Online Supplement

Summary of Findings table profiles

Question #1: In intubated patients suspected of having VAP should distal quantitative samples be obtained instead of proximal-quantitative samples?	Profile # 1 and 2
Question #2: Can patients suspected of having nosocomial pneumonia (HAP and VAP), who have early onset infection and no risk factors for MDR pathogens, be treated appropriately if they receive a different, and narrower spectrum empiric therapy than patients with late onset infection and/or the presence of MDR risk factors?	Profile # 3 and 4
Question #3: In patients with initial broad spectrum empiric therapy for HAP/VAP does an initial regimen combining two antibiotics targeting Gram-negative bacteria improve outcomes and when culture data are available, does combination therapy need to be continued as definitive therapy, compared to single antimicrobial agent therapy?	Profile # 5, 6 and 7
Question#4: In patients with HAP/VAP can duration of antimicrobial therapy be shortened to 7-10 days for certain populations, as compared to 14 days, without increasing rates of relapsing infections or decreasing clinical cure?	Profile # 8 and 9
Question #5: In patients receiving AB treatment for VAP or HAP, is bedside clinical assessment equivalent to the detection of serial biomarkers to predict adverse outcomes / clinical response at 72-96h?	Profile # 10 and 11
Question #6: In patients with HAP with severe sepsis or VAP, can serum procalcitonin be used to reduce the duration of antibiotic therapy, compared to care that is not guided by serial biomarker measurements?	Profile # 12
Question #7: In patients requiring mechanical ventilation for greater than 48 hours, does topical application of non-absorbable antimicrobials (antibiotics or chlorhexidine) in the oropharynx (SOD) or in the oropharynx and intestinal tract along with intravenous antibiotics (SDD) reduce the risk of VAP occurrence and/or improve patient outcome compared to standard care?	Profile # 13,14 and 15

Profile #1 Quantitative in comparison to qualitative samples in patients suspected of having VAP

Bibliography: Berton DC, Kalil AC, Teixeira PJZ. Quantitative versus qualitative cultures of respiratory secretions for clinical outcomes in patients with ventilator-associated pneumonia. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD006482

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Quantitative**	**qualitative culture**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mortality - 28 days												
3	randomised trials [1]	not serious [2]	not serious	not serious	serious [3]	none	142/614 (23.1%)	159/626 (25.4%)	**RR 0.91** (0.75 to 1.11)	**23 fewer per 1.000** (from 28 more to 63 fewer)	⊕⊕⊕◯ MODERATE	IMPORTANT
Antibiotic change												
2	randomised trials [4]	serious [5]	not serious	not serious	serious [3]	none	286/410 (69.8%)	284/417 (68.1%)	**RR 1.53** (0.54 to 4.39)	**361 more per 1.000** (from 313 fewer to 1.000 more)	⊕⊕◯◯ LOW	CRITICAL
Duration on mechanical ventilation (days)												
2	randomised trials [4]	serious [5]	not serious	not serious	not serious	none	410	417	-	MD **0.58 more** (0.51 fewer to 1.68 more)	⊕⊕⊕◯ MODERATE	IMPORTANT
ICU stay (days)												
3	randomised trials [1]	serious [5]	not serious	not serious	not serious	none	614	626	-	MD **0.95 more** (0.14 fewer to 2.04 more)	⊕⊕⊕◯ MODERATE	IMPORTANT
Number of antibiotic-free days												
2	randomised trials [6]	serious [5]	not serious	serious [7]	not serious	none	Fagon 2000: Invasive distal quantitative strategy vs. qualitative non-invasive methods: significant increase in the day-14 antibiotic free-days (5.0 ± 5.1 vs. 2.2 ± 3.5) and day-28 antibiotic free-days (11.5 ± 9.0 vs. 7.5 ± 7.6) CCTG 2006: no differences between groups in the day-28 antibiotic free-days				⊕⊕◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

1. CCTG 2006, Sole Violan 2000, Fagon 2000

2. Even though 2/3 studies were not blinded, it is unlikely that this affect this outcome. One study had incomplete outcome data but analysis was according to intention to treat population
3. 95% IC of the absolute values result in a appreciable benefit or appreciable harm
4. CCTG 2006 and Sole Violan 2000
5. One or more study(ies) was/were not blinded, review authors believe that this did affected subjective outcomes
6. CCTG 2006, Fagon 2000
7. One study used a guideline for antibiotic deescalation whereas the other did not.

Profile #2 Invasive in comparison to non-invasive samples in patients suspected of having VAP

Bibliography: Berton DC, Kalil AC, Teixeira PJZ. Quantitative versus qualitative cultures of respiratory secretions for clinical outcomes in patients with ventilator-associated pneumonia. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD006482

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Invasive**	**non-invasive method**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mortality												
5	randomised trials	not serious [1]	not serious	not serious	serious [2]	none	167/675 (24.7%)	184/692 (26.6%)	**RR 0.93** (0.78 to 1.11)	**19 fewer per 1.000** (from 29 more to 58 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

1. Even though some studies were not blinded, it is unlikely that this affect this outcome
2. 95%CI included appreciable benefit or harm

Profile #3 Prognostic factors of multi-drug resistant pathogens in ICU patients with pneumonia and frequency of MDR pathogens in early-onset VAP

Bibliography:

-Martin-Loeches I, Deja M, Koulenti D, Dimopoulos G, Marsh B, Torres A, Niederman MS, Rello J; EU-VAP Study Investigators. Potentially resistant microorganisms in intubated patients with hospital-acquired pneumonia: the interaction of ecology, shock and risk factors.Intensive Care Med. 2013;39(4):672-81.
-Verhamme KM1, De Coster W, De Roo L, De Beenhouwer H, Nollet G, Verbeke J, Demeyer I, Jordens P. Pathogens in early-onset and late-onset intensive care unit-acquired pneumonia. Infect Control Hosp Epidemiol. 2007;28(4):389-97.
-Ferrer M1, Liapikou A, Valencia M, Esperatti M, Theessen A, Antonio Martinez J, Mensa J, Torres A. Validation of the American Thoracic Society-Infectious Diseases Society of America guidelines for hospital-acquired pneumonia in the intensive care unit. Clin Infect Dis. 2010;50(7):945-52.
- Montravers P, Veber B, Auboyer C, Dupont H, Gauzit R, Korinek AM, Malledant Y, Martin C, Moine P, Pourriat JL. Diagnostic and therapeutic management of nosocomial pneumonia in surgical patients: results of the Eole study. Crit Care Med. 2002;30(2):368-75
- Arvanitis M1, Anagnostou T1, Kourkoumpetis TK2, Ziakas PD3, Desalermos A2, Mylonakis E. The impact of antimicrobial resistance and aging in VAP outcomes: experience from a large tertiary care center. PLOS One 2014; 9:e89984
- Leroy O, Jaffré S, D'Escrivan T, Devos P, Georges H, Alfandari S, Beaucaire G. Hospital-acquired pneumonia: risk factors for antimicrobial-resistant causative pathogens in critically ill patients. Chest. 2003;123(6):2034-42.
- Perbet S, Mongardon N, Dumas F, Bruel C, Lemiale V, Mourvillier B, Carli P, Varenne O, Mira JP, Wolff M, Cariou A. Early-onset pneumonia after cardiac arrest: characteristics, risk factors and influence on prognosis. Am J Respir Crit Care Med. 2011;184(9):1048-54
- Restrepo MI, Peterson J, Fernandez JF, Qin Z, Fisher AC, Nicholson SC. Comparison of the bacterial etiology of early-onset and late-onset ventilator-associated pneumonia in subjects enrolled in 2 large clinical studies.Respir Care. 2013 ;58(7):1220-5.

Quality assessment							Measure of effect	Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relative (95% CI) / Frequency (%)**		
Presence of severe sepsis / shock									
1	observational studies [1]	not serious	not serious	Very serious [2]	not serious	none	**OR 3.7** (1.5 to 8.9)	⊕⊕◯◯ LOW	IMPORTANT
Centres with >25% prevalence of MDR pathogens									
1	observational studies [1]	not serious	not serious	Very serious [2]	not serious	none	**OR 11.3** (2.1 to 59.3)	⊕⊕◯◯ LOW	IMPORTANT
Older age and previous antibiotic prophylaxis									

Quality assessment							Measure of effect	Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative (95% CI) / Frequency (%)		
1	observational studies [3]	not serious	not serious	Very serious [2]	not serious	none	**OR 4.6** (1.6 to 13.0)	⨁⨁◯◯ LOW	IMPORTANT
Previous antibiotic therapy									
1	observational studies [3]	not serious	not serious	Very serious [2]	not serious	none	**OR 8.2** (2.8 to 23.8)	⨁⨁◯◯ LOW	IMPORTANT
Incidence of MDR pathogens among ventilated patients with early-onset pneumonia									
7	observational studies[4]	not serious	serious [5]	Very serious [2]	not serious	none	From 10% to 51%	⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **OR:** Odds ratio

1. Martin-Loeches 2013
2. Not directly answering the question about the use of broad or narrow spectrum antibiotic use
3. Verhamme 2007
4. Martin-Loeches 2013, Ferrer 2010, Montravers 2002, Arvanitis 2014, Leroy 2003, Perbet 2011, Restrepo 2013
5. Estimates varied broadly

Profile #4 Narrow spectrum antibiotics in patients without risk factors for multi-drug resistant pathogens

Bibliography:

Ferrer M1, Liapikou A, Valencia M, Esperatti M, Theessen A, Antonio Martinez J, Mensa J, Torres A. Validation of the American Thoracic Society-Infectious Diseases Society of America guidelines for hospital-acquired pneumonia in the intensive care unit. Clin Infect Dis. 2010;50(7):945-52.

Leone M, Garcin F, Bouvenot J, Boyadjev I, Visintini P, Albanèse J, Martin C. Ventilator-associated pneumonia: breaking the vicious circle of antibiotic overuse. Crit Care Med. 2007;35(2):379-85

Quality assessment							Measure of effect Frequency (%)	Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Escalation to broader spectrum antibiotic									
1	observational studies [1]	not serious	not serious	serious [2]	not serious	none	43% of patients with early-onset VAP without risk factors, treated with narrow spectrum antibiotics presented initial non-response to therapy.	⊕◯◯◯ VERY LOW	IMPORTANT
Initial non-response to treatment									
1	observational studies [3]	not serious	not serious	serious [2]	not serious	none	26.6% of patients with early-onset VAP without risk factors, treated with narrow spectrum antibiotics had to receive a broader spectrum antibiotic.	⊕◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval

1. Ferrer 2010
2. Non-comparative results between narrow spectrum and broad spectrum in non-risk factors
3. Leone 2007

4.

Profile #5 Combination of two antibiotics compared to single antimicrobial agent therapy for patients suspected VAP (ventilator associated pneumonia)

Bibliography: Aarts MA, Hancock JN, Heyland D, McLeod RS, Marshall JC. Empiric antibiotic therapy for suspected ventilator-associated pneumonia: a systematic review and meta-analysis of randomized trials. Crit Care Med. 2008 Jan;36(1):108-17.

