Evidence Profile #1

Comparison: **Oral corticosteroids vs. no corticosteroids for ambulatory COPD exacerbations**
Bibliography: **16)** Aaron SD, Vandemheen KL, Hebert P, et al. Outpatient oral prednisone after emergency treatment of chronic obstructive pulmonary disease. New Engl J Med 2003; 348:2618-2625; **17)** Thompson W, Nielson C, Carvalho P, et al. Controlled Trial of Oral Prednisone in Outpatients with Acute COPD Exacerbation. Am J Respir Crit Care Med 1996; 154:407-412; **18)** Bathoorn E, Liesker JJ, Postma DS, et al. Anti-inflammatory effects of combined budesonide/formoterol in COPD exacerbations. COPD J Chronic Obstructive Pulm Dis 2008; 5:282-290.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral corticosteroids	Placebo	Relative (95% CI)	Absolute		
Treatment failure (an unscheduled visit to the physician, a return to the ER because of worsening of dyspnea, hospitalisation, or dyspnea requiring open label CS) (%)												
3	randomised trials	not serious[1]	serious[2]	serious[3]	serious[4]	none	26/98 (26.5%)	42/99 (42.4%)	**RR 0.69** (0.22 to 2.19)	132 fewer per 1000 (from 331 fewer to 505 more)	⊕OOO VERY LOW	CRITICAL
Hospital admission (%)												
3	randomised trials	not serious[1]	not serious	serious[3]	serious[4]	none	8/101 (7.9%)	17/100 (17%)	**RR 0.49** (0.23 to 1.06)	87 fewer per 1000 (from 131 fewer to 10 more)	⊕⊕OO LOW	CRITICAL
Mortality (%)												
2	randomised trials	not serious	not serious	serious[5]	serious[4]	none	1/87 (1.1%)	1/87 (1.1%)	**RR 0.99** (0.06 to 15.48)	0 fewer per 1000 (from 11 fewer to 166 more)	⊕⊕OO LOW	CRITICAL
Time to next exacerbation (days)												
NR[5]	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Change in quality of life (CRQ) (Better indicated by higher values)												

1	randomised trials	not serious	not serious	serious[6]	serious[4]	none	74	64	-	**MD 0.38 higher** (0.09 lower to 0.85 higher)	⊕⊕OO LOW	IMPORTANT
Serious adverse events (%)												
2	randomised trials	not serious	not serious	serious[5]	serious[4]	none	2/89 (2.2%)	1/88 (1.1%)	**RR 1.97** (0.18 to 21.29)	11 more per 1000 (from 9 fewer to 231 more)	⊕⊕OO LOW	IMPORTANT

Abbreviations: CI= confidence interval; ER= emergency room; CS= corticosteroids; RR= relative risk; COPD= chronic obstructive pulmonary disease; CRQ= chronic respiratory disease questionnaire; FEV1= forced expiratory volume in one second; MD= mean difference; NR= not reported.

[1] In one of the trials (Thompson, et al), the steroid group had more patients taking an inhaled corticosteroid than the placebo group; however, the task force did not deem the imbalance serious enough to warrant downgrading the quality of evidence.

[2] In two trials, the estimated effect favored steroids (Aaron, et al. and Thompson, et al.), whereas in one trial the estimated effect favored placebo (Bathoorn, et al).

[3] One of the trials enrolled patients who presented to the emergency department (Aaron, et al.) and, in another trial, more than half of patients were enrolled in the emergency department (Thompson, et al.), suggesting that many of the patients had a more severe exacerbation than those for whom the question is intended.

[4] The ends of the confidence interval lead to opposite clinical actions.

[5] The larger of the trials enrolled patients who presented to the emergency department (Aaron, et al.), suggesting that many of the patients studied had a more severe exacerbation than those for whom the question is intended.

[6] The trial enrolled patients who presented to the emergency department (Aaron, et al.), suggesting that many of the patients studied had a more severe exacerbation than those for whom the question is intended.

Evidence Profile #2

Comparison: Antibiotics vs. no antibiotics for COPD exacerbations
Bibliography: 27) Anthonisen NR, Manfreda J, Warren CP, Hershfield ES, Harding GK, Nelson NA. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. Anales de Medicina Interna 1987; 106(2):196–204; **31)** Llor C, Moragas A, Hernandez S, Bayona C, Miravitlles M. Efficacy of antibiotic therapy for acute exacerbations of mild to moderate COPD. Am J Respir Crit Care Med 2012;186:716-23.

