COPD Evidence Tables

The evidence tables are presented in section order.

The methodological quality of each paper was rated using the Scottish Intercollegiate Guidelines Network (SIGN) system (Scottish Intercollegiate Guidelines Network. SIGN 50 Guideline Developers Handbook, 2001; ID 19457):

++	All or most of the SIGN methodology checklist criteria were fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought very unlikely to alter.
+	Some of the criteria were fulfilled. Those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions.
-	Few or no criteria were fulfilled. The conclusions of the study are thought likely or very likely to alter.

Chronic Obstructive Pulmonary Disease: Management of adults with Chronic Obstructive Pulmonary Disease in Primary and Secondary Care

Management of exacerbations of COPD
Antibiotics
Index

Author	Publication Date	ID
Scottish Intercollegiate Guidelines Network (SIGN). Community management of lower respiratory tract infection (LRTI) in adults. Guideline 59. Section 4 Exacerbations of COPD. Point 4.2 Treatments. June 2002	2002	1316
McCrory, D. C., Brown, C., Gray, R. N., Goslin, R. E., MacIntyre, N. R., Kolimaga, J. T., Oddone, E. Z., & Matchar, D. 2001, *Management of acute exacerbations of chronic obstructive pulmonary disease.*, Agency for Healthcare Research and Quality., Rockville, MD, USA, 256.	2001	1145
Nouira, S., Marghli, S., Belghith, M., Besbes, L., Elatrous, S., & Abroug, F. 2001, "Once daily oral ofloxacin in chronic obstructive pulmonary disease exacerbation requiring mechanical ventilation: A randomised placebo-controlled trial", *Lancet*, vol. 15, no. 9298, p. pp-2025.	2001	349
Allegra, L., Blasi, F., de Bernardi, B., Cosentini, R., & Tarsia, P. 2001, "Antibiotic treatment and baseline severity of disease in acute exacerbations of chronic bronchitis: a re-evaluation of previously published data of a placebo-controlled randomized study", *Pulmonary Pharmacology & Therapeutics*, vol. 14, pp. 149-155.	2001	1151
Sin, D. D. & Tu, J. V. 2000, "Outpatient antibiotic therapy and short term mortality in	2000	416

elderly patients with chronic obstructive pulmonary disease", *Canadian Respiratory Journal*, vol. 7, no. 6, pp. 466-471.		
Saint, S., Bent, S., Vittinghoff, E., & Grady, D. 1995, "Antibiotics in chronic obstructive pulmonary disease exacerbations – a meta analysis", *Jama-Journal of the American Medical Association*, vol. 273, no. 12, pp. 957-960.	1995	44
Ball, P., Harris, J. M., Lowson, D., Tillotson, G., & Wilson, R. 1995, "Acute infective exacerbations of chronic bronchitis", *Quarterly Journal of Medicine*, vol. 88, no. 1, pp. 61-68.	1995	1152

Author / Title / Reference / Yr	Scottish Intercollegiate Guidelines Network (SIGN). Community management of lower respiratory tract infection (LRTI) in adults. Guideline 59. Section 4 Exacerbations of COPD. Point 4.2 Treatments. June 2002
Research Design	SIGN Guideline
Aim	The guideline focuses on the following in LRTI management: 1. When should antibiotics be prescribed? 2. How can the rates of re consultation be reduced? 3. When should patients be referred to secondary care? This evidence table focused on point 1 in application to exacerbations of COPD
Operational Definition	Guideline states, "There is currently no general agreement on the definition of an exacerbation in COPD. Definitions of exacerbations in COPD are based on increasing symptoms and / or increased health care utilisation (RCP 2002). In some studies exacerbations have been defined in operative terms according to the type and number of symptoms. A commonly used definition is based on an increase in symptoms of dyspnoea, sputum volume and sputum purulence with or without symptoms of upper respiratory infection. (Anthonisen, Manfreda Warren et al 1987).
Population	Exacerbations of COPD
Treatment	This section is quoted directly from the guidelines: "There have been a number of randomised placebo controlled trials of antibiotic therapy (usually aminopenicillin or tetracycline) in pts with exacerbation of COPD. A systematic review of these trials has shown a small benefit for those patients receiving antibiotic rather than placebo. Although a small number of pts was used in each of the original study groups (Saint et al 1995). **Evidence level 1-**

