¿Cómo Erradicamos gérmenes multiresistentes?

"Utopía o realidad"

Dra. María Gabriela Abalos
Médica Pediatra- Infectóloga Infantil
Comité Nacional de Infectología de la SAP
Asesora en Vacunas – Pfizer Argentina

¿Como Controlamos gérmenes multiresistentes?

" UNA OBLIGACION"

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MDR
multi-drug resistance
Resistencia simultanea a 3 o mas clases de agentes antimicrobianos
XDR
extreme-drug resistance
Resistencia a todas las drogas excepto a 2 o menos categorias de atbs
(i.e. colistin, tigecycline S)
PDR
Resistencia a todos los agentes antimicrobianos aprobados
Definiciones para S. aureus, Enterococcus, Enterobacteriaceae, P. aeruginosa & Acinetobacter. Una bacteria es considerada R si resulta R o I por EUCAST o CLSI
Definiciones propuestas
Grupo de Expertos ECDC & CDC, 2010

Patógenos ESKAPE

E	***Enterococcus faecium***
S	***Staphylococcus aureus***
K	***Klebsiella pneumoniae***
A	***Acinetobacter baumannii***
P	***Pseudomonas aeruginosa***
E	***Enterobacter* spp.**

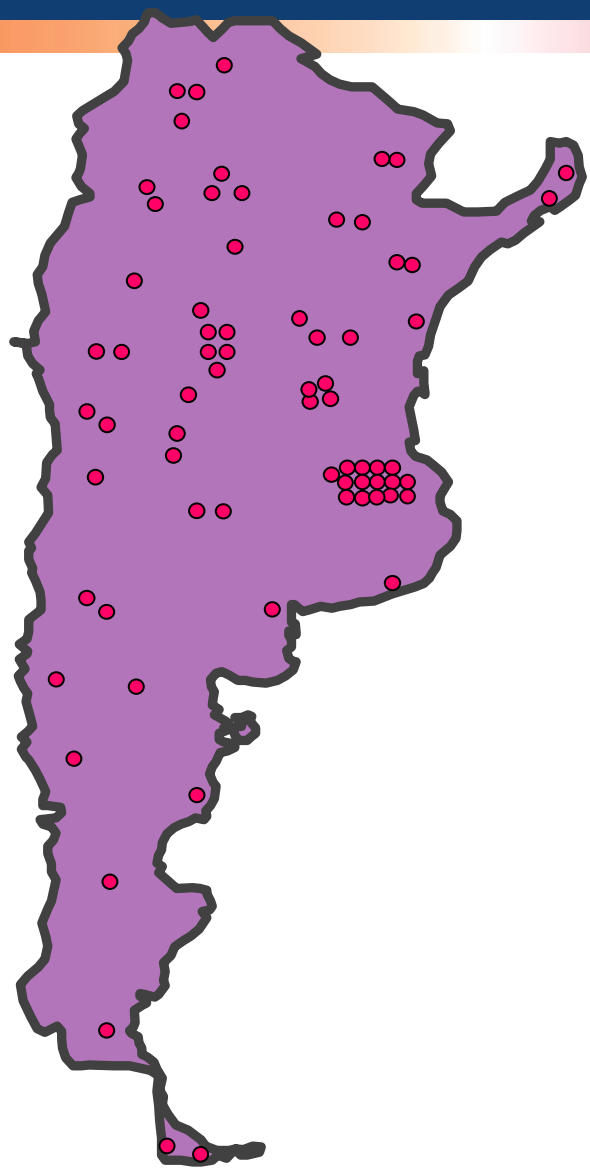
Rice LB. J Infect Dis. 2008;197:1079-1081.

Rice LB. Infect Control Hosp Epidemiol. 2010;31(Suppl 1):S7-S10.

¿COMO VIGILAMOS?

Red de Laboratorios – WHONET - Argentina 2009 – 71 LABS.

- JUJUY
- SALTA
- CATAMARCA
- TUCUMAN
- LA RIOJA
- SAN LUIS
- MENDOZA
- SAN JUAN
- CORDOBA
- LA PAMPA
- NEUQUEN
- CHUBUT
- RIO NEGRO
- SANTA CRUZ



- MISIONES
- CHACO
- CORRIENTES
- SANTA FE
- ENTRE RIOS
- FORMOSA
- CAPITAL FEDERAL
- PROV DE BUENOS AIRES
- MISIONES
- CHACO
- SANTIAGO DEL ESTERO
- TIERRA DEL FUEGO

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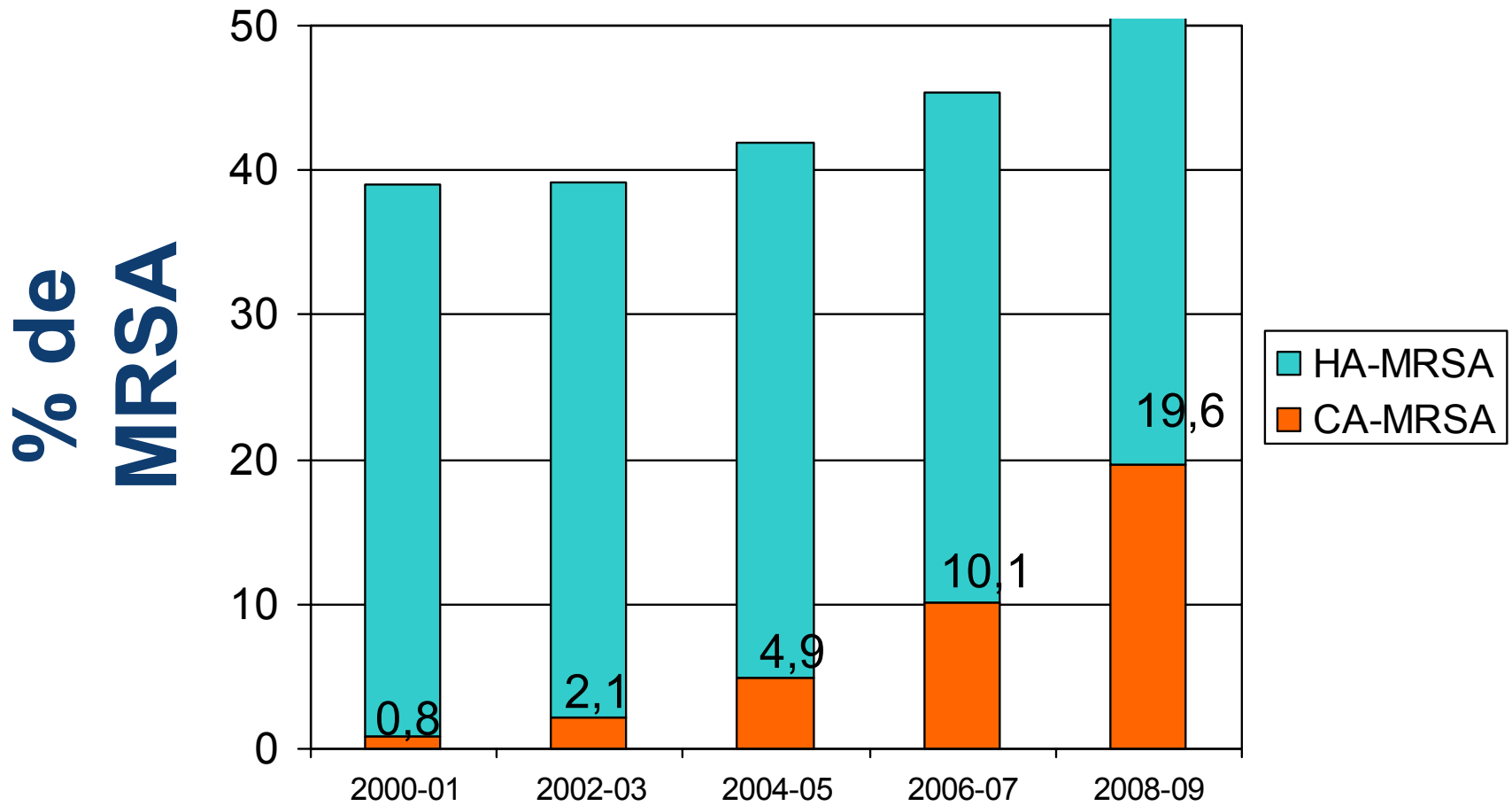
HA-MRSA versus CA-MRSA



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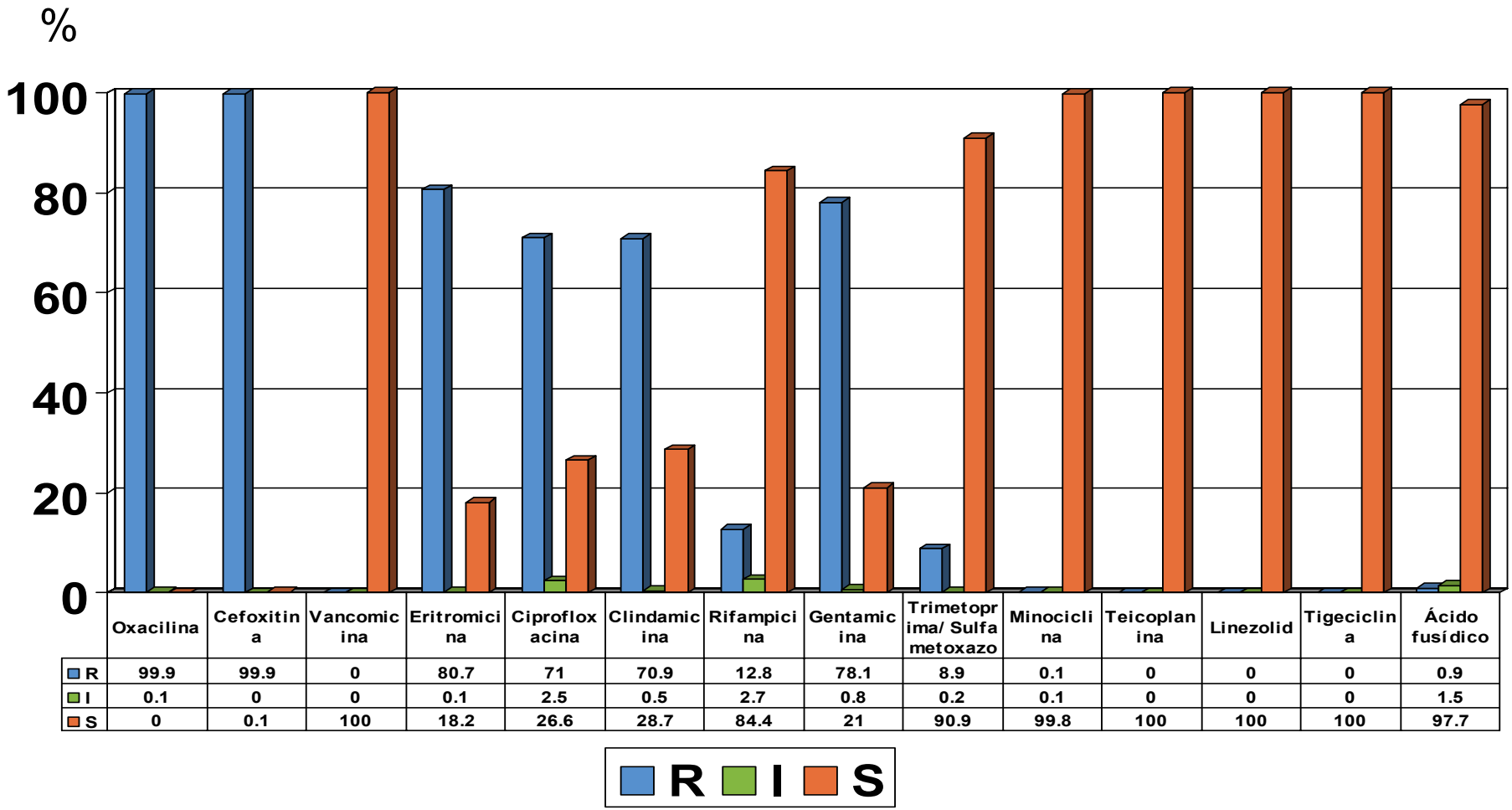
Actividad de ATBs en SAU Nosocomial Red WHONET-Arg 2007-2008 N=5322



