Table S1. Trials or case series of polymyxins based regimen

Author/ Country(year)	Trail type	Type of infection	Organisms isolated group	Experimental						Control group					
				Administration strategy	Sample size	Age(y)	Male gender n （%）	Nephrotoxicity	Neurotoxicity	Administration strategy	Sample size	Age	Male gender n （%）	Nephrotoxicity	Neurotoxicity
Kasiakou SK/ Greece (*16*) （2005）	retrospective, observational cohort study	pneumonia, bacteremia,UTI,intra-abdominal infection,meningitis, CRBSI, SSI,SSTI	MDR-GNB	IV COL alone or plus others	50(54 episodes)	59.2± 17.7 (24–90,)	29 (58)	4/50 (8),	1/50 (2)	/	/	/	/	/	/
Ioannides , K/ Greece.(*106*) （2007）	retrospective	VAP	Carb-S, only six Col-S, AB, *P. aeruginosa, K. pneumoniae*	IV COL with or without meropenem	52	NA	NA	NA	NA	/	/	/	/	/	/
Paksu MS/ Turkey (*21*)(2012)	retrospective	nosocomial infections	MDR-AB,MDR P. aeruginosa,K. pneumoniae	IV COL 5.4 ± 0.6 mg/kg/day 17.2 ± 8.4 days, alone or combined with others	79(87epicsodes)	30 (3–216)month	43/79 (54.4)	2(2.3%) concomitant gentamicin	generalised tonic–clonic seizures were seen in 2 episodes (2.3%)	/	/	/	/	/	/
Karbuz, A/ Turkey (*22*)(2014)	prospective and observational cohort study	VAP, CRBSI, bacteremia，shunt infection, peritonitis, pneumonia	AB (MDR/XDR), P.aureginosa(Non-MDR/MDR/XDR),K.pneumonia(ESBL +/ ESBL+ CPZ+/CPZ +), S. maltophilia, S. marcescens, E. coli	IV CMS (5.0 mg/kg/d (2.3–5.6mg/kg/d) for 12 days (2–28 days). Or 75,000 IU/kg/d (50,000–80,000 IU/kg/d) for 14 days (2–37 days)) and/or others	29(38 episodes)	17 (3–216 months)		1(3.4)	0	/	/	/	/	/	/
Khawcharoenporn T/ Thailand (*56*) （2014）	retrospective cohort	pneumonia(VAP/HAP)	XDR AB	an active XDR-AB regimen	184	75(17–95)	101 (55)	NA	NA	non-active XDR-AB regimen	52	72(21–91)	28 (65)/15 (50)	NA	NA
Falagas ME/ Greece (*17*) （2010）	retrospective study	pneumonia，bacteraemia,abdominal infections, central venous catheter-related infections，infections of other sites.	AB, P. aeruginosa, K. pneumoniae,Stenotrophomonas maltophilia, Enterobacter cloacae	IV colisitn(for 17.9 (10–22)) alone or combination	258	61(15–98)	174 (67%)	26(10.4)	NA	/	/	/	/	/	/

VAP: ventilator-associated pneumonia; HAP: hospital-acquired pneumonia; BSI: bloodstream infection; CRBSI: central venous catheter related blood stream infection; UTI: urinary tract infection; SSI: surgical site infection; MDR: multidrug-resistant; XDR: Extensively Drug-Resistant; PDR: pan-drug resistant; COS: colistin only susceptible; AB: A. baumannii; GNB: gram-negative bacilli; IV: intravenous; COL: colistin; CMS: colistin methanesulfonate

