Solutions for Uncontrolled Asthma
: Other than Pharmacological Management

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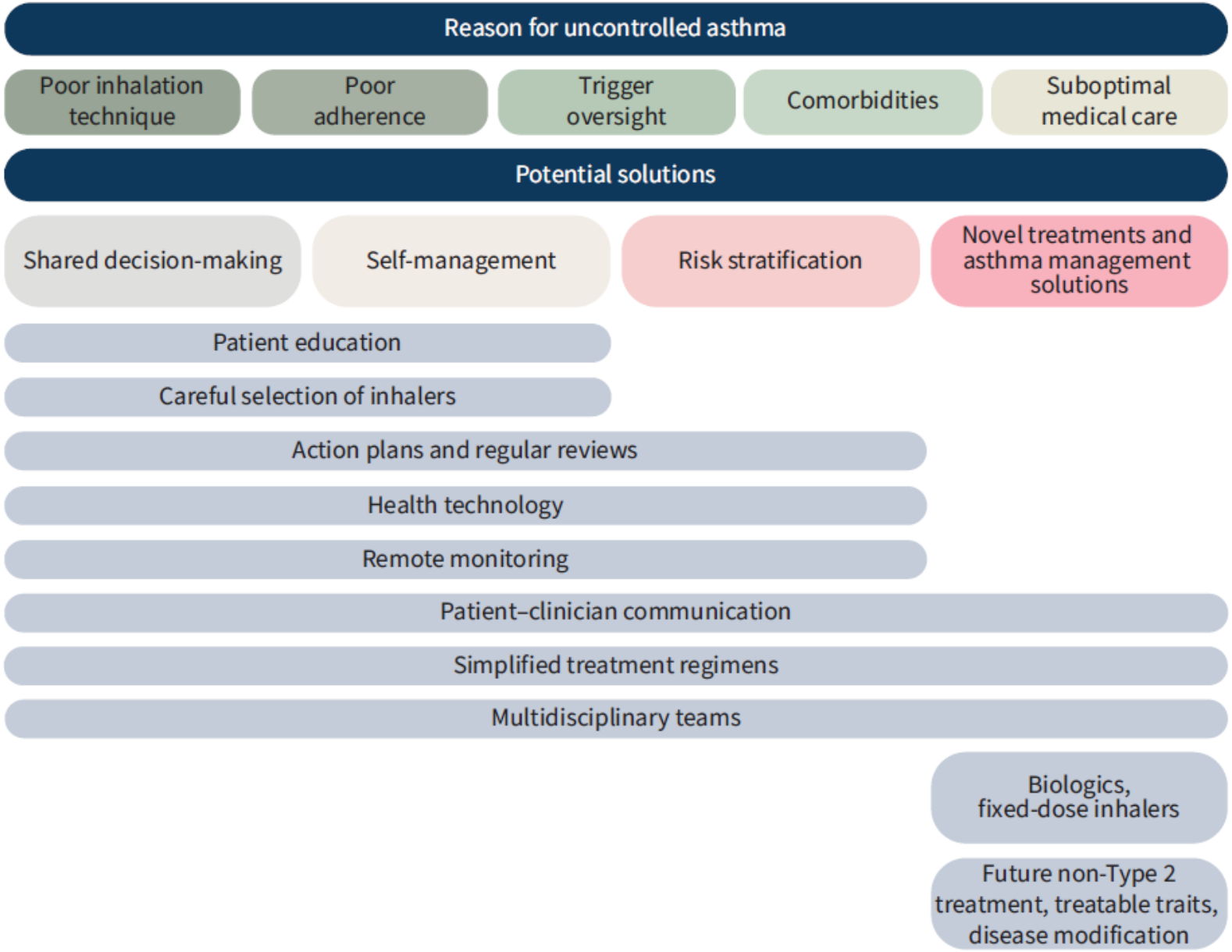
What is uncontrolled asthma?

- **Uncontrolled asthma** is defined by poor symptom control and/or frequent exacerbations that require OCS treatment or hospitalization.

Busse WW, Kraft M. Eur Respir Rev 2022; 31: 210176.

Interventions for uncontrolled asthma



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What is uncontrolled asthma?

- **Uncontrolled asthma** is defined by poor symptom control and/or frequent exacerbations that require OCS treatment or hospitalization.

- Reason for uncontrolled asthma
  - Poor inhalation techniques
  - Poor adherence
  - Trigger oversight
  - Comorbidities
  - Suboptimal medical care

Busse WW, Kraft M. Eur Respir Rev 2022; 31: 210176.

Agenda

- Poor inhalation techniques, poor adherence - Electronic monitoring
- Comorbid obese condition- diet, exercise for weight loss program
- Physiotherapy - Breathing technique
- Pulmonary rehabilitation
- Bronchial Thermoplasty
- Summary

Electronic monitoring

Errors in device technique

- A systematic search for articles reporting direct observation of inhaler technique by trained personnel covered the period from 1975 to 2014.
- Outcomes were the nature and frequencies of the three most common errors; the percentage of patients demonstrating **correct, acceptable, or poor technique**; and variations in these outcomes **over these 40 years**

Joaquin Sanchis et al. Chest 2016; 150(2): 394-406.

Asthma mobile health applications

- Many asthma apps have been produced over the past decade, offering functions that span health education, symptom tracking, environmental alerts, and medication reminders.
- The number of asthma apps continues to grow
- 209 English-language asthma-related apps in the Apple Store and/or Google Play in a 2015 review, **is now over 500.**

Blanca E. Himes et al. J Allergy Clin Immunol Pract 2019; 7(8): 2535-2543.

Apps for asthma management

App Name	Major Function	Secondary Functions	Study Population Characteristics	Evidence/Impact
Health App	Tracks symptoms and peak flow	-Receives customized advice -Medication reminders -General asthma information reminders	20 patients aged 12-17 year with persistent asthma recruited from pediatric specialty clinics at Arkansas Childrens Hospital	ACT score improved from 16 to 18 and asthma attack prevention domain improved from 34 to 36 [53]
t+ Asthma App	Tracks symptoms, drug use, and peak flow	-Sends information from patient to provider	288 patients aged 12+ years with poorly controlled asthma recruited from UK primary care practices	No significant change in asthma control, exacerbations, steroid courses, or unplanned clinic visits[54]
My Asthma Portal App (MAP) (web based application)	Tracks symptoms,physical activity, and medication	-Real-time feedback and monitoring from a nurse	100 patients aged 18-69 years with poor asthma control recruited from pulmonary clinics in two tertiary care hospitals located in Montreal,Canada	Increased quality of life but no better control over asthma [55]
POPET App (Physician On-call Engagement Trial)	Tracks health and medication compliance	-Sends information from patient to provider	136 patients aged 25-41 years with a diagnosis of mild to severe persistent asthma recruited from Pulmonary Diseases Departments across Turkey	ACT score improved [26]
SPA (Smartphone Application)	Tracks symptoms	-Receives environmental alerts and treatment advice	22 patients aged 18+ years with a physician diagnosis of asthma who reported symptoms worsening with exposure to air pollution recruited from the Primary Care Asthma Program in Windsor, Ontario.	Quality of life improved [56]
Breathe App (Available on iOS)	Tracks symptoms	-Gives customized advice based on asthma action plan -General asthma information -Send warning and risk reminders	344 patients with asthma and mean age 45.3 years recruited from six primary care and two specialty asthma clinics in Ontario, Canada.	Increased adherence to control plan and quality of life[57]
PCHMS App (Personally Controlled Health Management System)	Gives information on asthma and management tools	-Access to medical records	330 patients aged 18+ years with asthma recruited via advertisement through Asthma Foundation Australia and the National Asthma Council Australia.	No decreased hospitalization or increased adherence to asthma action plan [58]
AsthmaCare App*	Medication and treatment plan reminders	-Trigger reminders	239 patients aged 6 months to 21 years with persistent asthma were recruited when presenting with an asthma exacerbation to the Emergency Department from Nationwide Children's Hospital in Columbus, Ohio.	No decrease in hospital visits however increased asthma control 6 months later[59]
ASTHMAXcel App (Available on iOS)	Videos teach about how and when to use inhalers and spacers	-Teaches how to reduce triggers at home	130 participants aged 15-21 years with persistent asthma recruited at Montefiore Medical Center, Bronx, NY	Decreased hospitalizations, increased control and quality of life[60,61]

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Inhaler-based monitoring Devices available for asthma management

Device Name	Device Function	Corresponding App	Data/Results Reported	Study Population Characteristics	Evaluation
Inhaler Compliance Assessment (INCA)	Time-stamped audio recording of inhaler use.	Onboard data storage / no app	Raw audio files must be transferred to a computer for analysis.	184 participants with mean age 70.9 +/ – 9.65 years and asthma recruited at an academic teaching hospital in Dublin, Ireland	-Can measure impact of technique errors (failure to prime inhaler, low inhalation flow, dose dumping) on reduced medication delivery [34] -Can distinguish between intentional and unintentional adherence [35]
Flo-Tone	Inhaling speed and volume can be measured by sound and length of inhalation. Measures if user coordinates actuation with inhalation.	No data storage	Inhalation causes a whistle to sound as a signal to dispense medication. Keeping the whistle sounding is indicative of good technique. The function of the device is to give feedback on and improve inhaler usage technique.	62 patients aged 17-82 years with asthma (n=30) COPD (n=27) and asthma+COPD (n=5) were recruited from both in-patient wards and outpatient respiratory clinics at Beaumont Hospital, Dublin, Ireland	-Analysis of the audio-based method of data collection showed a frame-by-frame accuracy of 88.2% in classifying actuation, inhalation and exhalation. The analysis showed that 89% of patients made at least one technique error, even after training by an expert clinical reviewer [62]
SmartTrack	Records date, time, and number of actuations used, missed doses, and when inhaler is inserted and removed.	Hailie	App displays data to help track medication usage; provides alerts when medications are missed.	2,045 patients aged 6-15 years were recruited when admitted to the Auckland regional emergency department with a possible asthma diagnosis	-Use of device resulted in 84% median percentage of adherence in an intervention group versus 30% in control group [33]
SmartInhaler	-Records date and time of inhaler use. -Emits an audible reminder at preset times. -The device has a light, which is green before MDI use, changing to red once used.	Onboard data storage	Sensor data can be sent to a computer with a communication link, USB, or cellular upload for analysis.	110 patients aged 12-65 years with a diagnosis of asthma were recruited from research volunteer databases, newspaper advertisements, and informal contacts in Wellington, New Zealand.	-Those using device as intervention adhered to medication use 18% percentage points more than the control group; more participants in the intervention group used >50%, >80%, and >90% of their medication, with proportion ratios of use (compared to the control group) being 1.33, 2.27, and 3.25, respectively [63]
Propeller Health	-Records date and time of inhaler use -Records geographic location of use via the paired smartphone app	Propeller Health	-Records symptoms, medication usage, and environmental factors -Tracks inhaler usage data automatically so triggers and symptoms can be followed and recorded-customizable schedule available to set medication reminders -Uses the ACT or CAT to assess control of asthma or COPD, respectively -Integrates data to be able to see inhaler use along with possible triggers -App can send information from patient to the provider.	Barrett et al 2017: 120 participants aged 5- 67 years with a physician diagnosis of asthma were recruited from community asthma activities, clinics, and retail pharmacies. Merchant et al 2018: 224 patients aged 3-88 years old with a diagnosis of asthma were recruited during routine asthma care in specialty and primary care clinics. Merchant et al 2016: 495 participants with a mean age of 36 years with a diagnosis of asthma were recruited from Woodland Healthcare and Mercy Medical Group in Yolo and Scramento, California.	-Daily average SABA uses per person decreased by 0.41 for the intervention arm and by 0.31 for control arm between the first week and the remainder of the study period [29] -Asthma-related ED visits and combined ED and hospitalization events decreased before and after use of Propeller Health system [30] - SABA use was shown to drop by 39%, and symptom-free days were shown to increase by 12% in first month of intervention; each intervention month showed an increase in percent of patients with well-controlled asthma [31]

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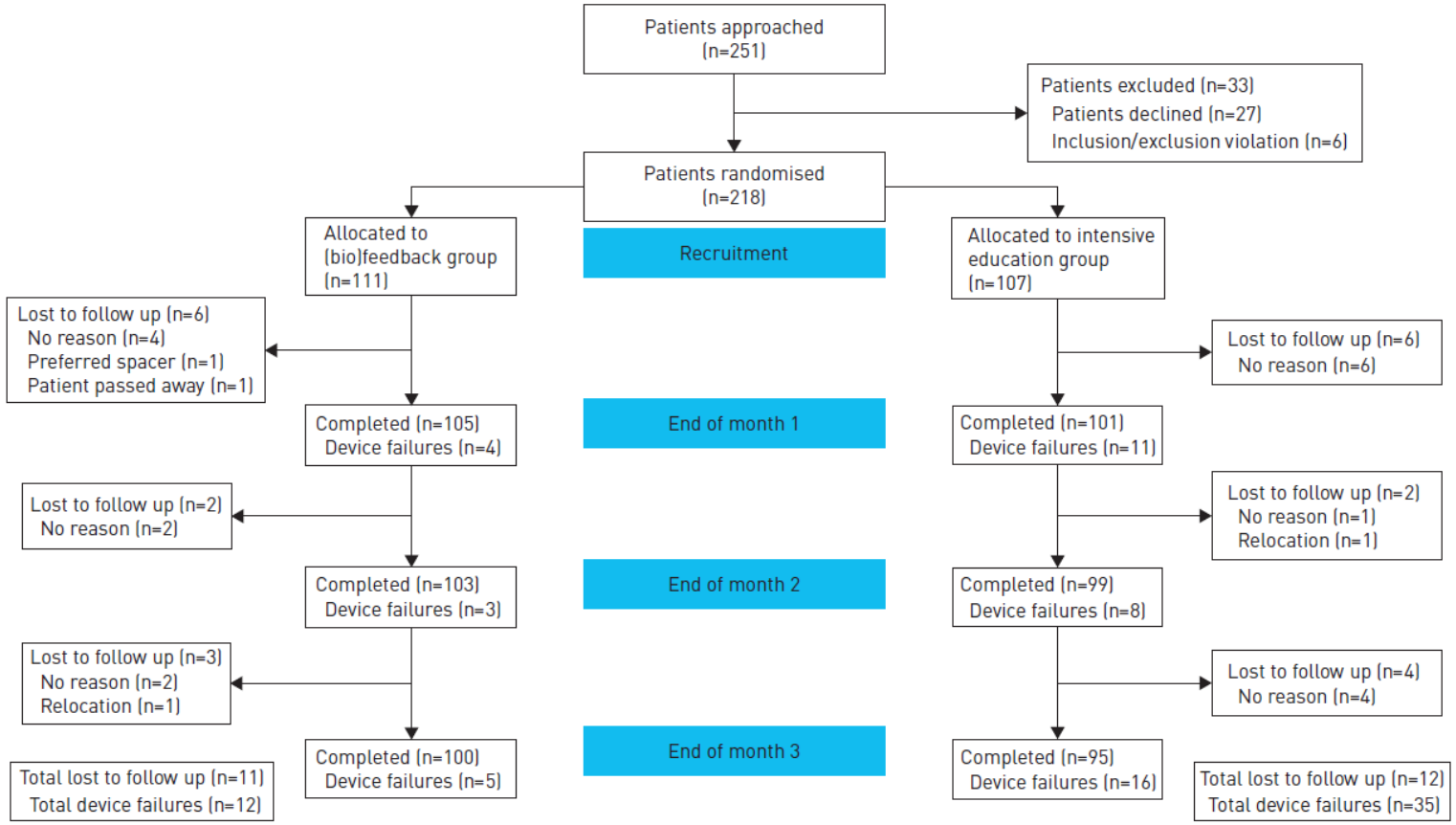
Feedback on inhaler adherence and technique in severe uncontrolled asthma pts.

