Antimicrobial Stewardship
"Bad Bugs, No Drugs"

Zahra Kassamali, PharmD, BCPS
Jennifer Curello, PharmD, BCPS

Infection Prevention Leadership Academy
UCLA Health System
June 24, 2014

Presentation adapted with permission from "Antimicrobial Stewardship: Bad Bugs, No Drugs" by Daniel Uslan, MD

UCLA Health

Antibiotics:

The Good, the Bad and the Multidrug-Resistant Bacteria

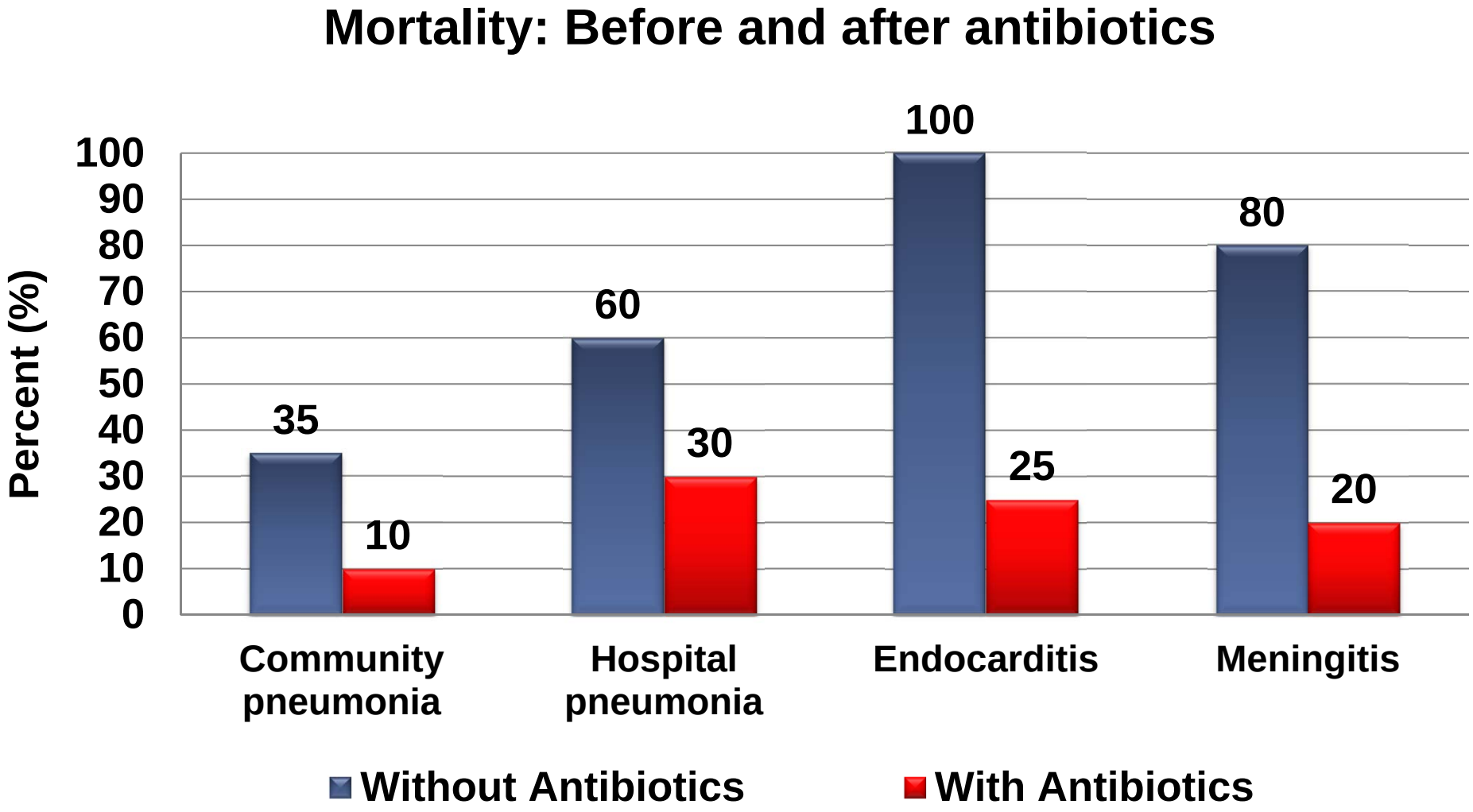
ZAHRA KASSAMALI, PHARM.D.

Prior to Antibiotics, Infection had the power to define civilization

Appl Microbiol Biotechnol (2011) 92:677–687

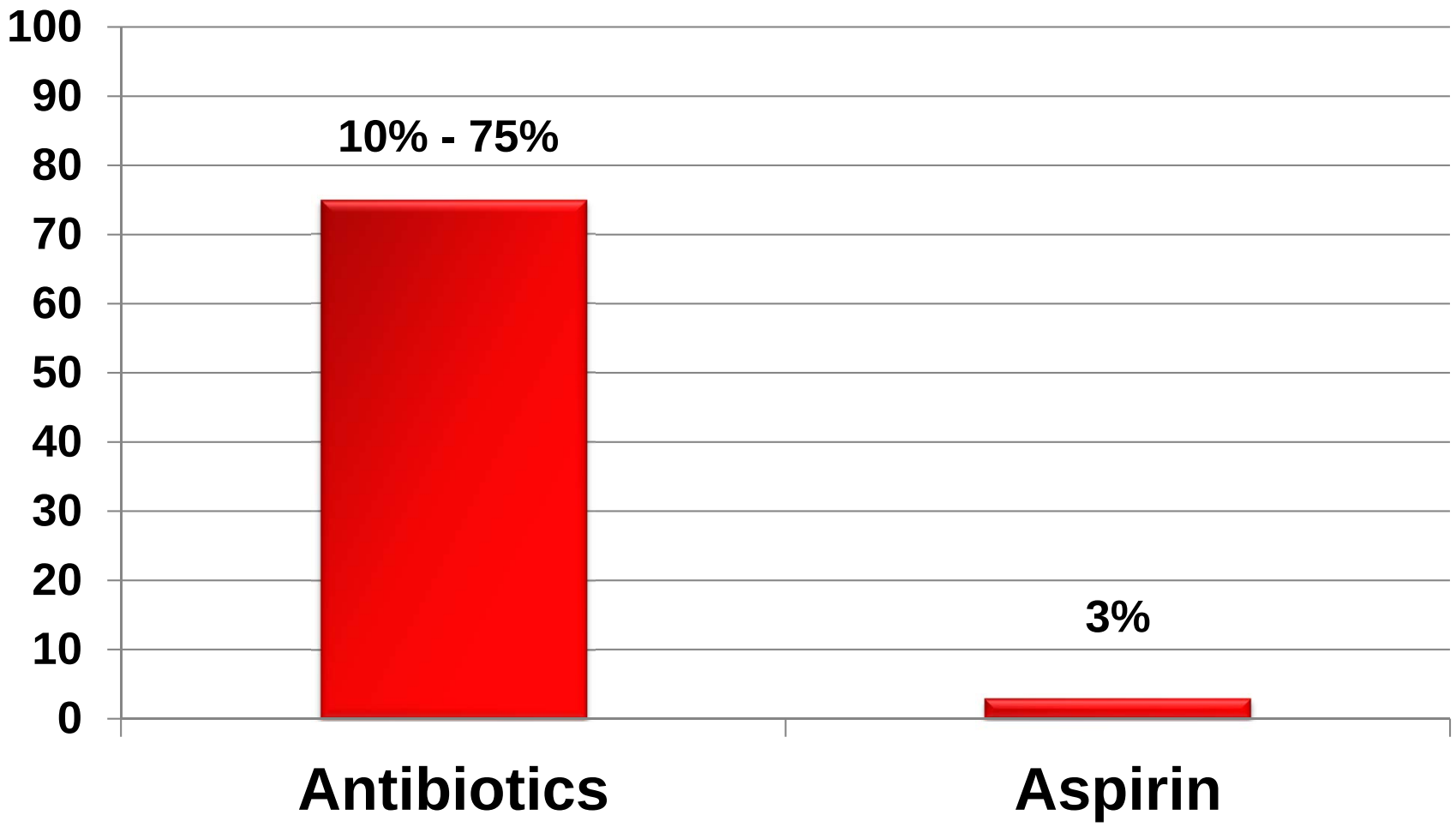

Thanks to PENICILLIN
...He Will Come Home!