Table S2. Trials or case series of monotherapy

Author/ Country	Trail type	Type of infection	Organisms isolated group	Experimental						Control group					
				Administration strategy	Sample size	Age(y)	Male gender n (%)	Nephrotoxicity	Neurotoxicity	Administration strategy	Sample size	Age	Male gender n (%)	Nephrotoxicity	Neurotoxicity
Levin AS/ Brazil (*107*) (1999)	Retrospective	pneumonia, UTI, primary BSI, CNS infection, peritonitis ,catheter-related infection,otitis media	P. aeruginosa /AB resistant to aminoglycosides, cephalosporins, quinolones, penicillins, monobactams, and imipenem	IV COL 152.8 ±62.8 for 12.6±6.8 day	59 (60 episodes)	42.1 ±21.4	39(65)	22/60 (36.7)	0	/	/	/	/	/	/
Elias LS/ Brazil (*23*) (2010)	retrospective cohort study	microbiologically confirmed infections and in patients with bacteraemia	P. aeruginosa AB	IV polymyxin B (150 mg)for 12d	276	NA	NA	119/235 (50.6%)	NA	/	/	/	/	/	/
Dalfino L/ Italy (*38*) (2012)	prospective, observational, cohort study	BSI, VAP	COS-AB, K. pneumoniae,P. aeruginosa	IV CMS	25 (28 episodes)	65 ± 18	21(75)	5 (17.8%)	NA	/	/	/	/	/	/
Kalin G/ Turkey (*33*) (2012)	retrospective	VAP	MDR-AB	IV COL(CMS)(2.5 mg/kg q6 h)	15	48.07 ± 24.86	9 (60)	6 (40)	NA	IV COL(2.5 mg/kg q12h or low dose,determined according to creatine clearance)	10 or 20	53.75 ± 17.86/45. 70 ± 18.89	16 (80)/ 7 (70)	7 (35) /2 (20)	NA
Karnik ND/ India (*24*) (2013)	a prospective, non-comparative, open label study	MDR-GNB infection	MDR-GNB	IV CMS(6 (2.5–6) MIU per day)(≥60 kg ,2 (MIU) every 8 h;<60 kg, 50,000 IU/kg/day in 3 divided doses)(XylistinTM; Batch number XP-9001; Cipla LtdMumbai Central, Mumbai, India	15	27.3 ±7.9	8(53.3)	0	2	/	/	/	/	/	/
Alan S/ Turkey (*93*) (2014)	retrospective	nosocomial infection	AB including MDR AB	3 mg/kg/d (2–5) IV COL for 9 days (3–26)	21	premature infants, 28 weeks (23–36)※	11(52)	NA		/	/	/	/	/	/
Rigatto MH/ Brazil (*25*) (2015)	multicentre prospective cohort study	respiratory tract, bloodstream, UTI,abdominal, skin and soft tissue, other sites, sepsis without a defined primary site	AB, P. aeruginosa, K. pneumoniae, Escherichia coli, Enterobacter aerogenes	IV polymyxin B 1.5–3.0 mg/kg/day in two divided (2.4+0.69 mg/kg and the median average daily dose was 150 mg (IQR¼140–187).)	410	64.0+16. 9	58.70%	189 (46.1%)		/	/	/	/	/	/
Binh NG/ Vietnam (*26*)(2015)	retrospective observational study	VAP, BSI	MDR-GNB(AB, P. aeruginosa, n (%)	IV Coly-Mycin 4.1 ± 1.6 MIU/d for 12.5 ± 5.2 days	28	60 (20.4; range: 19-88)	18 (64%)	6 (21.4%)	NA	/	/	/	/	/	/

