

MANAGEMENT OF HOSPITALISED PATIENTS WITH INFECTION AND IMPLICATIONS FOR ANTIMICROBIAL STEWARDSHIP

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Welcome to London



AIM

- Clinical Decision Making in managing hospitalised patients with potentially resistant infections
- Implications for hospital stewardship

Method?

Patient and organisational case
study with Q &A

PRESENTATION

1/2011

- 62 year old admitted to acute medical admissions unit with 3 day history of "flu like illness" followed by chills, vomiting, diarrhoea and increasing confusion. Incontinent of urine for 24 hours.
- Discharged from hospital 3 weeks earlier. Mainly tired & some sweats
- Type 2 DM, hypertension, peripheral vascular disease and PUD

Recent History

- 3rd hospitalisation in 12 months
- 4th course of antibiotic therapy in 12 months- 2UTI's & 2LRTI/s [FQ's and aminoglycoside and cephalosporins]
- Recent colonisation with MRSA
- Urinary catheter whilst in hospital recently
- 24 months ago removal of L renal calculus
- TB 30 years ago
- Smoker
- Co-amoxiclav started by GP
- Lisinopril
- Omeprazole
- Aspirin
- Glipizide
- Metformin
- Statin

EXAMINATION

- 39 C
- 28 breaths/minute
- 110 beats min
- Confused MSQ = 4/10
- Dehydrated
- Lower back tenderness
- Chest : spare basal crepitations
- Systolic murmur "all areas"
- Normal rectal examination

LABORATORY

- WCC 22.4
- PLT 98
- UREA 14.8
- Cr 196
- BG 23 mmol/l
- Po₂ 8.8
- Lactate 4.2
- CRP 345
- Glycosuria, ketonuria +, pyuria and nitrites

**What other laboratory
information would you like ?**

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RECENT MICROBIOLOGY

- MRSA colonisation
- *K.pneumoniae* in urine and blood 4 weeks earlier when in hospital
- *E.faecalis* in urine 6 months earlier
- Undertaken:
 - Blood and urine cultures

Q1: Differential diagnosis?

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Differential
Diagnosis?



How do you recognise a true Scotsman?

ANSWER 1

Severe Sepsis 2nd try to

- Urinary Tract Infection
 - +previous UTI
 - +diabetes mellitus
 - +recent catheterisation
 - +?BPH
 - +previous calculus
 - + nitrite positive

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ANSWER 1

- ENDOCARDITIS
 - -ve murmur not localised
 - -ve no previous valvular heart disease
 - + recent hospitalisation
 - + intravenous catheters recently
 - + MRSA colonisation

ANSWER 1

- LOWER
RESPIRATORY
TRACT INFECTION

- - ve cxr normal

- -ve minimal chest
findings

- + recent
hospitalisation

- +Smoker

- +MRSA colonisation

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**Q2: Is the infection hospital,
healthcare or community
acquired?**

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Community Acquired Infection

- An infection that was present at the time of infection to hospital or presented within 48 hours of admission

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Hospital acquired infection

- An infection that arose > 48 hours or more after admission to hospital which was not incubating at the time of admission

Healthcare Acquired Infection

- History of hospitalisation, surgery, dialysis or residence in LTCF within a year of contracting the infection, or the presence of a permanent indwelling catheter or percutaneous medical device e.g gastrostomy, tracheostomy or Foley catheter

**Q3: What is the likely
microbiological
epidemiology of the likely
syndromes ?**

Aetiology of clinically significant bacteraemia (bloodstream infection)

Organism	Hospital (HA) or community (CA) acquired	Incidence (% of total cases)
<i>Escherichia coli</i>	HA = CA	29
<i>Staphylococcus aureus</i>	HA > CA, 2:1	19
<i>Streptococcus pneumoniae</i>	CA > HA, 10:1	13
<i>Klebsiella</i> spp.	HA > CA, 3:1	7
<i>Pseudomonas aeruginosa</i>	HA > CA, 10:1	5
'Viridans' streptococci	CA > HA, 3:1	4
Coagulase-negative staphylococci	HA > CA, 20:1	4
Miscellaneous	Varies with organism	19

Likely source of clinically significant bacteraemia (bloodstream infection)

Organism	Common source
<i>Escherichia coli</i>	GU, biliary, peritoneal
<i>Staphylococcus aureus</i>	IV, skin, respiratory, B&J
<i>Streptococcus pneumoniae</i>	Respiratory (CNS)
<i>Klebsiella</i> spp.	GU, biliary, peritoneal
<i>Pseudomonas aeruginosa</i>	Respiratory, GU
Viridans' streptococci	Respiratory, cardiac, skin
Coagulase-negative staphylococci	IV, skin, prosthesis
<i>Enterococcus</i> spp.	GU, IV

Weinstein M, et al *CID* 1997; 24: 584-602

**What is your clinical
diagnosis?**

**What is your microbiological
diagnosis?**

**What empiric treatment would
you instigate ?**

ANSWER 3

- Site of infection
- Geographical location
 - Home v hospital (where in hospital) v healthcare facility etc
- Recent travel
- Outbreaks
- Co-morbidities
- Recent colonisation
- Recent antibiotics

EMPIRIC MANAGEMENT

- Probable health-care acquired UTI
- Worried about endocarditis also
- Started on Tazocin and Vancomycin

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CASE UPDATE

- BLOOD CULTURE
 - *K.pneumoniae* –ESBL
- CONTINUING MANAGEMENT
 - Switch to meropenem. Continue vancomycin just in case.

