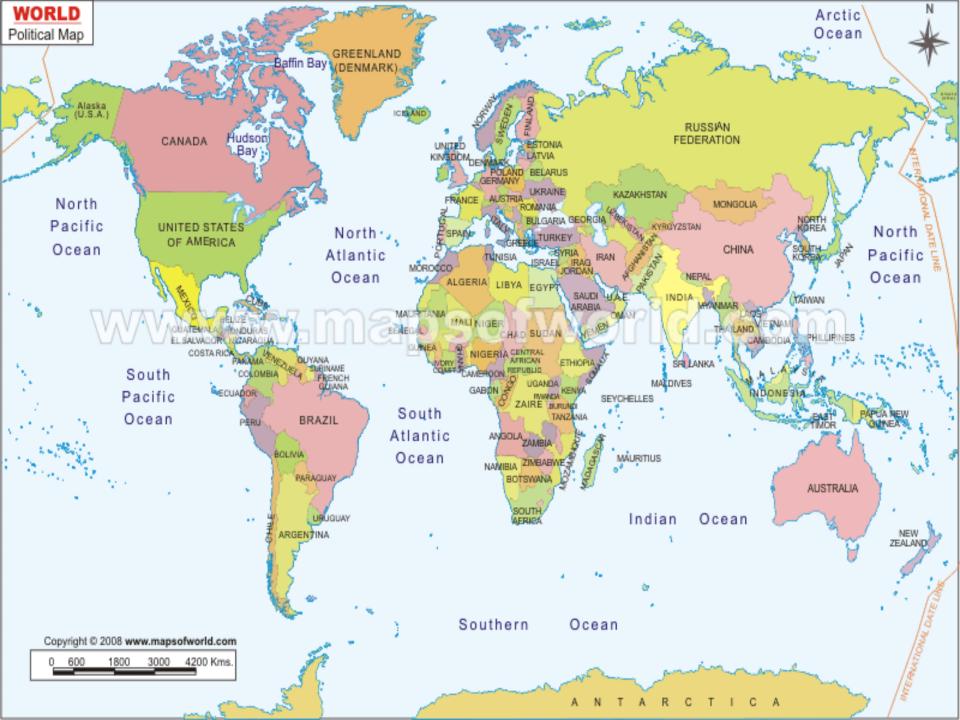
Impact of Antimicrobial Stewardship on MDR-Pathogens

Anucha Apisarnthanarak, MD Division of Infectious Diseases Thammasat University Hospital, Thailand

Adjunct Visiting Professor Washington University School of Medicine Saint Louis, MO, USA

Outlines

- > Understanding antibiotic use in Asia Pacific Regions
- Environment where antibiotic resistant develops and spreads
- > Incidence and patterns of inappropriate antimicrobial use
- > What work, not work in Thailand
- Implementing antibiotic stewardship programs
- Long-term success of antibiotic stewardship program
- Integration of antifungal stewardship program
- > Role of physicians



Inappropriate antibiotic use: Asia-Pacific region vs. USA

Country	Results	Reference
Philippines (OTC purchase)	Manila: 66%	Lansing et al. J Clin Epidemiol 1990
China Prescribing for viral infections	 Beijing Children's Hospital: 98% of cold Taiwan: 30% of all "colds" (45% aged ≤ 15 yrs)s and "RTIs 	Yang et al. PIDJ 1993 Chang et al. Int J Ant Ag 199)
Malaysia	53% inappropriate Rx in hospital	Lim Singapore Med J 1993; 1994
Hong Kong False diagnostic indicators and attitudes	Older, more senior, private practice = > AB Rx	Lam. Int J Clin Pract 2001/3
Thailand	Overall 80% inappropriate prescribing in drug store setting	Apisarnthanarak et al. ICHE, 2008
US	 Antibiotics for common cold 36% Antibiotics for acute resp infection 51% 	Gilberg, J Man Care Pharm 2003 Huang et al, J Clin Epidem 2005 4

Environment where antibiotic resistance develops and spreads

Nursing Homes



Homecare



Daycare





Tertiary Hospitals



Community Hospitals



Community



Foreign



Feedlots

Scenario and Overview of the Problems

Dispensing antibiotics at Thai Drug Stores

- Six interns trained as patients with common syndromic ailments presented to all drug stores in Pratumthani (central Thailand) from July-December 2006.
- Six presentations were simulated.

Apisarnthanarak A, et al. Non-judicious dispensing of antibiotic by drug store in Thailand. ICHE, 2008

Antibiotic Dispensing at Thai Drug Stores







Presentation and Treatment Guidelines

Presentation	Diagnosis	Treatment
Acute low grade fever and sore throat	Viral pharyngitis	No antibiotic
Acute fever, myalgia, rhinorrhea, cough	Influenza	No antibiotic
Acute fever, tender maxillary sinus with d/c	Viral sinusitis	No antibiotic
Acute watery diarrhea, no abdominal pain	Viral diarrhea	No antibiotic
Skin abrasion without exudate	Non infected wound	No antibiotic
Acute dysuria with suprapubic pain	Urinary tract infection	Quinolones

Slavin RG, et al. The diagnosis and management of sinusitis. J Allergy Immunology, 2005. Bisno AL. Pharyngitis. In: Principle and Practices in Infectious Diseases, 6th ed, 2005. Treanor j. Influenza virus. In: Principle and Practices in Infectious Diseases, 6th ed, 2005. Guerrant RL, et al. Practice guidelines for the management of infectious diarrhea. Clin Infect Dis, 2001 Stevens DL, et al. Practice guidelines for the diagnosis and management of SSTI. Clin Infect Dis, 2005 Gupta K, et al. Increasing antimicrobial resistance and the management of Uncomplicated CAUTI. Ann Intern Med , 2001 ¹¹



315 first-class drug stores were identified; 35 were no longer in business

>280 were surveyed

Appropriate antibiotic dispensed for all six indications at 56 (20%) drug stores

Dispensing of antibiotics at drug stores for 6 common syndromic ailments

	Antibiotic Dispensed ^a (%) Stores								
Clinical Syndrome	that prescribed antibiotics (N=280) No. (%)	Pen V	Amoxi cillin	Amoxi clav	TCN	Erythro	Azithro mycin	Rifam pin	Other(%)
Acute low-grade fever & sore throat	207 (74)	18	32	15	8	5	11	-	Cefu(8), Cefd(7)
Acute fever, myalgia, rhinorhea, cough	182 (65)	23	38	25	3	2	4		Cefd(5), Cefu(5)
Acute fever, tender maxillary sinus with non-purulent discharge	224 (80)	-	37	35	2	2	16	-	Nor(23), Olf(20)
Acute watery diarrhea without fever or abdominal pain	213 (76)	-	6	14	12	8	14		Cefu(4), Cefd(4)
Skin abrasion without exudates	179 (64)	14	24	18	8	6	4	-	Mupi(8), Fus(6), Cefp(10)
Acute dysuria & suprapubic pain	280(100)	3	14	15	17	-	-	12	Olf(13), Cipro(30), Cefp(6)