			K. pneumonia, n (%) COL MIC of Acinetobacter baumannii, mg/L, median (IQR))												
Qureshi, Z. A et al/ America (*45*)(2015)	retospecive	VAP (13 [65%]), bacteremia (2 [10%]), mediastinitis (1 [5%]), and HAP (1 [5%]).	COL-Resistant AB	18 (95%) IV CMS for 12.5 (range 2–76)days, 16 (84%) inhaled CMS for 10.5 (range, 5–84)days .	20	60.5±14.1	12（60）	NA	NA	/	/	/	/	/	/
Isguder R et al/ Turkey (*99*)（2016）	prospective	VAP(11 episodes) and CLABSI(3 episodes)	MDR AB	IV COL (4.1 ± 0.7 mg/kg/d, bid) for 18.5 ± 7.5 days	9	34 months（4-168）	3 (33.3)	NA	NA	/	/	/	/	/	/
Munster AM/ Maryland (*108*)(1989)	RCT	burn	NA	IV polymyxin B for 1500 iU/kg/d in 2 doses, 5000 iU/kg/d by day 4,1500 iU/kg/d on day 7	22	34.4	NA	0	NA	other antibiotics	23	38.8	NA		
Garnacho-Montero J/ Spain (*32*)(2003)	prospectively	VAP	MDR AB	IV COL(2.5–5.0 mg/kg qd divided into 3 doses)	21	56.9 ± 13.1	14(66.6)	5(24%),3 required dialysis	NA	IV impenem + cilastatin	14	64.5 ± 11	12(85.7)	6(42%)，3 required dialysis	
Reina R/ Argentina (*4*)(2005)	prospective cohort study	VAP, BSI，Catheter-related infections, central nervous system infections, peritonitis, surgical wound infection	Acinetobacter and Pseudomonas	IV COL for 13±5	55	40±16	19(34)	0	NA	Noncolistin for 13±6	130	41±16	57(44)	0	NA
Holloway KP/ USA (*43*)(2006)	retrospective chart	??	MDR AB	IV polymyxin B	33	??	??	NA	NA	IV doxycycline	4	??	??	NA	NA
Betrosian AP/ Greece (*42*)(2008)	prospective cohort	VAP	MDR AB	IV COL 3 MIU q8h	15	67 ± 9	7(46.7)	5 (33)	NA	IV ampicillin/sulbactam 9g q8h	13	72 ± 5	7(53.8)	2 (15.3)	NA
Gounden R/ South Africa (*39*)(2009)	retrospective cohort	Bloodstream infection,Sputum/tracheal aspirate,Wound pus swab,Cerebrospinal fluid,Central venous catheter tip, Urine	AB	IV COL(2 MU q8h) for 8(5-13)days	32	43.5 ± 15.6	NA	4 of 21 (19%)	NA	IV Tobramycin(5–6 mg/kg/d) for 7(6-10)days	32	45.6 ± 18.2	NA	2 of 23 (8.7%)	NA
Paul M/ Israel (*30*)(2010)	prospective cohort study	Pneumonia,VAP,UTI, deep or organ-space SSI, neurosurgical meningitis, bacteraemia of any source	GNB susceptible to COL, imipenem, meropenem or ampicillin/sulbactam	6–9 MU in three divided doses (equivalent to 480–720 mg of CMS or 180–270 mg of COL base activity) haemodialysis or haemofiltration received 1–2 MU twice daily	200	64.7+18.2	123(61.5)	week 1 26/168 (15.5) week 2 23/152 (15.1) week 4 13/128 (10.2)	0/195 Seizures, n/N 2/196	Comparators	295	61.2+18.8	179(61.7)	week 1 17/244 (7) week 2 15/227 (6.6) week 4 10/198 (5.1)	NA
Rigatto MH/ Brazil (*29*)(2013)	prospective cohort study	VAP，tracheobronchitis	P. aeruginosa or AB	polymyxin B 2.5 mg/kg/day q12 h (1 mg = 10,000 U). Not adjusted	45	60.4 ± 16.5	29 (64.4)	NA	NA	other antibiotic	22	62.7 ± 15.6	9 (40.9)	NA	NA

				according to renal function											
Chuang YC/ China (Taiwan)(*41*)(2014)	retrospective matched cohort	pneumonia	MDR-AB	IV COL based(Colimycin injection 3.0 (±0.8) mg/Kg/day for 14.0 ±11.2)	84	63.8±19.8	63 (75)	9.50%	NA	IV tigecycline based(100 mg loading, followed by 50 mg q12 hours for 12.9±9.3)	84	63.5 ±17.7	65 (77.4)	2.40%	NA
Chuang YC/ China (Taiwan)(*41*)（2014）	retrospective matched cohort	pneumonia	MDR-AB	IV COL based(Colimycin injection 3.0 (±0.8) mg/Kg/day for 14.6±13.7)	119	63.7 ± 19.5	86 (72.3)	NA	NA	IV tigecycline based(100 mg loading, followed by 50 mg q12 hours for 13.1±11.6)	175	63.8 ± 17.9	112 (64)	NA	NA
Kwon SH/ Korea (*36*)(2014)	retrospective observation	pneumonia, bacteremia,wound infection,peritonitis,UTI,biliary tract infection	XDR-AB	IV COL(75–300 mg/d)	39	59.0±19.2	24 (61.5)	NA	NA	IV Tigecycline (50–100 mg/d)	16	60.1±12.3	9 (56.3)	NA	NA
Balkan II/ Turkey (*37*)(2015)	retrospective, observational, multi-center study	BSI	MDR Acinetobacter spp	COL monotherapy(IV Colimycin 2.5–5.0 mg/kg/day)	36	58.3±20.5	15(41.7)	NA	NA	Non-colistin based combination	71	60.9±19.9	39(54.9)	NA	NA