	Oxacilina	Cefoxitina	Vancomicina	Eritromicina	Ciprofloxacina	Clindamicina	Rifampicina	Gentamicina	Trimetoprima/ Sulfametoxazo	Minociclina	Teicoplanina	Linezolid	Tigeciclina	Ácido fusídico
R	99.9	99.9	0	80.7	71	70.9	12.8	78.1	8.9	0.1	0	0	0	0.9
I	0.1	0	0	0.1	2.5	0.5	2.7	0.8	0.2	0.1	0	0	0	1.5
S	0	0.1	100	18.2	26.6	28.7	84.4	21	90.9	99.8	100	100	100	97.7

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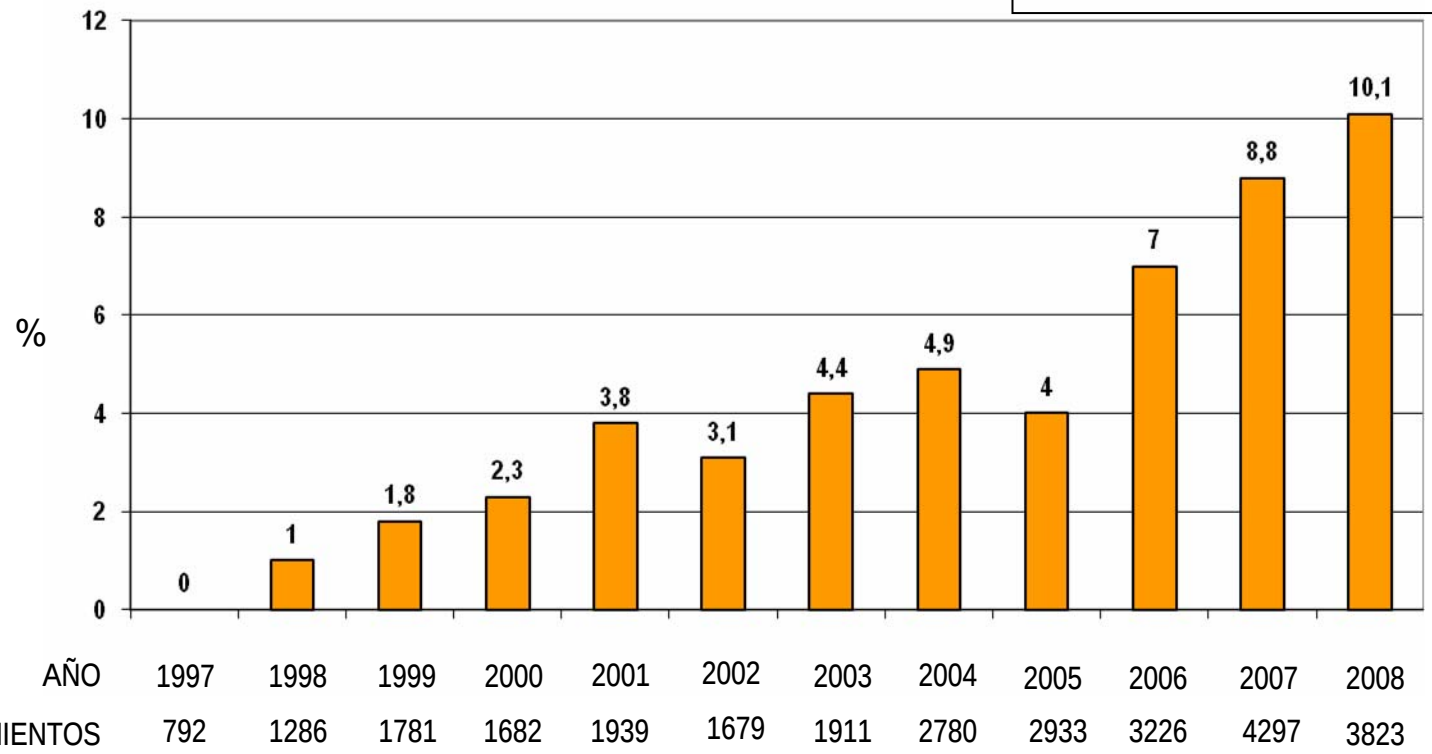
Red WHONET - Argentina

VRE

RESISTENCIA VANCOMICINA

Enterococcus sp., E. faecium, E. faecalis

Excluido: SCV, fecal, rectal



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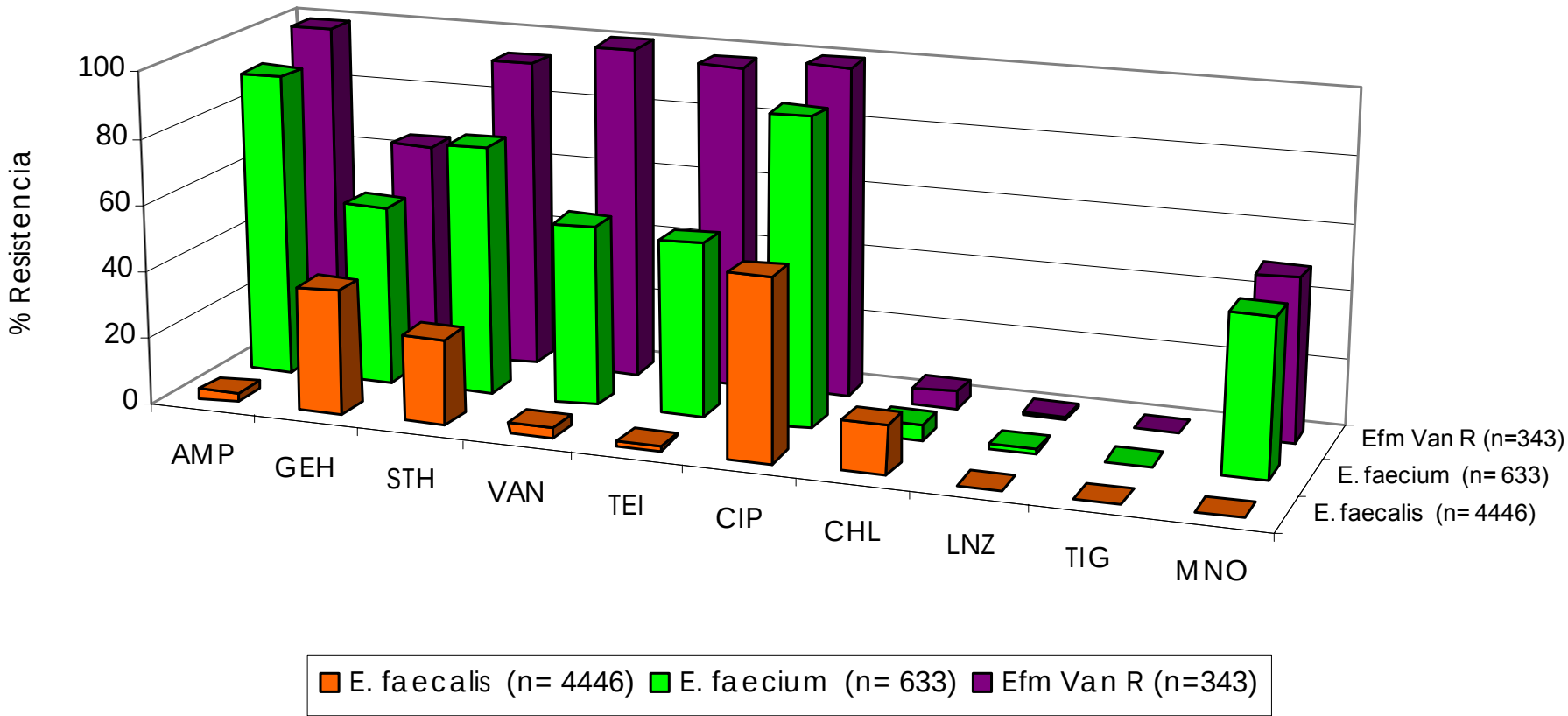
Red WHONET – Argentina 2008-2009