Quality assessment							No. of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Antibiotics**	**Placebo**	**Relative effect (95% CI)**	**Absolute effect**		
Treatment failure (defined as death or no resolution or deterioration of symptoms after a trial of medication of any duration) (%)												
2	randomised trials	not serious	not serious	not serious	serious[1]	none	60/215 (27.9%)	89/211 (42.2%)	**RR 0.67** (0.51 to 0.87)	139 fewer per 1000 (from 55 fewer to 207 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Adverse Events (%)												
1	randomised trials	not serious	not serious	not serious	serious[1]	none	23/158 (14.61%)	12/152 (7.9%)	**RR 1.84** (0.95 to 3.57)	66 more per 1000 (from 4 fewer to 203 more)	⊕⊕⊕O MODERATE	CRITICAL
Time to next exacerbation (days)												
1	randomised trials	not serious	not serious	not serious	not serious	none	158	152	-	**Diff med = 73 days**[2] Median 233 days (IQR 110-365) with antibiotics vs. 160 days (IQR 66 to 365) with placebo; p=0.015	⊕⊕⊕⊕ HIGH	CRITICAL
Mortality (%)												
NR	-	-	-	-	-	-	-	-	-	-	–	CRITICAL

Length of hospital stay (days)												
NR	-	-	-	-	-	-	-	-	-	-	–	CRITICAL
Hospital admission (%)												
NR	-	-	-	-	-	-	-	-	-	-	–	CRITICAL

Abbreviations: CI= confidence intervals; RR= relative risk; MD= mean difference; MeD= median difference.

[1] Wide confidence intervals; the ends of the confidence interval would lead to different clinical decisions

[2] Patient level data was not reported; therefore, the difference in the medians with 95% CI could not be calculated via a Wilcoxon-Mann-Whitney test.

Evidence Profile #3

Comparison: Intravenous corticosteroids vs. oral corticosteroids for COPD exacerbations
Bibliography: **34)** de Jong YP, Uil SM, Grotjohan HP, Postma DS, Kerstjens HA, and van den Berg JW. Oral or IV prednisolone in the treatment of COPD exacerbations: a randomized, controlled, double-blind study. Chest 2007; 132(6): 1741-1747; **35)** Ceviker Y, Sayiner A, et al. Comparisons of two systemic steroid regimens for the treatment of COPD exacerbations. Pulm Rehab Ther 2014; 27, 179-183.

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**IV CS**	**Oral CS**	**Relative (95% CI)**	**Absolute (95% CI)**		
Treatment failure (follow up at 90 days; defined as death, admission to the ICU, readmission to the ICU because of COPD, or intensification of pharmacological therapy) (%)												
2	randomised trials	serious[1]	not serious	not serious	serious [2]	none	68/127 (53.5%)	60/121 (49.6%)	**RR 1.09** (0.87 to 1.37)	45 more per 1000 (from 64 fewer to 183 more)	⊕⊕◯◯ LOW	CRITICAL
Mortality (%)												
2	randomised trials	serious[1]	not serious	not serious	serious [2]	none	7/127 (5.5%)	2/121 (1.7%)	**RR 2.78** (0.67 to 11.51)	29 more per 1000 (from 5 fewer to 174 more)	⊕⊕◯◯ LOW	CRITICAL
Readmission to hospital (%)												
2	randomised trials	serious[1]	not serious	not serious	serious [2]	none	18/127 (14.2%)	15/121 (12.4%)	**RR 1.13** (0.60 to 2.13)	16 more per 1000 (from 50 fewer to 140 more)	⊕⊕◯◯ LOW	CRITICAL
Length of hospital stay (days)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**IV CS**	**Oral CS**	**Relative (95% CI)**	**Absolute (95% CI)**		
2	randomised trials	serious[1]	not serious	not serious	serious [2]	none	127	121	-	**MD 0.71 days more** (1.35 fewer to 2.78 more)	⊕⊕◯◯ LOW	CRITICAL
Time to next exacerbation (days)												
NR	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Adverse events (%)												
1	randomised trials	serious[1]	not serious	not serious	serious [2]	none	14/20 (70%)	4/20 (20%)	**RR 3.50** (1.39-8.8)	500 more per 1000 (from 192 more to 695 more)	⊕⊕◯◯ LOW	IMPORTANT

Abbreviations: CS= corticosteroids; CI= confidence intervals; RR= relative risk; ICU= intensive care unit; COPD= chronic obstructive pulmonary disease; FEV1= forced expiratory volume in one second; SGRQ= St. George's Respiratory Questionnaire; MD= mean difference; NR= not reported.