Antibiotics Save Lives



1IDSA Position Paper '08 Clin Infect Dis 47(S3):S249-65; 2IDSA/ACCP/ATS/SCCM Position Paper '10 Clin Infect Dis In Press; 3Kerr AJ. Subacute Bacterial Endocarditis. Springfield IL: Charles C. Thomas, 1955 & Lancet 1935 226:383-4; 4Lancet '38 231:733-4 & Waring et al. '48 Am J Med 5:402-18; 5Spellberg et al. '09 Clin Infect Dis 49:383-91 & Madsen '73 Infection 1:76-81; 6'88 Lancet 2:349-60

Impact on Mortality Reduction



UCLA Health

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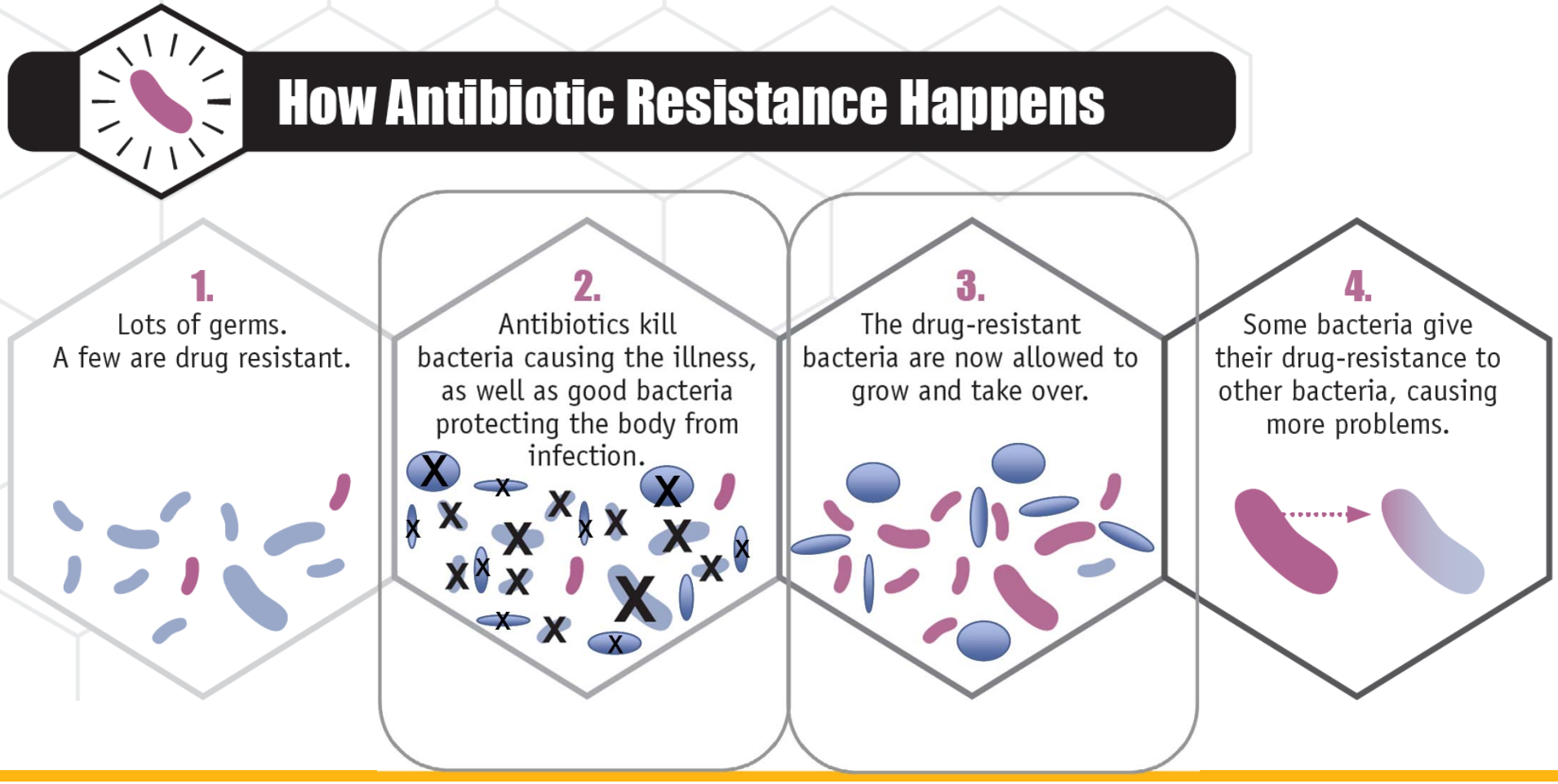
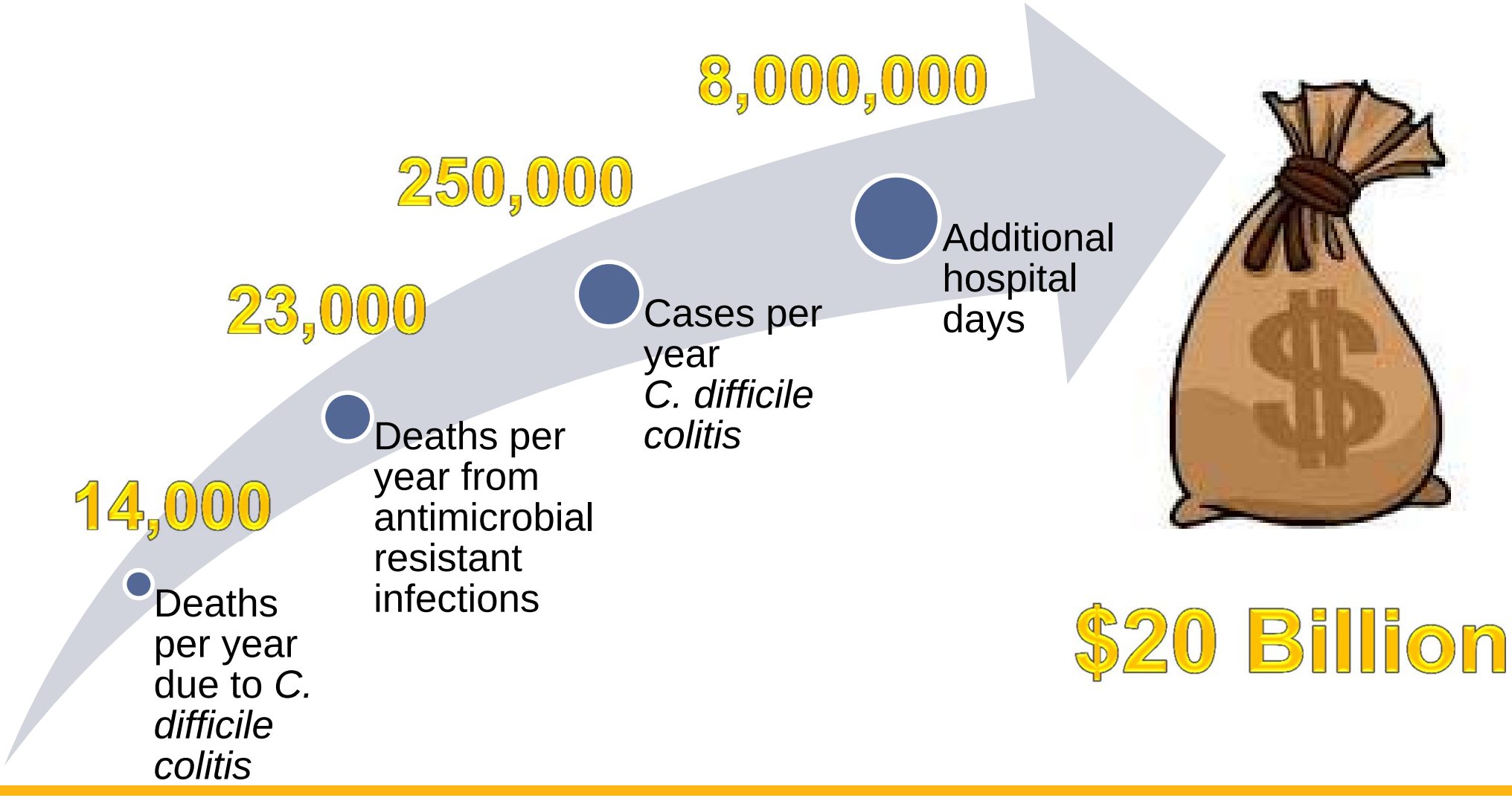
But Using Antibiotics Drives Bacterial Resistance



http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf#page=15

The Cost of Antimicrobial Resistance



CDC, Get Smart Nov 17, 2010
http://www.cdc.gov/getsmart/healthcare/resources/factsheets/pdf/antibiotic-use.pdf

What else could one buy for $20 Billion?

http://list25.com/25-things-facebook-could-buy-with-19-billion-instead-of-whatsapp/

Antimicrobial Resistance: Increases Mortality and Increases Costs

Organism	Increased risk of death (OR)	Attributable LOS (days)	Attributable cost
MRSA bacteremia	1.9	2.2	$6,916
MRSA surgical infection	3.4	2.6	$13,901
VRE infection	2.1	6.2	$12,766
Resistant Pseudomonas infection	3.0	5.7	$11,981
Resistant Enterobacter infection	5.0	9	$29,379

Cosgrove SE. *Clin Infect Dis*. 2006; 42:S82-9.