E. faecalis
E. faecium
E. faecium VAN R



Excluido: SCV, fecal, rectal

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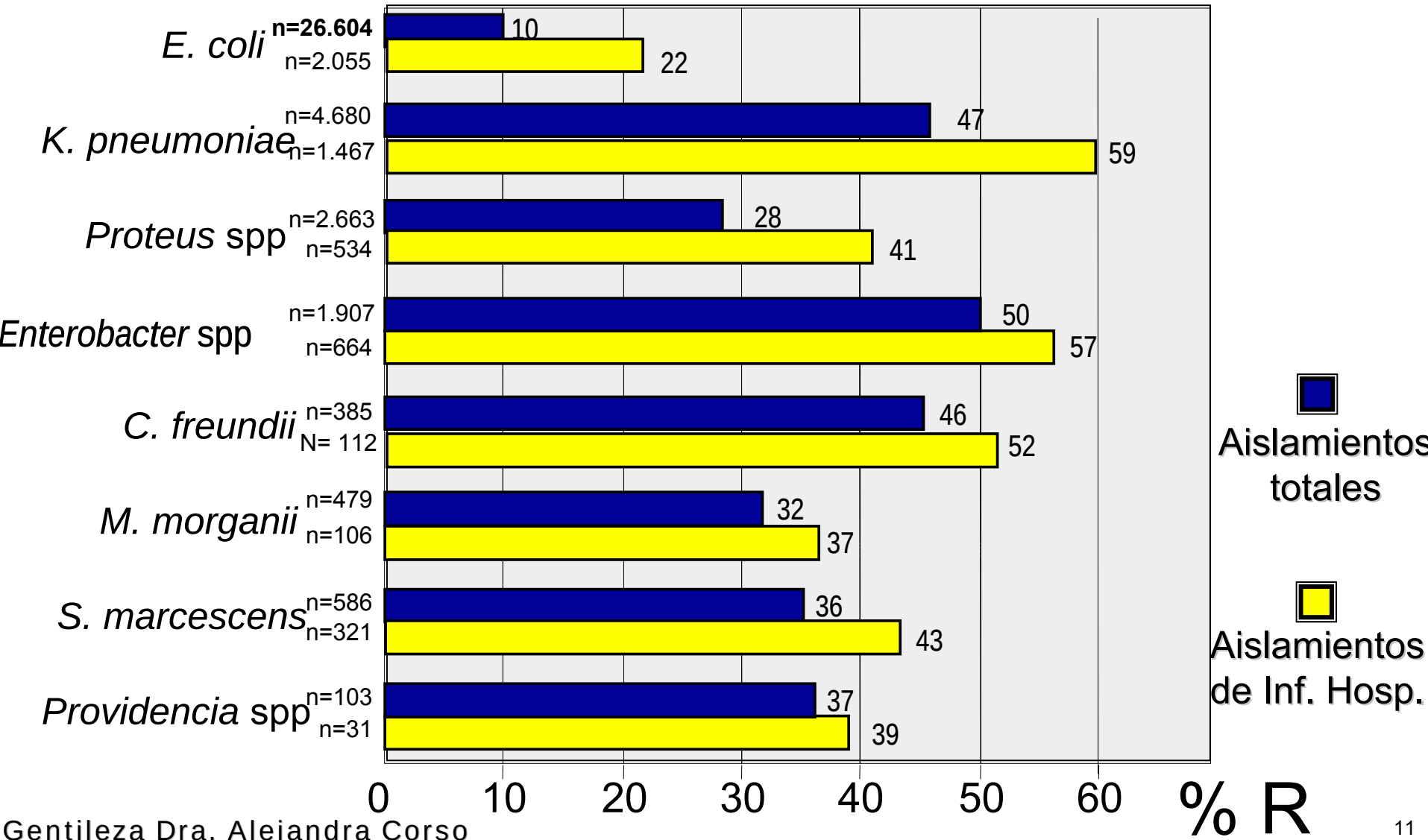
Resistencia a CEFALOSPORINAS de 3ª GENERACIÓN ENTEROBACTERIAS Red WHONET-Argentina (N= 37.407 - Año 2007)



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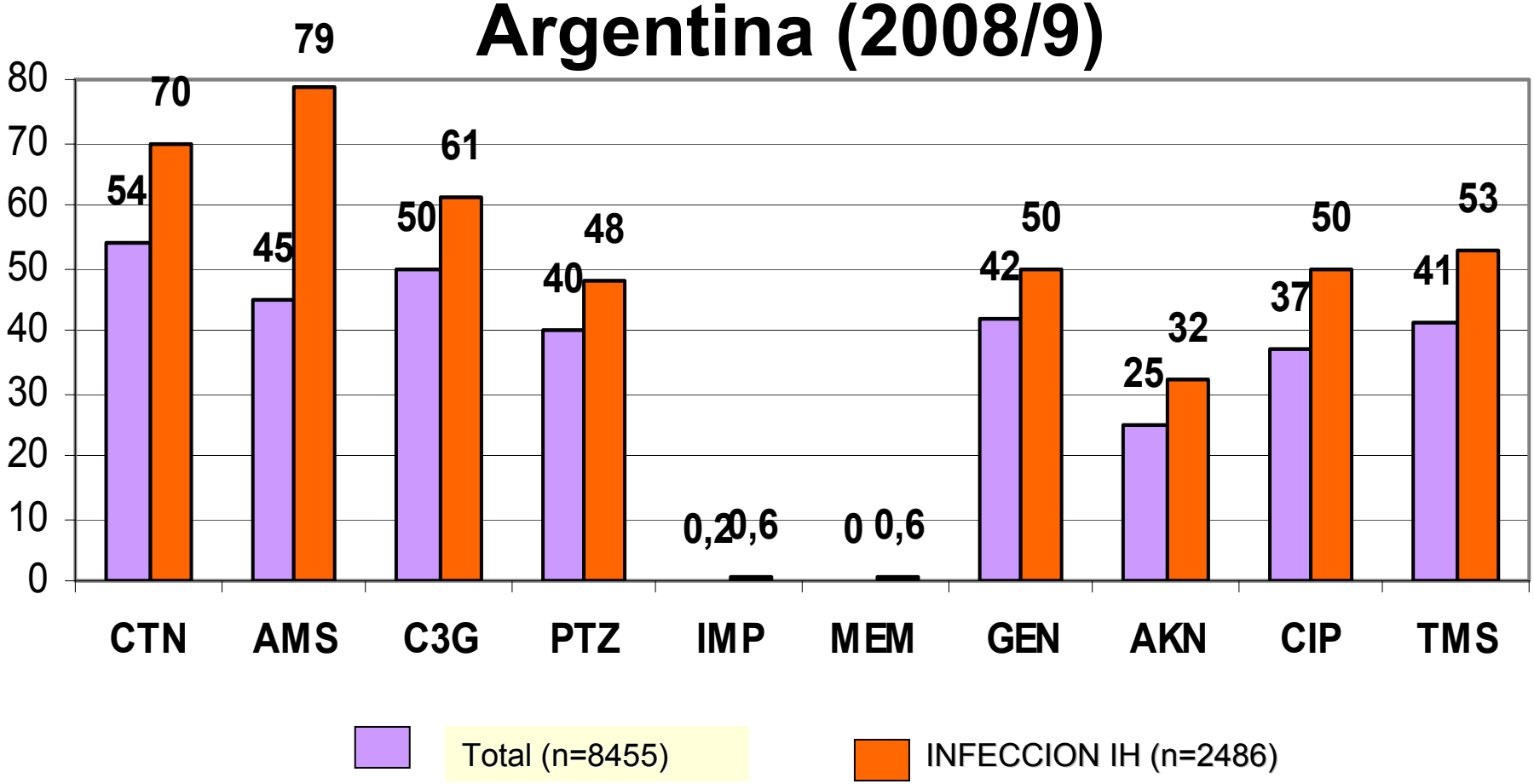
KLEBSIELLA PNEUMONIAE

Red WHONET-Argentina (2008/9)



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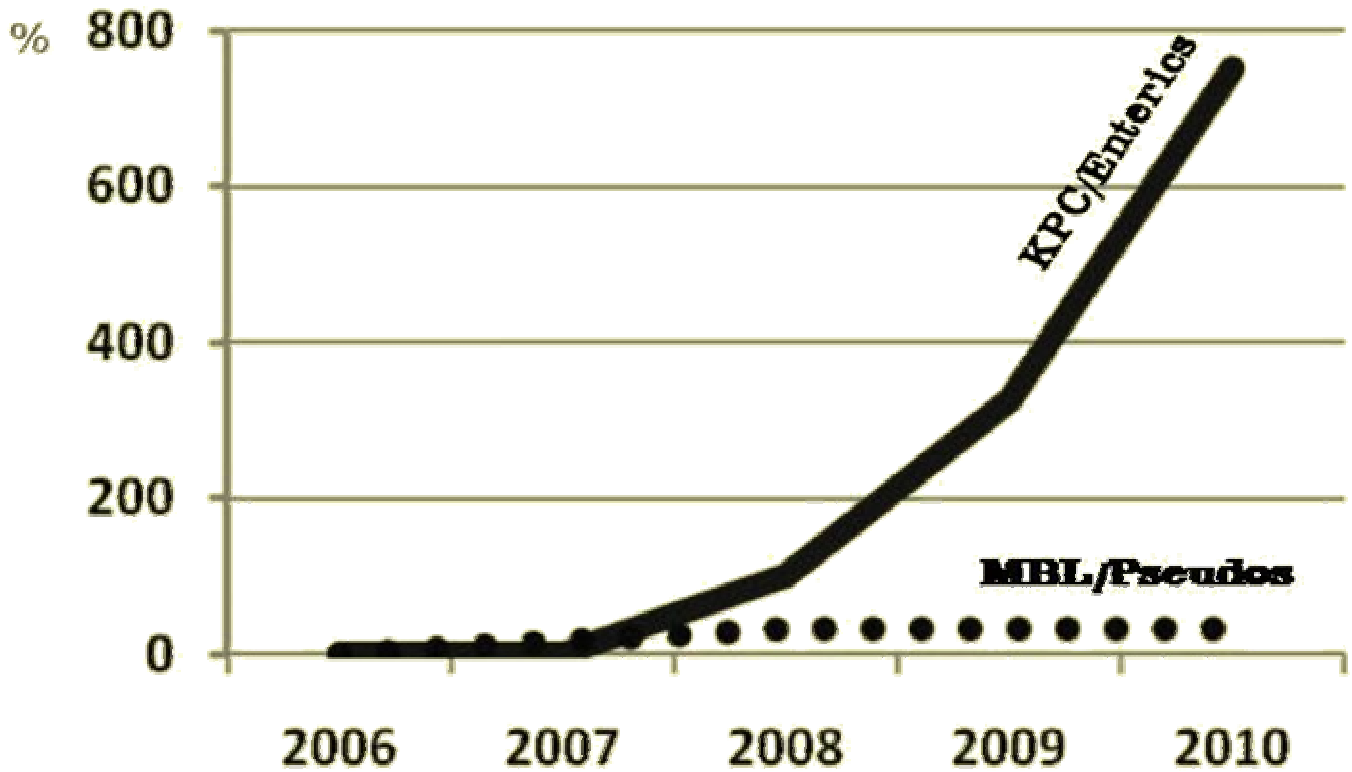
Curva epidemiologica de KPC en Enterobacterias. Argentina 2006-2010