**What happened to our
patient?**

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OUTCOME

- Cure after meropenem but develops CDI diarrhoea! Needed treatment with oral vancomycin.
- Microbiology concerned as 4th patient in 2 weeks with ESBL bacteraemia from same ward
- **You are a member of the antimicrobial management team and have been asked by the infection prevention lead to support the investigation of an outbreak**
- **What do you want to do from a stewardship perspective ?**

WHAT DATA [INTELLIGENCE] DO YOU NEED ?



What data do you need

Ward based, hospital based, national data on epidemiology?

- Microbiology
 - Surveillance data- blood, urine
 - IC practice review : Hand hygiene, CVC-PVC, Catheters , etc
 - Environment
- Consumption data on high risk antibiotics – cephalosporins, flouoroquinolones, etc
- Compliance with local policy
- Compliance with antibiotic review
- Patient flow and movement data
- Clinical data from case notes - risk factors e.g antibiotics; invasive interventions etc

National ESBL epidemiology

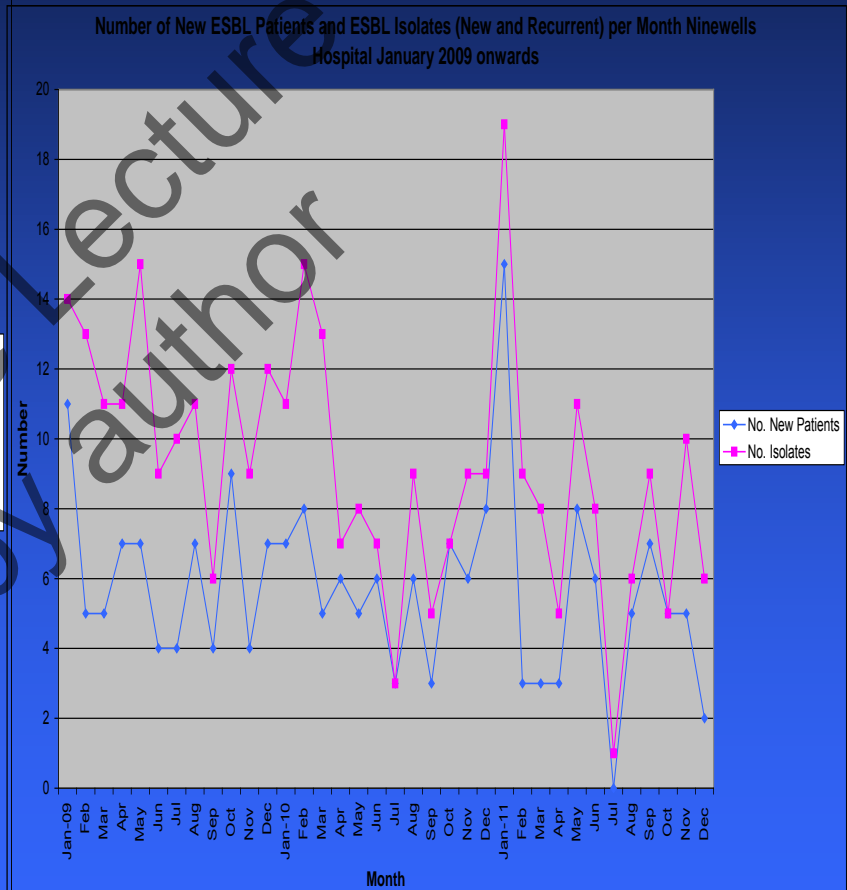
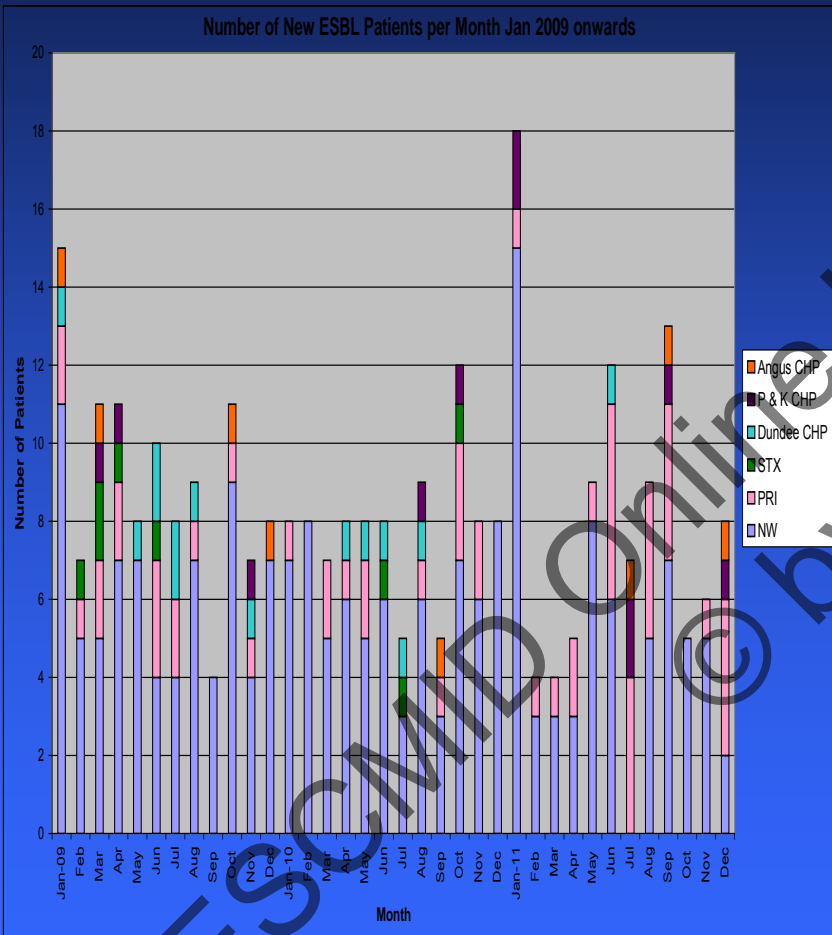
negative bacteraemias in 2008-2010; number of cases according to EARS-Net definition and percentage of