Who is Responsible for Antimicrobial Resistance?

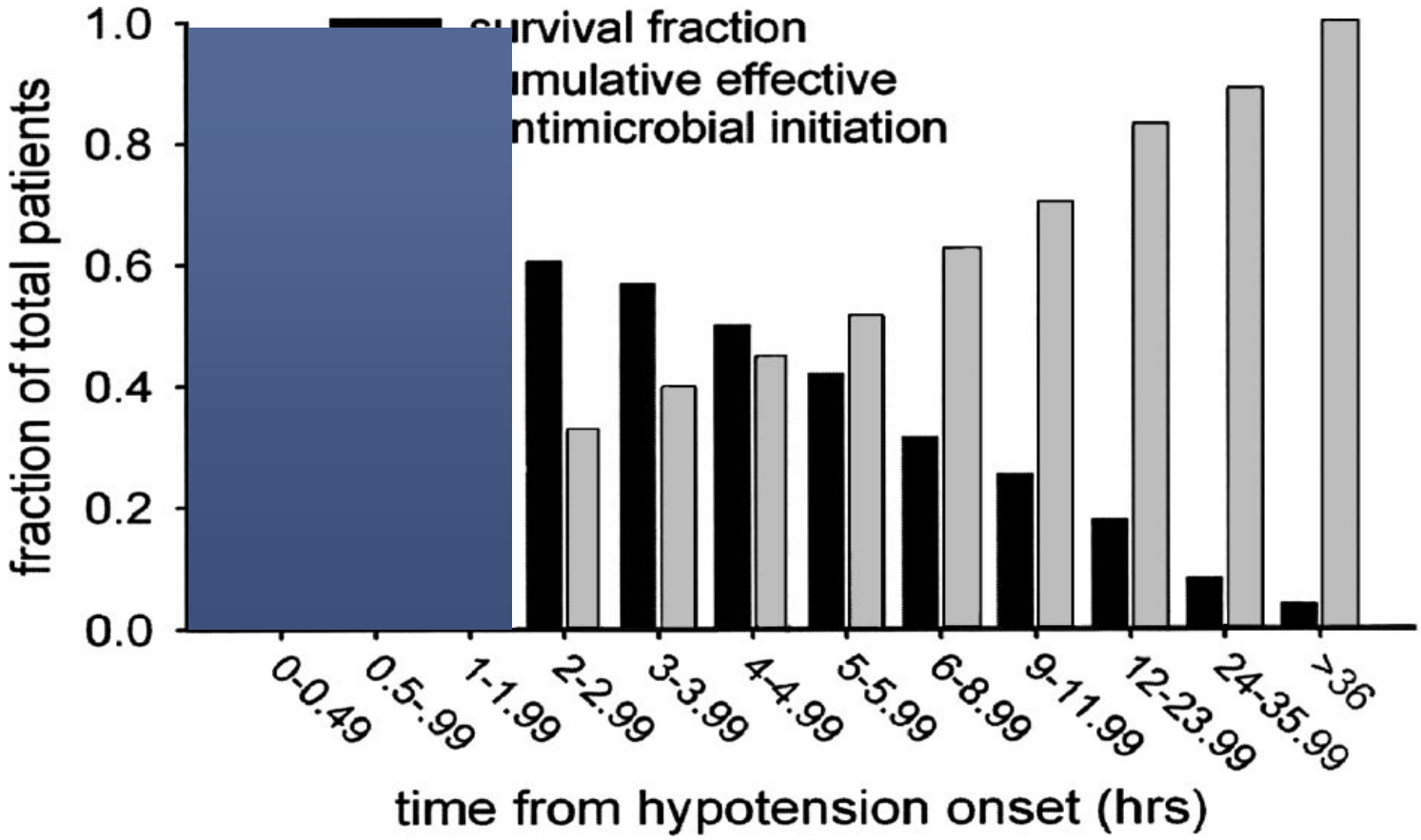
"…Microbes are educated to resist penicillin…which can be passed to other individuals…until they reach someone who gets a septicemia or a pneumonia which penicillin cannot save. In such a case the thoughtless person playing with penicillin treatment is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope the evil can be averted."

-Sir Alexander Fleming, 1946

Clinical Infectious Diseases 2013;56(10):1445–50

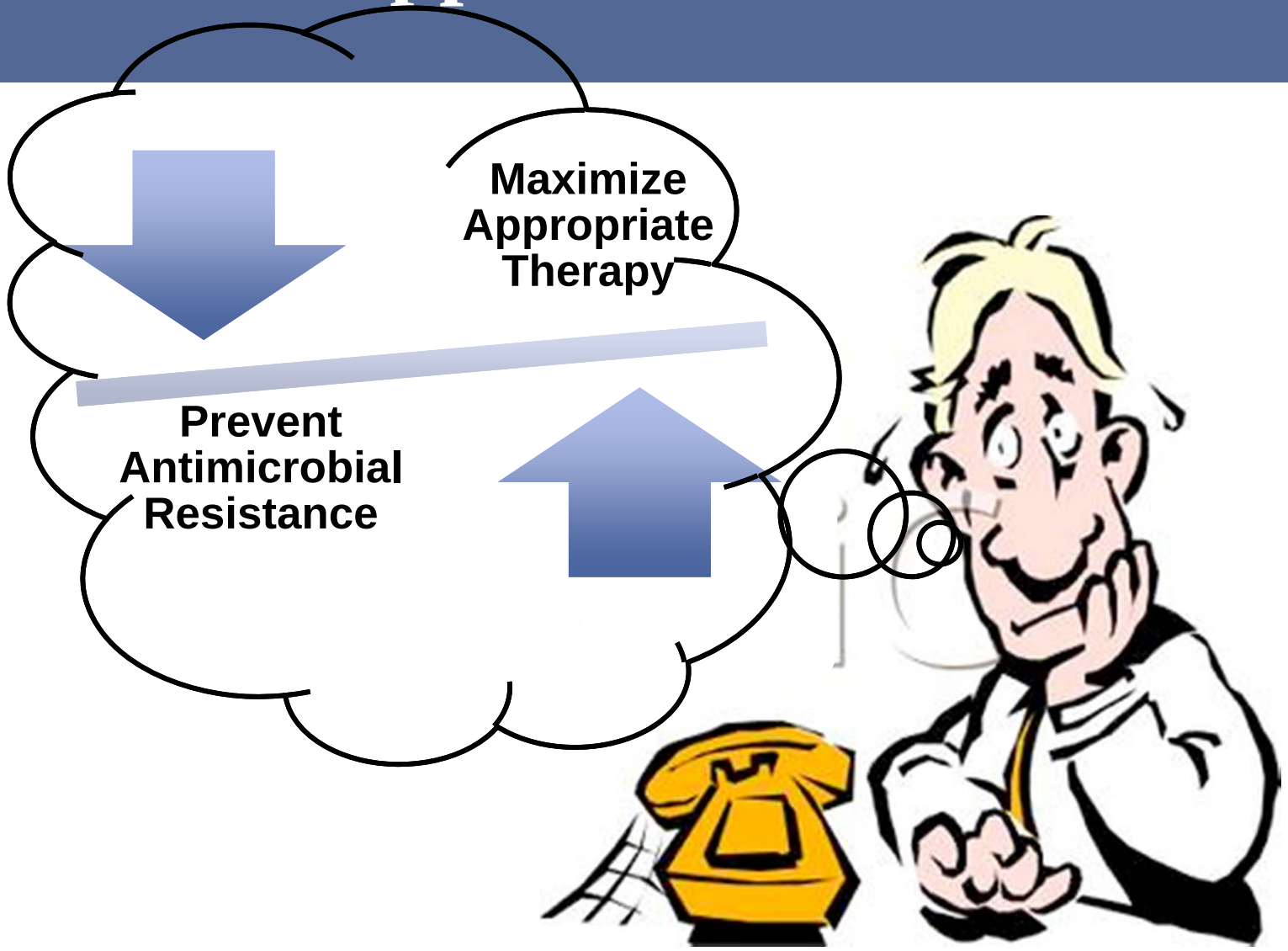
But in Our Defense…

- Timing of the first antibiotic dose matters!