Servicio Antimicrobianos INEI ANLIS Dr. Carlos G Malbran



Incremento internaual

Incremento inter-anual >700% para KPC desde 2008 al presente

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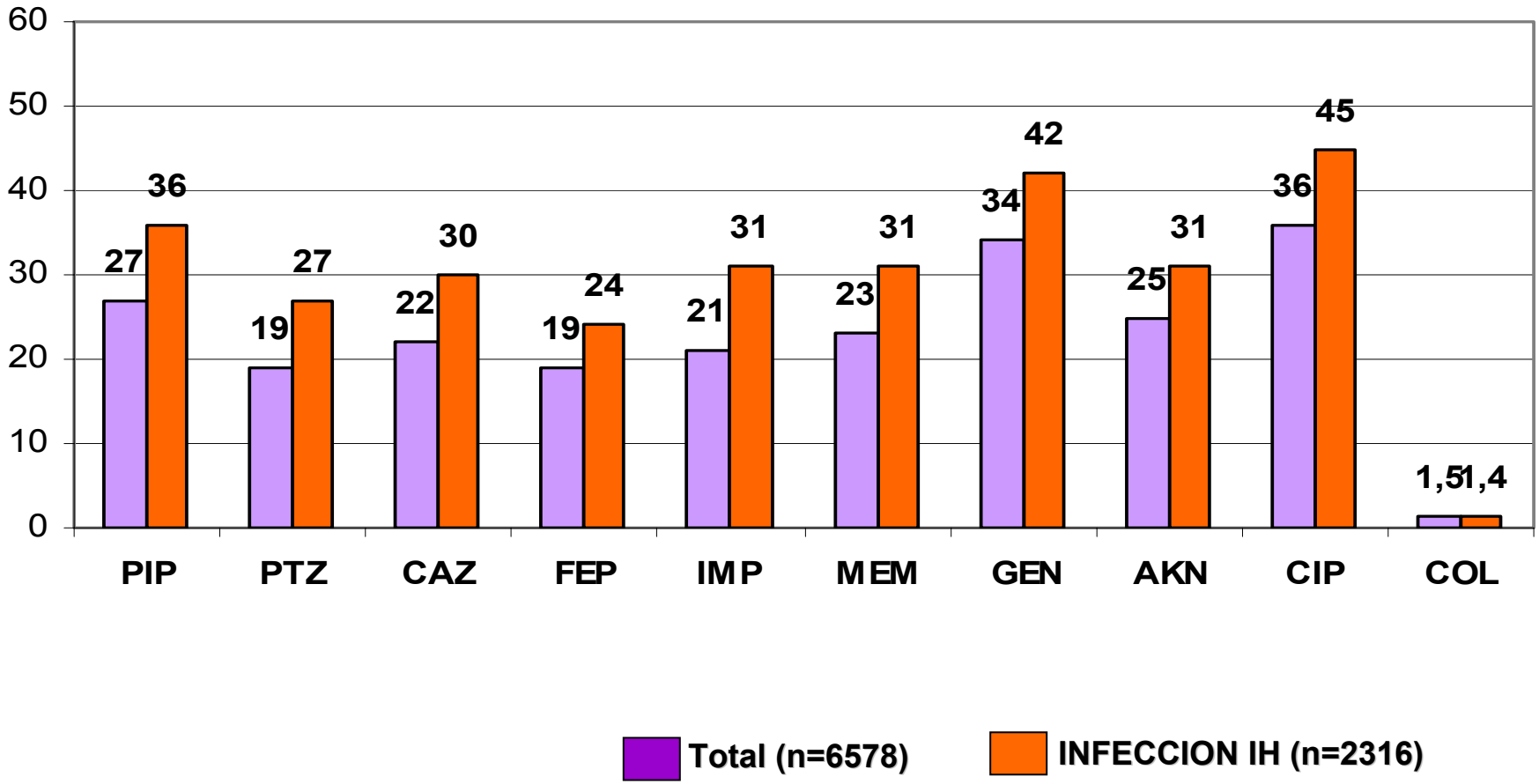
PSEUDOMONAS AERUGINOSA

Red WHONET-Argentina (2008/9)



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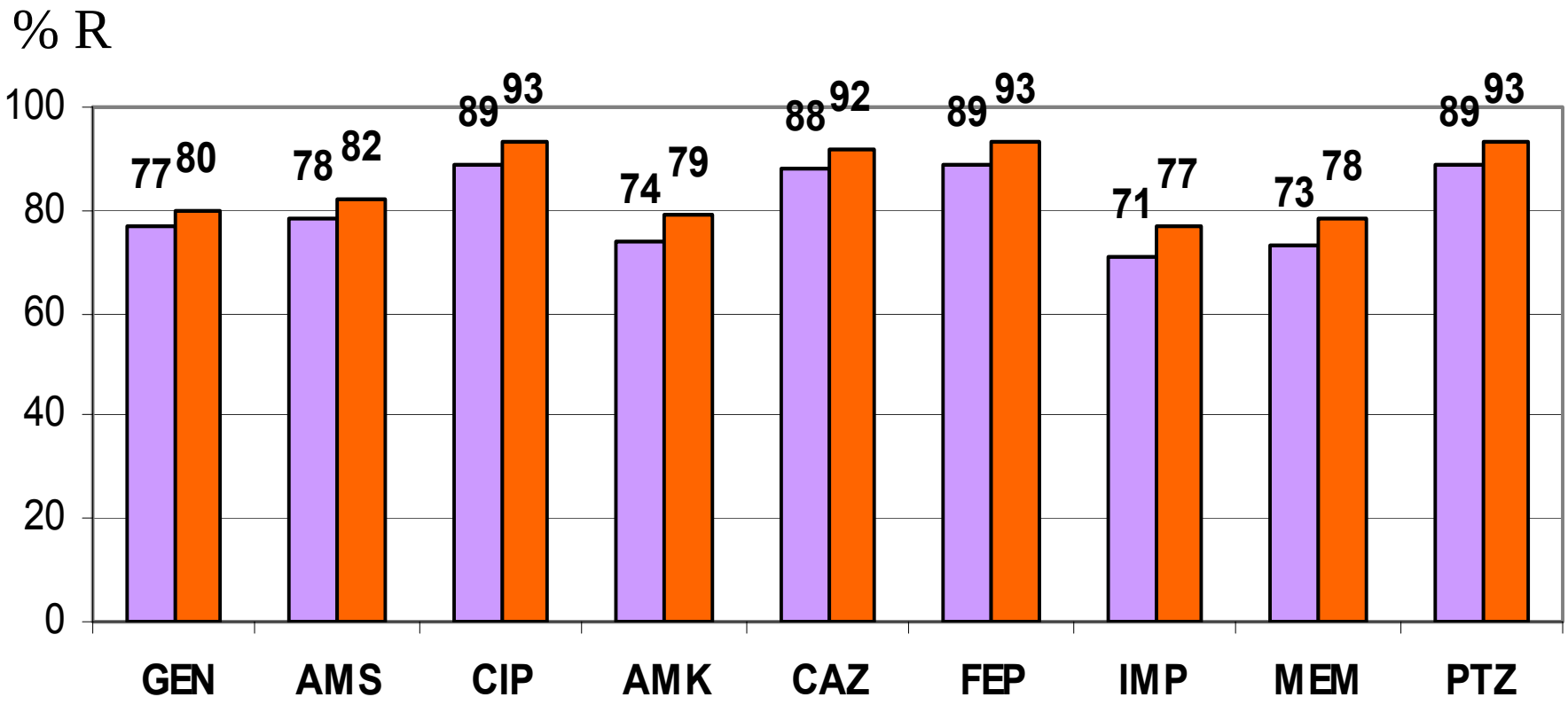
ACINETOBACTER SPP.

Red WHONET-Argentina (2008/9)



Minociclina^{R} 11% (total e IH) ; Colistina^{R} 3,6% (total) vs 2,9% (IH)

Total (n=3820) **INFECCIÓN IH (n=1977)**

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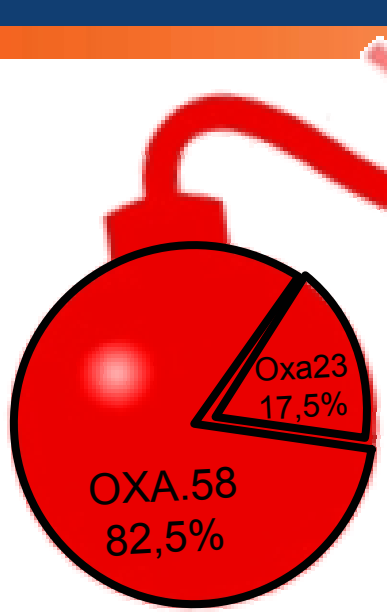

