

Table S5. Studies included in the systematic reviews with meta-analysis

Study	n	Characteristic of ICU/ patients	Diagnosis of VAP	Inclusion criteria	Exclusion criteria	Intervention (I) and Control (C) groups	Cointerventions ^a and VAP Bundle ^b
Mahmoodpoor et al, 2017	276	<p>Surgical ICU</p> <p>(I): APACHE II: 22.6 ± 5.1 ICU LOS: 15 ± 5 Duration MV: 11.6 ± 7.1</p> <p>(C): APACHE II: 21.4 ± 4.4 ICU LOS: 18 ± 10 Duration MV: 12.3 ± 10.5</p>	MV>48h, clinical features (CPIS) and bacterial pathogens ≥10 ⁴ CFU/ml in quantitative culture from bronchoalveolar lavage.	Age between 18 and 80 yr requiring mechanical ventilation for more than 72 hours with placement of an endotracheal tube	Patients transferred from other hospitals, urgent intubation in wards other than ICU, history of MV, pregnancy, HIV, immunosuppression, leukopenia, patient refusal, and acute respiratory distress syndrome. Patients who were receiving antibiotics at the time of intubation, and those who need a PEEP>5cm H ² O.	<p>(I): TaperGuard EVAC™ tubes: equipped with SSD port, polyurethane and cone shape cuff. Method of SSD: Intermittent every 6h</p> <p>(C): Conventional high-volume low-pressure endotracheal tubes</p>	<p>Cointervention: Polyurethane-cone shape cuff</p> <p>VAP bundle:</p> <ul style="list-style-type: none"> - Head elevation of 45°. - Protocolized enteral feeding. - Sedation with washout periods. - Oral hygiene with chlorhexidine. - Hand washing. - Pantoprazol for stress ulcer prophylaxis.
Deem et al, 2016	66	<p>ICUs at Harborview Medical Center.</p> <p>(I): SAPS II: 60 ± 12 ICU LOS: N/A Duration MV: 6.5 ± 12.7</p> <p>(C): SAPS II: 60 ± 14 ICU LOS: N/A Duration MV: 4.5 ± 4.3</p>	Modified Criteria of CDC	Adults (>18 yr of age) requiring emergency orotracheal intubation and critical care.	<p>Patients with out-of-hospital cardiac arrest.</p> <p>Use of a non-study-designated intubation device.</p> <p>Nasal intubation or tracheostomy.</p> <p>Children (age < 18 yr), pregnant women, and prisoners.</p>	<p>(I):</p> <ol style="list-style-type: none"> 1) a polyurethane-conical shaped cuffed tube 2) a polyurethane- conical shaped cuffed tube with a port for SSD <p>Method of SSD: Continuous</p> <p>(C): Standard polyvinylchloride-cylindrical cuffed tube</p>	<p>Cointervention: Polyurethane-cuffed</p> <p>VAP bundle:</p> <ul style="list-style-type: none"> - Head elevation of 45°. - Protocolized enteral feeding. - Oral care every 8h with 0.12% chlorhexidine. - Hand washing. - Stress ulcer prophylaxis. - Endotracheal tube cuff pressure measured and adjusted every 8h.

