Bijlage Evidencetabellen

Evidencetabel intervaltraining versus duurtraining

Studie	Land	Setting, duur en frequentie	Deelnemers	Interventie (intervaltraining)	Controle (duurtraining)	Opmerkingen	Uitkomstmaten	Schalen	Uitval (dropout)
Arnardottir 2007	Zweden	Setting: outpatient Duur: 16 wkn Frequentie: 2x/week	N=100 Lftd: 43-80 jr. Geslacht: 15%♂ FEV1: gem. 32-35% of predicted	Fietsen op 80% van Wmax 3 minuten lang, afgewisseld met 3 minuten op 30-40% van Wmax. In totaal 5 maal 80% en 4 maal 30-40% (27 minuten). Daarnaast warm-up en cool-down op 30-40% van Wmax, elk 6 minuten lang.	Fietsen op 65% van Wmax, 27 minuten lang. Daarnaast warm-up en cool-down op 30-40% van Wmax, elk 6 minuten lang.		C-P Exercise Test, Kortademigheid, Fysieke capaciteit	Wmax Borg (CR-10) 12MWT	N= 40 (unclear how many in each group)
Kortianou 2010	Griekenland	Setting: outpatient Duur: 10 wkn Frequentie: 3x/week	N= 46 Lftd: gem. 64-67 jr. Geslacht: 96%♂ FEV1: gem. 40-45% of predicted	Fietsen op 100% van Wmax, 30 seconden lang, afgewisseld met 30 seconden rust. Totaal 40 minuten lang.	Fietsen op 60% van Wmax, 40 minuten lang.		C-P Exercise Test, Kortademigheid, Kwaliteit van leven, Fysieke capaciteit	Wmax, Max dyspnoe, SGRQ, 6MWT	N= 3 (1 in interventie)
Mador 2009	USA	Setting: outpatient Duur: 8 wkn Frequentie: 3x/week	N= 41 Lftd: gem. 72 jr. Geslacht: 80%♂ FEV1: gem. 45% of predicted	Fietsen op 150% van continue doel, 1 minuut lang, afgewisseld met 2 minuten op 75%, in totaal 21 minuten lang. Vervolgens loopband op 150% van continue doel, 1 minuut lang, afgewisseld met 2 minuten op 75%, in totaal 21 minuten. Totale training 42 minuten.	Fietsen op 50% van Wmax, 20 minuten lang. Vervolgens loopband op 80% van snelheid in 6MWT en geen helling, 20 minuten lang. Totale training 40 minuten.	Vermogen (W) tijdens fietsen werd met 10% opgehoogd en vermogen op loopband werd met 5-15% opgehoogd.	C-P Exercise Test, Kwaliteit van leven, Fysieke capaciteit	Wmax, CRQ, 6MWT	N= 7 (4 in interventie)
Nasis 2009	Griekenland	Setting: outpatient Duur: 10 wkn Frequentie: 3x/week	N= 42 Lftd: gem. 66 jr. Geslacht: 79%♂ FEV1: gem. 42% of predicted	Fietsen op 100% van Wmax, 30 seconden lang, afgewisseld met 30 seconden rust. Totaal 40 minuten lang.	Fietsen op 60% van Wmax, 30 minuten lang.	Vermogen (W) is wekelijks opgehoogd per groep, maar niet specifiek beschreven.	C-P Exercise Test, Kortademigheid, Fysieke capaciteit	Wmax, Borg (CR-10) 6MWT	Geen

Studie	Land	Setting, duur en frequentie	Deelnemers	Interventie (intervaltraining)	Controle (duurtraining)	Opmerkingen	Uitkomstmaten	Schalen	Uitval (dropout)
Puhan 2006	Zwitserland	Setting: inpatient Duur: 3 wkn Frequentie: 5x/week	N= 86 Lftd: gem. 69 jr. Geslacht: niet gerapporteerd FEV1: gem. 34% of predicted	Fietsen op 90-100% van Wmax, 20 seconden lang, afgewisseld met 20-30% van Wmax, 40 seconden lang. In totaal 20 minuten lang. Daarnaast warm-up en cool-down op 20% van Wmax, 2 minuten elk.	Fietsen op 70% van Wmax, 20 minuten lang. Daarnaast warm-up en cool-down op 20% van Wmax, 2 minuten elk.	Vermogen (W) is met 10% opgehoogd ten opzichte van baseline.	Incremental exercise test, Fysieke capaciteit, Kwaliteit van leven	Wmax, 6MWT, CRQ	N= 11 (5 in interventie)
Varga 2007	Hongarije	Setting: outpatient Duur: 8 wkn Frequentie: 3x/week	N= 79 Lftd: gem. 64 jr. Geslacht: 77%♂ FEV1: gem. 57% of predicted	Fietsen op 90% van Wmax, 2 minuten lang, afgewisseld met 50% van Wmax, 1 minuut. In totaal 30 minuten lang. Daarnaast warm-up en cool-down van elk 7,5 minuten.	Fietsen op 80% van Wmax, 45 minuten lang.	3-armed study; 39 geïncludeerd in deze interventie- en controlegroep.	C-P Exercise Test, Kortademigheid	Wmax, Borg (CR-10)	Geen
Vogiatzis 2002	Griekenland	Setting: outpatient Duur: 12 wkn Frequentie: 2x/week	N= 36 Lftd: gem. 68 jr. Geslacht: 83%♂ FEV1: gem. 45% of predicted	Fietsen op 100% van Wmax, 30 seconden lang, afgewisseld met 30 seconden rust. In totaal 40 minuten.	Fietsen op 50% van Wmax, 40 minuten lang.	Maandelijkse ophoging van vermogen (W), gelijk in beide groepen.	C-P Exercise Test, Kortademigheid, Kwaliteit van leven	Wmax, Borg (CR-10), CRQ	N= 9 (5 in interval)
Vogiatzis 2005	Griekenland	Setting: outpatient Duur: 10 wkn Frequentie: 3x/week	N= 19 Lftd: gem. 65 jr. Geslacht: 84%♂ FEV1: gem. 42% of predicted	Fietsen op 100% van Wmax, 30 seconden lang, afgewisseld met 30 seconden rust. In totaal 45 minuten.	Fietsen op 60% van Wmax, 30 minuten lang.	Maandelijkse ophoging van vermogen (W), gelijk in beide groepen.	C-P Exercise Test	Wmax	

Evidencetabel duur-intervaltraining versus kracht én duur-/intervaltraining

Studie	Land	Setting, duur en frequentie	Deelnemers	Interventie (ET+RT)	Controle (ET)	Opmerkingen	Uitkomstmaten	Schalen	Uitval (dropout)
Ortega 2002	Spanje	Setting: outpatient Duur: 12 wkn FU: 12 wkn Frequentie: 3x/week	N=54 Lftd: gem. 64 jr. Geslacht: 85%♂ FEV1: 70% of predicted	*ET*: 20 minutes of cycling 70% of Wpeak þ *RT*: two series of five weightlifting procedures 70–85% of 1RM, 6–8 repetitions	*ET*: 40 minutes of cycle 70% of Wpeak	3-Armed study 36 patients randomized to our intervention and control groups	Adverse events, HRQoL, walking test, muscle strength, C-P exercise test	CRQ, SWT, leg extension 1RM in kilogram, VO2max in L/minute, watts	N= 6 (4 in controlegrorp)
Dourado 2009	Brazilië	Setting: inpatient Duur: 12 wkn Frequentie: 3x/week	N=51 Lftd: gem. 63 jr. Geslacht: 65%♂ FEV1: 58% of predicted	*ET*: 30 minutes of walking and low intensity strength þ *RT*: 30 minutes of two series of 8 repetitions at 50–80% of 1RM	*ET*: low intensity general training consisting of 30 minutes walking and 30 minutes of low-intensity general training	3-Armed study 33 patients randomized to our intervention and control group	HRQoL, walking test, muscle strength	SGRQ, 6MWT, leg extension and leg press 1RM in kg	N= 9 (3 in controlergroepgroup)
Vonbank 2012	Oostenrijk	Setting: outpatient Duur: 12 wkn Frequentie: 2x/week	N=43 Lftd: gem. 60 jr. Geslacht: 56% ♂ FEV1: 56% of predicted	*ET*: cycle ergometer training of increasing intensity þ *RT:* two to four series of 8 strength exercises, 8–15 repetitions until severe fatigue.	ET: 1 hour of cycle training of increasing intensity and time, 60% of VO2max	3-Armed study 24 patients randomized to our intervention and control group	HRQoL muscle strength, C-P exercise test	SGRQ, VO2 max in mL/kg/minute, watts	N= 7 (not reported in which group)
Bernard 1999	Canada	Setting: outpatient Duur: 12 wkn Frequentie: 3x/week.	N=45 Lftd: gem. 66 jr. Geslacht: 71% ♂ FEV1: gem. 42% of predicted	*ET*: 45 minutes on ergometer cycle at 80% of Wpeak rateþ *RT*: 45 minutes of 4 weightlifting exercises, 8–10 repetitions at 60% of 1RM increasing to 80%	*ET*: 45 minutes on ergometer cycle at 80% of Wpeak rate þ 45 minutes of relaxation and breathing exercises	-	Adverse events, HRQoL, walking test, muscle strength, C-P exercise test	CRQ, 6MWT, strength of quadriceps in kg, VO2max in L/minute, Wmax in watts	N= 9 (5 in controle)

