Supplemental file contents:

Table S1: *Pseudomonas* VAP data: observational studies (Benchmark groups) [a]

author	Year	Ref	Notes	MV%	Patients (n)	vap_n	PsVAP	PsVAP %
A'court	1993	1	T,	100	150	33	17	11.3
Alvarez-Lerma	1996	2		93	6494	519	174	2.7
Antonelli	1994	3	T, Md, B	67	124	41	5	4.0
Apostolopoulou	2003	4	Md,	100	175	56	17	9.7
Beck-Sague	1996	5	T, US,	100	145	15	5	3.4
Bekaert	2011	6	B	100	4479	685	155	3.5
Bercault_IHT	2005	7		100	118	31	9	7.6
Bercault_noINT	2005	7	I	100	118	12	3	2.5
Berrouane_all	2001	8	T, B	83	565	129	40	7.1
Bochicchio	2004	9	T, US,	100	678	125	22	3.2
Bonten'94	1994	10	B	100	64	11	6	9.4
Boots	2008	11	B	100	412	58	15	3.6
Bornstain	2004	12	B	100	747	80	23	3.1
Braun	1986	13	T, US,	100	66	15	0	0
Bregeon	1997	14	B	100	660	223	33	5.0
Bronchard	2004	15	T, B	100	109	45	0	0
Cade	1993	16		98	98	35	4	4.1
Cavalcanti	2006	17	T, Md, B	100	190	62	9	4.7
Cenderero	1999	18	Md, B	100	123	19	4	3.3
Chaari	2015	19	T, Md,	100	175	48	20	11.4
Chastre	1998	20	B	100	243	84	36	15.0
Chevret	1993	21	B	100	255	55	21	8.2
Cook_non-trauma	2010	22	US, B	100	2080	70	7	0.3
Cook_trauma	2010	22	T, US, B	100	511	91	16	3.1
Craven-medical	1988	23	US,	100	277	47	9	3.2
Craven-surgical	1988	23	US,	100	521	49	17	3.3
Daschner	1988	24		100	116	36	9	7.8
de_Latorre	1995	25	Md, B	100	80	12	7	8.8
Ensminger	2006	26	C, US,	100	92	17	2	2.2
Evans	2010	27	US, Tr	100	416	101	18	4.5
Ewig	1999	28	T, Md, B	100	48	10	4	8.3
Fagon'89	1989	29	B	100	567	49	16	2.8
Gacouin	2009	30	B	100	361	76	21	5.8
Garrouste-Orgas	1997	31	B	100	86	31	9	10.5
George	1998	32	US, B	100	223	28	6	2.7
Georges	2000	33	B	100	135	35	19	14.1
Giard	2008	34	B	100	7236	946	168	2.3
Gruson-95-96	2000	35	B	100	1004	231	62	6.2
Gruson-97-98	2000	35	B	100	1029	161	47	4.6
Gruson-99-01	2003	36	B	100	823	134	41	5.0

Table S1 (continued): *Pseudomonas* VAP data: observational studies (Benchmark groups)

author	Year	Ref	Notes	MV%	Patients (n)	vap_n	PsVAP	PsVAP %
Guérin	1997	37	B	100	260	27	14	5.4
Heyland	1999	38	US, B	100	1014	177	38	3.7
Hortal	2009	39	C, Md,	100	231	106	40	17.3
Hugonnet	2007	40	B	100	936	209	31	3.3
Hyllienmark	2013	41	T, B	100	135	45	4	3.0
Ibáñez	2000	42	Md,	100	30	6	1	3.3
Ibrahim'00	2000	43	US,	100	1882	397	130	6.9
Jaillette	2011	44		100	439	137	59	13.4
Jimenez	1989	45	Md,	100	77	18	7	9.1
Kallel	2005	46	T, Md,	100	241	77	34	14.1
Kollef' 93	1993	47	US,	100	277	43	4	1.4
Kollef '95	1995	48	US,	100	314	87	16	5.1
Kollef '97	1997	49	US,	100	521	77	15	2.9
Kollef '97_post	1997	50	C, US,	100	327	23	3	0.9
Kollef '97_pre	1997	50	C, US,	100	353	42	7	2.0
Kollef'14_Europe	2014	51		100	495	96	24	4.8
Kollef'14_USA	2014	51	US,	100	502	68	17	3.4
Koss– N	2001	52	US	100	87	17	4	4.6
Koss– P	2001	52	US, I	100	66	24	9	13.7
Kunac	2014	53	T, US, B	100	716	206	23	3.2
Lepelletier	2010	54	T,	100	161	34	10	6.2
Luyt	2005	55		100	290	69	11	3.8
Magnason	2008	56		100	280	21	5	1.8
Magret_non-trauma	2010	57		100	2082	337	64	3.1
Magret_trauma	2010	57	T,	100	354	128	17	4.8
Mahul	1992	58	B	100	145	30	8	5.5
Makris	2011	59	B	100	152	44	7	4.6
Markowicz	2000	60	B	100	744	162	58	7.8
Michel	2005	61	B	100	299	41	12	4.0
Moine	2002	62	B	80	764	89	27	3.5
Myny	2005	63		100	385	89	28	7.3
Nguile-Makao	2010	64	B	100	2873	434	130	4.5
Nielsen	1992	65		100	242	23	3	1.2
Nseir	2005	66		100	1241	77	32	2.6
Papazian	1996	67	B	100	586	97	26	4.4
Potgieter	1987	68		78	250	51	26	10.4
Raineri	2010	69	I, B	100	822	44	7	0.9
Raineri	2010	69	B	100	827	68	32	3.9
Rello'91	1991	70	Md, B	100	264	58	14	5.3
Rello'92	1992	71	Md, B, T	80	161	42	4	2.5
Rello'94	1994	72	Md, B	100	568	72	18	3.2
Rello'96	1996	73	Md, B	100	83	21	4	4.8
Rello'02	2002	74	US,	100	9080	842	119	1.3

Table S1 (continued): *Pseudomonas* VAP data: observational studies (Benchmark groups)

author	Year	Ref	Notes	MV%	Patients (n)	vap_n	PsVAP	PsVAP %
Reusser	1989	75		100	40	15	2	5.0
Rincón-Ferrari	2004	76	T, Md, B	100	310	72	6	1.9
Rodriguez	1991	77	T, US,	100	294	130	31	10.5
Ruiz-Santana	1987	78	B	100	1005	180	56	5.6
Salata	1987	79	US, B	100	51	21	7	13.7
Shahin	2013	80	US,	100	267	29	4	1.5
Sofianou	2000	81	Md,	100	198	67	19	9.6
Stéphan	2006	82	T,	100	175	78	14	8.0
Tejada-Artigas	2001	83	T, Md, B	100	103	23	5	4.9
Timsit	1996	84	B	100	387	56	11	2.8
Torres	1990	85	Md, B	100	322	78	5	1.6
Trouillet	1998	86	B	100	498	135	39	7.8
Urli	2002	87	Md,	95	178	116	27	15.2
Valles	2007	88	Md,	100	60	40	15	25.0
Vanhems	2011	89	B	100	3387	367	24	0.7
Verhamme	2007	90		84	4000	298	54	1.4
Violan	1998	91	Md, B	100	314	82	25	8.0
Woske	2001	92	B	100	103	49	8	7.8
Zahar	2009	93	B	100	1233	208	62	5.0

Table S1 footnotes

T – Data originating from a study for which the majority of ICU admission were for trauma

C - Data originating from a study for which the ICU admission were for cardio thoracic surgery

Md - Data originating from a study based in a country from the Mediterranean region.

US - Data originating from a study based in the United States of America or Canada

B – VAP diagnosis based on bronchoscopic based methods for sampling.

I – Infection control intervention to entire ICU

PsVAP - *Pseudomonas* VAP

Several (n = 43) of these studies were cited in the following source systematic reviews.

- Melsen WG, Rovers MM, Bonten MJM: Ventilator-associated pneumonia and mortality: A systematic review of observational studies. *Crit Care Med* 2009, 37:2709–2718.
- Safdar N, Dezfulian C, Collard HR, Saint S: Clinical and economic consequences of ventilator-associated pneumonia: a systematic review. *Crit Care Med* 2005, 33:2184–93.
- Agrafiotis M, Siempos II, Ntaidou TK, Falagas ME. Attributable mortality of ventilator-associated pneumonia: a meta-analysis. *Intern J Tub Lung Dis.* 2011;15(9):1154-1163.

Table S2: *Pseudomonas* VAP data: non-PM-based methods of VAP prevention [a]

author	Year	Ref	Notes	MV%	Patients (n)	vap_n	PsVAP	PsVAP %
control groups								
Acosta-escribano	2010	94	T, Md,	100	54	31	4	7.4
Bonten '95	1995	95	B	100	74	16	7	9.5
Boots'06_All	2006	96		100	381	59	14	3.7
Combes	2000	97	T,	100	50	4	0	0
Cook	1998	98	US,	100	596	114	20	3.4
Daumal	1999	99		100	174	25	11	6.3
Djedaini	1995	100	B	100	61	6	0	0
Drakulovic	1999	101	Md,	100	47	11	3	6.4
Dreyfuss ‘91	1991	102	B	100	35	11	3	8.6
Dreyfuss ‘95	1995	103	B	100	70	8	1	1.4
Driks	1987	104		100	69	16	5	7.2
Fabian	1993	105	T, US,	100	278	81	10	3.6
Forestier	2008	106	T, B	100	106	21	8	7.5
Fourrier'00	2000	107		100	30	15	4	13.3
Fourrier'05	2005	108		100	114	12	5	4.4
Genuit (C & T)	2001	109	US,	100	78	27	12	15.4
Heyland	1999	110	US,	100	46	7	0	0
Holzapfel_C_93	1993	111	B	100	149	17	0	0
Holzapfel_C_99	1999	112	B	100	200	51	6	3.0
Kantorova All	2004	113	T,	100	287	25	5	1.7
Kirschenbaum	2002	114	US, B	100	20	10	5	25.0
Kirton	1997	115	T, US,	100	140	22	6	4.3
Knight	2009	116		100	129	17	1	0.8
Koeman	2006	117		100	130	23	4	3.1
Kollef '95	1995	118	US,	100	300	80	23	7.7
Kollef'08	2008	119	US, B	100	743	56	11	1.5
Kortbeek	1999	120	T, US,	100	43	18	0	0
Kostadima	2005	121	Md,	100	21	8	2	9.5
Lacherade '05	2005	122	B	100	184	53	14	7.6
Lacherade '10	2010	123	B	100	164	42	16	9.8
Laggner	1989	124		100	16	2	0	0
Laueny	2014	125	T,	100	91	11	0	0

