Candida-Acinetobacter-Pseudomonas-interaction modelled within 286 ICU infection prevention studies

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Supplemental file contents:

Table S1: Observational studies (Benchmark groups) [a]

Author	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
A'court	1993	1	T	100	>10	150	17	0		6		
Alvarez -Lerma	1996	2		93	5to10	6494	174	56				
Antonelli	1994	3		70	>10	124	5	6	1			
Apostolo-poulou	2003	4		100	>10	175	17	6				
Arumugam	2018	5	T	100	5to10	332	7	4				
Azoulay	2006	6		100	>10	589	30					4
Azoulay	2006	6	crf	100	>10	214	19					2
Bailly	2015	7		100	>10	1491						11
Baraibar	1997	8		100	5to10	707		12				
Beck-Sague	1996	9		100	5to10	145	5	0				
Bekaert	2011	10		100	5to10	4479	155	24				
Bercault	2001	11		100	>10	1144			2			
Bercault_ IHT	2005	12		100	5to10	118	9	2				
Bercault _noINT	2005	12	I	100	>10	118	3	3				
Berrouane	1998	13		83	>10	565	40					
Blot 45_64	2014	14		100	5to10	670	20	15				
Blot 65_74	2014	14		100	5to10	549	20	14				
Blot >74	2014	14		100	5to10	516	10	8				
Bochicchio	2004	15	T	100	>10	678	22	10				
Bonten'94	1994	16		100	>10	64	6	0				
Bonten'96	1996	17		100	>10	141	12					
Boots	2008	18		100	>10	412	15	14	0			
Bornstain	2004	19		100	>10	747	23	1				
Borzotta	1999	20		85	5to10	459						7
Braun	1986	21		100	5to10	66	0					
Bregeon	1997	22		100	NS	660	33	10	3			
Bronchard	2004	23	T	100	>10	109	0					
Cade	1993	24		98	>10	98	4	0	5	1	0	1
Cavalcanti	2006	25		100	5to10	190	9	1	6			
Cenderero	1999	26		100	5to10	123	4	2	0			
Chaari	2015	27		100	5to10	175	20	12				
Charles	2005	28		75	>10	36						0
Charles	2005	28	crf	97	>10	56						1
Chastre	1998	29		100	>10	243	36	13	7			
Chevret	1993	30		100	5to10	255	21	5	4			
Combes	2000	31	T	100	>10	104	0					

Table S1 (continued): Observational studies (Benchmark groups)

Author	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Cook_ non-trauma	2010	32		100	5-10	2080	7	1	4			
Cook_trauma	2010	32	T	100	>10	511	16	8	1			
Craven-medical	1988	33		100	5-10	277	9	0	1	1		0
Craven-surgical	1988	33		100	5-10	521	17	0	5	6		3
Daschner	1988	34		100	5-10	116	9	1	4			
De waele	2003	35	crf	79	>10	28						0
de_Latorre	1995	36		100	>10	80	7	0	2			
de_Santis	2000	37		NS	NS	713				3		2
de_Santis	2013	37		NS	NS	1318				1		3
El-Masri	2004	38		NS	>10	361				1	3	6
Ensminger	2006	39	C	100	5-10	92	2	1				
Ertugrul	2006	40		100	5-10	100	3	6		0	2	
Esteve	2007	41		80	>10	404				8	1	0
Esteve	2007	41		78	>10	395				4	6	2
Evans	2010	42		100	5-10	416	18					
Ewig	1999	43		100	5-10	48	4	0	1			
Fabian	1993	44	T	100	>10	278	10	15				
Fagon	1989	45		100	>10	567	16	8				
Ferreira	2015	46		94	5-10	2527						23
Gacouin	2009	47		100	>10	361	21	4				
Garcı´a -Garmendia	2001	48		46	5-10	2640				14	42	11
Garrouste -Orgeas	1997	49		100	>10	86	9	11	1			
Garrouste -Orgeas	2006	50		75	>10	3247				19	1	15
George	1998	51		100	5-10	223	6	1	2			
Georges	2000	52		100	>10	135	19	8				
Giamarellos-Bourboulis	2009	53	T	100	>10	72	5	17	2	1	2	3
Giard	2008	54		100	5-10	7236	168					
Gruson-95-96	2000	55		100	NS	1004	62	20				
Gruson-97-98	2000	55	I	100	NS	1029	47	7				
Gruson-99-01	2003	56		100	NS	823	41	15				
Guérin	1997	57		100	>10	260	14	1	0			
Gursel	2010	58		100	5-10	92	10	23	1			
Heyland	1999	59		100	5-10	1014	38	6	26			5
Holzapfel_93	1993	60		100	5-10	300	0	1		0		
Huang_1SC	2013	61		NS	<5	15816				14	7	49
Huang_1pre	2013	61		NS	<5	23480				5	9	38

Table S1 (continued): Observational studies (Benchmark groups)

Author	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Hugonnet	2007	62		100	5-10	936	31	8	40			
Hyllienmark	2007	63		100	<5	221	0	1				
Hyllienmark	2013	64	T	42	<5	135	4	2				
Ibáñez	2000	65		100	5-10	30	1	1				
Ibrahim'00	2000	66		100	5-10	1882	130	16	19			
Ibrahim'00	2000	67		69	>10	4913				22	8	41
Ibrahim'01	2001	68		56	5-10	880	49	4				
Jacobs	1990	69		100	>10	24	4	0		1		
Jaillette	2011	70		100	>10	439	59	22				
Jensen_HE	2015	71		66	5-10	604						24
Jensen_SOC	2015	71		67	5-10	596						13
Jimenez	1989	72		100	5-10	77	7	6				
Kautzky	2014	73		37	>10	35			1			0
Kautzky	2014	73	crf	57	>10	30			1			2
Ko	2013	74		100	>10	1453				21	11	
Kollef' 93	1993	75		100	5-10	277	4	1				
Kollef '95	1995	76		100	NS	314	16	4				
Kollef '95	1995	77		100	>10	300	23	6				
Kollef '97	1997	78		100	5-10	521	15	2				
Kollef _post	1997	79	C I	90	<5	327	3	1	0	1	0	3
Kollef _pre	1997	79	C	90	<5	353	7	2	1	2	1	5
Kollef _Europe	2014	80		100	>10	495	24					
Kollef _USA	2014	80		100	>10	502	17					
Koss– N	2001	81		100	>10	87	4	2	10			
Koss– P	2001	81	I	100	>10	66	9	2	3			
Kunac	2014	82		100	NS	716	23	13		2	1	
Laggner	1989	83		100	>10	32	0	0	0			0
Lambert	2011	84		NS	5-10	119699				389	143	
Laupland	2002	85		NS	5-10	1017				2	0	3
Laupland	2004	86		84	5-10	4473				11	4	19
León	2006	87	crf	95	>10	1699						58
León	2009	88	crf	91	>10	1107						37
León	2016	89	crf	84	>10	233						11
Lepelletier	2010	90	T	100	>10	161	10					
Li	2012	91		17	>10	29			1			0
Li	2012	91	crf	40	>10	82			10			3
Luna	2003	92		100	5-10	427	13	25	2			

Table S1 (continued): Observational studies (Benchmark groups)

Author	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Luyt	2005	93		100	NS	290	11	3				
Magnason	2008	94		100	5-10	280	5	0	0	0	0	5
Mahul	1992	95		100	>10	145	8	3	3			
Makris	2011	96	I	100	>10	152	7					
Markowicz	2000	97		100	5-10	744	58	13				
Memish	2000	98		100	>10	202	21	14	4			
Michel	2005	99		100	>10	299	12					
Mitsogianni	2011	100		NS	>10	124				1	5	1
Mitsogianni	2010	100		NS	>10	143				2	12	0
Moine	2002	101		80	>10	764	27	1	2			
Montecalvo	1992	102		100	5-10	38				1		1
Myny	2005	103		100	<5	385	28	13				
Nguile-Makao	2010	104		100	5-10	2873	130					
Nielsen	1992	105		100	5-10	242	3	0				
Nseir	2005	106		100	5-10	1241	32	20				
Nseir	2007	107	crf	100	>10	102						3
Orsi	2007	108		98	>10	1741				29	16	10
Orsi	2012	108		100	>10	1165				12	23	4
Osmon	2003	109		72	5-10	893				9		26
Outcomerea	2019	110		100	5-10	7735	454	48				
Papazian	1996	111		100	NS	586	26	5				
Petri	1997	112	crf	95	>10	409						3
Potgieter	1987	113		78	5-10	250	26	32	5			
Prowle	2011	114		69	5-10	6339						51
Ramirez	2016	115		100	>10	440			0			
Rello'91	1991	116		100	5-10	264	14	2	1			
Rello'92	1992	117		80	5-10	208	10					
Rello'92	1992	118		67	5-10	161	4					
Rello'94	1994	119		72	NS	1650				16	5	4
Rello'96	1996	120		100	>10	83	4					
Rello'02	2002	121		100	5-10	9080	119					
Rello'03	2003	122		100	>10	99	8	2	0			
Resende	2013	123		100	>10	126	11	11	0			
Reusser	1989	124		100	5-10	40	2	1		0	0	
Rincón-Ferrari	2004	125		100	5-10	310	6	27				
Rodrigues	2009	126		100	5-10	133	10	14	2			
Rodriguez	1991	127	T	100	>10	294	31	11				
Ruiz-Santana	1987	128		100	5-10	1005	56	0	1			

Table S1 (continued): Observational studies (Benchmark groups)

Author	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Salata	1987	129		100	>10	51	7	0	1			
Shahin	2013	130		100	5to10	267	4		3			
Sofianou	2000	131		100	>10	198	19	35				
Stéphan	2006	132	T	100	>10	175	14	8				
Tan	2016	133		100	>10	618	49	114				
Tejada-Artigas	2001	134		100	>10	103	5	10				0
Thompson	2008	135		NS	5to10	4270				13	1	24
Timsit	1996	136		100	>10	387	11	8				
Torres	1990	137		100	<5	322	5	9				
Trouillet	1998	138		100	>10	498	39	22				
Urli	2002	139		95	>10	178	27		1	3		4
Valles	2007	140		100	>10	60	15	0				
Vanhems	2011	141		100	5to10	3387	24					
Verhamme	2007	142		84	5to10	4000	54	3	6			
Violan	1998	143		100	>10	314	25	1				
Warren	2001	144		28	<5	3163				3	0	4
Woske	2001	145		100	>10	103	8	1				
Xie	2011	146		100	5to10	4155	169	137	88			
Zahar	2009	147		100	5to10	1233	62					

