**Evidence Table H1. Data abstraction of systematic reviews**

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| **Author, Year**  **Country** | **Aims** | **Timeperiod Covered** | **Eligibility Criteria** |
| Aabenhus, 2014  Denmark | To assess the benefits and  harms of point-of-care biomarker tests of infection to guide antibiotic treatment in patients presenting with symptoms of acute respiratory infections in primary care settings regardless of age. | Through January 2014 | Study Designs:  Randomized controlled trials (RCTs) and cluster-RCTs in primary care.  Participants:  Patients of all ages defined as having ARIs.  Interventions:  (1) Point-of-care biomarkers including C-reactive protein, procalcitonin and white blood cell count. Excluded Strep A test or Monospot.  (2) Standard of care.  Outcome Measures: Primary  (1) Number of patients given an antibiotic prescription at the index consultation and at 28 days followup.  (2) Number of patients with substantial improvement (including full recovery) at day seven. (3) Total mortality at 28 days followup.  Secondary  (1) Number of patients in need of a reconsultation at 28 days followup.  (2) Number of patients in need of a hospital admission at 28 days followup.  (3) Duration of the ARI (e.g. mean or median days with restrictions in daily activities due to the infection).  (4) Number of satisfied patients.  (5) Number of patients with substantial improvement (including full recovery) at 28 days followup. |

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| **Author, Year**  **Country** | **Number of**  **Participants** | **Characteristics of Identified**  **Articles: Study Designs** | **Characteristics of Identified Articles:**  **Populations** | **Characteristics of Identified Articles:**  **Interventions** |
| Aabenhus, 2014  Denmark | 3,284 | RCTs studying the treatment of  ARIs with the C-reactive protein point-of-care test versus the standard of care. | Adults and children with:  (1) Cough  (2) Discolored/increased sputum  (3) Fever  (4) Runny nose  (5) Respiratory distress  (6) Feeling unwell  (7) Combinations of focal and systemic symptoms having a duration of less than four weeks  Diagnoses included:  (1) Lower or upper respiratory tract infection  (2) Pneumonia  (3) Bronchitis  (4) Acute exacerbations of chronic obstructive pulmonary disease or asthma (5) Pharyngitis  (6) Tonsillitis  (7) Laryngitis  (8) Rhinosinusitis, (9) Common cold  (10) Acute otitis media  (11) Influenza | (1) Point-of-care test vs. the standard of care  (no point-of-care test)  \*The only point-of-care biomarker of infection available to primary care at the time of this review was C-reactive protein. |

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| **Author, Year**  **Country** | **Main Results** | **Adverse Events** |
| Aabenhus, 2014  Denmark | KQ 1: A reduction in the use of antibiotic treatments was found in the C-reactive protein group (631/1685) versus  standard of care (785/1599). The pooled result showed a statistically significant effect of C-reactive protein testing on the number of antibiotic prescriptions issued in  primary care settings for ARIs, RR: 0.78, 95% CI: 0.66 to 0.92. Appropriateness of antibiotic prescribing and use  NR/not defined. KQ 2: NR  KQ 3: No deaths or serious complications were reported in any of the studies. Five of the six studies reported that there had been no hospitalizations in the followup period, 30 hospitalizations in the C-reactive protein group reported in Little  2013, 15 cases reviewed: cardiac (two); respiratory (eight), generally unwell/fever (two); gastrointestinal symptoms  (two); sinusitis (one). All hospitalizations may not have been directly related to the intervention.  KQ 4:  Patient satisfaction: Detected no differences. However, unable to draw clear conclusions as only 2 of the included studies reported this outcome.  Reconsultation rates: There were no significant differences in reconsultation rates.  Patient symptoms: No difference between using a C-reactive protein point-of-care test and standard care in clinical recovery (defined as at least substantial improvement at day 7 and 28 or need for re-consultations day 28). No differences were observed in patient-reported measures (e.g. mean or median days with restrictions in daily activities due to the infection).  KQ 5: NR | KQ 6: NR |

