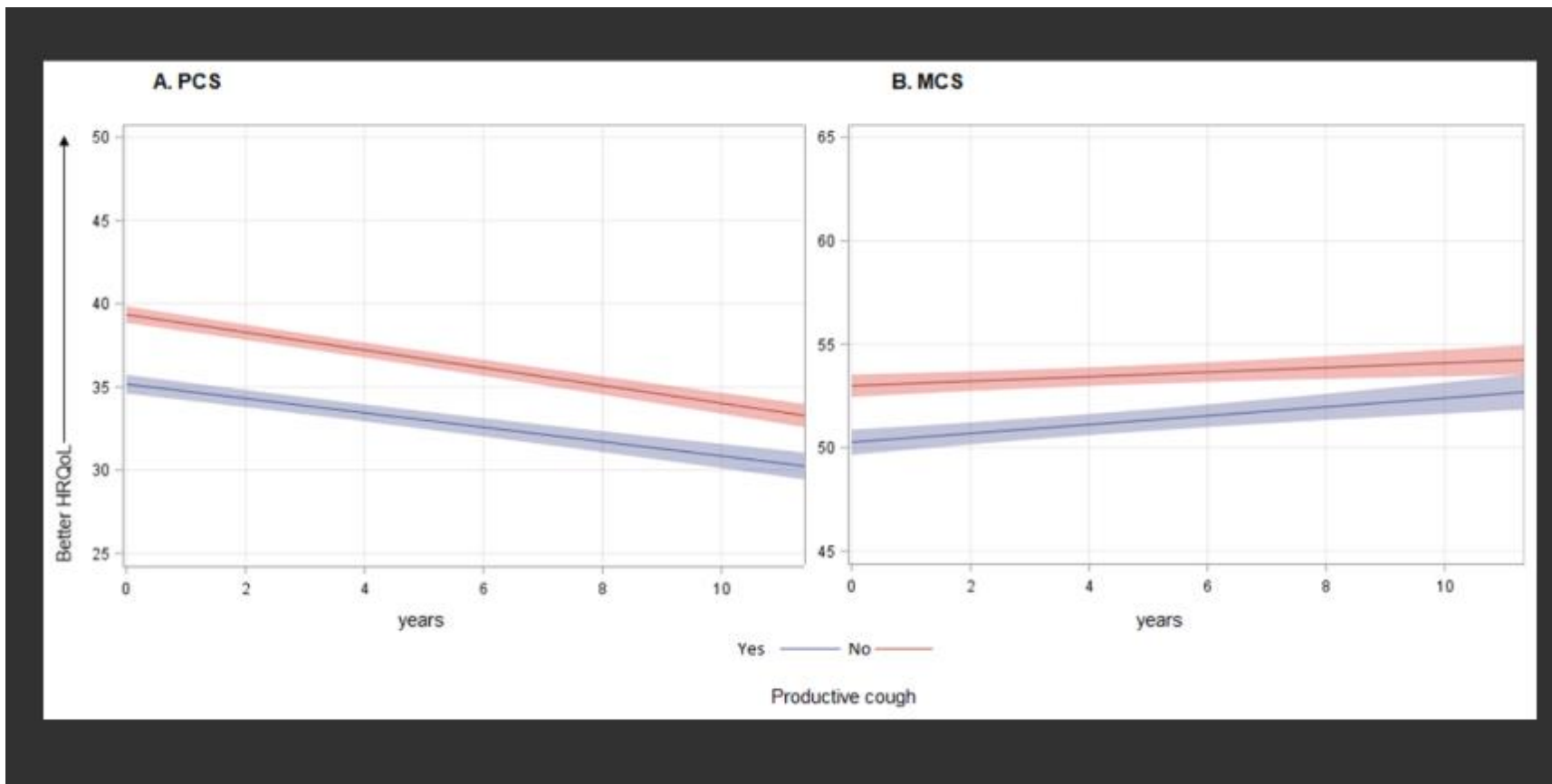
**Fig. 7.** Longitudinal trajectories of SF-36 summary scores by regular oxygen use in the past year at baseline.

PCS-Physical Component Summary; MCS-Mental Component Summary; norm-based, mean = 50 (SD = 10) in the general US population.

