Supplemental 1. Characteristics of the included studies.

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| Study type | Author | Year | Country | Study design | Sample size | Mean or median age (years) | study population | Cut-off (ng/ml) | Quality assessment1,2,3 |
| Diagnostic value of PCT | Chang15 | 2006 | China | Prospective | 45 | 67 | AECOPD patients in hospitalization, FEV1 %predicted (median)=47% | 0.155 | 10 |
| Daubin16 | 2008 | France | Prospective | 35 | 62.8 | AECOPD patients admitted to ICU, 77% patients with FEV1 %predicted below 50% | 0.25 | 12 |
| Nseir17 | 2008 | France | Prospective | 98 | 68.2 | AECOPD patients admitted to ICU, 97% patients with FEV1 %predicted below 50% | 0.5 | 12 |
| Falsey18 | 2012 | USA | Prospective | 184 | 66.7 | AECOPD patients in hospitalization, lung function was unclear | 0.25 | 9 |
| Tanriverdi19 | 2015 | Turkey | Prospective | 77 | 71.7 | AECOPD patients in hospitalization, FEV1 %predicted (mean)=47% | 0.4 | 13 |
| Ergan20 | 2016 | Turkey | Retrospective | 52 | 71 | AECOPD patients admitted to ICU, 81% patients with FEV1 %predicted below 50% | 0.25 | 12 |
| Li21 | 2017 | China | Prospective | 164 | 66.8 | AECOPD patients in hospitalization, all patients with FEV1 %predicted below 80% | 0.25 | 12 |
| Xiong22 | 2018 | China | Prospective | 78 | 61.9 | AECOPD patients in hospitalization, 42% patients with FEV1 %predicted below 50% | 0.76 | 12 |
| PCT guided antibiotic therapy | Christ-Crain23 | 2004 | Switzerland | Single-center, RCT | 60 | 70.5 | AECOPD patients from medical emergency department, FEV1 %predicted (mean)=44.7% | 0.25 | 4 |
| Stolz24 | 2007 | Switzerland | Single-center, RCT | 208 | 69.5 | AECOPD patients from medical emergency department, 75% patients with FEV1 %predicted below 50% | 0.25 | 3 |
| Schuetz25 | 2009 | Switzerland | Multi-center, RCT | 228 | NA | AECOPD patients from medical emergency department, lung function was unclear | 0.25 | 5 |
| Nangia26 | 2012 | Finland | Single-center, RCT | 100 | NA | AECOPD patients in hospitalization, lung function was unclear | 0.5 | 2 |
| Liu27 | 2015 | China | Single-center, RCT | 108 | 69.4 | AECOPD patients in hospitalization, 84% patients with FEV1 %predicted below 50% | 0.25 | 2 |
| Verduri28 | 2015 | Italy | Multi-center, RCT | 178 | 73 | AECOPD patients in hospitalization, 67% patients with FEV1 %predicted below 50% | 0.25 | 5 |
| Corti29 | 2016 | Denmark | Single-center, RCT | 120 | 72 | AECOPD patients from medical emergency department, FEV1 %predicted (median)=40% | 0.25 | 5 |
| Daubin30 | 2018 | France | Multi-center, RCT | 302 | 67 | AECOPD patients addmitted to ICU, 67% patients with FEV1 %predicted below 50% | 0.25 | 5 |
| Huang31 | 2018 | USA | Multi-center, RCT | 524 | NA | AECOPD patients from medical emergency department, lung function was unclear | 0.25 | 5 |
| Picart32 | 2016 | Reunion | Single-center, Retrospective | 245 | 75 | AECOPD patients from medical emergency department, 63% patients with FEV1 %predicted below 50% | 0.25 | 6 |
| Bremmer33 | 2018 | USA | Multi-center, Retrospective | 305 | 66 | AECOPD patients in hospitalization, lung function was unclear | 0.25 | 8 |
| Sabrine34 | 2018 | Tunisia | Single-center, Retrospective | 93 | NA | AECOPD patients admitted to ICU, lung function was unclear | 0.25 | 5 |
| Townsend35 | 2018 | USA | Single-center, Retrospective | 100 | NA | AECOPD patients from medical emergency department, 75% patients with FEV1 %predicted below 50% | 0.25 | 7 |
| Antibiotics treatment in low PCT levels | Wang36 | 2016 | China | Single-center, RCT | 191 | 72.9 | AECOPD patients in hopitalization with PCT level ＜0.1 ng/ml, FEV1 %predicted (mean)=37.6% | 0.1 | 5 |
| Bremmer37 | 2018 | USA | Multi-center, Retrospective | 356 | 66.2 | AECOPD patients in hopitalization with PCT level ＜0.25 ng/ml, lung function was unclear | 0.25 | 8 |

PCT, procalcitonin; RCT, randomized controlled trial; AECOPD, acute exacerbations of chronic obstructive pulmonary disease; ICU, intensive care unit; NA, not available.