	In one study the sub-group of patients showing most benefit from antibiotics were those with two or all of the following symptoms: increasing breathlessness, sputum volume and sputum purulence (Anthonisen et al 1987). Patients in this study had significant baseline obstruction with a mean FEV1 of 33% of predicted. In pts with COPD, sputum purulence is a good guide to the presence and number of bacteria and whether antibiotic treatment is likely to be beneficial (Sethi et al 2001) (Niroumand 1998). **Evidence level 1.** **Recommendation** Patients with significant airway obstruction who have an increase in breathlessness and sputum purulence should be treated with an antibiotic**.** Grade B **Good practice point** The antibiotic of choice should be an aminopenicillin, a macrolide or a tetracycline. Quinolones have performed equally well in clinical trials, but no clinical superiority over other antibiotics has yet been shown. (Davies 1986)".
SIGN Quality Rating	Key to evidence statements and grades of recommendations used by this SIGN guideline (assigned by SIGN team and not NCC CC Systematic Reviewer): **Levels of evidence** 1++ High quality meta analyses, systematic reviews of RCTs or RCTs with a very low risk of bias. 1+ Well conducted meta analyses, systematic reviews, or RCTs with a low risk of bias. 1- Meta analyses, systematic reviews or RCTs with a high risk of bias. 2++ High quality systematic review of case control or cohort or studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal. 2+ Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal. 2- Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal. 3 Non analytic studies, e.g. case reports, case series 4 Expert opinion. **Grades of recommendations** Grade B - A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results: or extrapolated evidence from studies rated as 1++ or 1+.
Hierarchy of Evidence Grading	SIGN Guideline
References	Anthonisen NR, Manfreda J, Warren CP et al. Antibiotic therapy in exacerbations of COPD. Ann Intern Med. 1987. 106: 196-204. Davies BI, Maesen FP. Quinolones in chest infections. J Antimicrob Chemother 1986; 18: 296-9. Niroumand M, Grossman RF. Airway infection. Infect Dis Clin North Am 1998 12: 671-88 RCP Consensus statement on COPD. Edinburgh: The College; 2002

	Saint S, Bent S, Vittinghoff E et al. Antibiotics in COPD exacerbations. A meta-analysis. JAMA 1995; 273: 957-60 Sethi S, Murphy TF. Bacterial infection in COPD in 2000: a state-of-the-art review. Clin Microbiol Rev 2001; 14: 336-63
NCC CC ID	1316

Author / Title / Reference / Yr	McCrory, D. C., Brown, C., Gray, R. N., Goslin, R. E., MacIntyre, N. R., Kolimaga, J. T., Oddone, E. Z., & Matchar, D. 2001, *Management of acute exacerbations of chronic obstructive pulmonary disease.*, Agency for Healthcare Research and Quality., Rockville, MD, USA, 256. Ref ID: 1145
N=	N=1 meta-analysis (Saint, Bent, Vittinghoff et al 1995 – See Evidence Table ID 44). Nine trials included in the meta analysis. Authors required studies to consider at least a 5-day duration of follow up. All antibiotic agents were considered together in the analysis. Adjustments were made for trials that used the number of exacerbations instead of the number of pts as the unit of analysis. N=11 placebo-controlled studies of antibiotic treatment. (Listed below). Two of the trials were included by AHRQ but were excluded from the meta analysis because one trial did not report outcomes as continuous variables (Pines, Raafat, Plucinski et al 1968) and the other was published after the meta-analysis was performed (Sachs, Koeter, Groenier et al 1995). Two other trials were excluded because one was reported in a letter (Manresa, Blavia, Martin et al 1987) and the other one was published in Italian (Allegra, Grassi, Grossi et al 1991).
Design	"In the preliminary literature review, AHRQ identified several hundred head-to-head comparisons of different antibiotic treatments for acute exacerbation of COPD. The Advisory Panel of Technical Experts suggested limiting the studies of antibiotic treatment to placebo-controlled trials. There was concern that this large and complex review could command all the resources that were available to the AHRQ project, to the exclusion of other questions".
Aim	How effective are the medical modalities (**antibiotics)** that are used to treat acute exacerbations of COPD in alleviating symptoms, resolving the cause of the exacerbation, preventing hospital admissions and decreasing LOS?
Operational Definition	Adults who had COPD based on clinical diagnosis, spirometry or known or suspected history; subjects must have been experiencing an acute exacerbation of respiratory symptoms. Respiratory symptoms included dyspnoea, increased quantity or purulence of sputum or acute respiratory failure.
Population	Acute exacerbations of COPD
Intervention	Antibiotic drugs studied were tetracycline, doxycycline, chloramphenicol, penicillin, streptomycin, ampicillin, amoxicillin and cotrimoxazole.
Comparison	Placebo
Outcome	PEFR, duration of exacerbation, PaO2, symptom score, and overall score by physician.
SIGN Quality Rating	++

