AMS Programs :
one size doesn't fit all

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Antimicrobial Stewardship

- **The Main Objective is:**

  To optimize the clinical outcome by minimizing the undesirable effects of using an antibiotic, such as:

1. Selection of other resistant bacteria
2. Emergence of resistance during treatment
3. Toxicity

- **The secondary objective is:**

  To reduce costs without compromising health care quality

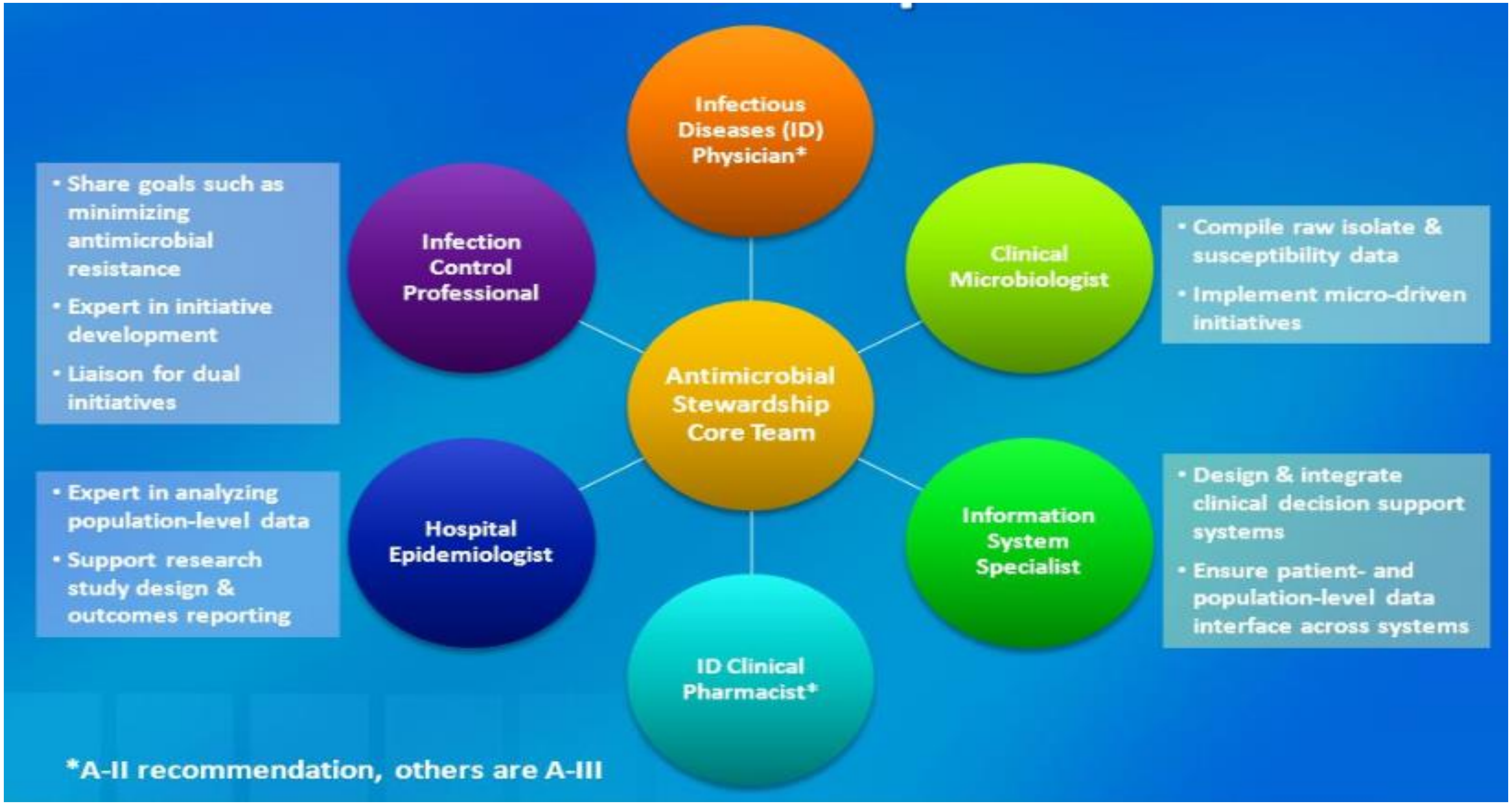
- It must be: **The combination of an Infection Control program + Antimicrobial Stewardship**

Dellit TH et al. *Clin Infect Dis.* 2007;44:159-177

Antimicrobial Stewardship GOAL

- Coordinated interventions to improve the use of antimicrobials by promoting selection of the
  - **Optimal drug**
  - **Optimal dose**
  - **Optimal route of administration**
  - **Optimal duration of therapy**
- **At a minimum the team should have a** microbiologist and pharmacist and /or physician, preferably with formal infectious diseases training
- Includes **education, development of guidelines**, pre-prescription approval or post-prescription review with feedback and other strategies according to each hospital.

Antimicrobial Stewardship Core Team



Dellit TH, et al. Clin Infect Dis 2007; 44: 159-177

Seven Core Elements for Successful Hospital AMS program

- **Leadership commitment: Dedicating necessary** human, financial, and information technology resources.
- **Accountability:** Appointing a **single leader responsible** for program outcomes. Experience with successful programs has shown that a physician leader is effective.
- **Drug expertise:** Appointing a **single pharmacist leader** responsible for working to improve antibiotic use.
- **Action: Implementing at least one recommended action**, i.e., "antibiotic time out" after 48 hours or only 5-7 days of treatment for IAI and UTI.
- **Tracking: Monitoring antibiotic prescribing and resistance patterns**.
- **Reporting: Regular reporting** information on antibiotic use and resistance to doctors, nurses and relevant staff members.
- **Education: Educating** clinicians about resistance and optimal prescribing.