Table S1 footnotes

Notes; T = Data originating from a study for which the majority of ICU admission were for trauma; C = cardio-thoracic ICU; I = Infection control intervention to entire ICU; crf = group wide candidemia risk factor

MV = percentage of group receiving mechanical ventilation; NS – Not stated; LOS is mean or median length of ICU stay; The ICU-LOS is the ICU length of stay. This is based on surrogate measures including mean (or median) length of MV were taken if the length of ICU LOS was not available in order to generate broad categories of ICU stay of <5 days, 5 to 10 days and >10 days

v_ps_n is the count of *Pseudomonas* VAP; v_sr_n is the count of *Staphylococcus aureus* VAP; v_ac_n is the count of *Acinetobacter* VAP and v_can_n is the count of *Candida* isolates from patients with VAP.

b_ps_n is the count of *Pseudomonas* bacteremia; b_sr_n is the count of *Staphylococcus aureus* bacteremia; and b_ac_n is the count of *Acinetobacter* bacteremia; b_can_n is the count of Candidemia; b_cns_n is the count of coagulative negative *Staphylococcus* bacteremia and b_ent_n is the count of *Enterococcal* bacteremia.

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: Groups of non decontamination studies [a]

Author	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Acosta -escribano	2010	148	T	100	>10	54	4	0	1			
Acosta -escribano	2010	148	T	100	>10	50	3	0	0			
Bonten '95	1995	149		100	>10	67	11	0				0
Bonten '95	1995	149		100	>10	74	7	1				0
Cook	1998	150		100	5to10	604	21		11			
Cook	1998	150		100	5to10	596	20		19			
Daumal	1999	151		100	>10	174	11		2			
Daumal	1999	151		100	5to10	187	12		6			
Djedaini	1995	152		100	5to10	68	3	0	1			
Djedaini	1995	152		100	5to10	61	0	3	0			
Drakulovic	1999	153		100	5to10	39	1	0	0			
Drakulovic	1999	153		100	5to10	47	3	1	0			
Dreyfuss	1991	154		100	5to10	28	1	2				
Dreyfuss	1991	154		100	>10	35	3	3				
Dreyfuss	1995	155		100	5to10	70	1	2				
Dreyfuss	1995	155		100	>10	61	0	3				
Driks	1987	156		100	>10	61	1		0			
Driks	1987	156		100	>10	69	5		0			
Forestier	2008	157		100	>10	106	8					
Forestier	2008	157		100	>10	102	3					
Heyland	1999	158		100	>10	49	0		0			
Heyland	1999	158		100	>10	46	0		0			
Holzapfel_C	1999	159		100	>10	200	6	3	3	0	0	1
Holzapfel_I	1999	159		100	>10	199	10	4	1	2	1	1
Kappstein	1991	160		100	5to10	49			3			
Kappstein	1991	160		100	5to10	55			7			
Kirschenbaum	2002	161		100	>10	20	5					
Kirschenbaum	2002	161		100	>10	17	1					
Kirton	1997	162		100	>10	140	6					
Kirton	1997	162		100	>10	140	6					
Knight	2009	163		100	5to10	130	0	3	0			
Knight	2009	163		100	5to10	129	1	1	0			
Kollef	2008	164		100	5to10	743	11	5	7			
Kollef _silverETT	2008	164		100	5to10	766	8	1	5			
Kortbeek	1999	165	T	100	5to10	37	0	1				
Kortbeek	1999	165	T	100	5to10	43	0	1				

Table S2 (continued): Groups of non decontamination studies [a]

Author	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Lacherade	2005	166		100	>10	185	9	2	0			
Lacherade	2005	166		100	>10	184	14	0	2			
Lacherade	2010	167		100	>10	164	16	2				
Lacherade	2010	167		100	>10	169	9	2				
Laueny	2014	168		100	>10	98	0	1	0			
Laueny	2014	168		100	>10	91	0	0	0			
Lorente '03	2003	169		100	>10	114	9	0	14			
Lorente '03	2003	169		100	>10	116	10	1	10			
Lorente '04	2004	170		100	>10	161	9	3	2			
Lorente '04	2004	170		100	>10	143	8	1	3			
Lorente '05	2006	171		100	>10	210	12	1	2			
Lorente '05	2006	171		100	>10	233	12	2	1			
Lorente '06a	2005	172		100	5to10	236	9	1	1			
Lorente '06a	2005	172		100	5to10	221	7	1	1			
Lorente '06b	2006	173		100	>10	53	2		0			
Lorente '06b	2006	173		100	>10	51	5		0			
Lorente '07	2007	174		100	>10	140	4	3	0			
Lorente '07	2007	174		100	>10	140	4	1	0			
Lorente'14	2014	175		100	>10	150	6	1				
Lorente'14	2014	175		100	>10	134	3	0				
Manzano	2008	176		100	>10	63	0	4				
Manzano	2008	176		100	5to10	64	0	2				
Martin	1993	177		100	5to10	65	0	1	1			
Martin	1993	177		100	5to10	66	2	0	0			
Morrow	2010	178		100	>10	73	0	3	0			
Morrow	2010	178		100	>10	73	6	2	1			
Nseir	2011	179		100	5to10	61	2	2				
Nseir	2011	179		100	>10	61	0	1				
Pickworth	1993	180	T	100	5to10	44	1		0			
Pneumatikos	2006	181		100	>10	39	0	1	0			
Pneumatikos	2006	181		100	>10	40	1	1	0			
Prod'hom_A	1994	182		100	5to10	81	4	0				
Prod'hom_R	1994	182		100	5to10	80	1	1				
Prod'hom_S	1994	182		100	5to10	83	1	0				
Reigneir	2013	183		100	5to10	227	12					
Reigneir	2013	183		100	5to10	222	9					

Table S2 (continued): Groups of non decontamination studies [a]

Author	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Rumbak	2004	184		100	5to10	60	1					
Rumbak	2004	184		100	>10	60	5					
Ryan_C	1993	185		100	5to10	56	2	1				
Ryan_S	1993	185		100	5to10	58	1	0				
Smulders	2002	186		100	>10	75	3		1			
Smulders	2002	186		100	>10	75	1		0			
Staudinger	2010	187		100	>10	75	5		2			
Staudinger	2010	187		100	5to10	75	3		0			
Thomachot	1998	188		100	>10	66	3	1	0			
Thomachot	1998	188		100	>10	70	2	1	0			
Thomachot	1999	189		100	>10	77	1	0	0			
Thomachot	1999	189		100	>10	63	2	0	0			
Thomachot	2002	190		100	5to10	71	0	1				
Thomachot	2002	190		100	5to10	84	2	0				
Valencia	2007	191		100	>10	69	1	0				
Valencia	2007	191		100	>10	73	3	1				
Valles	1995	192		100	5to10	77	12					
Valles	1995	192		100	5to10	76	12					
Walaszek	2017	193		100	5to10	804	5	39	5			
Walaszek	2017	193		100	5to10	1003	10	22	1			
Zeng	2016	194		100	>10	118	13	10	2			
Zeng	2016	194		100	>10	117	19	14	4			

Table S2 footNotes

Notes; T = Data originating from a study for which the majority of ICU admission were for trauma; C = cardio-thoracic ICU; I = Infection control intervention to entire ICU; crf = group wide candidemia risk factor

MV = percentage of group receiving mechanical ventilation; NS – Not stated; LOS is mean or median length of ICU stay, The ICU-LOS is the ICU length of stay. This is based on surrogate measures including mean (or median) length of MV were taken if the length of ICU LOS was not available in order to generate broad categories of ICU stay of <5 days, 5 to 10 days and >10 days

v_ps_n is the count of *Pseudomonas* VAP; v_sr_n is the count of *Staphylococcus aureus* VAP; v_ac_n is the count of *Acinetobacter* VAP and v_can_n is the count of *Candida* isolates from patients with VAP.

b_ps_n is the count of *Pseudomonas* bacteremia; b_sr_n is the count of *Staphylococcus aureus* bacteremia; and b_ac_n is the count of *Acinetobacter* bacteremia; b_can_n is the count of Candidemia; b_cns_n is the count of coagulative negative *Staphylococcus* bacteremia and b_ent_n is the count of *Enterococcal* bacteremia.