Hierarchy of Evidence Grading	1a
Results	The results presented here have been quoted directly from the AHQR report section entitled "Selected Treatment Strategies – Antibiotics" pp. 48-51. **"Meta analysis of the 9 trials:** • Three (individually) found statistically significant effects favouring antibiotics compared to placebo (Anthonisen, Manfreda, Warren et al 1987, Berry, Fry, Hindley et al 1960, Pines, Raafat, Greenfield et al 1972). • Three trials suggested a trend favouring antibiotics (Elmes, Fletcher and Dutton 1957, Elmes, King, Langlands et al 1965, and Fear, Edwards 1962. • Three trials failed to show any difference from placebo (Jorgensen, Coolidge, Pedersen et al 1992, Nicotra, Rivera and Awe 1982, Petersen, Esmann, Honcke et al 1967). • Results were combined to give an overall estimate of 0.22 (95% CI 0.1 to 0.34), a small but statistically significant effect favouring antibiotics over placebo. **Subgroup analysis:** PEFR (most frequently reported outcome measure (reported in 6 of the 9 trials)) One trial showed a statistically significant improvement in PEFR favouring antibiotics (Anthonisen, Manfreda, Warren et al 1987) and one trial showed a trend (Elmes, King, Langlands et al 1965). The trials were statistically homogeneous. A combined estimate of the difference in mean PEFR between antibiotic and placebo treated participants was 10.75 L/minute (95% CI, 4.96 to 16.54). **Level of care** Outpatient versus inpatient care. The summary effect size for outpatient studies was 0.17 (95%CI, 0.03 to 0.30) and 0.38 (95%CI, 0.13 to 0.62) for hospitalised patients. **Bacterial infection and severity of illness** In the meta analysis, it was not possible to investigate a relationship between antibiotic efficacy and severity of illness, sputum purulence, or bacterial cultures. Several of the trials analysed the efficacy of antibiotics according to subgroups that were defined either by evidence of bacterial infection or severity of illness (Anthonisen, Manfreda, Warren et al 1987, Berry, Fry, Hindley et al 1960 Elmes, King, Langlands et al 1965). Anthonisen, Mangreda, Warren et al 1987 found that a priori criteria that were proposed to select patients with signs of infection (Winnipeg criteria) showed a relationship of better outcomes with antibiotic versus placebo treatment. Pts with type-1 exacerbations (who met all three criteria: increases in amount of sputum, purulence of sputum and dyspnoea) benefited the most, with resolution of symptoms in 63% of the antibiotic treated exacerbations and 43% of the placebo treated exacerbations. Pts with type-3 exacerbations (who met one of the above three criteria) did not show any benefit, with 74% of exacerbations resolving on antibiotics and 70% resolving on placebo. Those with type-2 exacerbations (who met two of the above three criteria) showed an intermediate (and not statistically significant) benefit, with 70%