- Prospective, multicentre, randomised, controlled, open-label clinical trial, conducted between 2012.02 and 2015.12.
- Patients aged ⩾18 years with GINA stage 3 to 5 asthma were recruited from five specialist asthma clinics.
- All participants were asked to measure their peak expiratory flow (PEF) **using an electronic monitor (ASMA-1, Vitalograph, Ireland)** and to use their salmeterol/fluticasone Diskus inhaler, one puff, twice per day + **Audio recording device, the INhaler Compliance Assessment (INCA)**



Sulaiman I et al. Eur Respir J 2018; 51: 1701126.

	All	(Bio) feedback	Intensive education	p-value
Subjects n	218	111	107	
Age years	49.2±16.5	48.2±17.0	50.3±15.9	0.42
BMI	29.9±7.0	29.7±7.5	30.1±6.5	0.70
Females %	64	67	63	0.57
Smoking history %				0.29
Never smokers	56	60	52	
Ex-smokers	36	35	37	
Current smokers	8	5	11	
FEV_1 L	2.2±0.9	2.2±0.8	2.1±0.9	0.75
FEV_1 % predicted	73.0±22.1	75.1±20.8	70.8±23.3	0.23
FEV_1/FVC %	66.2±12	68.7±13	63.7±12	0.3
IgE $IU \cdot L^{-1}$	467.5±877.6	434.7±875.8	501.2±884.4	0.65
Serum eosinophils $cells \cdot mL^{-1}$	0.3±0.4	0.3±0.4	0.4±0.5	0.34
Atopy[#] % patients	57	55	59	0.76
Short oral steroid courses in the past year	3.9±3.4	4.1±3.7	3.8±3.2	0.60
Exacerbations in the past year n	4.5±3.5	4.5±3.7	4.5±3.3	0.94
Salmeterol/fluticasone dose % patients				0.83
250 µg	35	36	35	
500 µg	65	64	65	
Use of montelukast % patients	37	35	39	0.57
Use of LAMA % patients	17	16	17	0.93
GINA control % patients				0.64
Partly controlled	13	13	14	
Uncontrolled	87	87	86	
AQLQ	3.7±1.2	3.7±1.2	3.6±1.2	0.53
ACT	12.1±4.5	12.5±4.6	11.7±4.3	0.25
PEF $L \cdot min^{-1}$	376.1±135.5	378.8±128.2	373.2±143.3	0.37
PEF % expected	81.6±23.5	82.6±22.8	80.6±24.3	0.57
Inhaler Proficiency Score[¶]	7.5±2.7	7.6±2.6	7.5±2.8	0.70

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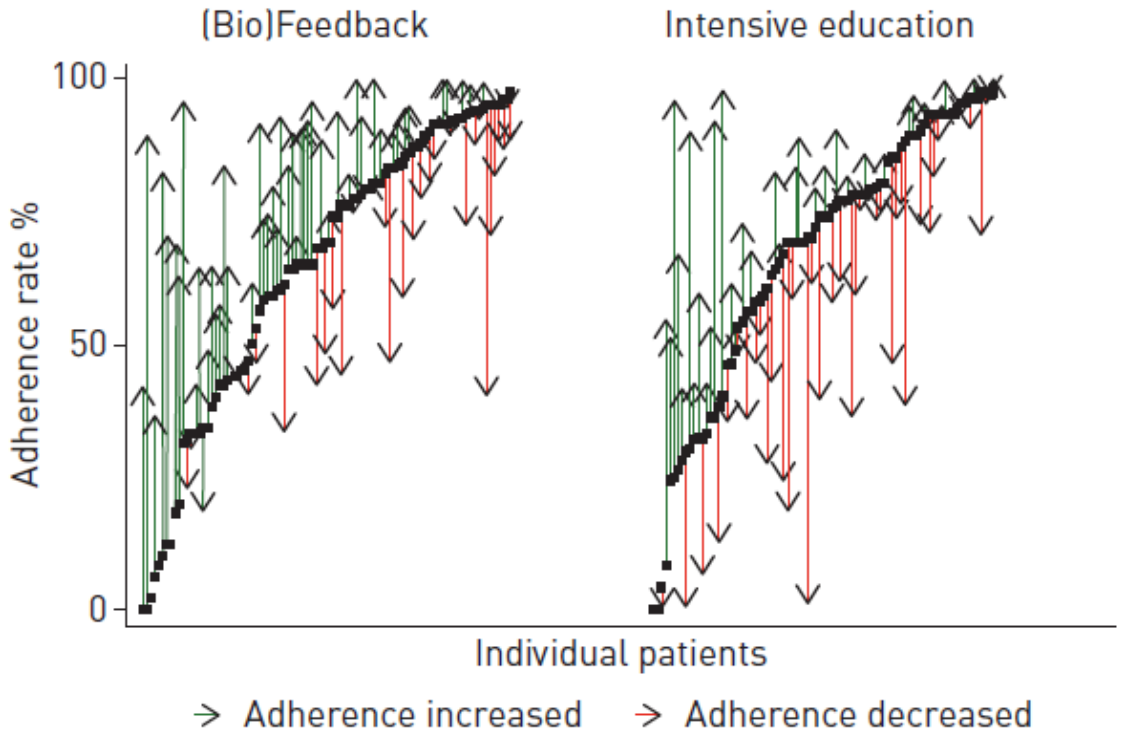

Adherence rate	Month 1			Month 3		
	(Bio)feedback	Intensive education	p-value #	(Bio)feedback	Intensive education	p-value ¶
Actual rate	63±27. 3	67±26.4	0.57	73±24*	63±26.0	<0.01
Average adherence from dose counter	86±24.7	92±46.8	0.27	92±15. 8	79±108.4	0.20
Attempted rate	82±18.7	78±22.5	0.11	73±26.2	82±18.1	0.01
Overdoses	6±8.7	7±10.4	0.55	3±5.2*	6±9.0	0.02
Missed doses	18±15.6	20±18.0	0.39	13±13.1	18±16.7	0.22
Technique error rate	11±19.2	8±18.9	0.36	11±13.9*	15±22.5	0.12

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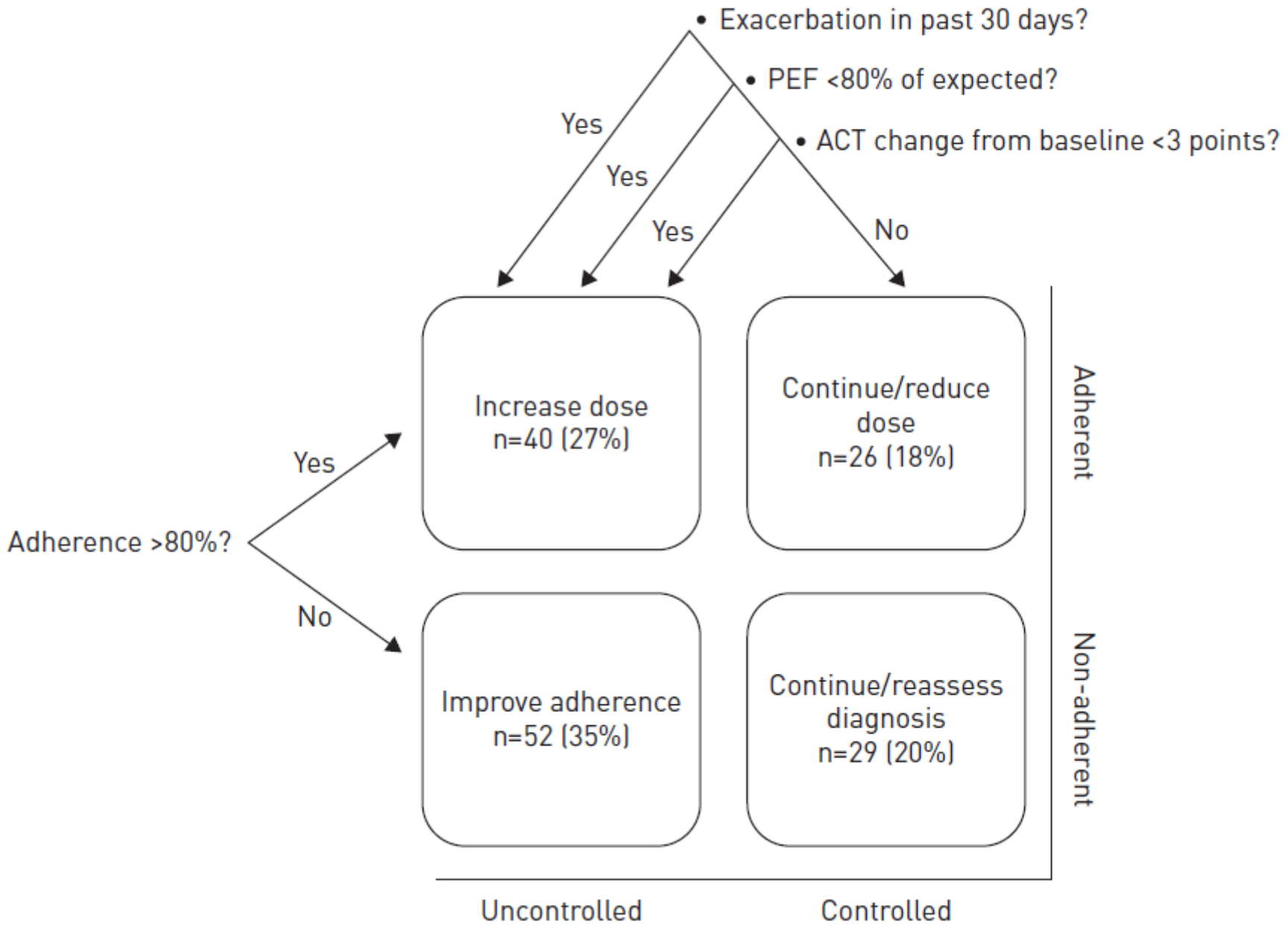