Table S2 (continued): *Pseudomonas* VAP data: non-PM-based methods of VAP prevention [a]

author	Year	Ref	Notes	MV%	Patients (n)	vap_n	PsVAP	PsVAP %
control groups (continued)								
Lorente '03	2003	126	Md, B	100	116	26	10	8.6
Lorente '04	2004	127	Md, B	100	143	33	8	5.6
Lorente'05	2005	128	Md, B	100	233	42	12	5.2
Lorente'06	2006	129	Md, B	100	221	31	7	3.2
Lorente'06	2006	130	Md, B	100	51	8	5	9.8
Lorente'07	2007	131	Md,	100	140	31	4	2.9
Lorente'12	2012	132	Md,	100	219	24	5	2.3
Lorente'14	2014	133	Md,	100	150	33	6	4.0
Manzano	2008	134	Md,	100	63	16	0	0
Martin	1993	135	US, Pl	100	66	6	2	3
Morrow	2010	136	US, B	100	73	28	6	8.2
Nseir	2011	137	B	100	61	16	2	3.3
Pickworth	1993	138	T, US,	100	44	5	1	2.3
Pneumatikos	2006	139	T, Md,	100	40	11	1	2.5
Prod'hom_A	1994	140		100	81	18	4	4.9
Reigneir	2013	141	B	100	222	35	9	4.1
Rumbak	2004	142	US,	100	60	15	5	8.3
Ryan_C	1993	143	US,	100	56	7	2	3.6
Seguin ‘06	2006	144	T, B	100	62	25	1	1.6
Seguin ‘14	2014	145	T, B	100	72	20	1	1.4
Smulders	2002	146		100	75	12	3	4.0
Staudinger	2010	147	B	100	75	17	5	6.7
Swan	2016	148	US	57	164	13	1	0.6
Thomachot ‘98	1998	149	B	100	66	21	3	4.5
Thomachot ‘99	1999	150	T,	100	77	24	1	1.3
Thomachot ‘02	2002	151	T,	100	84	22	2	2.4
Valencia	2007	152	Md, B	100	69	10	1	1.4
Valles	1995	153	Md, B	100	77	25	12	15.6

Table S2: *Pseudomonas* VAP data: non-PM-based methods of VAP prevention [a]

author	Year	Ref	Notes	MV%	Patients (n)	vap_n	PsVAP	PsVAP %
intervention groups								
Acosta-escribano	2010	94	T, Md,	100	50	16	3	6.0
Bonten '95	1995	95	B	100	67	15	11	16.4
Combes	2000	97	T,	100	54	10	0	0
Cook	1998	98	US,	100	604	98	21	3.5
Daumal	1999	99		100	187	30	12	6.4
Djedaini	1995	100		100	68	8	3	4.4
Drakulovic	1999	101	Md,	100	39	2	1	2.6
Dreyfuss	1991	102	B	100	28	8	1	3.6
Dreyfuss	1995	103	B	100	61	6	0	0
Driks	1987	104		100	61	7	1	1.6
Forestier	2008	106	T, B	100	102	19	3	2.9
Fourrier'00	2000	107		100	30	5	1	3.3
Fourrier'05	2005	108		100	114	13	6	5.3
Heyland	1999	110	US,	100	49	3	0	0
Holzapfel_I_99	1999	112	B	100	199	37	10	5.0
Kirschenbaum	2002	114	US, B	100	17	3	1	5.9
Kirton	1997	115	T, US,	100	140	9	6	4.3
Knight	2009	116		100	130	12	0	0
Koeman-Ch	2006	117		100	127	13	0	0
Kollef'08_silverETT	2008	119	US, B	100	766	37	8	1.0
Kortbeek	1999	120	T, US,	100	37	10	0	0
Kostadima	2005	121	Md,	100	20	2	0	0
Lacherade '05	2005	122	B	100	185	47	9	4.9
Lacherade '10	2010	123	B	100	169	25	9	5.3
Laggner	1989	124		100	16	1	0	0
Laueny	2014	125	T,	100	98	37	0	0

Table S2: *Pseudomonas* VAP data: non-PM-based methods of VAP prevention [a]

author	Year	Ref	Notes	MV%	Patients (n)	vap_n	PsVAP	PsVAP %
intervention groups (continued)								
Lorente '03	2003	126	Md, B	100	114	29	9	7.9
Lorente '04	2004	127	Md, B	100	161	37	9	5.6
Lorente'05	2005	128	Md, B	100	210	43	12	5.7
Lorente'06	2006	129	Md, B	100	53	21	2	3.8
Lorente'06	2006	130	Md, B	100	236	33	9	3.8
Lorente'07	2007	131	Md,	100	140	11	4	2.9
Lorente'12	2012	132	Md,	100	217	21	5	2.3
Lorente'14	2014	133	Md,	100	134	15	3	2.2
Manzano	2008	134	Md,	100	64	6	0	0
Martin	1993	135	US	100	65	2	0	0
Morrow	2010	136	US, B	100	73	13	0	0
Nseir	2011	137	B	100	61	6	0	0
Pneumatikos	2006	139	T, Md,	100	39	6	0	0
Prod'hom_R	1994	140		100	80	22	1	1.3
Prod'hom_S	1994	140		100	83	11	1	1.2
Reigneir	2013	141	B	100	227	38	12	5.3
Rumbak	2004	142	US,	100	60	3	1	1.7
Ryan_S	1993	143	US,	100	58	8	1	1.7
Seguin-PVI	2006	144	T, B	100	36	3	0	0
Seguin	2014	145	T, B	100	78	24	3	3.8
Smulders	2002	146		100	75	3	1	1.3
Staudinger	2010	147	B	100	75	8	3	4.0
Swan	2016	148	US	69	161	8	1	0.6
Thomachot	1998	149	B	100	70	26	2	2.9
Thomachot	1999	150	T,	100	63	21	2	3.2
Thomachot	2002	151		100	71	10	0	0
Valencia	2007	152	Md, B	100	73	11	3	4.1
Valles	1995	153	Md, B	100	76	14	12	15.8

Table S2 footnotes

T – Data originating from a study for which the majority of ICU admission were for trauma

C - Data originating from a study for which the ICU admission were for cardio thoracic surgery

Md - Data originating from a study based in a country from the Mediterranean region.

US - Data originating from a study based in the United States of America or Canada

B – VAP diagnosis based on bronchoscopic based methods for sampling.

PsVAP - *Pseudomonas* VAP

Several (n = 47) of these studies were cited in the following source systematic reviews.

- Messori A, Trippoli S, Vaiani M, Gorini M, Corrado A: Bleeding and pneumonia in intensive care patients given ranitidine and sucralfate for prevention of stress ulcer: meta-analysis of randomised controlled trials. *BMJ* 2000, 321:1103–1106.
- Huang J, Cao Y, Liao C, Wu L, Gao F: Effect of histamine-2-receptor antagonists versus sucralfate on stress ulcer prophylaxis in mechanically ventilated patients: a meta-analysis of 10 randomized controlled trials. *Crit Care* 2010, 14:R194.
- Alhazzani W, Almasoud A, Jaeschke R, Lo BW, Sindi A, Altayyar S, Fox-Robichaud A: Small bowel feeding and risk of pneumonia in adult critically ill patients: a systematic review and meta-analysis of randomized trials. *Crit Care* 2013, 17:R127.
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- Labeau SO, Van de Vyver K, Brusselaers N, Vogelaers D, Blot SI: Prevention of ventilator-associated pneumonia with oral antiseptics: a systematic review and meta-analysis. *Lancet Infect Dis* 2011, 11:845-854.
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- Safdar N, Dezfulian C, Collard HR, Saint S: Clinical and economic consequences of ventilator-associated pneumonia: a systematic review. *Crit Care Med* 2005, 33:2184–93.
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- Subirana M, Solà I, Benito S: Closed tracheal suction systems versus open tracheal suction systems for mechanically ventilated adult patients. *Cochrane Database Syst Rev* 2007, 4: CD004581;
- Siempos II, Vardakas KZ, Kopterides P, Falagas ME. Impact of passive humidification on clinical outcomes of mechanically ventilated patients: A meta-analysis of randomized controlled trials. *Crit Care Med* 2007; 35: 2843-51;
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- Delaney A, Gray H, Laupland KB, Zuege DJ. Kinetic bed therapy to prevent nosocomial pneumonia in mechanically ventilated patients: a systematic review and meta-analysis. *Crit Care* 2006; 10:R70;
- Sud S, Friedrich JO, Taccone P, Polli F, Adhikari NK, Latini R, Gattinoni L. Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis. *Inten Care Med* 2010; 36(4); 585-599.
- Siempos II, Vardakas KZ, Falagas ME. Closed tracheal suction systems for prevention of ventilator-associated pneumonia. *Brit J Anaesthesia*, 2008; 100(3): 299-306.

Table S3: *Pseudomonas* VAP data: Non-Concurrent control studies of topical PM based methods of VAP prevention [a]

author	Year	Ref	Notes	MV %	Patients (n)	vap_n	PsVAP	PsVAP %
control groups								
Bergmans NC	2001	154	B	100	61	14	5	8.2
Bonten NC	1994	155	B	100	54	7	4	7.4
Feeley	1975	156, 192	US	NS	711	78	45	6.3
Godard	1990	157	B	80	84	13	5	6
Klick	1975	158	US	NS	371	30	17	4.6
Konrad	1989	159		100	83	22	9	10.8
Stoutenbeek'84	1984	160	T	100	59	35	5	8.5
Stoutenbeek'87	1987	161	T	100	59	35	5	8.5
Winter NC	1992	162	B	92	84	11	2	2.4
intervention groups								
Bos	2017	163	[1, 2]	100	1573	69	4	0.3
Feeley	1975	156, 192	US [3]	NS	292	11	1	0.3
Garbino	2002	164	B [4]	100	204	20	4	2
Godard	1990	157	B [1]	100	97	2	0	0
Klick	1975	158	US [3]	NS	374	18	3	0.8
Konrad	1989	159	[2]	100	82	5	2	2.4
Leone	2002	165	T [5]	100	324	58	3	0.9
Nardi	2001	166	Md, B [1]	100	104	20	4	3.8
Nardi	2001	166	Md, B [6]	100	119	9	3	2.5
Rouby	1994	167	[7]	100	347	97	12	3.5
Silvestri'99	1999	168	[1]	100	117	5	2	1.7
Silvestri'02	2002	169	Md [1]	100	130	21	3	2.3
Stoutenbeek SDD	1984	160	T [2]	100	63	5	0	0
Stoutenbeek ED	1987	161	T [1]	100	42	23	1	2.4
Veelo	2008	170	[2]	100	231	14	2	0.9

Table S3 (continued): *Pseudomonas* VAP data: Non-Concurrent control studies of topical PM based methods of VAP prevention [a]

Footnotes

T – Data originating from a study for which the majority of ICU admission were for trauma

C - Data originating from a study for which the ICU admission were for cardio thoracic surgery

L - Data originating from a study for which all patients had severe liver disease or transplantation.

Md - Data originating from a study based in a country from the Mediterranean region.

US - Data originating from a study based in the United States of America or Canada

B – VAP diagnosis based on bronchoscopic based methods for sampling.

NS – Not stated

PsVAP - *Pseudomonas* VAP

The control group as published in this study [156] was derived from a previous series by these authors [192].

The control group in one study [160] appears also as the control group in another study by this author [161] and is used only once in the analysis here.

Several (n = 5) of these studies were cited in the following source meta-analyses.

- Vandenbroucke-Grauls CM, Vandenbroucke JP (1991) Effect of selective decontamination of the digestive tract on respiratory tract infections and mortality in the intensive care unit. Lancet 338:859-862.
- Hurley JC (1995) Prophylaxis with enteral antibiotics in ventilated patients: Selective decontamination or selective cross-infection? Antimicrob Agents Chemother 39:941–947.