	resolving on antibiotics and 60% resolving on placebo. Berry, Fry, Hindley et al 1960 assessed the severity of exacerbation at presentation on a subjective 4-point scale (baseline, mild, moderate or severe). For pts presenting with mild exacerbations there were no significant difference in severity of symptoms between antibiotic and placebo patients at any time point (two days, one wk and two wks). For pts presenting with moderate or severe exacerbations, antibiotic pts had significantly less severe symptoms on days 2 and 7 but were not significant at two wks. (Differences not quoted). Elmes, King, Langlands et al 1965 matched pts based on severity of illness which was defined as two or more criteria (temp higher than 37.5degrees cent, pulmonary consolidation or purulent sputum). The trial was not blinded to bacteriologic results. A later independent, blinded assessment failed to find a significant difference between antibiotic and placebo participants. Different trial populations appear to have clinically important differences in severity of illness (see attached table). **Adverse Effects** The most common adverse effect was diarrhoea, which was observed in the placebo group to four trials that described adverse effects in detail (Anthonisen, Manfreda, Warren, et al 1987, Elmes, Fletcher and Dutton 1957, Elmes, King, Langlands et al 1965, Jorgensen, Coolidge, Pedersen et al 1992)." **The AHQR authors conclude that in acute exacerbations of COPD:** **"**RCTs of antibiotic versus placebo treatment demonstrated improvement in pulmonary function. Trials suggest that the greater degree of bacterial infection (sputum purulence) and severe illness (worse PEFR) the greater degree of benefit from antibiotics, however this has not been conclusively demonstrated".
Studies Included	Meta-analysis by Saint, Bent, Vittinghoff et al 1995, included nine trials: Anthonisen, Manfreda, Warren et al 1987 (N=310), Berry, Fry, Hindley et al 1960 (N=33), Elmes, Fletcher, Dutton 1957 (N=113), Elmes, King, Langlands et al 1965 (N=56), Fear and Edwards 1962 (N=119), Jorgensen, Coolidge, Pedersen et al 1992 (N=262), Nicotra, Rivera and Awe 1982 (N=40), Petersen, Esmann, Honcke et al 1967 (N=19), Pines, Raafat, Greenfield et al 1972 (N=149). RCTs: Anthonisen, Manfreda, Warren et al 1987, Berry, Fry, Hindley, et al 1960, Elmes, Fletcher, Dutton 1957, Elmes, King, Langlands et al 1965, Fear and Edwards 1962, Jorgensen, Coolidge, Pedersen et al 1992, Nicotra, Rivera and Awe 1982, Petersen, Esmann, Honcke et al 1967, Pines, Raafat, Plucinski et al 1968, Sachs, Koeter, Groenier et al 1995.
ID	1145

Author / Title / Reference / Yr	Nouira, S., Marghli, S., Belghith, M., Besbes, L., Elatrous, S., & Abroug, F. 2001, "Once daily oral ofloxacin in chronic obstructive pulmonary disease exacerbation requiring mechanical ventilation: A randomised placebo-controlled trial"

	Lancet, vol. 15, no. 9298, p. pp-2025. Ref ID: 349
N=	N= 93 patients. Sites=Two hospitals. Duration=Jan 1996 to Dec 1999. Geographical location=Tunisia (N=3 excluded secondarily for non-invasive ventilation<6hrs).
Research Design	Prospective, randomised, double-blind, placebo-controlled RCT
Aim	To assess the efficacy of oral ofloxacin in the treatment of patients admitted to the ICU
Operational Definition	Exacerbation diagnosed on the basis of clinical history, physical examination and CXR. Acute respiratory failure requiring mechanical ventilation within the first 24 hr of admission – ARF defined as association of exacerbation of dyspnoea with at least two of the following: respiratory rate greater than 30 bpm; arterial partial pressure of CO2 greater than 6kPa; and arterial pH <7.30 after the pt had been breathing spontaneously for at least 10 min.
Population	Severe acute exacerbation of COPD requiring mechanical ventilation. "Patients were systematically assigned non-invasive ventilation. In case of failure of non-invasive ventilation or contraindication, patients were intubated and mechanically ventilated in the assist-control mode".
Intervention	Once daily does of ofloxacin 400mg. All treatments were given orally as two tables of 200 mg every day for 10 consecutive days in the morning. Intubated patients were given the same regimen via a NGT. Patients transferred from the ICU to another ward during this 10-day period were asked to complete the study treatment with the agreement of their physician. N=45
Comparison	Matched placebo N=45
Outcomes	Primary study outcomes: Death in hospital / need for additional course of antibiotics. Secondary study outcomes: Duration of mechanical ventilation / length of hospital stay.
Characteristics	Mean age 66 yrs Gender 90% male Baseline FEV1 antibiotic group 0.79 (0.25), placebo group 0.74 (0.23) (L/s) Initial ventilatory support – non-invasive 69% approx each group. Concomitant drugs 64% antibiotic group, 69% placebo group.
Results	**Deaths** 4% (N=2) patients receiving ofloxacin and 22% (N=10) in the placebo group died in hospital. Absolute risk reduction (ARR) 17.5%, 95% CI, 4.3 to 30.7, p=0.01. There were five times more deaths in hospital in the placebo group than in the ofloxacin group **Additional courses of antibiotics** 6% (N=3) patients receiving ofloxacin and 35% (N=16) in the placebo group required additional antibiotics.