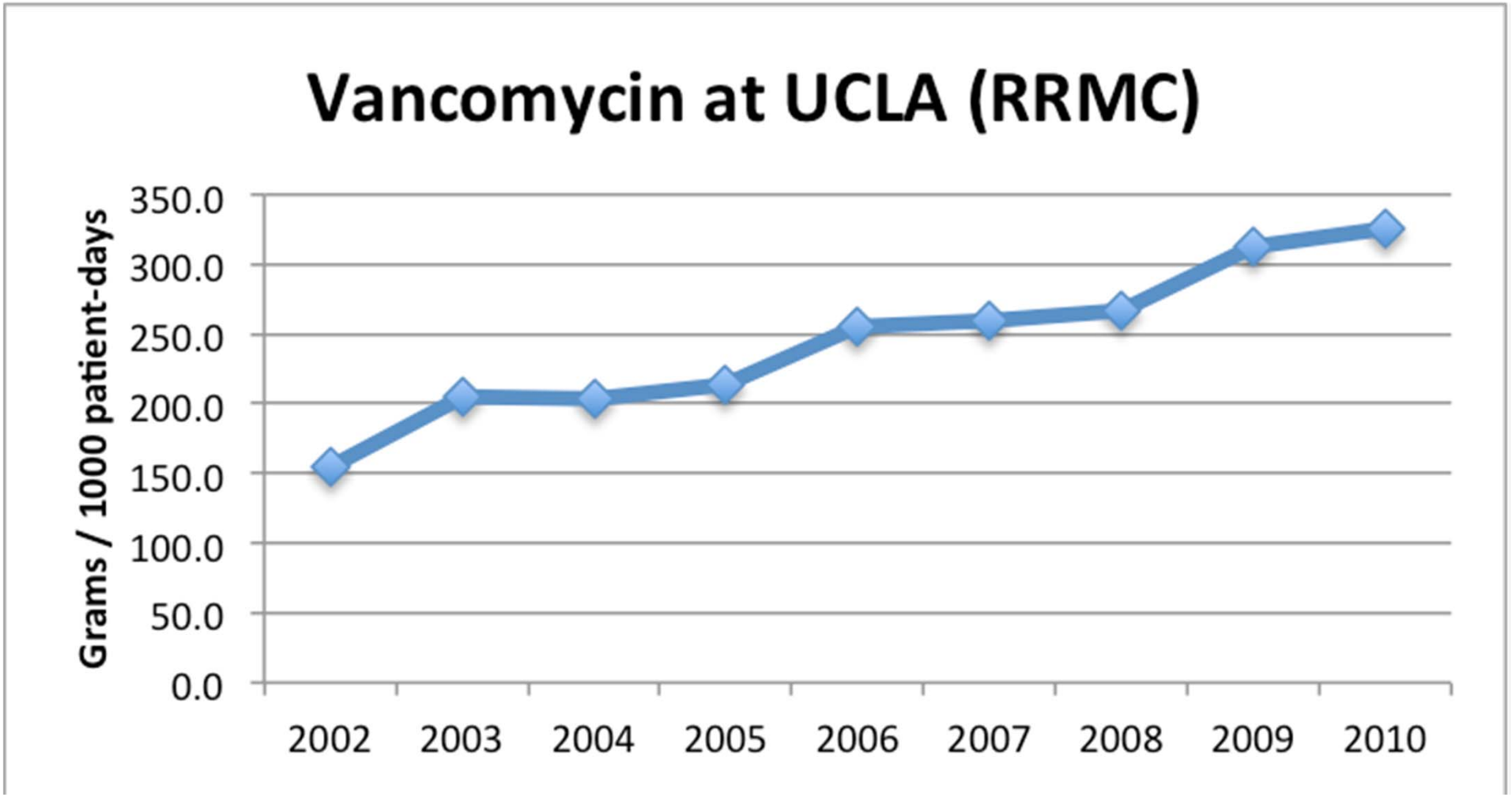


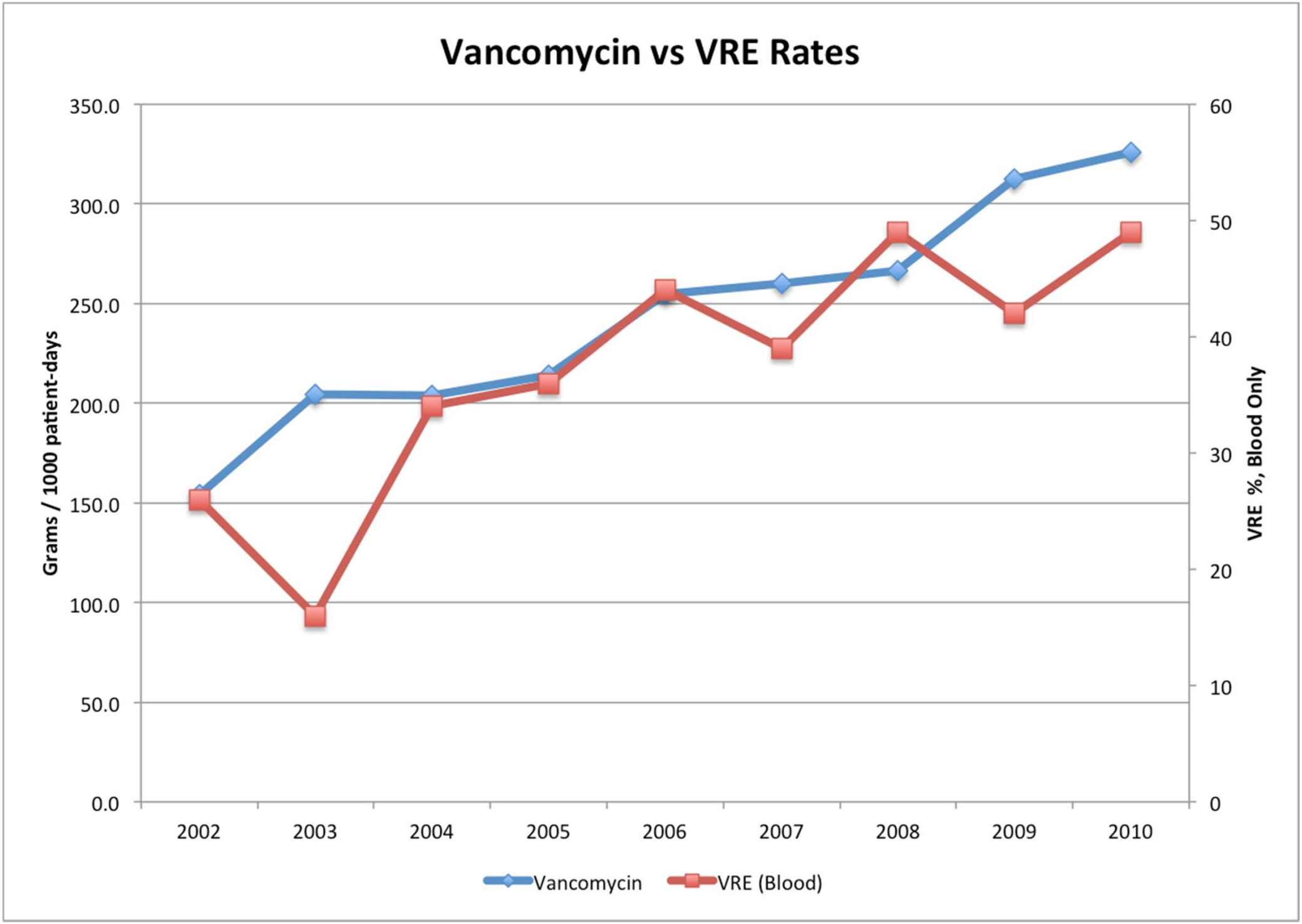
Kumar A, et al. *Crit Care Med*. 2006;34:1589-1596