Topical polymyxin intervention regimens

1. PTA (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin).
2. PTA-Ctx (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin; Ctx, parenteral cephalosporin).
3. P (P = polymyxin either aerosolized or topical)
4. PNeV (P = polymyxin; Ne = Neomycin; V = Vancomycin)
5. PGA-Ctx (=P, topical polymyxin; G, topical gentamicin; A, topical amphotericin; Ctx, parenteral cephalosporin).
6. PTAM (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin; topical mupirocin).
7. PE (=P, topical polymyxin; E, topical erythromycin)

Table S4: *Pseudomonas* VAP data: Concurrent control studies of topical PM based methods of VAP prevention [a]

author	Year	Ref	Notes	MV %	Patients (n)	vap_n	PsVAP	PsVAP %
control groups								
Abele-Horn	1997	171	T,	100	30	20	3	10.0
Aerdts	1991	172		100	39	27	10	25.6
Bergmans CC	2001	154	B	100	78	24	8	10.3
Bion	1991	173	L	100	31	8	3	9.7
Blair	1991	174		93	130	37	9	6.9
Bonten CC	1994	155	B	86	21	0	0	0
Cockerill	1992	175	US,	85	75	4	4	5.3
De le Cal	2005	176	Burn, Md	80	54	26	7	13
Ferrer	1994	177	Md, B	100	41	10	4	9.8
Hammond	1994	178	T	100	33	1	0	0
Jacobs	1992	179		100	43	4	0	0
Korinek	1993	180	B	100	60	25	3	5.0
Palomar	1997	181	T, Md,	100	42	21	6	14.3
Pneumatikos	2002	182	T, Md,	100	30	16	1	3.3
Quinio	1995	183	T,	100	72	37	12	16.7
Rocha	1992	184	T, Md,	100	54	25	8	14.8
Rodriguez_Roldan	1990	185	Md,	100	15	11	5	33.3
Rolando	1993	186	L,	75	31	11	2	6.5
Smith	1993	187	L, US,	100	18		1	5.6
Stoutenbeek '07	2007	188	T,	100	200	46	28	14.0
Unertl	1987	189		100	20	9	2	10.0
Verwaest	1997	190, 193		100	185	40	7	3.8
Wiener	1995	191	US, B	100	31	8	0	0
Winter CC	1992	162	B	92	92	17	8	8.7

Table S4 (continued): *Pseudomonas* VAP data: Concurrent control studies of topical PM based methods of VAP prevention [a]

author	Year	Ref	Notes	MV %	Patients (n)	vap_n	PsVAP	PsVAP %
intervention groups								
Abele-Horn	1997	171	T [2]	100	58	13	2	3.4
Aerdts	1991	172	T [8]	100	17	1	0	0
Bergmans	2001	154	B [9]	100	87	9	3	3.4
Bion	1991	173	L [2]	100	21	0	0	0
Blair	1991	174	[2]	93	126	11	1	0.8
Bonten TAP	1994	155	B [1]	100	22	0	0	0
Cockerill	1992	175	US [10]	85	75	3	1	1.3
De le Cal	2005	176	Burn, Md [2]	74	53	18	2	3.8
Ferrer	1994	177	Md, B [2]	100	39	7	1	2.6
Hammond	1994	178	T [2]	100	39	6	0	0
Jacobs	1992	179	[2]	100	36	0.5	0	0
KoemanChC	2006	117	[11]	100	128	16	2	1.6
Korinek	1993	180	T, B [12]	100	63	15	0	0
Palomar_1	1997	181	Md [2]	100	41	7	1	2.4
Pneumatikos	2002	182	T, Md [1]	100	31	5	0	0
Quinio	1995	183	T [13]	100	76	19	5	6.6
Rocha	1992	184	T, Md [2]	100	47	7	1	2.1
Rodriguez_Roldan	1990	185	T, Md [14]	100	13	0.5	0	0
Rolando	1993	186	L [1]	75	28	8	1	3.6
Smith	1993	187	L, US,	100	18		0	0
Stoutenbeek '07	2007	188	T [2]	100	201	19	11	5.5
Unertl	1987	189	[13]	100	19	1	0	0
Verwaest PTA	1997	190, 193	[2]	100	200	31	10	5.0
Wiener	1995	191	US, B [15]	100	30	8	2	6.7
Winter	1992	162	B [16]	92	91	3	3	3.3

Table S4 (continued): *Pseudomonas* VAP data: Concurrent control studies of topical PM based methods of VAP prevention [a]

Footnotes

T – Data originating from a study for which the majority of ICU admission were for trauma

C - Data originating from a study for which the ICU admission were for cardio thoracic surgery

L - Data originating from a study for which all patients had severe liver disease or transplantation.

Md - Data originating from a study based in a country from the Mediterranean region.

US - Data originating from a study based in the United States of America or Canada

B – VAP diagnosis based on bronchoscopic based methods for sampling.

NS – Not stated

PsVAP - *Pseudomonas* VAP

Several (n = 24) of these studies were cited in the following source systematic reviews.

- Liberati A, D'Amico R, Pifferi S, Torri V, Brazzi L, Parmelli E: Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care. *Cochrane Database Syst Rev* 2009, 4.
- Pileggi C, Bianco A, Flotta D, Nobile CG, Pavia M. Prevention of ventilator-associated pneumonia, mortality and all intensive care unit acquired infections by topically applied antimicrobial or antiseptic agents: a meta-analysis of randomized controlled trials in intensive care units. *Crit Care* 2011; 15:R155.
- Silvestri L, Van Saene HK, Milanese M, Gregori D. Impact of selective decontamination of the digestive tract on fungal carriage and infection: systematic review of randomized controlled trials. *Intensive Care Med* 2005, 31:898-910.
- Chan EY, Ruest A, Meade MO, Cook DJ. Oral decontamination for prevention of pneumonia in mechanically ventilated adults: systematic review and meta-analysis. *BMJ.* 2007; 334:889–900.

Topical polymyxin intervention regimens

1. PTA (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin).
2. PTA-Ctx (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin; Ctx, parenteral cephalosporin).
3. P (P = polymyxin either aerosolized or topical)
4. PNeV (P = polymyxin; Ne = Neomycin; V = Vancomycin)
5. PGA-Ctx (=P, topical polymyxin; G, topical gentamicin; A, topical amphotericin; Ctx, parenteral cephalosporin).
6. PTAM (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin; topical mupirocin).
7. PE (=P, topical polymyxin; E, topical erythromycin)
8. PNoA-Ctx (=P, topical polymyxin; No, topical norfloxacin; A, topical amphotericin; Ctx, parenteral cephalsporin).
9. PGV (=P, topical polymyxin; G, topical gentamicin; V, topical vancomycin).
10. PGNy-Ctx (=P, topical polymyxin; G, topical gentamicin; Ny, topical nystatin; Ctx, parenteral cephalsporin).
11. P-Ctx (=P, topical polymyxin; Ctx, parenteral cephalosporin).
12. PTAV (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin; V, topical vancomycin).
13. PGA (=P, topical polymyxin; G, topical gentamicin; A, topical amphotericin).
14. PTNeA (=P, topical polymyxin; T, topical tobramycin; Ne, topical Neomycin; A, topical amphotericin).
15. PGNy (=P, topical polymyxin; G, topical gentamicin; Ny, topical nystatin).
16. PTA-Cz (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin; Ctx, parenteral Ceftazidime).

Details of analytic methods used

Benchmarking: visual

Caterpillar plots were generated to facilitate a visual benchmark of the VAP and *Pseudomonas* VAP incidence rates and these were generated as follows. The data for VAP and *Pseudomonas* VAP were each logit transformed to generate caterpillar plots using the 'metan' command in STATA (release 12.0, STATA Corp., College Station, TX, USA) as previously [S194-S198]. For Pseudomonas VAP this transformation proceeds as follows; with the number of mechanically ventilated patients as the denominator (D), the number of patients with Pseudomonas VAP as the numerator (N), and R being the Pseudomonas VAP proportion (N/D), the logit(Pseudomonas VAP) is log(N/(D-N)) and its variance is 1/(D*R*(1-R)). Note that for any group with a zero event rate (N=0), the addition of the continuity correction (i.e. N+0·5) is required to avoid indeterminate transformations of the logit proportion and its variance. The visual benchmarks are the summary incidences for each of Pseudomonas VAP, and VAP as derived using the observational studies. These visual benchmarks were then used in the respective caterpillar plots of the component groups from the VAP prevention studies as a reference line. Dot plots were used to provide an 'at a glance' summary of the entire evidence base. These were derived as above for caterpillar plots but without the confidence limits.

Funnel plots were generated using the 'metafunnel' command in Stata [S199].

Benchmarking: Meta-regression

Group level regression models of VAP and Pseudomonas VAP proportions were developed using generalized estimating equation methods ('xtgee' command in STATA). Generalized estimating equation regression models include zero event groups without a need for the continuity correction and also accommodate any intra-cluster correlation. In these regression

models, the predictor variables were the component group membership as follows; membership of a group from an observational study; membership of a control group of a non-concurrent control or concurrent control designed study of polymyxin or a control group of a study of a non-polymyxin intervention; and membership of an intervention group of a non-concurrent control or concurrent control designed study of polymyxin or an intervention group of a study of a non-polymyxin intervention. Additional predictor variables were a group having less than 90% of patients receiving mechanical ventilation, origin from a North American ICU and year of study publication. The category of observational groups acts as the reference (benchmark) category in each model. All factors were entered into the regression models without any pre-selection step.

The regression models were repeated using meta-regression methods using DerSimonian and Laird random effects methods using the 'metareg' command in Stata.