	Treatment with ofloxacin significantly reduced the need for additional courses of antibiotics. ARR 28.4%, 95% CI, 12.9 to 43.9, p=0.0006. **Combined frequency of death in hospital and need for additional antibiotics** Was significantly lower in patients in the ofloxacin group than in those receiving placebo. ARR 45.9%, 95% CI, 29.1 to 62.7, p<0.0001. **Duration of mechanical ventilation** Was significantly shorter in the ofloxacin group than in the placebo group. Absolute difference 4.2 days, 95% CI, 2.5 to 5.9. **Duration of hospital stay** Was significantly shorter in the ofloxacin group than in the placebo group. Absolute difference 9.6 days, 95% CI, 3.4 to 12.8. **Nonsocomial pneumonia** Pts in the ofloxacin group were less likely to develop pneumonia than those in the placebo group, especially during the first week of mechanical ventilation. In the placebo group, most episodes of nosocomial pneumonia occurred within the first wk after admission to ICU (mean 7.2 days, SD 2.2, range 4 to 11) whereas all episodes in the ofloxacin group arose after this time (10.6 days, 2.9, 9 to 14; p=0.04). The mortality rate in the ICU was significantly higher in pts with nosocomial pneumonia than in those without this complication 13% (N=4/13) vs 8% (N=6/77), p=0.01). **Conclusion:** New fluoroquinolones, such as ofloxacin are beneficial in the treatment of COPD exacerbation requiring mechanical ventilation.
SIGN Quality Rating	++
Hierarchy of Evidence Grading	1b
NCC CC ID	349

Author / Title / Reference / Yr	Allegra, L., Blasi, F., de Bernardi, B., Cosentini, R., & Tarsia, P. 2001, "Antibiotic treatment and baseline severity of disease in acute exacerbations of chronic bronchitis: a re-evaluation of previously published data of a placebo-controlled randomized study", *Pulmonary Pharmacology & Therapeutics*, vol. 14, pp. 149-155. Ref ID: 1151
N=	N=46 Italian General Hospitals or University Hospitals. Date period – Eligible pts were followed as outpatients for the original study from Oct 1989 through to April 1990. Original RCT: N=957 screened / N=761 eligible / N=761 followed up / N=369 pts with first exacerbation randomised

	N=190 antibiotics / N=179 placebo 176 antibiotic group analysed (14 drop-out) 159 placebo group analysed (20 drop-out) Total N=335 The authors then retrospectively analysed the reported study data by re clustering pts on the basis of severity of baseline lung function. Cluster 1 N=104 / Cluster 2 N=109 / Cluster 3 N=122 / Total N=335
Research Design	Retrospective data analysis of a previously reported RCT
Aim	Antibiotic associated improvement may be particularly significant in pts with greater baseline pulmonary dysfunction although it is unclear whether all COPD pts need antibiotic treatment. In order to provide additional proof of the utility of antibiotic treatment in acute exacerbations of chronic bronchitis authors extended retrospectively the analysis on a previously reported study carried out within a relevant population.
Operational Definition	Scale fully documented to define exacerbation (unclear whether validated scale and scoring system).
Population	Acute exacerbations chronic bronchitis (asthmatics excluded)
Intervention	Amoxicillin-clavulanic acid 1g b.d. for 5 days
Comparison	Matched placebo for 5 days
Outcomes	FEV1
Retrospective re-clustering	Pts were retrospectively re-clustered on the basis of severity of baseline lung function: Cluster 1 mean screening FEV1 32.67+/- 6.83(SD) Cluster 2 mean screening FEV1 54.12 +/- 5.56 Cluster 3 mean screening FEV1 71.54 +/- 5.51
Characteristics	Gender m/f 246 / 89 Age 62.8yrs mean (Pts considered eligible if aged over 40 yrs) Pts receiving antibiotic or steroid therapy were excluded. FEV1 screening in antibiotic group 1.53 +/- 0.57 FEV1 screening in placebo group 1.49 +/- 0.51 FEV1 admission in antibiotic group 1.38 +/- 0.52 FEV1 admission in placebo group 1.35 +/- 0.51
Results	When clinical improvement was analysed on the basis of patient re clustering: **Mean number of exacerbations during the 12 months prior to enrolment** Cluster 1 = 3.05 +/- 0.96 Clusters 2 and 3 = 1.61 +/- 1.03 ($p<0.001$) **Cluster 1 (severe COPD)**