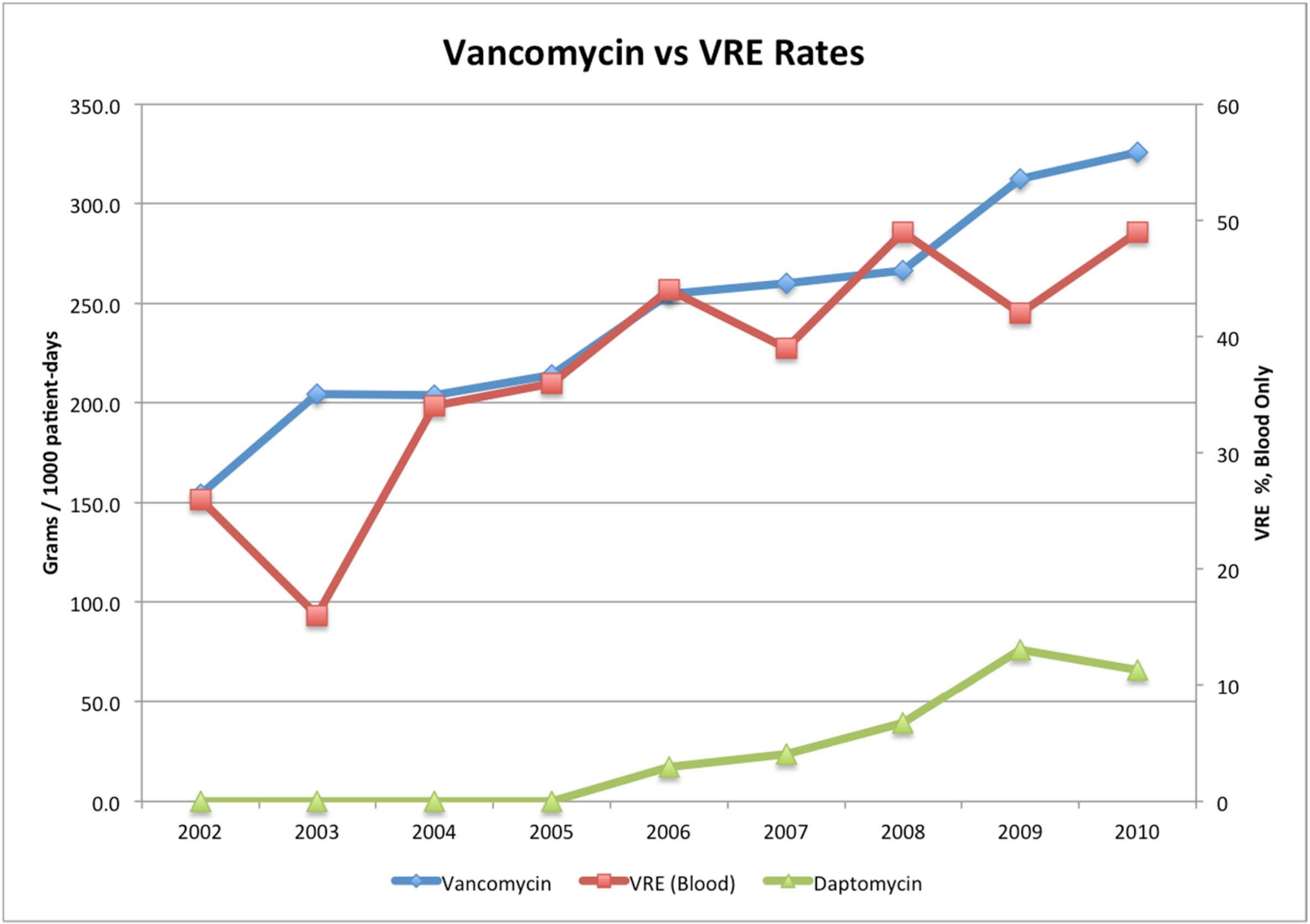
What Are We Supposed to Do?



The Situation at UCLA




Vancomycin vs VRE Rates
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
Grams / 1000 patient-days
60
50
40
30
20
10
0
VRE %, Blood Only
2002
2003
2004
2005
2006
2007
2008
2009
2010
Vancomycin
VRE (Blood)


Vancomycin vs VRE Rates
Grams / 1000 patient-days
VRE %, Blood Only
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
60
50
40
30
20
10
0
2002
2003
2004
2005
2006
2007
2008
2009
2010
Vancomycin
VRE (Blood)
Daptomycin

INVITED ARTICLE ANTIMICROBIAL RESISTANCE

George M. Eliopoulous, Section Editor

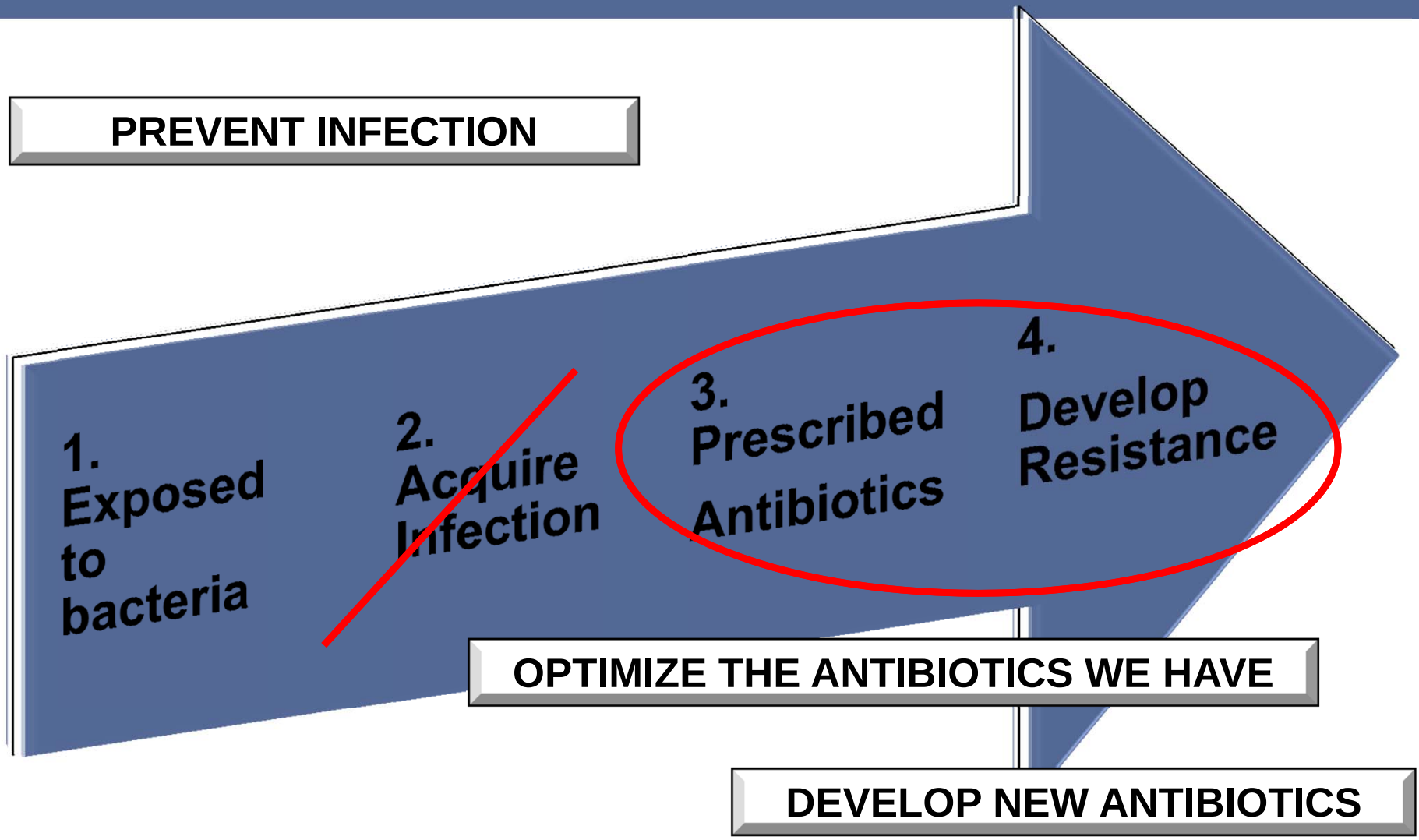
Daptomycin Nonsusceptible Enterococci: An Emerging Challenge for Clinicians

Theodoros Kelesidis,[1] Romney Humphries,[2] Daniel Z. Uslan,[1] and David A. Pegues[1]

[1]Department of Medicine, Division of Infectious Diseases, and [2]Department of Pathology and Laboratory Medicine, David Geffen School of Medicine at UCLA, Los Angeles, California

Daptomycin is the only antibiotic with in vitro bactericidal activity against vancomycin-resistant Enterococcus (VRE) that is approved by the Food and Drug Administration (FDA). Data on the potential emergence of daptomycin nonsusceptibility among enterococci remain limited. We systematically reviewed the published literature for reports of isolates of enterococci that were daptomycin nonsusceptible and assessed the clinical significance and outcome of therapy. Based on susceptibility breakpoints approved by the Clinical Laboratory Standards Institute (CLSI), daptomycin has in vitro activity against >90% of enterococcal isolates. Less than 2% of enterococcal isolates were daptomycin nonsusceptible, with minimum inhibitory concentrations (MICs) >4 μg/mL. The prevalence of nonsusceptibility of VRE isolates to daptomycin may be overestimated due to the spread of clonally related isolates in health care settings. Clinicians should be aware of the possibility of the emergence of daptomycin nonsusceptibility and should closely monitor daptomycin MICs of enterococci isolated during treatment.