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.
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Table S3: Groups of anti-septic studies [a]

Author & regimen	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Bellissimo-Rodrigues	2014	195		76	>10	127			1			
Bellissimo-Rodrigues Chlx	2014	195		77	>10	127			0			
Bleasdale	2007	196		35	<5	445				0		1
Bleasdale Chlx	2007	196		36	<5	391				0		0
Cabov	2010	197		57	5to10	30	4	0		0	0	
Cabov	2010	197		77	5to10	30	0	0		0	0	
Caruso	2009	198		100	>10	132	9	5	3			
Caruso Sal	2009	198		100	>10	130	7	1	0			
Climo	2013	199		NS	5to10	1398				2	2	16
Climo Chlx(BW)	2013	199		NS	5to10	1410				4	1	7
Fourrier	2000	200		100	>10	30	4	2	1	0	0	0
Fourrier Chlx	2000	200		100	>10	30	1	2	0	0	1	0
Fourrier	2005	201		100	>10	114	5	0	0	0	0	0
Fourrier Chlx	2005	201		100	>10	114	6	1	0	1	0	0
Huang_2pre	2013	61		NS	<5	15218				8	5	56
Huang_3pre	2013	61		NS	<5	17356				11	10	59
Huang_2TD	2013	61		NS	<5	24752				13	2	63
Huang_3UD	2013	61		NS	<5	26024				14	3	62
Koeman	2006	202		100	>10	130	4		1			
Koeman -Chlx	2006	202		100	>10	127	0		3			
Koeman ChlxC	2006	202		100	>10	128	2		4			
Kollef	2006	203		100	>10	347	9	2	6			
Kollef Iseganan	2006	203		100	>10	362	8	2	0			
Lorente	2012	204		100	5to10	219	5	0	0			
Lorente Chlx	2012	204		100	5to10	217	5	2	0			
Mori	2006	205		100	5to10	414	9	0	2			
Mori PVI	2006	205		100	5to10	1248	10	2	1			
Noto	2015	206		NS	<5	4852				2	0	6
Noto Chlx(BW)	2015	206		NS	<5	4488				4	0	2
Seguin	2006	207		100	>10	31	0					
Seguin	2006	207		100	>10	31	1					
Seguin-PVI	2006	207	T	100	>10	36	0					

Table S3 (continued): Groups of anti-septic studies [a]

Author & regimen	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Seguin	2014	208		100	>10	72	1					
Seguin-PVI	2014	208		100	>10	78	3					
Swan	2016	209		57	5to10	164	1	0	1	0	0	
Swan Chlx(BW)	2016	209		69	5to10	161	1	1	0	0	0	
Wittekamp Chlx	2018	210		100	5to10	2108				16		22

Table S3: Footnotes

Notes; T = Data originating from a study for which the majority of ICU admission were for trauma; C = cardio-thoracic ICU; I = Infection control intervention to entire ICU; crf = group wide candidemia risk factor

MV = percentage of group receiving mechanical ventilation; NS – Not stated; LOS is mean or median length of ICU stay; The ICU-LOS is the ICU length of stay. This is based on surrogate measures including mean (or median) length of MV were taken if the length of ICU LOS was not available in order to generate broad categories of ICU stay of <5 days, 5 to 10 days and >10 days

v_ps_n is the count of *Pseudomonas* VAP; v_sr_n is the count of *Staphylococcus aureus* VAP; v_ac_n is the count of *Acinetobacter* VAP and v_can_n is the count of *Candida* isolates from patients with VAP.

b_ps_n is the count of *Pseudomonas* bacteremia; b_sr_n is the count of *Staphylococcus aureus* bacteremia; and b_ac_n is the count of *Acinetobacter* bacteremia; b_can_n is the count of Candidemia; b_cns_n is the count of coagulative negative *Staphylococcus* bacteremia and b_ent_n is the count of *Enterococcal* bacteremia.

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

- 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.
- 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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Intervention regimens abbreviations

Chlx = chlorhexidine; Chlx BW = chlorhexidine body wash; ChC = chlorhexidine and colisitn; TD = targetted decolonization; UD = universal decolonization; PVI = povidone iodine; CC = concurrent control; SC = saline control; iseganan, is a synthetic variant of a porcine protegrin, which is a natural antibiotic peptide released by neutrophils in response to invasion by microbes [Kollef 2006].

Table S4: Groups of studies of topical antibiotics [a]

Author & regimen	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Groups from NCC studies												
Bergmans	2001	211		100	>10	61	5		1			
Bonten	1994	212		91	>10	54	4					
Camus	2014	213		28	<5	925				0	1	2
Camus PTA	2014	213		28	<5	1022				3	0	1
de Smet	2009	214		88	5-10	1990				36		16
de Smet PTA-Ctx	2009	214		93	5-10	2045				16		8
de Smet PTA	2009	214		94	5-10	1904				17		14
Frencken PTA-Ctx	2018	215		100	5-10	1874				15		
Garbino PNeV	2002	216		100	5-10	204	4		2			10
Godard	1990	217		80	>10	84	5					2
Godard PT	1990	217		81	>10	97	0					0
Hartenauer Ctx	1991	218		100	>10	101	20	4		1	1	
Hartenauer PTA-Ctx	1991	218		100	>10	99	0	0		1	0	
Hjortrup CefTMyco	1997	219	crf	100	NS	150			11	1	0	4
Konrad	1989	220		100	NS	83	9					
Konrad PTA-Ctx	1989	220		100	NS	82	2					
Landelle	2018	221		100	5-10	291	9	0				
Landelle PTNy	2018	221		100	5-10	413	12	1				
Landelle PTNy	2018	221		100	5-10	356	2	0				
Ledingham	1988	222		60	5-10	161	3					
Ledingham PTA-Ctx	1988	222		60	5-10	163	2					
Leone PTA-Cef	2002	223		100	>10	324	3	5				
Nardi	1990	224		100	>10	50		7				
Nardi PTA	1990	224		100	>10	47		4				
Nardi PTA	2001	225	T	100	>10	104	4	1	1			1
Nardi PTAM	2001	225	T	100	>10	119	3	0	0			0
Ong PTA-Ctx	2015	226		87	5-10	3080				10		17
Oostdijk PTA-Ctx	2014	227		51	5-10	5483				20	1	26
Oostdijk PTA	2014	227		52	5-10	5508				23	3	55
Rouby E	1994	228		100	>10	251	26					
Rouby P	1994	228		100	>10	347	12					

Table S4 (continued): Groups of studies of topical antibiotics [a]

Author & regimen	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Silvestri PTA-Ctx	1999	229		100	5to10	117	2		0	0		0
Steffen PTNy-Ctx	1994	230	crf	100	>10	127				1	0	0
Stoutenbeek	1984	231		100	>10	59	5	1	0	1	2	1
Stoutenbeek PTA-Ctx	1984	231		100	>10	63	3	1	0	0	0	0
Stoutenbeek	1987	232		100	>10	59	5	1	0			
Stoutenbeek PTA	1987	232		100	>10	42	1	2	0	1	0	
Stoutenbeek PTA-Ctx	1987	232		100	>10	63	0	0	0	0	0	0
Valles	2013	233		100	>10	58	2	0				
Valles Ctx	2013	233		100	5to10	71	1	0				
Veelo PTA-Ctx	2008	234		100	>10	231	2					
Winter	1992	235		92	5to10	84	2	0	0			0
Wittekamp	2018	210		100	5to10	2251				21		15
Wittekamp PTNy	2018	210		100	5to10	2224				15		23
Wittekamp PTNy	2018	210		100	>10	2082				9		18
Groups from CC studies												
Abele-Horn	1997	236	T	100	>10	30	3	0				
Abele-Horn PTA-Ctx	1997	236	T	100	>10	58	2	0				
Acquarolo	2005	236		100	>10	19	2	0	0	0		
Acquarolo Ampsul	2005	237		100	>10	19	2	0	0	0		
Aerdts	1991	238		100	>10	39	10	3	2			1
Aerdts PNoA-Ctx	1991	238		100	>10	17	0	0	0			0
Bergmans	2001	212		100	>10	78	8		3			
Bergmans PGV	2001	212		100	>10	87	3		1			
Bion	1991	239	crf	50	<5	31	3	0	2	0	0	0
Bion PTA-Ctx	1991	239	crf	50	<5	21	0	0	3	2	0	0
Blair	1991	240		93	5to10	130	9		1	3		0
Blair PTA-Ctx	1991	240		93	5to10	126	1		0	1		1
Blaise	1994	240	crf	33	5to10	45				1		
Blaise Ofl	1994	240	crf	37	5to10	46				1		

Table S4 (continued): Groups of studies of topical antibiotics [a]

Author & regimen	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Bonten	1994	213		86	5-10	21	0					
Bonten PTA	1994	213		100	>10	22	0					
Bouza	2013	242	C	100	>10	38	3		0			
Bouza Lnz-Mrp	2013	242	C	100	5-10	40	3		0			
Camus	2005	243		100	>10	126						
Camus MCh	2005	243		100	5-10	130						
Camus PT	2005	243		100	>10	130						
Camus PT&MCh	2005	243		100	>10	129						
Cerra	1992	244		26	>10	21				1	0	4
Cerra NoNy	1992	244		18	>10	25				1	0	1
Cockerill	1992	245		85	>10	75	4					2
Cockerill PGNy-Ctx	1992	245		85	5-10	75	1					1
de la Cal	2005	246	T	80	>10	54	7	5	0	7	3	0
de la Cal PTA-Ctx	2005	246	T	74	>10	53	2	6	2	9	6	1
Ferrer Ctx	1994	247		100	>10	41	4	0	2	0	0	0
Ferrer PTA-Ctx	1994	247		100	>10	39	1	0	0	1	0	0
Flaherty	1990	248	C	40	<5	56						0
Flaherty PGA-Ctx	1990	248	C	40	<5	51						0
Garbino_ PNeV	2004	249		100	>10	71			1			3
Garbino_ PNeV	2004	249	crf	100	>10	29			0			2
Gaussorgues	1991	250		100	NS	59			1			1
Gaussorgues PGA	1991	250		100	NS	59			0			0
Georges	1994	251		100	5-10	33		0	0			0
Georges PNeA	1994	251		100	5-10	31		1	0			0
Hammond Ctx	1993	252		100	>10	20		1				
Hammond PTA-Ctx	1993	252		100	>10	13		0				
Hammond Ctx	1994	253		100	>10	33	0	0				
Hammond PTA-Ctx	1994	253		100	>10	39	0	1				
Hellinger	2002	254	crf	NS	>10	43						0
Hellinger PGNy	2002	254	crf	NS	>10	37						0

Table S4 (continued): Groups of studies of topical antibiotics [a]