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**single agent**	**combination**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mortality												
8	randomised trials	not serious	not serious	not serious [1]	serious [2]	none	132/720 (18.3%)	145/739 (19.6%)	**RR 0.94** (0.76 to 1.16)	**12 fewer per 1.000** (from 31 more to 47 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Treatment failure												
7	randomised trials	serious [3]	not serious	not serious [1]	serious [2]	none	272/828 (32.9%)	284/803 (35.4%)	**RR 0.88** (0.72 to 1.07)	**42 fewer per 1.000** (from 25 more to 99 fewer)	⊕⊕◯◯ LOW	CRITICAL
Superinfections (assessed with: New, persistent, or worsening signs of infection associated with the isolation of a new pathogen or similar pathogen with a different antibiotic susceptibility profile or site of infection)												
n.s.	randomised trials	serious [3]	not serious	not serious	serious [2]	none	n.s.	n.s.	**RR 0.77** (0.48 to 1.22)		⊕⊕◯◯ LOW	IMPORTANT
Serious Adverse Events												
n.s.	randomised trials	serious [3]	not serious	not serious	serious [2]	none	n.s.	n.s.	**RR 0.84** (0.48 to 1.49)		⊕⊕◯◯ LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio; **n.s**: not specified

1. Although not all patients were under mechanical ventilation (85% approximately)
2. 95% CI includes appreciable benefit or harm.
3. Most studies not blinded, that would have affected this subjective outcome. Some with no ITT analysis

Profile #6 Combination of two antibiotics compared to single antimicrobial agent therapy for patients suspected HAP(hospital-acquired pneumonia)

Bibliography:

- Fernández-Guerrero M, Gudiol F, Rodriguez-Torres A, Arnau C, Valdés L, Vallvé C. Nosocomial pneumonia: comparative multicentre trial between monotherapy with cefotaxime and treatment with antibiotic combinations. Infection. 1991;19 Suppl 6:S320-5.
-Rubinstein E, Lode H, Grassi C. Ceftazidime monotherapy vs. ceftriaxone/tobramycin for serious hospital-acquired gram-negative infections. Antibiotic Study Group. Clin Infect Dis. 1995 May;20(5):1217-28.
-Jaspers CA, Kieft H, Speelberg B, Buiting A, van Marwijk Kooij M, Ruys GJ, Vincent HH, Vermeulen MC, Olink AG, Hoepelman IM. Meropenem versus cefuroxime plus gentamicin for treatment of serious infections in elderly patients. Antimicrob Agents Chemother. 1998 May;42(5):1233-8.
-Awad SS, Rodriguez AH, Chuang YC, Marjanek Z, Pareigis AJ, Reis G, Scheeren TW, Sánchez AS8, Zhou X, Saulay M, Engelhardt M. A phase 3 randomized double-blind comparison of ceftobiprole medocaril versus ceftazidime plus linezolid for the treatment of hospital-acquired pneumonia. Clin Infect Dis. 2014 Jul 1;59(1):51-61.

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**single agent**	**combination**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mortality (any combination vs. single therapy)												
2	randomised trials [1]	not serious [2]	not serious	not serious	serious [3]	none	84/567 (14.8%)	103/592 (17.4%)	**RR 0.85** (0.65 to 1.11)	**26 fewer per 1.000** (from 19 more to 61 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Subgroup: Mortality (cephalosporin vs. cephalosporin + aminoglycoside)												
1	randomised trials [4]	not serious [2]	not serious [5]	serious [6]	serious [3]	none	36/275 (13.1%)	52/273 (19.0%)	**RR 0.69** (0.47 to 1.02)	**59 fewer per 1.000** (from 4 more to 101 fewer)	⊕⊕◯◯ LOW	IMPORTANT
Subgroup: Mortality (cephalosporin vs. cephalosporin + oxazolidinone)												
1	randomised trials [7]	not serious	not serious [5]	not serious	serious [3]	none	48/287 (16.7%)	51/284 (18.0%)	**RR 0.93** (0.65 to 1.33)	**13 fewer per 1.000** (from 59 more to 63 fewer)	⊕⊕⊕◯ MODERATE	IMPORTANT
Clinical cure at the end of treatment (any combination vs. single therapy)												
4	randomised trials [8]	serious [9]	not serious	not serious	not serious	none	497/741 (67.1%)	360/605 (59.5%)	**RR 1.10** (1.02 to 1.19)	**60 more per 1.000** (from 12 more to 113 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Subgroup: Clinical cure at the end of treatment (cephalosporin vs. cephalosporin + aminoglycoside)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**single agent**	**combination**	**Relative (95% CI)**	**Absolute (95% CI)**		
2	randomised trials [10]	serious [11]	not serious	not serious	not serious	none	309/434 (71.2%)	177/300 (59.0%)	**RR 1.17** (1.05 to 1.30)	**100 more per 1.000** (from 30 more to 177 more)	⨁⨁⨁◯ MODERATE	IMPORTANT
Subgroup: Clinical cure at the end of treatment (cephalosporin vs. cephalosporin + oxazolidinone)												
1	randomised trials [7]	not serious	not serious [5]	not serious	serious [3]	none	171/287 (59.6%)	167/284 (58.8%)	**RR 1.01** (0.88 to 1.16)	**6 more per 1.000** (from 71 fewer to 94 more)	⨁⨁⨁◯ MODERATE	IMPORTANT
Subgroup: Clinical cure at the end of treatment (carbapenem vs. cephalosporin + aminoglycoside)												
1	randomised trials [12]	serious [13]	not serious [5]	not serious	serious [3]	none	17/20 (85.0%)	16/21 (76.2%)	**RR 1.12** (0.83 to 1.51)	**91 more per 1.000** (from 130 fewer to 389 more)	⨁⨁◯◯ LOW	IMPORTANT
Adverse events												
4	randomised trials	serious [9]	not serious [14]	serious [15]	not serious [16]	none	[Fernández-Guerrero 1991]: The frequency of serious adverse reactions was significantly higher in the group treated with antibiotic combinations. [Jaspers 1998]: Renal failure occurred during therapy in 2 of 39 (5%) meropenem recipients compared with 5 of 40 (13%) of those treated with combination therapy. [Rubinstein 1995]: Both regimens were well tolerated [Awad 2014]: Treatment-related AEs were reported for 96 ceftobiprole patients (24.9%) and 98 ceftazidime/linezolid patients (25.4%)				⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

1. Awad2014, Fernandez-Guerrero 1991
2. Even though one study was not blinded, this may not affect the results of this objective outcome
3. Low number of events. 95% CI includes appreciable harm or benefit
4. Fernandez-Guerrero 1991
5. single study
6. Only 60% of the combination therapy arm included a cephalosporin plus aminoglycoside
7. Awad 2014
8. Awad 2014, Jaspers 1998, Rubinstein 1995, Fernandez-Guerrero 1991
9. Two of four studies with serious limitations
10. Jaspers 1998, Rubinstein 1995
11. One study non-blinded, results from subgroup analysis in one study
12. Fernandez-Guerrero 1991

13. Post-hoc subgroup analysis, unblinded, large number of patients were lost of follow-up
14. Not pooled
15. Adverse events under different categories
16. Not pooled but probably not a problem

Profile #7 Combination of two antibiotics compared to single antimicrobial agent therapy for patients with high-risk life-threatening infections and MDR bacteria

Bibliography: Kumar A, Safdar N, Kethireddy S, Chateau D. A survival benefit of combination antibiotic therapy for serious infections associated with sepsis and septic shock is contingent only on the risk of death: A meta-analytic/meta-regression study. Crit Care Med 2010;38:1651-1664.