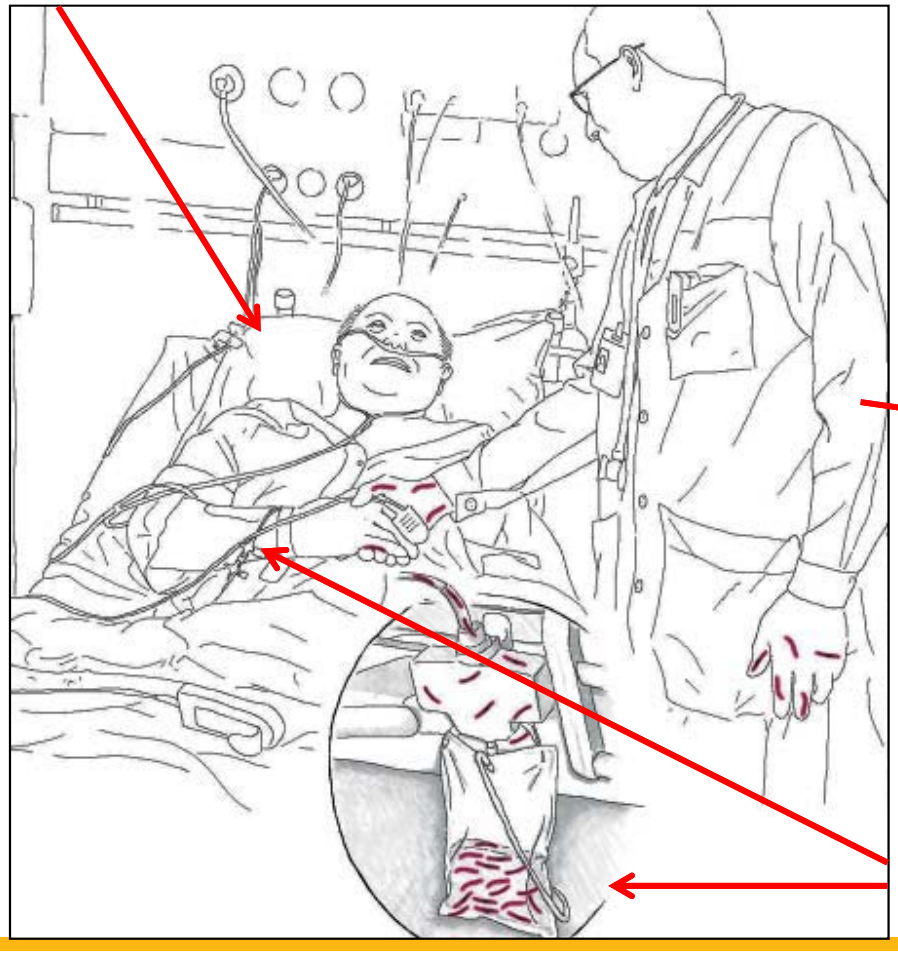
How Do We Combat Resistance?



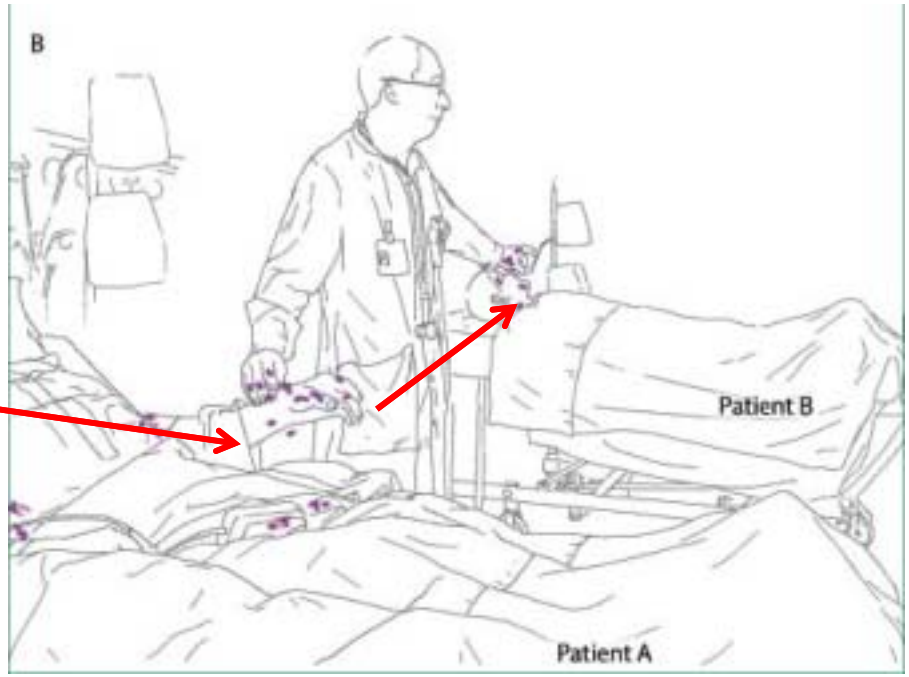
Prevent Infection

1. 2. 3. 4.