Table S5: Regression models (Random effect methods) [a]

Factor	VAP			*Pseudomonas* VAP		
	Coefficient [b]	95% CI	p	Coefficient [b]	95% CI	p
Groups from observational studies (reference group)	-1·2	-1·4 to -0·95	<0·001	-2·6	-2·8 to -2·3	<0·001
Control groups						
• Non-polymyxin studies	+0·05	-0·17 to +0·27	0·64	+0·05	-0·20 to +0·30	0·70
• NCC Topical polymyxin studies;	-0·05	-0·58 to +0·47	0·84	+0·25	-0·32 to +0·82	0·38
• CC Topical polymyxin studies;	+0·52	+0·18 to +0·87	0·003	+0·59	+0·21 to +0·97	0·002
Intervention groups						
• Non-polymyxin studies	-0·39	-0·62 to -0·16	0·001	-0·32	-0·60 to -0·04	0·024
• NCC Topical polymyxin studies;	-0·90	-1·29 to -0·51	0·001	-1·24	-1·72 to -0·77	0·001
• CC Topical polymyxin studies;	-0·65	-1·01 to -0·29	0·001	-0·57	-1·02 to -0·12	0·014
Trauma ICU [c]	+0·55	+0·36 to +0·74	0·001	+0·13	-0·11 to +0·36	0·29
Mode of diagnosis [d]	-0·03	-0·21 to +0·14	0·71	-0·04	-0·24 to +0·16	0·68
MV percent <90% [e]	-0·40	-0·73 to -0·08	0·015	-0·42	-0·80 to -0·06	0·026
North American study [f]	-0·38	-0·58 to -0·17	0·001	-0·46	-0·69 to -0·22	0·008
Year of publication [g]	-0·01	-0·02 to +0·002	0·10	-0·02	-0·03 to -0·01	0·02

Footnotes

a. Abbreviations; ICU, Intensive care unit; MV; Mechanical ventilation; PM polymyxin; NCC non concurrent control; CC concurrent control.

b. Interpretation. For each model the reference group is the observational study (benchmark) groups and this coefficient equals the difference in logits from 0 (a logit equal to 0 equates to a proportion of 50%; a logit equal to -1.4 equates to a proportion of 20%; a logit equal to -2.9

equates to a proportion of 5%) and the other coefficients represent the difference in logits for groups positive for that factor versus the reference group.

c. Trauma ICU arbitrarily defined as an ICU for which >50% of admissions were for trauma

d. Diagnosis of VAP using bronchoscopic versus tracheal based sampling

e. Less than 90% of the group receiving prolonged mechanical ventilation.

f. Originating from an ICU in The United States of America or Canada

g. Year of study publication with the coefficient representing the increment for each year post 1985

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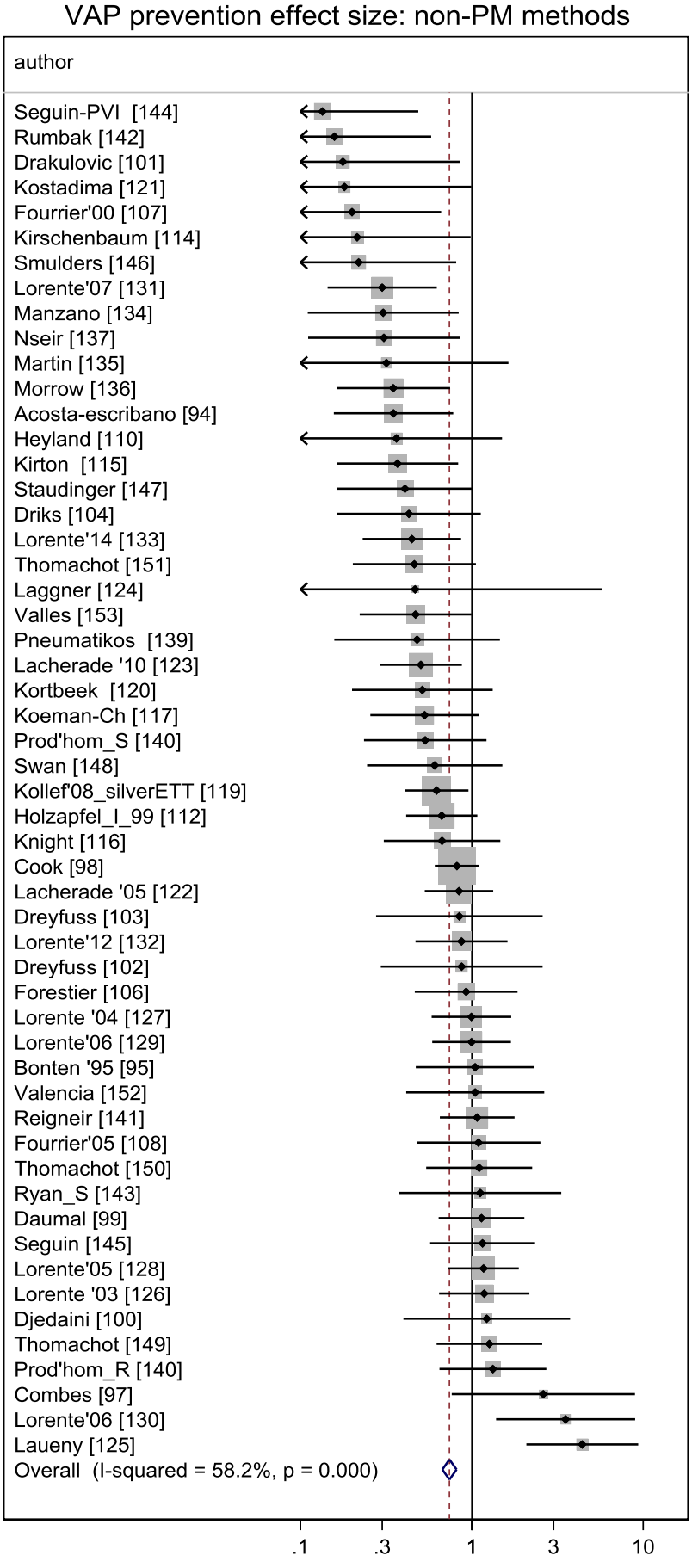


Fig S1

Caterpillar plots of the group specific (small squares) and summary (large open diamond, broken vertical line) effect size on the overall VAP incidence and 95 % CI among studies of non-PM methods of VAP prevention based methods of VAP prevention. Studies are listed in Table S2.

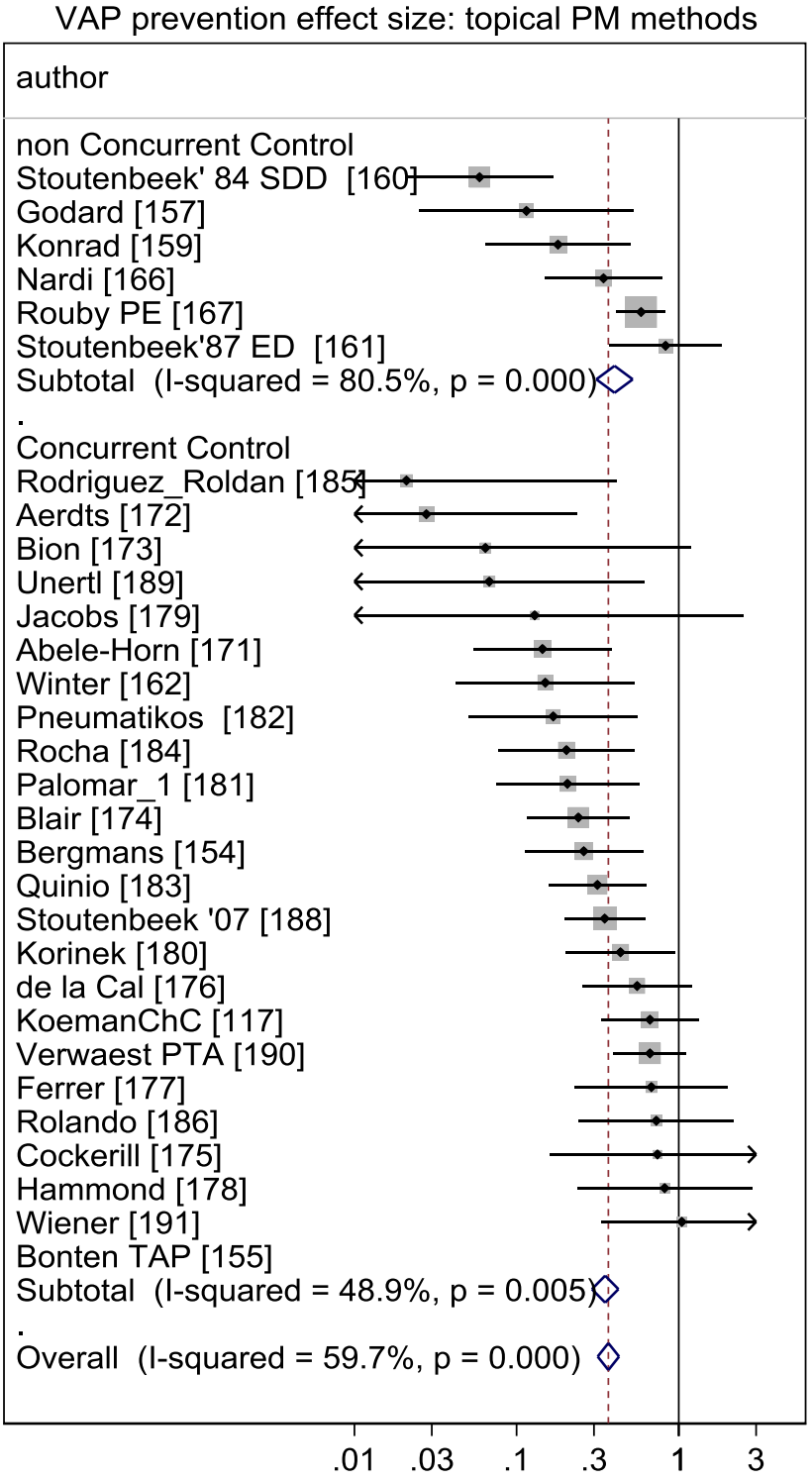


Fig S2

Caterpillar plots of the group specific (small squares) and summary (large open diamond, broken vertical line) effect size on the overall VAP incidence and 95 % CI among studies of topical PM based methods of VAP prevention. Studies are listed in Table S3 & S4.

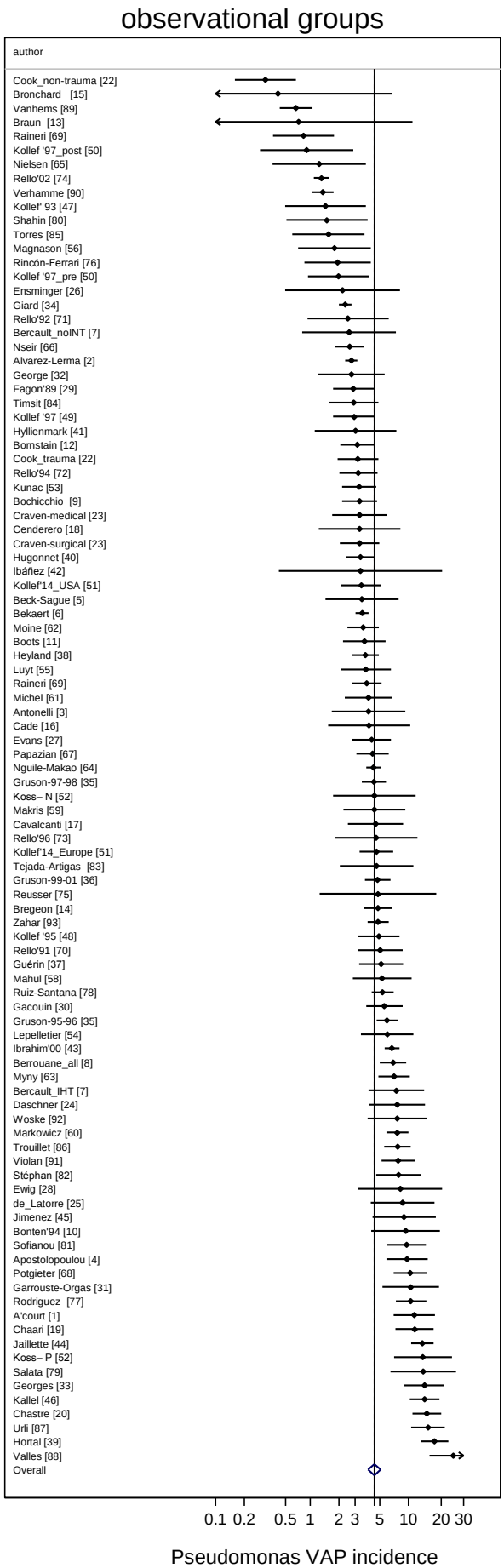


Fig S3

Pseudomonas VAP incidence among observational studies. Caterpillar plot of the group specific (small diamonds) and summary (central solid line and large open diamond) *Pseudomonas* VAP incidence proportion and 95 % CI. Groups are listed in Table S1. Note that the x axis is a logit scale and that groups with a zero event have a continuity correction (N+0.5) to enable them to appear in the plot. The central solid line is the *Pseudomonas* VAP benchmark. The corresponding funnel plot is presented in Fig S9.