[1] One of the trials (Ceviker, et al.) did not blind the patients or clinicians, thereby allowing the possibility of bias due to co-interventions.

[2] Wide confidence intervals; the ends of the confidence interval would lead to different clinical decisions

[3] Higher SGRQ scores normally indicate more physical limitations; however, the authors reported improvement in some domains.

Evidence Profile #4

Comparison: Usual care plus non-invasive mechanical ventilation vs. usual care alone for COPD exacerbations.

Bibliography: **39)** Andeev S, Tretyakov A, Grigoryants R, Kutsenko M, Chuchalin A. Noninvasive positive airway pressure ventilation: role in treating acute respiratory failure caused by chronic obstructive pulmonary disease. Anesteziologita Reanimatologia 1998;3:45-51. **40)** Barbe R, Togores B, Rubi M, Pons S, Maimo A, Agusti A. Noninvasive ventilatory support does not facilitate recovery from acute respiratory failure caused by chronic obstrucive pulmonary disease. Eur Respir J 1996;9:1240-5. **41)** Bott J, Carroll M, Conway J, Keilty S, Ward E, Brown A et al. Randomised controlled trial of nasal ventilation in acute ventilatory failure due to chronic obstructive airways disease. Lancet 1993;341(8860):1555-7. **42)** Brochard L, Mancebo J, Wysocki M, Lofaso F, Conti G, Rauss A et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. New Engl J Med 1995;333(13):817-22. **43)** Celikel T, Sungur M, Ceyhan B, Karakurt S. Comparison of nonivnasive positive pressure ventilation with standard medical therapy in hypercapnic acute respiratory failure. Chest 1998;114:1636-42. **44)** Conti G, Antonelli M, Navalesi P, Rocco M, Bufi M, Spadetta G et al. Non-invasive vs conventional mechanical ventilation in patients with chronic obstructive pulmonary disease after failure of medical treatment in the ward: a randomised trial. Intensive Care Medicine 2002;28(12):1701-7. **45)** del Castillo D, Barrot E, Laserna E, Otero R, Cayuela A, Castillo Gomez J. Noninvasive positive pressure ventilation for acute respiratory failure in chronic obstructive pulmonary disease in a general respiratory ward. Medicina Clinica (Barc) 203;120(17):647-51. **46)** Dikensoy O, Ikidag B, Filiz A, Bayram N. Comparison of noninvasive ventilation and standard medical therapy in acute hypercapnic respiratory failure: a randomised controlled trial at a tertiary health centre in SE Turkey. Int J Clinical Pract 2002;56(2):85-8. **47)** Khilnani GC, Saikia N, Banga A, Sharma SK. Non-invasive ventilation for acute exacerbation of COPD with very high PaCO(2): A randomized controlled trial. Lung India 2010 July;27(3):125-30. **48)** Kramer N, Meyer T, Meharg J, Cece R, Hill N. Randomised prospective trial of noninvasive positive pressure ventilation in acute respiratory failure. Am J Resp Crit Care Med 1995;151(6):1799-806. **49)** Plant P, Owen J, Elliott M. Early use of noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicenter, randomised, controlled trial. Lancet 2000;355(9219):1931-5. **50)** Servillo G, Ughi L, Rossano F, Leone D. Nonionvasive mask pressure support ventilation in COPD patients. Intensive Care Medicine 1994;20:S54. **51)** Thys F, Roeseler J, Reynaert M, Liistro G, Rodenstein D. Noninvasive ventilation for acute respiratory failure: a prospective randomised placebo-controlled trial. Eur Respir J 2002;20(3):545-55. **52)** Zhou R, Chen P, Luo H, Xiang X. Effects of noninvasive positive pressure ventilation on gas exchange and patients' transformation on chronic obstructive pulmonary disease and respiratory failure. Bulletin of Human Medical University 2001;26(3):261-2. **53)** Carrera M, Marin JM, Anton A, Chiner E, Alonso ML, Masa JF, Marrades R, Sala E, Carrizo S, Giner J, et al. A controlled trial of noninvasive ventilation for chronic obstructive pulmonary disease exacerbations. Journal of Critical Care 2009; 24(3):473-14; **54)** Keenan SP, Powers CE, and McCormack DG. Noninvasive positive-pressure ventilation in patients with milder chronic obstructive pulmonary disease exacerbations: a randomized controlled trial. Respiratory Care 2005; 50(5):610-616. **55)** Pastaka C, Kostikas K, Karetsi E, Tsolaki V, Antoniadou I, and Gourgoulianis KI. Non-invasive ventilation in chronic hypercapnic COPD patients with exacerbation and a pH of 7.35 or higher. European Journal of Internal Medicine 2007; 18(7):524-530; **56)** Schmidbauer W, Ahlers O, Spies C, Dreyer A, Mager G, and Kerner T. Early prehospital use of non-invasive ventilation improves acute respiratory failure in acute exacerbation of chronic obstructive pulmonary disease. Emergency Medicine Journal 2011; 28(7):626-627. **57)** Vargas F, Bui HN, Boyer A, Salmi LR, Gbikpi-Benissan G, Guenard H, Gruson D, and Hilbert G. Intrapulmonary percussive ventilation in acute exacerbations of COPD patients with mild respiratory acidosis: a randomized controlled trial. Critical Care 2005; 9(4):R382-R389. **58)** Wang C. Collaborative Research Group of Noninvasive Mechanical Ventilation for Chronic Obstructive Pulmonary Disease. Early use of non-invasive positive pressure ventilation for acute exacerbations of chronic obstructive pulmonary disease: A multicentre randomized controlled trial. Chinese Med J 2005; 118(24):2034-2040; **59)** Dhamija A, Tyagi P, Caroli R, Rahman M, Vijayan VK. Non-invasive ventilation in mild to moderate cases of respiratory failure due to acute exacerbations of chronic obstructive pulmonary disease. Saudi Med J 2005; 26(5):887-890.