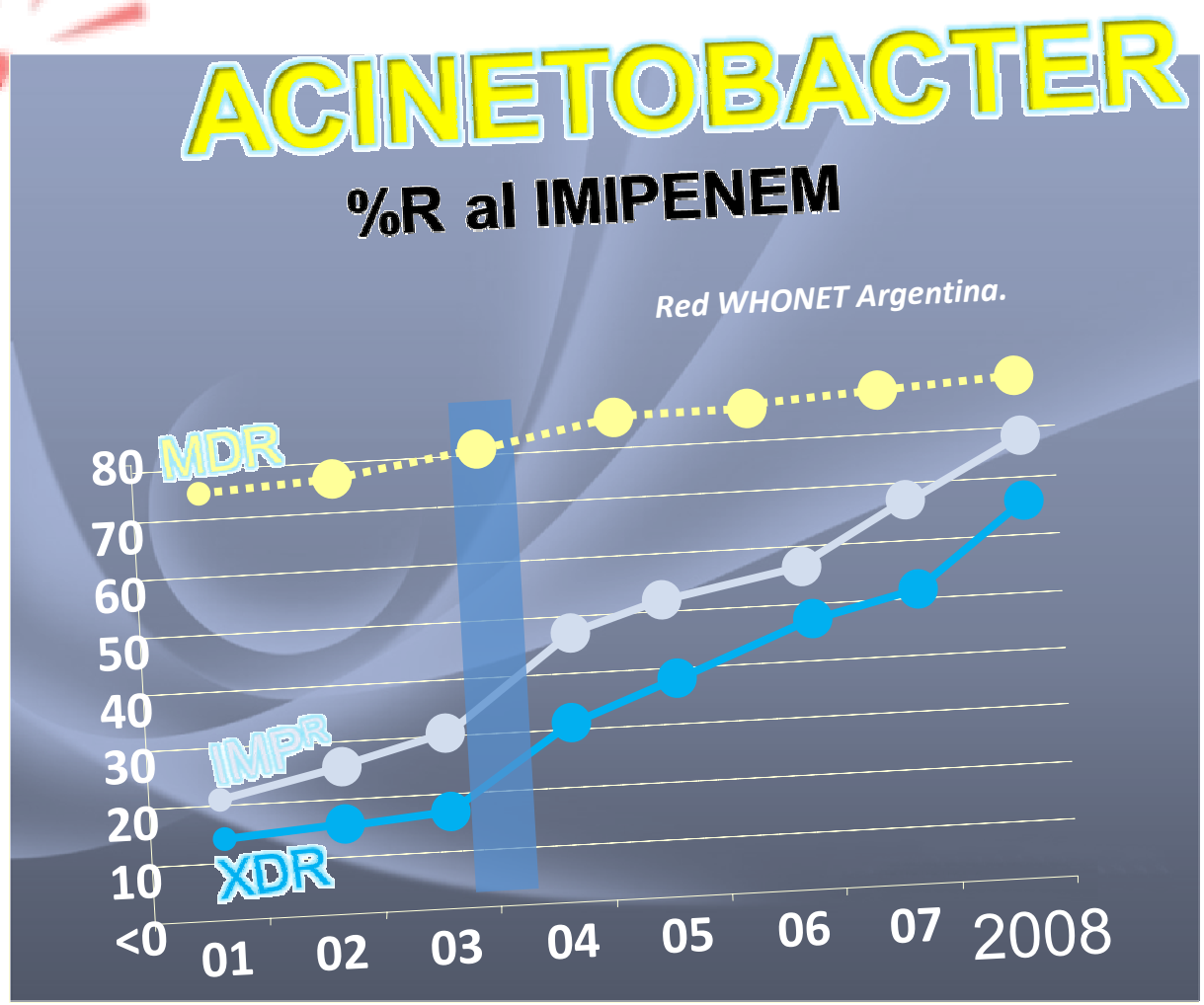

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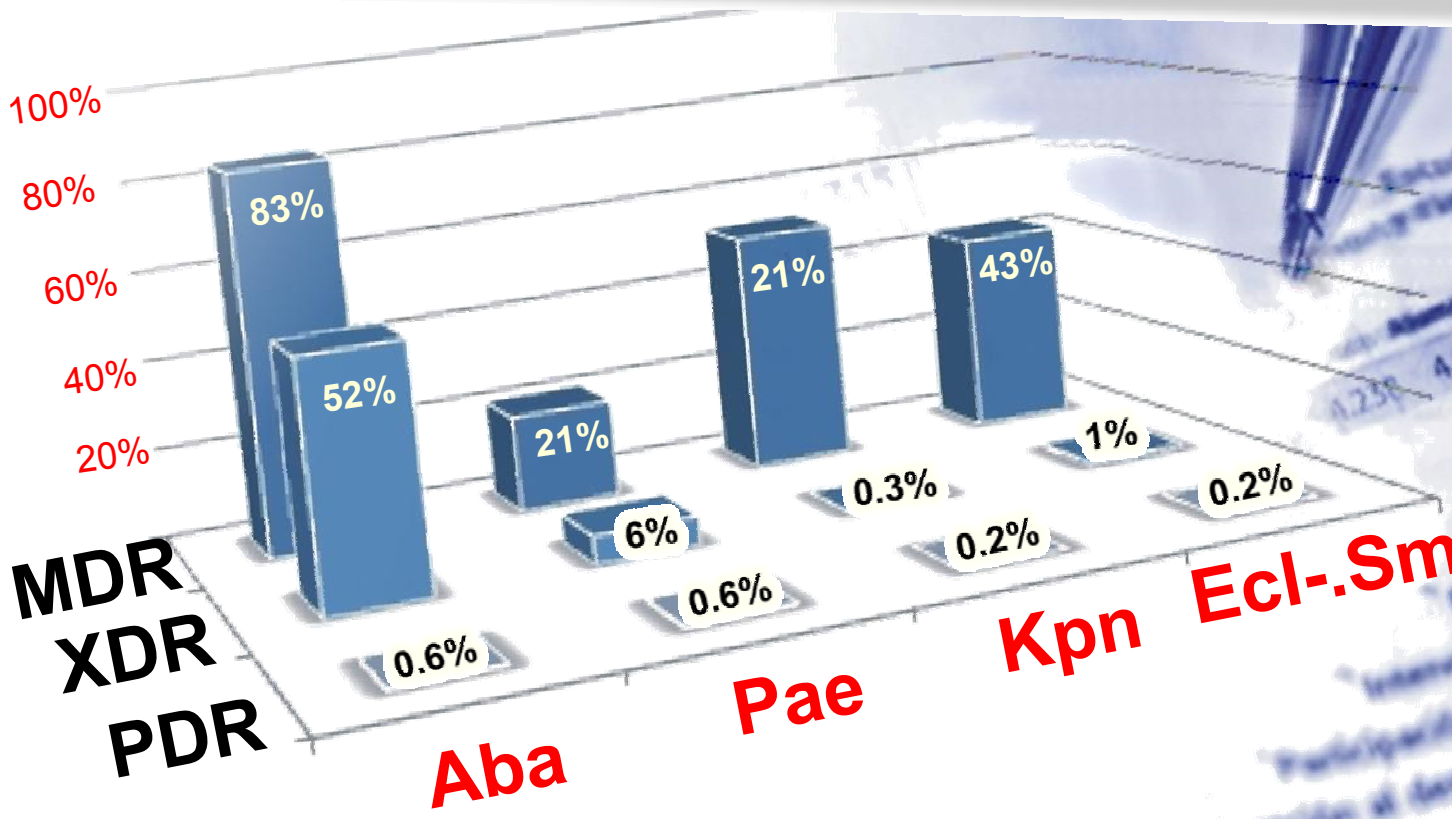
Prevalencia de microorganismos MDR, XDR y PDR asociado a infecciones nosocomiales



Red WHONET Argentina. Año 2007

Nro de microorganismos analizados: Kpn=1217; Par=1156; Aba=632; Ecl=426; Sma=252

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Patógenos "ESKAPE"
Mortalidad

	VRE	VSE	
Bacteremia[1]	n=683	n=931	OR 2.52*
	MRSA	MSSA	
Bacteremia[2]	11.8% (n=382)	5.1% (n=433)	p<0.001
	KPN-ESBL+	KPN-ESBL-	
Bacteremia[3]	52% (n=48)	29% (n=99)	p<0.05
	AB (IMP-R)	AB (IMP-S)	
Bacteremia[4]	57.5% (n=40)	27.5% (n=40)	p=0.007
	MDR-Pae	No-MDR-Pae	
Bacteriemia[5]	21% (n=40)	12% (n=40)	p=0.08
	EB (IMP-R)	EB (IMP-S)	
Serious infections[6]	33% (n=33)	9% (n=33)	p=0.038

*95% CI, 1.9–3.4

VRE=vancomycin-resistant enterococci
VSE=vancomycin-susceptible enterococci
MRSA=methicillin-resistant *S.aureus*
MSSA=methicillin-susceptible *S.aureus*
KPN=*K.pneumoniae*
ESBL=extended-spectrum β-lactamase
AB=*A.baumannii*
IMP=imipenem
Pae=*P.aeruginosa*
EB=*Enterobacter spp.*

1. DiazGranados et al. *Clin Infect Dis.* 2005; 41:327–33.
2. Melzer M, et al. *Clin Infect Dis.* 2003;37:1453-1460.
3. Tumbarello M, et al. *Antimicrob Agents Chemother.* 2006;50:498-504.
4. Kwon K. et al. *J Antimicrob Chemother.* 2007;59:525–530.
5. Aloush V. et al. *Antimicrob Agents Chemother.* 2006;50: 43–48.
6. Marchaim D. et al. *Antimicrob Agents Chemother.* 2008; 52:1413-1418.

Costos Hospitalarios y Sociales de las Infecciones Resistentes a Antimicrobianos (IRAs)

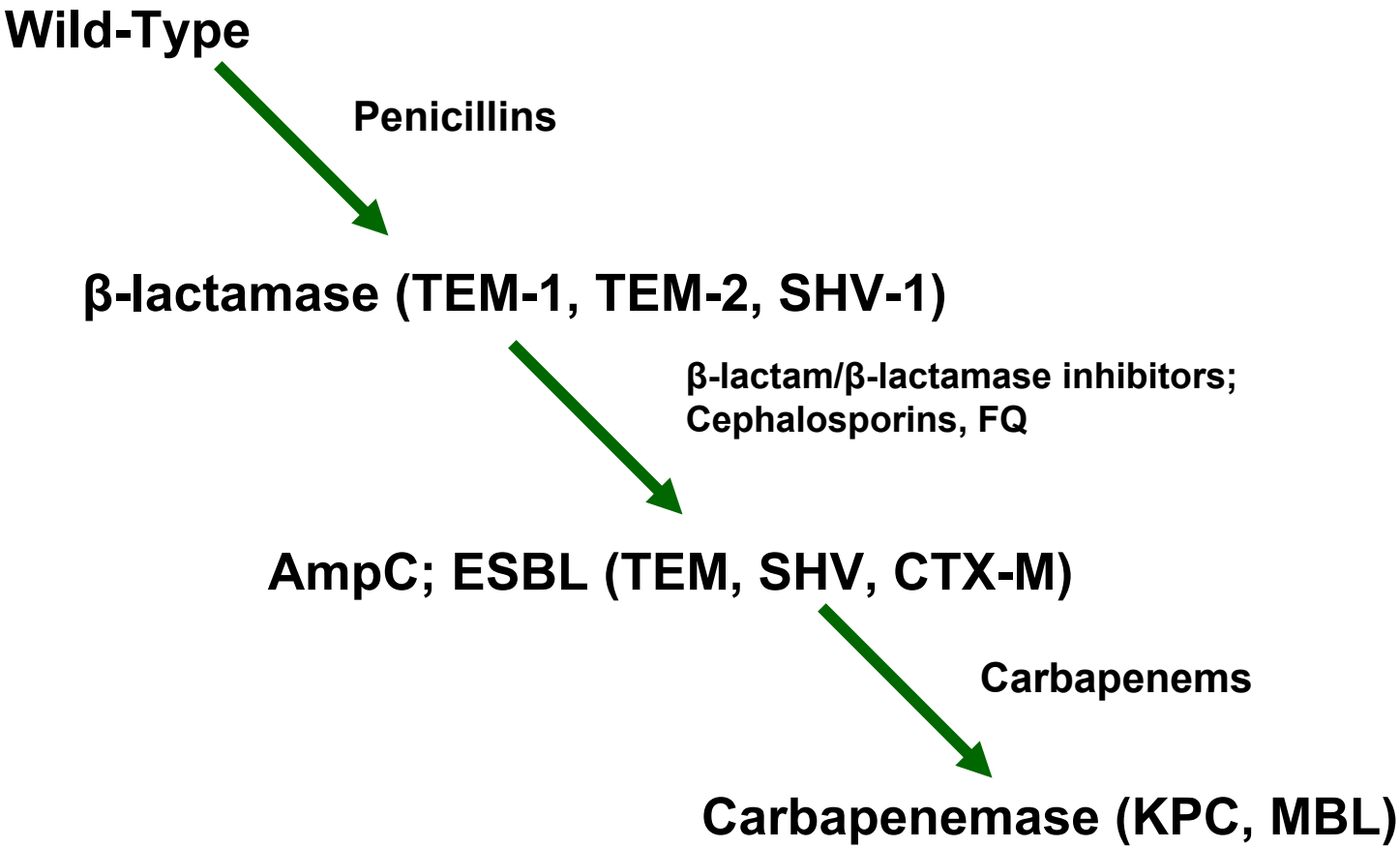
Analisis económico del
Chicago Antimicrobial Resistant Project dataset:

188 / 1391 pacientes (13.5%) with IRA

Costos Medicos atribuibles a IRA	$18.588 - $29.069 / paciente
Exceso en dias de internación	6.4 – 12.7 days
Mortalidad Atribuible	6.5%
Costos Sociales	$10.7 - $15.0 million

Roberts RR, et al. *Clin Infect Dis.* 2009;49:1175-84.

Evolución de β-Lactamasas



ESBL=extended-spectrum β-lactamase; KPC=*Klebsiella pneumoniae* carbapenemase; MBL=metallo-β-lactamase; TEM-1,TEM-2, SHV-1, TEM, SHV, CTX-M=types of β-lactamases.

Adaptado de Burgess DS, et al. Am J Health Syst Pharm. 2008;65:S4-S15.

Altas tasas de GMRs

Efecto Iceberg

Factores de Adquisición de GMRs

(CID2006; 43:S57–61)

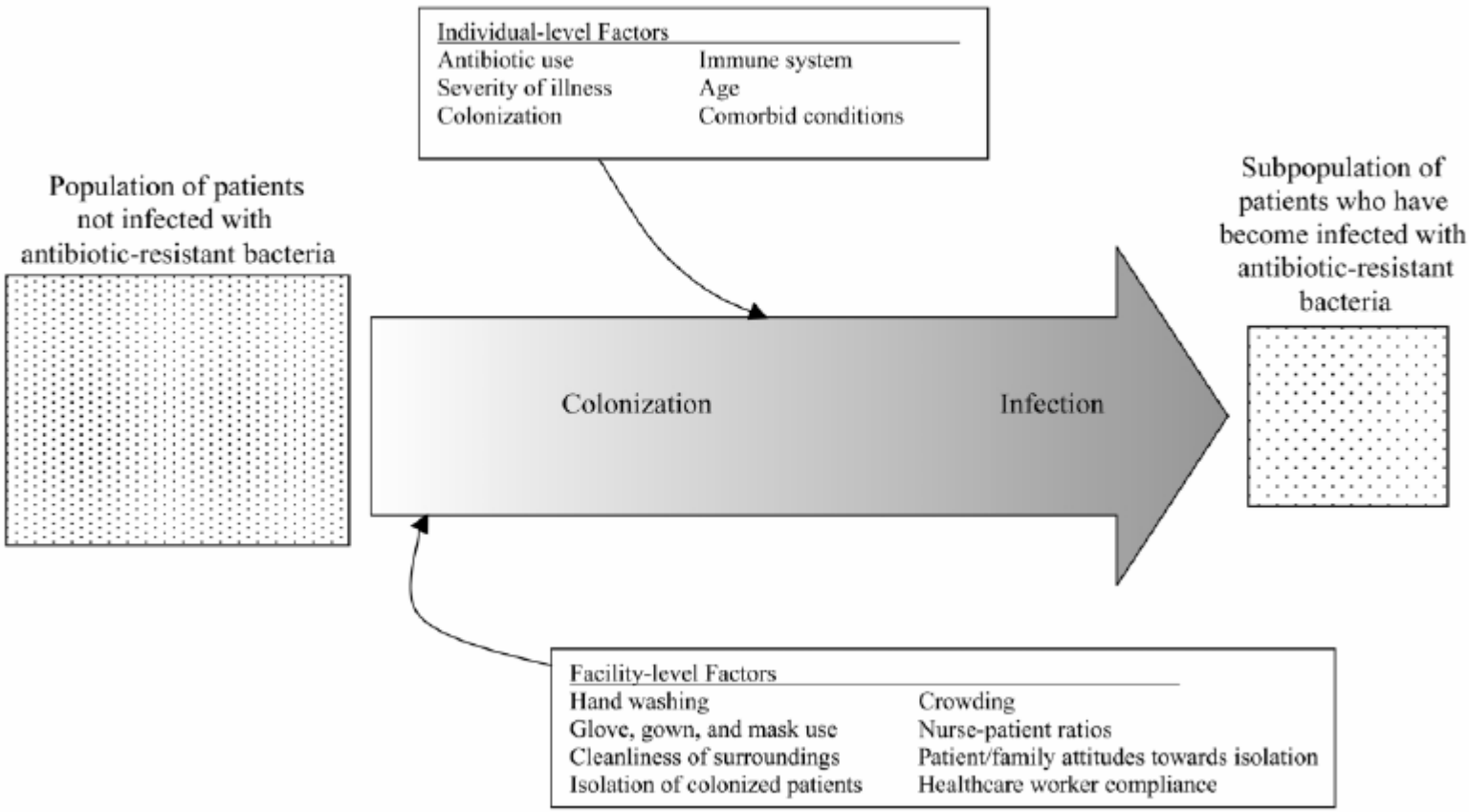


Figure 1. Factors that influence the acquisition of a nosocomial antibiotic-resistant bacterial infection

Prevención y estrategias de control

- **Los programas más exitosos en control de GMRs utilizan un conjunto de 6-7 medidas**
- **60% de intervenciones exitosas requieren ≥ 1 año de observación y seguimiento de la implementación.**
- **No existe evidencia contundente para sostener que una o un conjunto de medidas en particular, sean universalmente aplicadas a todos los ámbitos de atención de la salud.**

CDC: Management of MDROs in Healthcare Settings. 2006.

Table 2. Control measures for MDROs employed in studies performed in health care settings, 1982-2005

Focus of MDRO (No. of studies)	MDR-GNB (n = 30)	MRSA (n = 35)	VRE (n = 39)
	No. (%) of studies using control measure		
Education of staff, patients, or visitors	19 (63)	11 (31)	20 (53)
Emphasis on handwashing	16 (53)	21 (60)	9 (23)
Use of antiseptics for handwashing	8 (30)	12 (36)	16 (41)
Contact precautions or glove use*	20 (67)	27 (77)	34 (87)
Private rooms	4 (15)	10 (28)	10 (27)
Segregation of cases	4 (15)	3 (9)	5 (14)
Cohorting of patients	11 (37)	12 (34)	14 (36)
Cohorting of staff	2 (7)	6 (17)	9 (23)
Change in antimicrobial use	12 (41)	1 (3)	17 (44)
Surveillance cultures of patients	19 (63)	34 (97)	36 (92)
Surveillance cultures of staff	9 (31)	8 (23)	7 (19)
Environmental cultures	15 (50)	14 (42)	15 (38)
Extra cleaning and disinfection	11 (37)	7 (21)	20 (51)
Dedicated equipment	5 (17)	0	12 (32)
Decolonization	3 (10)	25 (71)	4 (11)
Ward closure to new admission or to all patients	6 (21)	4 (12)	5 (14)
Other miscellaneous measures	6 (22)†	9 (27)‡	17 (44)§

References for MDR-GNBs.[6,8,9,11,16,38,174,175,180,209,210,213-215,218,334,388,406,407] References for MRSA.[68,89,152,153,165-173,183,188,194,204,205,208,240,269,279,280,289,304,312,327,365,392,397,408-412]

*Contact precautions mentioned specifically, use of gloves with gowns or aprons mentioned, barrier precautions, strict isolation, all included under this heading.

†Includes signage, record flagging, unannounced inspections, selective decontamination, and peer compliance monitoring (1 to 4 studies employing any of these measures).

‡Includes requirements for masks, signage, record tracking, alerts, early discharge, and preventive isolation of new admissions pending results of screening cultures (1 to 4 studies employing any of these measures).

§Includes computer flags, signage, requirement for mask, one-to-one nursing, changing type of thermometer used, and change in rounding sequence (1 to 7 studies employing any of these measures).

(Am J Infect Control 2007;35:S165-193)

Organización de las Recomendaciones

- **Linea de Base para prevencion de infecciones y medidas de control**

Linea de Base para prevencion de infecciones y medidas de control

- **Soporte Administrativo (recursos humanos financieros y decision politica-filosofica)**
- **Programa de uso racional de ATB (selección, uso duración; formularios)**
- **Precauciones estandares.Precauciones de contacto. Programa de Lavado de Manos**
- **Procedimientos microbiologicos**