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. May 25 , 2016

Seven Core Elements for Successful Hospital AMS program

And if I have to pick ONE of the seven core elements

- **Leadership will be my number ONE !!!**
- **Because a leader maybe able to:**

- **Work with other experts in order that the AMS program IS IMPLEMENTED !!!**
- **Do the tracking :** monitoring antibiotic prescribing and resistance patterns.
- **Give the feedback** to the MDs about their antibiotic prescription (on site : optimal antibiotic that should be given according to the hospital Antibiotic Guideline including dose, time of duration, de-escalation).
- **Report** every month about the AMS program and antibiotic use.
- **Educate** about resistance and optimal prescribing.

- **However in order to be successful you have to:**

1. **Select an achievable goal (few antibiotics to follow, the most critical patients)**
2. **Share results to hospital staff and MDs in order that they see (+) results**

So how do we start

Creating Antibiotic Guidelines

1. Prophylactic
2. Therapeutic
3. Measuring adherence
4. Measuring other outcomes
   (economic impact)

Creating Antibiotic Guidelines (pros)

Prophylactic

- Generalized evidence of its benefit
- **Few discussions about antibiotic choices and administration**
- Is a safe issue for patients so becomes a priority to implement.
- Impact can be measured in SSI

Therapeutic

- **Changing the Paradigm of How we Steward: Syndrome-Specific Stewardship :**
- Easier to provide education and gather meaningful evidence for a specific infectious indication
- Focused message facilitates provider learning
- Less confounding when measuring outcomes
- Easier to collect relevant data

Pick the most common infections in your hospitals to start with (examples)

- **Empiric antibiotic selection in the ICU**
- **Urinary tract infections**
- Community-acquired pneumonia
- Healthcare-associated pneumonia
- Catheter-related infections
- Intra-abdominal infections
- Skin and soft tissue infections
- Central nervous system infections
- Surgical site infections
- ICU empiric therapy
- *C. difficile* infections

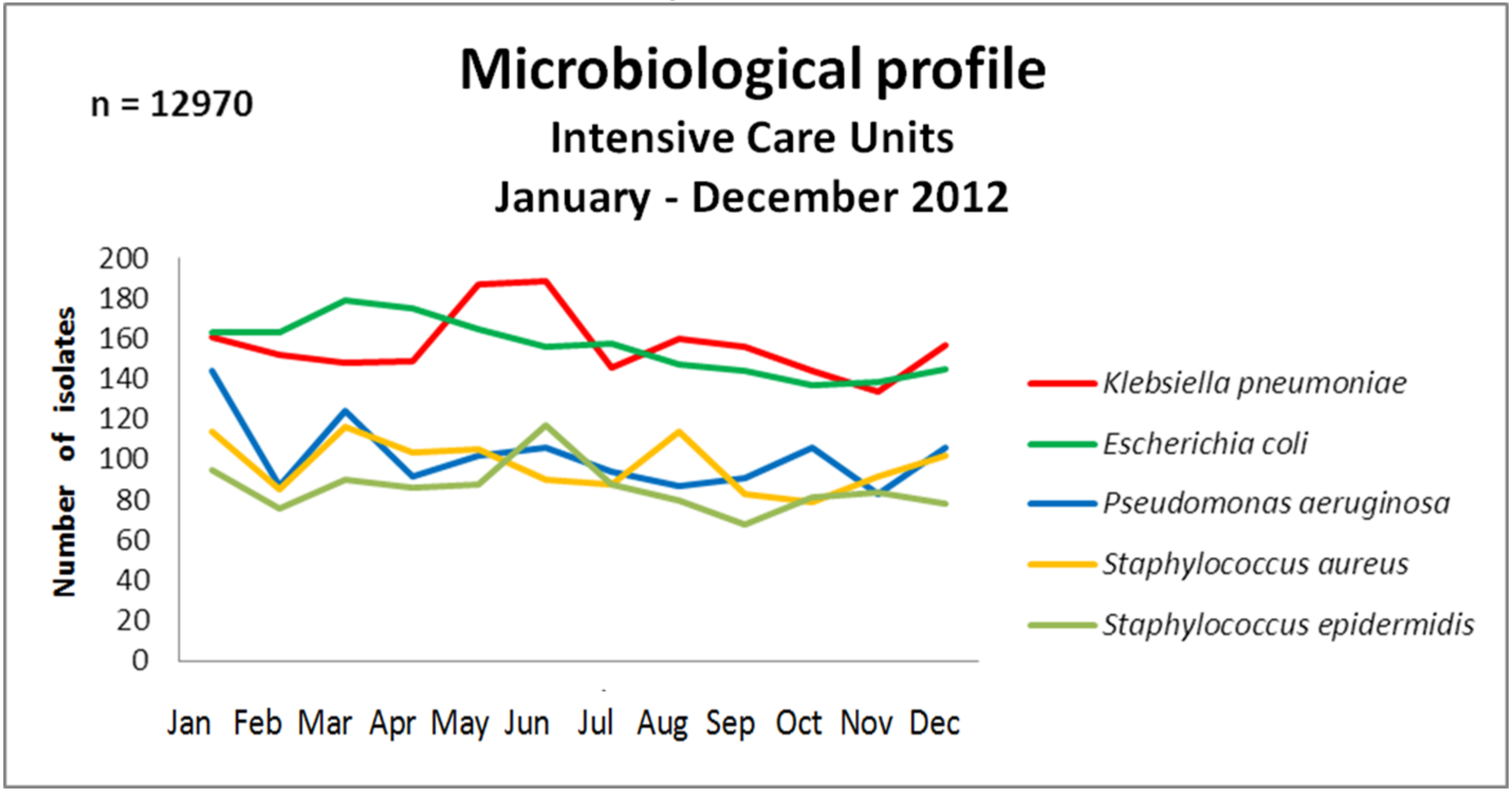
Creating Therapeutic Antibiotic Guidelines step by step

