

Study ID	Study Title	Author	Year	Design	Population	Intervention	Comparator	Primary Outcome	Secondary Outcome	Significance	Quality	Notes
1	Bacterial infections and risk factors in outpatients with acute exacerbation of chronic obstructive pulmonary disease: A 2-year prospective study	Arnscheidt, M., et al.	2007	Cohort	Germany	Amoxicillin	None	Number of bacterial infections	Number of hospitalizations	Yes	High	
5	Treatment with the immunomodulator AMI improves the health-related quality of life of patients with COPD	Alvarez-Gomez, G., et al.	2008	RCT	Spain	AMBIROL	None	Health-related quality of life	Number of exacerbations	Yes	High	
9	Exacerbations and impact of fatigue in patients with chronic obstructive pulmonary disease	Engel, K., et al.	2008	RCT	Germany	Respiratory medicine	None	Number of exacerbations	Number of hospitalizations	Yes	High	
9	The effect of oral corticosteroids on health status and quality of life in patients with COPD	Saravanan, K., et al.	2008	RCT	India	Respiratory medicine	None	Health status	Quality of life	Yes	High	
10	Effects of exacerbations and seasonality on exhaled nitric oxide (FeNO) in COPD	Saravanan, K., et al.	2007	RCT	India	Respiratory medicine	None	Exhaled nitric oxide	Number of exacerbations	Yes	High	
10	Relationship between respiratory symptoms and medical treatment in exacerbations of COPD	Chakraborty, R., et al.	2008	RCT	India	Respiratory medicine	None	Respiratory symptoms	Medical treatment	Yes	High	
7	Exacerbations in subjects with alpha-1 antitrypsin deficiency receiving augmentation therapy	Sampson, A., et al.	2009	Cohort	USA	Respiratory medicine	None	Number of exacerbations	Number of hospitalizations	Yes	High	
8	Influenza vaccination in subjects with alpha-1-antitrypsin deficiency	Campbell, S., et al.	2008	RCT	USA	Respiratory medicine	None	Number of exacerbations	Number of hospitalizations	Yes	High	
11	A long-term evaluation of once-daily inhaled budesonide in chronic obstructive pulmonary disease	Chakraborty, R., et al.	2007	RCT	India	Respiratory medicine	None	Number of exacerbations	Number of hospitalizations	Yes	High	
2	Withdrawal of inhaled corticosteroids in people with COPD in primary care: a randomized controlled trial	Choudhury, D., et al.	2007	RCT	India	Respiratory medicine	None	Number of exacerbations	Number of hospitalizations	Yes	High	
3	Exacerbation rates and quality of life in patients with COPD: a randomized controlled trial	Steen, M., et al.	2003	RCT	Denmark	Respiratory medicine	None	Number of exacerbations	Quality of life	Yes	High	
12	Exacerbations and time spent outdoors in chronic obstructive pulmonary disease	Donohue, J., et al.	2008	RCT	USA	Respiratory medicine	None	Number of exacerbations	Time spent outdoors	Yes	High	
11	Longitudinal changes in the season, severity and frequency of COPD exacerbations	Donohue, J., et al.	2008	RCT	USA	Respiratory medicine	None	Number of exacerbations	Severity and frequency	Yes	High	
1	Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease	Donohue, J., et al.	2003	Cohort	USA	Respiratory medicine	None	Lung function decline	Exacerbation frequency	Yes	High	
12	The relationship of chronic sputum expectoration to physiological and health status characteristics in alpha-1-antitrypsin deficiency	Stevens, G., et al.	2009	RCT	USA	Respiratory medicine	None	Physiological characteristics	Health status	Yes	High	
6	Exacerbations, a central of symptoms, fatigue, muscle weakness, and weight loss in chronic obstructive pulmonary disease	Stirling, J., et al.	1999	RCT	USA	Respiratory medicine	None	Exacerbations	Symptoms, fatigue, muscle weakness, weight loss	Yes	High	
1	Temporal clustering of exacerbations in chronic obstructive pulmonary disease	Hart, G., et al.	2008	RCT	USA	Respiratory medicine	None	Temporal clustering	Exacerbations	Yes	High	
1	Use of home telemonitoring at exacerbation of Chronic Obstructive Pulmonary Disease	Stevens, G., et al.	2008	RCT	USA	Respiratory medicine	None	Use of home telemonitoring	Exacerbation of COPD	Yes	High	