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**NIV**	**Usual Care**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mortality (%)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**NIV**	**Usual Care**	**Relative (95% CI)**	**Absolute (95% CI)**		
17	randomised trials	serious[1]	not serious	not serious	not serious	none	41/575 (7.1%)	81/581 (13.9%)	**RR 0.54** (0.38 to 0.76)	50 fewer per 1000 (from 20 fewer to 80 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Intubation rate (%)												
21	randomised trials	serious[2]	not serious	not serious	not serious	none	80/664 (12.0%)	205/670 (30.6%)	**RR 0.43** (0.35 to 0.53)	190 fewer per 1000 (from 120 fewer to 270 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Length of hospital stay (days)												
15	randomised trials	serious[3]	serious[4]	not serious	not serious	none	577	582	-	**MD 2.88 days fewer** (4.59 fewer to 1.17 fewer)[5]	⊕⊕◯◯ LOW	CRITICAL
Length of ICU stay (days)												
3	randomised trials	serious[6]	not serious	not serious	serious[7]	none	35	26	-	**MD 4.99 fewer** (9.99 fewer to 0)	⊕⊕◯◯ LOW	CRITICAL
Complications of treatment (%)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**NIV**	**Usual Care**	**Relative (95% CI)**	**Absolute (95% CI)**		
5	randomised trials	serious[8]	not serious	not serious	not serious	none	22/140 (15.7%)	60/143 (42.0%)	**RR 0.39** (0.26 to 0.59)	256 fewer per 1000 (from 172 fewer to 310 fewer)	⊕⊕⊕⊕ HIGH	IMPORTANT
pH one hour post-intervention												
13	randomised trials	serious[9]	serious[10]	not serious	serious[7]	none	521	522	-	**MD 0.02 higher** (0.01 lower to 0.06 higher)	⊕◯◯◯ VERY LOW	IMPORTANT
Nosocomial pneumonia (%)												
NR	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

Abbreviations: NIV= non-invasive mechanical ventilation; CI= confidence intervals; RR= relative risk; MD= mean difference; ICU= intensive care unit.