	Number of cases of bacteraemia reported (%ESBL)			
	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>P. aeruginosa</i>	<i>A. baumannii</i>
	2499 (7.2%)	512 (8.4%)	196 (0.0%)	53 (0.0%)
	3486 (7.5%)	672 (8.8%)	269 (0.4%)	64 (1.6%)
	3602 (7.6%)	715 (8.3%)	295 (0.3%)	36 (0.0%)

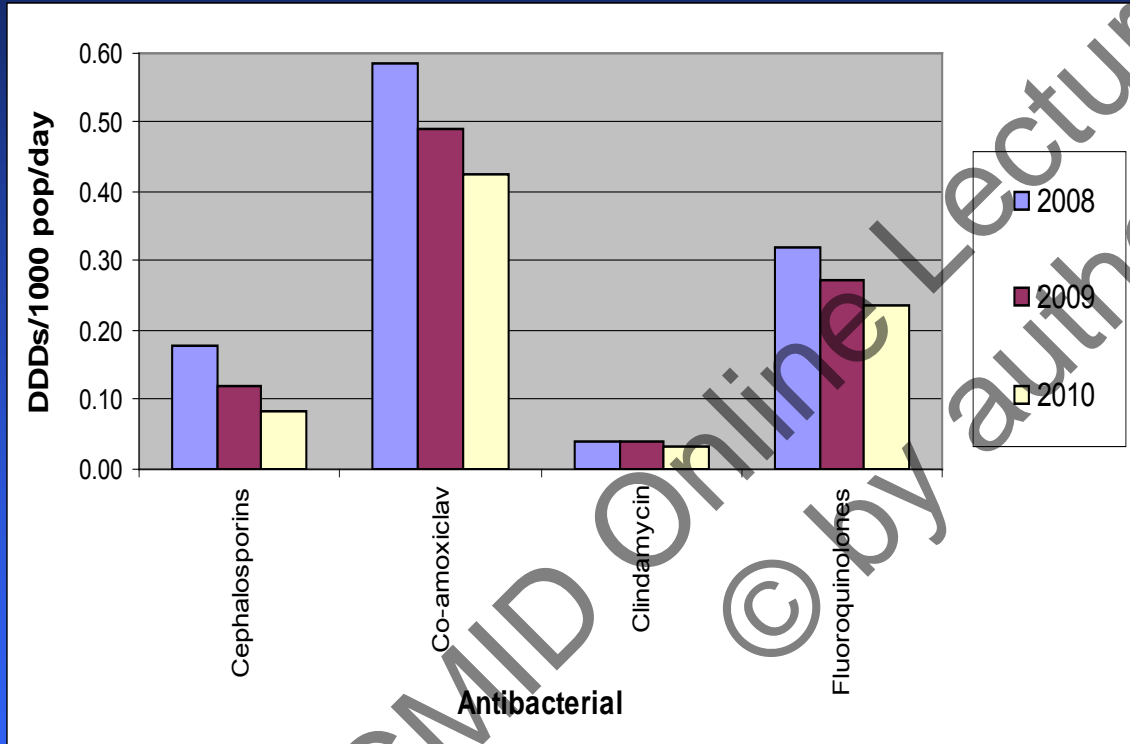
the resistance (and number of isolates tested) in *E. coli* and *K. pneumoniae* bacteraemias in 2008-2010

	% Resistance (number of isolates susceptibility tested)					
	<i>E. coli</i>			<i>K. pneumoniae</i>		
	2008	2009	2010	2008	2009	2010
	2499	3486	3602	512	672	715
	61.0 (464)	61.2 (975)	60.7 (858)	i.r.	i.r.	i.r.
	60.6 (1841)	62.8 (2725)	63.7 (2802)	i.r.	i.r.	i.r.
	2.0 (212)	5.7 (1077)	2.0 (2000)	5.5 (102)	1.5 (200)	5.5 (107)

LOCAL ESBL DATA



NHS Scotland: use of "high risk" C.diffgenic antibacterials in secondary care* DDD/1000/day 2008-2010.