PCS slopes: use of oxygen in the past year: No: 0.4925/year; Yes: 0.47138/year; (p-value for interaction use of oxygen\*time = 0.6766).

MCS slopes: use of oxygen in the past year: No: 0.2127/year; Yes: 0.0931/year; (p-value for interaction use of oxygen\*time = 0.0422).

Note: shaded areas indicate 95 % confidence intervals.



**Fig. 8.** Longitudinal trajectories of SF-36 summary scores by productive cough.

PCS-Physical Component Summary; MCS-Mental Component Summary; norm-based, mean = 50 (SD = 10) in the general US population; Productive cough refers to daily productive cough for at least 3 months each year over the past 2 years.

PCS slopes: productive cough: No: 0.5324/year; Yes: 0.4323/year; (p-value for interaction productive cough\*time = 0.0509).

MCS slopes: productive cough: No: 0.1100/year; Yes: 0.2134/year; (p-value for interaction productive cough\*time = 0.0819).

Note: shaded areas indicate 95 % confidence intervals.

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Cochrane



Cochrane Database of Systematic Reviews

## Alpha 1 antitrypsin augmentation for alpha 1 antitrypsin deficiency associated lung disease (Protocol)

Glaister P, Hindle Robinson N, Ward A, Bentham C, Crossingham I

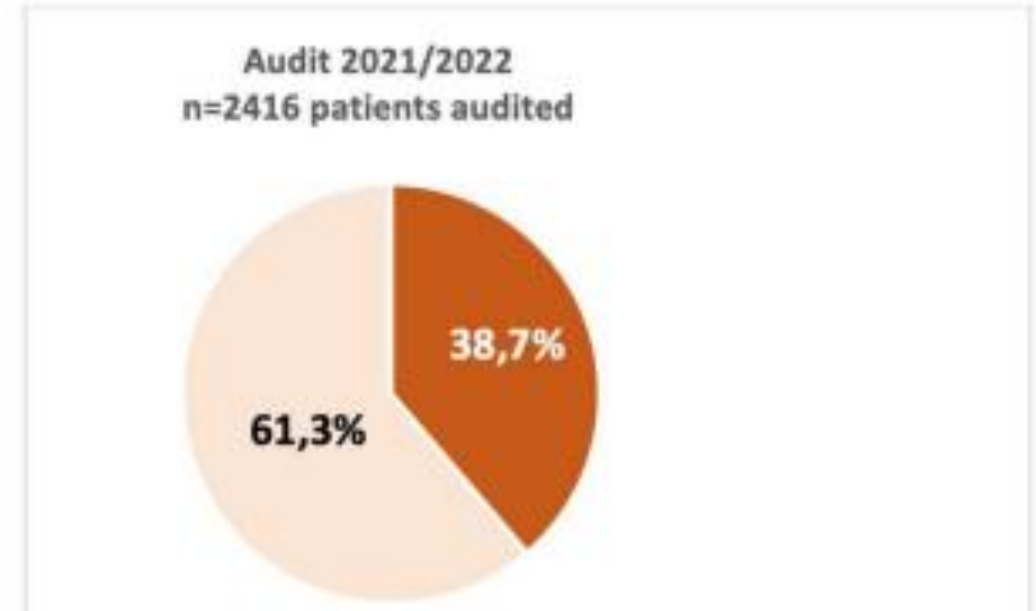
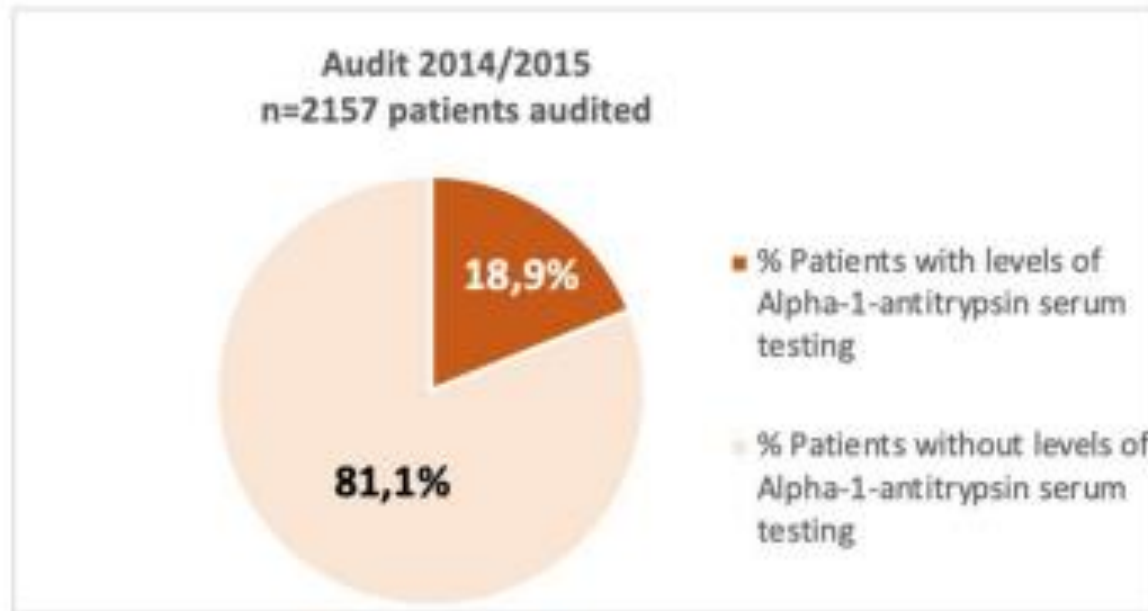