Tzouvelekis LS, Markogiannakis A, Piperaki E, Souli M, Daikos GL. Treating infections caused by carbapenemase-producing enterobacteriaceae. Clin Microbiol Infect 2014;20:862-872.

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**single agent**	**combination**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mortality – patients with shock / critical illness												
12	Randomised and observational studies	not serious	not serious	Serious [1]	not serious	none	128/252 (50.1%)	211/550 (38.4%)	**OR 0.51** (0.36 to 0.72)	**143 fewer per 1.000** (from 74 fewer to 201 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Mortality – patients with carbapenemase-producing Klebsiella pneumonia												
n.s	Observational studies	not serious	not serious[2]	Serious [3]	not serious	none	45/96 (46.7%)	72/247 (29.1%)	**OR 0.47** (0.29 to 0.76)	**22 fewer per 1.000** (from 13 fewer to 35 fewer)	⊕◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **n.s**: not specified

1. Studies including patients with different conditions (not all HAP or VAP). Data were only calculated for monotherapy treatment with beta-lactam and/or fluoroquinolones
2. Data not provided
3. Data only for one type of microorganism

Profile #8: Short (fixed)-course antibiotic therapy compared to prolonged-course antibiotic therapy for HAP in HAP (hospital-acquired pneumonia)

Bibliography: Dimopoulos G, IA, Armaganidis A, Kollef MH, Matthaiou DK. Short- vs long-duration antibiotic regimens for ventilator-associated pneumonia: a systematic review and meta-analysis. Chest 2013; 144(6):1759-67

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Short course**	**prolonged-course**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mortality - all cause (follow up: range 21-28 days to)												
4	randomised trials	not serious [1]	not serious	not serious	serious [2]	none	78/442 (17.6%)	68/441 (15.4%)	**OR 1.20** (0.84 to 1.72)	**25 more per 1.000** (from 21 fewer to 85 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Mortality in patients with nonfermentative gram-negative bacteria (follow up: range 28 days to)												
2	randomised trials	not serious [1]	serious [3]	not serious	serious [2]	none	27/111 (24.3%)	23/101 (22.8%)	**OR 1.33** (0.33 to 5.26)	**54 more per 1.000** (from 139 fewer to 380 more)	⊕⊕◯◯ LOW	IMPORTANT
Adverse events												
2	randomised trials	serious [4]	not serious [5]	not serious [6]	not serious [5]	none			Treatment discontinuation due to adverse events may be similar between both treatment options and shorter treatment duration is expected to be associated to better tolerability		⊕⊕⊕◯ MODERATE	CRITICAL
Emergence of resistances (assessed with: Secondary infections to resistant bacteria)												
2	randomised trials	not serious	not serious	not serious	serious [2]	none	42/98 (42.9%)	43/74 (58.1%)	**OR 0.56** (0.30 to 1.04)	**144 fewer per 1.000** (from 10 more to 287 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Antibiotic free days (follow up: median 28 days)												
2	randomised trials	not serious [1]	serious [3]	not serious	not serious	none	211	220	-	MD **3.4 more** (1.43 more to 5.37 more)	⊕⊕⊕◯ MODERATE	IMPORTANT
Relapses (follow up: median 60 days)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Short course**	**prolonged-course**	**Relative (95% CI)**	**Absolute (95% CI)**		
3	randomised trials	not serious [1]	not serious	not serious	serious [2]	none	40/329 (12.2%)	26/327 (8.0%)	**OR 1.67** (0.99 to 2.83)	**47 more per 1.000** (from 1 fewer to 117 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Mechanic ventilation free days												
2	randomised trials	not serious [1]	serious [3]	not serious	not serious	none	211	220	-	MD **0.75 more** (0.82 fewer to 1.82 more)	⨁⨁⨁◯ MODERATE	IMPORTANT
Duration of mechanic ventilation												
2	randomised trials	serious [4]	not serious	not serious	not serious	none	130	125	-	MD **0.15 more** (1.12 fewer to 1.42 more)	⨁⨁⨁◯ MODERATE	IMPORTANT
Length Intensive Care Unit stay												
3	randomised trials	serious [4]	not serious	not serious	not serious	none	327	329	-	MD **0.16 more** (0.99 fewer to 1.31 more)	⨁⨁⨁◯ MODERATE	IMPORTANT

CI: Confidence interval; **OR:** Odds ratio; **MD:** Mean difference

1. Overall of good quality. Some RCT open label
2. 95%CI includes large benefit or harm. Low number of events
3. Large heterogeneity
4. Two studies with open design, possible bias for a subjective outcome
5. Not pooled
6. Adverse events assessed using very different definitions

Profile #9: Short (fixed)-course antibiotic therapy compared to prolonged-course antibiotic therapy for HAP in HAP (hospital-acquired pneumonia)

Bibliography:

Singh N, Rogers P, Atwood CW, Wagener MM, Yu VL. Short-course empiric antibiotic therapy for patients with pulmonary infiltrates in the intensive care unit. A proposed solution for indiscriminate antibiotic prescription. American Journal of Respiratory and Critical Care Medicine 2000;162: 505–11