1. Chose one infection : ex: **ICU initial antibiotic selection and Complicated UTI**
2. Look for the epidemiology (R/S) in the last 6 months or 1 year (strong ¨n¨) of most common bacteria in the ICU and causing UTI (ex : in the ER).
3. Develop Antibiotic Guidelines including : Local epidemiology, Mechanisms of resistance, Selective pressure, Stratification of the infection with risk factors for MDR bacteria and De-escalation.
4. Do a consensus with the MDs/ specialists and go through the Antibiotic Guideline explaining why the antibiotics were selected
5. Listen to their concepts , ask about difficulties to implement the Guideline, about fears and/or doubts . **NEGOTIATE.**
6. Once the consensus is agreed, it should be implemented and followed (measure adherence and other easy outcomes) giving FEEDBACK to the specialists.

ICU initial antibiotic selection

Local Epidemiology in ICUs

Frequency trends of the first five microorganisms in ICUs in January-December 2012



Antibiotic Resistance Analysis in Gram-Negative Bacteria from ICUs

Antibiotic resistance percentages from the most frequently isolated Gram (-) bacteria in ICUs 2013

Microorganism	n	Cefotaxime %	Ceftazidime %	Ceftriaxone %	Aztreonam %	Cefepime %	Piperacillin / Tazobactam %	Ciprofloxacin %	Amikacin %	Tigecycline %	Ertapenem %	Imipenem %	Meropenem %	Doripenem %
K. pneumoniae	1883	35 (255/728)	33 (581/1765)	34 (582/1727)	34 (563/1638)	34 (623/1847)	30 (546/1814)	20 (373/1859)	7 (128/1861)	3 (37/1174)	12 (196/1614)	7 (127/1739)	8 (148/1832)	19 (21/110)
E. coli	1871	15 (132/858)	15 (271/1762)	16 (266/1623)	18 (251/1405)	17 (304/1839)	13 (201/1608)	31 (563/1837)	1 (23/1837)	0 (4/1002)	1 (10/1376)	0 (6/1606)	0 (6/1704)	0 (0/97)
P. aeruginosa	1222		24 (292/1193)		31 (288/920)	23 (273/1196)	23 (231/996)	25 (307/1207)	20 (236/1208)			31 (359/1156)	26 (308/1193)	22 (20/92)
E. cloacae	418	29 (52/179)	25 (96/380)	31 (119/382)	32 (117/370)	12 (50/407)	31 (124/395)	16 (65/409)	10 (41/408)		8 (29/361)	5 (18/392)	3 (14/408)	11 (2/18)
A. baumannii	373		55 (174/318)		83 (283/342)	63 (233/371)	71 (239/336)	65 (244/373)	22 (72/324)			64 (223/349)	60 (172/289)	100 (30/30)

Which is the Best Empirical Antibiotic Therapy in ICUs?

- We have to cover *P. aeruginosa* because is one of the most important pathogen.
- We could use any of the anti-pseudomonal antibiotics because of their high susceptibility : 70-80 % **but**

➢ if we start patients on cefepime or piperacillin/tazobactam, what do we do with ESBLs : **34 %**

➢ and/or KPCs : **12 %** given their broad-spectrum hydrolysis?

- We would probably use a carbapenem (high dose and prolonged infusion), and depending on patient severity:

➢ we add polymyxin and/or fosfomycin (septic shock)

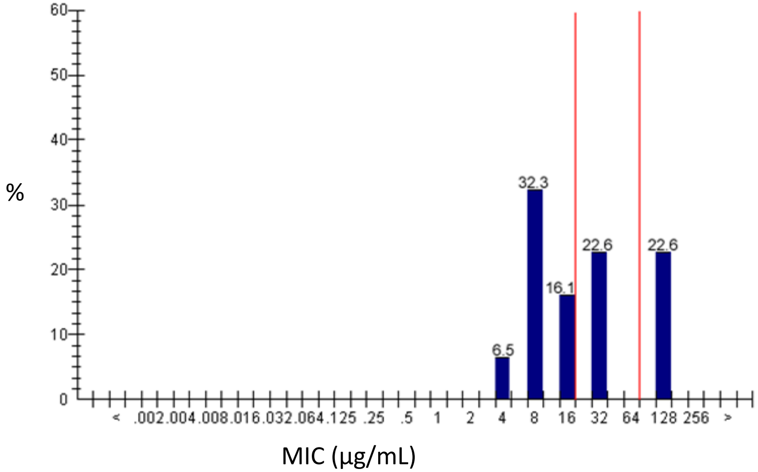
➢ or tigecyclin

Which is the Best Empirical Antibiotic Therapy in ICUs?

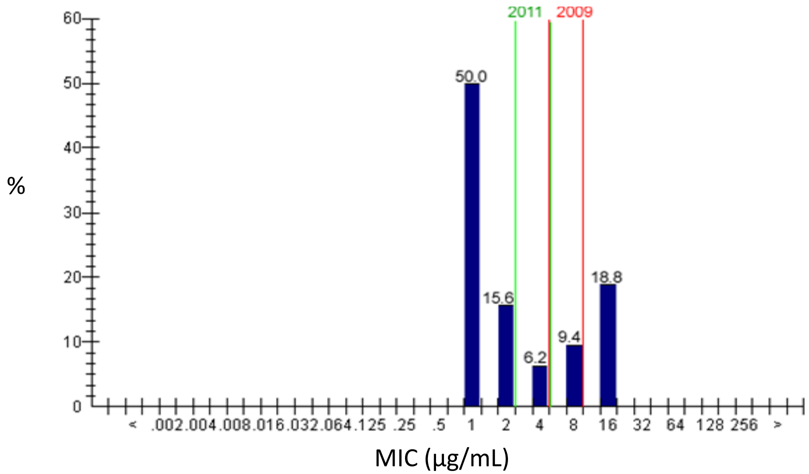
- Do we add an aminoglycoside to our therapy? Always? Sometimes?
- When do we de-escalate
- Should we always cover MRSA using vancomycin? Or only for sepsis of unknown origin in patients with central venous catheters?
- **Therefore, the antibiotic choice in ICUs should be based on additional data and local epidemiology.**