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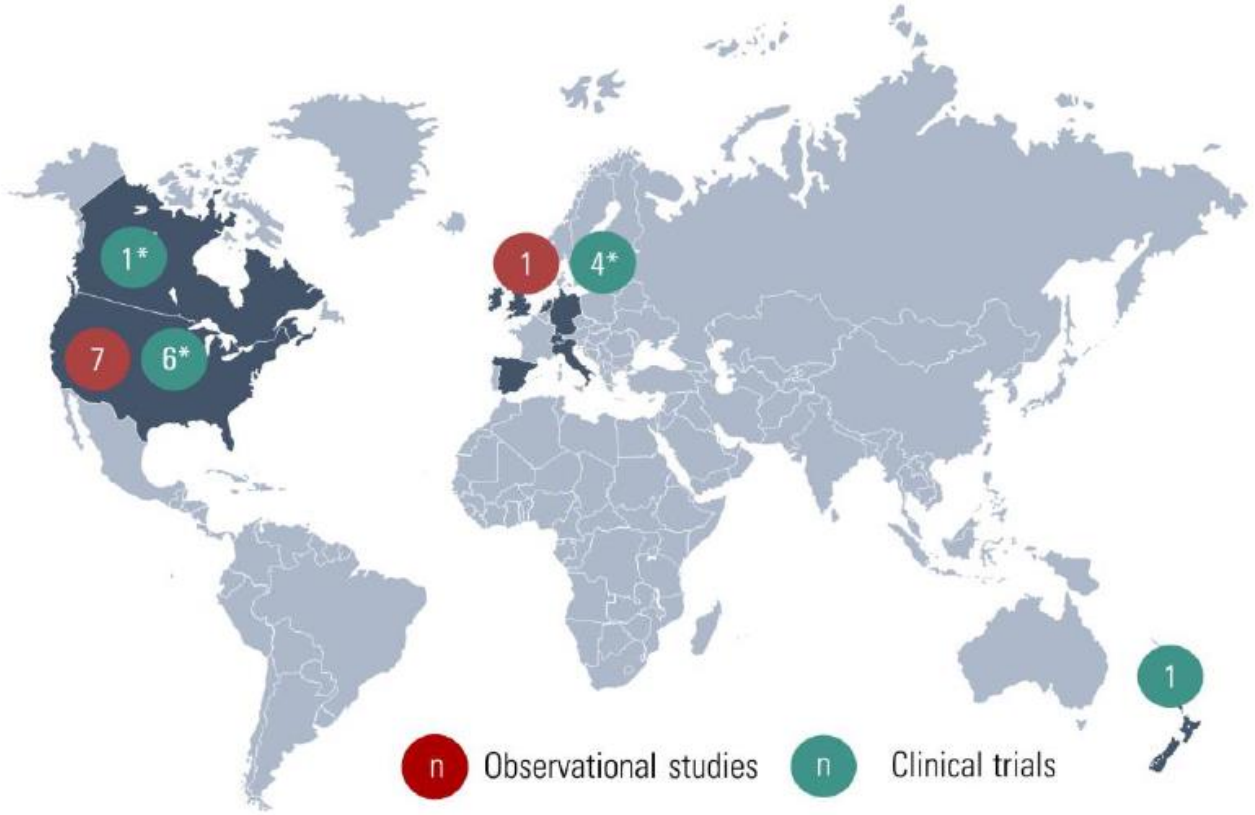
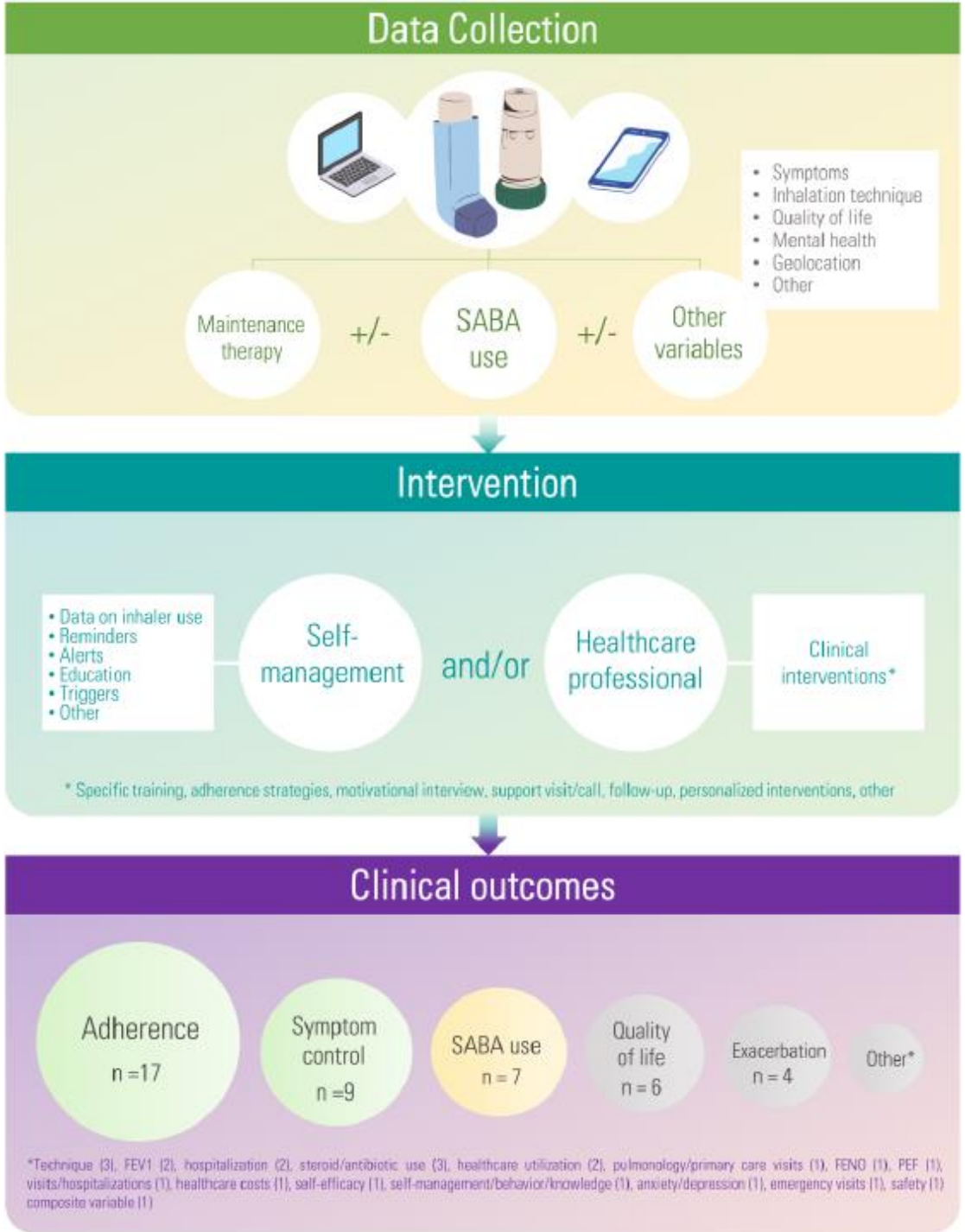
Impact of electronic monitoring devices in adult with asthma

- **Systematic review and meta-analysis** to gain insight into the characteristics and clinical impact of electronic monitoring devices of inhalers (EMDs) and their clinical interventions in adult patients with asthma or COPD
- The search included PubMed, Web of Science, Cochrane, Scopus and Embase databases, as well as official EMDs websites **(eight observational studies and ten clinical trials)**



Noe Garin et al. Pharmaceuticals 2023; 16: 414.



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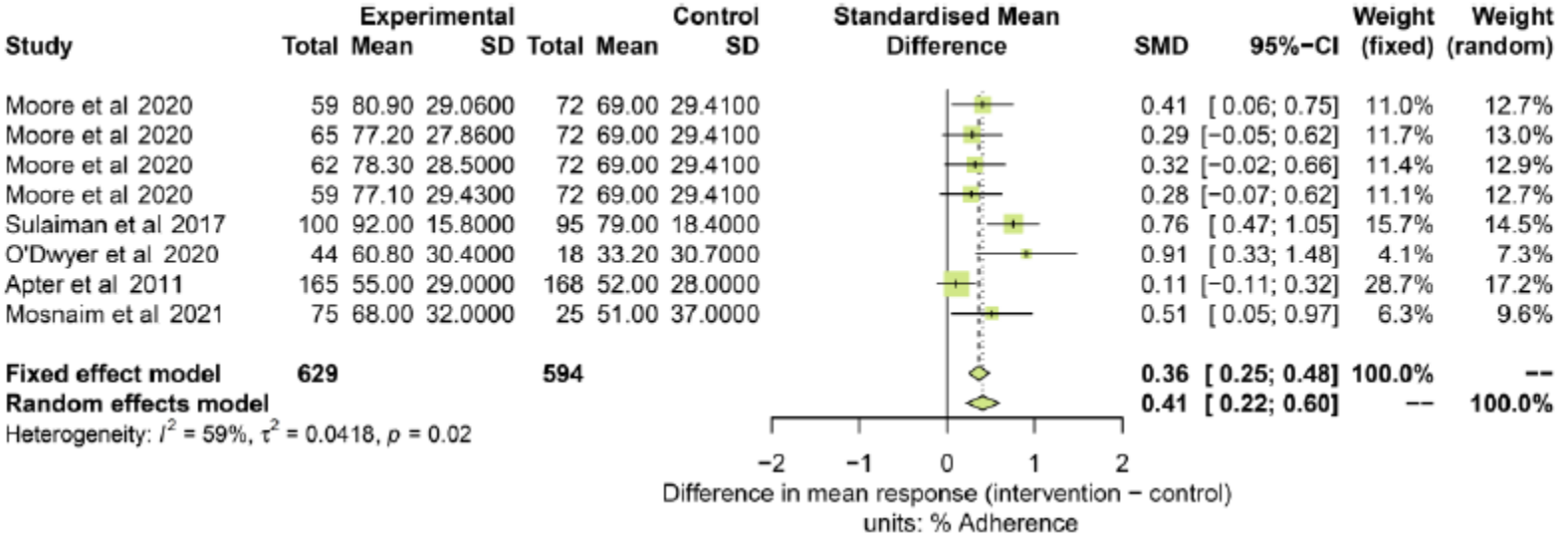
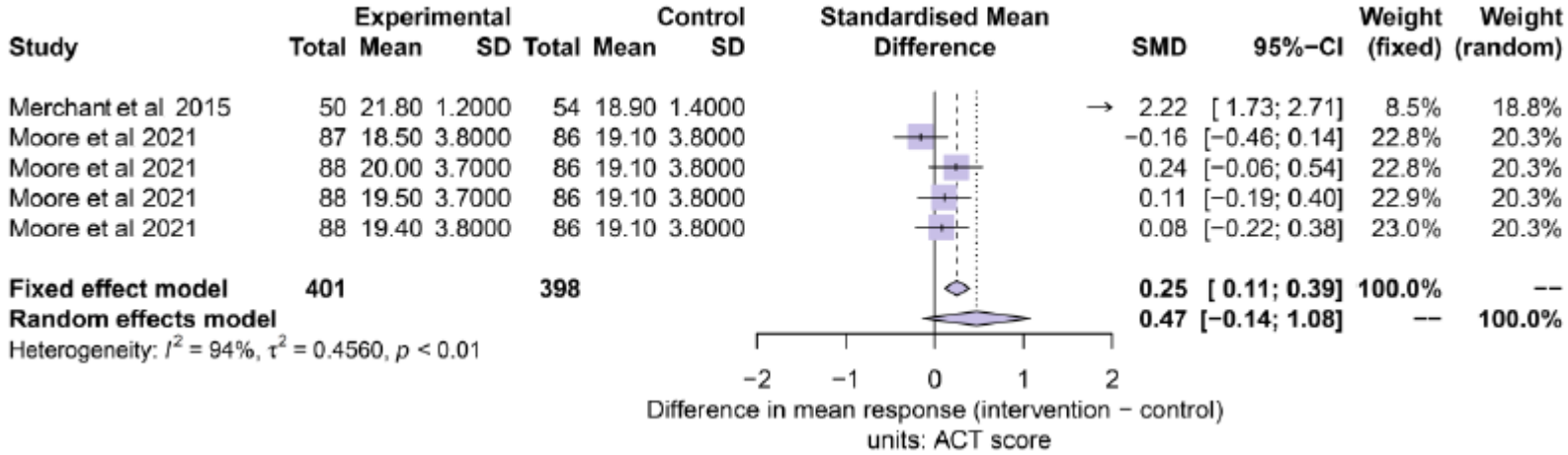
Adherence in studies 3months or longer



ACT score



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Diet & exercise for weight loss program

Obesity and asthma

- Obesity causes significant changes to normal lung physiology in adults.
- Excessive accumulation of fat in the thoracic and abdominal cavities leads to lung compression and an attendant reduction in lung volume.
- Inflammatory and metabolic changes from obesity cause airway reactivity or lung function.

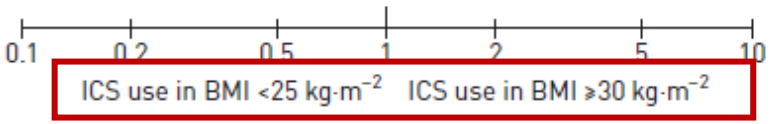
U. Peters et al. J Allergy Clin Immunol 2018; 141: 1169-79.

- **Systematic review/meta-analysis**
- Databases including CINAHL (Cumulative Index to Nursing and Allied Health Literature), Cochrane, Embase and MEDLINE were searched up to July 2019 for English-language studies that recorded medication use or dose in obese and healthy-weight adults with asthma.

a)

Study or subgroup	Obese Events	Obese Total	Healthy weight Events	Healthy weight Total	Weight %	OR M-H, Random, 95% CI
Adeyeye 2013	30	85	18	33	2.4	0.45 (0.20–1.03)
Camargo Jr (females) 1999	235	398	282	503	8.9	1.13 (0.87–1.47)
Chen 2016	12	59	12	77	2.1	1.38 (0.57–3.35)
Cohen (females) 2019	11	17	9	15	0.9	1.22 (0.29–5.13)
Cortes-Telles 2015	7	14	4	14	0.8	2.50 (0.52–11.93)
de Lima Azambuja 2015	2	25	6	25	0.6	0.28 (0.05–1.53)
Deesomchok 2010	32	45	30	51	2.2	1.72 (0.73–4.04)
Dixon 2006	172	228	95	133	5.1	1.23 (0.76–1.99)
Farah 2011	13	15	6	20	0.6	15.17 (2.58–88.99
Giouleka 2011	20	37	19	29	1.7	0.62 (0.23–1.60)
Hasegawa 2014	264	607	88	297	8.3	1.83 (1.36–2.46)
Holguin 2010	54	54	14	14		Not estimable
Holguin 2011	323	446	215	323	8.0	1.32 (0.97–1.80)
Lavoie 2006	89	94	125	139	1.5	1.99 (0.69–5.74)
Liu 2018	8	11	20	22	0.5	0.27 (0.04–1.91)
Lugogo 2018	236	243	204	211	1.5	1.16 (0.40–3.35)
Mosen 2008	243	412	183	291	8.0	0.85 (0.62–1.16)
Murphy (pregnant women) 2017	20	66	14	45	2.4	0.96 (0.42–2.19)
Nathell 2002	30	49	55	111	3.2	1.61 (0.81–3.19)
Rastogi 2017	25	648	2	144	0.9	2.85 (0.67–12.17)
Schatz 2013	5812	8611	2345	3526	12.5	1.05 (0.96–1.14)
Sutherland (females) 2008	17	20	16	19	0.6	1.06 (0.19–6.05)
Tang 2019	111	560	73	364	7.6	0.99 (0.71–1.37)
Taylor 2008	346	1022	296	1080	10.6	1.36 (1.13–1.63)
Thomson 2003	128	254	63	148	6.2	1.37 (0.91–2.06)
Vermette 2016	19	74	22	74	2.9	0.82 (0.40–1.60)
Total (95% CI)		14 094		7708	100.0	1.18 (1.03–1.36)
Total events	8259		4216			

Heterogeneity: Tau^2=0.04; Chi-squared=48.88, df=24 (p=0.002); I^2=51%
Test for overall effect: Z=2.37 (p=0.02)



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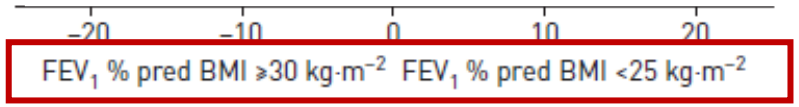
a)