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	3 day Short course	prolonged-course	Relative (95% CI)	Absolute (95% CI)		
Mortality - all cause (at day 3)												
1	randomised trials	not serious	not serious [1]	not serious	serious [2]	serious [3]	0/39 (0%)	3/42 (7%)	**RR 0.15** (0.01 to 2.88)	**1 fewer per 1.000** (from 0 fewer to 20 more)	⊕⊕◯◯ LOW	CRITICAL
Mortality - all cause (at day 30)												
1	randomised trials	not serious	not serious [1]	not serious	serious [2]	serious [3]	5/39 (13%)	13/42 (41%)	**RR 0.41** (0.16 to 1.05)	**17 fewer per 1.000** (from 7 fewer to 43 more)	⊕⊕◯◯ LOW	CRITICAL
Extrapulmonary infections												
1	randomised trials	serious	not serious [1]	not serious	serious [2]	serious [3]	7/39 (18%)	6/39 (15%)	**RR 1.17** (0.43 to 3.16)	**18 more per 1.000** (from 6 fewer to 47 more)	⊕⊕◯◯ LOW	IMPORTANT
Antimicrobial resistance and/or superinfections												
1	randomised trials	not serious	not serious [1]	not serious	serious [2]	serious [3]	5/37 (14%)	14/37 (38%)	**RR 0.36** (0.14 to 0.89)	**14 fewer per 1.000** (from 5 fewer to 34 fewer)	⊕⊕◯◯ LOW	CRITICAL
Length of ICU stay												
1	randomised trials	serious [4]	not serious [1]	not serious	not serious	serious [3]	39	42	-	Median (range) 4 (1-47) vs 9 (1-91), p=0.04	⊕⊕◯◯ LOW	IMPORTANT
CPIS equal or greater than 6 at day 3 (increased likelihood of bacterial pneumonia)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**3 day Short course**	**prolonged-course**	**Relative (95% CI)**	**Absolute (95% CI)**		
1	randomised trials	not serious	not serious [1]	not serious	serious [2]	serious [3]	8/39 (21%)	9/39 (23%)	**OR 0.89** (0.38 to 2.06)	**20 fewer per 1.000** (from 9 fewer to 47 more)	⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **OR:** Odds ratio; **MD:** Mean difference

1. Single study
2. Low number of events
3. Study terminated early (46% of the sample)
4. Study with open design, possible bias for a subjective outcome

Profile #10: Relationship of different biomarkers and clinical scores on 28 days mortality

Luna CM, Blanzaco D, Niederman MS, Matarucco W, Baredes NC, Desmery P, Palizas F, Menga G, Rios F, Apezteguia C. Resolution of ventilator-associated pneumonia: prospective evaluation of the clinical pulmonary infection score as an early clinical predictor of outcome. Crit Care Med. 2003; 31:676-82.

Luyt CE, Guerin V, Combes A, Trouillet JL, Ayed SB, Bernard M, Gibert C, Chastre J: Procalcitonin kinetics as a prognostic marker of ventilator-associated pneumonia. Am J Respir Crit Care Med 2005; 171:48-53.

Boeck L, Eggimann P, Smyrnios N, Pargger H, Thakkar N, Siegemund M, Marsch S, Rakic J, Tamm M, Stolz D. Midregional pro-atrial natriuretic peptide and procalcitonin improve survival prediction in VAP. Eur Respir J 2011; 37:595-603.

Seligman R, Seligman BGS, Teixeira PJ. Comparing the accuracy of predictors of mortality in ventilator-associated pneumonia J Bras Pneumol 2011 ;37; 495-503.

Seligman R, Meisner M, Lisboa TC, Hertz FT, Filippin TB, Fachel JM, Teixeira PJ. Decreases in procalcitonin and C-reactive protein are strong predictors of survival in ventilator-associated pneumonia. Crit Care. 2006;10:R125.

Póvoa P, Coelho L, Almeida E, Fernandes A, Mealha R, Moreira P, Sabino H. C-reactive protein as a marker of ventilator-associated pneumonia resolution: a pilot study. Eur Respir J. 2005 May;25:804-12.

Tanrıverdi H, Tor MM, Kart L, Altın R, Atalay F, SumbSümbüloğlu V. Prognostic value of serum procalcitonin and C-reactive protein levels in critically ill patients who developed ventilator-associated pneumonia. Ann Thorac Med. 2015; 10:137-42.

Boeck L, Eggimann P, Smyrnios N, Pargger H, Thakkar N, Siegemund M, Morgenthaler NG, Rakic J, Tamm M, Stolz D. The Sequential Organ Failure Assessment score and copeptin for predicting survival in ventilator-associated pneumonia. J Crit Care 2012; 27:523.e1-9. doi: 10.1016/j.jcrc.2011.07.081. Epub 2011 Sep 29.

Quality assessment							Effect	Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Procalcitonin									
4	Observational studies	not serious	not serious [1]	not serious	serious [2]	not serious	OR 4.43 (1.08–18.18) for any increase D0 to D4 OR 22.6 for levels >1 ng/mL on D3 Significant greater levels at D4 in non-survivors Sens/spec: 0.90 / 0.74; for Day 4values >0.47 ng/mL Sens/spec: 0.74 / 0.84; for Day 3values >1.5 ng/mL	⊕⊕⊕◯ MODERATE	CRITICAL

CRP									
4	Observational studies	not serious	not serious [1]	not serious	serious [2]	not serious	OR 7.40 (1.58–34.73) for any increase D0to D4 CRP ratio (0.1 increment); OR 1.401 (1.004–1.957) Non-significant differences in levels at D4between survivors and non-survivors Significant greater levels at D7 in non-survivors Sens/spec: 0.50 / 0.84; for Day 4values >155.5 mg/dL Sens/spec: 0.92 / 0.59; for Day 4CRP ratio >0.6	⊕⊕⊕◯ MODERATE	CRITICAL
MR-proANP									
2	Observational studies	serious	not serious [1]	not serious	serious [2]	not serious	Significant greater levels at D4 in non-survivors Sens/spec: 0.75 / 0.72; for Day 4values >465.5 pmol/L Sens/spec: 0.45 / 0.97; for Day 4values >660 pmol/L	⊕⊕⊕◯ MODERATE	CRITICAL
Copeptin									
2	Observational studies	serious	not serious [1]	not serious	serious [2]	not serious	Significant greater levels at D4 in non-survivors Sens/spec: 0.80 / 0.60; for Day 4values >43 pmol/L OR 1.07 (0.99-1.16) for 10 units increase at baseline	⊕⊕⊕◯ MODERATE	CRITICAL