[1] 7 out of 17 trials had unclear allocation concealment; none of the 17 trials was blinded.
[2] 9 out of 21 trials had unclear concealment of allocation; only one out of 21 trials was blinded.

[3] 5 out of 15 trials had unclear allocation concealment; only one of the 15 trials was blinded.

[4] There was significant heterogeneity, I^2=82%. In addition, one patient in Keenan et al. was an outlier; however sensitivity analysis excluding the outlier did not significantly change the result or the heterogeneity level.

[5] The values reported for Carrera et al. were assumed to be mean and standard deviation.

[6] 1 out of 3 trials had unclear concealment of allocation; 2 out of 3 studies were no blinded.

[7] Wide confidence intervals; the ends of the confidence interval would lead to different clinical decisions.
[8] 1 out of 5 studies had unclear concealment of allocation; none of the studies were blinded.
[9] 5 out of13 studies had unclear concealment of allocation; none of the studies were blinded.
[10] There was significant heterogeneity, I^2=93%.

Evidence Profile #5

Comparison: Hospital-at-home vs. hospital admission for acute exacerbations of COPD.

Bibliography: **65)** Cotton MM, Bucknall CE, Dagg KD, Johnson MK, MacGregor G, Stewart C, and Stevenson RD. Early discharge for patients with exacerbations of chronic obstructive pulmonary disease: a radnomised controlled trial. Thorax 2000; 55(11):902-906; **66)** Davies L, Wilkinso, M, Bonner S, Calverley PM and Angus RM. "Hospital at home" versus hospital care in patients with exacerbations of chronic obstructive pulmonary disease: a prospective randomised controlled trial. BMJ 2000; 321(7271):1265-1268; **67)** Hernandez C, Casas A, Escarrabill J, Alonso J, Puig-Junoy J, Farrero E, Vilagut G, Collvinent B, Rodriguez-Roisin R, Roca J, et al. Home hospitalisation of exacerbated chronic obstructive pulmonary disease patients. Eur Respir J 2003; 21(1):58-67; **68)** Nicholson C, Bowler S, Jackson C, Schollay D, Tweeddale M, and O'Rourke P. Cost comparison of hospital and home based treatment models for acute chronic obstructive pulomonary disease. Australia Helath Review 2001; 24(4):181-187; **69)** Nissen I and Jensen MS. Nurse supported discharge of patients with exacerbation of chronic obstructive pulmonary disease. Ugeskrift for laeger 2007; 169:2220-2223; **70)** Ojoo JC, Moon T, McGlone S, Martin K, Gardiner ED, Greenstone MA, and Morice AH. Patients' and carers' preferences in two models of care for acute exacerbations of COPD. Thorax 2002; 57(2):167-169; **71)** Ricuada NA, Tibaldi V, Leff B, Scarafiotti C, Marinello R, Zanocchi M, and Molaschi M. Substitutive "hospital at home" versus inpatient care for elderly patients with exacerbations of chronic obstructive pulmonary disease: a prospective, randomised, controlled trial. J Am Geriatrics Soc 2008; 56(493):500. **72)** Skwarska E, Cohen G, Skwarksi KM, Lamb C, Bushell D, Parker S, and MacNee W. Randomised controlled trial of supported discharge in patients with exacerbations of chronic obstructive pulmonary disease. Thorax 2000; 55(11):907-912. **73)** Utens C, Goossens L, Smeenk F, Rutten-van Mölken M, van Vliet M, Braken M, van Eijsden LM, van Schayck OC. Early assisted discharge with generic community nursing for chronic obstructive pulmonary disease exacerbations: results of a randomsied controlled trial. BMJ Open 2012; 2:e001684.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Hospital at home**	**Hospital admission**	**Relative (95% CI)**	**Absolute**		
Hospital readmission (%)												
All trials												
9[1]	randomised trials	not serious	not serious[2]	not serious	serious[3]	none	153/571 (26.8%)	150/438 (34.2%)	**RR 0.78** (0.62 to 0.99)	80 fewer per 1000 (from 0 fewer to 130 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Trials that discharged patients from the emergency department to a hospital-at-home												
5[4]	randomised trials	not serious	serious[5]	not serious	serious[3]	none	93/316 (29.4%)	92/245 (37.6%)	**RR 0.81** (0.54 to 1.20)	71 fewer per 1000 (from 173 fewer to 75 more)	——	——
Trials that discharged patients to a hospital-at-home following a brief hospitalization												