Study or subgroup	Obese Mean±SD	Obese Total	Healthy weight Mean±SD	Healthy weight Total	Weight %	Mean difference IV, Random, 95% CI
Bruno (severe asthma) 2014	55.7±14.9	24	64.8±16.8	42	2.6	−9.10 (−16.93– −1.27)
Chen 2016	82.6±14.9	59	86±16.4	77	4.5	−3.40 (−8.68–1.88)
Clerisme-Beaty 2009	69±16	183	72±23	44	2.9	−3.00 (−10.18–4.18)
Cohen (females) 2019	71±41.2	17	80±36.1	13	0.3	−9.00 (−36.72–18.72)
Cortes-Telles 2015	91±9	14	98±11	14	2.8	−7.00 (−14.44–0.44)
de Lima Azambuja 2015	64±19.12	25	76±23.29	25	1.3	−12.00 (−23.81– −0.19)
Deesomchok 2010	89±18	45	91±14	51	3.4	−2.00 (−8.51–4.51)
Desai (severe asthma) 2013	71.6±20.02	55	76.2±21.7	28	1.8	−4.60 (−14.22–5.02)
Dixon 2006	77±16	228	82±16	133	6.9	−5.00 (−8.42–1.58)
Farah 2011	66±19.76	15	79±11.41	20	1.4	−13.00 (−24.18–1.82)
Gibeon (severe asthma) 2013	66.9±24.26	322	69.9±28.03	149	4.5	−3.00 (−8.22–2.22)
Giouleka 2011	85±18	37	93±17	29	2.3	−8.00 (−16.48–0.48)
Holguin 2010	74.5±20.62	54	86±13.36	14	2.1	−11.50 (−20.40–2.60)
Holguin 2011	72.75±21.58	446	81.59±23.66	323	7.2	−8.84 (−12.11– −5.57)
Kwon 2012	81.5±19.1	42	85.2±18.9	577	3.8	−3.70 (−9.68–2.28)
Lavoie 2006	75±19	94	79±20	139	4.7	−4.00 (−9.08–1.08)
Liu 2018	68.2±18.8	11	71±21.2	22	0.9	−2.80 (−17.01–11.41)
Lugogo 2018	76.4±13.3	230	85.2±13.6	204	8.4	−8.80 (−11.34– −6.26)
Maalej 2012	68.42±14.72	60	79.78±12.66	77	5.1	−11.36 (−16.04– −6.68)
Murphy (pregnant women) 2017	95.1±15	66	93.3±13.9	45	4.3	1.80 (−3.64–7.24)
Nathell 2002	94.1±17.32	49	94±19.99	111	3.7	0.10 (−6.01–6.21)
Rastogi 2017	78.4±64.29	648	85±18.98	144	3.9	−6.60 (−12.44–0.76)
Sutherland (females) 2008	72.2±26.58	20	80.5±22.68	19	0.8	−8.30 (−23.78–7.18)
Tang 2019	84.5±14.4	560	89.8±13.3	364	9.7	−5.30 (−7.11– −3.49)
Vermette 2016	81.1±16.9	74	81.6±14.4	74	4.7	−0.50 (−5.56–4.56)
Wright 2010	76.5±19.8	171	78.8±20.9	234	6.0	−2.30 (−6.30–1.70)
Total (95% CI)		3549		2972	100.0	−5.32 (−6.75– −3.89)

Heterogeneity: Tau^2=4.61; Chi-squared=43.17, df=25 (p=0.01); I^2=42%
Test for overall effect: Z=7.31 (p<0.00001)



U. Peters et al. J Allergy Clin Immunol 2018; 141: 1169-79.

Diet-induced weight loss on asthma control

- Total of 55 obese individuals (BMI 30.0) with asthma were enrolled in the study and randomized into the diet or control groups
- To evaluate the effects of diet-induced weight loss on the characteristics of asthma in obese adults with asthma.

	Diet	Control	*p* value
Number: *n*	29	26	
Age (years)	50.4 ± 10.4	50.3 ± 10.0	0.928
Gender (%women)	93.1	100	0.161
BMI (kg/m^2)	37.5 (7.8)	35.7 (5.0)	0.649
Waist circumference (cm)	107.0 ± 10.8	105.9 ± 25	0.680
WHR	0.88 ± 0.07	0.89 ± 0.07	0.828
Total body fat (%)	44.3 (6.7)	43.3 (4.6)	0.482
Muscle mass (kg)	45.7 (8.1)	47.1 (6.6)	0.938
Abdominal fat	13.0 (5.5)	11.0 (3.5)	0.187
Body water ratio (%)	41.2 (4.6)	42.4 (3.5)	0.358
FVC (%)	90.8 ± 16.1	94 ± 15.8	0.480
FEV_1 (%)	93.8 ± 9.7	95.4 ± 8.3	0.433
FEV_1/FVC	98.0 (17.0)	96.0 (11.7)	0.694
PEF (%)	79.7 ± 18.8	82.8 ± 17.7	0.543
MEF_{25-75} (%)	49.8 ± 20.3	53.8 ± 22.9	0.513
MEF_{75} (%)	74.5 ± 26.7	78.7 ± 26.6	0.575
MEF_{50} (%)	55.8 ± 24.4	61.9 ± 28.3	0.415
MEF_{25} (%)	38.5 ± 15.0	39.0 ± 19.2	0.932
ACT score	21 (2)	21 (2.5)	0.152
AQLQ score	5.4 ± 0.6	5.7 ± 0.5	0.122
Asthma duration	10 (13.5)	10 (15)	0.992

Umus Ozbey et al. J Asthma 2020; 57(6): 618-626.

	Diet ($n=29$)		Control ($n=26$)		
	Baseline	Change (Δ)	Baseline	Change (Δ)	Intergroup p value
Body weight (kg)	85.1 (19.7)	−5.2 (4.5)**	87.5 ± 10.7	−0.1 (1.3)	0.000
BMI (kg/m^2)	37.5 (7.8)	−2 (1.7)**	35.7 (5.0)	0 (0.6)	0.001
Waist circumference (cm)	107.0 ± 10.8	−5.0 (5.0)**	105.9 ± 25	−0.2 (1.0)	0.001
WHR	0.88 ± 0.07	−0.05 (0.04)	0.89 ± 0.07	0.01 (0.01)	0.156
Total body fat (%)	44.3 (6.7)	−1.8 (2.8)**	43.3 (4.6)	0.4 (1.6)	0.001
Muscle mass (kg)	45.7 (8.1)	−1.1 (1.5)**	47.1 (6.6)	0.1 (1.2)	0.007
Abdominal fat	13.0 (5.5)	−1 (1)***	11.0 (3.5)	0 (0.5)	0.001
Body water ratio (%)	41.2 (4.6)	1.2 (2)**	42.4 (3.5)	−0.3 (1.0)	0.001
Total calories	1854.8 (258)	−309.4 (257)**	1815.3 (3459)	129.6 (283.7)**	0.001
Carbohydrates (g)	213.4 (112)	−35.4 (79.6)**	174.0 (70)	34.2 (61.8)**	0.001
Protein (g)	54.4 (29)	5.6 (5.8)	66.4 (15)	−3.5 (10.6)	0.091
Fats (g)	87.0 (13)	−13.4 (24.9)**	93.2 (19)	−4.0 (10.0)	0.002
SFA (g)	29.6 (7)	−5.6 (7.6)**	28.8 (22)	−1.5 (12.8)	0.008
MUFA (g)	25.4 (6)	−0.1 (8.0)	29.3 (14)	−2.7 (11.4)	0.205
PUFA (g)	25.3 (5)	−9.6 (14.8)**	25.3 (5)	−0.9 (9.4)	0.004
Vitamin A (μg)	881.8 (373)	82.2 (24.0)*	1257.1 (555)	63.9 (37.4)	0.673
Vitamin C (mg)	111.0 (88)	51.8 (26.6)*	230.7 (64)	−20.8 (47.9)	0.041
Vitamin E (mg)	26.1 (6)	−4.4 (10.6)	25.4 (23)	−0.5 (33.3)	0.091
Vitamin K (ug)	407.0 (110)	224.4 (75.7)*	449.7 (66)	−25.7 (37.4)	0.035
Zinc (mg)	7.65 (4.0)	1.4 (1.6)*	9.2 (2.0)	−1.5 (1.4)	0.092
Magnesium (mg)	224.0 (34)	127.7 (82.9)**	259.6 (105)	3.6 (1.6)	0.003

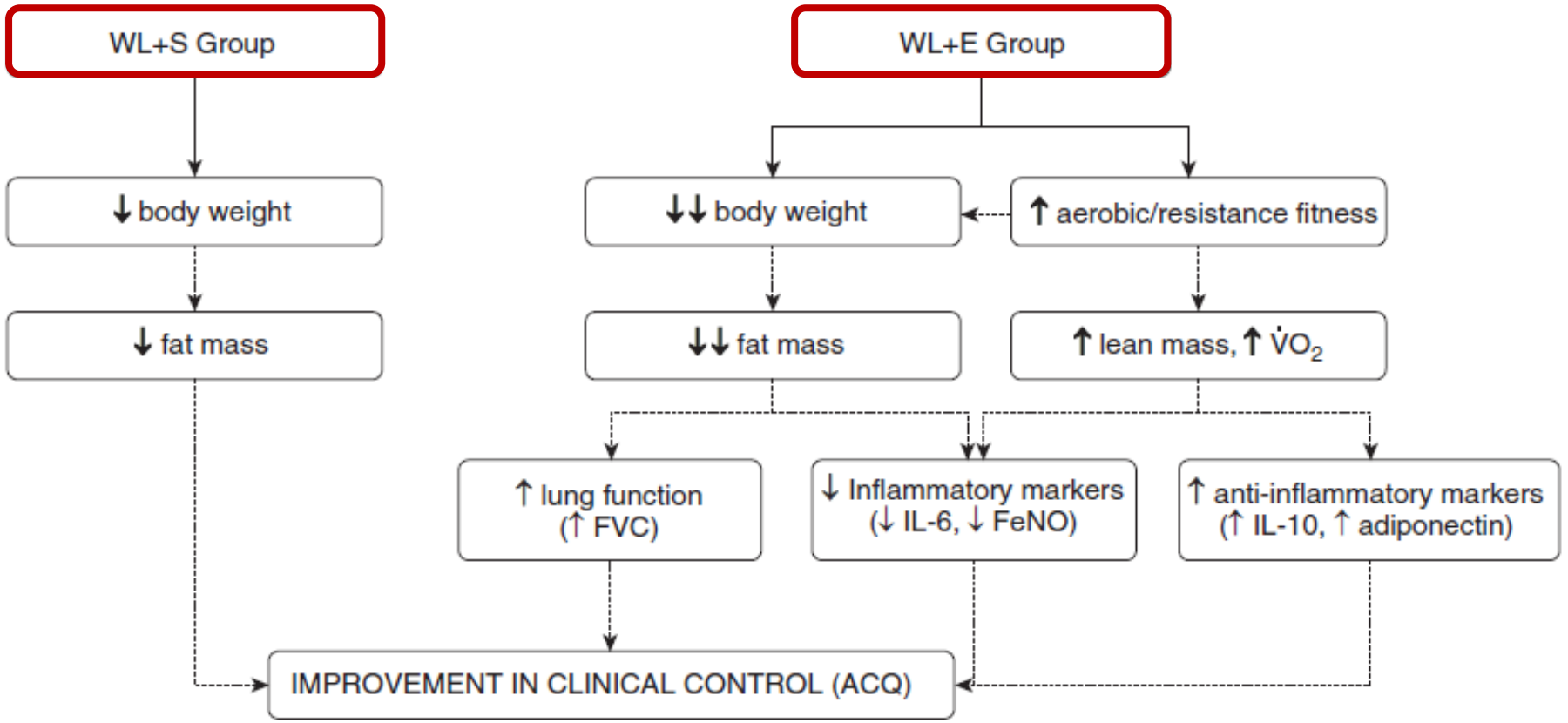
Umus Ozbey et al. J Asthma 2020; 57(6): 618-626.