Author & regimen	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Jacobs	1992	255		100	5-10	43	0	0	0	0	0	0
Jacobs PTA-Ctx	1992	255		100	5-10	36	0	0	0	0	1	0
Karvouniaris	2015	256		100	>10	84		11				
Karvouniaris P	2015	256		100	>10	84		2				
Kerver	1988	257		100	>10	47			0			0
Kerver PTA-Ctx	1988	257		100	>10	49			0			0
Korinek	1993	258		100	>10	60	3	1	0			
Korinek PTA-V	1993	258		100	>10	63	0	1	0			
Laggner	1994	259		100	>10	34	1		0	1	0	0
Laggner GA	1994	259		100	>10	33	0		0	0	0	0
Langlois -Karaga	1995	260		100	>10	50						
Langlois -Karaga PGA	1995	260		100	>10	47						
Palomar	1997	261		100	5-10	42	6	0	0			0
Palomar PTA-Ctx	1997	261		100	5-10	41	1	0	0			0
Palomar Ctx	1997	261		100	>10	46	1	2				1
Pneumatikos	2002	262	T	100	>10	30	1	1	0			
Pneumatikos PTA	2002	262	T	100	>10	31	0	1	0			
Quinio	1995	263	T	100	>10	72	12		0	0	0	0
Quinio PGA	1995	263	T	100	>10	76	5		0	0	0	0
Rimola	1985	264	crf	NS	5-10	72				0	0	
Rimola PGVNy	1985	264	crf	NS	>10	68				0	0	
Rocha	1992	265	T	100	>10	54	8	4		1	3	0
Rocha PTA-Ctx	1992	265	T	100	>10	47	1	1		0	0	0
Rodríguez -Roldán	1990	266		100	>10	15	5	2				
Rodríguez -Roldán PTNeA	1990	266		100	5-10	14	0	0				
Rolando	1996	267	crf	73	NS	61	2	0	1	0	0	1
Rolando PTA	1996	267	crf	73	NS	47	1	0	1	0	0	0
Rolando	1993	268	crf	75	5-10	31	2	0	3			0
Rolando PTAM-Cfu	1993	268	crf	75	5-10	28	1	0	0			0

Table S4 (continued): Groups of studies of topical antibiotics [a]

Author & regimen	Year	Ref	Notes	MV	LOS	Patients	VAP			Bacteremia		
				%	d	n	v_ps_n	v_ac_n	v_can_n	b_ps_n	b_ac_n	b_can_n
Sanchez-Garcia	1998	269		100	>10	140			0			
Sanchez-Garcia PTA-Ctx	1998	269		100	>10	131			0			
Sirvent	1997	270		100	>10	50	1	2	0			
Sirvent -Cef	1997	270		100	>10	50	3	1	0			
Smith	1993	271	crf	100	5to10	18	1		1			1
Smith PTA-Ctx	1993	271	crf	100	5to10	18	0		0			0
Stoutenbeek	2007	272	T	100	>10	200	28	23	21	2	3	0
Stoutenbeek PTA-Ctx	2007	272	T	100	>10	201	11	15	6	3	0	1
Ulrich	1989	273		83	>10	52			1			0
Ulrich_ PNoA-Tr	1989	273		77	>10	48			1			0
Unertl	1987	274		100	>10	20	2		0			
Unertl_PGA	1987	274		100	>10	19	0		0			
van Delden	2012	275		100	>10	45	6					
van Delden -Azith	2012	275		100	5to10	47	2					
Verwaest	1997	276		100	>10	185	7	4	0	1	2	4
Verwaest OfA-Of	1997	276		100	>10	193	2	4	1	2	2	0
Verwaest PTA-Ctx	1997	276		100	>10	200	10	4	0	6	2	0
Wiener	1995	277		100	>10	31	0	0	0			2
Wiener_ PGNy	1995	277		100	>10	30	2	1	0			0
Winter	1992	235		92	5to10	92	8	2	0			1
Winter_ PTA-Ctz	1992	235		92	5to10	91	3	0	0			0

Table S4: Footnotes

Notes; T = Data originating from a study for which the majority of ICU admission were for trauma; C = cardio-thoracic ICU; I = Infection control intervention to entire ICU; crf = group wide candidemia risk factor

MV = percentage of group receiving mechanical ventilation; NS – Not stated; LOS is mean or median length of ICU stay; The ICU-LOS is the ICU length of stay. This is based on surrogate measures including mean (or median) length of MV were taken if the length of ICU LOS was not available in order to generate broad categories of ICU stay of <5 days, 5 to 10 days and >10 days

v_ps_n is the count of *Pseudomonas* VAP; v_sr_n is the count of *Staphylococcus aureus* VAP; v_ac_n is the count of *Acinetobacter* VAP and v_can_n is the count of *Candida* isolates from patients with VAP.

b_ps_n is the count of *Pseudomonas* bacteremia; b_sr_n is the count of *Staphylococcus aureus* bacteremia; and b_ac_n is the count of *Acinetobacter* bacteremia; b_can_n is the count of Candidemia; b_cns_n is the count of coagulative negative *Staphylococcus* bacteremia and b_ent_n is the count of *Enterococcal* bacteremia.

* De Smet 2009 [214] The *Pseudomonas* and *Acinetobacter* counts in this study are available only as a combined category count for gram negative non-fermentative GNB and are provided here for reference but are not used in the analysis. The Pseudomonas counts in the study of Oostdijk [227] includes counts from the study by De Smet 2009 [214]. The Pseudomonas counts in the study of Oostdijk [227] are taken as given in Table 2 of Oostdijk [227] even though this Table appears to be mislabelled in comparison to the text and table 1 of Oostdijk [227] and in relation to the data in De Smet 2009 [214].

The control group in one study by Stoutenbeek [1987] appears also as the control group in another study by this Author [1984] and is used only once in the analysis here.

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.

TAP intervention regimens abbrevations; PTA (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin); PTA-Ctx (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin; Ctx, parenteral cephalosporin); P (P = polymyxin either aerosolized or topical); PNeV (P = polymyxin; Ne = Neomycin; V = Vancomycin); PGA-Ctx (=P, topical polymyxin; G, topical gentamicin; A, topical amphotericin; Ctx, parenteral cephalosporin); PTAM (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin; topical mupirocin); E (=E, topical erythromycin); PNoA-Ctx (=P, topical polymyxin; No, topical norfloxacin; A, topical amphotericin; Ctx, parenteral cephalsporin); PGV (=P, topical polymyxin; G, topical gentamicin; V, topical vancomycin); PGNy-Ctx (=P, topical polymyxin; G, topical gentamicin; Ny, topical nystatin; Ctx, parenteral cephalsporin); P-Ctx (=P, topical polymyxin; Ctx, parenteral cephalosporin); PTAV (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin; V, topical vancomycin); PGA (=P, topical polymyxin; G, topical gentamicin; A, topical amphotericin); PTNeA (=P, topical polymyxin; T, topical tobramycin; Ne, topical Neomycin; A, topical amphotericin); PGNy (=P, topical polymyxin; G, topical gentamicin; Ny, topical nystatin); PTA-Cz (=P, topical polymyxin; T, topical tobramycin; A, topical amphotericin; Cz, parenteral Ceftazidime).

Table S5: Groups of studies of antifungal prophylaxis

Author & regimen	Year	Ref	Notes	MV	LOS	Patients	RT Candida	Candidiemia
				%	d	n	v_can_n	b_can_n
Ables	2000	278	crf	95	5to10	60		0
Ables_Fluc	2000	278	crf	95	5to10	59		0
Eggimann	1999	279	crf	NS	>10	20		2
Eggimann_Fluc	1999	279	crf	NS	>10	23		0
Giglio	2012	280		100	>10	50	0	0
Giglio_Ny	2012	280		100	>10	49	0	0
Jacobs	2003	281		NS	>10	39		1
Jacobs_Fluc	2003	281		NS	>10	32		0
Lumbreras	1996	282	crf	NS	>10	67		0
Lumbreras_Fluc	1996	282	crf	NS	>10	76		1
Normand	2005	283		100	>10	47	0	0
Normand_Ny	2005	283		100	>10	51	0	0
Ostrosky-Zeichner	2014	284	crf	100	5to10	102		7
Ostrosky-Zeichner_ Casp	2014	284		100	5to10	117		1
Savino	1994	285		31	>10	72		0
Savino _Cl_ket_ny	1994	285		23	>10	80		0
Savino	1994	285	crf	33	5to10	65		2
Savino _Cl_ket_ny	1994	285	crf	39	>10	75		7
Schuster	2008	286		NS	>10	122		2
Schuster_Fluc	2008	286		NS	>10	122		0

Table S5: FootNotes

Notes; T = Data originating from a study for which the majority of ICU admission were for trauma; C = cardio-thoracic ICU; I = Infection control intervention to entire ICU; crf = group wide candidemia risk factor

MV = percentage of group receiving mechanical ventilation; NS – Not stated; LOS is mean or median length of ICU stay; The ICU-LOS is the ICU length of stay. This is based on surrogate measures including mean (or median) length of MV were taken if the length of ICU LOS was not available in order to generate broad categories of ICU stay of <5 days, 5 to 10 days and >10 days

RT Candida is respiratory tract candida. v_can_n is the count of *Candida* isolates from patients with VAP; b_can_n is the count of Candidemia;

Table S6: Development of Pseudomonas GSEM model [a, b]

Full models (all studies)						Models excluding studies ICU-LOS<5 days		
	Model 1	Model 2				Model 3	Model 4 .	
	Fig S3a	Fig S3b				Fig S4a	Fig S4a	
			95%CI					95%CI
Factor [c - k]								
b_Ps_n								
Pseudomonas colonization	1.09***	1.10***	0.71 to 1.5			1.30***	1.28***	0.84 to 1.7
ppap	0.85**	0.83**	0.25 to 1.4			0.98**	0.93**	0.31 to 1.7
_cons	-5.96***	-5.93***	-6.8 to -5.1			-5.16***	-5.05***	-5.5 to -4.5
v_Ps_n								
Pseudomonas colonization	1	1	(constrained)			1	1	(constrained)
mvp90	0.36	0.32	-0.04 to 0.7			0.42*	0.39*	0.02 to 0.76
non_D	-0.50***	-0.49***	-0.76 to -0.2			-0.48***	-0.46***	-0.73 to -0.2
_cons	-4.33***	-4.31***	-5.1 to -3.5			-3.51***	-3.45***	-3.9to -3.0
Pseudomonas colonization								
tap	-0.71***	-0.45***	-0.71 to -0.2			-0.64***	-0.39**	-0.66 to -0.12
year	-0.15*	-0.18**	-0.31 to -0.1			-0.14*	-0.18**	-0.3 to -0.05
los5	0.99*	0.51	-0.20 to 1.2					
los10	0.51***	0.52***	0.28 to 0.7			0.60***	0.54***	0.32 to 0.76
trauma	-0.14	-0.13	-0.47 to 0.2			-0.14	-0.12	-0.48 to 0.2
Anti-septic	-0.77***	-0.28	-0.77 to 0.2			-0.84***	-0.27	-0.75 to 0.22
crf	0.26	-0.46	-1.2 to 0.2			0.18	-0.54	-1.1 to 0.05
Candida colonization	-	0.33***	0.22 to 0.45				0.36***	0.24 to 0.48
b_can_n								
Candida colonization	0.50***	0.48***	0.3 to 0.64			0.58***	0.54***	0.36 to 0.73
_cons	-5.62***	-5.66***	-6.2 to -5.1			-5.02***	-5.09***	-5.6 to -4.6
v_can_n								
Candida colonization	1	1	(constrained)			1	1	(constrained)
mvp90	0.02	0.31	-0.53 to 1.1			0.2	0.3	-0.4 to 1.3
non_D	-0.28	-0.43	-1.1 to 0.21			-0.22	-0.21	-1.0 to 0.28
_cons	-6.53***	-6.86***	-8.4 to -5.3			-5.26***	-5.29***	-6.7 to -4.5