Studie	Land	Setting, duur en frequentie	Deelnemers	Interventie (ET+RT)	Controle (ET)	Opmerkingen	Uitkomstmaten	Schalen	Uitval (dropout)
Mador 2004	VS	Setting: outpatient Duur: 8 wkn, 24 sessions Frequentie: 3x/week	N=32 Lftd: gem. 68 en 74 jr. FEV1: gem. 42% of predicted	*ET*: cycle ergometer training adjusted to level of dyspnea by increasing intensity þ *RT:* four different strength exercises, increasing from 1 to 3 series of 10 repetitions at 60% of 1RM.	*ET*: cycle ergometer training adjusted to level of dyspnea by increasing intensity	Patients in intervention group were significantly older no information on gender	HRQoL, walking test, C-P exercise test, muscle strength	CRQ, 6MWT, Wmax in watts, VO2max in L/minute, quadriceps strengths in kilogram	N= 8 (4 dropouts in each group)
Nakamura 2008	Japan	Setting: outpatient Duur: 12 wkn Frequentie: 3x/week	N=42 Lftd: gem. 68–69 jr. FEV1: gem. 53% of predicted	*ET*: 20 minutes of walking at 3–5 on Borg scale þ *RT:* 30 minutes of seven strength exercises using self-weight or elastic bands, 3 sets of 10 repetitions, no progression	*ET*: 20 minutes of walking at Borg 3–5 þ 30 minutes of recreational activities of balance, agility and coordination	3 Armed study 28 patients randomized to our intervention and control group	HRQoL, walking test, muscle strength	SF 36, 6MWT, VO2 max in mL/kg/minute, Wmax in watts, grip strength in kilogram	N= 5 (4 in CT group)
Panton 2003	VS	Setting: outpatient Duur: 12 wkn Frequentie: 2x/week	N=18 Lftd: 50 - 72 jr. FEV1: gem. 40% of predicted	*ET*: 60 minutes of chair aerobic, cycling and walking at intensity of 50–70% þ *RT:* 45–60 minutes of 12 strength exercises, 3 sets of 12 repetitions, progressive increasing weight	*ET*: 60 minutes of chair aerobic, cycling and walking at intensity of 50–70%	-	Adverse events, ADLs, walking test, muscle strength, lean body mass	Time per ADLs, 12MWT, Leg extension in NM, Repetition, BMI	N= 1 (1 dropout in ET group)
Phillips 2006	VS	Setting: outpatient Duur: 8 wkn Frequentie: 2x/week	N=22 Lftd: gem. 70 jr FEV1: gem. 32% (C) en 42% (ET) of predicted	*ET*: 20–40 minutes of cycling (arms and legs) and walking exercises at METS 3 and low intensity to high repetition RT þ *RT:* five strength exercises at 50% of 1RM, progressive increasing weight	*ET*: 20–40 minutes of cycling (arms and legs) and walking exercises at METS 3 and low intensity to high repetition RT	More males (6) in CT group than control group (1)	Adverse events, walking test, muscle strength	6MWT, leg press in lb	N= 3 (unclear in which group)

Studie	Land	Setting, duur en frequentie	Deelnemers	Interventie (ET+RT)	Controle (ET)	Opmerkingen	Uitkomstmaten	Schalen	Uitval (dropout)
Ries 1988	VS	Setting: outpatient Duur: 6 wkn Frequentie: unclear	N=45 No baseline characteristics	*ET*: PR programme activities including walking training and 15–30 minutes of arm cycling þ *RT:* four strength exercises, 3 sets of 4–10 repetitions, progressive increasing weight	*ET*: PR programme activities including walking training	3 Armed study 20 patients completed 9 in CT group and 11 in ET group	Adverse events, ADLs, C-P exercise test	ADLs test in seconds, Wmax in watts (VO2max investigated but data not reported)	N= 17 (unclear in which group)
Würtemberger and Bastian 2001	Duitsland	Setting: inpatient Duur: 3 wkn Frequentie: 3 times per week	N=69 Lftd: gem. 61–65 jr. FEV1: range 30–62% of predicted Geslacht: 64%♂ Zuurstof: n=10 (C), n=12 (I)	*ET*: 20 minutes sessions on a calibrated ergo cycle, intensity of 70% of Wmax þ *RT:* include 5 strength exercises of muscle major groups, 2–4 series of 20–25 repetitions, intensity of 40% of Wmax	*ET*: 20 minutes sessions on a calibrated ergo cycle, intensity of 70% of Wmax	3 Armed study 46 patients randomized to our intervention and control groups	Walking test, ADLs	6MWT, ADLs in time	N= NB (Niet gerapporteerd)
Alexander 2008	VS	Setting: outpatient Duur: 8–10 wkn Frequentie: 16 sessions total	N=27 Lftd: gem. 65–73 jr. FEV1: gem. 30–39% of predicted	*ET*: 20–40 minutes of cycling (arms and legs) and treadmill walking intensity adjusted individually þ *RT:* 5 strength exercises of major muscle groups, 1 set of 12 repetitions at 50% of 1RM and progressive increasing weight	*ET*: 20–40 minutes of cycling (arms and legs) and treadmill walking, intensity adjusted individually þ low intensity upper extremity strength training	-	ADLs, muscle strength, walking test	6MWT, senior fitness test, seated leg press in lb	N= 7 (5 in CT group)
Aquino 2016	Italië	Setting: outpatient Duur: 4 wkn. Frequentie: 10x/week (5 ochtendsessies & 5 middagsessies)	N= 28 Lftd= gem. 67 jr. FEV1= 68,4%	*ET*: 's ochtends 30 min. treadmill exercise; Intensiteit: wk1: 70% HR wk2: 80%HR wk3: 85% HR wk4: 90% HR *RT:* 's middags training van deltoïdeus, quadriceps, biceps en dorsaalspieren; Intensiteit:	*ET*: 2x.dag 30 min. treadmill exercise; Intensiteit: wk1: 70% HR wk2: 80%HR wk3: 85% HR wk4: 90% HR	-	Aerobic capacity, muscle strength	6MWT, estimated one-repetition maximum	N= 0

Studie	Land	Setting, duur en frequentie	Deelnemers	Interventie (ET+RT)	Controle (ET)	Opmerkingen	Uitkomstmaten	Schalen	Uitval (dropout)
				wk1: 70% 1RM, 3 sets x 10 herhalingen wk2: 80%1RM, 3 sets x 8 herhalingen wk3: 85% 1RM, 3 sets x 6 herhalingen wk4: 90% 1RM, 3 sets x 4 herhalingen					
Covey 2014	VS	Setting: outpatient Duur: 8 wkn (met voorafgaand 8 wkn shamtherapie) Frequentie: 3x/week	N=75 Lftd= gem. 68 jr Geslacht= 89%♂ FEV1= 40% van voorspelde waarde	*ET*: Performed on a stationary cycle ergometer using an interval training protocol. Patients performed four work sets of five minutes duration separated by rest intervals of unloaded cycling lasting 2e4 min. This approach lessens symptoms of dyspnea and fatigue during training and enables even extremely dyspneic patients to train at progressively higher intensities without stopping or reducing training intensity. The initial work sets were at 50% of the peak work rate and were evaluated weekly with progressive increases targeted to achieve the highest work rate tolerated. The typical progression was: 50% peak work rate for weeks 1e2, 60% peak work rate for weeks 3e4, 70% peak work rate for weeks 5e6, and 80% peak work rate for	*ET*: Performed on a stationary cycle ergometer, calibrated with a 4 kg weight using an interval training protocol. For the interval training protocol patients performed four work sets of five minutes duration separated by rest intervals of unloaded cycling lasting 2e4 min. This approach lessens symptoms of dyspnea and fatigue during training and enables even extremely dyspneic patients to train at progressively higher intensities without stopping or reducing training intensity. The initial work sets were at 50% of the peak work rate and were evaluated weekly with progressive increases targeted to	3-Armed study 55 patients randomized to our intervention and control groups	C-P exercise test, muscle strength, aerobic capacity, dyspnea, ADLs,	Wmax in watts, one-repetition maximum, 6MWT, CRQ-dyspnea, FPI	N=15 (7 in CT group)

Studie	Land	Setting, duur en frequentie	Deelnemers	Interventie (ET+RT)	Controle (ET)	Opmerkingen	Uitkomstmaten	Schalen	Uitval (dropout)
				weeks 7e8. *RT*: performed with fitness equipment using 6 lifts: leg press, knee extension, knee flexion, calf raise, hip adduction, and hip abduction. Training was initiated at an intensity of 70% of the one repetition maximum (1RM) performed at baseline with a training volume of 2 sets of 8e10 repetitions for 2 weeks, followed by 2 weeks of training at 80% of the baseline 1RM at a volume of 2 sets. For the remaining 4 weeks the intensity was 80% of the 1RM (re-assessed after 4 weeks of training) at a volume of 3 sets of 8e10 repetitions.	achieve the highest work rate tolerated. The typical progression was: 50% peak work rate for weeks 1e2, 60% peak work rate for weeks 3e4, 70% peak work rate for weeks 5e6, and 80% peak work rate for weeks 7e8.				
Daabis 2017	Egypte	Setting: outpatient Duur: 8 wkn. Frequentie: 3x/week	N= 45 Lftd= gem. 60 jr. FEV1= 54,7% van voorspelde waarde	*ET*: 30 min at half the volume (i.e., 15 min of walking at a self-determined intensity and an additional 15 min at half the number of repetitions of low-intensity resistance training with free weights). *RT*: Consisted of exercises performed on weight training machines, for pectoralis major, deltoid, biceps brachii, triceps and quadriceps muscles. Patients were submitted to three sets of 12 repetitions	*ET:* Consisted of 30 minutes of treadmill training at an intensity of 75% of the results of the 6MWT and an additional 30-min of low-intensity resistance training with free weights. The number of repetitions used was based on physiologic endurance principles, including a high number of repetitions	3-Armed study 30 patients randomized to our intervention and control groups	Kortademigheid Perifere spierkracht Fysieke capaciteit, submaximaal Kwaliteit van leven	mMRC 1RM 6MWT SGRQ	N= NB (niet gerapporteerd)

Studie	Land	Setting, duur en frequentie	Deelnemers	Interventie (ET+RT)	Controle (ET)	Opmerkingen	Uitkomstmaten	Schalen	Uitval (dropout)
				with a 2- min rest between sets and with a workload at 50–80% of that achieved on the 1-RM test. The 1-RM test was repeated every 2 weeks to reestablish the workload.	with a low load.				
Pereira 2010	Portugal	Setting: outpatient Duur: 10 weken Frequentie: 3x/week	N= 100 Lftd = gem. 63,5 jr. Geslacht= 100%♂ FEV1 < 80% van voorspelde waarde	*ET:* 30 min aerobic exercise at 60-70% of reserve heart rate. *RT*: Strength exercises at an intensity of 50-70% of 1 RM. Patients performed 1-2 sets with 6-12 repetitions per set. The strength exercises included leg extensions, thigh and leg extensions, arm adductors, forearm flexes.	*ET: 4*0-60 min at 60-70% of reserve heart rate and strength exercise at an intensity of 50-70% of 1 RM.	3-Armed study 50 patients randomized to our intervention and control groups	HRQoL	SGRQ	N= NB (niet gerapporteerd)