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| **Author, Year**  **Country** | **Aims** | **Timeperiod Covered** | **Eligibility Criteria** |
| Doan, 2014  Canada | Determine if the use of a  rapid viral detection test for children with an ARI in EDs changes patient management and resource use (including precautionary testing, antibiotic use, and length of visit) in the ED, compared with not using a rapid viral detection test | Through December  2011 | Study Designs:  RCTs evaluating the use of rapid viral diagnosis in children admitted to the ED with an ARI  Participants:  (1) Studies of otherwise healthy children aged 0-18 years old  (2) Studies which reported separately on subgroups of children under 18 years of age, admitted to an ED with a clinical presentation consistent with ARI (fever and respiratory symptoms such as cough, runny nose, sore throat, or congested nose)  Interventions:  Rapid viral diagnosis from nasal pharyngeal aspirates or swabs by direct or indirect immunofluorescent test, enzyme immunoassays, optical immunoassay, or molecular testing such as multiplex polymerase chain reaction. Results are made available during the participants' stay in the ED  Outcome Measures  Primary Outcomes:  (1) Antimicrobial prescription rate in the ED (reduction of antibiotic use by 25% [RR=0.75]  as clinically important)  Secondary Outcomes:  (1) Length of ED stay (reduction of 30 minutes considered clinically important)  (2) Rate of ancillary tests (any blood tests or chest imaging or urine investigations) requested (reduction in ancillary testing of 25% [RR=0.75] considered clinically important) (3) Rate of physician visit (ED or office) within 2 weeks after discharged from ED (relative increase in physician visit within 2 weeks of discharge from an ED or 10% [RR=1.10] considered clinically important) |
| Doan, 2014  Canada  Continued. |  |  | (4) Hospital admission rate (reduction in admission rate of 25% [RR=0.75] considered  clinically important)  (5) Acceptability of nasal specimen collection sampling for rapid viral testing (discomfort level with invasiveness of the procedure) |

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| Doan, 2014  Canada | 1,588 (759 in  rapid viral testing group, 829 in control group) | Three RCTs and one quasi-RCT  were included | Bonner 2003: Previously healthy  participants, age 2 months to 21 years old, presenting to ED with fever, respiratory symptoms, malaise, or headaches of ≤ 72 hours duration  Poehling 2006: children < 5 years old presenting to ED with fever or acute respiratory symptoms during the 2002-  2003 and 2003-2004 influenza seasons  Iyer 2006: children 2 to 24 months of age presenting to ED with fever  Doan 2009: previously healthy children age 3 to 36 months old presenting to ED with fever and any respiratory symptoms | Bonner 2003:  Treatment: results of nasopharyngeal swab for rapid influenza testing using FluOIA test (turnaround time < 25 minutes) being revealed to treating physicians at initial patient assessment  Control: results of the rapid test were not made available to the treating physicians  Poehling 2006:  Treatment: results of rapid influenza testing were made available to the treating physician prior to patient assessment  Control: standard testing with results made unavailable until the subject had been discharged from the ED  Iyer 2006:  Treatment: nasal swab for rapid influenza testing (using Quickvue), providing a result within 30 minutes  Control: nasal swab for rapid influenza testing (using Quickvue), but these were performed only twice daily to simulate routine laboratory testing turnaround, and results were not made available to the treating physician using the patient had been discharged from the ED |
| Doan, 2014  Canada  Continued. |  |  |  | Doan 2009:  Treatment: nasopharyngeal aspirate for rapid respiratory virus panel (influenza A/B, parainfluenza 1/2/3, RSV, Adenovirus) using direct immunofluorescence assay (Light Diagnostics SimulFluor Respiratory Screening agent)  Control: routine admission to ED. Any test done was requested after assessment by treating physician |