Table S6: Development of Pseudomonas GSEM model (continued) [a, b]

Full models (all studies)					Models excluding studies ICU-LOS<5 days		
	Model 1	**Model 2**			**Model 3**	**Model 4**	
	Fig S3a	Fig S3b			Fig S4a	Fig S4a	
			95%CI				95%CI
Factor [c - k]							
Candida colonization							
tap	0.64	0.54	-0.31 to 1.4		0.62	0.62	-0.31 to 1.3
year	-0.01	0.08	-0.26 to 0.4		-0.03	-0.04	-0.23 to 0.37
los5	1.62**	1.59**	0.62 to 2.7				
los10	-0.09	-0.13	-0.59 to 0.4		0.17	0.16	-0.39 to 0.6
trauma	0.19	0.05	-0.9 to 0.9		0.19	0.16	-0.8 to 0.9
Anti-septic	-1.44**	-1.47**	-2.4 to -0.6		-1.66**	-1.59**	-2.6 to -0.77
Anti-fungal	-1.58***	-1.6***	-2.5 to -0.72		-1.43***	-1.46***	-2.3 to -0.63
crf	2.10***	2.25***	1.2 to 3.3		2.11***	2.17***	1.3 to 3.2
Error terms							
var (e. Candida colonization)	1.49***	1.49***	1.0 to 2.3		1.52***	1.53***	1.0 to 2.3
var (e. Pseudomonas colonization)	0.46***	0.30***	0.20 to 0.44		0.47***	0.29***	0.19 to 0.43
			-				
Model fit [l]							
AIC	3631.39	3600.45	-		3660.34	3622.49	-
Groups (n)	439	439	-		421	421	-
Clusters (n)	276	276			271	271	-
Factors	30	31	-		28	29	-

Footnotes

a. Legend: * p<0.05; ** p<0.01; *** p<0.001

b. Shown in this table are models derived with all studies including those with LOS<5 days (models 1, & 2) and models derived after excluding studies with LOS< 5 days (models 3 & 4). The figures corresponding to models 1 (Figure S5a), model 2 (Figure 1 & figure S5b) models 3 (Figure S6a), model 4 (figure S6b).

c. v_ps_n is the count of *Pseudomonas* VAP; v_ac_n is the count of *Acinetobacter* VAP; v_can_n is the count of *RT Candida*; b_ps_n is the count of *Pseudomonas* bacteremia and b_ac_n is the count of *Acinetobacter* bacteremia; b_can_n is the count of Candidemia.

d. PPAP is the group wide use of protocolized parenteral antibiotic prophylaxis; tap is topical antibiotic prophylaxis; non-D is a non-decontamination intervention; year = year of study publication in units of ten (decade)

e. MVP90 is use of mechanical ventilation by more than 90% of the group

f. Crf is group wide exposure to a candidemia risk factor.

g. LOS5 is a mean or median length of ICU stay for the group of less than 5 days

h. LOS10 is a mean or median length of ICU stay for the group of more than 10 days

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

j. Pseudomonas colonization (Pseudomonas col) is a latent variable

k. *Candida* colonization (*Candida* col) is a latent variable

l. Model fit; AIC is Akaike's information criteria. This indicates model fit taking into account the statistical goodness of fit and the number of parameters in the model. Lower values of AIC indicate a better model fit. Groups is the number of patient groups; clusters is the number of studies; N is the number of parameters in the model.

Table S7: Development of Acinetobacter GSEM model [a, b]

Full models (all studies)				Models excluding studies ICU-LOS<5 days		
	Model 5	**Model 6**		**Model 7**	**Model 8**	
	Fig S5a	Fig S5b		Fig S6a	Fig S7a	
			95%CI			95%CI
Factor [c - k]						
b_Ac_n						
Acinetobacter colonization	1.18***	1.17***	0.92 to 1.4	1.25***	1.23***	0.92 to 1.4
ppap	0.24	0.17	-0.87 to 1.4	0.31	0.21	-0.87 to 1.4
_cons	-8.14***	-8.08***	-9.2 to -6.9	-7.60***	-7.42***	-9.2 to -6.9
v_Ac_n						
Acinetobacter colonization	1	1	(constrained)	1	1	(constrained)
mvp90	0.58	0.54	-0.12 to 1.3	0.6	0.57	-0.12 to 1.3
non_D	-0.41	-0.37	-0.76 to 0.05	-0.39	-0.34	-0.76 to 0.05
_cons	-6.56***	-6.56***	-7.8 to -5.3	-5.92***	-5.85***	-7.8 to -5.3
Acinetobacter colonization						
tap	-0.69**	-0.43	-1.1 to 0.0	-0.66*	-0.4	-1.1 to 0.0
year	0.17	0.17	-0.12 to 0.4	0.16	0.17	-0.12 to 0.4
los5	0.76	0.34	-0.4 to 1.3			
los10	0.94***	0.91***	0.46 to 1.3	1.05***	0.95***	0.46 to 1.3
trauma	0.44	0.4	-0.03 to 0.95	0.45	0.4	-0.03 to 0.95
Anti-septic	-1.09**	-0.59	-1.5 to 0.1	-1.16**	-0.55	-1.5 to 0.1
crf	-0.27	-.095	-3.1 to 1.2	-0.29	-1.05	-3.1 to 1.2
Candida colonization	-	0.32*	0.01 to 0.5		0.36**	0.01 to 0.5
b_can_n						
Candida colonization	0.49***	0.49***	0.3 to 0.67	0.49***	0.49***	0.3 to 0.67
_cons	-5.6***	-5.56***	-6.1 to -4.9	-5.62***	-5.56***	-6.1 to -4.9
v_can_n						
Candida colonization	1	1	(constrained)	1	1	(constrained)
mvp90	0.02	0.12	-0.80 to 0.89	0.2	0.3	-0.80 to 0.89
non_D	-0.28	-0.27	-0.97 to 0.38	-0.22	-0.21	-0.97 to 0.38
_cons	-6.5***	-6.51***	-8.1 to -4.9	-5.26***	-5.29***	-8.1 to -4.9

Table S7: Development of Acinetobacter GSEM model (continued) [a, b]

Full models (all studies)					Models excluding studies ICU-LOS<5 days		
	Model 5	**Model 6**			**Model 7**	**Model 8**	
	Fig S5a	Fig S5b			Fig S6a	Fig S7a	
			95%CI				95%CI
Factor [c - k]							
Candida colonization							
tap	0.64	0.64	-0.22 to 1.5		0.62	0.62	-0.22 to 1.5
year	-0.01	-0.02	-0.36 to 0.28		-0.03	-0.04	-0.36 to 0.28
los5	1.62**	1.55**	0.51 to 2.7				
los10	-0.09	-0.08	-0.55 to 0.5		0.17	0.16	-0.55 to 0.5
trauma	0.19	0.16	-0.83 to 0.99		0.19	0.16	-0.83 to 0.99
Anti-septic	-1.44**	-1.39**	-2.4 to -0.5		-1.66**	-1.59**	-2.4 to -0.5
Anti-fungal	-1.58***	-1.6***	-2.5 to -0.69		-1.43***	-1.46***	-2.5 to -0.69
crf	2.10***	2.16***	1.05 to 3.1		2.11***	2.17***	1.05 to 3.1
Error terms							
var (e. Candida colonization)	1.49***	1.47***	1.0 to 2.3		1.52***	1.50***	1.0 to 2.3
var (e. Acinetobacter colonization)	1.42***	1.27***	0.95 to 1.7		1.42***	1.27***	0.95 to 1.7
Model fit [l]							
AIC	2723.04	2717.31	-		2736.76	2728.7	-
Groups (n)	395	395	-		378	378	-
Clusters (n)	247	247	-		239	239	-
Factors	30	31	-		28	29	-

Table S7: Development of Acinetobacter GSEM model (continued) [a]

Footnotes

a. Legend: * p<0.05; ** p<0.01; *** p<0.001
b. Shown in this table are models derived with all studies including those with LOS<5 days (models 5, & 6) and after excluding studies with LOS< 5 days (models 7 & 8). The figures corresponding to models 5 (Figure S7a), model 6 (figure S7b) models 7 (Figure S8a), model 8 (figure S8b).
c. v_ps_n is the count of *Pseudomonas* VAP; v_ac_n is the count of *Acinetobacter* VAP; v_can_n is the count of *RT Candida*; b_ps_n is the count of *Pseudomonas* bacteremia and b_ac_n is the count of *Acinetobacter* bacteremia; b_can_n is the count of Candidemia.
d. PPAP is the group wide use of protocolized parenteral antibiotic prophylaxis; tap is topical antibiotic prophylaxis; non-D is a non-decontamination intervention; year = year of study publication in units of ten (decade)
e. MVP90 is use of mechanical ventilation by more than 90% of the group
f. Crf is group wide exposure to a candidemia risk factor.
g. LOS5 is a mean or median length of ICU stay for the group of less than 5 days
h. LOS10 is a mean or median length of ICU stay for the group of more than 10 days
i. Trauma ICU arbitrarily defined as an ICU for which >50% of admissions were for trauma
j. Acinetobacter colonization (Acinteobacter col) is a latent variable
k. *Candida* colonization (*Candida* col) is a latent variable
l. Model fit; AIC is Akaike's information criteria. This indicates model fit taking into account the statistical goodness of fit and the number of parameters in the model. Lower values of AIC indicate a better model fit. Groups is the number of patient groups; clusters is the number of studies; N is the number of parameters in the model.