CLABSI: central line–associated bloodstream infection; VAP: ventilator-associated pneumonia; HAP: hospital-acquired pneumonia; BSI: bloodstream infection; UTI: urinary tract infection; CNS: central nervous system; SSI: surgical site infection; MDR: multidrug-resistant; XDR: Extensively Drug-Resistant; CR: Carbapenem-Resistant; COS: colistin only susceptible; AB: *A. baumannii*; GNB: gram-negative bacilli; IV: intravenous; COL: colistin; CMS: colistin methanesulfonate; MU: million unit

Table S3. Trials or case series of combination therapy

Author/ Country	Trail type	Type of infection	Organisms isolated group	Experimental						Control group					
				Administration strategy	Sample size	Age(y)	Male gender n (%)	Nephrotoxicity	Neurotoxicity	Administration strategy	Sample size	Age	Male gender n (%)	Nephrotoxicity	Neurotoxicity
Markou N/ Greece (*20*) (2003)	present observational study	sepsis(VAP,Post-traumatic meningitis,Urosepsis,Catheter-related sepsis,Sepsis of unknow imary origin,Empyema thoracis)	COS-GNB	IV COL for 13.5 days (range 4–24 days)+ceftazidime or piperacillin/tazobactam or carbapenem	24	44.3	17(70.8)	2/21 (14.3)	0	/	/	/	/	/	/
Petrosillo N/ Italy (*69*) (2005)	retrospective	VAP, BSI,SSI	CR-AB	IV CMS (2 MU threetimes-daily)+rifampicin(600 mg once-daily)	14	48.9 ± 23.5	10(71.4)	NA	NA	/	/	/	/	/	/
Motaouakkil S / Morocco (*70*)(2006)	present observational study	VAP, BSI, nosocomial meningitis	COS-AB	aerosolized /IV / IT COL+ IV rifampicin	26	43.6 ± 18.3	17(65.4)	No deterioration of kidney function	NA	/	/	/	/	/	/
Bassetti M/ Italy (*71*)(2008)	prospective uncontrolled case series	VAP, BSI	MDR-AB	IV CMS (6 MU/d) + IV rifampicin (10 mg/kg q12 h) for 17.03 + 3.68 days	29	47.2 ± 14.2	NA	3/ 29 (10%) (had previous renal failure)	0	/	/	/	/	/	/
Shields RK/ USA (*55*)(2011)	Case series	VAP;bacteremia;mediastinitis;empyema	XDR-AB	carberpenem + IV COL(5 mg/kg/d divided in 2–4 doses)	5	57.2 ±9.58	1(20 %)	NA	NA	IV COL+other antibiotics	11	57.82± 12.34	7/11(63.6)	NA	NA
Apisarnthanarak A/ Thailand (*109*)(2012)	retrospective	VABP HABP	CR P. aeruginosa	high-dose (1 g), 4-h infusion of doripenem in combination with fosfomycin for ≥2 days	25	45	15(60)	NA	NA	IV COL (5 mg/kg/day in two divided doses) in combination with fosfomycin for ≥2 days	24	46	13(54)	NA	NA
Crusio R/ U.S.A (*46*)(2014)	prospective observational cohort study	pneumonia,UTI,SSTI+OM,bacteremia,multiple sites	CR- K. pneumoniae,CR-P. aeruginosa,CR-AB	polymyxin B combination	104	77 ±12.9	62(59.6)	14.40%	NA	/	/	/	/	/	/
Khawcharoenporn T/ Thailand (*56*)(2014)	retrospective cohort	pneumonia(VAP/HAP)	XDR AB	9% IV COL(300 mg loading followed by 150 mg q12 h)/91% inhaled COL (40 mg q6 h)+high-dose sulbactam(6 g/day) for 14days	93	75 (17–92)	45 (48)	8(9)	NA	7% IV COL(300 mg loading followed by 150 mg q12 h)/93% inhaled COL (40 mg q6 h)+ tigecycline/7% IV COL(300 mg loading followed by 150 mg q12 h)/93% inhaled COL (40 mg q6	43/30	75 (45–94)/75 (23–88)	28 (65)/15 (50)	3(7) /2(7)	NA