	Diet ($n=29$)		Control ($n=26$)		
	Baseline	Change (Δ)	Baseline	Change (Δ)	Intergroup p value
FEV_1 (%)	80.4 ± 18.1	5.0 (10.5)**	84.9 ± 16.8	−4.3 (9.5)**	0.00
FVC (%)	90.8 ± 16.1	3.0 (12)**	94.4 ± 15.7	−4.0 (10.7)*	0.00
FEV1/FVC	93.8 ± 9.7	0 (65)	95.6 ± 8.1	−2.0 (4.2)	0.042
PEF (%)	79.7 ± 18.3	4.1 ± 12.3	84.3 ± 17.6	−3.0 ± 13.8	0.071
MEF_{25-75} (%)	49.8 ± 20.3	6.0 (15.5)*	54.6 ± 22.8	−1.5(9.0)	0.004
MEF_{75} (%)	74.5 ± 26.7	5.9 ± 15.5*	79.5 ± 26.3	−3.4 ± 11.5	0.021
MEF_{50} (%)	55.8 ± 24.4	6.0 (9.0)**	62.8 ± 28.1	−4.0 (9.5)*	0.000
MEF_{25} (%)	38.5 ± 15.0	5.0 (11.5)*	39.4 ± 19.0	0 (8.7)	0.010
ACT	21.0 (2)	2.0 (2.0)**	21.0 (2.5)	0 (1.7)	0.000
AQLQ	5.4 ± 0.6	0.8 ± 0.1**	5.7 ± 0.5	−0.02 ± 0.5	0.000

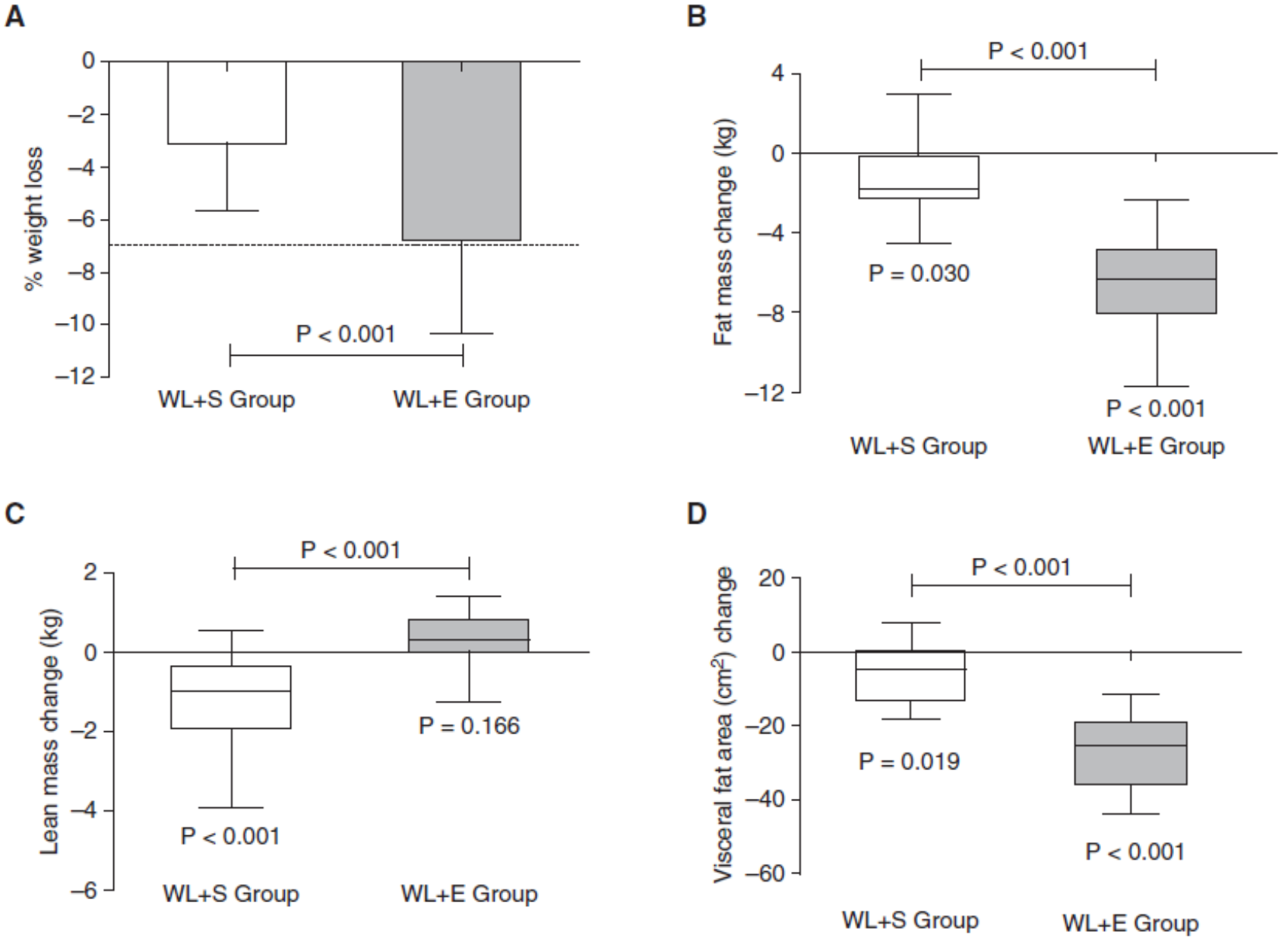
Umus Ozbey et al. J Asthma 2020; 57(6): 618-626.

Exercise in a weight loss program on clinical control

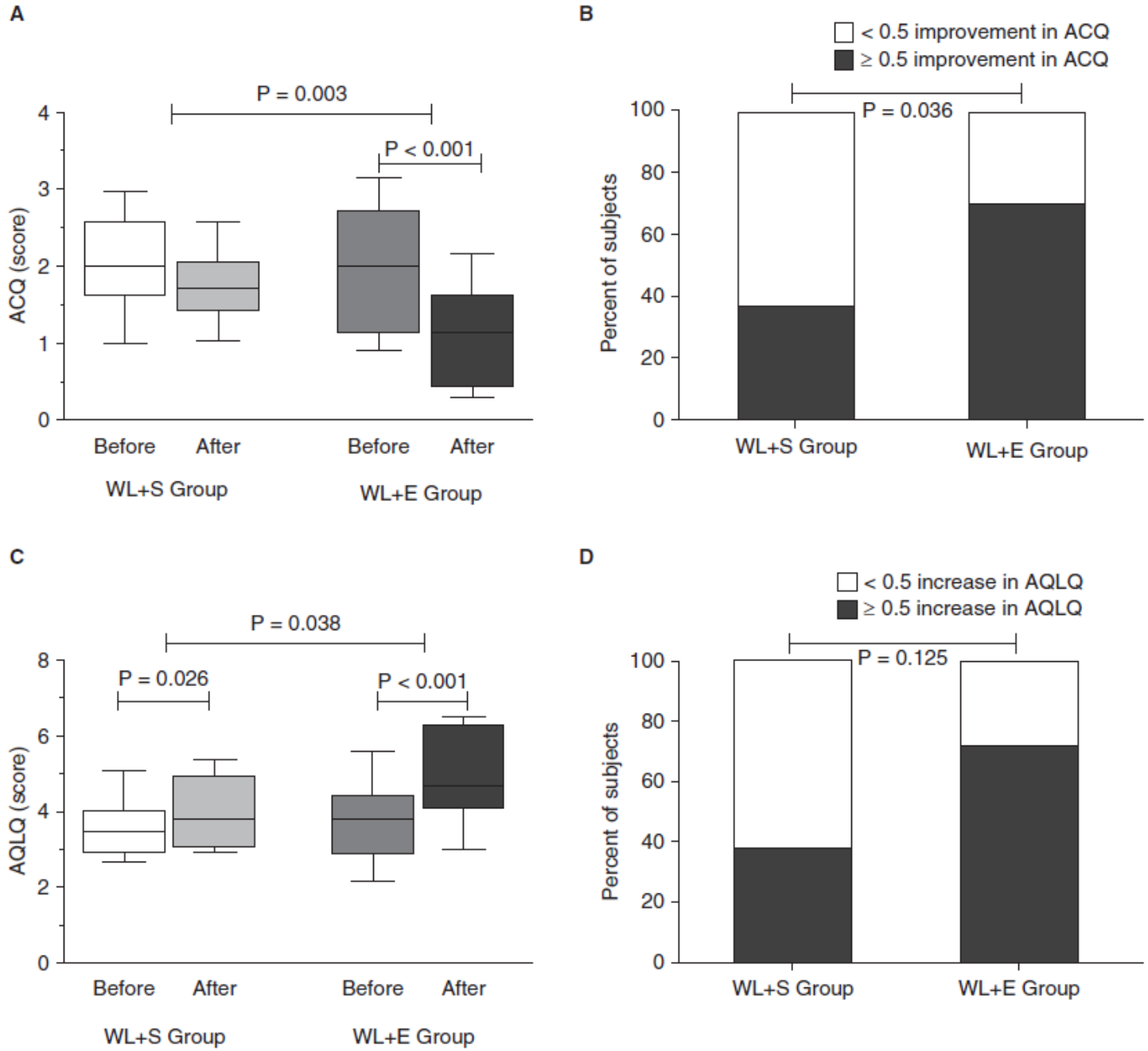
- Randomized clinical trial, N=55, obese pts.
- WL+S group (weight loss program) vs. WL+E (weight loss + exercise)
- Outcome: To examine the effect of exercise training on asthma control, quality of life, etc.



Patriacia D. Freitas et al. Am J Respir Crit Care Med 2017; 195(1): 32-42.



Patriacia D. Freitas et al. Am J Respir Crit Care Med 2017; 195(1): 32-42.



Patriacia D. Freitas et al. Am J Respir Crit Care Med 2017; 195(1): 32-42.

Physiotherapy, pul rehabilitation

Breathing exercise for asthma control

- Breathing exercises have been widely used worldwide as a non-pharmacological therapy to treat people with asthma.
- Breathing exercises
  - the Papworth Method
  - the Buteyko breathing technique
  - yogic breathing
  - deep diaphragmatic breathing
- The training of breathing usually focuses on tidal and minute volume and encourages relaxation, exercise at home, the modification of breathing pattern, nasal breathing, holding of breath, lower rib cage and abdominal breathing.

Santino TA et al. Cochrane Database of Systematic Reviews 2020, Issue 3. Art. No.: CD001277

Breathing exercise for pts with asthma in specialist care

- Adult patients with incompletely controlled asthma attending respiratory specialist clinics were **randomized to usual specialist care (UC, n=99) or UC and BrEX (UC1BrEX, n=94)** with **three individual physiotherapist-delivered sessions and home exercises**.
- To investigate the effectiveness of BrEX as adjuvant treatment on QoL in patients with **uncontrolled moderate to severe asthma**.

	UC + BrEX (*n* = 94)			UC (*n* = 99)		
Sex						
Female	—	58	(61.7%)	—	64	(64.7%)
Male	—	36	(38.3%)	—	35	(35.4%)
Age at inclusion	—	55	(44–65)	—	51	(42–61)
Smoking status						
Never-smokers	—	89	(55.3%)	—	95	(65.7%)
Smokers	—	5	(5.3%)	—	4	(4.0%)
Former smokers	—	37	(39.4%)	—	30	(30.3%)
Body mass index						
Underweight	—	1	(1.1%)	—	1	(1.0%)
Normal weight	—	24	(25.5%)	—	22	(22.2%)
Overweight	—	29	(30.9%)	—	44	(44.4%)
Obese	—	26	(27.7%)	—	20	(20.2%)
Severely obese	—	8	(8.5%)	—	7	(7.1%)
Extremely obese	—	6	(6.4%)	—	5	(5.1%)
PROMs						
Mini-AQLQ	—	4.3	(3.7–5.1)	—	4.4	(3.6–5.1)
ACQ6	—	2.2	(1.5–2.7)	—	2.0	(1.2–2.7)
NQ*	—	22.9	(10.9)	—	23.1	(11.3)
HADS-anxiety	—	5	(3–10)	—	6	(3–9)
HADS-depression	—	3	(1–7)	—	3	(1–6)
EQ-5D-5L index	—	0.742	(0.648–0.859)	—	0.754	(0.700–0.824)
EQ-5D-5L VAS*	—	62.0	(20.7)	—	62.1	(19.0)
GINA steps						
1	—	0	(0%)	—	0	(0%)
2	—	1	(1.1%)	—	2	(2.0%)
3	—	16	(17.0%)	—	13	(13.1%)
4	—	31	(33.0%)	—	34	(34.3%)
5	—	46	(48.9%)	—	50	(50.5%)

Karen H. Andreasson et al. Ann Am Thorac Soc 2022; 19(9): 1498-1506.

	Total No. of Assessments*		Intent-to-Treat Population			
	UC + BrEX	UC	UC + BrEX (*n* = 94) Mean Change	UC (*n* = 99) Mean Change	Between-Group Difference Difference in Mean Change	
Mini-AQLQ	262	287	0.65 (0.46 to 0.85)	0.31 (0.12 to 0.49)	0.35	(0.07 to 0.62)
ACQ6	256	285	−0.32 (−0.5 to −0.15)	−0.21 (−0.38 to −0.05)	−0.11	(−0.35 to 0.13)
NQ	255	285	−3.83 (−5.52 to −2.13)	−2.78 (−4.39 to −1.17)	−1.05	(−3.38 to 1.29)
HADS-anxiety	255	284	−1.06 (−1.73 to −0.38)	−1.11 (−1.75 to −0.47)	0.06	(−0.87 to 0.98)
HADS-depression	255	284	−1.16 (−1.71 to −0.61)	−0.26 (−0.78 to 0.27)	−0.90	(−1.67 to −0.14)
6MWT (m)	160	176	2.03 (−10.2 to 14.27)	9.03 (−2.44 to 20.5)	−7.00	(−23.77 to 9.77)
FEV_1% pred	150	163	0.48 (−2.19 to 3.14)	−0.53 (−3.01 to 1.96)	1.00	(−2.64 to 4.65)
Steps per day	82	89	84.74 (−973.24 to 1,142.72)	−245.85 (−1282.1 to 790.4)	330.59	(−1149.86 to 1,811.04)
PAL	82	89	0.03 (−0.02 to 0.08)	−0.02 (−0.06 to 0.03)	0.05	(−0.02 to 0.11)
	Total No. of Assessments*		Per-Protocol Population			
	UC+BrEX	UC	UC + BrEX (*n* = 76) Mean Change	UC (*n* = 99) Mean Change	Between-Group Difference Difference in Mean Change	
Mini-AQLQ	222	287	0.68 (0.47 to 0.89)	0.31 (0.12 to 0.49)	0.38	(0.1 to 0.66)
ACQ6	216	285	−0.39 (−0.58 to −0.2)	−0.21 (−0.38 to −0.05)	−0.18	(−0.43 to 0.07)
NQ	215	285	−4.03 (−5.88 to −2.19)	−2.78 (−4.41 to −1.16)	−1.25	(−3.71 to 1.21)
HADS-anxiety	215	284	−1.13 (−1.84 to −0.42)	−1.11 (−1.74 to −0.48)	−0.02	(−0.97 to 0.93)
HADS-depression	215	284	−1.46 (−2.03 to −0.89)	−0.26 (−0.76 to 0.25)	−1.20	(−1.97 to −0.44)
6MWT (m)	140	176	2.50 (−10.2 to 15.19)	9.03 (−2.53 to 20.58)	−6.53	(−23.69 to 10.63)
FEV_1% pred	131	163	0.87 (−1.89 to 3.63)	−0.52 (−3.02 to 1.99)	1.39	(−2.34 to 5.11)
Steps per day	79	89	139.09 (−921.97 to 1,200.14)	−248.85 (−1282.53 to 784.83)	387.93	(−1093.4 to 1,869.27)
PAL	79	89	0.03 (−0.02 to 0.08)	−0.01 (−0.06 to 0.03)	0.05	(−0.02 to 0.11)