Clinical scores									
7	Observational studies	serious	not serious [1]	not serious	serious [2]	not serious	**SOFA:** OR 2.25 (0.48–10.46) for any decrease of scores at Day 0 to Day 4 Significant greater levels at D4 in non-survivors Sens/spec: 0.57 / 0.82; for Day 4SOFA score >6 D0 SOFA score (1-point increment); OR 1.469 (1.014–2.127) D0 SOFA score (1-point increment); OR 1.28 (1.10-1.49) **SOFA components:** Age : two studies with significant relationship and two studies with non-significant relationship White Blood Cell counts : two studies with significant relationship and one study with non-significant relationship Temperature: one study with significant relationship and two studies with non-significant relationship Lack of improvement of PaO2/FiO2 values: with significant relationship with mortality in three studies **APACHE II score:** No significant relationship with mortality in multivariate regression analysis **CPIS:** Non-significant differences in levels at D4between survivors and non-survivors. Significant decrease of CPIS scores from onset to Day3,5 and 7	⊕⊕⊕◯ MODERATE	CRITICAL
Combination of biomarkers and clinical scores									
2	Observational studies	serious	not serious [1]	not serious	serious [2]	not serious	Combination of SAPS II, SOFA, ODIN, PCT, MR-proANP serum levels has better diagnostic performance in comparison to single assessment.	⊕⊕⊕◯ MODERATE	CRITICAL

CI: Confidence interval; **OR:** Odds ratio; **MD:** Mean difference

1. No serious inconsistency between studies
2. Pooled results not obtained, most probably results are imprecise for decision making

Profile #11: Relationship of different biomarkers and adequacy of antibiotic therapy

Luna CM, Blanzaco D, Niederman MS, Matarucco W, Baredes NC, Desmery P, Palizas F, Menga G, Rios F, Apezteguia C. Resolution of ventilator-associated pneumonia: prospective evaluation of the clinical pulmonary infection score as an early clinical predictor of outcome. Crit Care Med. 2003; 31:676-82.
Póvoa P, Coelho L, Almeida E, Fernandes A, Mealha R, Moreira P, Sabino H. C-reactive protein as a marker of ventilator-associated pneumonia resolution: a pilot study. Eur Respir J. 2005 May;25:804-12.

Quality assessment							Effect	Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
CRP									
1	Observational studies	not serious	not serious [1]	not serious	serious [2]	not serious	Patients who initially received adequate antibiotics showed a marked CRP ratio decrease in comparison to those with initially inadequate therapy (p<0.001).	⊕⊕⊕◯ MODERATE	CRITICAL
Clinical scores									
1	Observational studies	serious	not serious [1]	not serious	serious [2]	not serious	**CPIS:** Significant improvement in patients receiving adequate AB therapy and worsening in those patients with inadequate AB therapy at Day 3 **SOFA components:** PaO2/FiO2: Significant improvement in patients receiving adequate AB therapy and worsening in those patients with inadequate AB therapy at Day 3	⊕⊕⊕◯ MODERATE	CRITICAL

CI: Confidence interval; **OR:** Odds ratio; **MD:** Mean difference

1. Single study
2. Low number of patients and events

Profile #12 Discontinuation of antibiotic therapy according to serum procalcitonin level compared to not guided discontinuation in HAP / VAP patients

Bibliography: Bouadma L, Luyt CE, Tubach F, et al.. Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial. Lancet 2010;375(9713):463-74. Stolz D, Smyrnios N, Eggimann P, et al. Procalcitonin for reduced antibiotic exposure in ventilator-associated pneumonia: a randomised study. Eur Respir J 2009;34:1364-7. Pontet J, Paciel D, Olivera W, et al. Procalcitonin (PCT) guided antibiotic treatment in ventilator associated pneumonia (VAP). Multicentre, clinical prospective, randomized-controlled study. American Thoracic Society International Conference, San Francisco, California, USA. 2007:A76. de Jong E, van Oers JA, Beishuizen A, et al. Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial. Lancet Infect Dis. 2016 Jul;16(7):819-27