9	Underreporting of exacerbations in the common cold and influenza	Stevens, G., et al.	2009	RCT	USA	Respiratory medicine	None	Underreporting of exacerbations	Common cold and influenza	Yes	High	
1	Long-term evaluation of once-daily inhaled budesonide in chronic obstructive pulmonary disease	Saravanan, K., et al.	2007	RCT	India	Respiratory medicine	None	Number of exacerbations	Number of hospitalizations	Yes	High	
1	Microbiome DNA instability and COPD exacerbations	Marik, T., et al.	2008	Cohort	USA	Respiratory medicine	None	Microbiome DNA instability	COPD exacerbations	Yes	High	
2	Exacerbations and lung function decline in COPD: new insights in current and ex-smokers	Marik, T., et al.	2007	RCT	USA	Respiratory medicine	None	Exacerbations	Lung function decline	Yes	High	
2	Use of accelerometers to characterize physical activity in COPD	Neggers, S., et al.	2008	RCT	Belgium	Respiratory medicine	None	Use of accelerometers	Physical activity	Yes	High	
1	Impact of COPD exacerbations on quality of life in primary care	Ortiz, J., et al.	2008	RCT	Spain	Respiratory medicine	None	Impact of COPD exacerbations	Quality of life	Yes	High	
25	Bronchitis, exacerbation incidence, and inflammation in chronic obstructive pulmonary disease	Patel, V., et al.	2004	RCT	USA	Respiratory medicine	None	Bronchitis, exacerbation incidence, inflammation	Chronic obstructive pulmonary disease	Yes	High	
26	Relationship between bacterial colonization and the frequency, character, and severity of COPD exacerbations	Patel, V., et al.	2008	RCT	USA	Respiratory medicine	None	Relationship between bacterial colonization and COPD exacerbations	Frequency, character, severity of COPD exacerbations	Yes	High	
13	Acetylcysteine reduces the exacerbation rate in patients with moderate to severe COPD	Pau, C., et al.	1999	RCT	Taiwan	Respiratory medicine	None	Acetylcysteine	Exacerbation rate	Yes	High	
1	Effect of corticosteroids on symptom and inflammatory markers and exacerbations in COPD	Patel, V., et al.	2007	RCT	USA	Respiratory medicine	None	Effect of corticosteroids	Symptom and inflammatory markers, exacerbations	Yes	High	
1	Relationship between depression and exacerbations in COPD	Patel, V., et al.	2008	RCT	USA	Respiratory medicine	None	Relationship between depression and exacerbations	COPD	Yes	High	
1	Relationship between chronic nasal and respiratory symptoms in patients with COPD	Patel, V., et al.	2008	RCT	USA	Respiratory medicine	None	Relationship between chronic nasal and respiratory symptoms	Patients with COPD	Yes	High	
1	Long-term effectiveness of a placebo associated with decreased chronic obstructive pulmonary disease	Saravanan, K., et al.	2008	RCT	India	Respiratory medicine	None	Long-term effectiveness of a placebo	Decreased chronic obstructive pulmonary disease	Yes	High	
1	Detection of rhinovirus in induced sputum at exacerbation of COPD	Saravanan, K., et al.	2007	RCT	India	Respiratory medicine	None	Detection of rhinovirus	Induced sputum at exacerbation of COPD	Yes	High	
1	The course and recovery of exacerbations in patients with COPD	Saravanan, K., et al.	2008	RCT	India	Respiratory medicine	None	The course and recovery of exacerbations	Patients with COPD	Yes	High	
1	Effects of exacerbations on quality of life in patients with COPD	Saravanan, K., et al.	1999	RCT	India	Respiratory medicine	None	Effects of exacerbations	Quality of life in patients with COPD	Yes	High	
8	Removal of oral medication in patients with COPD: a feasible study using a novel device	Saravanan, K., et al.	2009	RCT	India	Respiratory medicine	None	Removal of oral medication	Patients with COPD	Yes	High	
1	Impact of gastro-oesophageal reflux disease symptoms on COPD exacerbation	Tarada, M., et al.	2008	Cohort	Spain	Respiratory medicine	None	Impact of gastro-oesophageal reflux disease symptoms	COPD exacerbation	Yes	High	