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| **Author, Year**  **Country** | **Main Results** | **Adverse Events** |
| Doan, 2014  Canada | KQ 1:  Antibiotics Prescribed in ED (Rapid Viral Testing vs. Control RR): RR=0.89; 95% Cl, 0.71 to 1.12  Antibiotics Prescribed in ED, sensitivity analysis: 0.86 (0.61 to 1.22) KQ 2: NR  KQ 3: NR  KQ 4:  Blood investigations (e.g. cell count and/or culture) (Rapid Viral Testing vs. Control RR): RR=0.79; 95% Cl, 0.62 to1.00  Blood investigations, sensitivity analysis: 0.61 (0.42 to 0.89)  Urine testing (Rapid Viral Testing vs. Control RR): RR=0.97; 95% Cl, 0.79 to 1.19  Urine testing, sensitivity analysis: 0.93 (0.70 to 1.25)  Chest radiography (Rapid Viral Testing vs. Control RR): RR=0.77; 95% Cl, 0.65 to 0.91  Chest radiography, sensitivity analysis: 0.59 (0.43 to 0.81)  Visits to physician or ED post ED discharge (Rapid Viral Testing vs. Control RR): RR=1.00; 95% Cl, 0.77 to 1.29  KQ 5: NR | KQ 6:  Mean ED length of visit in minutes (Rapid Viral Testing vs. Control, mean  difference; 95% CI): -10.61;  95% Cl, -22.47 to 1.25  Mean ED length of visit in minutes, sensitivity analysis: -19.47 (-51.38 to  12.44) |
| Doan, 2014  Canada  Continued. |  |  |

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| **Author, Year**  **Country** | **Aims** | **Timeperiod Covered** | **Eligibility Criteria** |
| Huang, 2013  China | To systematically review  studies that have examined the association between POC C- reactive protein testing and antibiotic prescribing for RTIs in general practice | Through June 2013 | Population and Interventions:  Studies were included that examined patients who had been diagnosed with RTIs and compared the antibiotic prescribing rate of a POC CRP testing group with a no-POC CRP testing group  Study Designs:  RCTs (including parallel-group RCTs, cluster RCTs, crossover RCTs, and factorial RCTs)  or observational studies |

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| Huang, 2013  China | 10,005 patients  with RTIs | 3 cluster RCTs, 4 parallel-group  RCTs, and 6 observational studies | Included studies of populations from the  Netherlands (4 studies), Norway (3 studies), Denmark (2 studies), Spain (2 studies), Ireland (1 study), and the US (1 study) | POC testing vs. no-POC testing |

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| **Author, Year**  **Country** | **Main Results** | **Adverse Events** |
| Huang, 2013  China | KQ 1:  Antibiotic prescribing at the index consultation\*: RR=0.75; 95% Cl, 0.67 to 0.83  Antibiotic prescribing at any time during the 28-day followup period\*: RR=0.85; 95% Cl, 0.70 to 1.01  KQ 2: NR KQ 3: NR KQ 4:  Patient satisfaction\*: RR=1.07; 95% Cl, 0.98 to 1.17  KQ 5: NR | KQ 6: NR |

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| **Author, Year**  **Country** | **Aims** | **Timeperiod Covered** | **Eligibility Criteria** |
| Schuetz, 2011  Schuetz, 2012  United States, Canada | Schuetz 2011:  Summarize the evidence based on previous RCTs for using PCT measurement in respiratory infections and sepsis from the clinical settings for which the most RCT data are available, namely, primary care, the ED, the medical ICU, and the surgical ICU. Proposed clinical algorithms for use in future US trials  Schuetz 2012:  Assess the safety and efficacy of using procalcitonin for starting or stopping antibiotics over a large range of patients with varying severity of ARIs and from different clinical  settings | Through 2011 | Study Designs:  Schuetz 2011:  RCTs including adults with a diagnosis of respiratory tract infections (i.e. pneumonia, acute exacerbations of COPD, or other respiratory tract infections) or sepsis  Schuetz 2012:  RCTs of adult participants with ARIs who received an antibiotic treatment either based on a procalcitonin algorithm or usual care/guidelines  Clinical Settings:  Primary care, the ED, or the ICU  Interventions:  Measurement of PCT levels to inform decisions regarding antibiotic therapy (i.e. regarding its initiation and/or duration)  Primary Endpoints:  Schuetz 2012: all-cause mortality and treatment failure at 30 days  Secondary Endpoints:  Schuetz 2012: antibiotic use, length of hospital stay, length of ICU stay, number of days with restricted activities within 14 days after randomization |