Correlations of outpatient antibiotic use and drug resistance

Inappropriate use of rifampin: primary rifampin resistance approached 15%
Riantawan P, et al. Resistant of MTB to anti-tuberculosis *in Central Thailand. Int J Tuberc Lung Dis, 1999*

Inappropriate use of 2nd & 3rd cephalosporins Apisarnthanarak A, et al. Clinical and molecular epidemiology of CO-ESBL E. coli in Thailand. Am J Infect Control 2008

Table 1. Dispensing of antibiotics by drug stores for six common syndromic ailments

	No.(%) Drug		Α	ntibiotic	Dispe	n <mark>sed</mark> a ('	%)		
Clinical Syndrome	stores that prescribed antibiotics (N=280)	Pen V	Amoxi cillin	Amoxi cillin/ Clavulonic acid	Tetra cycline	Erythro mycin	Azithro mycin	Rifam pin	Other(%)
Acute low-grade fever and sore Throat	207 (74)	18	32	15	8	5	11	-	Cefu(8), Cefd(7)
Acute fever, myalgia, rhinorhea, cough	182 (65)	23	38	25	3	2	4	-	Cefd(5), Cefu(5)
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Emergence of mupirocin resistance in Thailand

Point prevalence survey in January 2010 detected 3.8% (9/250 pts) with MRSA nasal carriage.

Low level mupirocin-resistance detected in 22% (2/9 pts); all had history of skin abrasion and self-purchase mupirocin and fluoroquinolone from a local pharmacy within 3 months prior to admission.

Apisarnthanarak A, et al. Prevalence of nasal carrier with mupirocin-resistant MRSA in Thailand. ICHE 2011 (in press) Harbarth S, et al. Risk factors for persistent carrier of MRSA. Clin Infect Dis 2000

Antibiotic prescription is so easy?

Sale of antibiotics according to the clinical case and statement made to obtain the drug.

	Clinical case presented, no. (%) of pharmacies visited								
Result and level of demand (statement)	UTI	Sore throat	Acute bronchitis	Total					
	(n=69)	(n=69)	(n=59)	(n=197)					
Antibiotic obtained									
 (Can you give me something to alleviate the symptoms of the infection?) 	52 (75.4)	12 (17.4)	1 (1.7)	65 (33.0)					
2. (Can't you give me something stronger?)	2 (2.9)	10 (14.5)	5 (8.5)	17 (8.6)					
3. (I would like an antibiotic.)	1 (1.4)	2 (2.9)	4 (6.8)	7 (3.6)					
All	55 (79.7)	24 (34.8)	10 (16.9)	89 (45.2)					
Antibiotic not obtained	14 (20.3)	45 (65.2)	49 (83.1)	108 (54.8)					

Llor C, et al. Sale of antibiotic without prescription in Spain. CID 2009.

Explanation and questions from the pharmacist to the simulated patient in the pharmacies in which the antibiotic was obtained.

	Clinical case presented, no. (%) of pharmacies providing antibiotic							
Pharmacist statement	UTI	Sore throat	Acute bronchitis	Total				
	(n=55)	(n=24)	(n=10)	(n=89)				
Explained how often to take the antibiotic	52 (94.5)	17 (70.8)	5 (50.0)	74 (83.1)				
Explained how long the antibiotic should be taken	52 (94.5)	9 (37.5)	1 (10.0)	62 (69.7)				
Asked patient about other symptoms	38 (69.1)	17 (70.8)	6 (60.0)	61 (68.5)				
Asked patient about possible drug allergies	5 (9.1)	17 (70.8)	6 (60.0)	61 (68.5)				
Asked patient whether she might be pregnant	2 (3.6)			2 (3.6)				
Recommended that patient see a physician if there is no improvement	1 (1.8)	3 (12.5)	0 (0)	4 (4.5)				

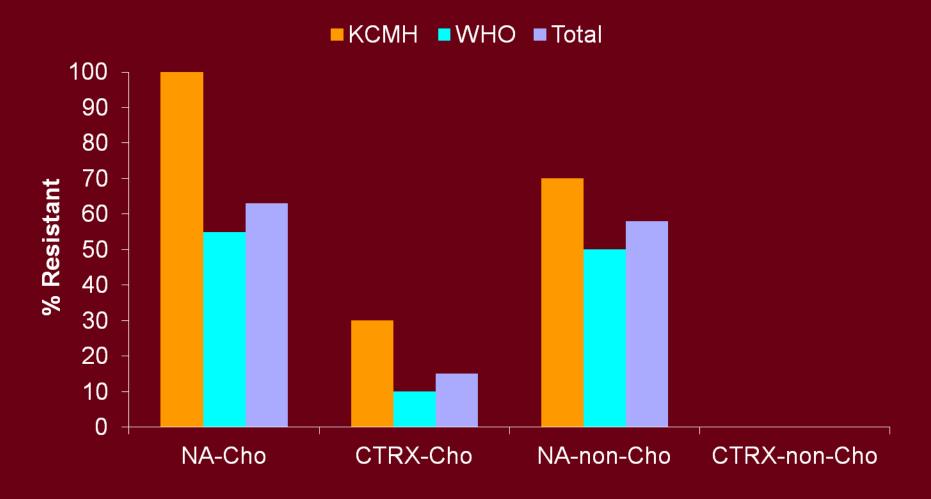
Llor C, et al. Sale of antibiotic without prescription in Spain. CID, 2009

This is a global issue!

- Tangden T, et al. Foreign travel is a major risk factor for colonization with Escherichia coli producing CTX-M-type extended-spectrum {beta}-lactamases. AAC 2010
- Leverstein-van Hall MA. Carbapenem resistant K. pneumoniae following foreign travel. Ned Tijdschr Geneeskd. 2010
- Emergence of new antibiotic resistant mechanism in India, Pakistan and the UK. Lancet Infect Dis 2010
- Rolain JM, et al. New Delhi metallo-beta-lactamase (NDM-1): towards a new pandemia? CMI 2010

Salmonella spp. E. coli Clostridium difficile Vancomycin-resistant Enterococci Illing and and and all

Drug Resistant Non-Typhoidal Salmonella Bacteremia in Thailand



Kulwichit W, et al. EID, 07

International Spread of Multidrug-resistant Salmonella Schwarzengrund in Food Products

	No. isolates		No. isolates resistant to antimicrobial drugs*									
Country/ source	tested/ total no. isolates	AMP	CHL	CIP	GEN	NAL	STR	SUL	TET			
Denmark												
Humans	14/14	8	3	1	6	8	11	9	8			
Pigs on farm	22/22	0	2	0	0	0	4	2	2			
Pork	4/4	0	0	0	0	0	0	0	0			
Chicken meat of unknown origin	7/7	4	1	0	4	5	5	6	4			
Imported chicken	13/13	11	0	0	11	11	12	13	13			
Imported turkey	9/9	1	0	0	1	1	4	4	4			
Others	0/4	-	-	-	-	-	-	-	-			
Thailand												
Humans**	46/57	30	13	10	27	42	45	41	35			
Chicken meat	44/48	23	16	2	28	39	39	36	23			
Turkey meat	2/4	0	0	0	0	0	0	0	0			
United States												
Humans	38/390	13	08	16	4	17	4	20	22			
Chicken meat	0/3	-	-	-	-	-	-	-	-			
Turkey on farm	0/1	-	-	-	-	-	-	-	-			
Pigs on farm	2/2	0	0	0	0	0	0	1	1			
Imported food	3/3	1	2	1	2	3	2	3	3			
Total	204/581	91	45	30	83	126	126	135	115			