7	Continuous and on demand use of bronchodilators in patients with non-asthmatic obstructive pulmonary disease: a randomized controlled study	van Schalk, D., et al.	1999	RCT	Netherlands	Respiratory medicine	None	Continuous and on demand use of bronchodilators	Patients with non-asthmatic obstructive pulmonary disease	Yes	High	
4	Reported and unreported exacerbations of COPD	Vijayarathna, S., et al.	2007	Cohort	India	Respiratory medicine	None	Reported and unreported exacerbations	COPD	Yes	High	
9	Early therapy improves outcomes of exacerbations of COPD	Wilson, D., et al.	2009	RCT	USA	Respiratory medicine	None	Early therapy	Improves outcomes of exacerbations of COPD	Yes	High	
3	Independent Effect of Depression and Anxiety on COPD Exacerbations and Hospitalizations	Yu, C., et al.	2008	RCT	USA	Respiratory medicine	None	Independent Effect of Depression and Anxiety	COPD Exacerbations and Hospitalizations	Yes	High	
2	Effect of corticosteroids on acute exacerbation of COPD: a meta-analysis	Yu, C., et al.	2008	RCT	USA	Respiratory medicine	None	Effect of corticosteroids	Acute exacerbation of COPD	Yes	High	
12	Positive benefits of theophylline in a randomized, double-blind, parallel-group, placebo-controlled study of low-dose inhaled theophylline in the treatment of COPD: a meta-analysis	Yuan, Z., et al.	2008	RCT	China	Respiratory medicine	None	Positive benefits of theophylline	Low-dose inhaled theophylline in the treatment of COPD	Yes	High	
1	Exacerbations of COPD are accompanied by elevations of plasma fibrinogen and serum IL-6 levels	Medina, S., et al.	2003	Cohort	Spain	Respiratory medicine	None	Exacerbations of COPD	Elevations of plasma fibrinogen and serum IL-6 levels	Yes	High	
4	Inflammatory changes, recovery and relapse at COPD exacerbations	Perera, H., et al.	2007	RCT	USA	Respiratory medicine	None	Inflammatory changes, recovery and relapse	COPD exacerbations	Yes	High	
1	Effect of sputum inflammatory markers on symptoms and lung function changes in COPD exacerbations	Perera, H., et al.	2003	Cohort	USA	Respiratory medicine	None	Effect of sputum inflammatory markers	Symptoms and lung function changes in COPD exacerbations	Yes	High	
1	Respiratory viruses, symptoms, and inflammatory markers in acute exacerbations and stable chronic obstructive pulmonary disease	Saravanan, K., et al.	2008	RCT	India	Respiratory medicine	None	Respiratory viruses, symptoms, and inflammatory markers	Acute exacerbations and stable chronic obstructive pulmonary disease	Yes	High	
2	The long-term effects of treatment of exacerbations of COPD patients: the COPD-CARE study	Wang, L., et al.	2009	RCT	China	Respiratory medicine	None	The long-term effects of treatment	Exacerbations of COPD patients	Yes	High	
3	Negative impacts of unreported COPD exacerbations on HRQoL	Yu, C., et al.	2009	RCT	USA	Respiratory medicine	None	Negative impacts of unreported COPD exacerbations	HRQoL	Yes	High	
9	Diagnostic Pulmonary Function at Exacerbation of Chronic Obstructive Pulmonary Disease: prospective pilot study	Hart, G., et al.	2010	Cohort	USA	Respiratory medicine	None	Diagnostic Pulmonary Function	Exacerbation of COPD	Yes	High	
14	Effect of a new once-daily long-acting inhaled L2 agonist in COPD	Wang, L., et al.	2010	RCT	China	Respiratory medicine	None	Effect of a new once-daily long-acting inhaled L2 agonist	COPD	Yes	High	

1	Predictive accuracy of patient reported exacerbation frequency in chronic obstructive pulmonary disease.	Saint, Donaldson, Hunt, Godding, Baumgaertl, Weidicha	for Ragoz 1	2012	Cohort	no	207	12	Yes, major	Yes, major	Yes, minor	Yes, minor	Yes, minor	Yes, minor	Yes, minor	No	no	no	no	No	2	increase in two symptoms including one major	1-day moving average below or equal to day -14 to -8	Symptom score back to an individual predefined baseline	not reported	not reported	not reported	Symptom report and location	yes	Phys Cards	not reported	not reported	not reported
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