3[6]	randomised trials	not serious	not serious	not serious	serious[3]	none	56/233 (24.0%)	50/171 (29.2%)	**RR 0.82** (0.59 to 1.13)	53 fewer per 1000 (from 120 fewer to 38 more)	——	——
Mortality (%)												
All trials												
8[7]	randomised trials	not serious	not serious	not serious	serious[3]	none	31/558 (5.6%)	36/426 (8.5%)	**RR 0.66** (0.41 to 1.05)	30 fewer per 1000 (from 50 fewer to 5 more)	⊕⊕⊕O MODERATE	CRITICAL
Trials that discharged patients from the emergency department to a hospital-at-home												
4[8]	randomised trials	not serious	not serious	not serious	serious[3]	none	24/303 (7.9%)	26/233 (11.1%)	**RR 0.74** (0.43 to 1.27)	29 fewer per 1000 (from 64 fewer to 30 more)	——	——
Trials that discharged patients to a hospital-at-home following a brief hospitalization												
3[6]	randomised trials	not serious	not serious	not serious	serious[3]	none	6/233 (2.6%)	10/171 (5.8%)	**RR 0.37** (0.14 to 1.00)	37 fewer per 1000 (from 50 fewer to 0 fewer)	——	——
Time to first readmission (days)												
1	randomised trials	not serious	not serious	not serious	serious[3]	none	70	69	-	**MD 8 higher** (3.7 lower to 19.7 higher)	⊕⊕⊕O MODERATE	CRITICAL
Hospital acquired infections (%)												
NR	-	-	-	-	-	-	-	-	-	-	_	IMPORTANT
Quality of Life (SGRQ) (Better indicated by lower values)												

NR[9]	-	-	-	-	-	-	-	-	-	-	–	IMPORTANT

Abbreviations: CI= confidence intervals; RR= relative risk; FEV1= forced expiratory volume in one second; MD= mean difference; SMD= standard mean difference; QoL= quality of life; SGRQ= St. George's Respiratory Questionnaire; NR= not reported.

[1] Davies 2000; Hernandez 2003; Ojoo 2002; Ricauda 2008; Nicholson 2001; Cotton 2000; Skwarska 2000; Nissen 2007; and, Utens 2012.
[2] Some heterogeneity was detected, i^2=30%; however, the panel elected to not downgrade the quality of evidence because it was judged too mild to reduce their confidence in the estimated effects.
[3] Wide confidence intervals; the ends of the confidence interval would lead to different clinical decisions.
[4] Davies 2000; Hernandez 2003; Nicholson 2001; Ojoo 2002; and, Ricauda 2008.
[5] Inconsistency: I^2=56%. P(het)=0.06.
[6] Cotton 2000; Skwarska 2000; and, Utens 2012.
[7] Davies 2000; Hernandez 2003; Ojoo 2002; Ricauda 2008; Cotton 2000; Skwarska 2000; Nissen 2007; and, Utens 2012.
[8] Davies 2000; Hernandez 2003; Ojoo 2002; and, Ricauda 2008.
[9] Not reported in a useful manner. Among the three trials that reported the outcome, one did not provide standard deviations, another only provided SGRQ scores for a subgroup of the participants, and the third measured generic HRQoL using the EuroQoL-5D. The analyses were not considered by the panel.

