

Do self-management interventions in COPD patients work and which patients benefit most? An individual patient data meta-analysis

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Supplementary material

Supplementary Table 1: Sensitivity analysis of pooling published effects with main effects of included studies of self-management interventions in patients with COPD.

Outcome	N studies	n patients	Effect measure	Treatment effect	95% CI
<i>Health-related quality of life</i>					
at 6 months additional studies: Khdour 2009 ²¹ , Wakabayashi 2011 ²⁴ , Watson 1997 ²⁵ , Wood-baker 2006 ²⁶	13	2346	SMD	0.08	(-0.01-0.17)
at 12 months additional studies: Fan 2012 ⁹ , Khdour 2009 ²¹ , Wakabayashi 2011 ²⁴ , Wood-baker 2006 ²⁶	14	3503	SMD	0.08	(0.01-0.15)
<i>Respiratory-related hospitalization</i>					
Time-to-first-event additional study: Fan 2012 ⁹	7	2298	HR	0.83	(0.70-0.97)
within 6 months Pooled analysis with published effects not possible due to reporting.					
within 12 months additional studies: Fan 2012 ⁹ , Khdour 2009 ²¹ , Rea 2004 ²³ , Wood-baker 2006 ²⁶	13	3299	RR	0.78	(0.67-0.92)
<i>All-cause hospitalization</i>					
Time-to-first-event additional study: Fan 2012 ⁹	5	1985	HR	0.83	(0.72-0.95)
within 6 months Pooled analysis with published effects not possible due to reporting.					
within 12 months additional studies: Fan 2012 ⁹ , Khdour 2009 ²¹ , Rea 2004 ²³ , Wakabayashi 2011 ²⁴	9	2653	RR	0.84	(0.67-1.05)
<i>Mortality</i>					
Time-to-event additional study: Fan 2012 ⁹	8	2546	HR	1.19	(0.91-1.56)
within 6 months additional study: Khdour 2009 ²¹	10	2663	RR	1.01	(0.75-1.35)
within 12 months additional studies: Fan 2012 ⁹ , Khdour 2009 ²¹ , Rea 2004 ²³ , Wood-baker 2006 ²⁶	11	3055	RR	1.30	(0.88-1.90)

Abbreviations: CI, confidence interval; HR, hazard ratio; RR, risk ratio; SMD, standardized mean difference.

Supplementary Table 2: Effects of self-management interventions on additional outcomes in patients with COPD.

Outcome	N studies	n patients	Effect size	Treatment effect	95% CI
<i>Generic quality of life</i>					
PCS <i>at 6 months</i>	3	600	MD	0.92	(-1.89-3.73)
PCS <i>at 12 months</i>	2	383	MD	-1.05	(-3.45-1.35)
MCS <i>at 6 months</i>	3	600	MD	0.19	(-2.38-2.76)
MCS <i>at 12 months</i>	2	383	MD	0.47	(-2.32-3.25)
<i>Total days respiratory-related hospital stay</i>					
<i>at 6 months</i>	3	566	RR	1.06	(0.48-2.33)
<i>at 12 months</i>	5	1295	RR	0.83	(0.46-1.48)
<i>Total days all-cause hospital stay</i>					
<i>at 6 months</i>	2	378	RR	1.01	(0.48-2.17)
<i>at 12 months</i>	4	1559	RR	0.79	(0.62-1.00)

Abbreviations: CI, confidence interval; MCS, mental component scale Short Form Health Survey; MD, mean difference; PCS, physical component scale Short Form Health Survey; RR, risk ratio.

Supplementary Table 3: Effects of self-management interventions on additional outcomes in subgroups of patients with COPD.

Outcome	n patients	Subgroup	UNIVARIABLE ANALYSIS				MULTIVARIABLE ANALYSIS		
			Effect size	Treatment effect	95% CI	P-value for interaction	Treatment effect	95% CI	P-value for interaction
<i>Generic quality of life</i>									
PCS at 6 months		No subgroup effects.							
PCS at 12 months		No subgroup effects.							
MCS at 6 months		No subgroup effects.							
MCS at 12 months		No subgroup effects.							
<i>Total days respiratory-related hospital stay</i>									
at 6 months†	283	≥50% FEV1 % predicted	RR	0.77	(0.26-2.24)	0.001	*		
	283	<50% FEV1 % predicted		1.34	(0.45-4.01)				
at 12 months		No subgroup effects.							
<i>Total days all-cause hospital stay</i>									
at 6 months		No subgroup effects.							
at 12 months†	1099	Males	RR	0.65	(0.49-0.87)	0.020	1.10	(0.68-1.78)	0.016
	460	Females		1.22	(0.79-1.87)				
	432	≥50% FEV1 % predicted	RR	1.38	(0.88-2.17)	0.010	1.10	(0.68-1.78)	0.014
	1127	<50% FEV1 % predicted		0.68	(0.51-0.89)				

Notes: Results of the subgroup analyses are only presented if a potential effect modifier showed an effect with $P < 0.10$ in the univariable analysis.