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Jena et al, 2016	50	Neurological ICU (I): APACHE/SAPS II: N/A ICU LOS: 29.8 ± 20.1 Duration MV: 21.5 ± 17.6 (C): APACHE/SAPS II: N/A ICU LOS: 24.4 ± 14.2 Duration MV: 17.2 ± 11.5	MV>48h, clinical features and microbiological confirmation of VAP by bronchoalveolar lavage fluid.	Patients with neurological illnesses aged > 18 years and requiring endotracheal intubation and VM > 48 h were	Patients who arrived to ICU already intubated or reintubated during the study period, patients with a tracheostomy, and patients intubated for cardiac arrest or ventilated for <48 h	(I): Portex Blue Line endotracheal tube (suction above cuff endotracheal tube). Method of SSD: Intermittent every 2h. (C): Standard endotracheal tube	Cointervention: None specified VAP bundle: - Oral intubation. - Use of nasogastric tubes. - Early enteral nutrition. - Semi-recumbent position. - Stress ulcer prophylaxis. - Maintenance of cuff pressure between 20-30 cm H ² O.
Gopal et al, 2015	240	Cardiothoracic surgery ICU (I): EuroSCORE: 6.4 ± 2.2 ICU LOS: N/A Duration MV: N/A (C): EuroSCORE: 6.4 ± 2.6 ICU LOS: N/A Duration MV: N/A	Hospital in Europe Link for Infection Surveillance (HELICS)	Age over 70 years and/ or left ventricular ejection function <50% and urgent cardiac surgery.	N/A	(I): Venner-PneuX™ endotracheal tube. Method of SSD: N/A (C): Standard endotracheal tube (Portex tracheal tube) Intermittent every 6h	Cointervention: Tracheal seal monitor that allow continuous cuff inflation pressures monitorization and maintenance. VAP bundle: - Semi-recumbent position. - Change of ventilator circuits when soiled or at 7 days. - Mouthwash every 6h with 2% chlorhexidine. - Appropriate hand hygiene. - Stress ulcer prophylaxis with ranitidine 50mg I.V every 8h.

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Damas et al, 2015	352	5 ICUs in a tertiary hospital I): SAPS III: 70 ± 14.5 ICU LOS: 16.2 ± 13.5 Duration MV: 11.7 ± 11.9 (C): SAPS III: 69 ± 16.6 ICU LOS: 15.8 ± 13.2 Duration MV: 10.9 ± 9.8	Clinical features and quantitative bacterial culture ≥ 10 ⁶ CFU/ml from bronchoalveolar lavage.	Expected MV>48h, age over 18 years and intubation with a Teleflex Isis™	Patient participating in another study or having already participated in this study.	(I): Teleflex Isis™ endotracheal tube that allow the SSD Method of SSD: N/A (C): Teleflex Isis™ endotracheal tube without SSD technique	Cointervention: None specified VAP bundle: - Semi-recumbent position of at least 30°. - Oral care and teeth brushing with 0.2% chlorhexidine and application of 1% chlorhexidine gel. - Daily assessment of sedation. - Control of cuff pressure between 20-30 cm H ² O.
Tao et al, 2014	149	N/A I): SAPS III: N/A ICU LOS: N/A Duration MV: N/A (C): SAPS III: N/A ICU LOS: N/A Duration MV: N/A	MV>48h, clinical features and culture of endotracheal aspirate, reduction of oxygen.	Expected MV>48h and APACHE score 20-30	Lung infection when MV beginning	(I): 1) Intermittent SSD every 4h 2) Continuous SSD (C): Not SSD	Cointervention: None specified

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Seyfi et al, 2013	80	ICU of Hospital of Tehran I): SAPS/APACHE: N/A ICU LOS: N/A Duration MV: N/A (C): SAPS/APACHE: N/A ICU LOS: N/A Duration MV: N/A	Clinical features (CPIS)	N/A	N/A	(I): Special tracheal tube for SSD Method of SSD: Intermittent every 1-2h (C): Ordinary tracheal tube	Cointervention: N/A VAP bundle: N/A
Lacherade et al, 2010	333	Medical-surgical ICU I): SAPS III: 51 [40–64] ^c ICU LOS: 11 [7–19] ^c Duration MV: 8 [5–13] ^c (C): SAPS III: 52 [39–63] ^c ICU LOS: 11 [6–20] ^c Duration MV: 7 [3–15] ^c	Clinical features and quantitative bacterial culture $\geq 10^4$ CFU/ml from bronchoalveolar lavage or quantitative culture $\geq 10^3$ CFU/ml from protected telescoping catheter sample.	Expected MV > 48h, older than 18 years, intubated with HI-Lo Evac tube	Intubated before ICU and/ or with a tube different than HI-Lo Evac tube, tracheostomy, physhotropic drug overdose, acute drunkenness, cardiac arrest.	(I): Specific tracheal tube for SSD (HI-Lo Evac tube) Method of SSD: Intermittent every 1h. (C): Conventional tracheal tube and/or HI-Lo Evac tube without SSD technique.	Cointervention: none specified. VAP bundle: - Semi-recumbent body position. - Oral route of insertion of the tracheal and gastric tubes. - Enteral delivery of nutritional support. - Maintenance of cuff pressure between 20-30 cm H ² O.