Evidencetabel neuromusculaire elektrostimulatie van de onderste ledematen

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up	Uitkomstmaten (studies) & Effectgrootte (95% BI)
Hill, 2018	SR en meta-analyse van RCT's *Literatuursearch: Hill 2018 tot maart 2018, update KNGF tot 7 juni 2018** *16 studies geïncludeerd:* *- NMES vs. gebruikelijke zorg (n=10),* *- Oefentherapie met vs. zonder NMES (n=6)*	Selectiecriteria SR: "Randomised controlled trials that recruited adults with COPD if they had compared outcomes between a group that received NMES and a group that received usual care or compared outcomes between a group that received NMES plus conventional exercise training and a group that participated in conventional exercise training alone."	Neuromusculaire elektrostimulatie van de onderste ledematen (NMES) met of zonder oefentherapie	Gebruikelijke zorg of oefentherapie	Eind v/d follow-up (range): onbekend	Kwaliteit van leven Fysiek functioneren Fysieke capaciteit Ongewenste voorvallen
	NMES vergeleken met gebruikelijke zorg (stand alone)					
	D: Bourjeily-Habr 2002 *Setting*: Poliklinisch (pulmonary rehabilitation or outpatient centre)	D: 18 patiënten met stabiel COPD I: n= 9; ♂= 6; lftd= 58 (2) jr; FEV1, % voorspelde waarde, gem (SEM)= 36 (4) % C: n= 9; ♂= 4; lftd, gem(SEM)= 62 (2) jr; FEV1, % voorspelde waarde, gem (SEM)= 41 (4) %	D: <u>NMES</u> Bilateraal; hamstrings, quadriceps & kuitspieren; *Golfvorm:* asymmetrisch, vierkante puls *Frequentie*: 50 Hz *Pulsduur:* 200 ms elke 1500 ms *Intensiteit*: 55-120 mA + 5 mA toename per week *Serietijd:* 200 ms elke 1500 ms *Sessieduur*: 20 min./dag; *Aantal sessies:* 18 sessies (3 dgn/week gedurende 6 wkn)	D: <u>Shamtherapie</u> Identieke opstelling maar zonder elektrische stimulatie	D: Eind v/d follow-up: onbekend Incomplete uitkomsten: onbekend	<u>Kwaliteit van Leven</u> *SGRQ:* H: SMD= -0,03 [-0,58; 0,51] L: SMD= -0,98 [-1,92; -0,04] Gepoold effect (n= 72; random[§]; I^2= 74%): SMD= -0,43 [-1,34; 0,49] ten gunste van NMES; <u>Fysiek functioneren</u> Niet gerapporteerd. <u>Kortademigheid</u> *Na afloop van inspanningstest (Borg):* I: MD= -0,93 [-1,43; -0,43]
	G: Latimer 2013 *Setting*: Thuis (combination of supervised and unsupervised home training)	G: 16 patiënten met stabiel COPD ♂= 8; lftd, gem (sd)= 64 (9) jr.; FEV1, % voorspelde waarde, gem (sd)= 50 (22) % *I:* 16 benen *C:* 16 benen	G: <u>NMES</u> Unilateraal; Quadriceps; *Golfvorm:* bifasisch puls *Frequentie*: 50 Hz *Pulsduur:* 300 µs *Intensiteit*: maximale tolerantie *Serietijd (op/af)*= 15/5 sec.	G: <u>Geen stimulatie</u>	G: Eind v/d follow-up: onbekend Incomplete uitkomsten: onbekend	

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up	Uitkomstmaten (studies) & Effectgrootte (95% BI)
			Sessieduur: 30 min. *Aantal sessies*: 30 sessies (5x/week [3 met en 2 sessies zonder supervisie], gedurende 6 wkn)			L: MD= -2,20 [-3,60; -0,80] N: MD= 0,40 [-1,56; 2,36] Gepoold effect (n= 55; random[§], I^2= 59%): MD= 1,03 [2,13; 0,06] ten gunste van NMES. <u>Inspanningsvermogen</u> *6MWT* H: SMD= 0,80 [0,23; 1,37] L: SMD= 0,87 [-0,06; 1,80] Gepoold effect (n=72; random[§], I^2=0%): SMD= 0,82 [95% BI: -0,33; 1,30] ten gunste van NMES, NS; *ISWT* D: Significant effect ten gunste van NMES, geen data beschikbaar *Endurance time (constant power bike test [I, L] oF ESWT [N])* I: SMD= 2,15 [-0,79; 3,52] L: SMD= 0,82 [-0,11; 1,74] N: SMD= 2,17 [1,01; 3,34] Gepoold effect (n= 55; random[§], I^2= 62%):
	H: Maddocks 2016 *Setting*: Thuis	H: 15 patiënten met stabiel COPD (n=52); I: n= 25; ♂= 11; lftd, gem. (sd)= 70 (11) jr; FEV1, % voorspelde waarde, gem (sd)= 31 (11) % C: n= 27; ♂= 10; lftd, gem. (sd)= 69 (9) jr; FEV1, % voorspelde waarde, gem. (sd) = 31 (13)%	H: <u>NMES</u> Bilateraal; Quadriceps; *Golfvorm:* - *Frequentie*: 50 Hz *Pulsduur:* 350 µs *Intensiteit* ≈ 15-25% MVC *Serietijd (op:af)*= week 1: 2/15 sec; week 2: 5/20 sec; week 3-6: 10/15 sec *Sessieduur*: 30 min/dag; *Aantal sessies:* 42 sessies (7 dgn/week; 6 wkn lang)	H: <u>Shamtherapie</u> Identieke opstelling, de 0-20 mA stroom geeft een voelbare stimulus maar is onvoldoende om een contractie op te wekken.	H: Eind v/d follow-up: onbekend Incomplete uitkomsten: onbekend	
	I: Neder 2002 *Setting*: eerste week poliklinisch, daarna thuis	I: 15 patiënten met stabiel COPD (♂=9) *I:* n= 9; lftd, gem. (sd)= 67 (8) jr; FEV1, % voorspeld, gem. (sd)= 38 (10)% *C*: n= 6; lftd, gem. (sd)= 65 (5) jr; FEV1, % voorspeld, gem.(sd) = 40 (13)%	I: <u>NMES</u> Bilateraal; Quadriceps *Golfvorm:* bifasisch symmetrisch, square puls *Frequentie:* 50 Hz *Pulsduur:* 300-400 µs *Intensiteit*= max. tolerantie *Serietijd (op/af)*= week 1: 2/18 sec; week 2: 5/25 sec; week 3-6: 10/30sec *Sessieduur:* 15 (week 1 per been) tot 30 min. *Aantal sessies:* 30 sessies (5 dgn/week gedurende 6 wkn; Supervisie in week 1)	I: <u>Geen stimulatie</u>	I: Eind v/d follow-up: onbekend Incomplete uitkomsten, N (%): onbekend	
	L: Vieira 2014 *Setting*: (waarschijnlijk) thuis	L: 24 patiënten met stabiel COPD (♂= 24) I: n= 12; lftd, gem. (sd)= 56 (11) jr; FEV1, % voorspelde waarde, gem. (sd)= 36 (10)	L: <u>NMES</u> Bilateraal; Quadriceps; *Golfvorm:* bifasisch, symmetrisch, vierkante puls	L: <u>Shamtherapie</u> Identical setup for the electrodes, but no current was provided.	L: Eind v/d follow-up: onbekend Incomplete uitkomsten, N	

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up	Uitkomstmaten (studies) & Effectgrootte (95% BI)
		% C: n= 12; lftd, gem. (sd)= 56 (13) jr.; FEV1, % voorspelde waarde, gem. (sd)= 40 (14) %	*Frequentie:* 50 Hz (,) *Pulsduur:* 300-400 µs *Intensiteit*: maximale tolerantie *Serietijd (op/af)*: week 1: 2/18 sec; week 2: 5/25 sec; week 3-8: 10/30 sec *Sessieduur*: 60 min./sessie *Aantal sessies*: 80 sessies (2x/dag; 5 dgn/week; 8 wkn lang)	Both groups received respiratory PT (i.e. airway clearance) and stretching exercises for the upper limbs, lower limbs and back.	(%): I= 1/12 (8%); C= 3/12 (25%)	SMD= 1,63 [0,64; 1,75] ten gunste van NMES; <u>Perifere spierkracht</u> D: SMD= 0,35 [-0,58; 1,28] G: SMD= 0,20 [-0,50; 0,89] H: SMD= 0,33 [-0,21; 0,88] I: SMD= 0,77 [-0,31; 1,85] N: SMD= 0,30 [-0,60; 1,20] Gepoold effect (n= 137; random[§]; I^2= 0%): SMD= SMD= 0,34 [0,00; 0,68]. <u>Mortaliteit</u> D: RV= 0,00 [-0,19; 0,19] H: RV= -0,04 [-0,14; 0,06] I: RV= 0,00 [-0,23; 0,23] L: RV= 0,00 [-0,15; 0,15] N: RV= 0,00 [-0,17; 0,17] Gepoold effect (n= 142; random[§]; I^2= 0%): RV= RV= -0,01 [-0,09; 0,06] <u>Ongewenst voorval</u> D: RV= 0,33 [0,009;
	N: Vivodtzev 2012 *Setting*: Thuis	N: COPD stabiel (n= 22) *I*: n= 13; ♂= 8; lftd, gem.(SEM)= 70 (1) jr.; FEV1, % voorspelde waarde, gem (SEM)= 34 (3) % *C*: n= 9; ♂= 5; lftd, gem. (sem)= 68 (3) jr.; FEV1, % voorspelde waarde, gem (sem)= 30 (4) %	N: <u>NMES</u> Bilateraal; Quadriceps (35 min) & kuitspieren (25 min); *Golfvorm:* bifasisch symmetrisch, square puls *Frequentie:* 50 Hz *Pulsduur:* 400 µs *Intensiteit*: maximale tolerantie *Serietijd*: 6 sec (50 Hz) / 10 sec (5 Hz) *Sessieduur*: - *Aantal sessies:* 30 sessies (5 dgn/week gedurende 6 wkn)	N: <u>Shamtherapie</u> Identiek stimulatieprogramma, continue stimulatie met 5 Hz.	N: End-point of follow-up: onbekend Incomplete uitkomsten, N (%): I= 1/13 (8%); C= 1/9 (11%)	