4C antibacterials in 2010

30.7% lower than 2008

Cephalosporins ↓ 54%

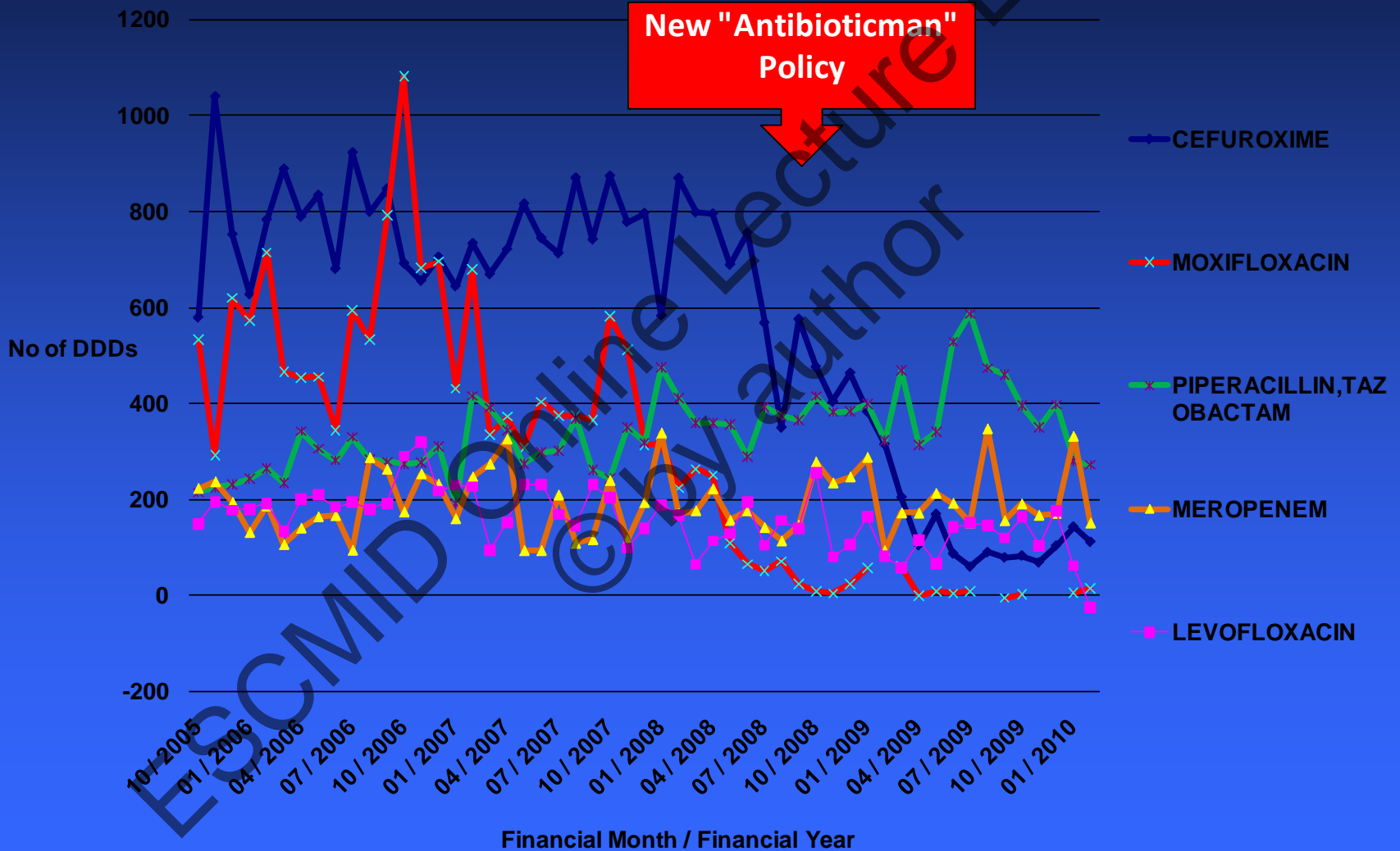
Co-amoxiclav ↓ 27%

Fluoroquinolones ↓ 26%

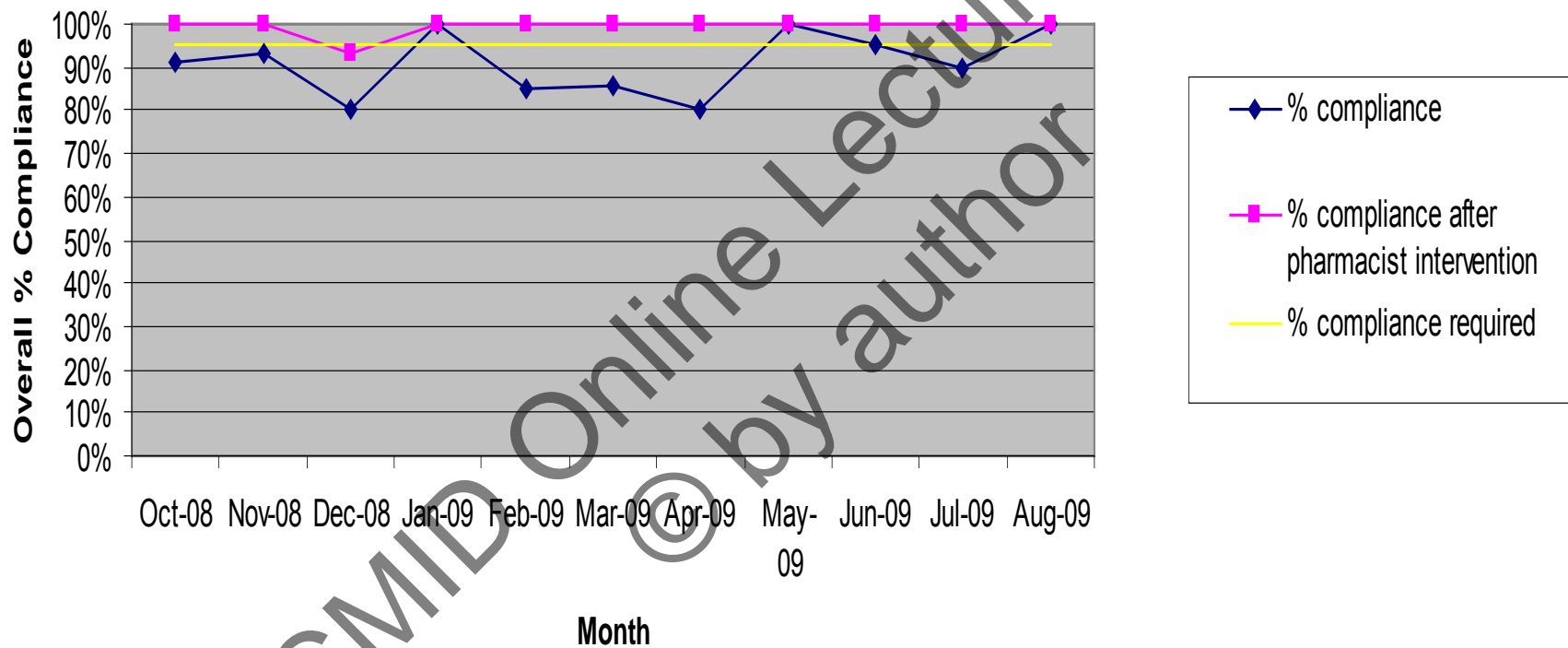
Clindamycin ↓ 13%