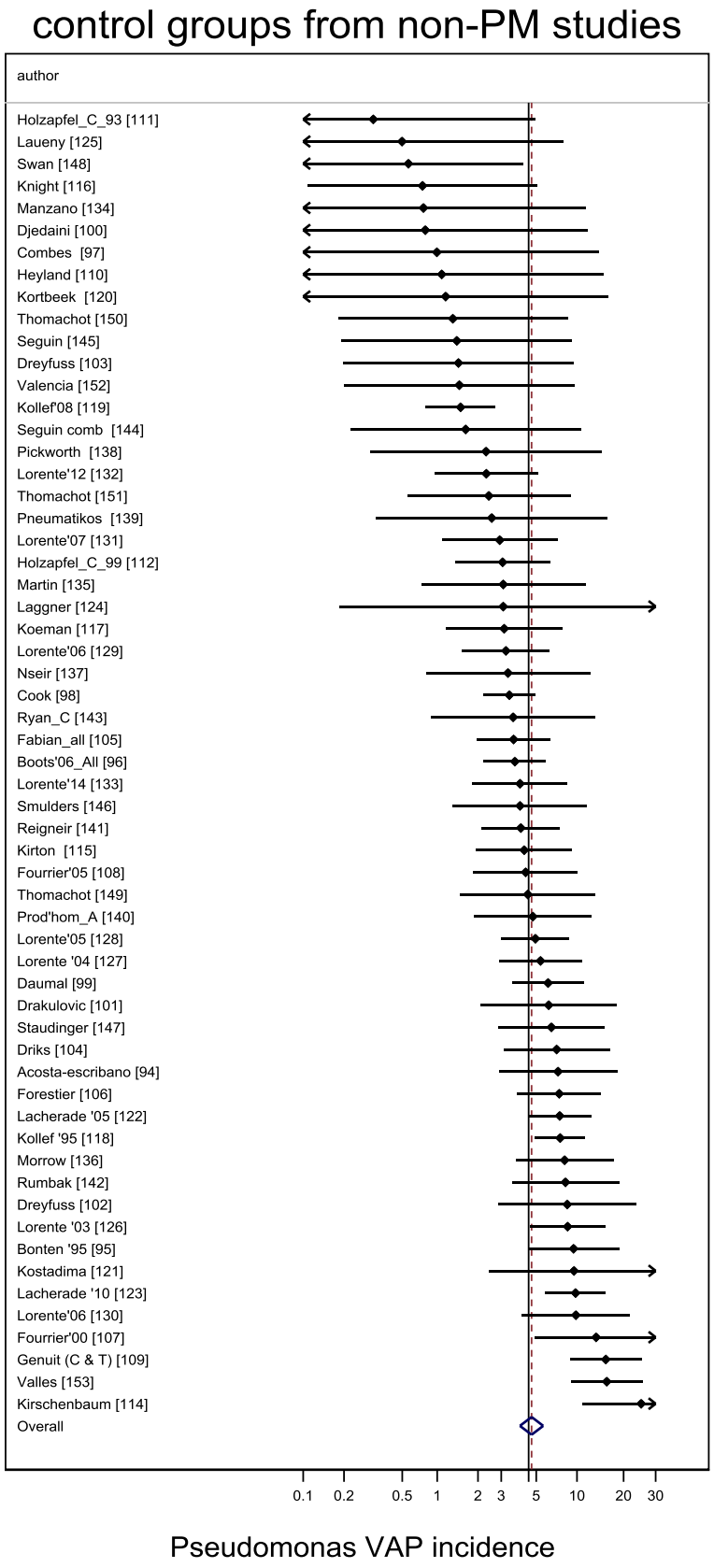


Fig S4

Pseudomonas VAP incidence among control groups from studies of non-polymyxin methods. Caterpillar plots of the group specific (small diamonds) and summary (central broken line and large open diamond) *Pseudomonas* VAP incidence and 95% CI. Groups are listed in Table S2. Note that the x axis is a logit scale and that groups with a zero event have a continuity correction (N+0.5) to enable them to appear in the plot. The central solid line is the *Pseudomonas* VAP benchmark from Figure S3. The corresponding funnel plot is presented in Fig S10.

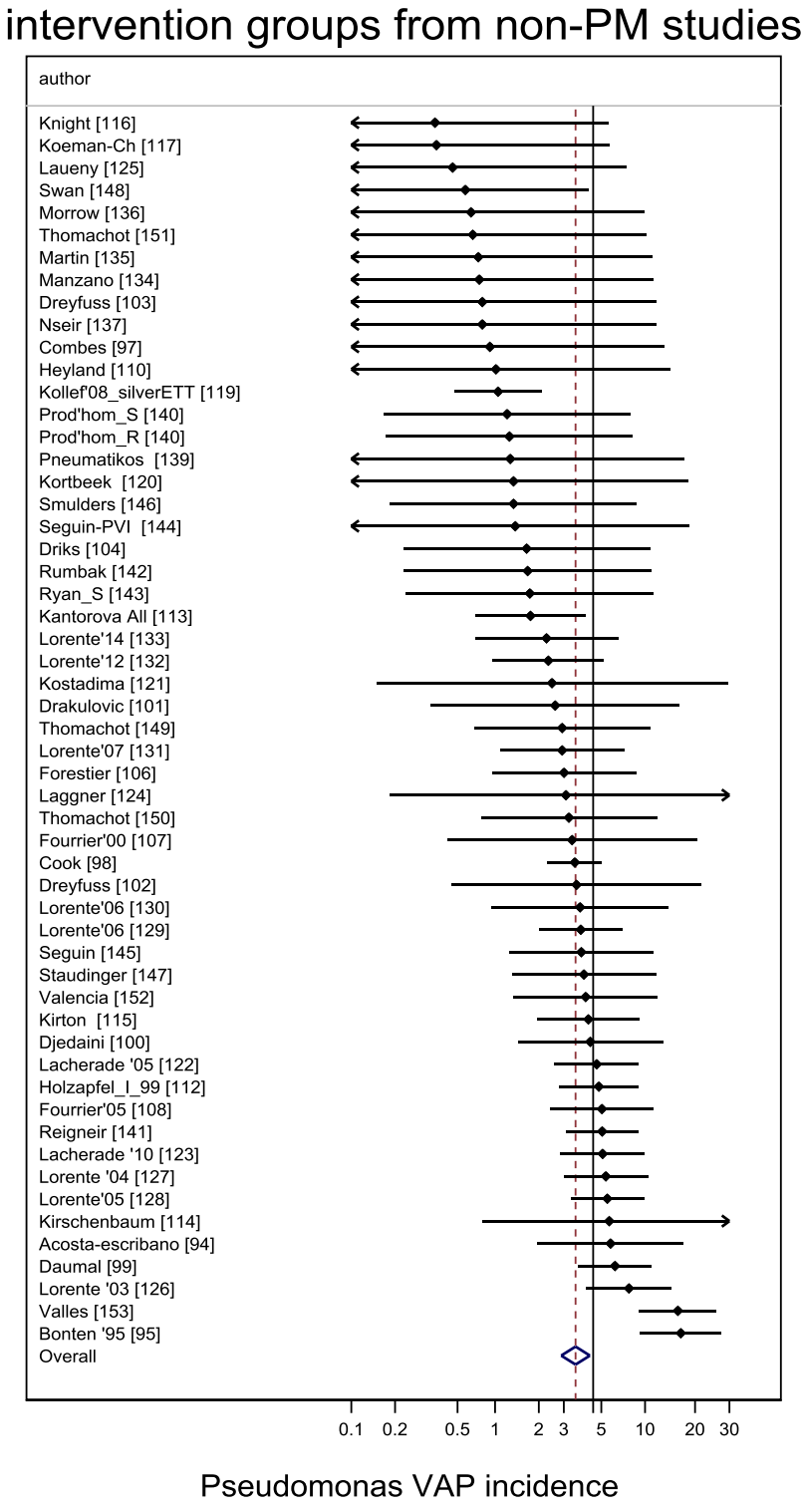


Fig. S5

Pseudomonas VAP incidence among intervention groups from studies of non-polymyxin methods. Caterpillar plots of the group specific (small diamonds) and summary (central broken line and large open diamond) *Pseudomonas* VAP incidence and 95% CI. Groups are listed in Table S2. Note that the x axis is a logit scale and that groups with a zero event have a continuity correction (N+0.5) to enable them to appear in the plot. The central solid line is the *Pseudomonas* VAP benchmark from Figure S3. The corresponding funnel plot is presented in Fig S11.