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Discontinuation according to procalcitonin**	**Not guided**	**Relative (95% CI)**	**Absolute (95% CI)**		
28-day mortality												
4	randomised trials	not serious	not serious	not serious	not serious	none	71/735 (18.9%)	96/373 (25.7%)	**OR 0.67** (0.48 to 0.96)	**69 fewer per 1.000** (from 8 fewer to 115 fewer)	⊕⊕⊕ HIGH	CRITICAL
Duration of antibiotic therapy												
3	randomised trials	serious [2]	not serious	not serious	not serious	none	157	151	-	MD **3.2 fewer** (4.45 fewer to 1.95 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
In-hospital mortality												
1	randomised trials	not serious	not serious [3]	not serious	serious [1]	none	10/51 (19.6%)	14/50 (28.0%)	**OR 0.63** (0.25 to 1.58)	**83 fewer per 1.000** (from 101 more to 191 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Intensive Care Unit mortality												
1	randomised trials	serious [4]	not serious [3]	not serious	serious [1]	none	8/31 (25.8%)	11/35 (31.4%)	**OR 0.76** (0.26 to 2.22)	**56 fewer per 1.000** (from 190 more to 208 fewer)	⊕⊕◯◯ LOW	IMPORTANT
Recurrence of pneumonia												
1	randomised trials	serious [5]	not serious [3]	not serious	serious [1]	none	14/31 (45.2%)	10/35 (28.6%)	**OR 2.06** (0.74 to 5.70)	**166 more per 1.000** (from 57 fewer to 409 more)	⊕⊕◯◯ LOW	IMPORTANT
28-day antibiotic-free days												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Discontinuation according to procalcitonin	Not guided	Relative (95% CI)	Absolute (95% CI)		
3	randomised trials	serious [2]	not serious	not serious	serious [6]	none	157	151	-	MD **2.8 more** (1.39 more to 4.21 more)	⨁⨁◯◯ LOW	IMPORTANT
Non-resolution of pneumonia												
1	randomised trials	serious [5]	not serious [3]	not serious	serious [1]	none	8/31 (25.8%)	8/35 (22.9%)	**OR 1.17** (0.38 to 3.62)	**29 more per 1.000** (from 127 fewer to 289 more)	⨁⨁◯◯ LOW	IMPORTANT
Recurrence due to resistant organism												
1	randomised trials	serious [5]	not serious [3]	not serious	serious [1]	none	7/31 (22.6%)	5/35 (14.3%)	**OR 1.75** (0.49 to 6.21)	**83 more per 1.000** (from 67 fewer to 366 more)	⨁⨁◯◯ LOW	IMPORTANT
Intensive Care Unit duration of stay												
2	randomised trials	serious [2]	not serious	not serious	serious [6]	none	82	85	-	MD **2.68 fewer** (6.01 fewer to 0.66 more)	⨁⨁◯◯ LOW	IMPORTANT
Duration of hospital stay												
1	randomised trials	serious [2]	not serious [3]	not serious	serious [6]	none	51	50	-	MD **2.4 fewer** (6.4 fewer to 1.6 more)	⨁⨁◯◯ LOW	IMPORTANT
Duration of mechanical ventilation												
2	randomised trials	serious [2]	not serious	not serious	serious [7]	none	82	85	-	MD **0.35 fewer** (3.24 fewer to 2.54 more)	⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **OR:** Odds ratio; **MD:** Mean difference

1. 95%CI includes large benefit or harm. Low number of events
2. Most studies not blinded assessing subjective outcome
3. Single study
4. Potential source of bias as this is a per-protocol analysis; exclusion of 9 patients with low PCT measurements in the PCT group may exclude a higher proportion of relatively well patients compared with the control group

5. Non blinded study assessing a subjective outcome, which excluded patients with low PCT values
6. 95% CI ranging from futility to large benefit

95% CI ranging from appreciate benefit or harm

1.

Profile #13 Topical application of chlorhexidine in comparison to usual care or placebo in patients requiring mechanical ventilation.

Bibliography: Klompas M, Speck K, Howell MD, Greene LR, Berenholtz SM. Reappraisal of routine oral care with chlorhexidine gluconate for patients receiving mechanical ventilation: systematic review and meta-analysis. JAMA Intern Med. 2014 May;174(5):751-61

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Chlorhexidine**	**Usual care or placebo**	**Relative (95% CI)**	**Absolute (95% CI)**		
Lower respiratory tract infections (HAP and VAP)												
16	randomised trials	not serious	not serious	not serious	not serious	none	207/1833 (11.3%)	277/1797 (15.4%)	**RR 0.73** (0.58 to 0.92)	**42 fewer per 1.000** (from 12 fewer to 65 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Lower respiratory tract infections - Cardiac surgery												
3	randomised trials	not serious	not serious	not serious	not serious	none	52/928 (5.6%)	92/940 (9.8%)	**RR 0.56** (0.41 to 0.77)	**43 fewer per 1.000** (from 23 fewer to 58 fewer)	⊕⊕⊕⊕ HIGH	IMPORTANT
Lower respiratory tract infections - NON cardiac surgery												
13	randomised trials	not serious	not serious	not serious	serious [1]	none	155/905 (17.1%)	185/857 (21.6%)	**RR 0.78** (0.60 to 1.02)	**47 fewer per 1.000** (from 4 more to 86 fewer)	⊕⊕⊕◯ MODERATE	IMPORTANT
Mortality												
12	randomised trials	not serious	not serious	not serious	serious [2]	none	283/1637 (17.3%)	247/1597 (15.5%)	**RR 1.13** (0.99 to 1.28)	**20 more per 1.000** (from 2 fewer to 43 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Mortality - cardiac surgery												
3	randomised trials	not serious	not serious	not serious	very serious [3]	none	16/928 (1.7%)	19/940 (2.0%)	**RR 0.88** (0.25 to 3.14)	**2 fewer per 1.000** (from 15 fewer to 43 more)	⊕⊕◯◯ LOW	IMPORTANT
Mortality - NON cardiac surgery												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Chlorhexidine**	**Usual care or placebo**	**Relative (95% CI)**	**Absolute (95% CI)**		
9	randomised trials	not serious	not serious	not serious	serious [2]	none	267/709 (37.7%)	228/657 (34.7%)	**RR 1.13** (0.99 to 1.29)	**45 more per 1.000** (from 3 fewer to 101 more)	⨁⨁⨁◯ MODERATE	IMPORTANT
Duration of mechanical ventilation (assessed with: days)												
6	randomised trials	not serious	not serious	not serious	not serious	none	838	826	-	MD **0.01 more** (1.12 fewer to 1.14 more)	⨁⨁⨁⨁ HIGH	IMPORTANT
Duration of mechanical ventilation - cardiac surgery (assessed with: days)												
1	randomised trials	not serious	not serious [4]	not serious	not serious	none	485	469	-	MD **0.05 lower** (0.14 lower to 0.04 higher)	⨁⨁⨁⨁ HIGH	IMPORTANT
Duration of mechanical ventilation - NON cardiac surgery (assessed with: days)												
5	randomised trials	not serious	not serious	not serious	not serious	none	353	357	-	MD **0.15 fewer** (2.18 fewer to 1.89 more)	⨁⨁⨁⨁ HIGH	IMPORTANT
Duration of ICU stay (assessed with: days)												
6	randomised trials	not serious	not serious	not serious	not serious	none	838	826	-	MD **0.1 fewer** (0.25 fewer to 0.05 more)	⨁⨁⨁⨁ HIGH	IMPORTANT
Duration of ICU stay - cardiac surgery (assessed with: days)												
1	randomised trials	not serious	not serious	not serious	not serious	none	485	469	-	MD **0.1 fewer** (0.25 fewer to 0.05 more)	⨁⨁⨁⨁ HIGH	IMPORTANT
Duration of ICU stay - NON cardiac surgery (assessed with: days)												
5	randomised trials	not serious	not serious	not serious	not serious	none	353	357	-	MD **0.08 more** (1.47 fewer to 1.57 more)	⨁⨁⨁⨁ HIGH	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