* 10 boards, covering 58% Scottish population

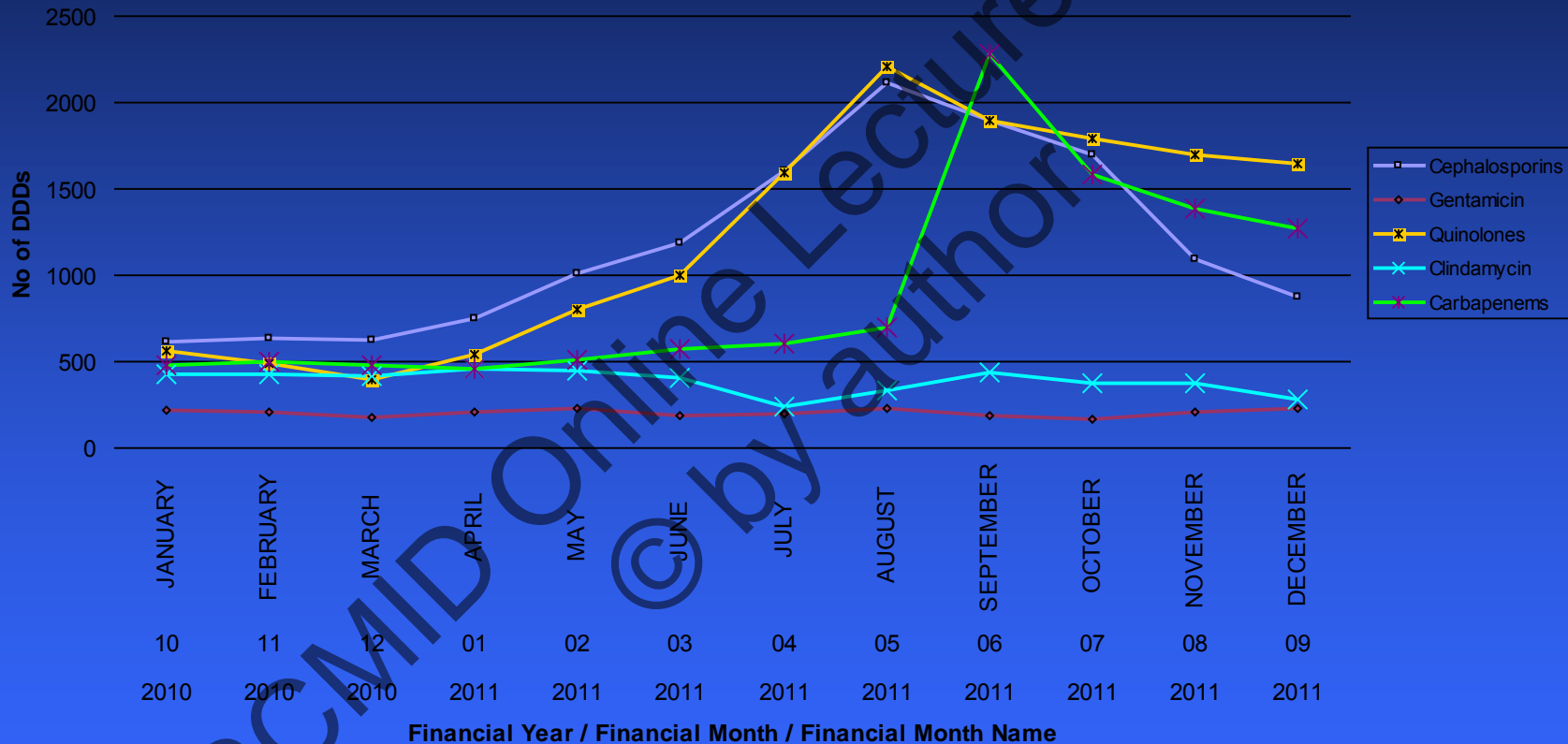
Hospital : Restricted Drugs



Compliance data from Ward 8



LOCAL UNIT BASED DATA



How do you interpret the data?