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Fig S1. (p 45) Search method, screening criteria and resulting classification of eligible studies and subsequent decant of component groups. The four numbered arrows are as follows;

(1) An electronic search for systematic reviews or meta-analysis (SR/MA) containing potentially eligible studies using search terms; “ventilator associated pneumonia”, “mechanical ventilation”, “intensive care unit”, each combined with either “meta-analysis” or “systematic review” up to December 2018;

(2) The systematic reviews were then searched for studies of patient populations requiring prolonged (> 24 hours) ICU admission

(3) The studies were triaged from the systematic reviews into one of five categories; studies in which there was no intervention (observational studies), studies of various non-decontamination methods such as methods delivered either via the gastric route, the airway route or via the oral care route, studies of anti-septic methods, studies with a TAP (in any formulation) based intervention, and studies of antifungal prophylaxis as a single agent.

(4) All studies were reviewed for potentially eligible studies and screened against inclusion and exclusion criteria. Any duplicate or ineligible studies were removed and

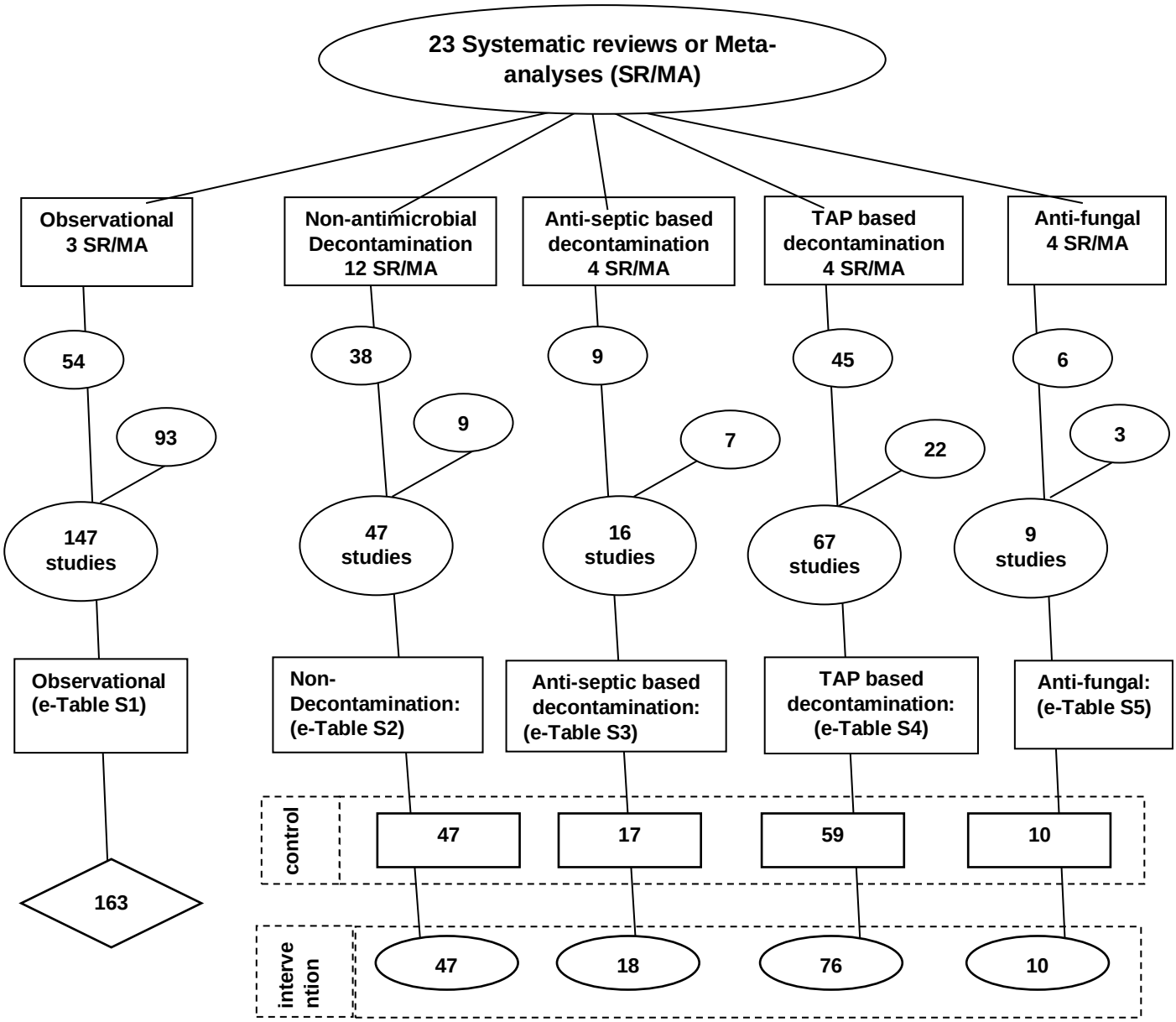
(5) Studies identified outside of systematic reviews were included;

(6) The component groups were decanted from each study being control (rectangles), intervention (ovals) and observation (diamond) groups.

Note; the total numbers do not tally as some systematic reviews provided studies in more than one category and some studies provided groups in more than one category and some studies have unequal numbers of control and interventions groups.

TAP = Topical antibiotic prophylaxis

Figure 1: Flow chart of literature search and study and group decant



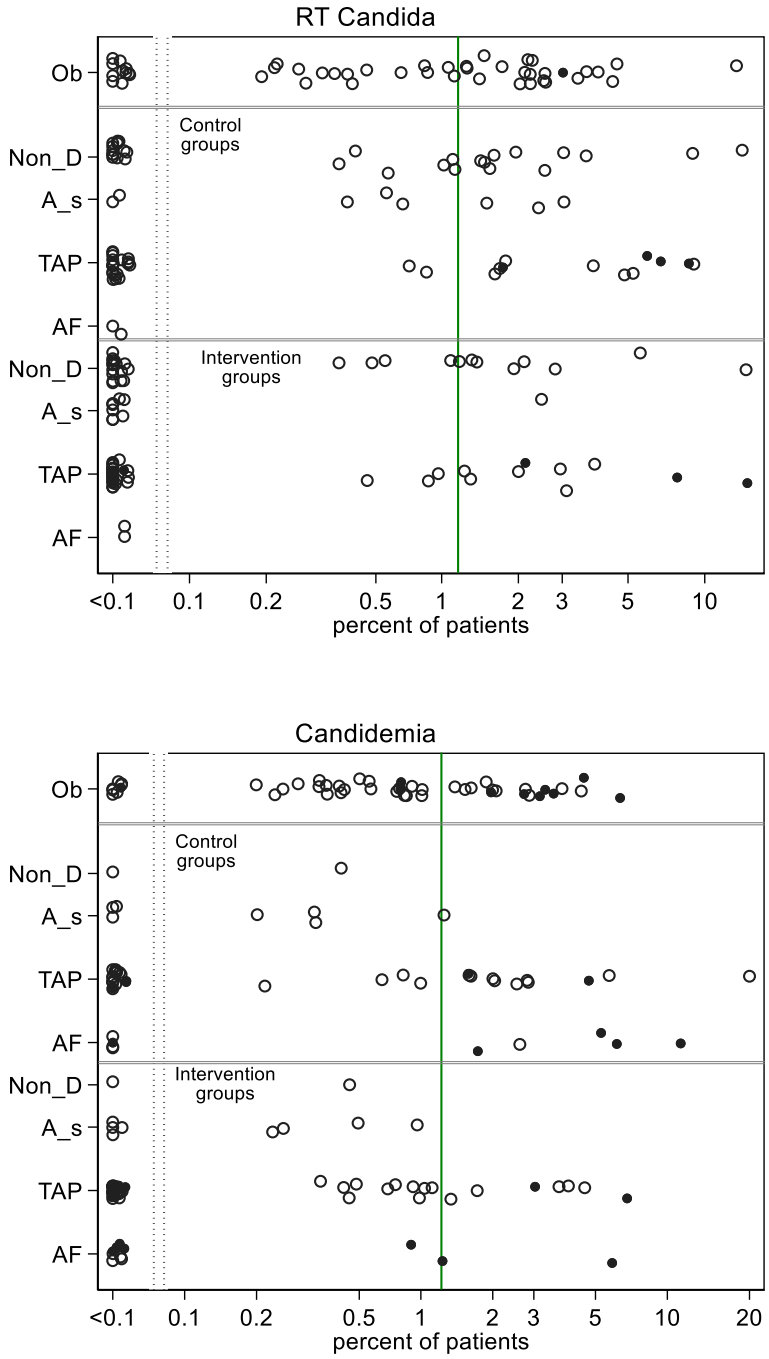


Figure s2a & b Scatter plots (logit scale) of RT Candida incidence (top) and Candidemia (bottom) in component (control and intervention) groups of various methods of infection prevention in the ICU (all studies). The benchmark incidence in each plot is the summary mean derived from the observation studies (central vertical line). The groups wide presence of candidemia risk factors (CRF) is identified by solid symbols versus not (open).
non-D is non-decontamination, A_s is anti-septic, TAP is topical antibiotic prophylaxis and AF is anti-fungal