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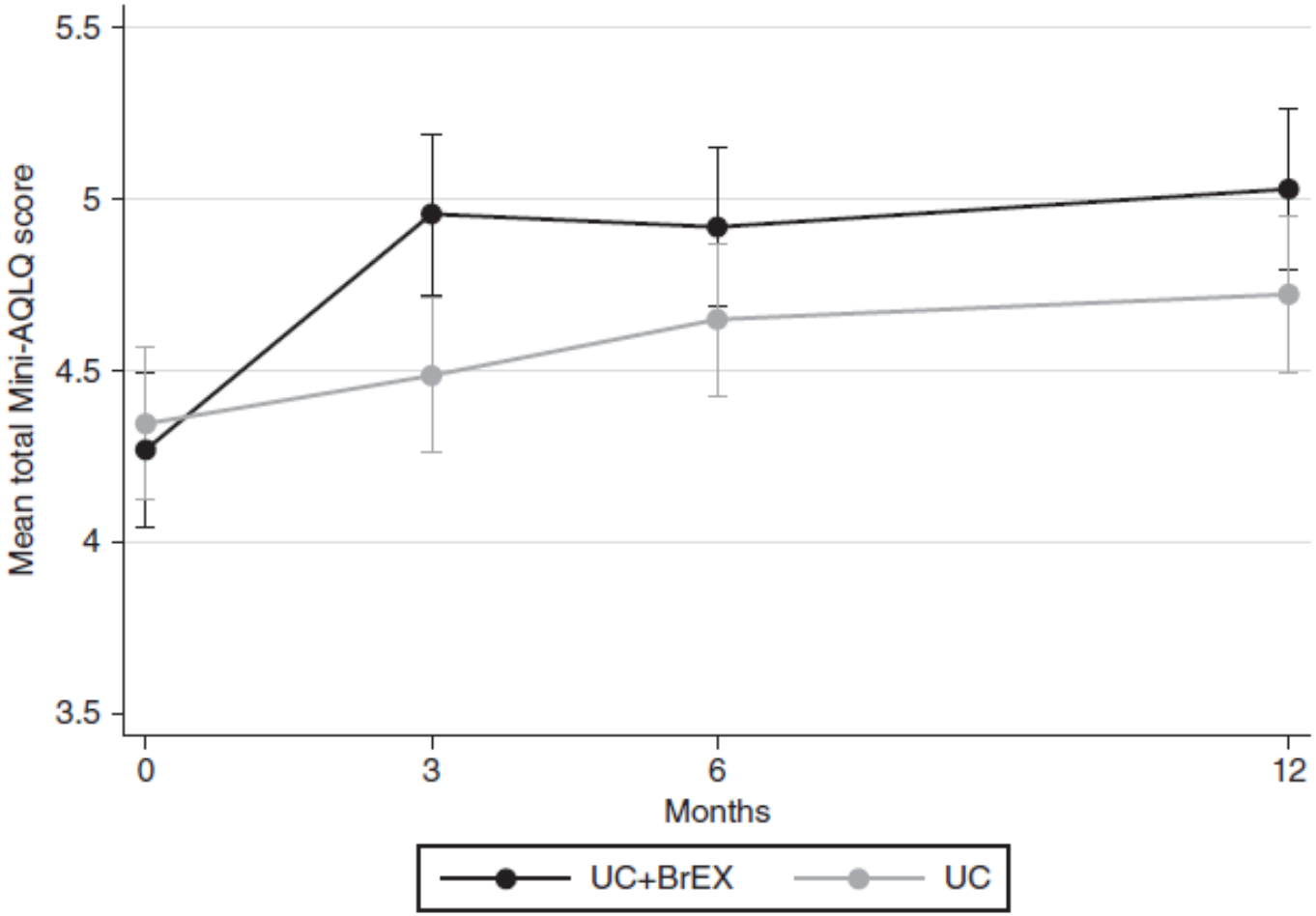

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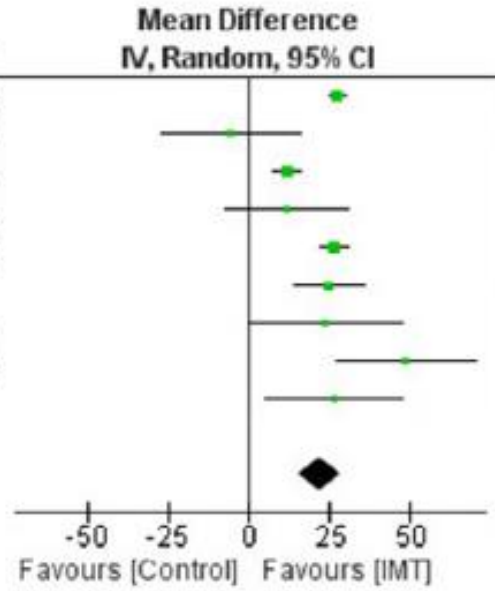
Effect of respiratory muscle training in asthma

- Systematic review of research included up to September 2021 in PubMed/MEDLINE, PEDro, Scopus, Web of Science, CINAHL, LILACS, Cochrane Central Register of Controlled Trials and ClinicalTrials.gov.
- **Eleven studies (270 participants)** were included, **10 with only adults** and were included in the meta-analysis.

Maximal inspiratory pressure (PImax) between IMT and control group

	IMT			Control				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Weiner 1992 [9]	107	4.8	15	79.6	2.1	15	18.4%	27.40 [24.75, 30.05]	1992
McConnell 1998 [5]	121	30.1	9	126.4	14.5	9	6.5%	-5.40 [-27.23, 16.43]	1998
Weiner 2000 [36]	109.7	5.2	11	98.1	5.3	11	17.5%	11.60 [7.21, 15.99]	2000
Sampaio 2002 [43]	78.7	22.2	10	66.9	21.5	10	7.7%	11.80 [-7.35, 30.95]	2002
Weiner 2002 (2) [37]	111.5	6.2	15	85.1	5.4	15	17.7%	26.40 [22.24, 30.56]	2002
Turner 2011 [44]	145.4	11.7	7	120.6	9.2	8	12.9%	24.80 [14.04, 35.56]	2011
Delgado 2014 [42]	136.4	22.5	5	112.6	15.5	5	5.8%	23.80 [-0.15, 47.75]	2014
Duruturk 2018 [39]	88.92	42.73	16	40.18	7.95	14	6.7%	48.74 [27.39, 70.09]	2018
Lage 2021 [40]	118.05	32.38	20	91.45	35.16	19	6.8%	26.60 [5.36, 47.84]	2021
Total (95% CI)			**108**			**106**	**100.0%**	**21.95 [15.05, 28.85]**	

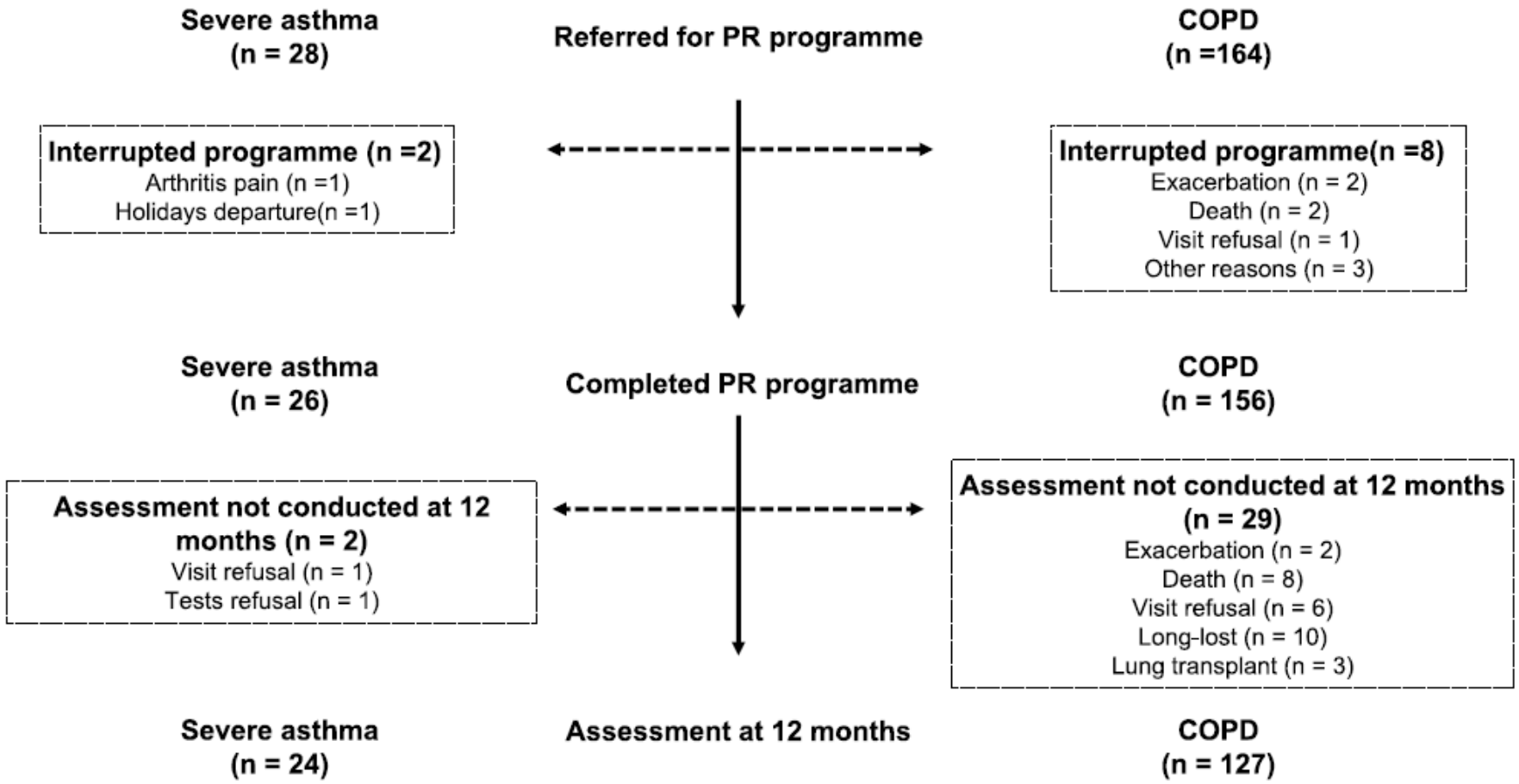
Heterogeneity: Tau² = 65.66; Chi² = 52.00, df = 8 (P < 0.00001); I² = 85%
Test for overall effect: Z = 6.23 (P < 0.00001)



Ana Lista-Paz et al. Annals of Physical and Rehabilitation Medicine 2023; 66: 101691.

Long term effect of home-base PR in severe asthma

- Retrospective study which included **28 patients with severe asthma** (61.5 ± 16.2 yrs, FEV1:51.4 ± 17.3%) and **164 matched COPD patients** (64.3 ± 11.6 yrs, FEV1: 47.7 ± 15.5%) who had completed a home-based PR program and pursued at least 12 months of f/u.



J-M Grosbois et al. Respiratory Medicine 2019; 157: 36-41.

	Severe asthma (n = 28)	COPD (n = 164)	p
Socio-demographic data			
Age, years	61.5 ± 16.2	64.3 ± 11.6	0.398
Women, n (%)	22 (78.6)	76 (46.3)	0.002
BMI, kg/m^2	29.6 ± 6.5	28.7 ± 8.1	0.901
Tobacco, n (%)			< 0.001
Non-smokers, n (%)	17 (60.7)	25 (15.2)	< 0.001
Ex-smokers, n (%)	9 (32.1)	114 (69.5)	< 0.001
Smokers, n (%)	2 (7.1)	14 (8.5)	1.000
Missing data, n (%)	0 (0)	11 (6.7)	0.372
≥3 comorbidities, n (%)	24 (85.7)	133 (81.1)	0.279
Treatment			
Combined LABA-ICS, n (%)	20 (82.1)	73 (44.5)	0.013
ICS, n (%)	5 (17.8)	26 (15.8)	0.784
LABA, n (%)	11 (39.3)	63 (38.4)	0.949
LAMA, n (%)	8 (28.6)	112 (68.3)	< 0.001
SABA, n (%)	28 (100)	81 (49,4)	< 0.001
Oral corticosteroids, n (%)	10 (35.7)	29 (17.7)	0.030
Montelukast, n (%)	10 (35.7)	0 (0)	< 0.001
Omalizumab, n (%)	2 (7.1)	0 (0)	0.021
Mepolizumab, n (%)	2 (7.1)	0 (0)	0.021
LTOT, n (%)	7 (25)	50 (30.5)	0.544
NIV, n (%)	5 (17.9)	41 (25)	0.404
CPAP, n (%)	3 (10.7)	19 (11.6)	1.000
Pulmonary function test			
FEV1 (% of the predicted value)	51.4 ± 17.3	47.7 ± 15.5	0.236
FVC (% of the predicted value)	81.4 ± 21.8	71.1 ± 18.1	0.026
FEV1/FVC (%)	59.9 ± 14.0	56.8 ± 9.9	0.376

J-M Grosbois et al. Respiratory Medicine 2019; 157: 36-41.

Exercise tolerance, anxiety, depression and QOL

	Baseline	Post-PR	ES post-PR	M12	ES M12	Global p
6MST, number of steps						
Severe asthma	450 ± 148	504 ± 150 p = 0.043	+0.35	538 ± 163 p = 0.016	+0.54	0.003
COPD	407 ± 142	466 ± 151 p < 0.001	+0.41	460 ± 181 p = 0.004	+0.33	< 0.001
VSRQ, score						
Severe asthma	32.2 ± 12.4	38.7 ± 15.8 p = 0.119	+0.45	39.0 ± 18.6 p = 0.049	+0.42	0.039
COPD	32.7 ± 15.4	40.4 ± 16.4 p < 0.001	+0.49	38.8 ± 16.9 p < 0.001	+0.37	< 0.001
HAD, score						
Severe asthma	17.9 ± 6.6	14.8 ± 7.5	−0.43	16.7 ± 10.0	−0.14	0.197
COPD	17.8 ± 7.1	14.8 ± 7.7 p < 0.001	−0.41	14.4 ± 7.9 p < 0.001	−0.45	< 0.001
HAD-A, score						
Severe asthma	9.8 ± 3.3	8.4 ± 3.7	−0.41	9.3 ± 4.9	−0.12	0.292
COPD	10.1 ± 4.7	8.7 ± 4.5 p < 0.001	−0.31	8.5 ± 4.7 p < 0.001	−0.34	< 0.001
HAD-D, score						
Severe asthma	8.0 ± 4.0	6.4 ± 4.4	−0.38	7.4 ± 5.9	−0.13	0.235
COPD	7.7 ± 4.0	6.1 ± 4.1 p < 0.001	−0.41	5.9 ± 4.5 p < 0.001	−0.43	< 0.001

J-M Grosbois et al. Respiratory Medicine 2019; 157: 36-41.