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up	Uitkomstmaten (studies) & Effectgrootte (95% BI)
						0,76] G: RV=0,0 [-0,11; 0,11] H: RV= 0,00 [-0,10; 0,11] I: RV= 0,0 [-0,23; 0,23] N: RV= -0,11 [-0,35; 0,13] Gepoold effect (D/G/H/I/N; n=139; random[§]; I^2=0%): RV= -0,00 [95% BI: -0,07; 0,07]
	Oefentherapie met NMES vergeleken met oefentherapie zonder NMES (add-on)					
	C: Akinlabi 2013 *Setting*: Thuis	C: COPD stabiel *I*: n= 5; ♂= 2; lftd, gem. (sd)= 73 (6) jr; FEV1, % voorspeld, gem. (sd)= 24 (9)% *C*: n= 5; ♂= 3; lftd, gem. (sd)= 77 (10) jr; FEV1, % voorspeld, gem. (sd)= 26 (8)%	C: <u>NMES + laag-intensieve oefentherapie</u> Bilateraal; Hamstrings & quadriceps; *Golfvorm:* - *Frequentie*: 10-50 Hz *Pulsduur*: 200-400 µs *Intensiteit*: 10-120 mA *Serietijd:* - *Sessieduur:* - *Aantal sessies*: 16 sessies (2 dgn/ week gedurende 8 wkn).	C: <u>Oefentherapie</u> Laag-intensieve oefentherapie symptom-limited exercise	C: Eind v/d follow-up: onbekend Incomplete uitkomsten, N (%): I= 0/5 (0%); C= 0/5 (0%)	<u>Kwaliteit van Leven</u> C: SMD= -0,26 [-1,51; 0,99] P: SMD=-0,49 [-1,04; 0,07] E: SMD= -1,72 [-2,92; -0,52] J: SMD= -0,22 [-0,76; 0,33] M: SMD= -0,77 [-1,77; 0,22] Gepoold effect (C/P/E/J/M; n=164; random[§]; I^2= 27%): SMD= -0,55 [-0,96; -0,13] <u>Fysiek functioneren</u> Niet gerapporteerd.
	E: Dang 2011 *Setting*: Poliklinisch	E: participants participated in a comprehensive 'ambulatory' respiratory rehabilitation programme for 12 weeks. I: n= 8; ♂= 3; lftd, gem (sd)= 63 (4) jr; FEV1, % voorspelde waarde, gem (sd)= 36 (7) % C: n= 8; ♂= 5; lftd, gem (sd)= 61 (8) jr; FEV1, % voorspelde waarde, gem (sd)= 40 (6) %	E: <u>NMES + PR</u> Bilateraal; Quadriceps; *Golfvorm:* symmetrisch rechthoek puls *Frequentie:* 45 Hz *Pulsduur:* 350 µs *Intensiteit*: maximale tolerantie *Serietijd (op/af)*: 4 sec (45Hz) / 8 sec (8 Hz) *Sessieduur:* 36 min.	E: <u>PR</u> Usual respiratory rehabilitation (no other details given)	E: Eind v/d follow-up: onbekend Incomplete uitkomsten, N (%): I= ../.. (..%); C: ../.. (..%)	

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up	Uitkomstmaten (studies) & Effectgrootte (95% BI)
			Aantal sessies: 36 sessies (3x/week gedurende 12 weken)			Kortademigheid Na afloop van inspanningstest (Borge): P: SMD= -0,20 [-0,28; -0,12] K: SMD= 0,38 [-0,73; 1,49] M: SMD= -1,50 [-3,22; 0,22] Gepoold effect (P/K/M; n= 95; random[§]; I^2= 38%): SMD= -0,22 [-0,83; 0,40] Inspanningsvermogen C: SMD= 31,00 [-93,72; 155,72] P: SMD= -3,83 [-8,38; 0,72] E: SMD= -19,00 [-141,10; 103,10] F: SMD= 13,80 [-38,18; 65,78] J: SMD= -1,00 [-49,63; 47,63] M: SMD= 33,00 [-4,10; 70,10] Gepoold effect (C/P/E/F/J/M; n= 174; random[§]; I^2= 0%): SMD= -3,12 [-7,59; 1,35]
	F: Kucio 2016 *Setting*: Inpatient rehabilitation	F: Ziekenhuispatiënten met stabiel COPD *I*: n= 15; ♂= 11; lftd, gem (sd)= 68 (6) jr.; FEV1, gem (sd)= 1,66 (0,69) L *C:* n= 15 ♂= 10; lftd, gem (sd)= 61 (8) jr.; FEV1, gem (sd)= 1,78 (0,78) L	F: NMES + PR Bilateraal; Quadriceps & gastrocnemius; *Golfvorm:* symmetrisch rechthoek puls *Frequentie:* 35 Hz *Pulsduur:* 300 µs (0,3 ms) *Intensiteit:* - *Serietijd (op/af)*= 2/4 sec. *Sessieduur:* 36 min. *Aantal sessies:* 18 sessies (6 dg/week gedurende 3 weken)	F: Geen stimulatie + PR PR: 6 gesuperviseerde sessies oefentherapie gedurende 3 wkn. met ademhalingsoefeningen, cardiorespiratoire en krachttraining.	F: Eind v/d follow-up: onbekend Incomplete uitkomsten, N (%): onbekend	
	J: Tardif 2015 *Setting*: Thuis	J: 52 patiënten met stabiel COPD (♂= 45; lftd, gem.(sd)= 59 (9) jr.; FEV1, % voorspelde waarde= 24-59%; I: n=27 C: n=25	J: NMES + PR Bilateraal; Quadriceps; *Golfvorm:* - *Frequentie*: 35 Hz *Pulsduur*: - *Intensiteit*: maximale stimulatie zonder pijn *Serietijd*: - *Sessieduur*: 30 min./dag; *Aantal sessies*: 40 sessies (5 dgn/week gedurende 8 wkn)	J: Geen stimulatie + PR PR: 18-24 sessies gedurende 8 wkn.	J: Eind v/d follow-up: onbekend Incomplete uitkomsten, N (%): onbekend	
	K: Tasdemir 2015 *Setting*: Poliklinisch	K: COPD stabiel I: n= 17 (data: n= 13; ♂=11); lftd, gem.(sd)= 62 (8) jr.; FEV1, % voorspelde waarde, med. (range)= 29 (16-71)% C: n= 17 (data: n= 14;♂= 13); lftd, gem.(sd)= 63 (8) jr; FEV1, % voorspelde waarde, med.(range)= 42 (23-66)%	K: NMES + PR Bilateraal; Quadriceps; *Golfvorm:* symmetrisch, bifasisch constante stroom *Frequentie:* 50Hz *Pulsduur*: 300 µs *Intensiteit:* maximale tolerantie *Serietijd (op/af)*: 10/20 sec *Serieduur*: gedurende 20 min.	K: Shamtherapie + PR Sham: Gelijk protocol, intensiteit (5 Hz) was voldoende voor een zichtbare spiertrekking PR: 2 dgn/week gedurende 10 wkn.	K: Eind v/d follow-up: onbekend Incomplete uitkomsten, N (%): I= 4/17 (24%); C= 3/17 (18%)	

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up	Uitkomstmaten (studies) & Effectgrootte (95% BI)
			Aantal sessies: 20 sessies (2 dgn/wk gedurende 10 wkn)			Perifere spierkracht E: SMD= 0,57 [-0,44; 1,58] J: SMD= -0,10 [-0,85; 0,66] M: SMD= 0,33 [-0,63; 1,29] Gepoold effect (E/J/M; n= 60; random[§]; I^2= 0%): SMD= 0,20 [-0,32; 0,71]. Mortaliteit C: RV= 0,00 [-0,31; 0,31] E: RV= 0,00 [-0,21; 0,21] F: RV= 0,00 [-0,12; 0,12] J: RV= 0,00 [-0,07; 0,07] K: RV= 0,00 [-0,11; 0,11] Gepoold effect (C/E/F/J/K; n= 142; random[§]; I^2= 0%): RV= 0,00 [-0,06; 0,06] Ongewenste voorvallen C: RV= 0,00 [-0,31; 0,31] E: RV= 0,00 [-0,21; 0,21] J: RV= 0,00 [-0,07; 0,07] K: RV= 0,00 [-0,13; 0,13]
	M: Vivodtzev 2006 *Setting*: Inpatient rehabilitation	M: COPD stabiel, maar kort na acute ziekte. "All participants were admitted to a PR for 1 month following hospitalisation." I: n= 9; ♂= 6; lftd, gem. (sd)= 59 (15) jr; FEV1, % voorspelde waarde, gem= 27 (sd 3) C: n= 8; ♂= 5; lftd, gem. (sd)= 68 (12) jr; FEV1, % voorspelde waarde, gem. (sd) = 34 (11)	M: NMES + Revalidatie Bilateraal; Quadriceps; *Golfvorm:* bifasisch symmetrisch, vierkant puls *Frequentie:* 35 Hz *Pulsduur*: 400 µs *Intensiteit*: maximale tolerantie + 5 mA toename/dag *Serietijd (op/af):* 7 sec (35 Hz) / 8 sec (5 Hz) *Sessieduur:* 30 min (5 min. warm-up [continu; 5 Hz, 400 µs\; 25 min. stimulatie); *Aantal sessies*: 16 sessies (4x / week, 4 wkn lang)	M: PR Both groups received active limb exercises. De sterkste patiënten liepen ook op een loopband en kregen 5-10 min armkracht-oefeningen	M: Eind v/d follow-up: onbekend Incomplete uitkomsten, N (%): onbekend	
	P*: Bonnevie 2018 *Setting*: Thuis	P*: COPD stabiel, n= 73 (data van n= 51) *I*: n= 27; ♂= 25; lftd, gem. (sd)= 61,2 (10,2); FEV1, % voorspeld, gem. (IQR)= 34,6 (28,3-38,5) *C*: n= 24; ♂= 19; lftd, gem. (sd)= 57 (8,6); FEV1, % voorspelde waarde, gem. (sd)= 37 (8,3) %	P*: NMES + PR Bilateraal; Quadriceps; *Golfvorm:* bifasisch symmetrische stroom *Frequentie:* 35 Hz *Pulsduur:* 400 µs *Intensiteit*: maximale tolerantie zonder pijn *Serietijd (op/af):* 0,5 sec (35Hz) / 1,5 sec (4Hz) *Sessieduur*: 30 min. (2 min. warm-up [continu, 6Hz]; 25 min. stimulatie; 3 min. herstelperiode [3Hz]); *Aantal sessies*: 40 sessies (5x/week gedurende 8 wkn)	P*: PR Poliklinisch or home-based PR program including respiratory PT and strength and endurance training on a cycloergometer; 3-5 keer per week gedurende 8wkn	P*: Eind v/d follow-up: onbekend Incomplete uitkomsten: I= 9/36 (25%); C= 13/37 (35%)	