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Zheng et al, 2008	61	Medical-surgical ICU I): APACHE II: 17.6 ± 2.9 ICU LOS: 9.3 ± 2.9 Duration MV: 7.9 ± 2.6 (C): APACHE II: 17.6 ± 3.5 ICU LOS: 12.3 ± 5.7 Duration MV: 10.4 ± 0.9	Criteria of United States of VAP clinical standard diagnosis of infection monitoring system (NNIS)	Age over 18 years and expected MV>48h	N/A	(I): Special tracheal tube for SSD Method of SSD: Continuous (C): Standard tracheal tube	Cointervention: N/A VAP bundle: - Semi-recumbent body position. - Body position changes every 4h. - Maintenance of cuff pressure between 25-30 cm H ² O.
Yang et al, 2008	91	Medical-surgical ICU I): SAPS/APACHE: N/A ICU LOS: N/A Duration MV: N/A (C): SAPS/APACHE: N/A ICU LOS: N/A Duration MV: N/A	Clinical features or positive tracheal/blood cultures or CPIS ≥ 5	Age over 18 years and expected MV>48h	Intubated before ICU	(I): SSD Method of SSD: Continuous (C): Not SSD	Cointervention: N/A VAP bundle: - Peptic ulcer prophylaxis with sucralfate. - Endotracheal tube cuff control twice a day. - Head elevated - Open system single-use catheters - Weekly circuit changes - Oral decontamination

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Bouza et al, 2008	690	<p>Cardiothoracic surgery ICU</p> <p>I): APACHE II: 10.2 ± 2.4 ICU LOS: 7 [3-27] ^c Duration MV: 3 [2-9] ^c</p> <p>(C): APACHE II: 10.4 ± 3.3 ICU LOS: 16.5 [6.5-39.5] ^c Duration MV: 7 [3-11] ^c</p>	<p>MV>48h, Clinical features (CDC criteria) and quantitative bacterial culture ≥10⁴ CFU/ml from endotracheal aspiration and ≥10³ CFU/ml from telescopic brushing.</p>	Major Heart Surgery	N/A	<p>(I): Special tracheal tube for SSD (HI-Lo Evac) Method of SSD: Continuous</p> <p>(C): Standard tracheal tube (Hi-Contour)</p>	<p>Cointervention: None specified</p> <p>VAP bundle:</p> <ul style="list-style-type: none"> - Tracheal aspiration. - Maintenance of cuff pressure between 20-30 mm Hg. - Pantoprazol for stress ulcer prophylaxis.

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Lorente et al, 2007	280	<p>Medical-surgical ICU</p> <p>I): APACHE II: 14.9 ± 6.6 ICU LOS: 14.1 ± 17.9 Duration MV: 10.5 ± 15.9</p> <p>(C): APACHE II: 15.1 ± 6.3 ICU LOS: 15.5 ± 19.9 Duration MV: 11.1 ± 15.2</p>	Clinical features and quantitative culture of respiratory secretions by endotracheal aspirate >10 ⁶ CFU/ml	Expected MV>24h	Age less than 18 years, pregnancy, infection with human immunodeficiency virus, blood leukocyte count less than 1,000 cells/mm ³ , solid or hematological tumor, and/or immunosuppressive therapy.	<p>(I): Special tracheal tube with polyurethane cuff and SSD (SealGuard Evac) Method of SSD: Intermittent every 1 h</p> <p>(C): Conventional endotracheal tube with polyvinyl cuff without SSD (Hi-Lo)</p>	<p>Cointervention: Polyurethane-cuffed</p> <p>VAP bundle:</p> <ul style="list-style-type: none"> - Verification every 4h of semi-recumbent body position 40° - Nasogastric tubes. - Continuous enteric nutrition. - Ranitidine for stress ulcer prophylaxis. - Verification every 4h of cuff pressure to maintain a pressure of 25 cm H²O. - Oral cleaning with chlorhexidine every 8h. - Protocol of sedation. - Protocol for MV weaning. - No selective digestive decontamination. - Verification of gastric volume every 6h. - Tracheal suction when necessary. - No routine change of ventilator circuits.