Aarestrup FM, et al. Emerg infect Dis 2007

"CTX-M-type beta-lactamases non-Typhi Salmonella were detected in 2.5% in US during 2007"

Sjölund-Karlsson M, et al. CTX-M producing non-Typhi Salmonella spp. isolated from humans, United States. Emerg Infect Dis 2011

Al-Mashhadani M, et al. Foreign travel and decreased ciprofloxacin susceptibility in *Salmonella enterica* Infections. Emerg Infect Dis 2011

Environment where antibiotic resistance develops and spreads

Nursing Homes



Homecare



Daycare





Tertiary Hospitals



Community Hospitals



Community



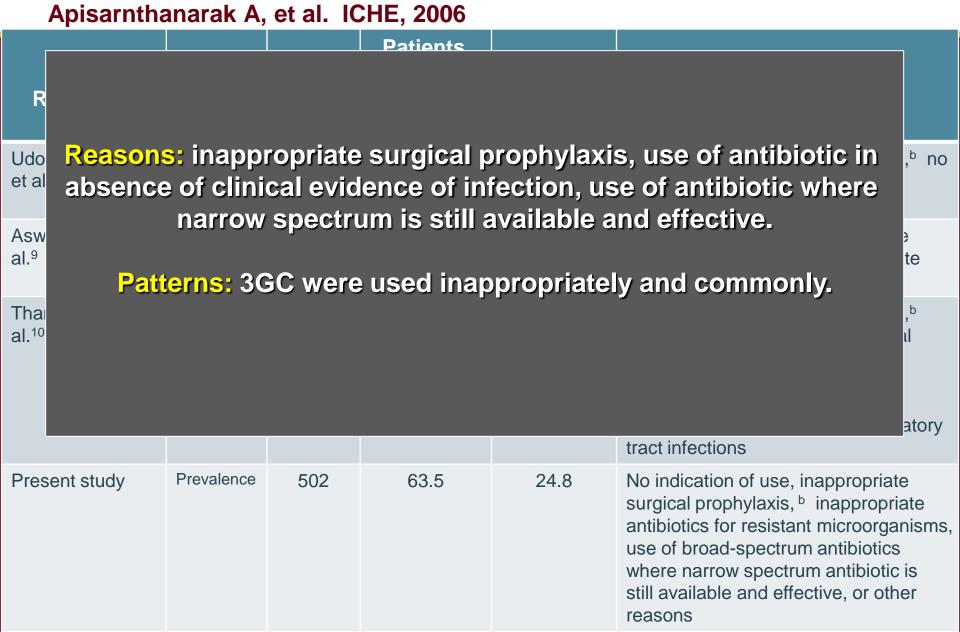
Foreign



Feedlots

Incidence/Prevalence and Patterns of Inappropriate Antibiotic Use in Thailand

Prevalence/Incidence, and Patterns of Inappropriate Antibiotic Use in Thailand



Factors Associated with Inappropriate Antibiotic Use

Variables	aOR	<u>95% CI</u>
Admission to surgery	2.0	1.1-3.4
Admission to OB & GYN	2.0	1.1-4.1
ID Consultation	0.15	0.03-0.65

Apisarnthanarak A, et al. Inappropriate antibiotic use: an incidence study and review of Thailand experience. Infect Control Hosp Epidemiol, 2006

What works & What doesn't work in Thailand?: Lessons Learned

Antimicrobial Stewardship Program in Thailand: Lessons Learned

Education

Formulary restriction

Antibiotic approval program using Drug Use Evaluation (DUE) Form

Comprehensive programs

Education Works

Thamlikitkul V, et al. Impact of an educational program on antibiotic use in a tertiary care hospital in

Interventions were performed in less than % a year, so long-term outcome cannot be drawn from these interventions

Doominavomsak B, et al. Intervention of inappropriate antibiotic use at a university teaching hospital, 1991.

Antibiotic Approval Program

Suwangool P, et al. Effect of a selective restriction policy on antibiotic expenditure and use: an institutional model. J Med Asso Thai, 1991.

 Reduction in IAU (pre vs post)
 33% vs 18% (P<0.001)</th>

Hospital expense on antibiotics (pre vs post) 2.2 mB vs 1.9 mB (13%)

May or May Not Work

Ayuthaya S, et al. Utilization of restricted antibiotics in a university hospital in Thailand. Southeast Asian J Trop Med Public Health, 2003.
 AOF, closely monitored, enforcement 75% of appropriate antibiotic use

sian

ture

What Doesn't Work?

Aswapokee N, et al. The failure of a preprinted order form to alter physicians' antimicrobial prescribing pattern. J Med Assoc Thai, 1992

AOF alone

Fail

Implementing Antimicrobial Stewardship Program

Introduction of Antibiogram, Antibiotic Guideline and Prescription Forms

> Interventions:

- 1. Monthly Education Target High-Risk Units
- 2. Introduction of Antibiotic Order Form
- **3.**Presence of Clinical Pharmacist
- 4.Real-time Feedback
- **5**.Encourage ID Consultation