MIC Analysis for selecting the Anti-pseudomonal Antibiotic

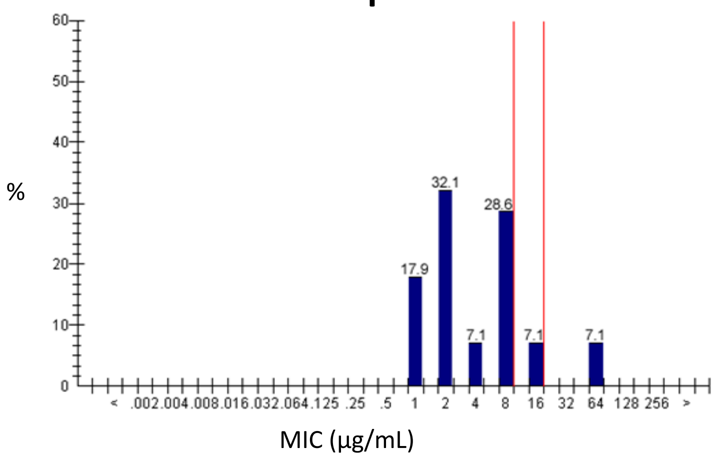
Piperacillin/Tazobactam



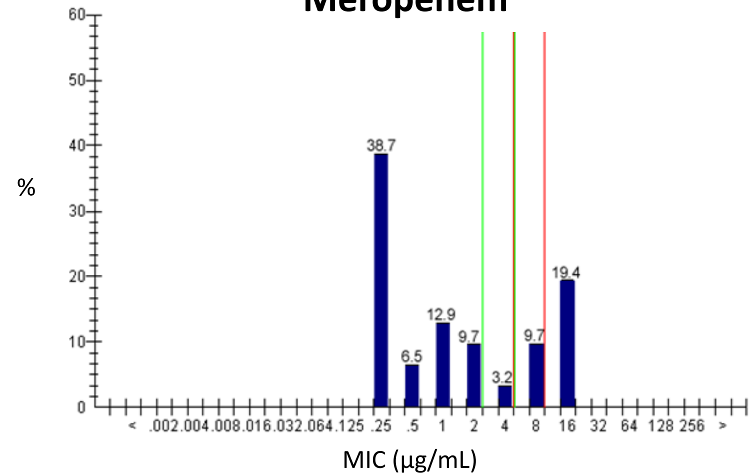
Imipenem



Cefepime



Meropenem



Example of Adding or Not amikacin and meropenem for *P. aeruginosa*

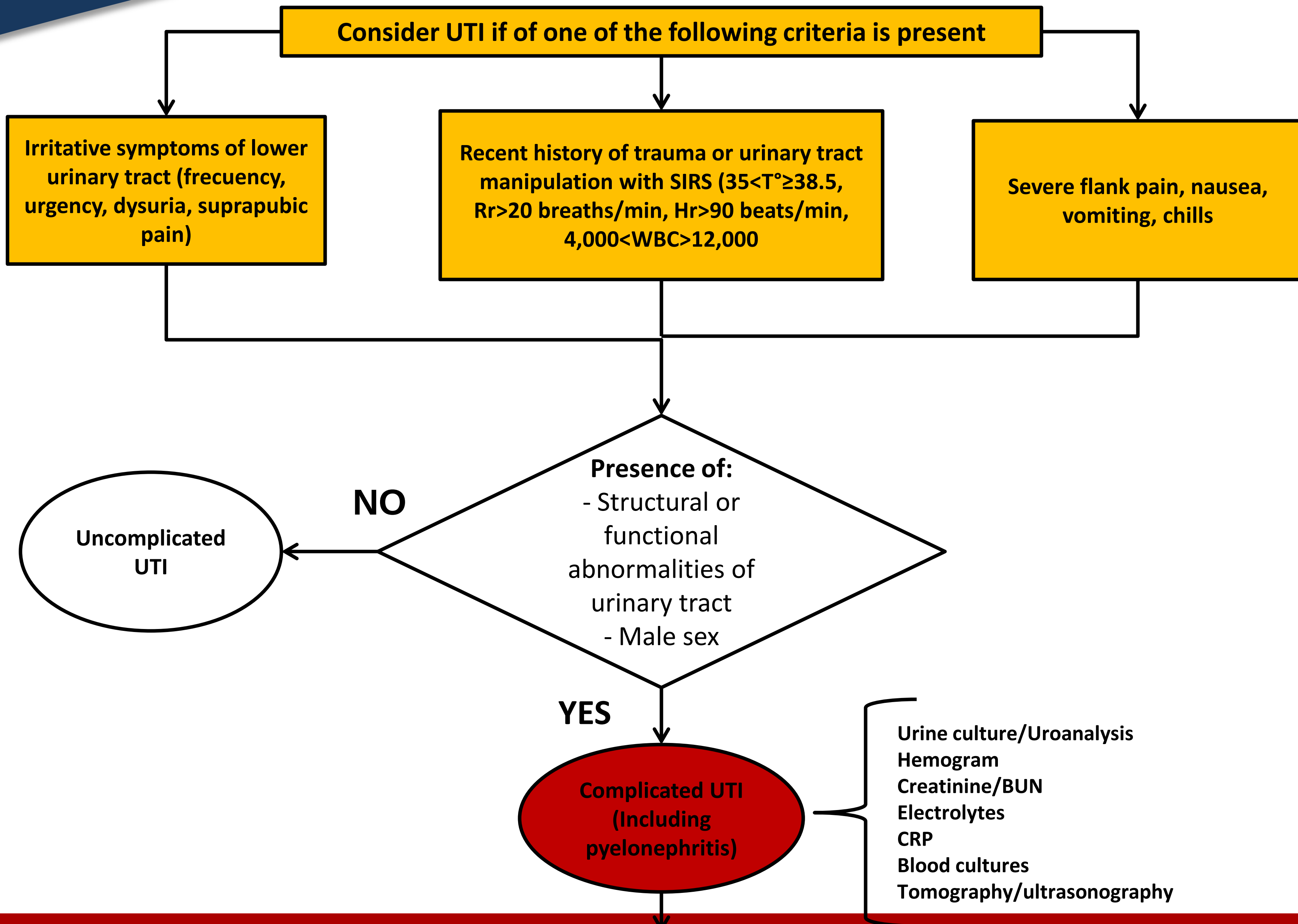
AMK (MIC)	MEM S	MEM I	MEM R
R			17.2%
I			3.4%
S	69%		10.3%