										h)+high-dose prolonged-infusion carbapenem					
Batirel A/ Turkey (*47*)(2014)	retrospective, multicenterobservational, multicenter	BSI	XDR-AB	COL(5 mg COL base activity/kg/day divided into 2–3 doses)+carbapenem/ sulbactam/ other antimicrobial	214	59.1 ± 19.6	141 (65)	36 (21.8)	Present 3 (1.4),Unconscious/pharmacologic sedation 211 (98.6)	COL(5 mg COL base activity/kg/day divided into 2–3 doses)	36	58.3 ± 20.5	21 (58)	9 (25)	Present 0(0),Unconscious/pharmacologic sedation 36 (100)
Ceccarelli G/Italy (*72*)(2015)	Case series	BSI, VAP	MDR-AB	VAN + COL(6mg/kg /d into 3 divided for 12-19d) + MEM	4	3-25 mons	NA	NA	NA	/	/	/	/	/	/
Cheng A et al/ China (Taiwan)(*61*) (2015)	Prospective, observational, multicenter study	bacteremia	XDR AB	COL(2.5–5 mg/kg/d divided over 8 or 12hours)-tigecycline	29	62 (45–81)	19 (65.5)	AKI after COL 6/16	NA	COL-carbapenem	26	62 (44–73)	17 (65.4)	AKI after COL 5/19	NA
Falagas ME/ Greece (*27*) （2006）	retrospective cohort study	pneumonia,UTI,abdominal spondylodiscitis,SSI /SSTI, bacteremia,catheter-related,empirical	AB,P. aeruginosa,K. pneumoniae,Stenotrophomonas maltophilia,Enterobacter cloacae,Escherichia coli	IV CMS(4.6 ± 2.3 MIU) for 14.2 ± 7.3 days	14	56.2 ± 19.8	8／14 (57.1 %)	0／14 (0)	NA	IV CMS(5.5 ± 2.2 MIU)for 17.8 ± 11.4 days, +meropenem(4.8 ± 1.6 g for a mean of 15.7 ± 9.6 days)	57	61.5 ± 18.9	34／57 (59.6 %)	4／57 (7%)	NA
Jang HJ/ Korea (*35*) （2009）	retrospective	VAP	MDR-AB	COL only for 12.3±6.8days	22	62.5±17.5	12 (75.0)	10(45.5%)	NA	COL + synergistic antibiotics for 19.1±11.2 days	19	57.0±16.5	13 (68.4)	6(31.6)	NA
Simsek F/ Turkey (*19*) （2012）	retrospective case-control study	VAP,BSI, nosocomial pneumonia, UTI, SSI+VAP,CLABSI, intra-abdominal infection	COS-AB	Either IV COL sulphate or CMS alone or plus other antibiotics	51	51.71 ± 18.82	31 (70)	NA	NA	/	/	/	/	/	/
Durante-Mangoni E/ Italy (*53*) （2013）	multicenter, parallel, randomized, open-label	VAP,BSI,HAP, Complicated intra-abdominal infection	XDR-AB	IV COL(CMS)(160 mg every 8 hours) + IV Rifampicin(600 mg every 12 hours)	104	62 ± 15.1	67 (64.4 %)	24 (23.7)	1 (0.99)	IV COL(CMS)(160 mg every 8 hours)	105	61 ± 15.7	70 (66.7 %)	29 (28.7)	0
Garnacho-Montero J/ Spain (*51*)(2013)	retrospective	VAP or bacteremia	CR AB	IV COL (6.5 ± 1.63 MU/d for 13.4 ± 7.3 days) plus IV VAN(2 g/day)	29	54 ± 14.8	19(65 .5)	16/29 (55.2)	NA	IV COL (7 ± 3.62 MU for 13.1 ± 7.7 days)	28	63 ± 11.6	16 (57.1)	8/28 (28.6)	NA
Aydemir H/ Turkey (*52*)(2013)	open, comparative, prospective, randomized, single-centre	VAP	CRAB	IV COL(CMS) （300mg divided into three i.v. doses） + rifampicin (600 mg/day) nasogastrically for 9.8±2.9 days	21	58 ± 23	14(66 .7)	NA	NA	IV COL(CMS) （300mg divided into three i.v. doses） for 8.9±3.5	22	63± 17	16(72. 7)	NA	NA
Petrosillo N,/ Italy, Croatia, Turkey (*28*)(2014)	retrospective multicenter cohort study	VAP，BSI,SSI,UTI,Intra-abdominal infection	MDR AB,MDR P. aeruginosae,CR K. pneumoniae,Non-MDR AB,Non-MDR P. aeruginosa, ESBL-producing Escherichia coli,Morganella morganii	COL alone	61	65, 45.5–75.5	35 (57.4)	8 (13.1)	NA	COL-glycopeptide	42	68, 46.5–67.5	28 (66.7)	3 (7.1)	NA