http://www.cdc.gov/ncidod/dhqp/ps_5handHygiene.html

Organización de las Recomendaciones

- NIVEL 1: Recomendaciones para prevencion y control de GMRs

Recomendaciones de Nivel 1

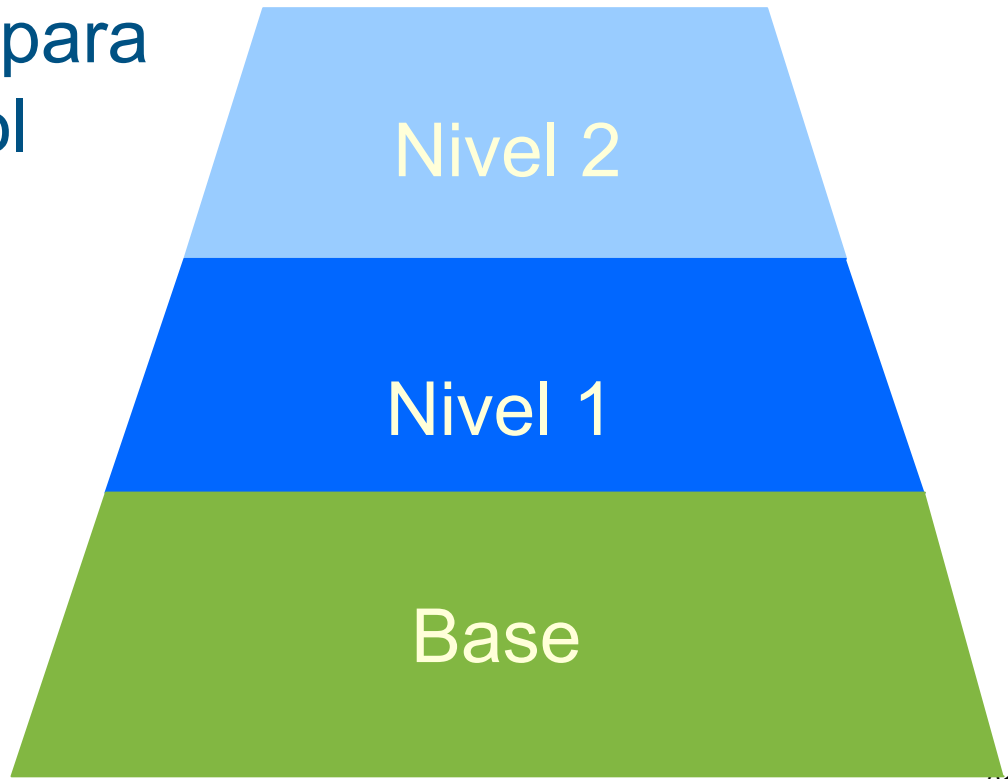
1. **Soporte Administrativo**
2. **Uso racional de ATB**
3. **Sistema de vigilancia**
4. **Precauciones standards y de contacto**
5. **Medidas ambientales**
6. **Educación**
7. **Decolonización**

Tier 1. General Recommendations for Routine Prevention and Control of MDROs in Healthcare Settings

Administrative Measures/Adherence Monitoring	MDRO Education	Judicious Antimicrobial Use	Surveillance	Infection Control Precautions to Prevent Transmission	Environmental Measures	Decolonization
Make MDRO prevention/control an organizational priority. Provide administrative support and both fiscal and human resources to prevent and control MDRO transmission. *(IB)* Identify experts who can provide consultation and expertise for analyzing epidemiologic data, recognizing MDRO problems, or devising effective control strategies, as needed. *(II)* **Implement systems to communicate information about reportable MDROs to administrative personnel and state/local health departments. *(II)*** Implement a multi-disciplinary process to monitor and improve HCP adherence to recommended practices for Standard and Contact Precautions.*(IB)* Implement systems to designate patients known to be colonized or infected with a targeted MDRO and to notify receiving healthcare facilities or personnel prior to transfer of such patients within or between facilities. *(IB)* Support participation in local, regional and/or national coalitions to combat emerging or growing MDRO problems.*(IB)* Provide updated feedback at least annually to healthcare providers and administrators on facility and patient-care unit MDRO infections. Include information on changes in prevalence and incidence, problem assessment and performance improvement plans. *(IB)*	Provide education and training on risks and prevention of MDRO transmission during orientation and periodic educational updates for HCP; include information on organizational experience with MDROs and prevention strategies. *(IB)*	In hospitals and LTCFs, ensure that a multi-disciplinary process is in place to review local susceptibility patterns (antibiograms), and antimicrobial agents included in the formulary, to foster appropriate antimicrobial use. *(IB)* Implement systems (e.g., CPOE, susceptibility report comment, pharmacy or unit director notification) to prompt clinicians to use the appropriate agent and regimen for the given clinical situation. *(IB)* Provide clinicians with antimicrobial susceptibility reports and analysis of current trends, updated at least annually, to guide antimicrobial prescribing practices. *(IB)* In settings with limited electronic communication system infrastructures to implement physician prompts, etc., at a minimum implement a process to review antibiotic use. Prepare and distribute reports to providers. *(II)*	Use standardized laboratory methods and follow published guidelines for determining antimicrobial susceptibilities of targeted and emerging MDROs. Establish systems to ensure that clinical micro labs (in-house and outsourced) promptly notify infection control or a medical director/designee when a novel resistance pattern for that facility is detected. *(IB)* In hospitals and LTCFs: ...develop and implement laboratory protocols for storing isolates of selected MDROs for molecular typing when needed to confirm transmission or delineate epidemiology of MDRO in facility. *(IB)* ...establish laboratory-based systems to detect and communicate evidence of MDROs in clinical isolates *(IB)* ...prepare facility-specific antimicrobial susceptibility reports as recommended by CLSI; monitor reports for evidence of changing resistance that may indicate emergence or transmission of MDROs *(IA/IC)* ...develop and monitor special-care unit-specific antimicrobial susceptibility reports (e.g., ventilator-dependent units, ICUs, oncology units). *(IB)* ...monitor trends in incidence of target MDROs in the facility over time to determine if MDRO rates are decreasing or if additional interventions are needed. *(IA)*	Follow Standard Precautions in all healthcare settings. *(IB)* Use of Contact Precautions (CP): --- In *acute care settings* : Implement CP for all patients known to be colonized/infected with target MDROs.*(IB)* --- In *LTCFs: Consider the individual patient's clinical situation and facility resources in deciding whether to implement CP (II)* --- In *ambulatory and home care settings, follow Standard Precautions (II)* ---In *hemodialysis units*: Follow dialysis specific guidelines *(IC)* No recommendation can be made regarding when to discontinue CP. (*Unresolved issue*) Masks are not recommended for routine use to prevent transmission of MDROs from patients to HCWs. Use masks according to Standard Precautions when performing splash-generating procedures, caring for patients with open tracheostomies with potential for projectile secretions, and when there is evidence for transmission from heavily colonized sources (e.g., burn wounds). Patient placement in hospitals and LTCFs: When single-patient rooms are available, assign priority for these rooms to patients with known or suspected MDRO colonization or infection. Give highest priority to those patients who have conditions that may facilitate transmission, e.g., uncontained secretions or excretions. When single-patient rooms are not available, cohort patients with the same MDRO in the same room or patient-care area. *(IB)* When cohorting patients with the same MDRO is not possible, place MDRO patients in rooms with patients who are at low risk for acquisition of MDROs and associated adverse outcomes from infection and are likely to have short lengths of stay. *(II)*	Follow recommended cleaning, disinfection and sterilization guidelines for maintaining patient care areas and equipment. Dedicate non-critical medical items to use on individual patients known to be infected or colonized with an MDRO. Prioritize room cleaning of patients on Contact Precautions. Focus on cleaning and disinfecting frequently touched surfaces (e.g., bed rails, bedside commodes, bathroom fixtures in patient room, doorknobs) and equipment in immediate vicinity of patient.	Not recommended routinely

Organización de las Recomendaciones

- NIVEL 2:
  Refuerzo de Recomendaciones para prevencion y control



Recomendaciones de Nivel 2

1. **Soporte Administrativo**
2. **Uso racional de ATB**
3. **Sistema de vigilancia**
4. **Precauciones standards y de contacto**
5. **Medidas ambientales**
6. **Educación**
7. **Decolonización**

Tier 2. Recommendations for Intensified MDRO control efforts

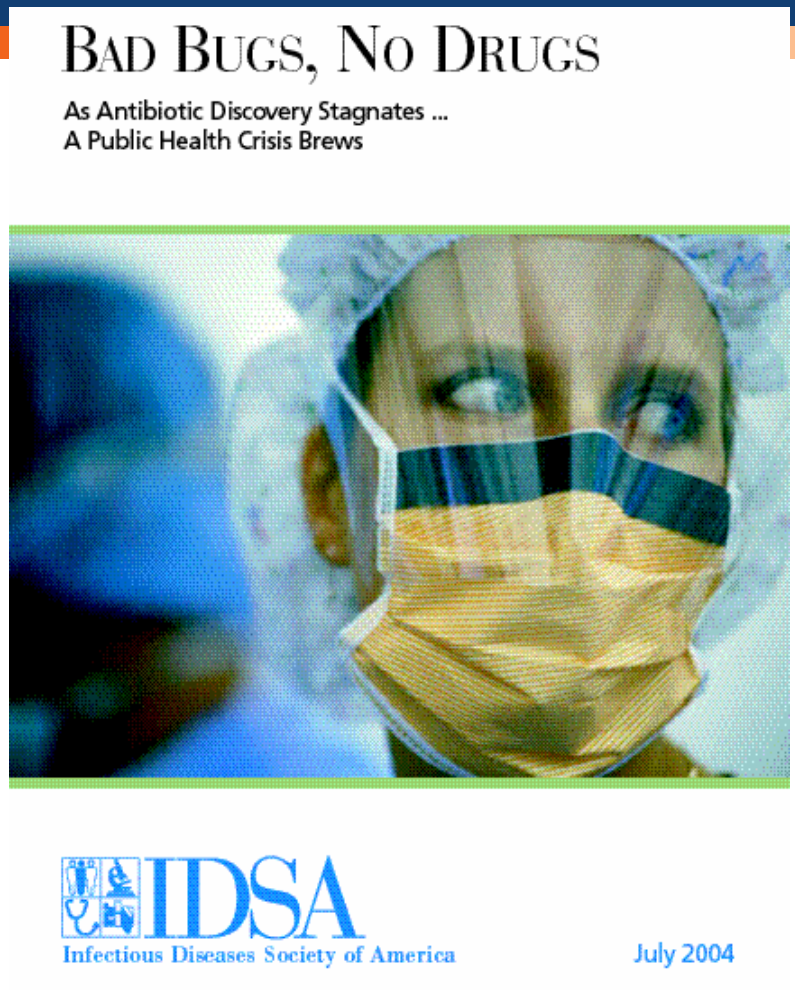
Institute one or more of the interventions described below when 1) incidence or prevalence of MDROs are not decreasing despite the use of routine control measures; or 2) the *first* case or outbreak of an epidemiologically important MDRO (e.g., VRE, MRSA, VISA, VRSA, MDR-GNB) is identified within a healthcare facility or unit *(IB)* Continue to monitor the incidence of target MDRO infection and colonization; if rates do not decrease, implement additional interventions as needed to reduce MDRO transmission.