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| Schuetz, 2011  Schuetz, 2012  United States, Canada | 4,221 total  (2,610 in studies applicable to present review, e.g. primary care and select ED settings) | 4 RCTs applicable to present  review (2 multicenter noninferiority; 1 ED only, single center; 1 ED and inpatient multicenter) | Subjects with upper and lower RTI (2  studies) or CAP, AECOPD, bronchitis (2 studies) | Algorithm by PCT Level (µg/L)  Primary care setting: <0.10, SRAA; 0.10-0.25, RAA; > 0.25, FRA; recheck PCT level at 6-24 hours if no antibiotics initiated; or <0.25, RAA;  >0.25. RFA  ED settings: <0.10, SRAA; 0.10-0.25, RAA;  0.25-0.50, RFA; >0.50, SRFA; recheck PCT level after 6-24 hours if no antibiotics initiated; or <0.10, SRAA; 0.10-0.25, RAA; 0.25-0.50, RFA; >0.50, SRFA; retest PCT level every 2 days; discontinue antibiotics with same cutoffs |

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| **Author, Year**  **Country** | **Main Results** | **Adverse Events** |
| Schuetz, 2011  Schuetz, 2012  United States, Canada | KQ 1:  *Schuetz 2011*  Briel 2008:  Antibiotics Use, Control vs. PCT Prescription: 97% vs. 25% Duration (mean): 7.1 vs. 6.2 days Relative Reduction, % Prescription: -74  Duration: -13  Burkhardt 2010:  Antibiotics Use, Control vs. PCT Prescription: 36.7% vs. 21.5% Duration (mean): 7.7 vs. 7.8 days Relative Reduction, % Prescription: -42  Duration: 1  *Schuetz 2012*  PCT (n (%)) vs. Control (n (%)), Adjusted OR; 95% CI; p  Initiation of antibiotics, Upper ARI: 43 (15) ED. 129 (48), OR=0.14; 95% Cl, 0.09 to 0.22; p< 0.001  Initiation of antibiotics, Acute bronchitis: 61 (24) vs. 185 (66), OR=0.15; 95% Cl, 0.10 to 0.23; p< 0.001  PCT (median (IQR)) vs. Control (median (IQR)), Adjusted OR; 95% CI; p  Duration of antibiotics in days, Upper ARI: 7 (5 to 8) vs. 7 (6 to 7), OR=-1.16; 95% Cl, -2.08 to -0.24; p=0.013  Total exposure of antibiotics in days, Upper ARI: 0 (0 to 0) vs. 0 (0 to 7), OR=-2.64; 95% Cl, -3.16 to -2.11; p< 0.001  Duration of antibiotics in days, Acute bronchitis: 7 (4 to 9) vs. 7 (5 to 8), OR=-0.38; 95% Cl, -1.21 to 0.46; p=0.375  Total exposure of antibiotics in days, Acute bronchitis: 0 (0 to 0) vs. 5 (0 to 7), OR=-3.06; 95% Cl, -3.69 to -2.43; p<  0.001 | KQ 6: NR |