Evidence Profile #6

Comparison: Early pulmonary rehabilitation vs. usual care (i.e., late pulmonary rehabilitation or no pulmonary rehabilitation) for COPD exacerbations

Bibliography: **77)** Behnke M, Taube C, Kirsten D, Lehnigk B, Jurres RA, and Magussen H. Home-based exercise is capable of preserving hospital-based improvements in severe chronic obstructive pulmonary disease. Respir Med 2000; 94(12):1184-1191. **79)** Eaton T, Young P, Fergusson W, Moodie L, Zeng I, O'Kane F, Good N, Rhodes L, Poole P, and Kolbe J Does early pulmonary rehabilitation reduce acute health-care utilization in COPD patients admitted with an exacerbation? A randomized controlled study. Respirology 2009; 14(2):230-238. **80)** Kirsten DK, Taube C, Lehnigk B, Arres RA, and Magnussen H. Exercise training improves recovery in patients with COPD after an acute exacerbation. Respir Med 1998;92(10):1191-1198. **81)** Man WD, Polkey MI Donaldson N, Gray BM, and Moxham, J. Community pulmonary rehabilitation after hospitalisation for acute exacerbations of chronic obstructive pulmonary disease: randomised controlled study. BMJ 2004; 329:1209. **82)** Murphy N, Bell C, and Costello RW. Extending a home from hospital care programme for COPD exacerbations to include pulmonary rehabilitation. Respiratory Medicine 2005; 99(10):1297-1302. **83)** Nava S. Rehabilitation of patients admitted to a respiratory intensive care unit. Arch Phys Med Rehab 1998; 79(7):849-854. **84)** Seymour JM, Moore L, Jolley CJ, Ward K, Creasey J, Steier JS, Yung B, Man WD, Hart N, Polkey PI, and Moxham J. Outpatient pulmonary rehabilitation following acute exacerbations of COPD. Thorax 2010; 65(5):423-428. **85)** Troosters T, Probst VS, Crul T, Pitta F, Gayan-Ramirez G, Decramer M, and Gosselink R. Resistance training prevents deterioration in quadriceps muscle function during acute exacerbations of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2010; 181(10):1072-1077. **86)** Ghanem M, Elaal EA, Mehany M, and Tolba K. Home-based pulmonary rehabilitation program: Effect on exercise tolerance and quality of life in chronic obstructive pulmonary disease patients. Ann Thorac Med 2010; 5(1):18-25. **87)** Ko FW, Dai DL, Ngai J, Tung A, Ng S, Lai K, Fong R, Lau H, Tam W, and Hui DS. Effect of early pulmonary rehabilitation on health care utilization and health status in patients hospitalized with acute exacerbations of COPD. Respirology 2011; 16(4):617-624. **88)** Deepak TH, Mohapatra PR, Janmeja AK, Sood P, and Gupta M. Outcome of pulmonary rehabilitation in patients after acute exacerbation of COPD. Indian J Chest Dis Allied Sci 2014; 56:7-12. **89)** Tang CY, Blackstock FC, Clarence M, Taylor NF. Early rehabilitation exercise program for inpatients during acute exacerbation of chronic obstructive pulmonary disease: a randomized controlled trial. J Cardiopulm Rehabil Prev 2012; 32(3):163-9. **90**) Greening NJ, Williams JEA, Hussain SF et al. An early rehabilitation intervention to enhance recovery during hospital admission for an exacerbation of chronic respiratory disease: randomised controlled trial 2014;349:g4315.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Early rehabilitation versus control**	**Control**	**Relative (95% CI)**	**Absolute**		
Hospital readmission												
All trials												
7[1]	randomised trials	serious[2]	serious[3]	not serious	serious[4]	none	165/367 (45.0%)	187/368 (50.8%)	**RR 0.65** (0.42-1.00)	178 fewer per 1000 (from 0 fewer to 295 fewer)	⊕⊕⊕O VERY LOW	CRITICAL
Pulmonary rehabilitation initiated during hospitalization												
3[5]	randomised trials	serious[2]	serious[6]	not serious	serious[4]	none	145/274	143/274	**RR 0.88**	63 fewer per 1000 (from 230 fewer to 193 more)	—	—