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up	Uitkomstmaten (studies) & Effectgrootte (95% BI)
						Gepoold effect (C/E/J/K; n= 105; random[§]; I^2= 0%): RV= 0,00 [-0,06; 0,06].
	Mobilisatie met en zonder NMES op IC- en HC-afdeling van het ziekenhuis					
	A: Abdellaoui 2011 *Setting*: Ziekenhuis - Intensive care	A: IC-opname i.v.m. longaanval (n=17). Patiënten ontvangen zuurstof (n=5); niet-invasieve ventilatie (n=5), invasieve mechanische ventilatie (n=5). *I*: n= 10; ♂= 7; lftd, med.(IQR)= 59 (57-69) jr; FEV1, % voorspelde waarde, med.(IQR)= 25 (17-41)% *C*: n= 7; ♂= 6; lftd, med. (IQR)= 67 (59-72) jr; FEV1, % voorspelde waarde, med. (IQR)= 15 (10-27)%	A: <u>NMES + daily active passive mobilisation</u> Bilateraal; Hamstrings & quadriceps; *Golfvorm:* bifasisch symmetrisch, constant stroom *Frequentie:* 35 Hz *Pulsduur*: 400 µs *Intensiteit*: maximaal getolereerd *Serietijd*: 6 s contractie / 12 s pauze *Sessieduur*: 60 min. *Aantal sessies*: 30 sessies (5 dgn/week; gedurende 6 wkn)	A: <u>Shamtherapie + daily active passive mobilisation</u> Stimulatie zonder zichtbare of tastbare contracties + Daily active-passive mobilisation	A: Eind v/d follow-up: onbekend Incomplete uitkomsten, N (%): I= 1/10 (10%); C= 1/7 (14%)	<u>Kwaliteit van Leven</u> Niet gerapporteerd. <u>Fysiek functioneren</u> B: SMD= -7,35 [-11,58; -3,12] O: SMD= -3,58 [-5,56; -1,60] Gepoold effect (B/O; n=44; random[§]; I^2= 60%): SMD= -4,98 [-8,55; -1,41] <u>Kortademigheid</u> <u>Inspanningsvermogen</u> *6MWT:* A: SMD= 92,00 [21,36; 162,64] <u>Perifere spierkracht</u> O: SMD= 1,20 [0,32; 2,08] <u>Mortaliteit</u> A: RV= 0,00 [-0,21; 0,21] O: RV= 0,00 [-0,15;
	B: Akar 2017 *Setting*: Ziekenhuis - Intensive care	B: IC-opname i.v.m. respiratory failure. Patiënten worden beademd (invasieve mechanische ventilatie). *I*: N= 10; ♂= 4; lftd, gem. (sd)= 70(12) jr *C*: N= 10; ♂= 5; lftd, gem. (sd)= 68 (18) jr	B: <u>NMES + oefentherapie</u> Bilateraal; Deltoïdeus & quadriceps; *Golfvorm:* bifasisch symmetrisch square waves *Frequentie:* 50Hz *Pulsduur:* - *Intensiteit*: 20-25 mA (maximale tolerantie); *Serietijd:* 6 sec contractieduur (1,5 sec toename en 0,75 s afname) *Sessieduur:* - *Aantal sessies:* 20 sessies (5 dgn/week).	B: <u>Oefentherapie</u> Both groups received active exercise (active joint ROM exercise for upper and lower limbs). Participants who could not manage active exercise received active-assisted or passive ROM exercise	B: Eind v/d follow-up: onbekend Incomplete uitkomsten, N (%): onbekend	
	O: Zanotti 2003	O: COPD stabiel, maar kort na acute ziekte. Patiënten worden beademd (invasieve	O: <u>NMES + Revalidatie</u> Bilateraal; Quadriceps & vastus gluteï;	O: <u>PR</u> Both groups received	O: Eind v/d follow-up:	

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up	Uitkomstmaten (studies) & Effectgrootte (95% BI)
	Setting: Ziekenhuis – High care (Respiratory high dependency unit for inpatient rehabilitation)	mechanische ventilatie). "All participants had chronic hypercapnic respiratory failure due to COPD, needed mechanical ventilation via a tracheostomy and had marked muscle atrophy. They had been referred to a high dependency unit from an ICU and had been confined to bed for ≥30 days. However, they were clinically stable." *I*: n= 12; ♂= 9; lftd, gem. (sd)= 66 (8) jr. *C*: n= 12; ♂= 8; lftd, gem. (sd)= 64 (4) jr.	*Golfvorm:* bipolair, bifasisch, asymmetrisch, rechthoek puls *Frequentie: 35 Hz* *Pulsduur*: 350 µs *Intensiteit*: - *Serietijd*: - *Sessieduur*: 30 min. (5 min [8 Hz, 250 µs], 25 min [35 Hz, 350 µs]) *Aantal sessies*: -	rehabilitation that comprised active limb exercises	onbekend Incomplete uitkomsten, N (%): onbekend	0,15] Gepoold effect (A/O; n= 41; random[§]; I^2= 0%): RV= 0,00 [-0,13; 0,13] <u>Ongewenste voorvallen</u> A: RV= 0,00 [-0,23; 0,23] O: RV= 0,00 [-0,15; 0,15] Gepoold effect (A/O; n= 41; random[§]; I^2= 0%): RV= 0,00 [-0,12; 0,12].

* Toegevoegd aan review n.a.v. update op [datum], [§] random = random effects model;
Afkortingen: NMES= Neuromusculaire elektrostimulatie van de onderste ledematen; PR= longrevalidatie (pulmonary rehabilitation); ROM= range of motion; MVC= maximum voluntary contraction; PT= fysiotherapie (physiotherapy / physical therapy); IC = Intensive Care; ♂ = man; dgn= dagen; mnd= maanden; jr. = jaar; lftd = leeftijd; med. = mediaan; gem.= gemiddeld; sd= standaard deviatie; SEM= standard error of the mean; IQR= interkwartielbereik (interquartile range); 6MWT= Zes Minuten Wandeltest; ISWT= incremental shuttle walk test; LoS: opnameduur (length of stay); SGRQ= Saint George Respiratory Questionnaire; VAS= visual analogue scale; MD= gemiddeld verschil (mean difference); SMD = gestandaardiseerd gemiddeld verschil (standardised mean difference); RV= risicoverschil (risk difference; RD); BI= betrouwbaarheidsinterval; (m)MRC= (modified) Medical Research Council Dyspnoe vragenlijst.

Evidencetabel ademhalingstechnieken

Borge 2015*	
Methods	A double-blind randomized control study, four-week intervention.
Participants	150 patient with moderate or severe stages of COPD, mean age 67,4 years FEV1 57,6% predicted.
Intervention	3 groups which used the same device to measure their breathing pattern, but different instructions were given via earphones/earplugs. The device was used for the first time at the hospital for 15 min and later at home, twice a day for four weeks. Guided deep breathing group (GDBG): used the device and received instructions about how to breathe slowly based on their RR, which was measured by a sensor belt that was placed around the waist. The device played soft, non-rhythmic music in the background, and a voice instructed the participants to breathe out while the musical note lasted during expiration, whereas a new musical note followed during inspiration Music listening group (MLG) listened to the same music being played in the background as the GDBG group members, but they were not given any instructions to breathe slowly. Sham group sitting still (SSG)only received an introductory instruction to sit down and listen to the same music for 1–2 min, but without any instructions about breathing or music during the at the rest of the session.
Outcomes	A questionnaire booklet covering self-reported outcomes related to sociodemographic variables, breathlessness, and QOL was sent by postal mail at baseline (T1), in the follow up after four weeks (T2) and four months after baseline (T3). Primary outcomes: Relief of symptoms using the St George's Respiratory Questionnaire (SGRQ) and reported changes in breathlessness using the Global Rating of Change scale (GRC). The secondary outcomes were scores for diseases related to QOL (i.e., activity and impact according to the SGRQ) and the breathing pattern (i.e., TIN, TEX, and RR).
Collins 2008	
Methods	Randomised controlled trial, 3 groups, all had 36 sessions of training over a mean of 14.8 weeks
Participants	91 participants recruited from outpatient clinic; aged 40 years or more, post-bronchodilator FEV1 <70% predicted, FEV1/FEV <70%, PaO_2 ≥56 mmHg at rest; mean SpO2 ≥85%at peak exercise (with or without supplemental oxygen), stable clinical condition without an exacerbation during the preceding 6 weeks, and MMSE score > 23
Intervention	All groups trained in the laboratory 3 times weekly Intervention 1: VF training alone 30 to 35 minutes of VF training at each session. The VF system consisted of a heated pneumotachometer interfaced to a computer. Goals of respiratory rate and the exhalation to inhalation ratio during feedback training were based on the breathing pattern recorded during baseline exercise stress test. Expiratory time goals were shown as targets on the computer screen. Progression of training by decrease in respiratory rate and increase in expiratory time. Included a 10-minute period of low-intensity exercise so that participants could experience VF during exercise Intervention 2: VF training during exercise training as described below Control: exercise training alone - interval training commencing at 60% of VO2peak, increasing to 85% of VO2peak; training duration commenced at 25 minutes total and increased to 45 minutes; 18 sessions of leg cycle exercise followed by 18 sessions of treadmill exercise; light upper body strength training at all sessions Breathing exercises for chronic obstructive pulmonary disease (Review) 36