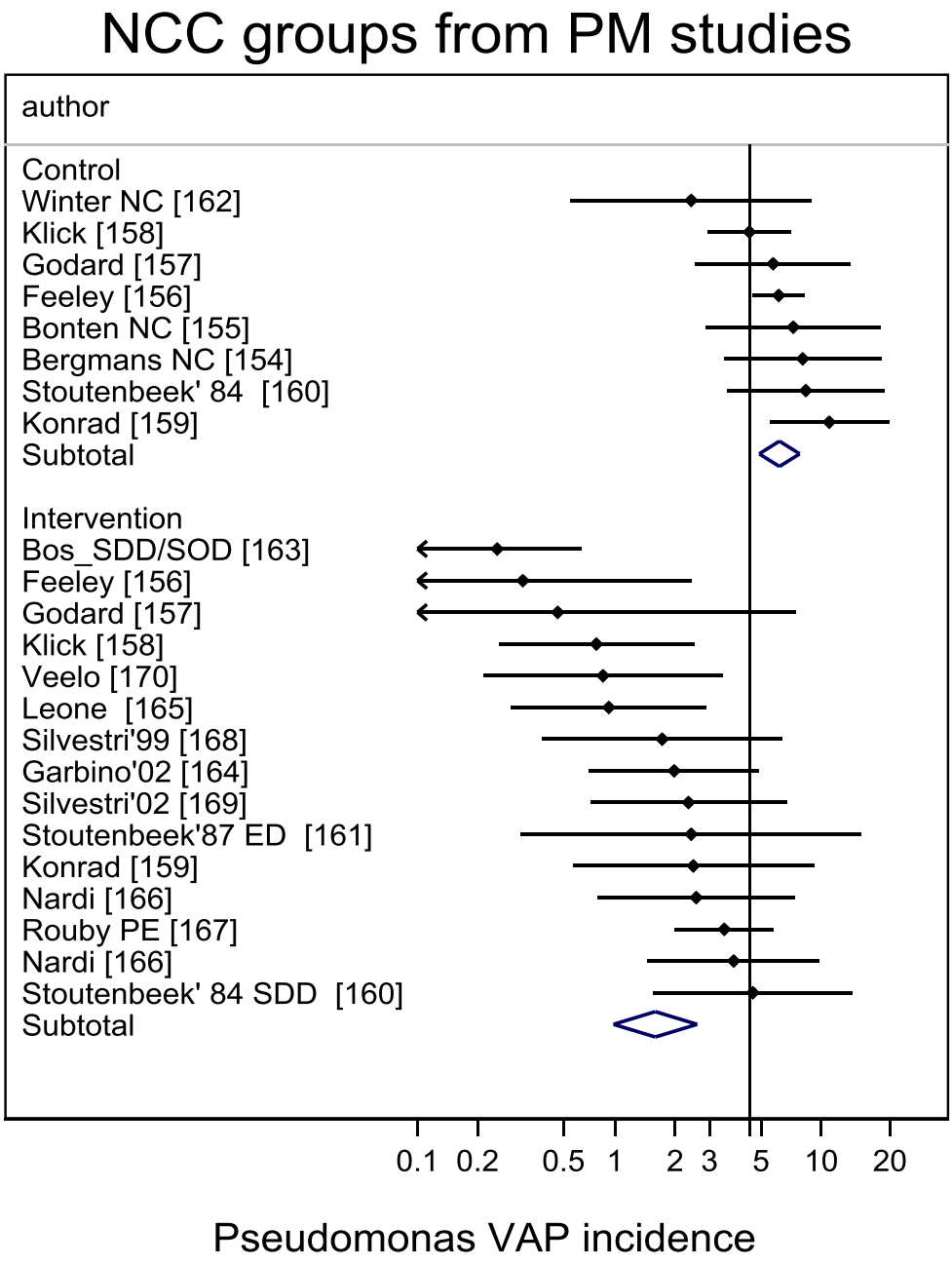


Fig S6

Pseudomonas VAP incidence among non-concurrent controlled studies of topical polymyxin. Caterpillar plots of the group specific (small squares) and summary (large open diamonds) *Pseudomonas* VAP incidence proportion and 95 % CI. Groups are listed in Table S3. Note that the x axis is a logit scale and that groups with a zero event have a continuity correction (N+0.5) to enable them to appear in the plot. The central solid line is the *Pseudomonas* VAP benchmark from Figure S3. The corresponding funnel plot for the control groups are presented in Fig S12 & S14.

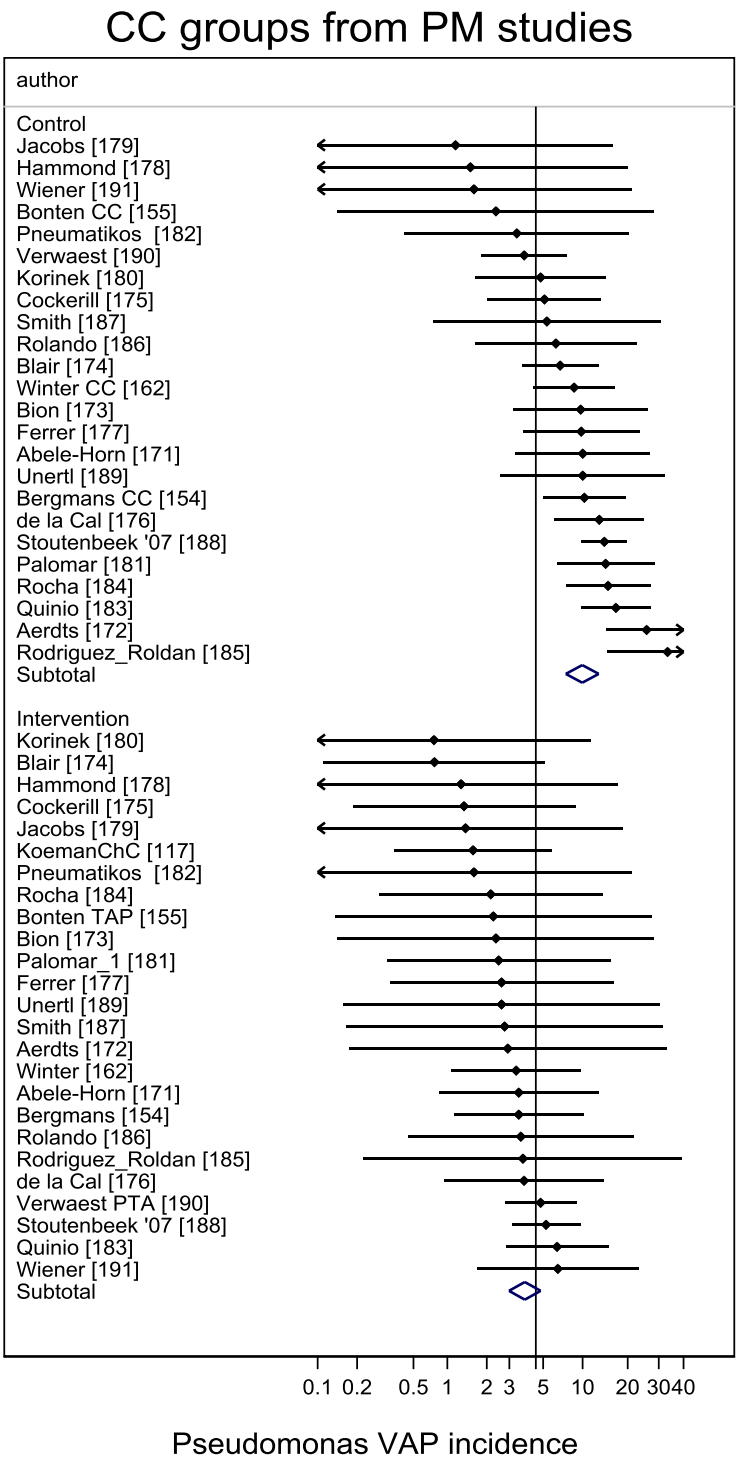


Fig S7

Pseudomonas VAP incidence among concurrent controlled studies of topical polymyxin. Caterpillar plots of the group specific (small squares) and summary (large open diamonds) *Pseudomonas* VAP incidence proportion and 95 % CI. Groups are listed in Table S4. Note that the x axis is a logit scale and that groups with a zero event have a continuity correction (N+0.5) to enable them to appear in the plot. The central solid line is the *Pseudomonas* VAP benchmark from Figure S3. The corresponding funnel plot for the control groups are presented in Fig S14 & S15.

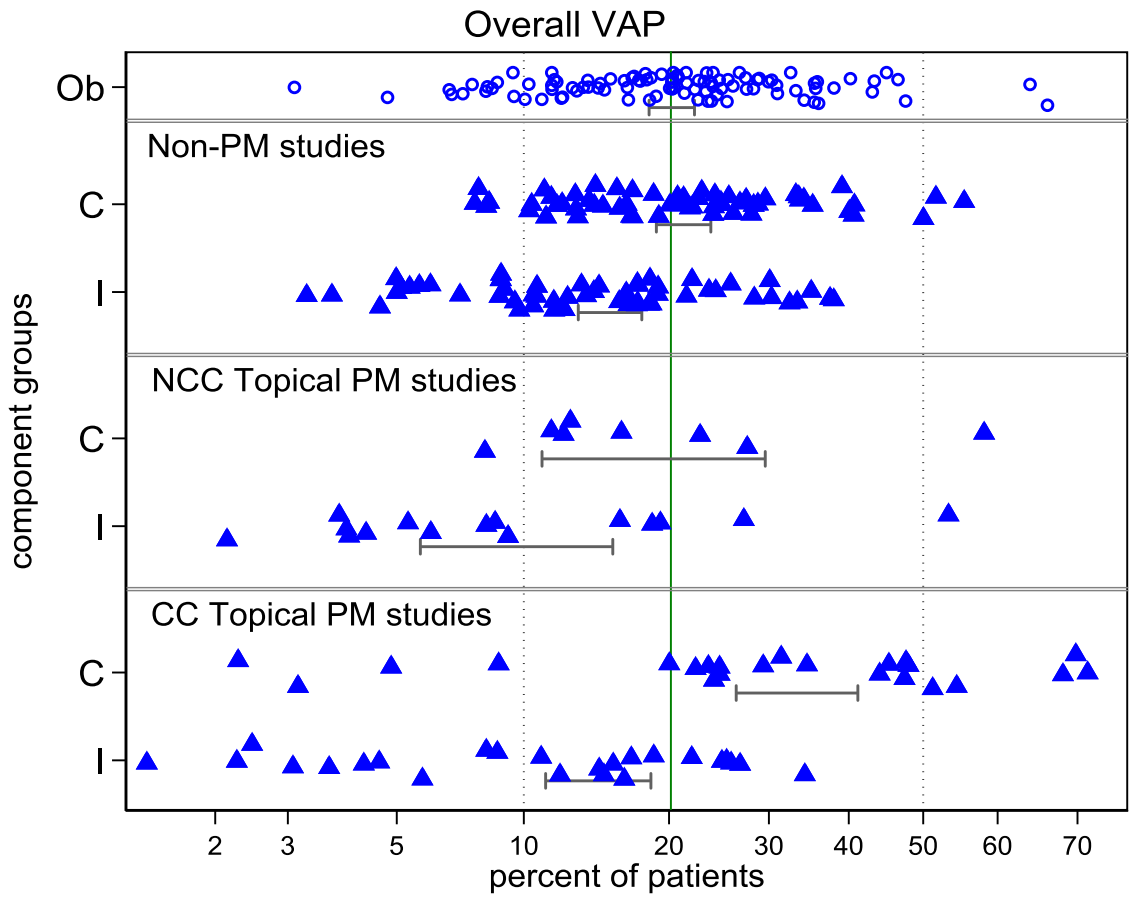


Fig S8. Overall VAP incidence per 100 patients for all component groups together with 95 % confidence intervals of summary incidence. Ob is observational groups (open symbols), C is control groups, I is interventional groups (closed triangles). Note that the x axis is a logit scale and that groups with a zero event have a continuity correction (N+0.5) to enable them to appear in the plot. The vertical line is the VAP benchmark derived from the observational groups.