Petrosillo N,/ Italy, Croatia, Turkey (*28*)(2014)	retrospective multicenter cohort study	VAP, BSI,SSI,UTI,Intra-abdominal infection	MDR AB,MDR P. aeruginosae,CR K. pneumoniae,Non-MDR-AB,Non-MDR P. aeruginosa, ESBL-producing Escherichia coli,Morganella morganii	COL plus other anti-GNB drugs	37	56.5, 45–67.5	25 (67.6)	5 (13.5)	NA	COL-glycopeptide plus other anti-GNB drugs	26	55, 39.2–74.7	15 (57.7)	5 (19.2)	NA
Batirel A/ Turkey (*47*)(2014)	retrospective, multicenterobservational, multicenter	BSI	XDR-AB	COL(5 mg COL base activity/kg/day divided into 2–3 doses)+carbapenem/ sulbactam/ other antimicrobial	214	59.1 ± 19.6	141 (65)	36 (21.8)	Present 3 (1.4),Unconscious/pharmacologic sedation 211 (98.6)	COL(5 mg COL base activity/kg/day divided into 2–3 doses)	36	58.3 ± 20.5	21 (58)	9 (25)	Present 0(0),Unconscious/pharmacologic sedation 36 (100)
Sirijatuphat R/ Thailand (*54*)(2014)	reliminary open-label randomized controlled	pneumonia,primary bacteremia,UTI,SSTI,intra-abdominal or gastrointestinal infection,CNS infection,others	CR AB	IV COL（CMS）(4.4 ± 1.5 mg/kg/day for 10.3 ± 3.9days） + fosfomycin	47	67.4 ± 17.2	20 （42.6）	53.4	NA	IV COL（4.0 ± 1.5mg/kg/day for 12.1 ± 8.2days）	47	69.2 ± 16.3	24 （51.1）	59.6	NA
Kalin G/ Turkey (*34*)(2014)	retrospective	VAP	MDR AB	IV COL 2.5 mg/kg every 12 h	52	52 (19–96)	36 (69.2)	NA	NA	IV COL/sulbactam	37	63 (20–89)	18 (48.6)	NA	NA
Yilmaz GR/ Turkey (*31*)(2015)	retrospective observational	VAP	MDR and XDR AB	IV COL(Colistincolistimethate sodium (100 mg COL base, colomycine) was administered either 75 mg three times per day or 150 mg IV twice per day. The ose was adjusted for patients with renal impairment.) for 12.3 ± 3.2days	17	59.8 ± 21.5	7 (41.2)	3/17 (17.6)	NA	IV COL + carbapenem/sulbactam (imipenem 500 mg IV four times per day, meropenem 1 g IV three times per day, and sulbactam 1 g IV three times per day.)for 11.7 ± 5.6/10.8 ± 4.2	33/20	59.6 ± 20.5/70.6 ± 14.7	10 (50)	4/33 (12.1) / 2/20 (10.0)	NA

CLABSI: central line–associated bloodstream infection; VAP: ventilator-associated pneumonia; HAP: hospital-acquired pneumonia; BSI: bloodstream infection UTI: urinary tract infection; CNS: central nervous system; SSI: surgical site infection; SSTI: Skin and soft tissue infection; OM, osteomyelitis, MDR: multidrug-resistant; XDR: Extensively Drug-Resistant; COS: colistin only susceptible; AB: *A. baumannii*; GNB: gram-negative bacilli; IV: intravenous; COL: colistin; VAN: vancomycin; MEM: meropenem; CMS: colistin methanesulfonate; MU: million unit