1. 95%CI include appreciable benefit and harm
2. 95%CI include appreciable harm or benefit

3. Very low number of events
4. Single study

Profile #14: Selective oropharyngeal decontamination (SOD) compared to placebo or standard care in patients requiring mechanical ventilation

Bibliography:
-Li J1, Xie D, Li A, Yue J. Oral topical decontamination for preventing ventilator-associated pneumonia: a systematic review and meta-analysis of randomized controlled trials. J Hosp Infect. 2013 Aug;84(4):283-93
-Price R, MacLennan G, Glen J; SuDDICU Collaboration. Selective digestive or oropharyngeal decontamination and topical oropharyngeal chlorhexidine for prevention of death in general intensive care: systematic review and network meta-analysis. BMJ. 2014 Mar 31;348:g2197

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**SOD**	**standard care**	**Relative (95% CI)**	**Absolute (95% CI)**		
ventilator-associated pneumonia												
3	randomised trials	not serious	not serious	serious [1]	serious [2]	none [3]	22/158 (13.9%)	58/123 (47.2%)	**RR 0.27** (0.18 to 0.42)	**344 fewer per 1.000** (from 273 fewer to 387 fewer)	⨁⨁◯◯ LOW	CRITICAL
All-cause mortality												
3	randomised trials	not serious	not serious	serious [1]	serious [4]	none [3]	40/158 (25.3%)	37/123 (30.1%)	**RR 0.85** (0.50 to 1.46)	**45 fewer per 1.000** (from 138 more to 150 fewer)	⨁⨁◯◯ LOW	CRITICAL
All-cause mortality (including cluster clinical trials)												
4	randomised trials	serious [5]	not serious	serious [1]	not serious	none	**n.s.**	**n.s.**	**OR 0.85** (0.74 to 0.97)		⨁⨁◯◯ LOW	CRITICAL
Duration of mechanical ventilation (assessed with: days)												
1	randomised trials	not serious	not serious [6]	serious [1]	serious [4]	none [3]	58	30	-	MD **1.7 more** (4.67 fewer to 1.27 more)	⨁⨁◯◯ LOW	IMPORTANT
Duration of Intensive Care Unit stay (assessed with: days)												
1	randomised trials	not serious	not serious [6]	serious [1]	serious [4]	none [3]	58	30	-	MD **4 fewer** (7.73 fewer to 0.27 fewer)	⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio; **MD:** Mean difference; **n.s.:** not specified

1. SOD definition varied widely across studies and reviews included different studies under same concept
2. Low number of events and patients.
3. No explanation was provided
4. Low number of events and patients. 95%CI includes benefit or harm
5. Biggest study (deSmet) was a cluster trial and thus did not randomized patients with a potential for selection bias
6. single study

Profile #15: Selective oropharyngeal decontamination (SOD) and selective digestive decontamination (SDD) compared to placebo or standard care in patients requiring mechanical ventilation

Bibliography:
-D'Amico R, Pifferi S, Torri V, Brazzi L, Parmelli E, Liberati A. Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care. Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD000022
-Daneman N, Sarwar S, Fowler RA, Cuthbertson BH; SuDDICU Canadian Study Group. Effect of selective decontamination on antimicrobial resistance in intensive care units: a systematic review and meta-analysis. Lancet Infect Dis. 2013;13(4):328-41.
-Price R, MacLennan G, Glen J; SuDDICU Collaboration. Selective digestive or oropharyngeal decontamination and topical oropharyngeal chlorhexidine for prevention of death in general intensive care: systematic review and network meta-analysis. BMJ. 2014 Mar 31;348:g2197

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**SOD and SDD**	**Usual care**	**Relative (95% CI)**	**Absolute (95% CI)**		
Overall mortality												
17	randomised trials [1]	not serious [2]	not serious	serious [3]	not serious	none	496/2025 (24.5%)	614/2050 (30.0%)	**OR 0.75** (0.65 to 0.87)	**57 fewer per 1.000** (from 28 fewer to 82 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Overall mortality (including cluster clinical trials)												
15	randomised trials	serious [4]	not serious	serious [3]	not serious	none	**n.s.**	**n.s.**	**OR 0.73** (0.64 to 0.84)		⊕⊕◯◯ LOW	CRITICAL
Methicillin-resistant staphylococcus aureus infection or colonisation												
9	randomised trials [5]	serious [6]	not serious	not serious	serious [7]	none	110/2780 (4.0%)	61/1753 (3.5%)	**OR 1.46** (0.90 to 2.37)	**15 more per 1.000** (from 3 fewer to 44 more)	⊕⊕◯◯ LOW	IMPORTANT
Vancomycin-resistant enterococci infection or colonisation												
5	randomised trials [5]	serious [6]	not serious	not serious	serious [8]	none	31/2014 (1.5%)	139/2837 (4.9%)	**OR 0.63** (0.39 to 1.02)	**18 fewer per 1.000** (from 1 more to 29 fewer)	⊕⊕◯◯ LOW	IMPORTANT

CI: Confidence interval; **OR:** Odds ratio; **n.s.:** not specified

1. SOD / SDD with topical AND systemic antibiotics
2. Most studies open and 7/17 with inadequate allocation concealment, but sensitivity analysis did not change the results
3. Included patients in ICU, some not under mechanical ventilation

4. 5. Biggest study (deSmet) was a cluster trial and thus did not randomized patients with a potential for selection bias
5. SOD / SDD with topical OR systemic antibiotics
6. Overall, most randomized and observational studies had adequate quality. It cannot be ruled out a selective outcome reporting
7. 95% CI includes no effect or appreciable harm
8. 95% CI includes appreciable benefit or no effect