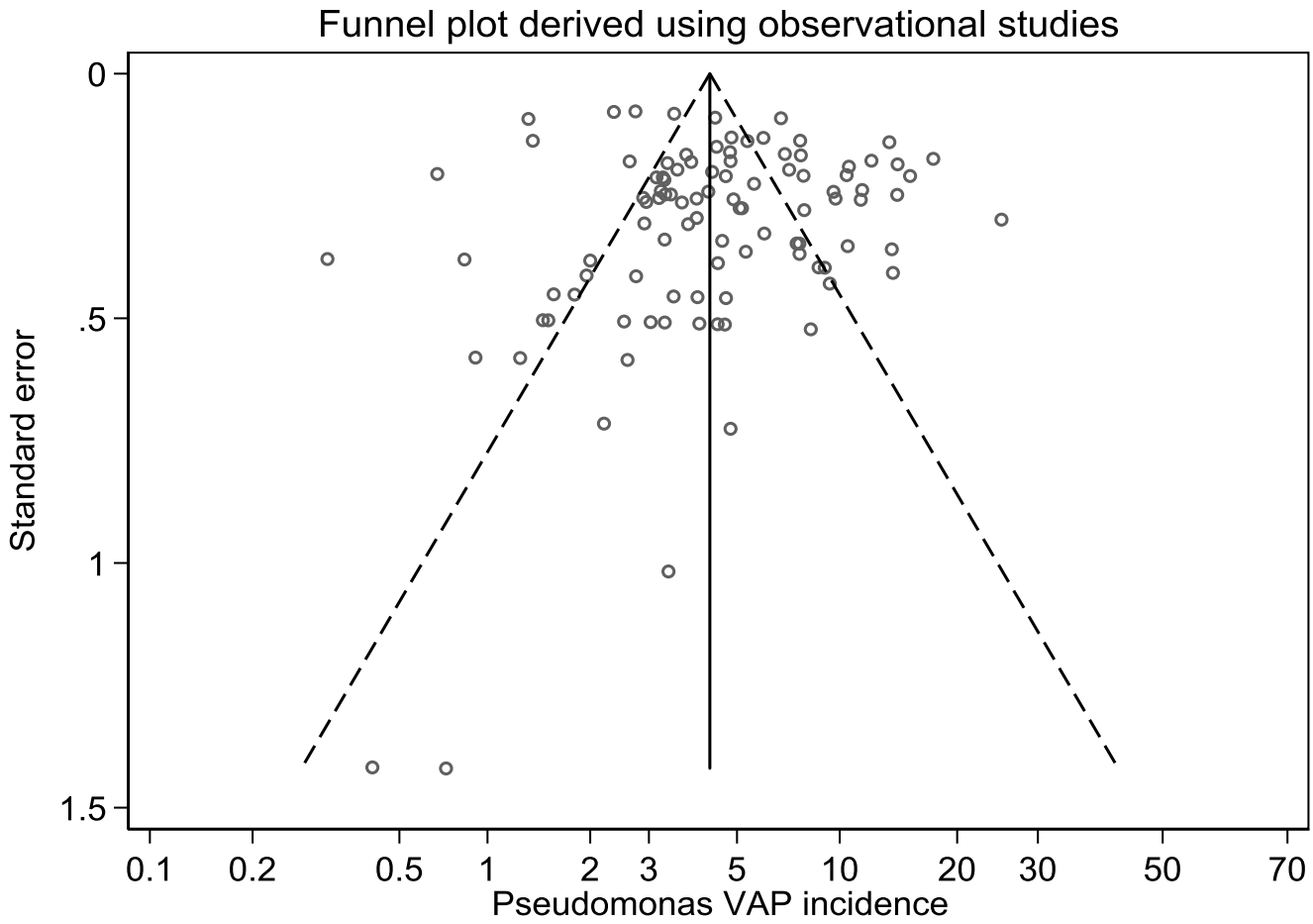
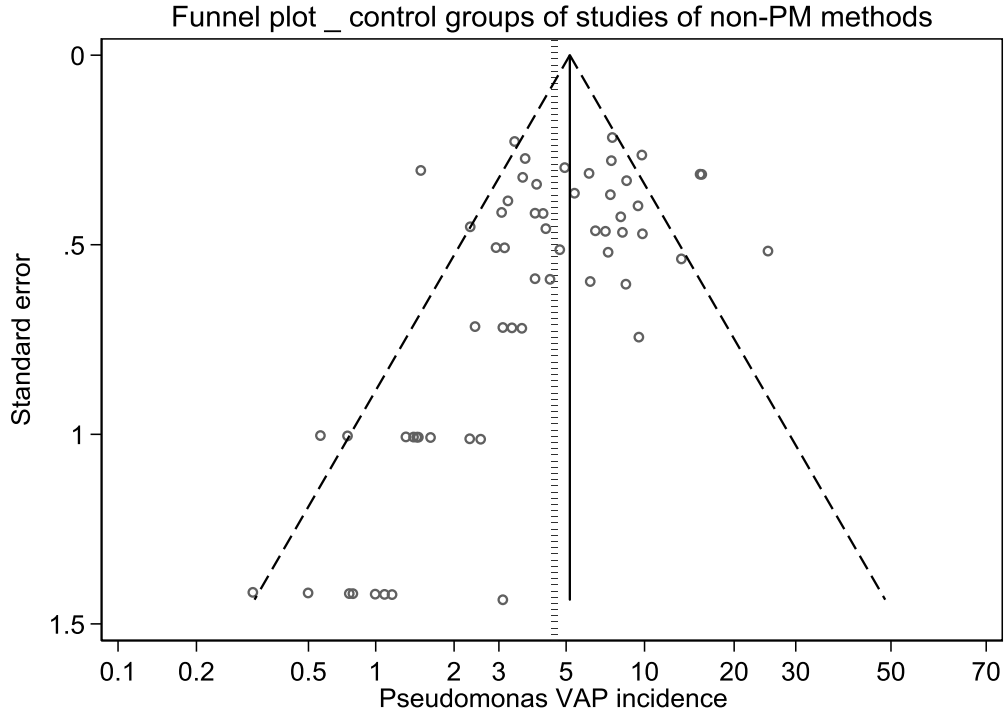


Fig S9 PsVAP incidence funnel plots for groups from observational studies. Note that the x axis is a logit scale and that groups with a zero event have a continuity correction (N+0.5) to enable them to appear in the plot. The vertical dotted line is the PsVAP benchmark derived from the observational groups.



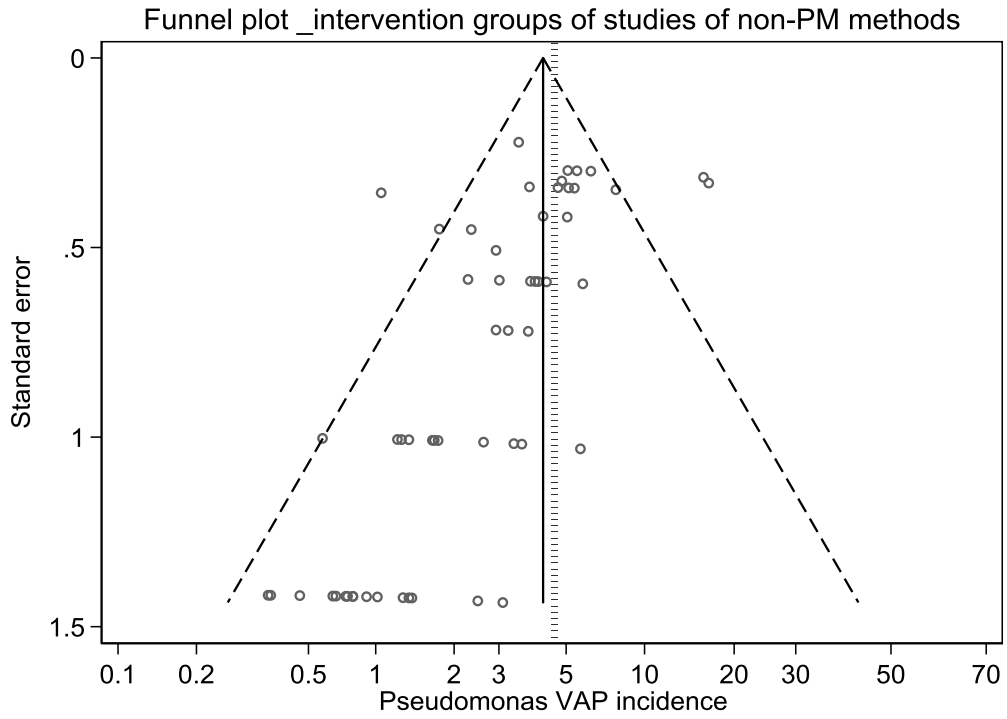
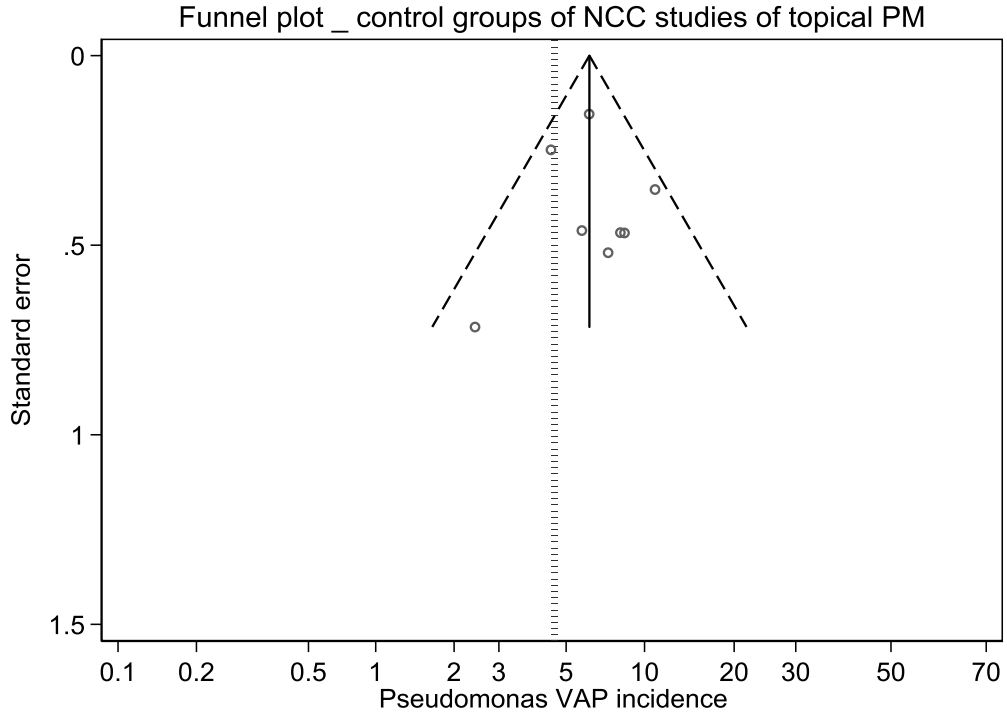


Fig S10 & S11 PsVAP incidence funnel plots for control (Fig S10 top) and intervention (Fig S11 bottom) groups studies of non-PM methods. Note that the x axis is a logit scale and that groups with a zero event have a continuity correction (N+0.5) to enable them to appear in the plot. The vertical dotted line is the PsVAP benchmark derived from the observational groups.