INVESTIGATION OF TRENDS

- ESBL NATIONALLY AND LOCALLY STABLE UNTIL THIS OUTBREAK
- EMPIRIC THERAPY COMPLIANCE SEEMS TO BE GOOD;
- LOOK AT DDD DATA- GOOD BUT 4-6 MONTHS NOTE RISE IN CEPHALOSPORIN AND QUINOLONE USE
- SHARE WITH PRESCRIBING TEAM
- LOOK FOR FACTORS THAT MAY HAVE INFLUENCED THIS PRESCRIBING
- CONSIDER CASE NOTE REVIEW
- SHARE WITH INFECTION CONTROL TEAM

Actions to deal with ESBL

- What would you do to support prescribing actions from this outbreak?

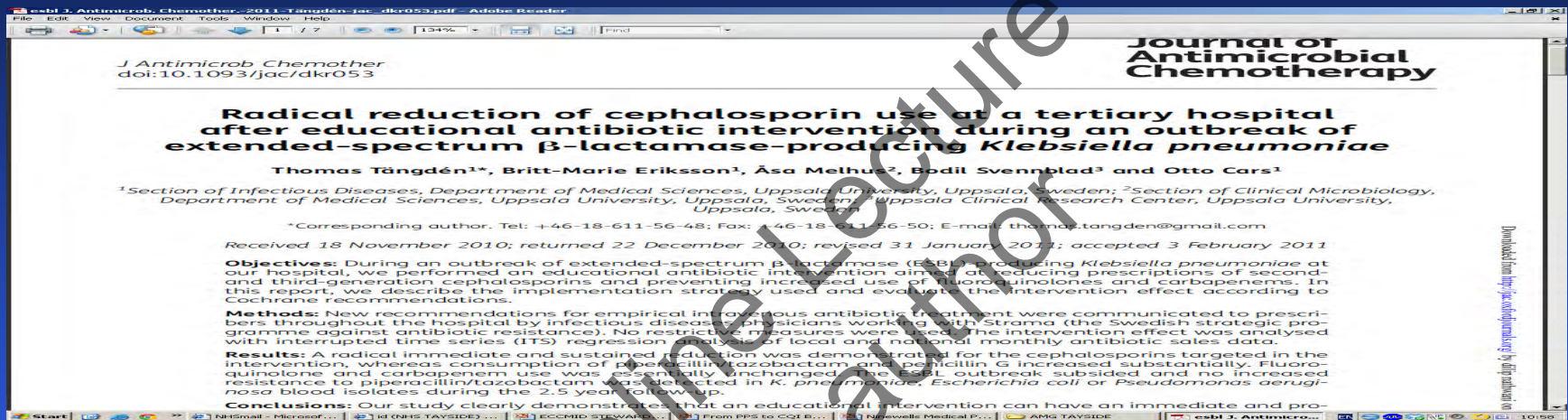


Actions to deal with ESBL

- Remove or restrict "high risk antibiotics-
 - Pre-authorisation approval, post-prescription review, promote carbapenem sparing agents- temocillin, tigecycline, fosfomycin, 3 day review /automatic stop order
- Educational or persuasive
 - Regular ID infection input with feedback, regular educational sessions, improvement measures [review bundles, monitoring compliance, case note review/root cause analysis, run charts]

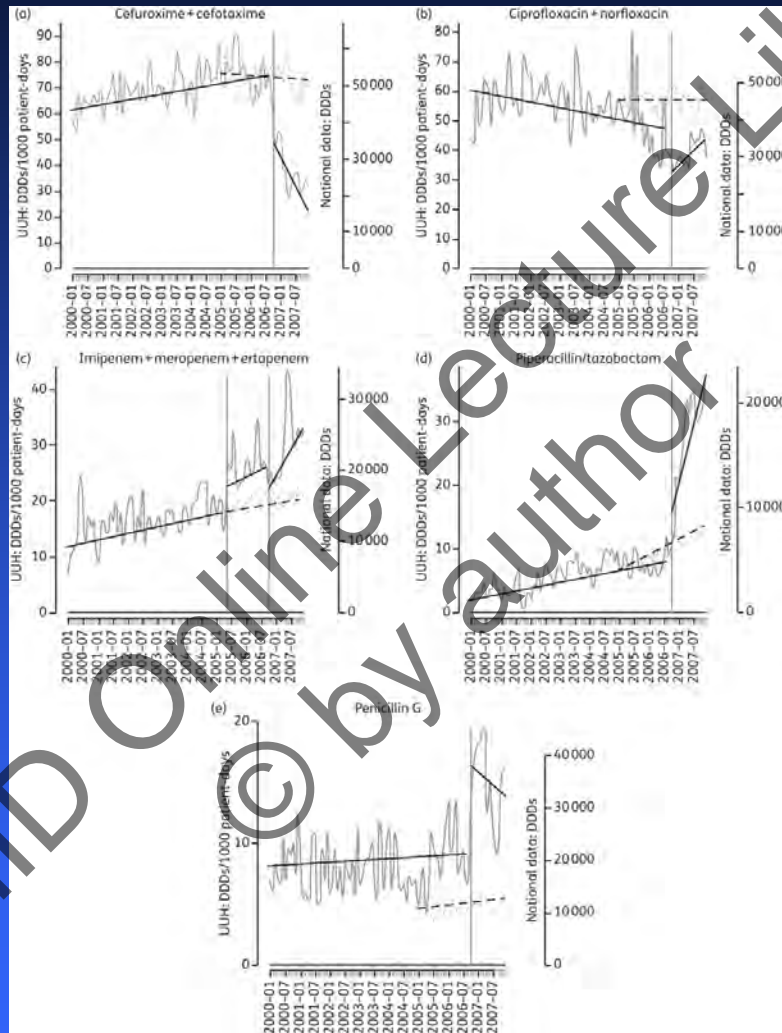
COMBINATION OF EDUCATIONAL AND RESTRICTIVE