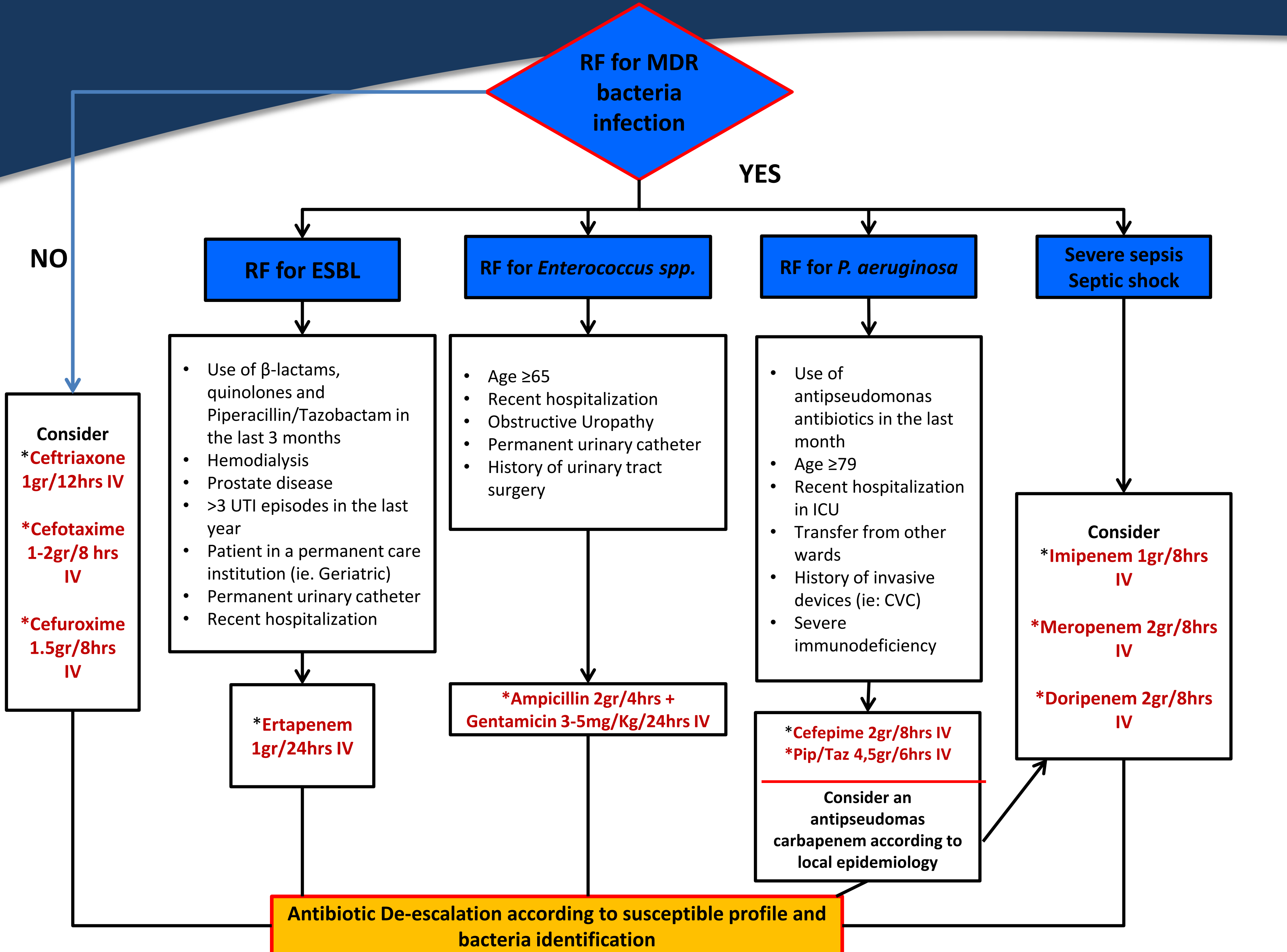
MEM (MIC)

"According to the susceptibility tests performed, 69% of *P. aeruginosa* are susceptible to both amikacin and meropenem. Combination therapy with meropenem and amikacin would increase chance of appropriate therapy in 10.3%."