Administrative Measures/Adherence Monitoring	MDRO Education	Judicious Antimicrobial Use	Surveillance	Infection Control Precautions to Prevent Transmission	Environmental Measures	Decolonization
Obtain expert consultation from persons with experience in infection control and the epidemiology of MDROS, either in-house or through outside consultation, for assessment of the local MDRO problem and guidance in the design, implementation and evaluation of appropriat4e control measures. *(IB)* Provide necessary leadership, funding and day-to-day oversight to implement interventions selected. *(IB)* Evaluate healthcare system factors for role in creating or perpetuating MDRO transmission, including staffing levels, education and training, availability of consumable and durable resources; communication processes, and adherence to infection control measures.*(IB)* Update healthcare providers and administrators on the progress and effectiveness of the intensified interventions. *(IB)*	Intensify the frequency of educational programs for healthcare personnel, especially for those who work in areas where MDRO rates are not decreasing. Provide individual or unit-specific feedback when available. *(IB)*	Review the role of antimicrobial use in perpetuating the MDRO problem targeted for intensified intervention. Control and improve antimicrobial use as indicated. Antimicrobial agents that may be targeted include vancomycin, third-[d] generation cephalosporins, anti-anaerobic agents for VRE; third generation cephalosporins for ESBLs; and quinolones and carbapenems. *(IB)*	Calculate and analyze incidence rates of target MDROs (single isolates/patient; location-, service-specific) *(IB)* Increase frequency of compiling, monitoring antimicrobial susceptibility summary reports *(II)* Implement laboratory protocols for storing isolates of selected MDROs for molecular typing; perform typing if needed *(IB)* Develop and implement protocols to obtain active surveillance cultures from patients in populations at risk. *(IB)* (See recommendations for appropriate body sites and culturing methods.) Conduct culture surveys to assess efficacy of intensified MDRO control interventions. Conduct serial (e.g., weekly) unit-specific point prevalence culture surveys of the target MDRO to determine if transmission has decreased or ceased.*(IB)* Repeat point-prevalence culture-surveys at routine intervals and at time of patient discharge or transfer until transmission has ceased. *(IB)* If indicated by assessment of the MDRO problem, collect cultures to assess the colonization status of roommates and other patients with substantial exposure to patients with known MDRO infection or colonization. *(IB)* Obtain cultures from HCP for target MDROs when there is epidemiologic evidence implicating the staff member as a source of ongoing transmission. *(IB)*	**Use of Contact Precautions:** **Implement Contact Precautions (CP) routinely for all patients colonized or infected with a target MDRO. *(IA)*** **Don gowns and gloves *before or upon entry* to the patient's room or cubicle. *(IB)*** **In LTCFs, modify CP to allow MDRO-colonized/infected patients whose site of colonization or infection can be appropriately contained and who can observe good hand hygiene practices to enter common areas and participate in group activities** **When active surveillance cultures are obtained as part of an intensified MDRO control program, implement CP until the surveillance culture is reported negative for the target MDRO *(IB)*** No recommendation is made for universal use of gloves and/or gowns. (*Unresolved issue*) **Implement policies for patient admission and placement as needed to prevent transmission of the problem MDRO. *(IB)*** When single-patient rooms are available, assign priority for these rooms to patients with known or suspected MDRO colonization or infection. Give highest priority to those patients who have conditions that may facilitate transmission, e.g., uncontained secretions or excretions. When single-patient rooms are not available, cohort patients with the same MDRO in the same room or patient-care area. *(IB)* When cohorting patients with the same MDRO is not possible, place MDRO patients in rooms with patients who are at low risk for acquisition of MDROs and associated adverse outcomes from infection and are likely to have short lengths of stay. (*II*) **Stop new admissions to the unit or facility if transmission continues despite the implementation of the intensified control measures. *(IB)*** Implement patient.-dedicated use of non-critical equipment *(IB)* Intensify and reinforce training of environmental staff who work in areas targeted for intensified MDRO control. Some facilities may choose to assign dedicated staff to targeted patient care areas to enhance consistency of proper environmental cleaning and disinfection services *(IB)* **Monitor cleaning performance to ensure consistent cleaning and disinfection of surfaces in close proximity to the patient and those likely to be touched by the patient and HCWs (e.g., bedrails, carts, bedside commodes, doorknobs, faucet handles) *(IB)*.** Obtain environmental cultures (e.g., surfaces, shared equipment) only when epidemiologically implicated in transmission *(IB)* **Vacate units for environmental assessment and intensive cleaning when previous efforts to control environmental transmission have failed *(II)*** Consult with experts on a case-by-case basis regarding the appropriate use of decolonization therapy for patients or staff during limited period of time as a component of an intensified MRSA control program *(II)* When decolonization for MRSA is used, perform susceptibility testing for the decolonizing agent against the target organism or the MDRO strain epidemiologically implicated in transmission. Monitor susceptibility to detect emergence of resistance to the decolonizing agent. Consult with microbiologists for appropriate testing for mupirocin resistance, since standards have not been established. Do not use topical mupirocin routinely for MRSA decolonization of patients as a component of MRSA control programs in any healthcare setting. *(IB)* Limit decolonization to HCP found to be colonized with MRSA who have been epidemiologically implicated in ongoing transmission of MRSA to patients. *(IB)* No recommendation can be made for decolonization of patients who carry VRE or MDR-GNB.

Necesitamos multiples intervenciones para controlar el problema!!!

- **Educación, lavado de manos, precauciones de contacto, cultivos de vigilancia epidemiologica de pacientes, cultivos de staff, cultivos de superficies ambientales, evitar compartir equipos entre los pacientes….**
- **Por lo tanto, no solo el aislamiento del paciente colabora en reducir la transmisión de GMR**
- **Sencillamente….. CUMPLIMIENTO, CUMPLIMIENTO y CUMPLIMIENTO sobre todo …..del Lavado de Manos!!!!**

Bad Bugs, No Drugs[1]



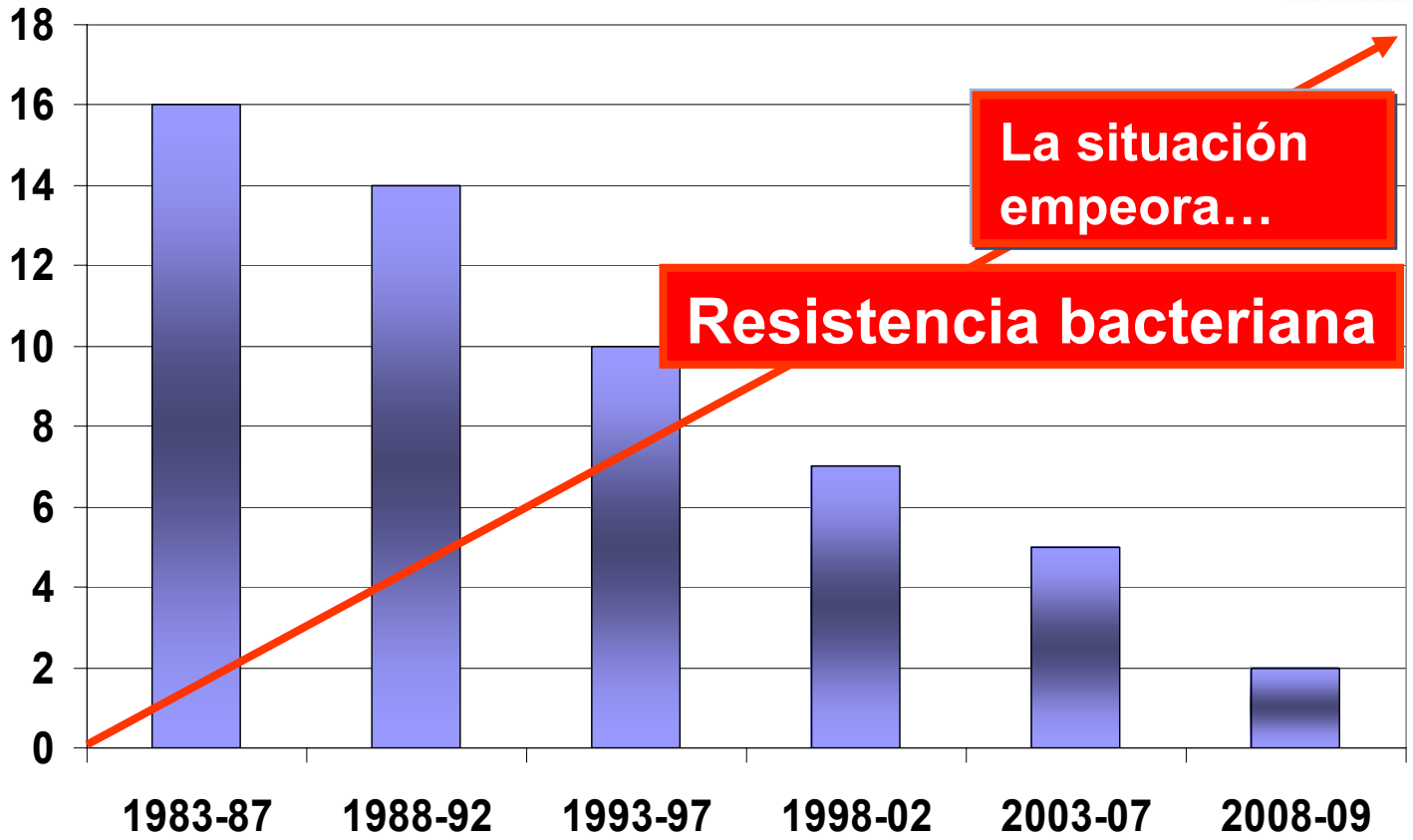
Declining research investments in antimicrobial development[2]

The Antimicrobial Availability Task Force of the IDSA identified, among others, *Acinetobacter baumannii*, ESBL-producing *Enterobacteriaceae*, vancomycin-resistant *Enterococcus*, & *Pseudomonas aeruginosa* as particularly problematic pathogens[2]

ESBL = extended spectrum β-lactamase

1. Infectious Diseases Society of America. Bad Bugs, No Drugs: As Antibiotic Discovery Stagnates, A Public Health Crisis Brews. http://www.idsociety.org/pa/IDSA_Paper4_final_web.pdf. July, 2004. Accessed March 17, 2007. 2. Talbot GH, et al. *Clin Infect Dis*. 2006:42:657-68.

2009-Opciones Antibióticas Declinan: Iniciativa10 x '20



http://www.idsociety.org/badbugsnodrugs.html; last access Feb 12, 2010

En resumen...

- **Las infecciones por GMRs representan una causa importante de prolongación de hospitalización y traen aparejadas aumentos en la mortalidad y en los costos de atención médica.**
- **No existe una UNICA HERRAMIENTA para controlar el problema.**
- **Se necesita una estrategia multidisciplinaria agresiva para ayudar en el control de la emergencia de cepas de GMRs.**
- **El compromiso DEBE ser de todos los actores del sistema de salud.**

“Donde hay un gran desafío,

Hay una gran oportunidad”

MUCHAS GRACIAS