แบบบันทึกการสั่งใช้ยา Ceftazidime/Ceftriaxone/Cefotaxime/

Cefoperazone-sulbactam/Piperacillin-Tazobactam/Cefrom

1	น้ำหน่	เ ๊กตัว		kg CrCl			.ml/r	nin	ประวัติการแพ้ยา							
เคย admit หรือเคยไ	ด้รับ 3	rd ge	nerati	on Cephalosporins ໃ	เนช่วง	3เดี	อนก่	อนเ	หน้านี้ 🗌 YES		NO					
2. ข้อบ่งใช้หรือต่ำเ	แหน่ง	เติดเรี	ส้้อที่จ	ะใช้ยาต้านจุลชีพ		หมา	ยเหตุ	1 CA	P=Community Acquir	ed Pne	umon	ia , HA	P= Hospital Acquired P	neumo	nia	
Bone & joint in	fectio	on			Mer	ningiti	is or	CN	IS infection				Skin & soft tissue in	nfectio	n	
Febrile neutro	penia	а			Pne	umor	nia (CAP HAP)				UTI or Pyelonephri	tis		
Intra-abdomir									remia				Other			
3. ลักษณะการใช้ย	า			ctic Antibiotic ก่อนกา										เนข้อ4เ	.ເລະ 5	<i>б</i>)
_				therapy เชื้อที่น่าจะเบ็												
				มูลเพียงพอ กรุณากรอ	-											
<u> </u>				nd on > 3 days of Ant				al A	TB or Anti-pseudo	mona	⊢β-la	actarr	n- eta lactamase inhibi	tor (β	_/βι)*	
(ถ้ามีข้	-		-	นากรอกข้อมูลในข้อ 4												
				therapy (กรุณากรอกข้	-11	เนข้อ	4 แส	ละใข	นข้อ 5)							
	-	เารถเ	เลือกไ	ด้มากกว่า 1 ตัวเลือง	-								-			
Specim	ien			By Gram s				_			C	rgan	ism			
Blood				Gram + ve ba			\rightarrow		P. aeruginosa							
Sputum				Gram – ve bad			\rightarrow	S. pneumoniae								
CSF				Gram + ve co				<i>E. coli + K. pnuemoniae</i> (non-ESBL)								
Urine				Gram – ve coo	cci			Enterobacter spp.								
Pus				Mixed organis	m				E. coli + K. pnu	emon	iae (p	previc	ous ESBL or suspect	ed ES	BL)	
Not done				Not done					Acinetobacter s	pp.						
Other				Negative gram					No growth / Unk	nown						
5. ผลความไวของเ	ชื้อจา	กห้อ	งปฏิบั	ไดิการ () NOT AVA	AILAE	BLE			() AVAILABLE A	S BEI	ow					
Antimicrobial	S	Т	R	Antimicrobial	S	Т	R		Antimicrobial	S	Т	R	Antimicrobial	S	Т	R
Penicillin				Ceftriaxone					Gentamicin				Cefotaxime			
Amox/Clav				Ceftazidime	Amikacin Cefpirome											
Piperacillin				Cefo/sulb					Ciprofloxacin				Erythromycin			
			L	เบบบันทึกนี้ 1 ใบ	ใช้ร	สำหรั	ับยา	1	รายการ ควรใช	ช้ได้ไม	เเกิน	7 วัเ	J			
				ขนาดย									ใช้(จำนวนวัน)			

Pocket size antibiogram

Percentage of Antibiotic	Si	15
Organisms	Amnia	Ame
Acinetobacter baumannii	:	:
Acinetobacter baumannii (MDR)	:	:
Aeromonas spp.	21 (28)	4:
Burkholderia (Pseudomonas) pseudomallei	(20)	(*
Coagulase Negative Staphylococci	:	98 (34
Coagulase Negative Staphylococci (MRSE)	:	3 (63
E.coli (ESBL-producing strain)	5 (554)	53
Enterobacter cloacae	0	(55
Enterobacter spp.	(111)	(11
Enterococcus spp.	(94) 80	(93
Escherichia coli	(30) 18	- 74
Haemophilus influenzae	(1423)	(134
	(8)	(8 84
Klebsiella pneumoniae	(558) 2	(55 67
Kleb.pneumoniae (ESBL-producing strain)	(135) 42	(13 84
Proteus mirabilis	(235)	(23
Proteus vulgaris	30 (33)	38 (32
Pseudomonas aeruginosa	:	-
Pseudomonas aeruginosa (MDR)	:	:
Salmonella serogroup B	44 (18)	88 (8)
Salmonella serogroup C	48 (29)	87 (15
Salmonella serogroup D	39 (36)	76
Staphylococcus aureus	:	97 (32)
Staphylococcus aureus (MRSA)	:	3 (19
Stenotrophomonas maltophilia (X.maltophi)	:	-
Streptococcus gr.D - not Enterococci	:	-
Streptococcus pneumoniae	•	-
the second se	-	-



Antimicrobial Susceptibility

Thammasat University Hospital 2006

a	kia	t H	10	sp	ita		200	06
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			"/ ä		3/ 3			ំ/រៀ
Ċ	5/3	12	1ª	120	10	/ ပီ	15	/ రి
	1	:	58 (232)	64 (230)	1	1	1	1
-	-	-	4	8	-	-	-	-
-	-	-	(132)	(132)	-	- 67	•	-
1	:	-	(21)	(28)	1	(21)	1	-
-	-		100	-	-		-	-
-	-	•	(8)	-	-	•	-	•
10		:	:	87 (343)	89 (342)	99 (343)	:	:
3	35		0	51	81	1	-	-
(63		•	(1)	(629)	(631)	(631)	-	-
-	-	•	75	28	-	82	97	0
-	•		(554)	(552) 71		(554) 7	(37)	(42)
-	1	:	66 (111)	(111)	1	(110)	100 (10)	2
-	•	•	69	63 (94)	:	23	75	38
-			(93)	(94)	98	(93)	(4)	(24)
	-	-	-	(2)	(47)	-	-	-
-	:	:	88 (1341)	41 (1423)	1	88 (1339)	100 (68)	71 (83)
-	•	-	1	50 (8)	:	:	:	:
-			85	79	-	86	100	93
-	-	•	(556)	(559)	-	(556)	(32)	(44)
1	:	1	64 (135)	47 (135)	1	81 (135)	91 (11)	1
-			94	51		88	100	72
-	•	•	(233)	(236)	-	(234)	(13)	(18)
1	:	:	97 (32)	64 (33)	1	88 (32)	100 (4)	:
-			87	(33)		0	100	
-			(773)	(434)	-	(1)	(1)	
-	-	:	44 (108)	0 (68)	1	1	:	1
•	-		100	56	-	88	•	-
-			(8)	(18)	-	(8) 87	- 100	
-			(15)	(29)	-	(15)	(3)	1
•	-	-	79	75	•	86	•	•
99	- 88		(29)	(36) 97	91	(29)		
(326		1	1	(326)	(325)	(326)		1
0 (191	15 (190)	:	:	14 (190)	91 (190)	1 (188)	:	1
-	-	-	29	83	-	-	-	-
-	•	•	(52)	(52)	-	•	-	-
	:	1	:	:	2	:	:	1
100) -			37	-			-
				0.000				

- - - (19)

Combination Antibiogram of *A. baumannii*

	Per	cents	of Iso	lates S	uscept	ible to at	Least 1	of the	e con	nbinati	on agen	ts, by	drug
Drug	GEN	AMI	NET	CEFP	CEFZ	CP/SB	AM/SB	CIP	IMI	MER	PIP/TZ	COL	CP/SB +NET
GEN				28	21	39	34	21	31	30	36	100	
AMI				30	23	42	36	24	34	32	35	100	
NET				31	34	54	39	31	40	39	35	100	
CEFP	28	30	31					25				100	
CETZ	21	23	34					20				100	
CP/SB	39	42	54					31				100	
AM/SB	34	36	39					31				100	
CIP	21	24	31	25	20	31	31		29	30	24	100	49
IMI	31	34	40					29				100	65
MER	30	32	39					30				100	61
PIP/TZ	36	35	35					24				100	
COL	100	100	100	100	100	100	100	100	100	100	100		100
CP/SB +NET								49	65	61		100	

NOTE: 560 A. baumannii isolates were identified

Apisarnthanarak A, et al. The Role of Combination Antibiogram for Empiric Treatment of Multidrug Resistant *A. baumannii*. ICHE, 2008