Complicated Urinary Tract Infections

Flowchart for cUTI in the Emergency Department

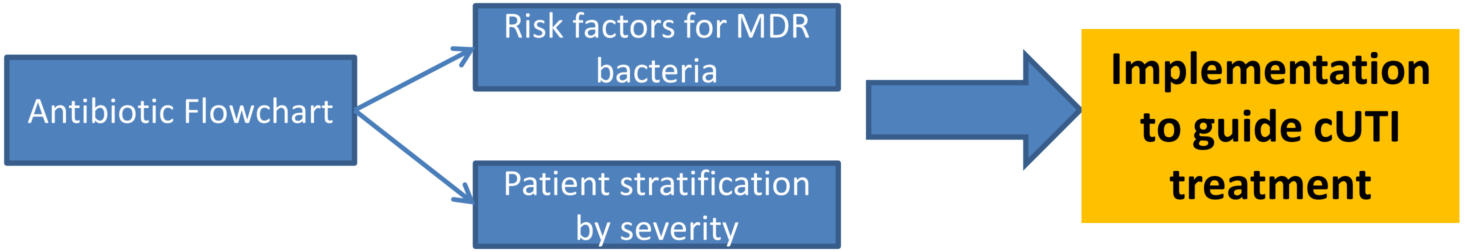


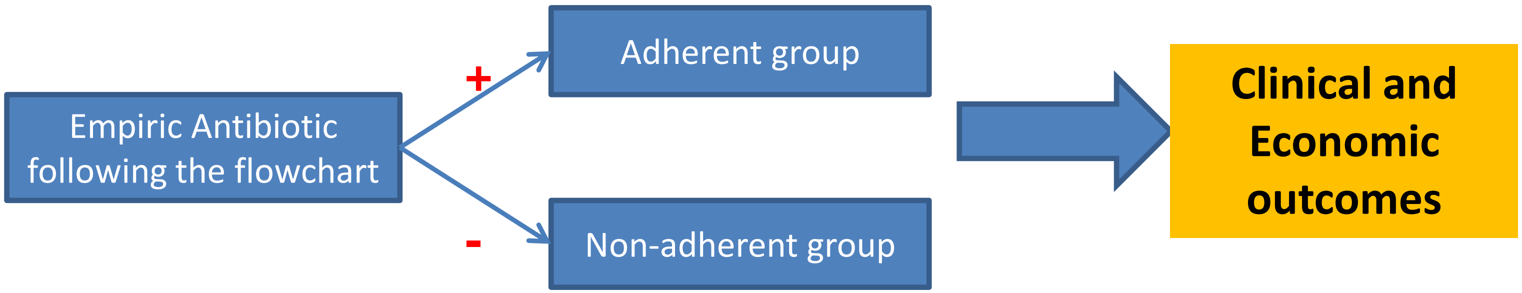

RF for MDR bacteria infection
NO
YES
RF for ESBL
RF for Enterococcus spp.
RF for P. aeruginosa
Severe sepsis Septic shock
Consider *Ceftriaxone 1gr/12hrs IV
*Cefotaxime 1-2gr/8 hrs IV
*Cefuroxime 1.5gr/8hrs IV
• Use of β-lactams, quinolones and Piperacillin/Tazobactam in the last 3 months
• Hemodialysis
• Prostate disease
• >3 UTI episodes in the last year
• Patient in a permanent care institution (ie. Geriatric)
• Permanent urinary catheter
• Recent hospitalization
*Ertapenem 1gr/24hrs IV
• Age ≥65
• Recent hospitalization
• Obstructive Uropathy
• Permanent urinary catheter
• History of urinary tract surgery
*Ampicillin 2gr/4hrs + Gentamicin 3-5mg/Kg/24hrs IV
• Use of antipseudomonas antibiotics in the last month
• Age ≥79
• Recent hospitalization in ICU
• Transfer from other wards
• History of invasive devices (ie: CVC)
• Severe immunodeficiency
*Cefepime 2gr/8hrs IV
*Pip/Taz 4,5gr/6hrs IV
Consider an antipseudomas carbapenem according to local epidemiology
Consider
*Imipenem 1gr/8hrs IV
*Meropenem 2gr/8hrs IV
*Doripenem 2gr/8hrs IV
Antibiotic De-escalation according to susceptible profile and bacteria identification

Clinical and Economic Impact of the Implementation of an Antibiotic Flowchart for Complicated Urinary Tract Infection (cUTI) in a Tertiary Care Hospital in Colombia

METHODS

Adult patients admitted to the emergency department
One tertiary care hospital in Colombia
Preliminary data: January-April, 2016
Treatment with empiric antibiotics for cUTI
Patients were followed until completion of their antibiotic regimen





Total: 50 patients

E. coli: 36 cases (72%)

VARIABLE	ADHERENT GROUP (n=39, 78%)	NON-ADHERENT GROUP (n=11, 22%)	*p*
Age (years)	66 (+/-21)	66 (+/-21)	0.78
Sex Male (n=21, 42%) Female (n=29, 58%)	17 22	4 7	0.67
Complications	5 (13%)	5 (45%)	**0.01**
48 h - Symptom´s improvement	31 (79%)	1 (9%)	0.48
End of treatment Symptom´s resolution	31 (79%)	4 (36%)	**0.006**
Mortality	1 (2.5%)	2 (18%)	0.06
Clinical tests – Mean cost per patient	$113 USD	$282 USD	**0.01**

ID WEEK. October 2016. New Orleans. Session: 134. Antibiotic Stewardship: General Acute Care Implementation and Outcomes. Friday, October 28, 2016: 12:30 PM

COST-EFFECTIVENESS OF ANTIMICROBIAL STEWARDSHIP PROGRAMS IN FIVE HIGH COMPLEXITY HOSPITALS IN COLOMBIA

A real example in limited resource settings

Institution A: Private teaching-hospital, 400 beds

Institution C: Public teaching-hospital, 900 beds

Institution E: Private not-teaching hospital, 250 beds

Cristhian Hernández-Gómez, Christian Pallares, Kevin Escandón-Vargas, Sergio Reyes, Soraya Salcedo, Lorena Matta, and Maria Virginia Villegas. Economic Impact of an Antimicrobial Stewardship Program Implementation in Three High-Complexity Hospitals in Colombia. Open Forum Infect Dis. 2016; 3 (suppl 1): doi:10.1093/ofid/ofw172.726.