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Liu et al, 2006	86	N/A I): SAPS/APACHE: N/A ICU LOS: N/A Duration MV: N/A (C): SAPS/APACHE: N/A ICU LOS: N/A Duration MV: N/A	Clinical features and culture of endotracheal aspirate.	Age over 18 years and expected MV>48h	Expected death within 48h; Expected weaning within 48h; existing lung infection when MV beginning	(I): Special tracheal tube for SSD Method of SSD: Continuous (C): Standard endotracheal tube	Cointerventions: Semi-recumbent position and mosapride citrate VAP bundle: N/A
Liu et al, 2006	98	Respiratory ICU I): SAPS/APACHE: N/A ICU LOS: N/A Duration MV: N/A (C): SAPS/APACHE: N/A ICU LOS: N/A Duration MV: N/A	MV >48 h, the chest radiograph showed pulmonary new or progressive infiltrates, and excluding atelectasis, pulmonary edema, and pleural effusion	Age over 60 years and expected MV>48h	N/A	D): Special tracheal tube for SSD Method of SSD: Intermittent (C): Standard tracheal tube	Cointervention: N/A VAP bundle: N/A

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Girou et al, 2004	18	10-bed medical ICU D): APACHE II: 27 [20-40] ^c ICU LOS: N/A Duration MV: N/A (C): APACHE II: 27 [24-33] ^c ICU LOS: N/A Duration MV: N/A	Clinical features and quantitative culture of protected specimen brush or bronchoalveolar lavage specimen with more than 5% of cells containing intracellular bacteria	Expected MV>5 days	Patients intubated within the 15 days preceding ICU admission.	(I): Special tracheal tube for SSD (HI-Lo Evac) Semi-recumbent position Method of SSD: Continuous (C): Standard tracheal tube Supine position	Cointervention: Semi-recumbent position 30°. VAP bundle: - Sucralfate for stress ulcer prophylaxis. - Verification every 8h of cuff pressure to maintain between 20-30 mm Hg. - Verification every 4h of permeability of drainage system.
Smulders et al, 2002	105	12- bed general ICU D): APACHE II: 23.1 ± 7.6 ICU LOS: 9.3 ± 7.4 Duration MV: 5.8 ± 4.4 (C): APACHE II: 22.3 ± 8.6 ICU LOS: 12.3 ± 3.6 Duration MV: 7.1 ± 5.4	Adaptation of the American College of Chest Physicians. Clinical features and culture of endotracheal aspirate.	Expected MV>72 h	MV<72 h Pneumonia developed within 72h.	(I): Special endotracheal tube for SSD (HI-Lo Evac) Method of SSD: Intermittent (C): Standard endotracheal tube	Cointervention: None specified VAP bundle: - Sucralfate for stress ulcer prophylaxis. - Changes of body position from the right to the left decubitus every 4h. - Endotracheal suction every 4h or according to need. - Control of cuff pressure every 4h.