Abbreviations: CI, confidence interval; FEV1, forced expiratory volume in 1 second; MCS, mental component scale Short Form Health Survey; PCS, physical component scale Short Form Health Survey; RR, risk ratio.

* Multivariable analysis was only performed if ≥ 2 potential effect modifiers in the univariable analysis to adjust for other potential effect modifiers.

† Fitted with random intercepts only due to convergence problems.

Supplementary Table 4: Effects of self-management interventions in subgroups of patients with COPD based on exacerbation frequency prior to enrolment.

Study	0 PRIOR EXACERBATIONS			1 PRIOR EXACERBATION			>1 PRIOR EXACERBATIONS			P-value interaction
	n	Effect	95% CI	n	Effect	95% CI	n	Effect	95% CI	
Respiratory-related health-related quality of life - 6 months (SMD)										
Bischoff 2012 ⁸	59	0.02	(-0.38-0.43)	36	-0.27	(-0.81-0.28)	35	0.16	(-0.40-0.73)	0.52
Bucknall 2012 ⁷	4	*	*	20	0.08	(-0.19-0.36)	114	0.07	(-0.61-0.75)	0.97
Casas 2006 ²⁹	40	0.00	(-0.52-0.52)	22	0.39	(-0.38-1.16)	13	-1.00	(-1.86--0.13)	0.05
Effing 2009 ³¹	0	*	*	11	-0.04	(-1.68-1.61)	111	0.06	(-0.29-0.41)	0.91
Monninkhof 2003 ³⁴	89	0.05	(-0.20-0.29)	68	0.00	(-0.28-0.29)	82	-0.04	(-0.30-0.23)	0.90
Trappenburg 2011 ³⁷	105	0.00	(-0.24-0.23)	34	0.32	(-0.11-0.74)	36	-0.02	(-0.42-0.38)	0.39
Respiratory-related health-related quality of life - 12 months (SMD)										
Bischoff 2012	56	0.08	(-0.30-0.46)	35	-0.16	(-0.66-0.34)	35	0.85	(0.34-1.36)	0.01
Bucknall 2012	4	*	*	17	0.28	(-0.01-0.57)	99	0.36	(-0.36-1.09)	0.84
Casas 2006	33	0.34	(-0.21-0.89)	19	0.24	(-0.54-1.02)	10	-0.70	(-1.66-0.27)	0.16
Effing 2009	0	*	*	11	0.86	(-0.31-2.03)	111	0.08	(-0.25-0.41)	0.20
Monninkhof 2003	89	-0.11	(-0.37-0.16)	66	-0.18	(-0.49-0.14)	79	0.20	(-0.09-0.49)	0.16
Respiratory-related hospitalization - time-to-event (HR)										
Bucknall 2012	17	0.64	(0.06-7.08)	61	1.84	(0.68-4.99)	383	0.99	(0.75-1.32)	0.45
Casas 2006	81	0.32	(0.14-0.73)	37	0.67	(0.28-1.63)	37	0.65	(0.32-1.31)	0.34
Trappenburg 2011	128	1.17	(0.34-4.03)	50	0.50	(0.10-2.58)	47	1.45	(0.35-6.06)	0.59
Respiratory-related hospitalization - 6 months (RR)										
Bucknall 2012	17	*	*	61	1.13	(0.34-3.82)	383	1.09	(0.83-1.43)	0.77
Casas 2006	81	0.31	(0.09-1.02)	37	0.82	(0.21-3.12)	37	0.38	(0.08-1.74)	0.55
Trappenburg 2011	128	1.13	(0.34-3.73)	50	0.51	(0.11-2.38)	47	1.35	(0.36-4.99)	0.59
Respiratory-related hospitalization - 12 months (RR)										
Bucknall 2012	17	0.62	(0.07-5.14)	61	1.66	(0.70-3.92)	383	0.98	(0.80-1.21)	0.44
Casas 2006	81	0.25	(0.09-0.69)	37	0.44	(0.11-1.73)	37	0.06	(0.00-Inf)	0.19
Effing 2009	0	*	*	11	0.44	(0.07-2.82)	111	0.81	(0.37-1.76)	0.58
Monninkhof 2003	62	0.18	(0.04-0.78)	51	0.00	(0.00-Inf)	56	0.87	(0.26-2.90)	0.05

Abbreviations: CI, confidence interval; HR, hazard ratio; RR, risk ratio; SMD, standardized mean difference.

* Could not be estimated reliably due to limited/no measurements in level.

Definition of exacerbations

Bischoff 2012 ⁸	Unscheduled physician contacts for COPD in 24 months prior to study enrolment
Bucknall 2012 ⁷	Courses prednisolone in 12 months prior to study enrolment
Casas 2006 ²⁹	Hospitalizations and/or emergency department visits for COPD in 12 months prior to study enrolment
Effing 2009 ³¹	Course prednisolone and/or antibiotics in 24 months prior to study enrolment
Monninkhof 2003 ³⁴	Courses prednisolone and/or antibiotics in 12 months prior to study enrolment as confirmed by physician
Trappenburg 2011 ³⁷	Courses prednisolone and/or antibiotics in 6 months prior to study enrolment