METHODS AND RESULTS

- **Specific Objective #1:** To describe the structure, resources and costs of implementing the AMS programs.

The modified Antimicrobial Stewardship index (ICATB1) was applied

Criteria	Institution A	Institution B	Institution C	Institution D	Institution E
Level of dedication of the AMS team	3	2	4	1	2
Existence of an antimicrobial prescribing referent	2,5	4	4	3,2	4
Digital Clinical Records	1	1	1	1	1
Computerized antimicrobial prescription	2	2	2	1,8	2
Training for those who prescribe antibiotics	1	1	1	0,8	1
Antimicrobial Guidelines in use	2	2	2	1,8	1,4
List of available antibiotics for prescription	0,25	0,25	0,25	0	0
List of restricted antibiotics	1	0,25	0,25	0	0
Time control for the time of administration of the antibiotic during therapy	0,25	0,25	0,25	0,15	0,25
Follow up of antibiotics consumption	2,5	2,5	2,5	2	2,5
Evaluation of antibiotics prescription	2,5	2,5	2,5	2	2,5
Global average score (Biannual measurement during two years)	**18**	**17,75**	**19,75**	**13,75**	**16,65**

Percentile 70= 13.5 Percentile 90 = 15.78

METHODS AND RESULTS

- **Specific Objective #1:** To describe the structure, resources and costs of implementing the AMS programs.

Monthly used resources during the execution of the AMS Program

Resource	Institution A	Institution B	Institution C	Institution D	Institution E
Number of hours assigned for an ID per month	20	20	20	20	40
Number of hours assigned for an epidemiologist per month	0	128	4	192	0
Number of hours assigned for a general MD per month	0	192	264	0	40
Number of hours assigned for nursing per month	120	58	72	64	0,4
Number of hours assigned for a pharmacist per month	8	58	9	5	40
Number of hours assigned for a microbiologist per month	12	29	6	5	0
Number of hours assigned for an administrative assistant per month	20	58	0	20	0
Number of hours used of the working stations (table-chair) per month	96	192	143	192	40
Number of hours of use of the computers per month	96	192	141	192	40
Software licence for operation and statistics per month	Excel	SPSS V.20	SPSS V.20	Excel	Excel
Number of hours of use of the software per month	96	96	96	64	20

METHODS AND RESULTS

- **Specific Objective #1:** To describe the structure, resources and costs of implementing the AMS programs.

Average monthly costs associate with the execution of the AMS Program

Resource	Institution A	Institution B	Institution C	Institution D	Institution E
Number of hours assigned for an ID per month	USD 1.571	USD 1.571	USD 1.571	USD 1.565	USD 1.414
Number of hours assigned for an epidemiologist per month	USD 0	USD 1.571	USD 258	USD 1.739	USD 1.571
Number of hours assigned for a general MD per month	USD 0	USD 1.583	USD 3.166	USD 0	USD 0
Number of hours assigned for nursing per month	USD 730	USD 353	USD 389	USD 431	USD 2
Number of hours assigned for a pharmacist per month	USD 49	USD 353	USD 46	USD 34	USD 243
Number of hours assigned for a microbiologist per month	USD 73	USD 353	USD 31	USD 34	USD 0
Number of hours assigned for an administrative assistant per month	USD 31	USD 91	USD 0	USD 135	USD 0
Number of hours of the working stations used (table-chair) per month	USD 5	USD 10	USD 7	USD 2	USD 2
Number of hours of use of the computers per month	USD 7	USD 13	USD 10	USD 3	USD 3
Software licence for operation and statistics per month	USD 3	USD 9	USD 9	USD 2	USD 2
Number of hours of use of the software per month	USD 2.469	USD 5.907	USD 5.488	USD 3.945	USD 3.237

METHODS AND RESULTS

- **Specific Objective #2:** To compare the tendencies of antibiotic use during the period before and after the implementation of the AMS programs.

Tendency in DDD (per 1000 days-bed) of antimicrobials consumed

DDD	Institution A	Institution B	Institution C	Institution D	Institution E
Sem -4 pre	36,73	59,51	351,34	0,00	107,54
Sem -3 pre	43,04	63,86	353,42	0,00	148,88
Sem -2 pre	50,01	70,79	351,94	69,18	136,30
Sem -1 pre	56,96	79,11	374,66	69,13	134,30
Sem 1 pos	53,24	74,18	303,85	92,16	105,25
Sem 2 pos	48,29	71,71	183,62	56,70	100,06
Sem 3 pos	51,86	62,27	129,72	42,15	120,93
Sem 4 pos	45,60	44,87	112,00	63,81	116,31
Sem 5 pos	56,78	52,00	105,69	65,15	137,10

Sumatory of the monthly average during a periods of six months (ICU and hospitalization) of the DDD of CRO, FEP, MEM, TZP, ETP and VAN, four periods of six months previously and five periods of six months after implementing AMS (pos).

Rate of increase	**35% →7%**	**7% → - 49%**	**20% → - 16%**

METHODS AND RESULTS

- **Specific Objective #2:** To compare the tendencies of antibiotic use during the execution period of the programs and during the period before and after the implementation of the AMS programs.