Antibiotic Guideline



คู่มือการใช้ยาต้านจุลชีพ ประจำปี 2549-2551

โรงพยาบาลธรรมศาสตร์ เฉลิมพระเกียรติ

- Guidelines for empirical therapy
- Guidelines for documented infection in specific organ system
- Guidelines for surgical/OB-GYN prophylaxis

All Guidelines are agreed and accepted by all department

Antimicrobial Stewardship at Thammasat University Hospital

> Educations to intern, residents, staffs

- Five-sessions education for all intern, residents and staffs in the hospital
- One on one feedback to externs, interns and residents

Intervention target at specific units

- Structured teaching on medicine, surgery and OB-GYN
- Monthly education for medical students, interns and residents
- Presence of clinical pharmacist on medicine, surgery and OB-GYN units

> Encourage Infectious Diseases consultation

Initiated in July,

04

Apisarnthanarak A, et al. Effectiveness of Educational and Antibiotic Control Program in a tertiary care hospital in Thailand, Clin Infect Dis, 2006

Table 3. Incidence of inappropriate antibiotic use, reasons forinappropriateness, and departments associated with inappropriateantibiotic use during the pre- and postintervention periods.

Variable	Preintervention period (<i>n</i> = 4305)	Postintervention period (<i>n</i> = 2830)	Р
Inappropriate antiobiotic use	1808 (42)	566 (20)	<.001
Reason for inappropriateness ^a			
Inappropriate sugical prophylaxis ^b	452 (25)	115 (20)	.02
Use of antibiotic without any evidence of infection	723 (40)	200 (35)	.04
Redundant spectrum	217 (12)	50 (9)	.03
Bacterial resistance ^c	235 (13)	91 (16)	.07
Narrow spectrum was available ^d	181 (10)	41 (7)	.04
Department ^e			
Surgery	633 (35)	170 (30)	.01
Obstetrics and gynecology	452 (25)	125 (22)	.17
Internal medicine	416 (23)	113 (20)	.14
Other ^f	307 (17)	113 (20)	.12

Bacterial resistance rates during the pre and post intervention periods

Microorganism	Resistanc Pre intervention	Post intervention	Associated antibiotic class	Type of variation	R Þ	Ρ
MRSA	period 48	period 33.5	Glycopeptides 3 rd gen. Cephalo.	Decrease Decrease	0.55 0.93	<.001 <.001
ESBL <i>E.coli</i>	33	21	3 rd gen. Cephalo.	Decrease	0.74	<.001
ESBL <i>K.pneumonia</i> e	30	20	3 rd gen. Cephalo.	Decrease	0.69	<.001
3 rd GC-resistant <i>A. baumanii</i>	27	19	3 rd gen. Cephalo.	Decrease	0.78	<.001
Imipenem-resis <i>P. aeruginosa</i>	5	4	None	-	-	
MDR <i>A.baumanii</i>	4	5	None	-	-	

^a Calculated using the total number of strains.

^b Linear regression analysis between evolution in the resistance rate and antibiotic use throughout the study

What components are needed for long-term success?

Long-Term Outcomes of Antibiotic Control Program With vs. Without Education

> Period 1: July 1, 2004-June 30, 2005

Introduced obligatory antibiotic order form, monthly education, bed-side discussion

Period 2: July 1, 2005-June 30, 2006 Similar activities to period 1, but without education

> Period 3: July 1, 2006-June 30, 2007

Similar to both period 1 and 2; educational program was re-introduced

Apisarnthanarak A, et al. Long-term outcomes of antibiotic control program with vs. without education. Clin Infect Dis, 2007

Long-Term Outcomes of Antibiotic Control Program With vs. Without Education

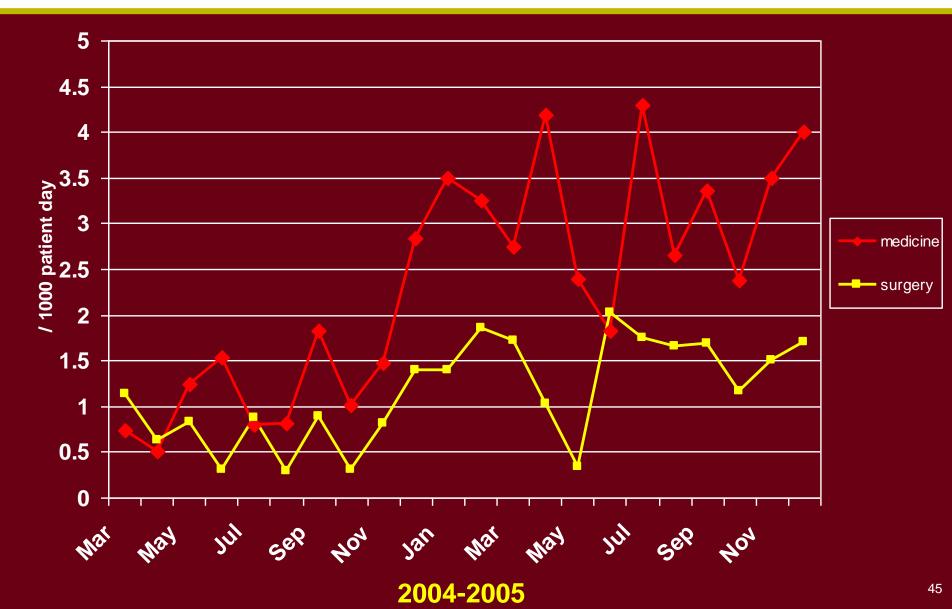
Characteristic	Period 1 (n=2830)	Period 2 (n=2915)	Period 3 (n=2714)
Inappropriate antibiotic use	566 (20)	654 (23)	515 (19)
Reason for inappropriate antibiotic use Inappropriate surgical prophylaxis	115 (20)	170 (26)	93 (18)
Use of antibiotic without evidence of infection	200 (35)	235 (36)	175 (34)
Redundant spectrum	50 (9)	52 (8)	46 (9)
Bacterial resistance	91 (16)	98 (15)	77 (15)
Narrow spectrum available	41 (7)	39 (6)	28 (5)

Controlling Antibiotic Use and Resistant (Editorial Note)