## Primary outcomes

- Exacerbations of COPD or airways disease
- All-cause mortality
- Serious adverse events, as defined by the US Food and Drug Administration ([FDA 2023](#))

## Secondary outcomes

- Lung function measures (preferentially forced expiratory volume in 1 second (FEV<sub>1</sub>), gas transfer (TLco), then other lung function measures)
- Quality of life (preferring St George's Respiratory Questionnaire (SGRQ) above other measures)
- Need for lung transplantation



Calle-Rubio et al. J. Clin Med 2024

Sex issues in the European Alpha-1 Research Collaboration (EARCO) registry, a prospective, international, observational cohort study.

N=1283 PiZZ individuals

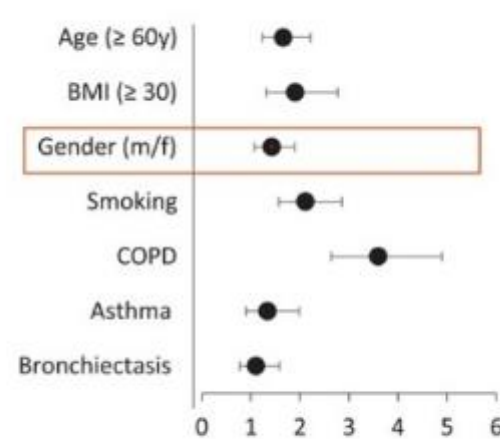


Female gender was an independent risk factor for exacerbations and symptom burden.

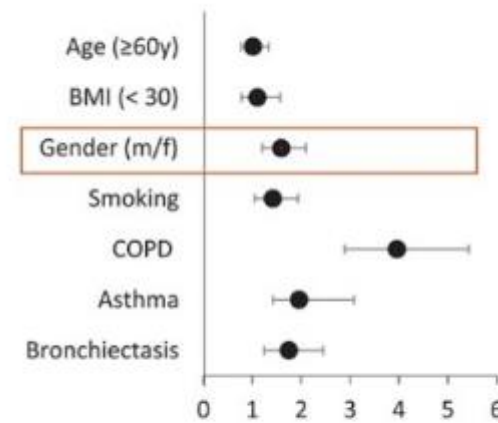


Women: Less tobacco use, occupational exposure and alcohol consumption than men

Men: Higher prevalence of COPD and liver disease, lower prevalence of bronchiectasis than women