Costs of monthly consumption of antibiotics in UCI and wards per institution

ATB cost	Institution A	Institution B	Institution C	Institution D	Institution E
Sem -4 pre	$ 17.525	$ 61.606	$ 69.609	$ -	$ 23.589
Sem -3 pre	$ 24.205	$ 66.396	$ 80.622	$ -	$ 25.107
Sem -2 pre	$ 86.210	$ 215.780	$ 92.537	$ 6.745	$ 51.089
Sem -1 pre	$ 110.851	$ 244.294	$ 102.121	$ 6.760	$ 53.195
Sem 1 pos	$ 42.074	$ 82.845	$ 93.116	$ 9.932	$ 28.034
Sem 2 pos	$ 42.847	$ 85.462	$ 70.864	$ 8.363	$ 25.425
Sem 3 pos	$ 44.929	$ 82.420	$ 59.425	$ 5.999	$ 27.109
Sem 4 pos	$ 39.547	$ 71.260	$ 54.214	$ 7.404	$ 30.255

Efectiveness	Institution A	Institution B	Institution C	Institution D	Institution E
Global reduction	29%	45%	20%	-135%	28%

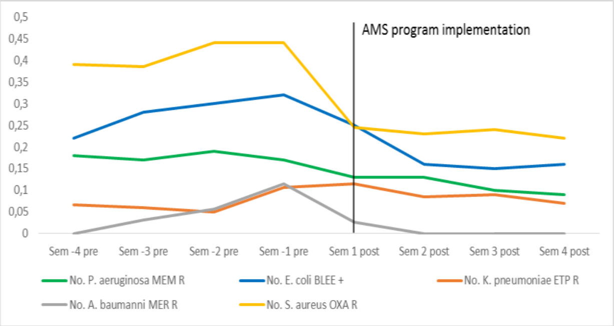
Sumatory of the monthly average during periods of six months (ICU and wards) of the consumption costs in grams of CRO, FEP, MEM, TZP, ETP and VAN, four periods of six months previously and four periods of six months after AMS (pos).

METHODS AND RESULTS

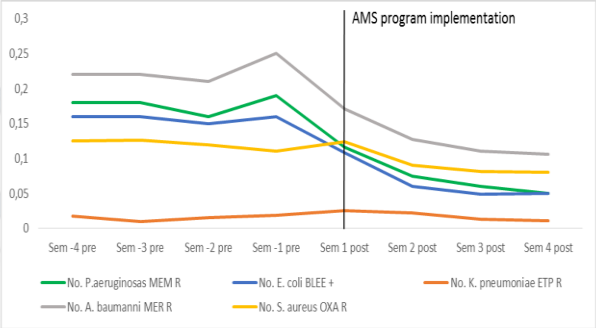
- **Specific Objective #3:** To compare the incidence of MDR microorganisms during the period before and after the implementation of the AMS programs.

Average of monthly MDR incidence in Intensive Care Units and wards (MDR per 1000 discharges)

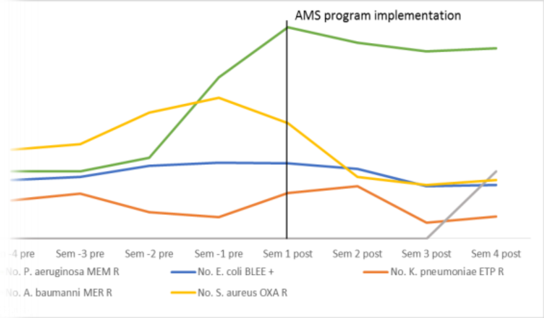
Institution A



Institution C



Institution E



MICROORGANISM	PRE	POST	Decrease %	p Value
# P. aeruginosa MEM R	1,95	1,80	-7,53	0,248
# E. coli BLEE +	1,63	0,92	-43,77	0,020
# K. pneumoniae ETP R	0,39	0,85	116,62	0,021
# A. baumanni MER R	2,37	0,20	-91,79	0,021
# S. aureus OXA R	3,02	1,09	-64,07	0,021

Conclusions

- **Results :**
- The study was implemented in medical-surgical intensive care units (ICUs) and general wards.
- All hospitals had empirical antibiotic guidelines according to the local epidemiology and staff monitored prospectively the AMS program.
- In every hospital there was a different way of following the AMS program.
- The antibiotic consumption in the ICUs decreased post-implementation
- The cost of AMS program implementation was in average $4,305 USD per month.
- There was a clear decrease of MDR bacteria

- **In summary :**
- Our study outcomes confirm the importance and economic impact of implementing an AMS program in healthcare institutions.
- When instituting an AMS program, a hospital should tailor its choice of strategies to its needs and available resources. Similar programs in several other institutions in the country are underway.

Cristhian Hernández-Gómez, Christian Pallares, Kevin Escandón-Vargas, Sergio Reyes, Soraya Salcedo, Lorena Matta, and Maria Virginia Villegas. Economic Impact of an Antimicrobial Stewardship Program Implementation in Three High-Complexity Hospitals in Colombia. Open Forum Infect Dis. 2016; 3 (suppl 1): doi:10.1093/ofid/ofw172.726.

Summary

- Antimicrobial stewardship (AMS) programs have demonstrated to reduce morbidity and mortality, bacterial resistance, collateral damage, adverse effects and costs.
- Any AMS should start with Antibiotic Guidelines and their implementation.
- Consider syndrome-specific approach
  - Consider selecting one syndrome at a time (give it plenty of time)
  - Emphasize that the goal is improving the outcomes of patients
  - Encourage team approach (make them think this is their idea)
- Demonstrate benefit to the individual patient and the hospital
- Streamline rather than complicate practice
- Transparent evaluation (and reevaluation) of successes and failures with all team members
- **Passion, faith and leadership !!!!**

Thank you!