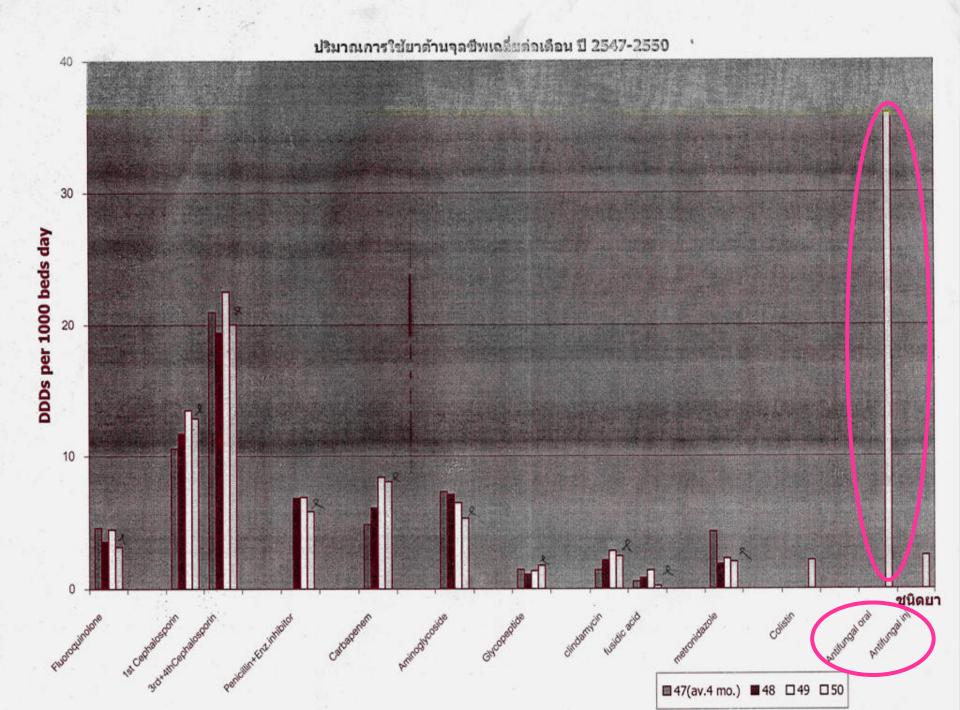
".....To sustain or even further improve these results, lasting and repeated efforts will be needed. Integrating infection-control efforts into this education and antibiotic-control program is warranted."

Nouven JL, Clin Infect Dis, 2006

Despite effective antimicrobial stewardship program, *PDR-A. baumannii* was emerged....



Integration of Antifungal Stewardship Program



Inappropriate Use of Antifungal Medications in a Tertiary Care Center in Thailand: A Prospective Study

Anisada Sutenvarnon. MD:

Most mistakes occur in treatment of candiduria and inappropriate antifungal dose adjustment

an-The

incidence of inappropriate antifungal use was 74% (in 42 of 57 patients). Isolation of *Candida* species from urine (P = .004) was a risk factor, whereas receipt of an infectious diseases consultation (P = .004) was protective.

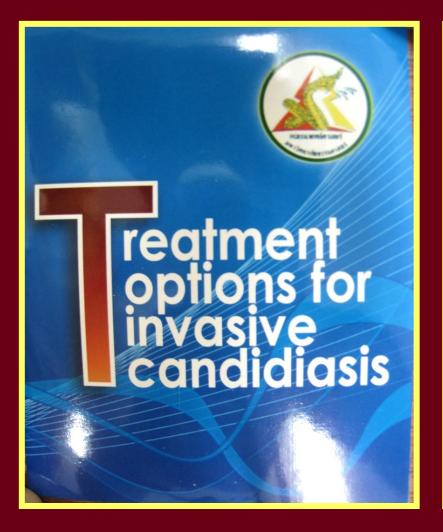
Infect Control Hosp Epidemiol 2008; 29:370-373

Interventions Incorporated to Existing Antimicrobial Stewardship Program

- Education on antifungal treatment and prophylaxis for Physicians/Resident/Intern
- Intervention to reduce inappropriate urinary catheterization
- Implement the clinical care practices for Candidemia
- Implement renal dose adjustment for antifungal dose as a poster
- Implement antifungal DUE and encourage ID consultation for complicated cases

Apisarnthanarak A, et al. Impact of education and antifungal control program. ICHE, 2010

Pocket Size for Invasive Candidasis a Care Map



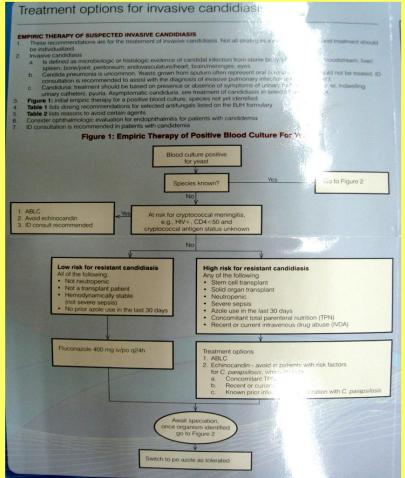
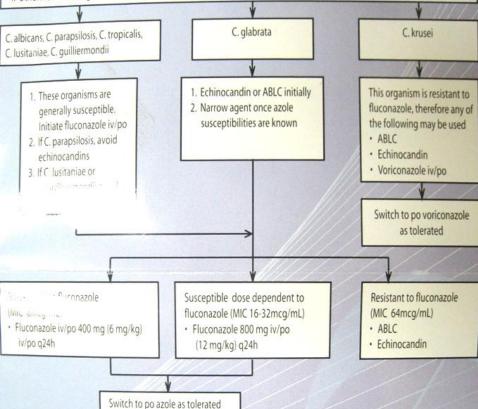


Figure 2: Species-Specific Therapy

- 1. If severe sepsis or persistantly neutropenic, use echinocandin or ABLC until these conditions resolve.
- 2. If patient on azole in last 30 days or bloodstream growing non-albicans species, review antifungal susceptibilities before switching to azole.
- 3. If history of colonization with C. lusitaniae or C. guilliermondii. Avoid amphotericin.
- 4. Otherwise follow algorithm below



SPECIES-SPECIFIC THERAPY

- 1. After initial cultures are drawn and empiric therapy has been started, all patients should be re-evaluated in 2-3 days when the fungal species has been identified and when anti-fungal susceptibilities are known
- 2. Figure 2 lists species-specific treatment options. Note that fluconazole exhibits variable activity against C. glabrata and is ineffective against C. krusei.
- 3. For uncomplicated, line-related candidemia, fluconazole 400-800 mg iv/po q24h is preferred. Decrease dose to 400 mg iv q24h if C. albicans or susceptible C. glabrata is identified. 4.
- If C. glabrata is identified from blood, caution is warranted since this organism exhibits three fluconazole susceptibility patterns. Interpretive breakpoints for each pattern are;
- Fluconazole susceptible: MIC 8 mcg/ml
- lool-

C.FL

b. Fluconazole susceptible, dose dependent Site 16-32 mcg/ml. High dose (800 mg q24h) fluconazole is effective for these

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Renal Dose Adjustment Poster

Antifunnale		Renal Impairment Patient			
All uli yais		Renal Impairment			
	All Severity	No Adjustment			
	Hepatic Impairment				
Cancidas	Mild (Child-Pugh Score < 7)	No Adjustment			
	Moderate	Loading Dose : 70 mg OD			
(Caspofungin acetate	(Child-Pugh Score 7-9)	Maintenance Dose: 35 mg OD			
	Severe	No Clinical Experience			
50 mg.70 mg)	(Child-Pugh Score >9)				
		Renal Impairment			
		Oral Form			
	Mild-Severe	No adjustment			
	IV Form				
	Moderate-Severe	Switch to Oral Form			
V-fend	Hemodialysis	No adjustment			
(Voriconazole)	(Within 4 hrs)				
		Hepatic Impairment			
	Mild-Moderate	Loading Dose : Same Normal Patient			
	(Child-Pugh A or B)	Maintenance Dose : Half of Normal Patient			
	Severe (Child-Pugh C)	No Study			