SUSTAINED IMPACT OF EDUCATION IN AN ESBL OUBREAK



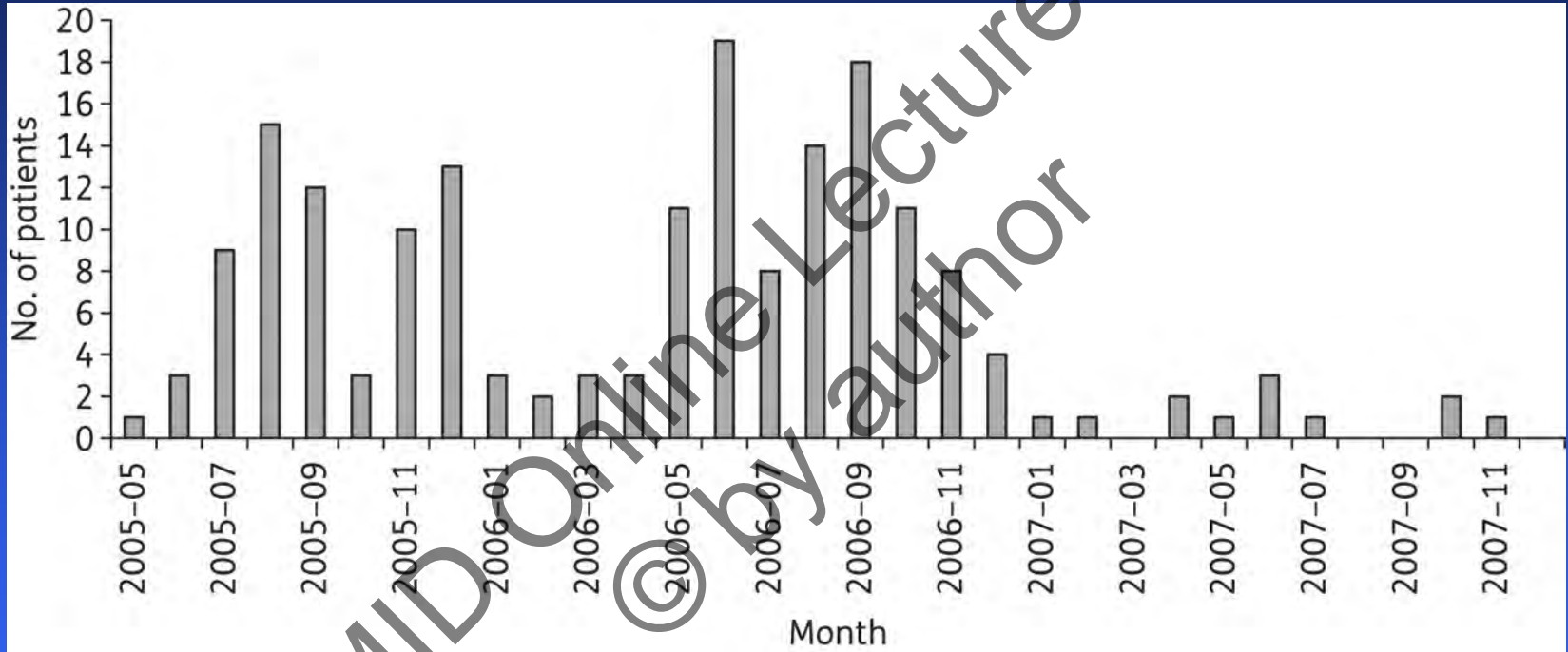
- New recommendations for empirical intravenous antibiotic treatment were communicated to prescribers throughout the hospital by infectious diseases physicians working with Strama (the Swedish strategic programme against antibiotic resistance). No restrictive measures were used. The intervention effect was analysed with interrupted time series (ITS) regression analysis of local and national monthly antibiotic sales data.

Segmented trend lines (grey) for monthly antibiotic use at UUH during January 2000–December 2007.



Tängdén T et al. *J. Antimicrob. Chemother.* 2011;66:1161-1167

Monthly numbers of patients infected by the ESBL-KP outbreak strain at UoH during May 2005–December 2007.



Tängdén T et al. *J. Antimicrob. Chemother.* 2011;66:1161-1167

THREE KEY MESSAGES

- ASSESMENT FOR RISK OF RESISTANCE CAN BE CLINICAL VALUE AND IMPORTANT TO GUIDE THERAPY IN UNWELL PATIENTS
- A RANGE OF STEWARDSHIP TOOLS CAN SUPPORT IMPROVEMENT THE QUALITY OF ANTIBIOTIC PRESCRIBING- THEY PROBABLY NEED TO BE MULTI-FACETED
- CONSUMPTION AND SURVEILLANCE DATA, DATA, DATA..... INTEGRATED, LOCAL AND NATIONAL



THANK YOU
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& Immunity

Interactive case study

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Once upon a time...