	31.4% pts treated with antibiotics showed clinical improvement and 58.8% successfully recovered 13.2% pts receiving placebo improved and 17% successfully recovered (p<0.001) **Cluster 2 and 3 (grouped together)** 31.2% improvements and 53.6% recovered pts among antibiotic treated group 29.2% improvements and 30.2% successful recoveries among placebo pts (p<0.001) **Placebo treated group** The improvement / success vs failure rate was significantly different in Cluster 1 patients compared to Cluster 2 and 3 patients (p<0.01). **Differences in final FEV1 values** In the treatment group and placebo group were significantly different (p<0.01) in favour or the active treatment group. **Comparison between screening and follow-up** Among cluster 1 subjects, the comparison between screening and follow up FEV1 values showed an improvement following antibiotic treatment and worsening after placebo (p<0.01). In cluster 2 and 3 the difference between screening and follow up FEV1 values was not significant for both treatment groups. In patients with severe functional impairment and higher number of exacerbations per year are those who derive the greatest benefit from antibiotic treatment.
SIGN Quality Rating	++
Hierarchy of Evidence Grading	1b – Caution this grading is attributed to the original study. The data presented in the evidence table is post hoc / retrospective analysis of previously reported RCT data. Retrospective re-clustered patients on the basis of severity of baseline lung function.
NCC CC ID	1151

Author / Title / Reference / Yr	Sin, D. D. & Tu, J. V. 2000, "Outpatient antibiotic therapy and short term mortality in elderly patients with chronic obstructive pulmonary disease", *Canadian Respiratory Journal*, vol. 7, no. 6, pp. 466-471. Ref ID: 416
N=	N=26,301. Geographical location=Canada
Research Design	A population-based retrospective cohort study
Aim	To determine the association between outpatient use of oral antibiotics and 30-day all-cause mortality following hospitalisation in a group of elderly COPD patients.
Operational Definition	COPD defined using ICD-9 codes (International Classification of Diseases, ninth revision).
Population	Patients aged 65 yrs or older who were hospitalised for COPD between 1992 and 1996.
Factor of interest	• Elderly pts admitted at least once with an ICD-9 diagnosis of COPD were identified through the Canadian

	Institute for Health Information database. • The data was then linked to the Ontario Drug Benefit database to determine the use of antibiotics within 30-days of the index hospitalisation. • Relevant data was then matched to the Ontario registered persons database to determine the 30-day mortality following the index hospitalisation.
Medical information	• For those with multiple admissions, only the initial hospitalisation was used in the analysis in order to avoid double counting of pts. • Pts transferred from chronic care to acute care were excluded because outpatient drug information was unavailable. • Pts younger than 65yrs were excluded as the databases did not contain any prescription medication information for this group. • During the study period the Ontario government offered prescription medication free of charge. • The Ontario Drug Benefit database contained comprehensive data on all outpatient medications including the name, the formulation and the amount that was dispensed to all pts in the cohort. • From the database, the use of oral antibiotics within 30-days of the index hospitalisation was ascertained. • Medications selected were amoxicillin (ampicillin), penicillin, sulfa drugs, cephalosporins, fluoroquinolones, tetracyclines and macrolides. • By law, all deaths occurring in Ontario must be reported. The information is then registered on the Ontario Registered Persons Database. This database was used in the present study to determine mortality.
Outcomes	14-day and 30-day mortality from the date of the index hospitalisation. Use of antibiotics within 30-days before the index hospitalisation.
Characteristics	Mean age 75yrs
Results	**Demographics** • N=26,301 pts included in the study • 7% (N=1937) of pts died within 30-days of hospitalisation • 34% (N=9037) of the pts used an oral antibiotic within 30 days of their index hospitalisation date. • Pts who were 80 yrs of age or older had the highest rate of antibiotic use (30%), while those between 65-70yrs had the lowest rate of use (22%). • The Charlson-Deyo co morbidity scores were similar between the two groups*. **Mortality** • Patients who used antibiotics within 30-days of the index hospitalisation date experience lower odds for all-cause 30-day mortality after hospitalisation than those who did not receive antibiotics. • Odds ratio (OR) 0.83, 95% CI, 0.75 to 0.92. (N.B This result takes into account adjustments made for important baseline covariates including age, sex, Charlson-Deyo co morbidity scores and use of other COPD medications).