Antifungal DUE

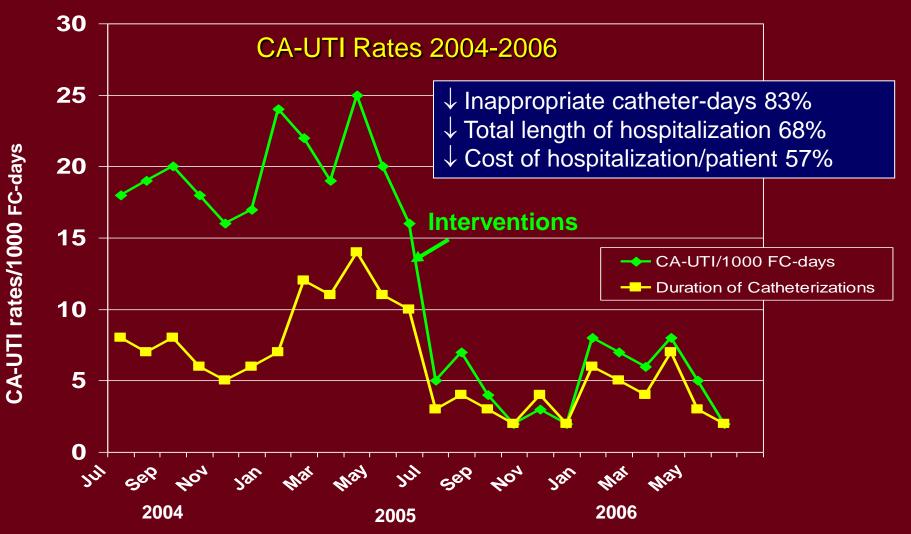
แบบบันทึกการสั่งใช้ยา Fluconazole/Caspofungin/Voriconazole

)		หแพ้อา	
เคย admit หรือเคยได้รับ Flucon	azole ในช่วง 3 เดือนก่อนหน้านี้ 🗌	YES NO		
 ข้อบ่งใช้หรือตำแหน่งติดเชื้อ 	อที่จะใช้อาต้านเชื้อรา			
Bone & joint infection	Meningi	tis or CNS infection		Skin & soft tissue infection
Febrile neutropenia	Candide	emia		Peritonitis
Intra-abdominal infection	Catheter	-associated infection		Other
\sim	 (ถ้ามีร้อมูลเพียงพอ กรุณากรอก 	ร้อมุลใบร้อ 4)		2 hr. on admission
🗌 Spec	cific therapy (กรุณากรอกร้อมูลในรัฐ โอกได้มากกว่า 1 ตัวเลือก)	ร้อมูลในร้อ 4) 14)		
 4. ตารางการธรรจ (สามารอเลี 	cific therapy (กรุณากรอกร้อมูลในรัง มือกได้มากกว่า 1 ตัวเมือก) Specimen	ร้อมูลในร้อ 4) 54) Organisr		
 4. สารางการอรวจ (สามารอเลื 1. ยิเองป 	cific therapy (กรุณากรอกร้อมูลในรัง ออกได้มากกว่า 1 ตัวเลือก) Specimen	ร้อมูลในร้อ 4) : 4) Organisr spergillus spp.		
	cific therapy (กรุณากรอกร้อมูลในร้อ ออกได้มากกว่า 1 ตัวเลือก) Specimen	ร้อมูลในร้อ 4) (4) Organism spengillus spp. anolida albican		
Spec Spec	cific therapy (กรุณากรอกชื่อมูลในชั่ง ออกได้มากกว่า 1 ตัวเลือก) Specimen	Seyaluše 4) (4) Organism spengillus spp. andida albican andida non-albican		
Spec	cific therapy (กรุณากรอกชื่อมูลในชั่ง ออกได้มากกว่า 1 ตัวเลือก) Specimen	ร้อมูลในร้อ 4) (4) Organism spengillus spp. anolida albican		
Spec Spec	cific therapy (กรุณากรอกร้อมูลในรัง ออกได้มากกว่า 1 ตัวเลือก) Specimen	Seyaluše 4) (4) Organism spengillus spp. andida albican andida non-albican		
Spec Urine Urine	cific therapy (กรุณากรอกร้อมูลในร้อ ออกได้มากกว่า 1 ตัวเรือก) Specimen	Seyaluže 4) (14) Organist spergilus spp. antida albican antida non-albican spotococcus spp.		
Spec Spec	cific therapy (กรุณากรอกชื่อมูลในชั่ง ออกได้มากกว่า 1 ตัวเรือก) Specimen	Provincia de la construction de la construction de la construcción de		
Spec Spec	cific therapy (กรุณากรอกร้อมูลในร้อ ออกได้มากกว่า 1 ตัวเรือก) Specimen	Provide albican Provide albican Protococcus app. Protococcus app. Protoccus app. Protococcus app. Protococus app. Protococus app. Protocus		

แบบบันทึกนี้ 1 ใบ ใช้สำหรับอา 1 รายการ ควรใช้ได้ไม่เกิน 7 วัน

อาทีไข้ แพทย์ผู้สั่งใช้อา		แพทย์เจ้าของไว้(Staff)	ะะเวลาที่ไร้(จำนวนวัน)
ความเห็นเภสัชกร เชื่องจาก			🔲 ส่งปรึกษาแพทย์โรคติดเชื้อ
เกล้รกะรู้รับใบ DUE ความเห็นแพทย์โรคติดเชื่อ เรื่องจอง	🔲 เห็นสมควรใช่ไร้	วันที่ได้รับใบ DUI 🔲 ไม่เห็นสมควรให้ไว้	E
		แพทยโรคลิลเชื้อ	

Urinary Tract Infection Intervention



Apisarnthanarak A, et al. Effectiveness of multifaceted hospital wide quality improvement program featuring intervention to remove IUC in a tertiary care center in Thailand. ICHE, 2007

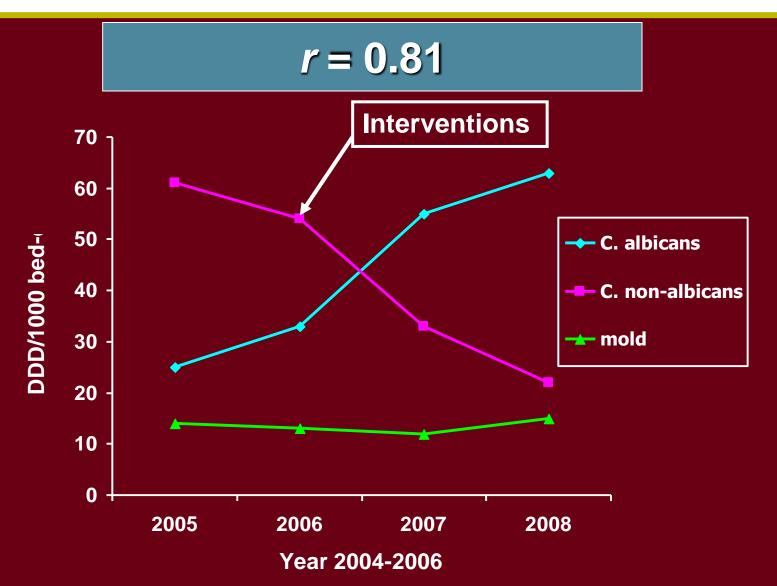
Table 4. Summary of antifungal prescribing practices for 1,106 patients by hospital service, drug and evidence of appropriate use during a three-years study period.