Elevate head of bed



Hand washing

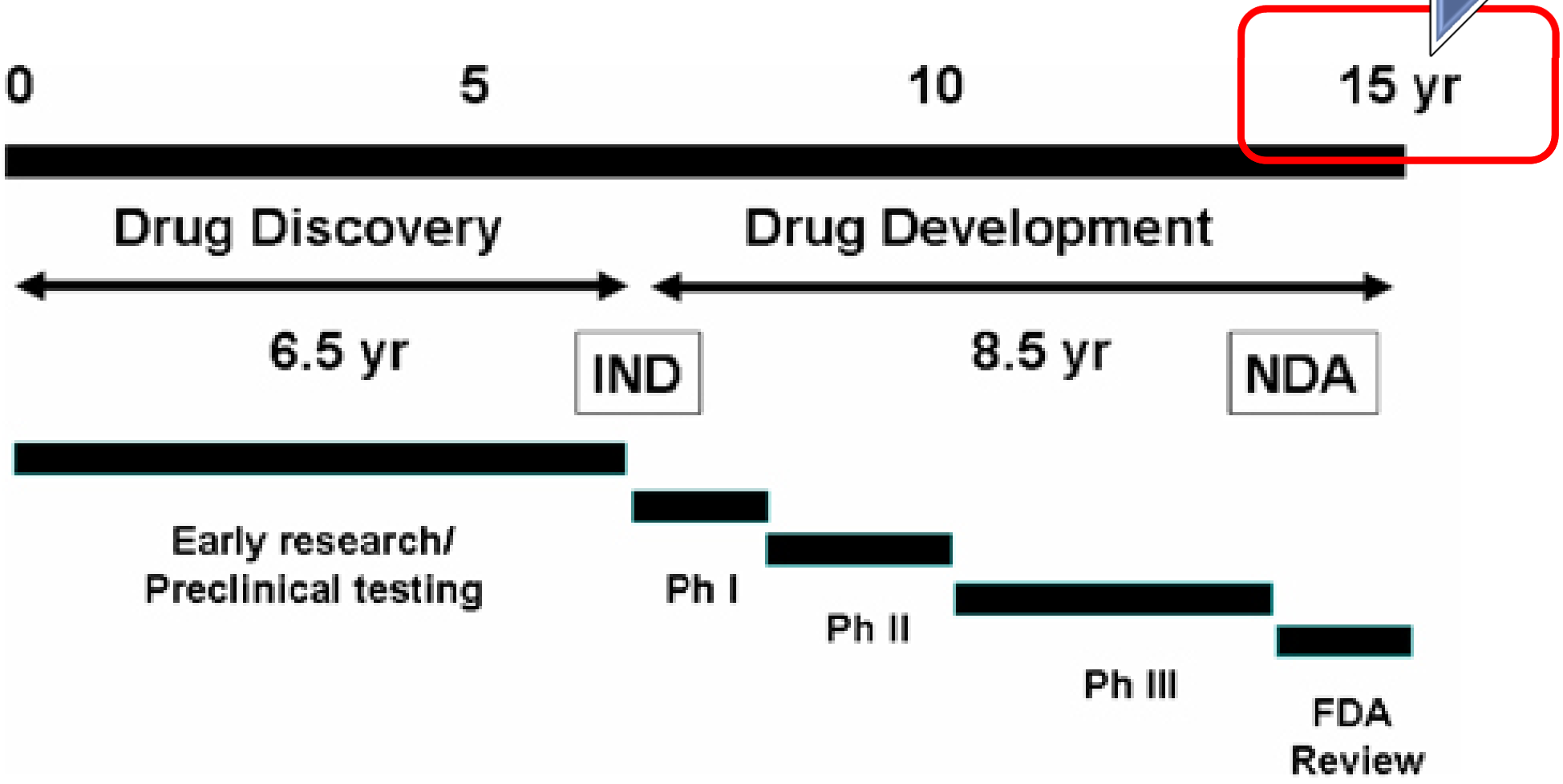


Reduce portals of entry

Lancet ID. 2006;6:641-52.

Develop New Antibiotics

1. 2. 3. 4.



http://www.palgrave-journals.com/jcb/journal/v15/n3/fig_tab/jcb200836f1.html

Challenges for Antimicrobial Research and Development

- **Smaller market:**
  - **Antibiotics work well and fast (days – weeks)**
  - **Compared with chronic, long-term conditions or lifestyle issues (months – years)**
- **Limited long-term potential:**
  - **bacteria will become resistant**

Challenges for Antimicrobial Research and Development

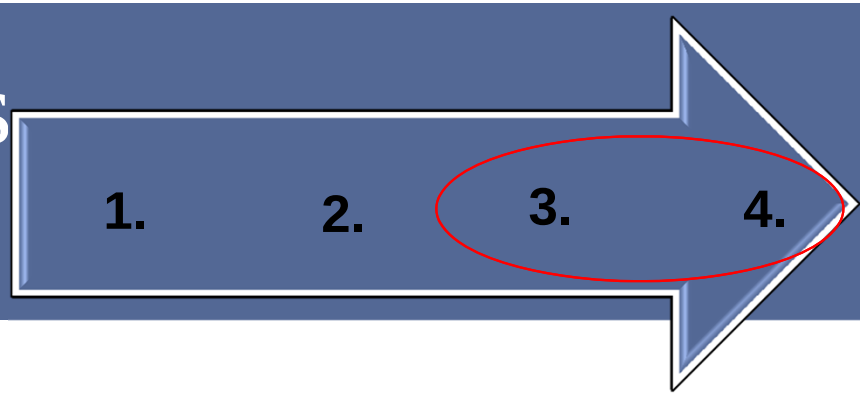
Cardiologists:

“Here’s a new drug—everyone use it!”

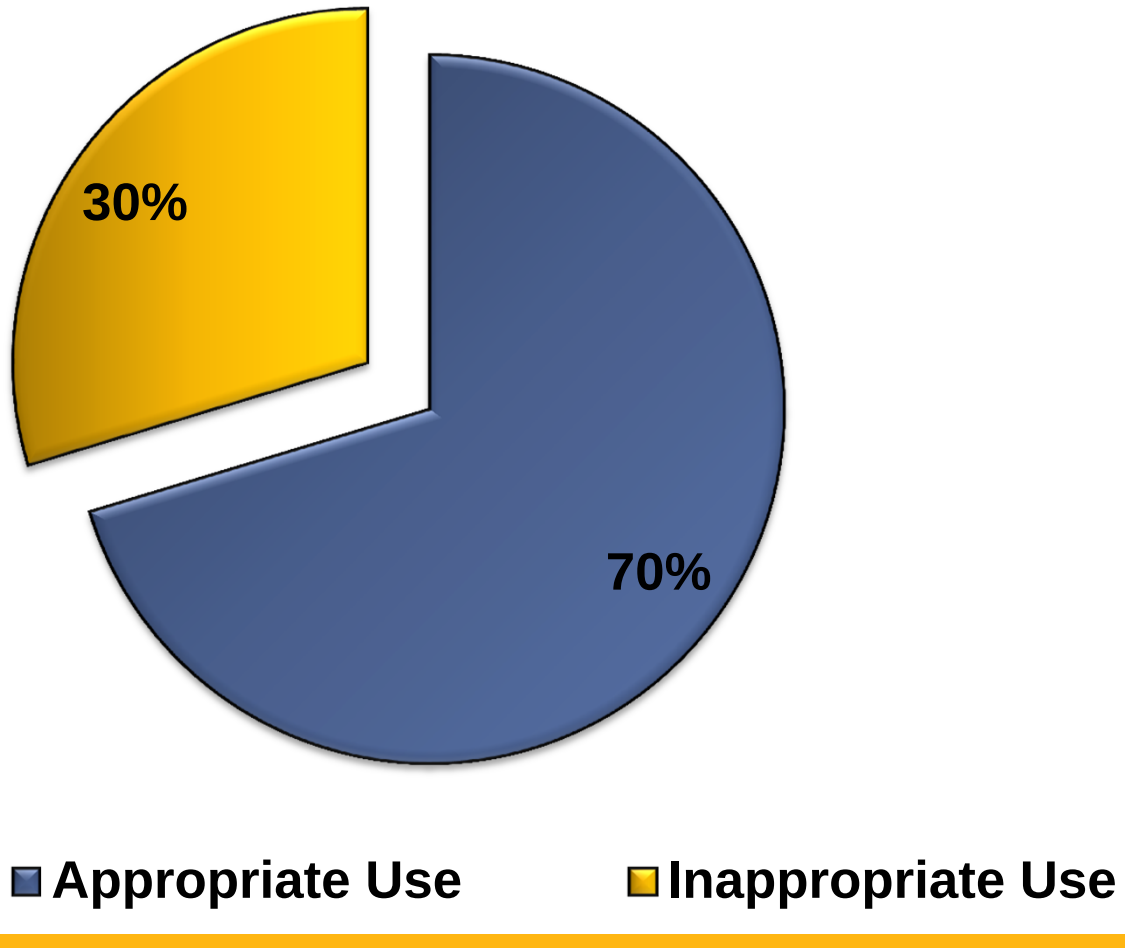
ID:

“Here’s a new drug—no one use it!”