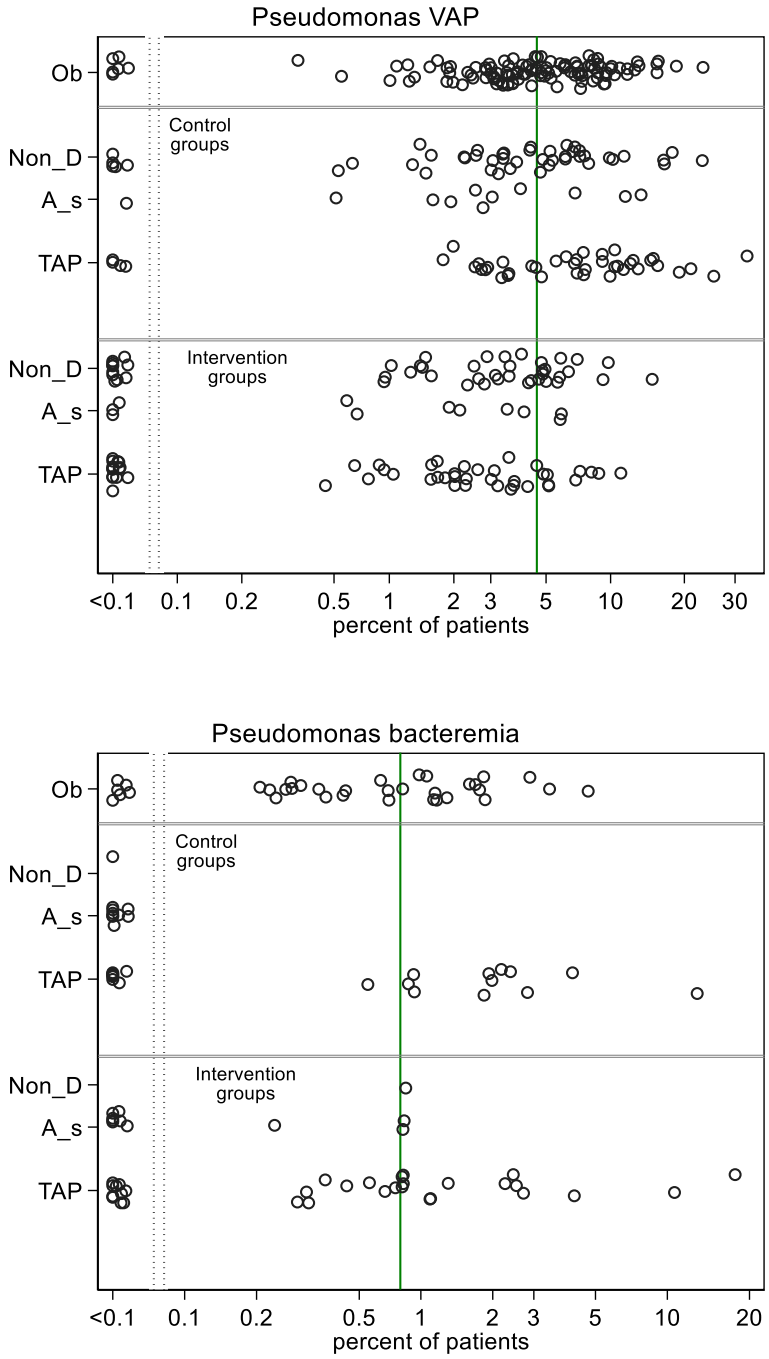


Figure s3a & b Scatter plots (logit scale) of Pseudomonas VAP incidence (top) and Pseudomonas bacteremia (bottom) in (control and intervention) component groups of various methods of infection prevention in the ICU (all studies). The benchmark incidence in each plot is the summary mean derived from the observation studies (central vertical line). non-D is non-decontamination, A_s is anti-septic, TAP is topical antibiotic prophylaxis and AF is anti-fungal

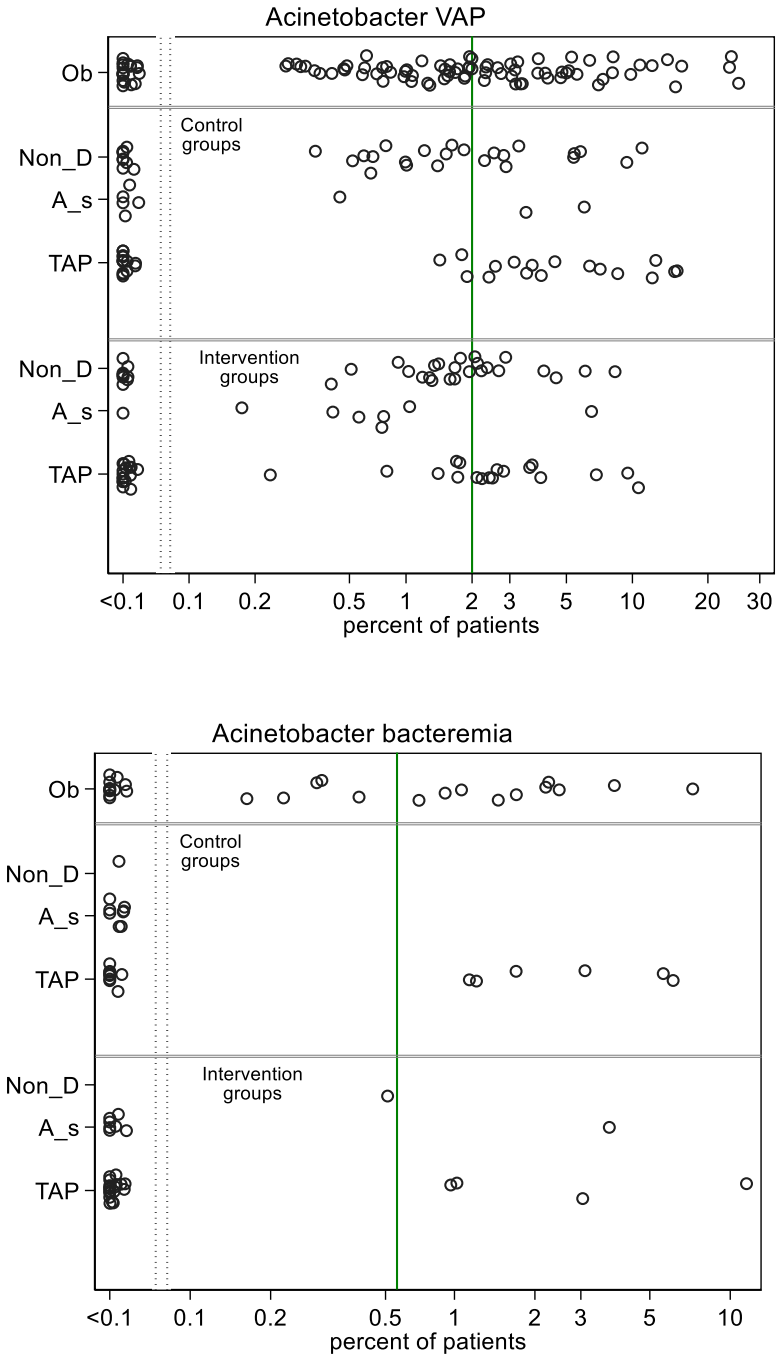


Figure s4a & b Scatter plots (logit scale) of Acinetobacter VAP incidence (top) and Acinetobacter bacteremia (bottom) in (control and intervention) component groups of various methods of infection prevention in the ICU (all studies). The benchmark incidence in each plot is the summary mean derived from the observation studies (central vertical line). non-D is non-decontamination, A_s is anti-septic, TAP is topical antibiotic prophylaxis and AF is anti-fungal

Figure s5a & b. GSEM model 1 (top) & 2 (bottom) – Pseudomonas – all studies (see Table S6 for abbreviations)

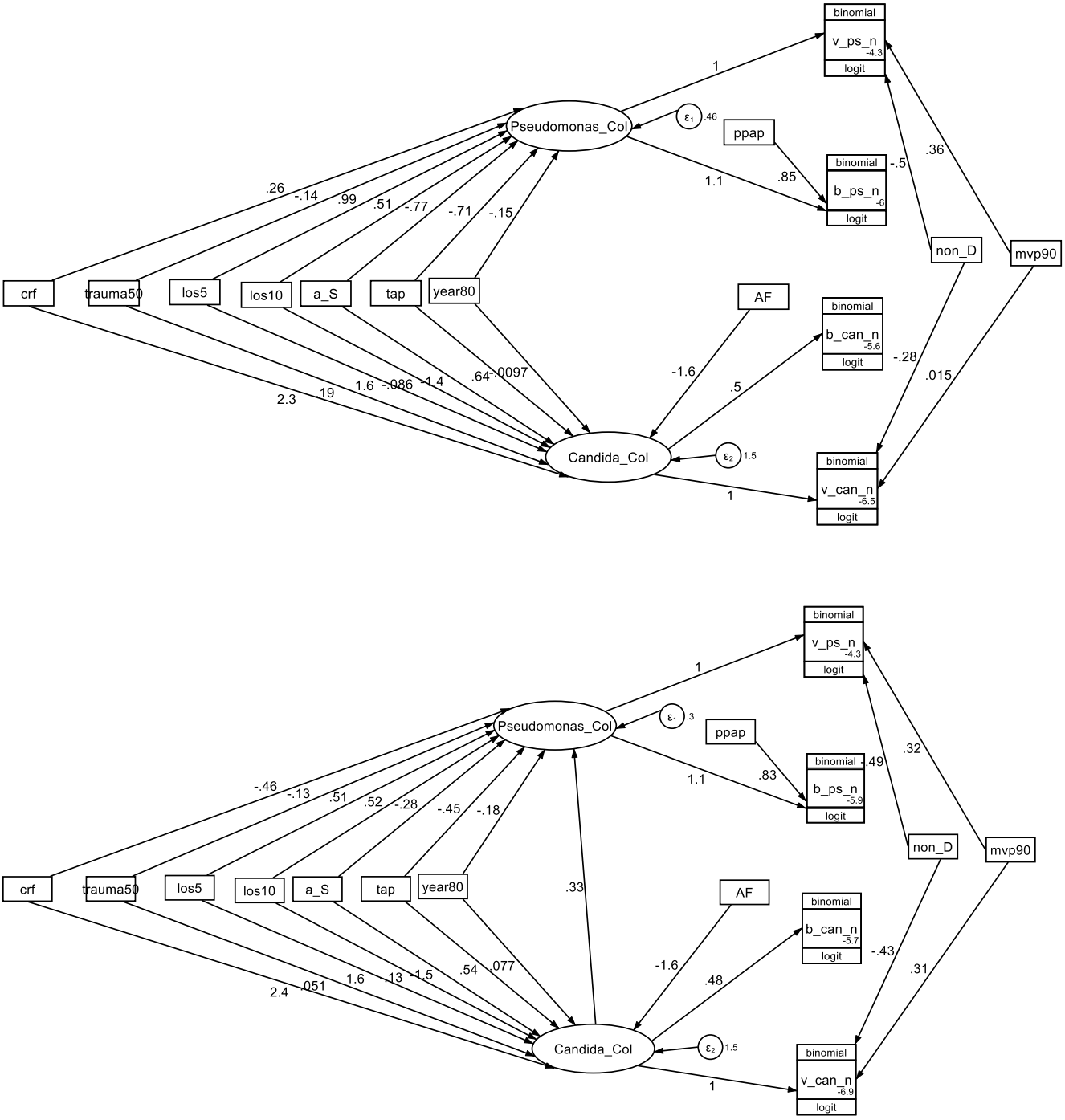


Figure s6 a & b. GSEM model 3 (top) & 4 (bottom) – Pseudomonas excluding studies with ICU-LOS<5 days (see Table S6 for abbreviations)