Exercise tolerance, anxiety, depression and QOL between severe asthma and COPD

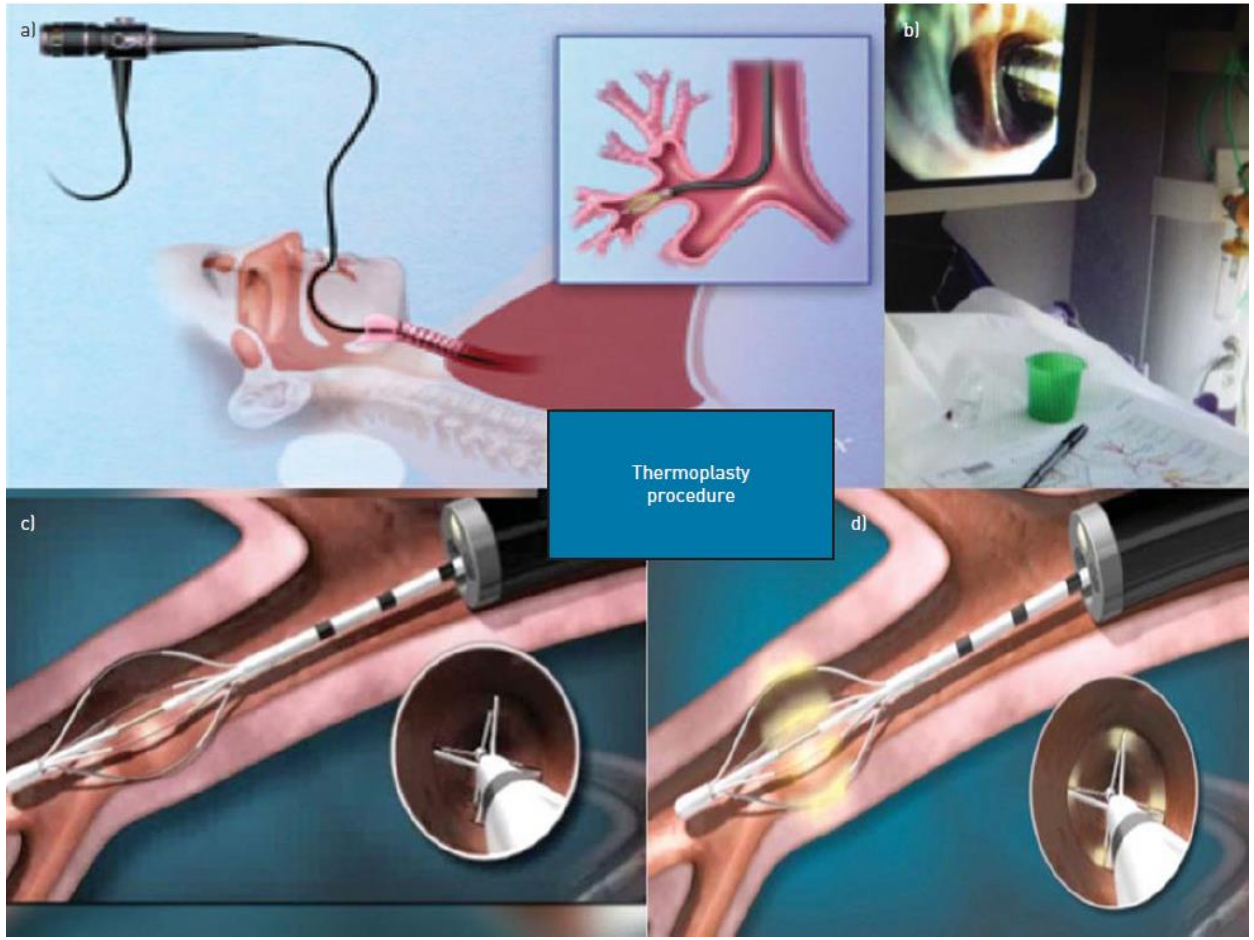
	Severe asthma	COPD	p	Effect size
6MST, number of steps				
post-PR - baseline	+86.8 ± 85.8	+56.1 ± 98.0	0.210	−0.32
M12 - baseline	+70.2 ± 104.9	+52.2 ± 131.0	0.436	−0.14
VSRQ, score				
post-PR - baseline	+8.8 ± 13.8	+6.9 ± 12.6	0.277	−0.15
M12 - baseline	+6.8 ± 11.9	+6.1 ± 16.2	0.841	−0.05
HAD-A, score				
post-PR - baseline	−1.7 ± 2.9	−1.4 ± 3.5	0.702	0.08
M12 - baseline	−0.5 ± 4.8	−1.6 ± 3.9	0.311	−0.27
HAD-D, score				
post-PR - baseline	−1.5 ± 2.9	−1.4 ± 3.5	0.911	0.02
M12 - baseline	−0.7 ± 5.1	−1.8 ± 4.1	0.260	−0.26

J-M Grosbois et al. Respiratory Medicine 2019; 157: 36-41.

Bronchial Thermoplasty

Bronchial thermoplasty: new therapeutic option

- Bronchial thermoplasty is a nonpharmacological, device-based therapy that delivers controlled thermal energy to the airway wall as part of a series of three bronchoscopic procedures.
- Approved by the US FDA for the treatment of severe persistent asthma in patients aged o18 years whose asthma is not well controlled with inhaled corticosteroids (ICS) and long-acting b2-agonists (LABAs) in 2010



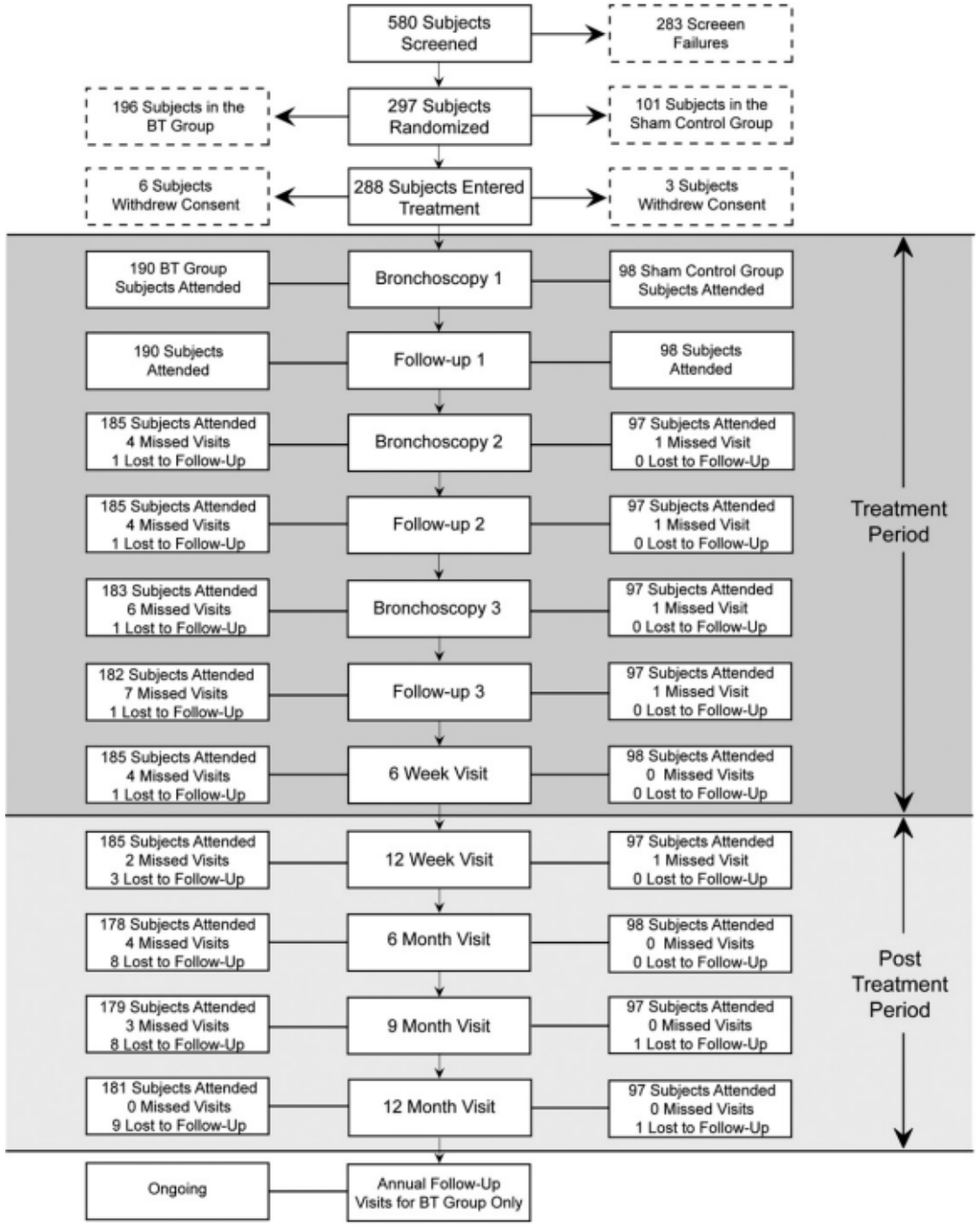
M-C Dombret et al. Eur Respir Rev 2014; 23: 510-518.

Effectiveness and safety of bronchial thermoplasty for severe asthma

- Of 580 subjects screened, 297 were randomized to the BT group (196 subjects) or the sham control group (101 subjects).
- Of these, **190 subjects in the BT group** and **98 subjects in the sham group** underwent at least one bronchoscopy (ITT population).
- The primary outcome was the difference in Asthma Quality of Life Questionnaire (AQLQ) scores from baseline to average of 6, 9, and 12 months (integrated AQLQ).

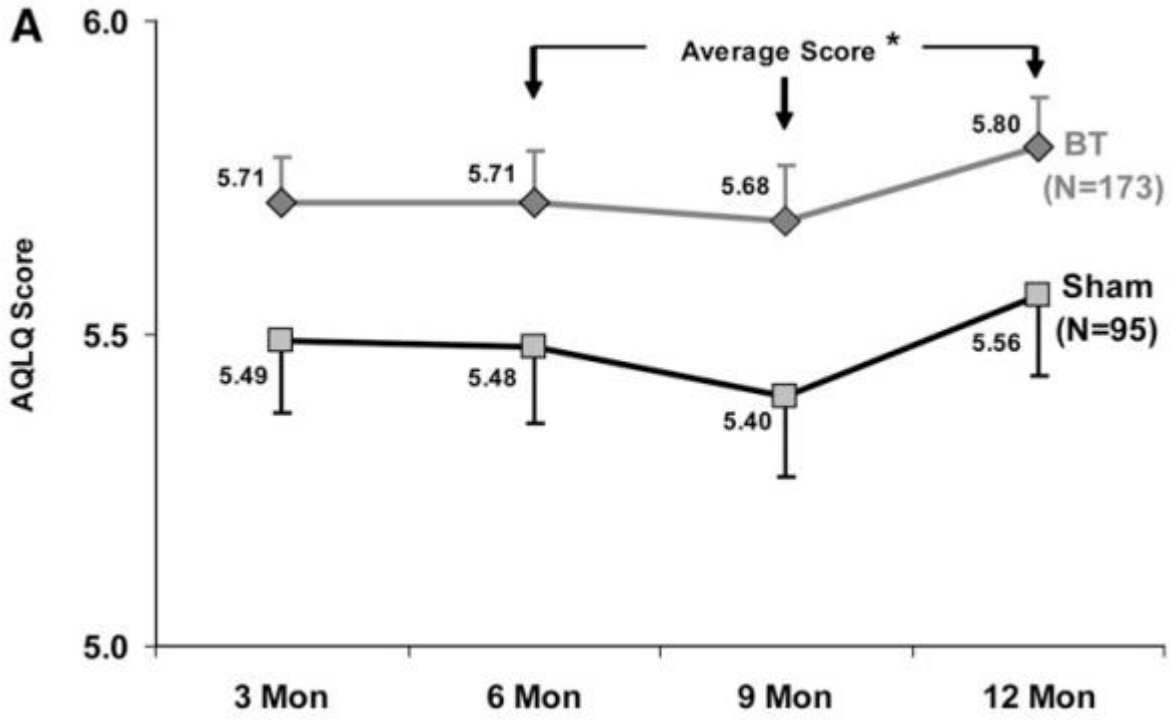
	BT (n = 190)*	Sham (n = 98)*
Age (years)	40.7 ± 11.89	40.6 ± 11.85
Sex, n (%)		
Male	81 (42.6)	38 (38.8)
Female	109 (57.4)	60 (61.2)
Race/Ethnicity, n (%)		
White	151 (79.5)	72 (73.5)
African American/Black	19 (10.0)	15 (15.3)
Other	20 (10.5)	11 (11.2)
Methacholine PC_{20} (mg/ml)		
Geometric mean	0.27 (n=178)	0.31 (n=94)
95% Confidence interval bounds	(0.22, 0.34)	(0.22, 0.43)
Prebronchodilator FEV_1 (% predicted)	77.8 ± 15.65	79.7 ± 15.14
Inhaled corticosteroid dose† (μg/d), mean (median)	1960.7 (2,000)	1834.8 (2,000)
Long-acting β_2-agonist dose‡ (μg/day)	116.8 ± 34.39 (n=189)	110.3 ± 26.70 (n=97)
AQLQ baseline score	4.30 ± 1.17	4.32 ± 1.21
Percent symptom-free days§	16.4 ± 24.04	16.8 ± 23.10
Number and percentage of subjects on other asthma maintenance medications		
Oral corticosteroids	7 (3.7)	1 (1.0)
Methylxanthines	6 (3.2)	5 (5.1)
Leukotriene modifiers	47 (24.7)	18 (18.4)
Omalizumab	2 (1.1)	3 (3.1)
Other	15 (7.9)	9 (9.2)
Any of the above maintenance medications	59 (31.1)	25 (25.5)
Oral corticosteroids dose (mg/d)	6.4 ± 1.97 (n = 7)	5.0 (n = 1)

Mario Castro et al. Am J Respir Crit Care Med 2010; 181: 116-124.