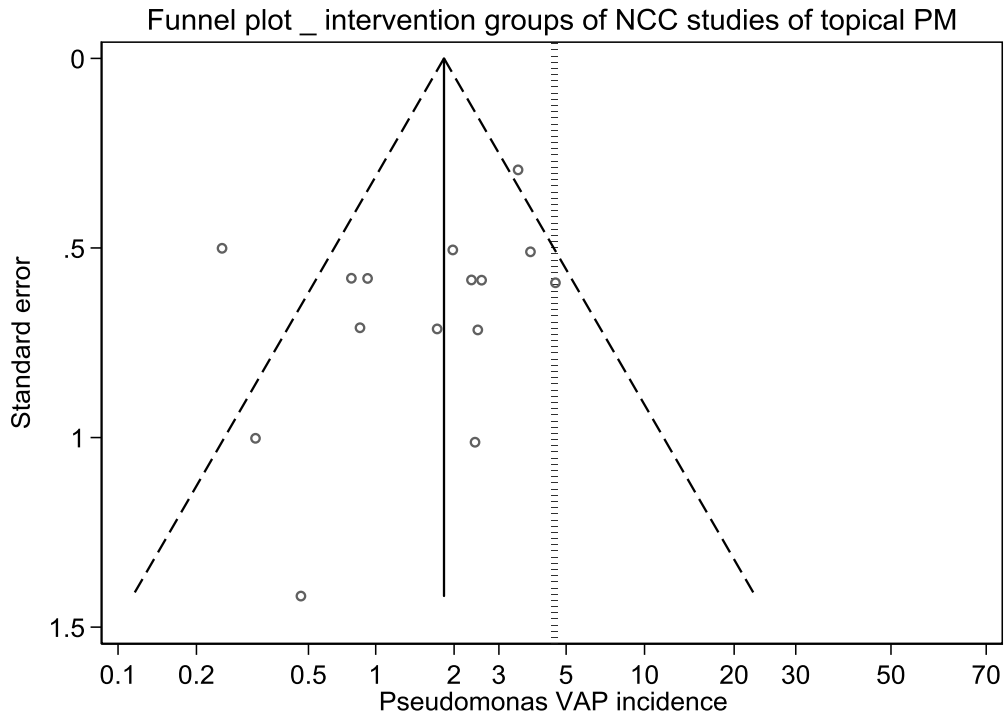
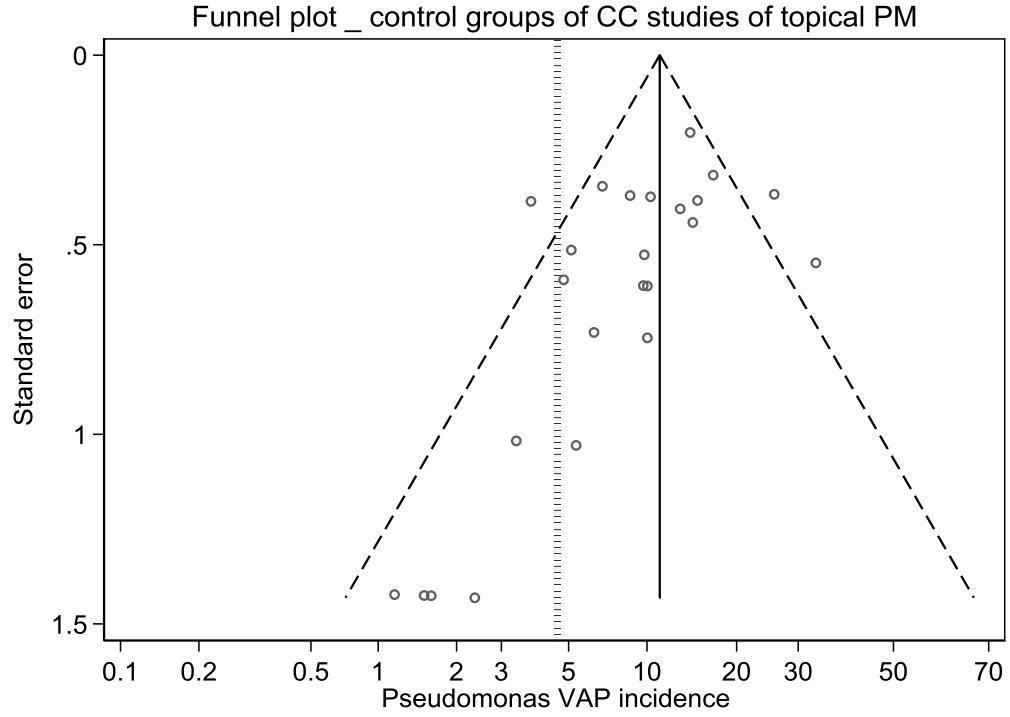


Fig S12 & S13 PsVAP incidence funnel plots for control (Fig S12 top) groups and intervention (Fig S13 bottom) of NCC design studies of PM methods. Note that the x axis is a logit scale and that groups with a zero event have a continuity correction (N+0.5) to enable them to appear in the plot. The vertical dotted line is the PsVAP benchmark derived from the observational groups.



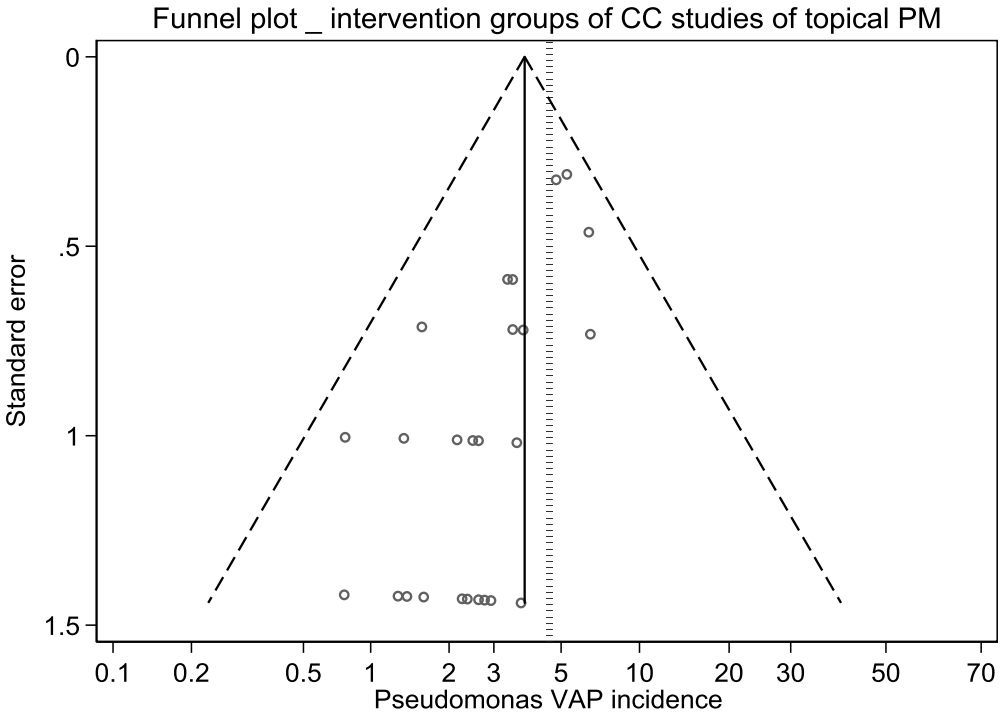


Fig S14 & S15 PsVAP incidence funnel plots for control (Fig S14 top) groups and intervention (Fig S15 bottom) of CC design studies of PM methods. Note that the x axis is a logit scale and that groups with a zero event have a continuity correction (N+0.5) to enable them to appear in the plot. The vertical dotted line is the PsVAP benchmark derived from the observational groups.

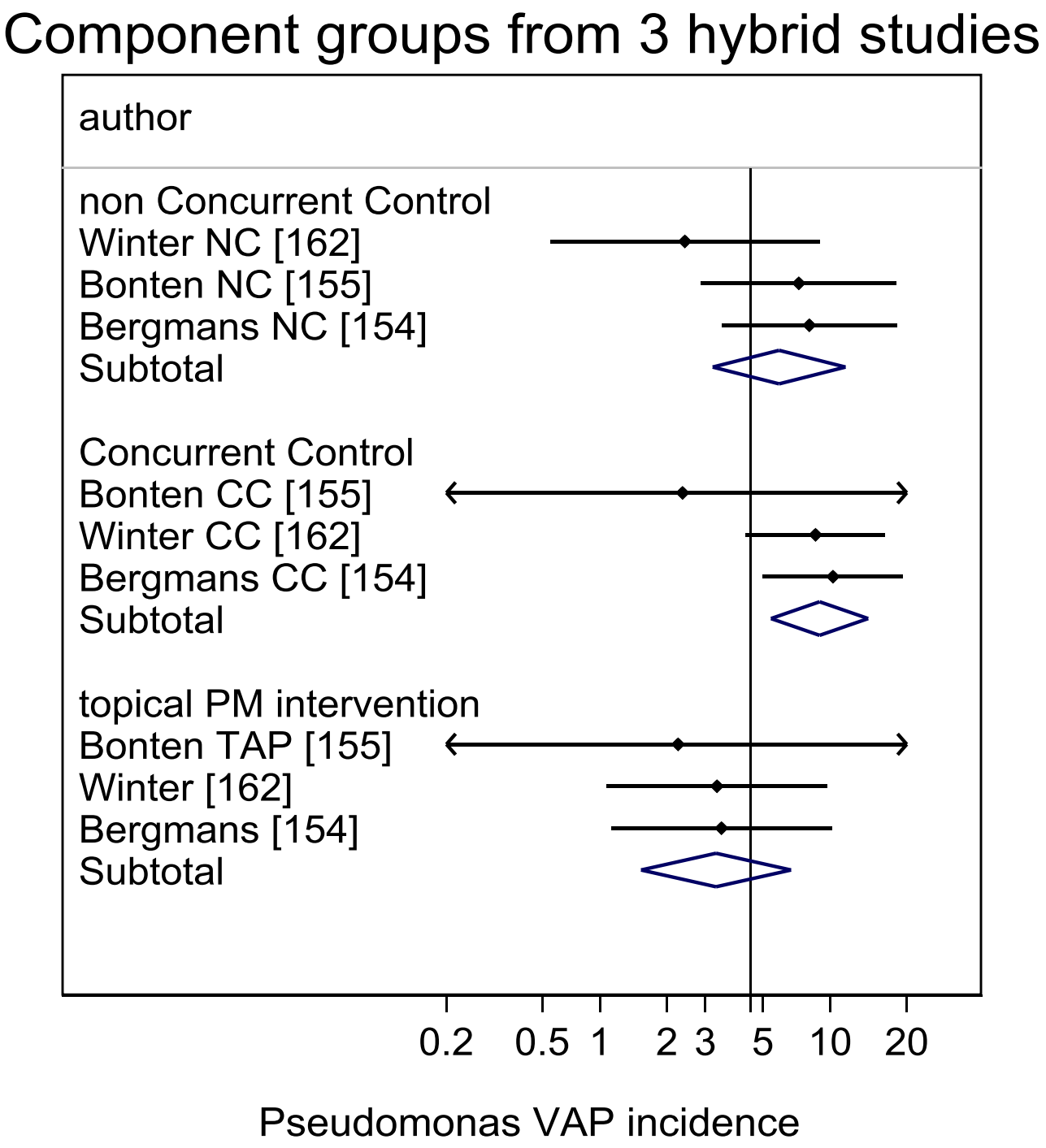


Fig S16 *Pseudomonas* VAP incidence among component groups of three studies of topical polymyxin with hybrid non-concurrent and concurrent controlled design. Caterpillar plots of the group specific (small squares) and summary (large open diamonds) *Pseudomonas* VAP incidence proportion and 95 % CI. Groups are listed in Table S3 and S4. Note that the x axis is a logit scale and that groups with a zero event have a continuity correction (N+0.5) to enable them to appear in the plot. The central solid line is the *Pseudomonas* VAP benchmark from Figure S3.