Outcomes	Treadmill constant work rate test (primary outcome); incremental treadmill test; Chronic Respiratory Disease Questionnaire; dyspnoea at isotime on constant work rate test; minute ventilation, oxygen consumption and oxyhaemoglobin saturation at isotime; respiratory rate, inspiratory time and expiratory time at isotime. Measured following 36 sessions of intervention at approximately 12 weeks.
Nield 2007	
Methods	Randomised controlled trial, 12-week intervention period
Participants	40 participants (38male), FEV1/FVC< 70%, FEV1 < 80%predictedwith no reversibility following bronchodilator, dyspnoea during walking, modified Borg score of 3 or more on screening 6MWT, no exacerbation in last 4 weeks
Intervention	Intervention 1: PLB with a pulse oximeter provided for home use; participants were instructed to practice for 10 minutes per day in the first week, 15 minutes per day in the second week, 20 minutes per day in the third week and 25 minutes per day by the fourth week. Four weekly visits to the research laboratory for supervision. Prolonged expiration reinforced during monitoring sessions by observation of breathing pattern on a monitor. Practiced PLB during walking at each monitoring session, with cadence paced to breathing pattern. Daily diary was completed and reviewed at monitoring sessions. Intervention 2: expiratory muscle training with resistive load of 4 to 20 cm H2O during exhalation. Expiratory load initially set at 10% of baseline PEmax. Duration and frequency of practice sessions and visits as for intervention 1 Control: participants received the American Lung Association health education pamphlet 'About Lungs and Lung Disease'; they visited the laboratory on the same number of occasions as the intervention subjects and received the same amount of attention during their visits.
Outcomes	Measured at 4 and 12 weeks: University of San Diego Shortness of Breath Questionnaire Modified Borg at end 6MWT Human Activity Profile Physical function dimension of the Short Form 36-item Health Survey, Version 2.0 Breathing pattern - respiratory rate, inspiratory time, expiratory time, inspiratory to expiratory ratio Respiratory muscle strength
Sun 2003	
Methods	Randomised controlled trial, 6-month intervention period
Participants	99 participants (57 males) with COPD class II or III (FEV1 < 80% predicted); mean age 69 years; condition stable for 1 month
Intervention	Intervention: PLB: 3 times per day (morning, midday and evening). 10 minute per session. Breathing frequency - 7 to 10 breaths per minute Respiratory muscle gymnastics: 5 parts - various forms of breathing with trunk rotation or bending, as well as breathing with leg exercise. Twice a day (morning and evening), 10 minute each session Control - no details provided
Outcomes	Quality of Life questionnaire for COPD; resting FEV1, FEV1/FVC in the morning; blood gases measured in supine position: PaO2, PaCO2. Measured at baseline and 6 months.
Valenza 2014*	
Methods	Randomised clinical trial, 10 day controlled breathing program.
Participants	46 patients, 67-86 years old, hospitalized with acute COPD exacerbation.
Intervention	Subjects were randomly and equally divided into a control group and a controlled breathing intervention group. Subjects in the standard care group received the standard medical

	treatment. The controlled breathing program was delivered by a trained physiotherapist twice a day for 30 min during hospitalization. The controlled breathing program included relaxation exercises, pursed-lips breathing, and active expiration.
Outcomes	Outcome measures: Hospital anxiety and depression scale, St George's Respiratory Questionnaire, Modified Medical Research Council Dyspnea Scale, European Quality of Life Questionnaire, Hand-Grip Strength, Respiratory Muscle Strength.
Van Gestel 2011	
Methods	Randomised controlled trial, 4-week intervention period
Participants	40 participants with COPD, mean age 66 years, mean FEV1 46% predicted
Intervention	Intervention: 4-week pulmonary rehabilitation programme (as per control group) with addition of controlled breathing using respiratory biofeedback. 10 sessions of RBF, 30 minutes each session. Practiced for 10 minutes at rest, and during the 20 minutes of endurance training on a cycle ergometer. Instructions for daily home practice. Patients trained to modify 4 respiratory characteristics: rapid shallow breathing, breath to breath irregularity in rate and depth, predominant thoracic breathing. Patients encouraged to deep breathe with outwards motion of abdominal wall, while reducing upper rib cage motion; prolonged expiration using PLB. Breathing pattern was monitored using respiration sensors at umbilical and abdominal level; RBF training provides simple acoustic tones and visual graphic signals to inform patient of their breathing pattern Control: conventional 4-week pulmonary rehabilitation programme - 3 times a week for 3 to 4 weeks, 10 sessions in total, 1.5-hour sessions, dynamic strength training 3 x 10 repetitions starting at 70% 1RM, cycle ergometer 20 minutes starting at 30% peak work load, stepping exs and arm cranking.
Outcomes	FEV1, 6MWT, CRQ, cardiac autonomic function. Measured at baseline and 4 weeks
Wu 2006	
Methods	Randomised controlled trial, 3-month intervention period.
Participants	30 inpatients with mean age 70 years, condition stabilised after an exacerbation.
Intervention	Intervention: PLB training in hospital for 2 weeks, 10 minutes each session, 3 times per day. Continue exercises at home for 3 months Control: routine medical treatment.
Outcomes	FEV1, FVC, FEV1/FVC, Quality of Life questionnaire for COPD, Activities of Daily Living assessment. Measured at baseline and 3 months.
Xi 2015*	
Methods	Randomised controlled trial, 12 months intervention.
Participants	60 COPD patients were randomized and divided into two groups, an intervention (n =30) and control (n=30) group. Mean FEV1 was 41.9% in the intervention group vs 43.33% in the control group.
Intervention	The control group in their once monthly visit to the outpatient clinic received routine health education from a physiotherapist about the development and progression of COPD. The intervention group received the Respiratory training (RT) program. The RT method was based on studies by Collins [16], Tiep [17] and Mendes de Oliveira [18]. Briefly, the method was performed by a combination of pursed-lip breathing, abdominal breathing (diaphragmatic breathing) and upper and lower limb exercises. A minimum of 1 h of the exercise was

	performed on their monthly visit at the outpatient clinic and participants were advised to continue their exercises at home for a minimum of 5 days per week.
Outcomes	Participants' height and weight were measured. The modified Medical Research Council (MMRC) dyspnea scale [3], COPD assessment test (CAT) and the Saint George's respiratory questionnaire (SGRQ) were applied [19]. The 6-Minute Walk Test (6MWT) was conducted in a 50 metre long corridor. Heart rate, dyspnoea, and oxygen saturation were measured before and after each test. The body mass, airflow obstruction, dyspnoea and exercise capacity index (BODE index) for COPD was calculated accordingly [20]. A COPD assessment test (CAT) was performed by an experienced observer.
Yamaguti 2012	
Methods	Randomised controlled trial with 4-week intervention period
Participants	30 participants with mean FEV1 42% predicted
Intervention	Intervention: diaphragmatic breathing training programme, supervised 3 times a week for 4 weeks
Outcomes	Ratio of rib cage to abdominal movement (primary outcome), diaphragmatic mobility; 6MWT, modified MRC dyspnoea scale; St Georges Respiratory Questionnaire. Measured at baseline and 4 weeks
Zhang 2008	
Methods	Randomised controlled trial with 8-week intervention period
Participants	60 participants (51 male) in GOLD stage III or IV, no acute exacerbation in last 4 weeks
Intervention	Intervention 1: quick inspiration (0.8 to 1 second) and slow expiration (3 to 4 seconds). Reported to be "in relation to respiratory pathophysiology": quick inspiration to total lung capacity, hold, slow expiration - 3 times per day, 15 minutes each session, for 8 weeks Intervention 2: PLB - 3 times per day, 15 minutes each session, for 8 weeks Control: no breathing training
Outcomes	6MWT,MRC Dyspnoea scale, Activity of Daily living, Quality of Life score, MIP, MEP. Measured at baseline and 8 weeks

* Studies toegevoegd aan systematische review Holland 2012 n.a.v. update.

Evidencetabel bevordering mucusklaring bij patiënten met stabiel COPD

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up
Osadnik, 2012	SR en meta-analyse van randomised controlled trials (RCT's) en randomised crossover trials (RXT's) *Literatuursearch Osadnik 2012 tot 2012, update KNGF tot 3 augustus 2018**	Patiënten met stabiel COPD: Patiënten met COPD, emfyseem of chronische bronchitis (>50% van de patiëntpopulatie), geen patiënten met bronchiectasis of asthma, cystic fibrose of patiënten met kunstmatige beademing Patiënten die vier weken of langer vrij zijn van een longaanval die medicijnen benodigd. No exclusions were made on the basis of disease severity, age, gender or smoking history. *13 studies geïncludeerd:*	Technieken die primair bedoeld zijn voor mucusklaring zoals 'actieve ademhalingstechnieken (huffen, ACBT, AD, FET, ELTGOL), positieve uitademingsdruk (PEP) en trillende positieve uitademingsdruk (O-PEP). Het uitzuigen van de luchtwegen, ademhalingsoefeningen voor andere doeleinden dan mucusklaring (zie module C4.1 Ademhalingsoefeningen), interventies tegen hyperinflatie tijdens inspanning, en training van de ademhalingsspieren (zie module C3.3 Adempiertraining) Tevens zijn interventies die slechts zeer beperkt worden toegepast bij stabiel COPD zoals intrapulmonary percussive ventilation (IPV of IPPV), high-frequency chest wall oscillation (HFCWO) en conventionele interventies zoals percussie en vibratie zijn buiten beschouwing gelaten.	Geen interventie/ gebruikelijke zorg, shaminterventie of alleen hoesten	
	PEP				
	C: Christensen & Simonsen 1990 Design: RCT Setting: Longpoli Land: Denemarken	C: 60 patiënten met stabiel ernstig COPD en chronische mucus hypersecretie. Geslacht, ♂= 21/47 (45%); Lftd, gem= 64 jr; FEV_1, mediaan= 0,97L	C: PEP PEP mask (PEEP-ventiel, 10 cm H_2O) Dose: ≥ 15 minutes, 3 times/day	C: Sham PEP mask (PEEP-ventiel, 0 cm H_2O) Dose: ≥ 15 minutes, 3 times/day	C: Eind v/d follow-up: 6 mnd Incomplete uitkomsten, N (%): 47/60 (78)
	D: Christensen 1991b Design: RCT Setting: Ziekenhuis Land: Denemarken	D: 30 patiënten met stabiel chronische bronchitis Lftd, gem (range)= 64 [58 to 73] jr; FEV_1, gem. = 2,1 [1,1-3,3]L	D: PEP, masker 10-20 cm H_2O via masker as control, except PEP of 10 to 20 cm H2O a PEP mask (10-20 cm H2O). Dose: 10 tidal breaths, twice/day for 4 weeks.	D: Sham usual oral bronchodilators + 2 puffs (0.5 mg) terbutaline via spacer connected to a PEP mask (0 cm H2O). Dose: 10 tidal breaths, twice/day for 4 weeks.	D: Eind v/d follow-up: 4 wkn Incomplete uitkomsten, N (%): 28/30 (93)
	E: Christensen 1991a	E: 10 patiënten met stabiel COPD en	E: PEP, masker	E: Sham	E:

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up
	Design: RXT Setting: polikliniek Land: Denemarken	dagelijkse hoest, expectoratie en dyspneu en dagelijks bronchodilators nodig. Geslacht, ♂= 7/10 (70%); Lftd, gem= 54,4 (16,6) jr; FEV_1, gem= 34,7 (15,3) %	10-15 cm H_2O via masker Same as control except 10 to 15 cm H2O Dose: tidal breathing until end of nebuliser (8 to 10minutes), 3 times/day for 2 weeks.	Inhalation of 2 ml 5 mg nebulised terbutaline via PARI-Inhaler-boy connected to a PEPmask (0 cmH2O). Dose: tidal breathing until end of nebuliser (8 to 10minutes), 3 times/day for 2 weeks. Additional terbutaline was allowed when needed	Eind v/d follow-up: 3 x 2 wkn Incomplete uitkomsten, N (%): 0/10 (0%)
	I: Mascardi 2016* Design: RCT Setting: ziekenhuis Land: Italië	I: 80 patiënten met ernstig COPD (FEV_1 <50%; GOLD III en IV) I: n= 40; Geslacht, ♂= 30 (75%) Lftd, gem(sd)= 71 (6) jr FEV_1, gem= 36 (10) % Fysieke capaciteit (6MWT in meters)= 243 [180-280] Ziektelast (CAT), gem [range]= 22,5 [19-27] C: n= 40; Geslacht, ♂= 28 (72%); Lftd, gem(sd)= 71 (6) jr; FEV_1, gem= 33 (11) % Fysieke capaciteit (6MWT in meters)= 260 [220-310] Ziektelast (CAT), gem [range]= 25 [19-29]	I: T-PEP, tijdelijke PEP + farmacotherapie Thuisgebruik van T-PEP, Tweemaal daags 30 minuten gedurende 15 dagen	I: farmacotherapie	X: Eind v/d follow-up: 3 mnd Incomplete uitkomsten, N (%): 16/80 (20%)
	J: Nicolini 2014* Design: RCT Setting: ziekenhuis Land: Italië	J: 30 patiënten met ernstig tot zeer ernstig stabiel COPD I: n= 15; Geslacht, ♂= 9/15 (60%); Lftd, gem(sd)= 73 (6) jr; Ziektelast (CAT), gem (sd)= 27 (6) *C:* n= 15;	J: T-PEP, tijdelijke PEP ~~10-20 cm H_2O via masker~~ The TPEP-device delivered a fixed positive pressure (1 cm H2O) only in the expiratory phase. This increase in low pressure was created through a pulsatile flow approximately 42 Hz in frequency. The TPEP therapy was delivered by a use-specific mouthpiece. Treatment lasted 30 min per session and were given twice daily (morning and late afternoon).	J: Controle Alleen farmacotherapie	J: Eind v/d follow-up: direct na interventie (15 dgn) Incomplete uitkomsten, N

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up
		Geslacht, ♂= 8/15 (53%); Lftd, gem(sd)= 70 (6) jr; Ziektelast (CAT), gem (sd)= 27 (6)	The duration of the treatment was fifteen days and the treatment was administered five days per week.		(%): 0/30 (0%)
	K: Nicolini 2018a*¥ Design: RCT Setting: longpoli Land: Italië	K: 80 patiënten met ernstig tot zeer ernstig COPD (chronische bronchitis dagelijks hoesten meer dan drie maanden in meer dan twee jaar en luchtwegobstructie GOLD 3/4). I: n= 40; Geslacht, ♂= 29/40 (%); Lftd, gem(sd)= 72 (1) jr; Ziektelast (CAT), gem (sd)= 23 (7) Fysieke capaciteit (6MWT in meters)= 261 (61) FEV_1, gem= 35 (12) % C: n= 40; Geslacht, ♂= 30/40 (%); Lftd, gem(sd)= 71 (2) jr; Ziektelast (CAT), gem (sd)= 25 (6) Fysieke capaciteit (6MWT in meters)= 276 (64) FEV_1, gem= 32 (11) %	K: T-PEP, tijdelijke PEP 10-20 cm H_2O via masker Treatment lasted 30 min per session and were given twice daily (morning and late afternoon). The duration of each treatment was 12 days. After the end of the treatment a 26 weeks follow-up began.	K: Geen interventie Alleen farmacotherapie	K: Eind v/d follow-up: 26 weken Incomplete uitkomsten, N (%):
	O-PEP				
	L: Cegla 1997 Design: RCT Setting: Longpoli Land: Duitsland	L: 90 patiënten met COPD met tracheobronchial instability en sputumproductie FEV_1, gem (sd)= 1,74 (0,8)L Geslacht, ♂= 61 (68%) Lftd, gem(sd)= 56,0 (10,4) jr	L: O-PEP (Cornet/Flutter) I_1): 'standard medical therapy' plus Cornet. Dose: 5 minutes, 4 times/day for 7 days. First session (only) supervised I_2): 'standard medical therapy' plus Flutter. Dose: 5 minutes, 4 times/day for 7 days. First session (only) supervised	L: Gerbruikelijke zorg standard medical therapy' (steroids, theophylline, bronchodilators +/- shortterm oxygen)	L: Eind v/d follow-up: 7 dgn Incomplete uitkomsten, N (%): 0/43 (0%)

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up
	M: Cegla 2002 Design: RCT Setting: Longonderzoeksinsituut Land: Duitsland	M: 81 patiënten met stabiel ernstig COPD. Geslacht, ♂= 38/50 (76%) Lftd, gem(sd)= 63,4 (9,2) jr FEV_1, gem (sd)= 41 (12)%	M: O-PEP (Cornet) Drug therapy + Cornet. Dose: used inthe start position for ≥ 5mins, 3 times/day plus whenever they noticed mucus or dyspnoea	M: Gebruikelijke zorg Drug therapy (theophylline, salmeterol, Atrovent, glucocorticosteroids)	M: Eind v/d follow-up: 2 jr Incomplete uitkomsten, N (%): 31/81 (38%)
	N: Weiner 1996 Design: RCT Setting: ? Land: ?	N: 20 patiënten met COPD en bronchiale hypersecretie (>30 ml) Geslacht, ♂= 13/20 (%); Lftd, gem(sd)= 63 (10) jr; FEV_1, gem(sd)= 35 (9)%	N: O-PEP (Flutter) Flutter (from TLC + 1 to 2-sec breath hold to RV) x 10 breaths followed by 30-sec rest x 4 to 8 sets (approx. 10 minutes), daily for 3 months.	N: Sham Same as intervention except steel ball removed.	N: Eind v/d follow-up: 3 mnd Incomplete uitkomsten, N (%):
	O: Wolkove 2002 Design: RXT Setting: ziekenhuis Land: Canada	O: 23 patiënten met ernstig COPD Geslacht, ♂= 10/23 (%); Lftd, gem(sd)= 72 (6) jr; FEV_1, gem(sd)= 34,5 (12,7)%	O: O-PEP (Flutter) 10 minutes Flutter (used in the position which generated the best 'flutter' sensation within the chest) followed by 4 puffs Combivent via MDI and spacer.	O: Sham same as intervention except 10 minutes sham Flutter (steel ball removed)	O: Eind v/d follow-up: 3 dgn Incomplete uitkomsten, N (%):
	P: Wolkove 2004 Design: RXT Setting: Land:	P: 15 patiënten met COPD Geslacht, ♂= 9 (60%); Lftd, gem(sd)= 71 (10) jr; FEV_1, gem(sd)= 29 (9)%	P: O-PEP (Flutter) 10 minutes Flutter (used in the position which generated the best 'flutter' sensation within the chest), 4 times/day prior to usual bronchodilator therapy (administered via spacer) for 1 week.	P: Sham same as intervention (self selected mouth position) except steel ball removed from Flutter (sham Flutter)	P: Eind v/d follow-up: 22 dgn Incomplete uitkomsten, N (%):
	Q: Gastaldi 2015* Design: RXT Setting: polikliniek Land: VK	Q: n=15 Geslacht, ♂= onbekend Lftd, gem(sd)= 67,3 (9) jr; GOLD-stadium: I, n=2; II, n=7; III, n=5; IV,	Q: O-PEP (Flutter) Ademhalingsoefeningen met flutterapparaat. Subjects were seated upright and held the flutter device with no inclination. The breathing exercises were undertaken for 30 min using	Q: Sham The ''flutter-sham'' intervention was used as a control where the flutter device was used without the	Q: Eind v/d follow-up: Incomplete

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up
		n=1 I: n= 7; C: n= 8;	quiet breath in a controlled manner where they inhaled through the nose and then exhaled through their mouth with a slow and prolonged expiration. They were instructed to perform the exercises feeling the vibration in their external chest wall. They did 1 min of rest every 4 min of flutter and the flutters were interrupted any time that the subjects wanted to cough or expectorate sputum.	stainless steel ball.	uitkomsten, N (%):)
	R: Sethi 2014* Design: RCT Setting: Ziekenhuis Land: VS	R: 69 patiënten met COPD en chronische bronchitis. I: n= 33; Geslacht, ♂= 29 (88%); Lftd, gem(sd)= 69 (1) jr; FEV_1, gem (sd)= 51 (3)% C: n= 36; Geslacht, ♂= 32 (89%); Lftd, gem(sd)= 68 (1) jr; FEV_1, gem (sd)= 49 (3)%	R: O-PEP (Lung flute) Twee cycli, tweemaal daags gedurende 26 dgn. Cyclus: Blaas twee keer krachtig in de Lung Flute om het rietje te doen trillen, gevolgd door 5 normale ademhalingen. Herhaal 10 keer, gevolg door 3 hufs.	R: gebruikelijke zorg Gebruikelijke COPD-medicatie gedurende 26 dgn Geen CPT, ademhalingsoefeningen of PR	R: Eind v/d follow-up: direct na interventie Incomplete uitkomsten, N (%): 10/69 (14%)
	S: Nicolini 2018a*¥ Design: RCT Setting: longpoli Land: Italië	S: 80 patiënten met ernstig tot zeer ernstig COPD (chronische bronchitis dagelijks hoesten meer dan drie maanden in meer dan twee jaar en luchtwegobstructie GOLD 3/4). I: n= 40; Geslacht, ♂= 28/40 (%); Lftd, gem(sd)= 71 (2) jr; Ziektelast (CAT), gem (sd)= 25 (6) Fysieke capaciteit (6MWT in meters)= 266 (73) FEV_1, gem= 33 (11) % C: n= 40; Geslacht, ♂= 30/40 (%);	S: O-PEP, oscillerende PEP cm H_2O Treatment lasted 30 min per session and were given twice daily (morning and late afternoon). The duration of each treatment was 12 days. After the end of the treatment a 26 weeks follow-up began.	S: Geen interventie Alleen farmacotherapie	S: Eind v/d follow-up: 26 weken Incomplete uitkomsten, N (%):