1 The quality and bias of the diagnostic studies were assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) checklist.

2 The quality and bias of the RCT studies were assessed using the Jadad score.

3 The quality and bias of the cohort studies were assessed using the modified Newcastle-Ottawa scale (NOS).

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Supplemental 2. Deek’s funnel plot asymmetry test for publication bias of studies evaluating the value of PCT for the diagnosis of respiratory bacterial infections.

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Supplemental 3. Risk of bias graph on included randomized controlled trials.

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Supplemental 4. Risk of bias summary on included randomized controlled trials.

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Supplemental 5. A funnel plot of PCT-guided treatment on treatment failure for the index exacerbation in patients with AECOPD.

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Supplemental 6. A funnel plot of PCT-guided treatment on length of hospital stay for the index exacerbation in patients with AECOPD.

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Supplemental 7. Fagan’s nomogram for calculation of post-test probabilities. Fagan’s nomogram for PCT illustrates post-test probability with fixed pre-test probability of 50 % for respiratory bacterial infection in AECOPD. LR likelihood ratio, *pos* positive, *neg* negative.

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Supplemental 8. Univariate meta-regression and subgroup analysis of studies evaluating PCT for the diagnosis of respiratory bacterial infections.

Supplemental 9. Quality of the evidence (GRADE) on PCT-guided antibiotic treatment in COPD exacerbation.

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| **Quality assessment** | | | | | | | **No of patients** | | **Effect** | | **Quality** | **Importance** |
|
| **No of studies** | **Design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **PCT algorithm** | **Control** | **Relative (95% CI)** | **Absolute** |
| **Treatment failure** | | | | | | | | | | | | |
| 6 | randomised trials | serious1 | no serious inconsistency | no serious indirectness | serious2 | none | 83/469  (17.7%) | 99/473  (20.9%) | RR 0.85 (0.66 to 1.09) | 31 fewer per 1000 (from 71 fewer to 19 more) |  LOW | CRITICAL |
| **Lenght of hospitalization for the index exacerbation (Better indicated by higher values)** | | | | | | | | | | | | |
| 9 | randomised trials | serious1 | no serious inconsistency | no serious indirectness | no serious imprecision2 | none | 914 | 914 | - | MD 0.17 higher (-0.88 lower to 1.22 higher) |  MODERATE | IMPORTANT |
| **Antibiotic exposure** | | | | | | | | | | | | |
| 9 | randomised trials | serious1 | no serious inconsistency | no serious indirectness | no serious imprecision | none | 454/914  (49.7%) | 670/914  (73.3%) | RR 0.68 (0.63 to 0.73) | 235 fewer per 1000 (from 198 fewer to 271 fewer) |  MODERATE | IMPORTANT |
| **Mean duration of the use of antibiotics (Better indicated by lower values)** | | | | | | | | | | | | |
| 7 | randomised trials | serious1 | no serious inconsistency | no serious indirectness | no serious imprecision | none | 760 | 752 | - | MD -2.60 lower (-4.48 to 0.72 lower) |  MODERATE | IMPORTANT |
| **Mortality at longest follow-up** | | | | | | | | | | | | |
| 8 | randomised trials | no serious risk of bias | no serious inconsistency | no serious indirectness | Serious2 | none | 50/649  (7.7%) | 45/655  (6.9%) | RR 1.12 (0.77 to 1.63) | 8 more per 1000 (from 16 fewer to 43 more) |  MODERATE | IMPORTANT |
| **Exacerbation recurrence rate at longest follow-up** | | | | | | | | | | | | |
| 5 | randomised trials | serious1 | no serious inconsistency | no serious indirectness | Serious2 | none | 133/378  (35.2%) | 140/386  (36.3%) | RR 0.99 (0.83 to 1.16) | 4 fewer per 1000 (from 62 fewer to 58 more) |  LOW | IMPORTANT |
| **Re-hospitalization rate at longest follow up** | | | | | | | | | | | | |
| 6 | randomised trials | serious1 | no serious inconsistency | no serious indirectness | Serious2 | none | 91/482  (18.9%) | 80/486  (16.5%) | RR 1.15 (0.88 to 1.5) | 25 more per 1000 (from 20 fewer to 82 more) |  LOW | IMPORTANT |

1 None of the included trials was blinded  
2 Not meeting optimal information size (OIS) criterion. OIS criterion was calculated accepting a Type 1 error rate a=0.05 and Power 1-β=80%

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Supplemental 10. Forrest plot of antibiotic treatment for patients with low PCT levels on re-hospitalization rate at 30-day follow up.

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Supplemental 11. Forrest plot of antibiotic treatment for patients with low PCT levels on overall mortality rate at 30-day fellow up.