- you were having dinner with a urologist. He is on call. During the soup, he has to answer his telephone. It is about a 72 year-old male who underwent prostatic surgery that morning, and who now having a high fever (and chills) and signs of sepsis.
- He tells the resident to start the patient the usual antibiotic treatment with Superpenem®. After the phone call (you have finished your soup), he asks whether you would agree with the treatment.



While he is eating his snails,

- you say that you wonder whether Superpenem® being a last resort drug should be used for such a simple urosepsis.
- You say that you even wonder whether Superpenem® has the optimal spectrum towards enterococci and Pseudomonas species



Waiting for the lobster,

- he tells you that formerly they would treat all these patients with ciprofloxacin, but more and more patients appeared to have 'these nasty cipro-resistant bugs'. They even encountered a few deaths...
- What would you like to know?



While he pours the Chablis,

- you ask him whether these patients have been exposed to cipro before they are being operated...
- He responds that that is indeed the case. You propose that you will come by next morning to study the charts of these patients that suffered from cipro-resistant microorganism...
- How would you proceed?



The next morning...

- you start looking at the chart of the patient who was given Superpenem the night before.
- While you are reading the chart, the urological resident receives a call that another patient on the ward has a positive blood culture with a *Candida* spp.



'Not again!'

- the resident exclaims...
He tells this is the 3d patient with a Candida in the blood in the last 4 months.
- What would you like to know?

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Indeed,

- all three cases were on a prolonged course of Superpenem
- When you ask what he means by prolonged he tells you these were very complicated cases that received more than 3 weeks of Superpenem®

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Nosocomial fungaemia: a 2-year prospective study.

- 68 consecutive patients with fungaemia were studied during a period of 2 years, 81% had two or more positive blood cultures. Gastrointestinal tract (28%) and haematological diseases (17%) were the most common underlying conditions. The majority of cases had received vancomycin and/or imipenem (87%) and a central venous catheter (78%). *Candida albicans* (50%) and *Candida parapsilosis* (17%) were the most frequent isolates.

Costa et al. J Hosp Inf 2000

Enrique Maraví-Poma
Joan Gener
Francisco Alvarez-Lerma
Pedro Olaechea
Armando Blanco
J. Enrique Domínguez-Muñoz
Spanish Group for the Study
of Septic Complications
in Severe Acute Pancreatitis

**Early antibiotic treatment (prophylaxis)
of septic complications in severe acute
necrotizing pancreatitis: a prospective,
randomized, multicenter study comparing
two regimens with imipenem-cilastatin**

Infection by *Candida albicans*
occurred in 7% of patient treated for
14 days and 22% of patients treated
longer



While you are still there,

- a sales representative of MaxiPharm comes in and offers the resident a trip to a meeting on 'Superpenem in serious infection' which will take place in Ibiza in May...
- ' By the way doc, if you are also interested, I could see what I can do for you...'
- What is your response?



You return to the chart,

- and find out that the patient presented with lower urinary tract complaints and had a high PSA, in which case it is hard to tell whether it is chronic prostatitis or cancer. For that reason he was treated with ciprofloxacin 500 mg bid for 6 weeks about 2 months ago. The PSA did not fall.



Some weeks later,

- The patient underwent prostatic biopsies, for which he received 3 days of ciprofloxacin prophylaxis...
- A small prostatic cancer was found, and that was the reason to operate him yesterday, again under ciprofloxacin prophylaxis...
- What would you do next?



You decide to

- review the charts of the last 10 patients that were treated with Superpenem
- You ask the Medical Microbiology lab for the positive blood cultures over the past 6 months
- You ask the pharmacy for the deliveries of Superpenem over the past 6 months



In the meantime...

- Escherichia coli Bloodstream Infection After Transrectal Ultrasound-Guided Prostate Biopsy: Implications of Fluoroquinolone-Resistant Sequence Type 131 as a Major Causative Pathogen. Williamson DA, et al Clin Infect Dis. 2012 Mar 14. [Epub]
- Bacteriuria and antibiotic resistance in catheter urine specimens following radical prostatectomy. Banks JA, et al Urol Oncol. 2012 Jan 25. [Epub]
- Prevalence of Antibiotic Resistance in Fecal Flora of Patients Undergoing Transrectal Ultrasound-Guided Prostate Biopsy in Thailand. Siriboon S, et al. Urol Int. 2012 Jan 21. [Epub]
- Ciprofloxacin-resistant infection after transrectal ultrasonography-guided prostate biopsy: should we reassess our practice? Ismail M, et al BJU Int. 2011 108(3):305-6.
- Fluoroquinolone-resistant acute prostatitis requiring hospitalization after transrectal prostate biopsy: effect of previous fluoroquinolone use as prophylaxis or long-term treatment. Ekici S et al Int Urol Nephrol. 2012;44(1):19-27.



You find

- all 10 patients were males previously exposed to ciprofloxacin for weeks (and often repeatedly).
- The blood cultures reveal mostly ciprofloxacin-resistant E coli (12 x in 9 patients); many of these were susceptible to 2nd gen cephalosporins. There was one culture with Klebsiella (cipro R) and indeed 3 patients with positive cultures for Candida spp.



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and

- a high expenditure on Superpenem®

So what are you going to do now?

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Discuss with the urologists:

- Rethink longterm ciprofloxacin in patients with high PSA
- Rethink cipro prophylaxis for prostatic biopsies and surgery
- Rethink empiric treatment for postoperative urosepsis
- Regard Superpenem as a last resort drug