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| **Author, Year**  **Country** | **Aims** | **Timeperiod Covered** | **Eligibility Criteria** |
| Schuetz, 2011  Schuetz, 2012  United States, Canada  Continued. |  |  |  |
| Spurling, 2013  Australia, United  States | Evaluate use of delayed  antibiotics compared with immediate or no antibiotics as a prescribing strategy for ARTIs | Through February  2013 | Study Designs:  Randomized controlled trials and open randomized trials  Participants:  Patients of all ages defined as having ARTIs  Interventions:  (1) Delayed antibiotic use defined as strategy involving use of or advice to use antibiotics more than 48 hours after initial consultation  (2) Immediate antibiotic use defined as immediate use of prescription oral antibiotics given at initial consultation  (3) No antibiotic use defined as no prescription of antibiotics at initial consultation  Outcome Measures: Primary  (1) Clinical outcomes for sore throat, AOM, bronchitis, common cold  (2) Antibiotic use  (3) Patient satisfaction  (4) Antibiotic resistance  Secondary  (1) Adverse events of antibiotics  (2) Complications of disease  (3) Re-consultation  (4) Use of alternative therapies |

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| Schuetz, 2011  Schuetz, 2012  United States, Canada  Continued. |  |  |  |  |
| Spurling, 2013  Australia, United  States | 3,157 | RCTs studying the treatment of  ARTIs with delayed antibiotics versus immediate or no antibiotics | Adults and children with:  (1) common cold or  (2) cough or  (3) sore throat or  (4) cough and at least one symptom or sign localizing to lower respiratory tract  Children with: (1) AOM or  (2) sore throat | (1) Delayed antibiotics vs. immediate  antibiotics  (2) No antibiotics vs. delayed antibiotics  (3) Delayed antibiotics vs. immediate antibiotics vs. no antibiotics |

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| **Author, Year**  **Country** | **Main Results** | **Adverse Events** |
| Schuetz, 2011  Schuetz, 2012  United States, Canada  Continued. | KQ 2: NR  KQ 3:  *Schuetz 2011*  PCT Algorithm vs. No PCT Algorithm, Total; Weight, %; Fixed, Peto OR; 95% CI Mortality in Primary Care Trials: 507 vs. 501, 0.3, OR=0.13; 95% Cl, 0 to 6.64  *Schuetz 2012:* PCT (n (%)) vs. Control (n (%)), Adjusted OR; 95% CI; p  Mortality, Upper ARI: 0 (0) vs. 1 (0.4); NR; NR  Treatment failure, Upper ARI: 93 (33.0) vs. 92 (34.5), OR=0.95; 95% Cl, 0.73 to 1.24; p=0.687  Mortality, Acute Bronchitis: 0 (0) vs. 2 (0.8); NR; NR  KQ 4:  *Schuetz 2012:* PCT (median (IQR)) vs. Control (median (IQR)), Adjusted OR; 95% CI; p  Days with Restricted Activities: 9 (6 to 14) vs. 9 (5 to 14), OR=0.05; 95% Cl, -0.46 to 0.56, p=0.854  KQ 5: NR |  |
| Spurling, 2013  Australia, United  States | KQ 1: Delayed antibiotics resulted in a significant reduction in antibiotic use compared with immediate antibiotics. A 'no  antibiotics' strategy resulted in the least antibiotic use. Appropriateness of antibiotic prescribing and use NR/not defined.  KQ 2: NR  KQ 3: Minor differences in clinical AEs of antibiotics with no significant difference in complication rates. Antibiotic resistance: NR.  KQ 4:  Patient satisfaction  Delayed vs. immediate antibiotics, OR; 95% CI: OR=0.52; 95% Cl, 0.35 to 0.76  Overall 92% of participants in immediate antibiotics arms were satisfied vs. 87% in the delayed arms. Delayed vs. no antibiotics, OR; 95% CI: OR=1.44; 95% Cl, 0.99 to 2.10  Reconsultation rates: no difference between immediate and delayed groups  Patient symptoms: no difference between delayed, immediate, and no prescribed antibiotics for clinical outcomes evaluated in cough and common cold. In patients with AOM and sore throat, immediate antibiotics were more effective than delayed for fever, pain, and malaise in some studies.  KQ 5: NR | KQ 6: NR |