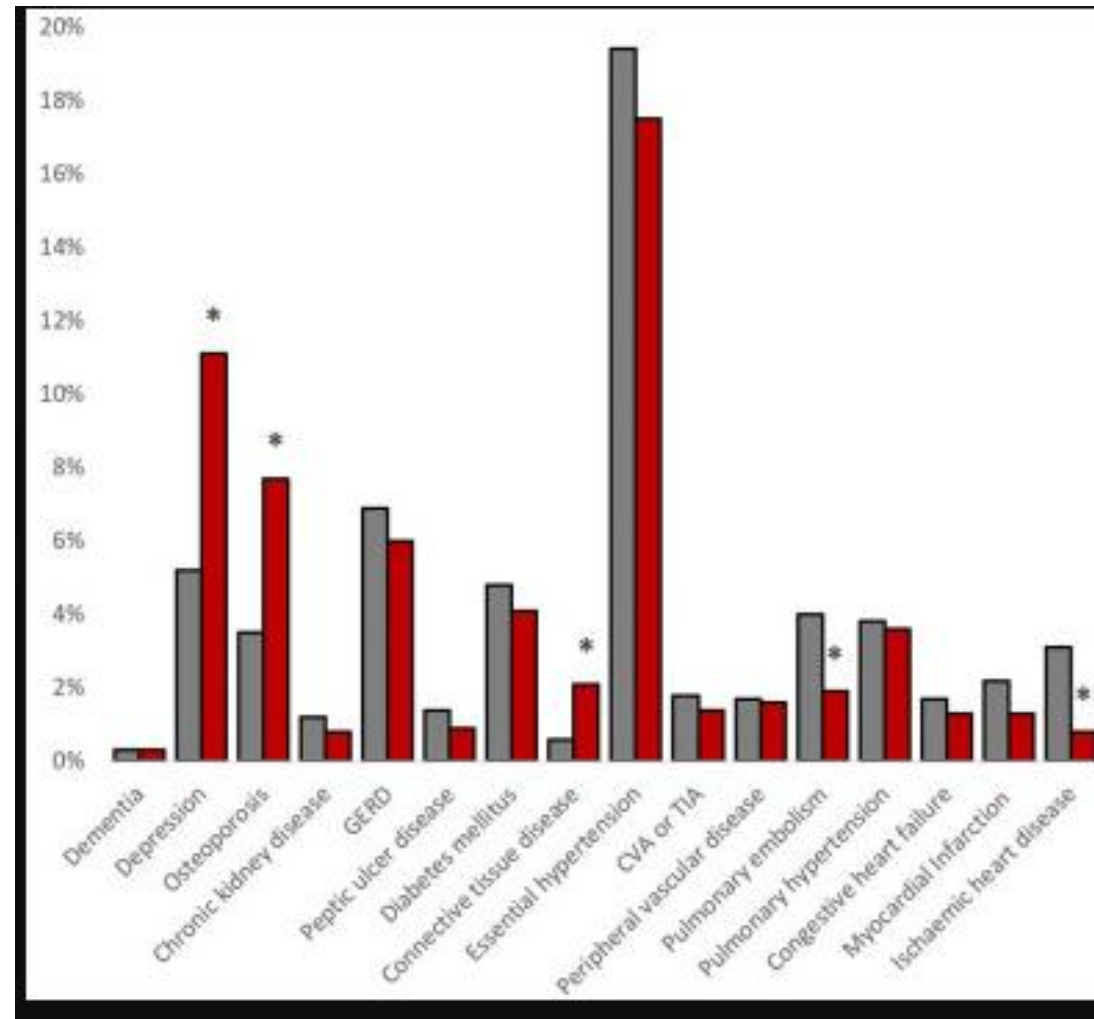


Symptoms (CAT ≥ 10)