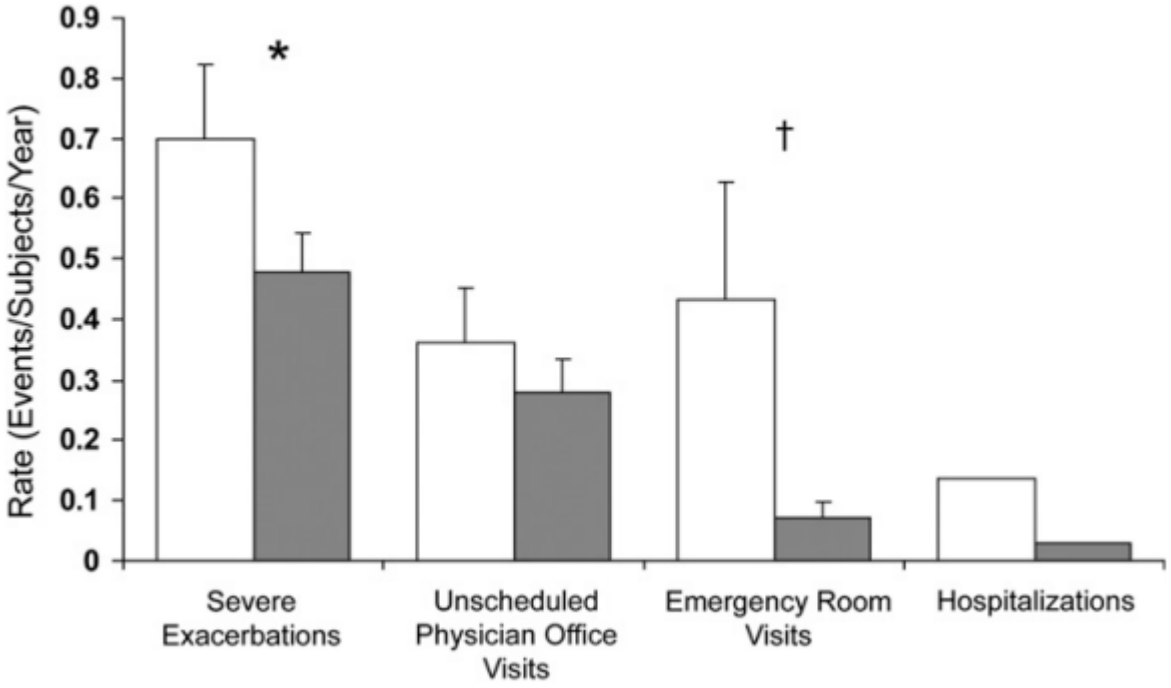


Mario Castro et al. Am J Respir Crit Care Med 2010; 181: 116-124.

Change in asthma QOL by treatment group



Healthcare utilization events during the Post Tx



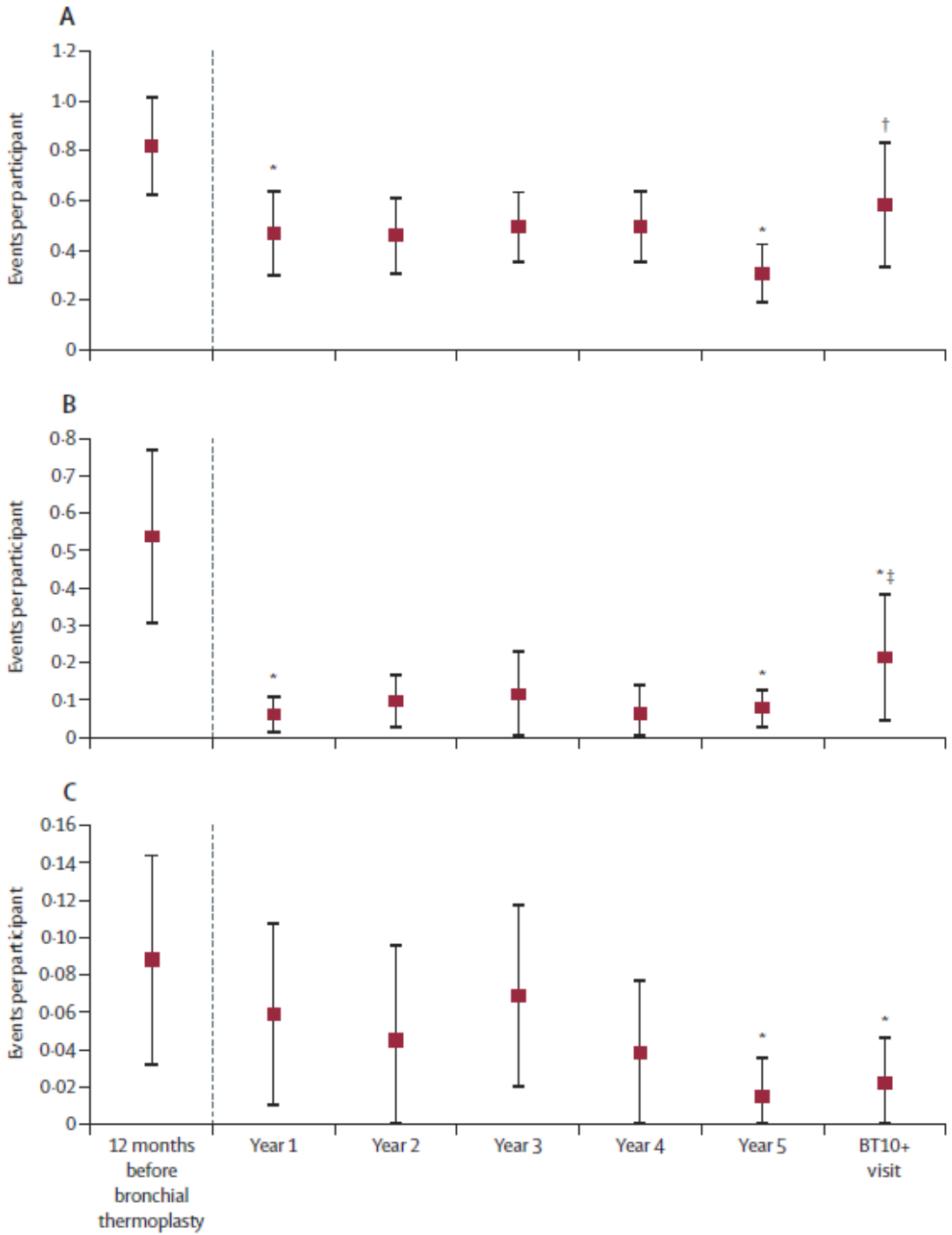
Mario Castro et al. Am J Respir Crit Care Med 2010; 181: 116-124.

Long term efficacy and safety of bronchial thermoplasty from three RCTs

- BT10+ was an international, multicentre, follow-up study of participants who were previously enrolled in the AIR, RISA, and AIR2 trials and who had 10 or more years of follow-up since bronchial thermoplasty treatment.
- To investigate the efficacy and safety of bronchial thermoplasty **after 10 or more years of follow-up**.

	Control or sham with no post-study bronchial thermoplasty (n=38)	Control or sham with post-study bronchial thermoplasty (n=18)	Bronchial thermoplasty (n=136)
Age (years)	54·4 (11·8)	54·2 (8·9)	53·6 (11·4)
Sex			
Female	19 (50%)	7 (39%)	82 (60%)
Male	19 (50%)	11 (61%)	54 (40%)
Weight (kg)	80·4 (19·1)	96·5 (14·0)	83·7 (19·8)
Height (cm)	167·7 (11·3)	166·6 (8·8)	165·2 (9·1)
Body-mass index (kg/m²)	28·5 (5·7)	34·9 (5·2)	30·6 (6·5)
Meet current European Respiratory Society and American Thoracic Society Guidelines for Severe Asthma*	26 (68%)	13 (72%)	103 (76%)
FEV_1			
Pre-bronchodilator, % predicted	74·4 (17·4)	73·4 (17·1)	72·9 (19·4)
Post-bronchodilator, % predicted	80·7 (16·3)	80·1 (15·2)	79·4 (18·5)
Pre-bronchodilator, measured (L)	2·3 (0·8)	2·3 (0·8)	2·2 (0·8)
Post-bronchodilator, measured (L)	2·5 (0·8)	2·5 (0·8)	2·4 (0·7)
Forced vital capacity			
Pre-bronchodilator, % predicted	93·2 (16·4)	87·7 (14·1)	90·2 (15·1)
Post-bronchodilator, % predicted	97·8 (16·3)	93·2 (11·8)	96·5 (14·3)
Pre-bronchodilator, measured (L)	4·0 (1·1)	3·7 (1·0)	3·7 (0·9)
Post-bronchodilator, measured (L)	4·2 (1·1)	3·9 (1·0)	4·0 (0·9)
Residual volume, % predicted	121·2 (41·8)	121·2 (21·2)	120·9 (34·6)
Total lung capacity, % predicted	102·1 (14·7)	101·8 (13·0)	105·1 (14·0)

Rekha Chaudhuri et al. Lancet Respir Med 2021; 9: 457-66.

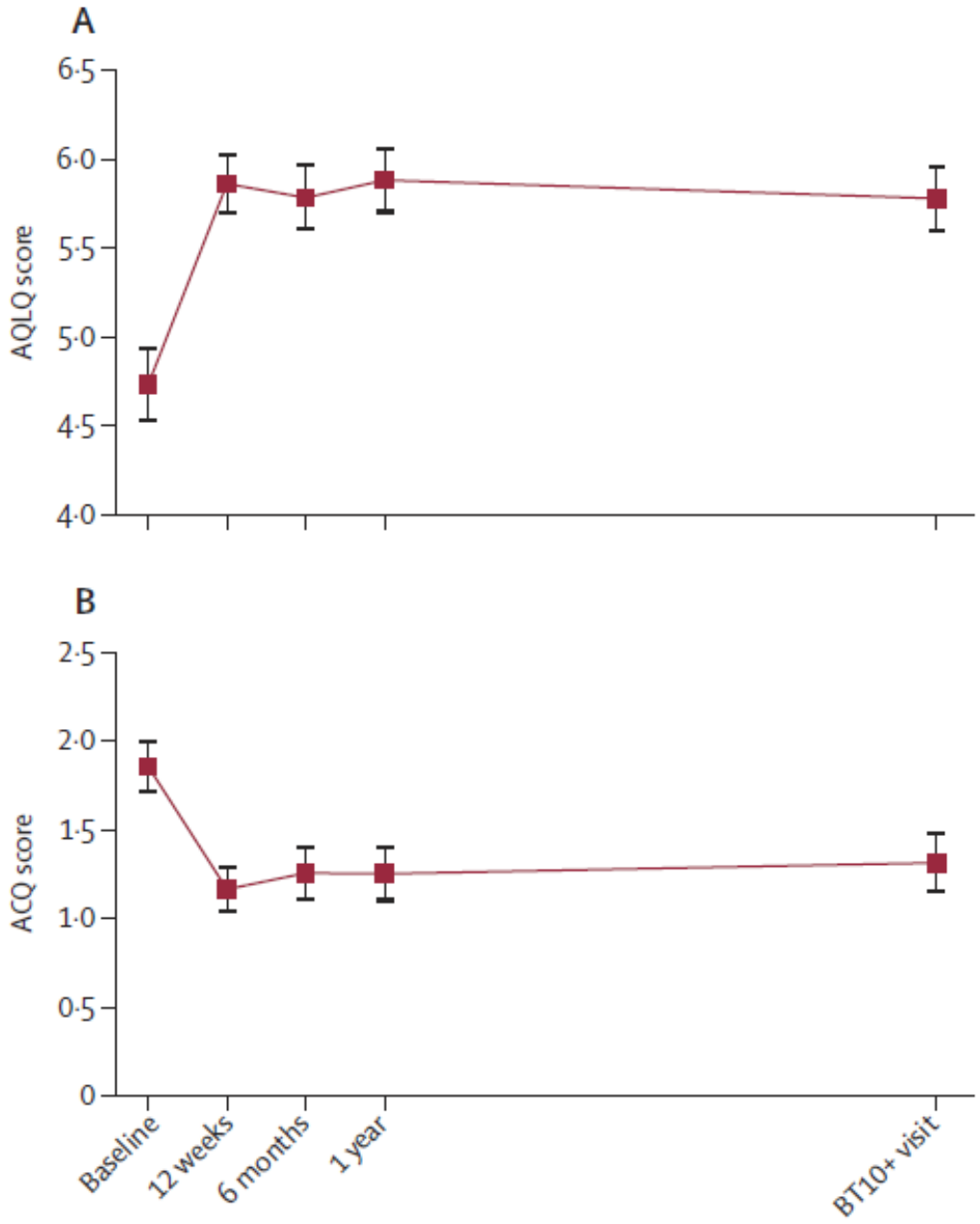


Severe asthma exacerbation

Hospital emergency department visits

Admission to hospital for asthma

Rekha Chaudhuri et al. Lancet Respir Med 2021; 9: 457-66.



Rekha Chaudhuri et al. Lancet Respir Med 2021; 9: 457-66.

Summary

- Various reasons for uncontrolled asthma
- Electronic monitoring for inhaler adherence
- Diet and weight loss program in obese asthmatic patients
- Physiotherapy (breathing technique), Pulmonary rehabilitation in asthma
- Bronchial Thermoplasty – long term effect (+)

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