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up
		Lftd, gem(sd)= 71 (2) jr; Ziektelast (CAT), gem (sd)= 25 (6) Fysieke capaciteit (6MWT in meters)= 276 (64) FEV_1, gem= 32 (11) %			
	Fridlener 2012 Design: RCT Setting: Ziekenhuis Land: Israel	T: 29 patiënten met COPD (FEV1/FVC < 0.7) Alleen karakteristieken beschreven van patiënten die studie afgemaakt hebben. I: n= 11; Geslacht, ♂= 8/11 (73%); Lftd, gem(sd)= 67,7 (2,6) jr; Ziektelast (CRQ), gem (sd)= 5,1 (0,3) Fysieke capaciteit (6MWT in meters)= 397 (31) FEV_1, gem= 49,6 (3,6) % C: n= 11; Geslacht, ♂= 10/11 (91%); Lftd, gem(sd)= 69,0 (1,9) jr; Ziektelast (CRQ), gem (sd)= 4,6 (0,5) Fysieke capaciteit (6MWT in meters)= 426 (24) FEV_1, gem= 52,6 (4,9) %	T: O-PEP	T: Sham	T: Eind v/d follow-up: Direct na interventie (2 weken) Incomplete uitkomsten, N=7/29, (24%)
	Ademhalingstechnieken (Autogene drainage, ACBT, Huffen, Forced expiration technique (FET), ELTGOL)				
	Geen studies geïncludeerd				

* Toegevoegd aan review n.a.v. update op 3 augustus 2018, § random = random effects model;
¥ De studie Nicolini 2018a bevat drie behandelgroepen. Net als in de review Osadnik 2012 ("Where multiple ACTs were investigated in a single study, we only included data from independent comparisons of each ACT to the control condition. We did not include studies which compared one ACT to another ACT only") zijn de resultaten van Nicolini 2018a opgesplitst en meegenomen in 'losse' vergelijkingen (TPEP vs controle en OPEP vs controle).
Afkortingen:
6MWT= zes-minuten-wandeltest; SGRQ= Saint George Respiratory Questionnaire; VAS= visual analogue scale; CAT= COPD Assessment Test; (m)MRC= (modified) Medical Research Council Dyspneu vragenlijst; ♂ = man; dgn= dagen; mnd= maanden; jr. = jaar; lftd = leeftijd; med. = mediaan; gem.= gemiddeld; sd= standaard deviatie; SEM= standard error of the mean; IQR= interkwartielbereik (interquartile range); MD= gemiddeld verschil (mean difference); SMD = gestandaardiseerd gemiddeld verschil (standardised mean difference); RV= risicoverschil (risk difference; RD); BI= betrouwbaarheidsinterval.

Evidencetabel mucusklaring bij patiënten met een COPD-longaanval

SR	Studiekarakteristieken	Patiëntkarakteristieken	Interventie (I)	Controle (C)	Follow-up
Osadnik, 2012	SR en meta-analyse van randomised controlled trials (RCT's) en randomised crossover trials (RXT's) *Literatuursearch Osadnik 2012 tot 2012, update KNGF tot 3 augustus 2018**	Patiënten met stabiel COPD: Patiënten met COPD, emfyseem of chronische bronchitis (>50% van de patiëntpopulatie), geen patiënten met bronchiectasis of asthma, cystic fibrose of patiënten met kunstmatige beademing. Patiënten die vier weken of langer vrij zijn van een longaanval die medicijnen benodigd. No exclusions were made on the basis of disease severity, age, gender or smoking history. *7 studies geïncludeerd*	Technieken die primair bedoeld zijn voor mucusklaring zoals 'conventional' techniques, breathing exercises, and PEP or mechanical devices. Geen suctioning and breathing strategies for purposes of relaxation (e.g. relaxed controlled breathing) or respiratory muscle strengthening (e.g. inspiratory/ expiratory muscle training).	Geen interventie/ gebruikelijke zorg, shaminterventie of alleen hoesten	
	Ademhalingstechnieken				
	Basri 2014* Setting: 1 ziekenhuis Land: Pakistan	N=60, Hospitalized COPD patients with acute exacerbation and pronounced symptoms of sputum retention with coughing. Lftd= gem. 54 jr.	Medical treatment + ACBT ACBT in 3 stappen: 1. Breathing control exercise: this step consisted breathe in through the nose and breathe out through pursed lips, while the abdomen was supposed to move up with inspiration and move down with expiration. The step repeated for 8-10 times. 2. Thoracic expansion exercises: this step consisted of full inspiration with holding air inside lungs for 1-3 seconds and then full end with pursed lips. It was performed 3-4 times on atients. 3. Forced expiration technique included 1-2 huffs followed by force full cough for 1 or 2 times. Step 1 was considered as a relaxation technique and used at any time for correction breathlessness. Sessieduur: 30-40 min. Behandelduur: 2 wkn.	Medical treatment (bronchodilators, anti-inflammatory drugs, smoking cessation and other life style and diet modification.)	FU: 2 wkn.

	Kodric 2009 Setting: 1 ziekenhuis Land: Italië	N=59, ptnt with an acute exacerbation of COPD (GOLD) Lftd= gem. 70,2 jr. FEV1 = gem. 54,0% van voorspelde waarde	Standaard medical therapy + ELTGOL (slow expiration with glottis open in the lateral position) Sessieduur: 30-40 min. tweemaal daags Behandelduur: 7 dgn	Standaard medical therapy (steroids, bronchodilators, antibiotics according to GOLD guidelines)	FU: 6 mnd.
	Inal-Ince 2004 Setting: 1 IC Land: Turkije	N= 35, ptnt with acute hypercapnic respiratory failure requiring ICU and NIV. Lftd= gem. 66,5 jr.	usual ICU care + NIV + ACBT (2 cycles of 4 to 6 RCBs, 3 to 4 thoracic expansion exercises +/- percussion and vibration with FET, 4 to 6 RCBs, 2 to 3 huffs) in upright positions, supervised. Sessieduur: 15-30 min. eenmaal daags Behandelduur: tot ontslag van IC	usual ICU care + NIV (≤ continuous first 24/24, then progressive wean according to study protocol)	FU: tot ontslag van IC
	Manuele technieken				
	Cross 2012* Setting: 4 ziekenhuizen Land: VK	N=526 patients hospitalised with acute COPD exacerbation Lftd, gem= 69 jr;	D: Manuele technieken (percussion, vibration & cough) + advies over mucusklaring 3.1 Auscultate patient 3.2 Select 2 most appropriate positions according to clinical findings. Turn patient to position 1. 3.3 Encourage patient to breathe deeply during treatment 3.4 Percuss* thorax with cupped hand(s) directly over the lung segment(s) being drained. 3.5 Vibrate* chest over percussed area using two hands 3.6 Encourage cough* (spontaneous, directed, FET, manually assisted as deemed necessary) 3.7 Turn patient to position 2 3.8 Repeat 3.4 to 3.6 3.9 Modify treatment within above parameters depending on patient's condition/tolerance 3.10 Select further position(s) if deemed necessary 3.11 After last position, return patient to original/suitable position 3.12 Record main treatment parameters (i.e. positions & total time taken to deliver MCT) 3.13 Record major deviations from treatment protocol with brief explanation 3.14 Monitor and record oxygen saturation until return to baseline	C: advies over mucusklaring	FU: 6 mnd na randomisatie

	PEP				
	Bellone 2002 Setting: 1 respiratoire IC Land: Italië	N=30, ptnt with an acute exacerbation of COPD (ATS criteria) with hypersecretion and acute hypercapnic respiratory failure requiring NIV. Lftd= gem. 64,5 jr. FEV1 = gem. % van voorspelde waarde	Standardised medical care + PEP PEP therapy comprised 5 to 7 cycles of 2 minutes tidal breathing through mask followed by assisted coughing and 2 minutes undisturbed breathing. druk: 10-15 cm H20 sessieduur: 30-40 minuten, driemaal daags behandelduur: 3 dagen	standardised medical care (bronchodilators, steroids, antibiotics, oxygen, Bi- PAP) + assisted coughing (tracheal stimulation)	FU: Tot ontslag van respiratoire IC
	Osadnik 2014* Setting: 2 ziekenhuizen Land: Australië	N= 92 patients hospitalised due to an AECOPD and with evidenceof sputum expectoration or a history of chronic sputum production (‘regularly expectorated sputum on most days’) Lftd = gem. 68 jr. FEV1 = gem. 41% van voorspelde waarde	Usual care + PEP PEP therapy via a mask in an upright position with elbows resting on a table. Participants were instructed to breathe at tidal volume with a slightly active expiration for 8–10 breaths to achieve a pressure of 10–20 cm H2O, monitored initially via a manometer. This was followed by one huff from a low lung volume (small inspiration, prolonged expiration), one huff from a mid-lung volume (moderate inspiration, moderate expiration) and two strong coughs. druk: 10–20 cm H2O Supervisie: eenmaal, daarna zelfstandig mbv schriftelijke instructiekaart. Sessieduur: eenmaal daags, 5 herhalingen gedurende ca. 20 min. Behandelduur: until hospital discharge or 24 h without sputum expectoration	Usual care UC: medical therapy (bronchodilators, corticosteroids, antibiotics, supplemental oxygen), non-invasive ventilation (NIV) if indicated, and allied health assessment and intervention, as required. Physiotherapists delivered a standardised physical exercise training regime that commenced as early as possible with the aim of achieving 30 min/day of walking or equivalent lower limb exercise. Participants did not perform any ACTs except coughing, as needed.	FU: 6 mnd.
	O-PEP				
	Geen studies	-	-	-	-

* Toegevoegd aan review n.a.v. update op 3 augustus 2018. Afkortingen: dgn= dagen; mnd= maanden; jr. = jaar; lftd = leeftijd; med. = mediaan; gem.= gemiddeld; sd= standaard deviatie; SEM= standard error of the mean; IQR= interkwartielbereik (interquartile range); MD= gemiddeld verschil (mean difference); SMD = gestandaardiseerd gemiddeld verschil (standardised mean difference); RV= risicoverschil (risk difference; RD); BI= betrouwbaarheidsinterval.