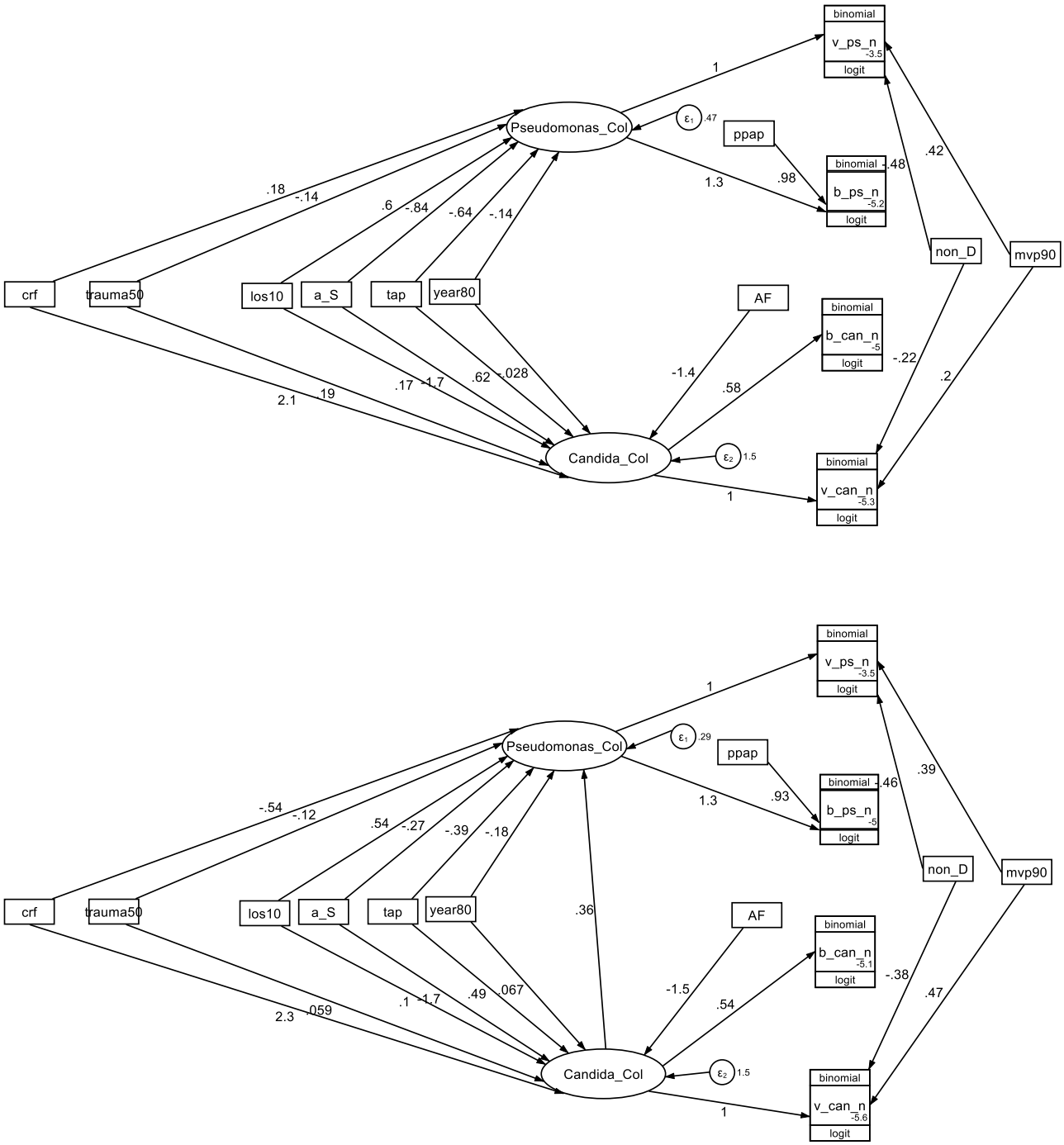
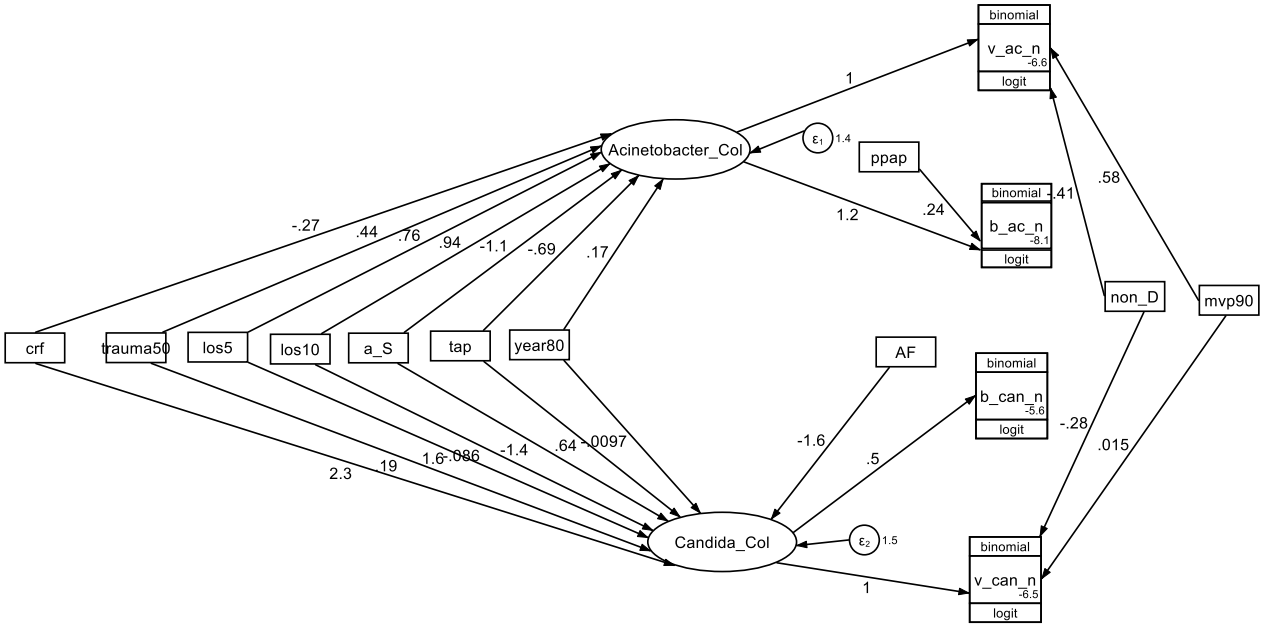


Figure s7 a & b. GSEM model 5 (top) & 6 (bottom) Acinetobacter – all studies (see Table S7 for abbreviations)



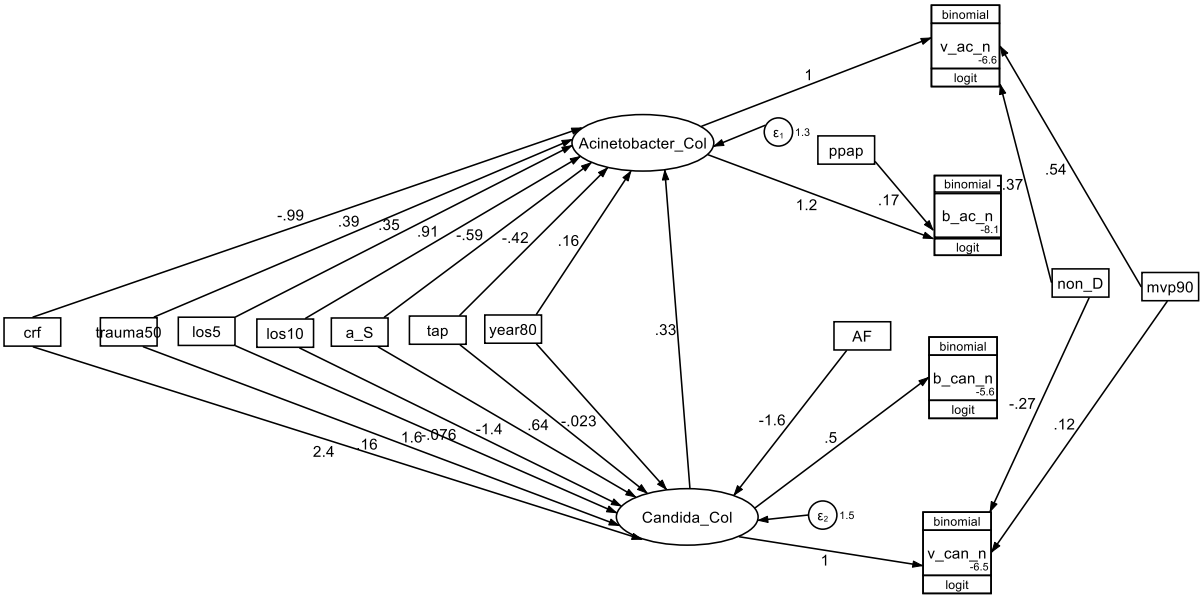


Figure s8 a & b. GSEM model 7(top) & 8 (bottom) – Acinetobacter excluding studies with ICU-LOS<5 days (see Table S7 for abbreviations)