Variables	Pre-intervention period (n=694)	Post-intervention period (n=412)	<i>P</i> Value
Inappropriate antifungal use	493 (71)	98 (24)	<0.001
Department			
Medicine	153 (31)	28 (28)	0.42
Surgery	74 (15)	17 (18)	
Intensive care unit	217 (44)	38 (39)	
Others	49 (10)	15 (15)	
Antifungal agent			
Polyenes	128 (26)	23 (24)	0.64
Azoles	335 (68)	62 (63)	
Echinocandins	30 (6)	13 (13)	
Antifungal regimen			
Empiric therapy	30 (6)	7 (7)	0.86
Documented therapy	375 (76)	71 (73)	
Prophylaxis	74 (15)	16 (16)	
Other	15 (3)	4 (4)	
Inappropriate antifungal criteria			
Unnecessary	217 (44)	34 (35)	0.009
Lack of hepatic/renal dose adjustment	118 (24)	20 (20)	
Inappropriate dose or duration	118 (24)	20 (20)	
Inappropriate prophylaxis	89 (18)	16 (16)	
Others	104 (21)	21 (21)	

Table 2. Antifungal prescribing practices, sites of ingections, and Candida species detected during a three-year study period.

Characteristics	Pre-intervention	Post-intervention	P Value
Isolations positive for Candida spp.	796	799	NA
Site of specimen source			
Urine	430 (54)	439 (55)	0.91
Bloodstream	287 (36)	288 (36)	
Other ^a	79 (10)	72 (9)	
Yeast isolated			
Candida albicans	430 (54)	591 (74)	0.04
Candida glabrata	207 (26)	112 (14)	
Candida krusei	111 (14)	48 (6)	
Other ^b	48 (6)	48 (6)	
Antifungal prescription	694	412	NA
Site of antifungal prescription			
Urine	350 (55)	112 (27)	<0.001
Bloodstream	287 (41)	278 (67)	
Other ^a	57 (8)	22 (6)	
Yeast isolated			
Candida albicans	382 (55)	309 (75)	<0.001
Candida glabrata	173 (25)	41 (10)	
Candida krusei	83 (12)	25 (6)	
Other ^b	56 (8)	36 (9)	

Antifungal Consumption (iv and oral)



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Antimicrobial Stewardship: Can physicians help?

- Physicians play an important roles for successful antimicrobial stewardship program
- Potential role of physicians: input for antibiotic guidelines, consultation with infectious diseases, comply with policies
- Involvement of ID specialists in the program is more likely associated with successful outcomes
- Patterns of antibiotic use among different physicians will have an impact on how you select appropriate intervention
- Target physicians responsible for IAU in the group that likely comply with the program
- Additional studies to evaluate physicians behaviors that likely comply with antibiotic policy would help strengthen the antimicrobial stewardship program

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Thank you very much for your attention

"Kob-Koon-Krub" ขอบคุณครับ Can antimicrobial stewardship help reduce MDR-pathogens in hospitals where MDR-pathogens are highly prevalent?

Molecular epidemiology of 71 extended-spectrum betelactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* infections.

Bacteria	Molecular typing	No (%)
Escherichia coli	CTX-M-14	32 (63)
(n = 51)	CTX-M-15	7 (14)
	CTX-M-15, VEB-1	4 (8)
	CTX-M-55	8 (16)
Klebsiella pneumoniae	CTX-M-14	4 (20)
(n = 20)	CTX-M-14, SHV-12	7 (35)
	CTX-M-15	2 (10)
	CTX-M-15, SHV-12	2 (10)
	CTX-M-15, VEB-1	2 (10)
	CTX-M-55	1 (5)
	SHV-12, VEB-1	2 (10)

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Molecular Epidemiology, Risk Factors and Outcomes of HA-ESBL with Multiple ESBL-genes

Variable	Patient in entire cohort (N = 71)	HA-ESBL with multiple ESBL genes (n =17)	HA-ESBL with single ESBL gene (n =54)	P Value
Age (years): median (range)	58 (15-89)	56 (15-80)	58 (15-89)	0.83
Male, sex	36 (51)	9 (53)	27 (50)	0.43
Underlying disease				
Diabetes	23 (32)	8 (47)	16 (30)	0.18
Cerebrovascular accident	22 (31)	7 (41)	15 (22)	0.30
Other	15 (21)	5 (30)	10 (19)	0.34
Admission APACHE-II score:	17 (4-23)	18 (6-23)	17 (4-22)	0.71
median (range)				
Time at risk (days): median (range)	10 (0-27)	12 (6-27)	5 (0-14)	0.005
Source of infection				
Urinary tract	44 (62)	10 (59)	34 (63)	0.75
Pneumonia	12 (17)	4 (24)	8 (15)	0.40
Bloodstream infection	6 (8)	2 (12)	4 (7)	0.57
Other	9 (13)	2 (12)	7 (13)	0.89
Previous exposure to ≥3 class of antibiotics	45 (63)	15 (88)	30 (67)	0.01

Molecular Epidemiology, Risk Factors and Outcomes of HA-ESBL with Multiple ESBL-genes

Variable	Patient in entire cohort (N = 71)	HA-ESBL with multiple ESBL genes (n =17)	HA-ESBL with single ESBL gene (n =54)	P Value
Empirical antibiotic regimen				
Third/fourth generation cephalosporins	40 (56)	9 (53)	31 (57)	0.74
Quinolones	12 (17)	4 (24)	8 (15)	0.40
β -lactam / β -lactamase inhibitors	12 (17)	3 (18)	9 (17)	0.92
Other	8 (11)	2 (12)	6 (11)	0.48
Inadequate antibiotic treatment	60 (85)	17 (100)	43 (80)	0.04
Outcomes				
Failure of initial antimicrobial therapy	44 (62)	16 (94)	28 (52)	0.001
Crude mortality	22 (31)	5 (30)	17 (31)	0.87
Length of hospitalization: median (range)	24 (1-48)	25 (1-48)	24 (1-40)	0.71
Hospital costs accrued after	2,145	2,155	2,089	0.83
Infection (SUS):median (range)	(45-3,225)	(85-3,225)	(45-2,990)	