							(52.9%)	(52.2%)	(0.56-1.37)			
Pulmonary rehabilitation initiated following discharge from the hospital												
4[7]	randomised trials	serious[2]	serious[8]	not serious	serious[4]	none	20/93 (21.5%)	44/94 (46.8%)	**RR 0.37** (0.14 to 0.97)	270 fewer per 1000 (from 120 fewer to 420 fewer)	⨁⨁OO LOW	CRITICAL
Mortality												
All trials												
4[9]	randomised trials	serious[2]	not serious	not serious	serious[4]	none	51/260 (19.6%)	36/256 (14.1%)	**RR 1.44** (0.97 to 2.13)	0 more per 1000 (from 100 fewer to 100 more)	⨁⨁OO LOW	CRITICAL
Pulmonary rehabilitation initiated during hospitalization												
2[10]	randomised trials	serious[2]	not serious	not serious	serious[4]	none	50/210 (23.8%)	32/205 (15.6%)	**RR 1.54** (1.03 to 2.29)	80 more per 1000 (from 0 more to 150 more)	⨁⨁OO LOW	CRITICAL
Pulmonary rehabilitation initiated following discharge from the hospital												
2[11]	randomised trials	serious[2]	not serious	not serious	serious[4]	none	1/50 (2.0%)	4/51 (7.8%)	**RR 0.37** (0.06 to 2.29)	60 fewer per 1000 (from 150 fewer to 30 more)	⨁⨁OO LOW	CRITICAL
Quality of Life- St. George's Respiratory Questionnaire score (Better indicated by lower values)												
All trials												
5[12]	randomised trials	serious[2]	serious[13]	not serious	serious[4]	none	112	113	-	**MD** 11.75 lower (19.76 to 3.75 lower)	⨁⨁⨁O VERY LOW	CRITICAL
Pulmonary rehabilitation initiated during hospitalization												
0	—	—	—	—	—	—	—	—	—	—	—	—

Pulmonary rehabilitation initiated following discharge from the hospital												
5[12]	randomised trials	serious[2]	serious[13]	not serious	serious[4]	none	112	113	-	**MD** 11.75 lower (19.76 to 3.75 lower)	⨁⨁OO LOW	IMPORTANT
6 minute walking test (Better indicated by higher values)												
All trials												
8[14]	randomised trials	serious[2]	serious[15]	not serious	not serious	none	239	183	-	**MD** +88.89 m (+26.67 m to +151.11 m)	⨁⨁OO LOW	IMPORTANT
Pulmonary rehabilitation initiated during hospitalization												
5[16]	randomised trials	serious[2]	serious[15]	not serious	not serious	none	156	111	-	**MD** +107.92 m (+17.57 m to +198.27 m)	⨁⨁OO LOW	IMPORTANT
Pulmonary rehabilitation initiated following discharge from the hospital												
3[17]	randomised trials	serious[2]	serious[18]	not serious	not serious	none	83	72	-	**MD** +57.47 m (+20.04 m to +94.89 m)	⨁⨁OO LOW	IMPORTANT

[1] Behnke 2000; Eaton 2009; Greening 2014; Ko 2011; Man 2004; Murphy 2005; Seymour 2010; and Troosters 2010.
[2] None of the trials was blinded. Many of the trials had unclear concealment of allocation and either unclear or no adherence to intention-to-treat principle.
[3] Inconsistency: I^2=73%, P(het)=0.001.
[4] Wide confidence intervals: the ends of the confidence interval would lead to different clinical decisions.
[5] Behnke 2000; Eaton 2009; Greening 2014; and Troosters 2010.
[6] Inconsistency: I^2=71%, P(het)=0.03.
[7] Ko 2011; Man 2004; Murphy 2005; and Seymour 2010.
[8] Inconsistency: I^2=65%, P(het)=0.03.
[9] Behnke 2000; Greening 2014; Ko 2011; and, Man 2004. The five trials did not include Nava S, et al, which we excluded because it counted patients dying while they were still admitted to ICU. A sensitivity analysis demonstrated that exclusion of the trial had little effect on the results
[10] Behnke 2000 and Greening 2014.
[11] Ko 2011 and Man 2004.
[12] Deepak 2014; Ko 2011; Man 2004; Murphy 2005; and Seymour 2010.
[13] Inconsistency: I^2=70%, P(het)=0.009.
[14] Behnke 2000; Deepak 2014; Eaton 2009; Ghanem 2010; Kirsten 1998; Ko 2011; Nava 1998; and, Troosters 2010.
[15] Inconsistency: I^2=97%, P(het)=0.00001.
[16] Behnke 2000; Eaton 2009; Kirsten 1998; Nava 1998; and, Troosters 2010.
[17] Deepak 2014; Ghanem 2010; and, Ko 2011.
[15] Inconsistency: I^2=70%, P(het)=0.04.