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Bo et al, 2000	68	<p>Surgical ICU</p> <p>I): SAPS/APACHE: N/A ICU LOS: N/A Duration MV: N/A</p> <p>(C): SAPS/APACHE: N/A ICU LOS: N/A Duration MV: N/A</p>	Quantitative bacterial culture of secretions obtained by protected specimen brush	Expected MV>72 h	Intubated outside hospital; high-risk surgery or trauma; pre-existing infection	<p>D): Special tracheal tube for SSD Method of SSD: Continuous</p> <p>(C): Standard tracheal tube</p>	<p>Cointervention: None specified</p> <p>VAP bundle: - Intra-cuff pressure monitored every 4h. - Stress ulcer prophylaxis with histamine-2 receptor or proton pump inhibitor.</p>
Kollef et al, 1999	343	<p>Cardiothoracic ICU</p> <p>I): APACHE II: 11.1 ± 3.7 ICU LOS: 3.7 ± 4.6 Duration MV: 1.5 ± 3.3</p> <p>(C): APACHE II: 11.0 ± 3.6 ICU LOS: 3.2 ± 4.5 Duration MV: 1.9 ± 5.1</p>	Adaptation of the American College of Chest Physicians. Clinical features and culture of endotracheal aspirate.	Age >18 years and required MV in the cardiothoracic ICU after undergoing cardiac surgery	Patients transferred from an outside hospital and had already received MV	<p>(I): Special endotracheal tube for SSD (HI-Lo Evac) Method of SSD: Continuous</p> <p>(C): Standard endotracheal tube without SSD</p>	<p>Cointervention: None specified</p> <p>VAP bundle: - Head elevated - Circuit change - Stress ulcer prophylaxis (not specific drug data)</p>

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Valles et al, 1995	153	Medical-surgery ICU I): APACHE II: 20.5 ± 7.0 ICU LOS: N/A Duration MV: N/A (C): APACHE II: 18.9 ± 7.1 ICU LOS: N/A Duration MV: N/A	Clinical features after 72h of MV and protected specimen brush culture containing >10 ³ CFU/ml or bronchoalveolar lavage culture with >10 ⁴ CFU/ml or good response to antibiotic agents.	Expected MV>72h, intubation in ICU or in the emergency department.	Patients intubated in other areas of the hospital, tracheostomy, develop pneumonia during the first 72 hours of MV	(I): Special tracheal tube for SSD (HI-Lo Evac) Method of SSD: Continuous (C): HI-Lo Evac with SSD lumen closed	Cointervention: None specified VAP bundle: - Intra-cuff pressure monitored every 4h. - Stress ulcer prophylaxis with sucralfate. - No selective decontamination regimen or antibiotic prophylaxis.
Mahul et al, 1992	145	Medical-surgical ICU I): SAPS/APACHE: N/A ICU LOS: N/A Duration MV: N/A (C): SAPS/APACHE: N/A ICU LOS: N/A Duration MV: N/A	New and persistent infiltrate on the chest X-ray after 2 days of intubation and aerobic microorganism on bronchoalveolar lavage culture ≥ 10 ⁵ CFR/ml.	Expected MV>3 days	No intubation, tracheostomy, intubated <3 days, vital risk for new intubation, intubated before ICU, gastric bleeding, oesogastrectomy	(I): Special tracheal tube for SSD (HI-Lo Evac) with/without stress ulcer prophylaxis Method of SSD: Intermittent every 1h (C): HI-LO EVAC tube without SSD technique with/without stress ulcer prophylaxis	Cointervention: Stress ulcer prophylaxis: Antacids (aluminum hydroxide) 20ml/6h or cytoprotective agent (sucralfate) 1g/6h. VAP bundle: - Intra-cuff pressure monitored every 8h and kept up to 30mm Hg.

MV, mechanical ventilation; ICU, intensive care unit; I, intervention; C, control; CPIS, Clinical infection pulmonary score; SSD, subglottic secretion drainage; PEEP, positive end-expiratory pressure; CFU, colony-forming units; CDC, Centers for Disease Control and Prevention; APACHE II, Acute Physiology and Chronic Health Evaluation; SAPS II, Simplified Acute Physiologic Score; LOS, length of stay.

^a Cointervention only in intervention group.

^b VAP bundle carried out in both groups: control and intervention.

^c Median [IQR]