	• 14-day mortality – relative odds associated with antibiotic exposure before hospitalisation was 0.79, 95% CI, 0.70 to 0.90 **Antibiotics** • Use of macrolides had the lowest relative odds for mortality. • OR 0.58, 95% CI, 0.47 to 0.73 • Use of fluoroquinolones had the highest relative odds. • OR 0.98, 95% CI, 0.84 to 1.15 **Conclusion:** In elderly pts with COPD who required hospitalisation for COPD, treatment with oral antibiotics on an outpatient basis before the COPD related admission was associated with a reduced mortality rate. COPD pts who received at least one course of antibiotic therapy before hospitalisation were 17% less likely to die within 30-days following hospitalisation for their COPD than those who did not receive any antibiotic therapy.
SIGN Quality Rating	++
Hierarchy of Evidence Grading	III
NCC CC ID	416

Author / Title / Reference / Yr	Saint, S., Bent, S., Vittinghoff, E., & Grady, D. 1995, "Antibiotics in chronic obstructive pulmonary disease exacerbations. A Meta analysis", *Jama-Journal of the American Medical Association*, vol. 273, no. 12, pp. 957-960. Ref ID: 44
N=	N=9 trials (1,101 pts) of which 6 included PEFR as an outcome measure (836 pts)
Research Design	Meta analysis of RCTs
Aim	To estimate the effectiveness of antibiotics in treating exacerbations of COPD
Operational Definition	Participants with a diagnosis of COPD (chronic bronchitis or emphysema) and thought to be having an exacerbation followed up for at least 5 days.
Population	In and out patients with acute exacerbation of COPD
Intervention	Antibiotic regimens including oxytetracycline, ampicillin, chloramphenical, amoxicillin, tetracycline and a combination of sulfamethoxazole and trimethoprim, amoxicillin or doxycycline.
Comparison	Placebo
Outcomes	Days of illness, overall symptom score, overall score by physician and change in peak expiratory flow rate.

Characteristics	Not documented
Results	**See AHRQ Evidence Table ID 1145** In summary: Overall summary effect size of the 9 trials was 0.22 (95% CI, 0.10 to 0.34) indicating a small benefit in the antibiotic treated group. Similar analysis of the 6 studies that provided data on PEFR changes revealed a summary effect size of 0.19 (95% CI, 0.03 to 0.35) and a summary change in PEFR of 10.75 L/min (95% CI, 4.96 to 16.54) in four of the antibiotic treated group. Sensitivity analyses did not significantly affect the results.
SIGN Quality Rating	+
Hierarchy of Evidence Grading	1a
NCC CC ID	44

Author / Title / Reference / Yr	Ball, P., Harris, J. M., Lowson, D., Tillotson, G., & Wilson, R. 1995, "Acute infective exacerbations of chronic bronchitis", *Quarterly Journal of Medicine*, vol. 88, no. 1, pp. 61-68. Ref ID: 1152
N=	N=127 GPs joined the study / N=471 pts entered / N=48 (10%) lost to F/U / N=423 outcome fully documented Geographical location = UK. Duration=Nov 1992 to March 1993.
Research Design	Computer based general practice prospective data collection study
Aim	To determine whether feature of past history, presenting symptoms, or findings on examination were **predictive** of failure to recover from a COPD exacerbation.
Operational Definition	No operational definitions provided.
Population	Patients presenting with acute infective exacerbations of chronic bronchitis
Data collection	• GP computer network which recorded history, examination findings and management decisions. • If pt returned for any reason to the practice during the next 28 days from the first presentation the reason for return and details were recorded. • Data was analysed in stages: 1) First analysis was of factors relating to the pts past and current history at the time of presentation. 2) Second analysis was undertaken at the 4 wk follow up visit when outcome was assessed, attempted to relate the variables to outcome so as to establish which features were predictive of particular clinical results. 3) In addition, an aggregate clinical score thought to be representative of severity of an exacerbation was calculated.
Characteristics	Median age 68 yrs. Range 31 to 94 yrs. / Gender – 56% male / 82% current or ex smokers
Results	• The only factors significantly ($p<0.05$) predicting failure to recover from an acute exacerbation of chronic bronchitis were historical.

	• The best combination predicting return with a chest problem was history of cardiopulmonary disease (OR 2.30, 95% CI, 1.30 to 4.10) and more than four previous exacerbation in the last 12 months (OR 2.11, 95% CI, 1.05 to 4.23). The sensitivity was 75% and specificity 47%.
SIGN Quality Rating	-
Hierarchy of Evidence Grading	III
NCC CC ID	1152