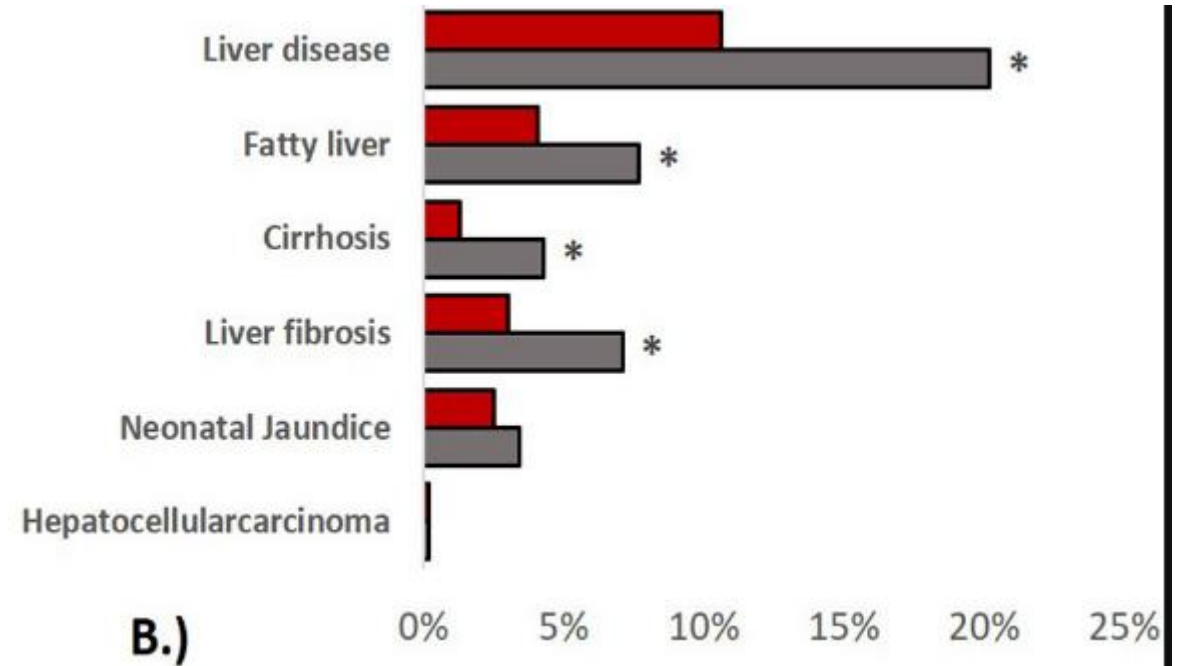
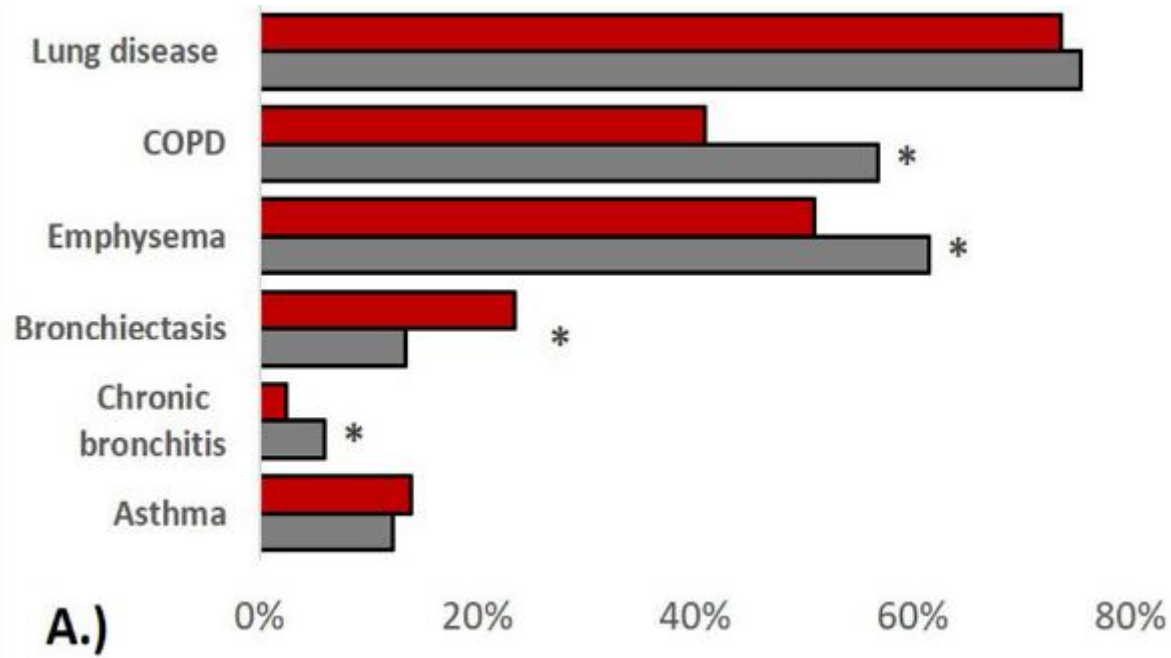


Exacerbations (≥ 1)

A Year in review



Ersöz et al. Arch Bronconeumol 2024 et al.



Ersöz et al. Arch Bronconeumol 2024 et al.