Optimize Current Antibiotics
Identify scope of the Problem

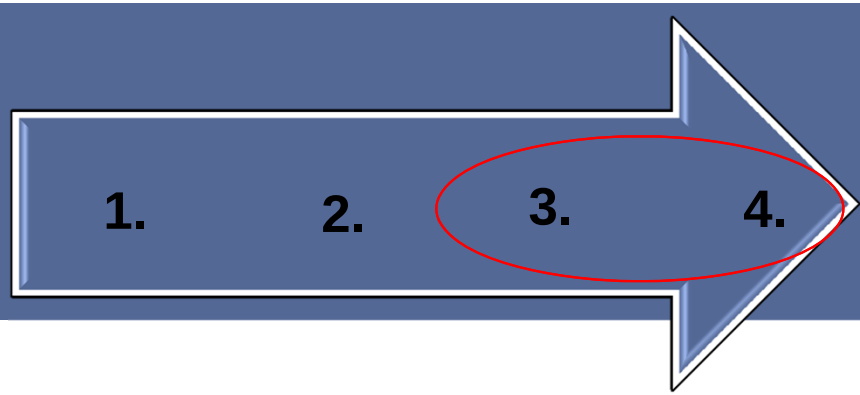


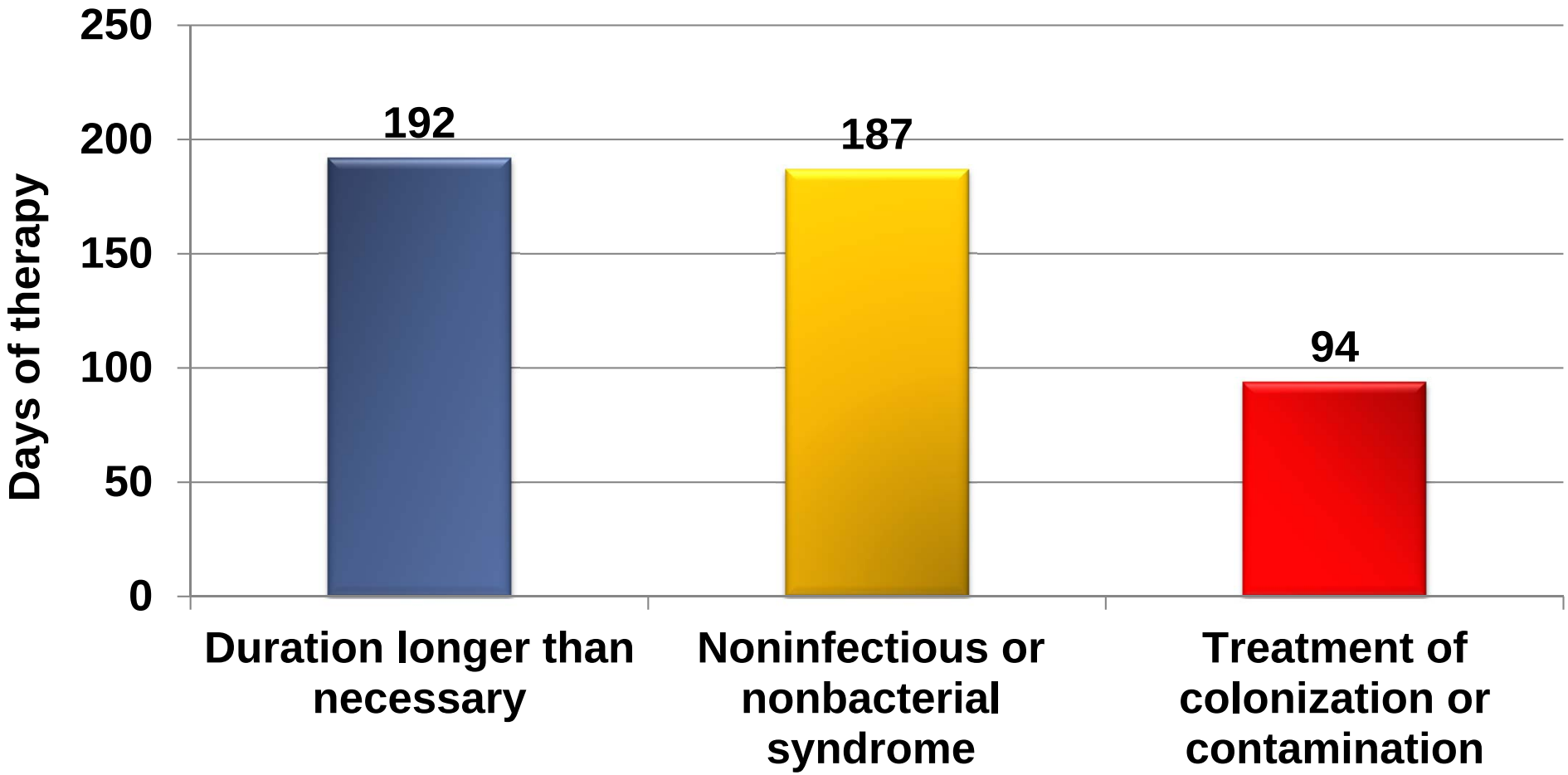
N = 1941 days of antimicrobial therapy



Hecker MT et al. Arch Intern Med 2003;163:972-978

Optimizing the Antibiotics: Address overuse





Hecker MT et al. Arch Intern Med 2003;163:972-978

California Senate Bill 739

SECTION 1. (a) The Legislature finds and declares all of the following:

- **(1) Health care facilities across the nation have seen a steady increase in the risk of healthcare associated infection (HAI) during recent decades.**
- **(2) According to published estimates, approximately 5 to 10 percent of**

January 1, 2008
This bill would establish the
Hospital Infectious Disease Control Program

and surgical site infections account for more than 80 percent of all HAI.

- **(4) Approximately 25 percent of HAI cases occur among patients in intensive care units, and two-thirds of those cases are linked to antimicrobial resistance.**
- **(5) Conservative estimates indicate that approximately 240,000 patients admitted to California hospitals each year develop HAI, which results in an estimated cost of $3.1 billion to the state.**

Stewardship at UCLA Medical Center

JENNIFER CURELLO, PHARM.D.

Antimicrobial stewardship program (ASP)

The mission of the antimicrobial stewardship program is to *optimize clinical outcomes* of antimicrobial use in patients across the UCLA Health System.

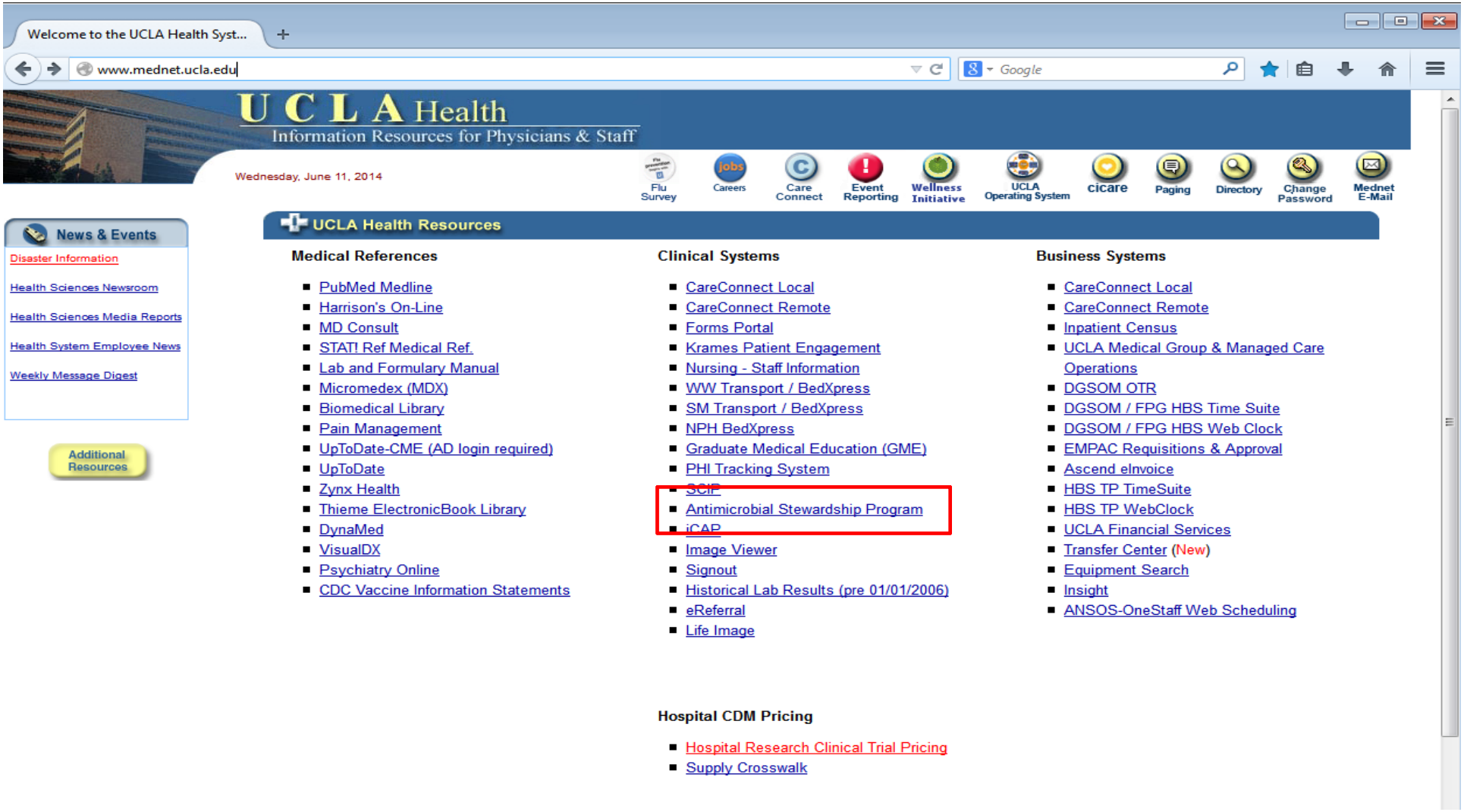
- Optimal antimicrobial selection, dose, route, & duration
- Maximize efficacy while minimizing drug related-toxicity
- Minimize emergence of resistance
- Minimize risk of unintentional consequences of antimicrobial use

Our team

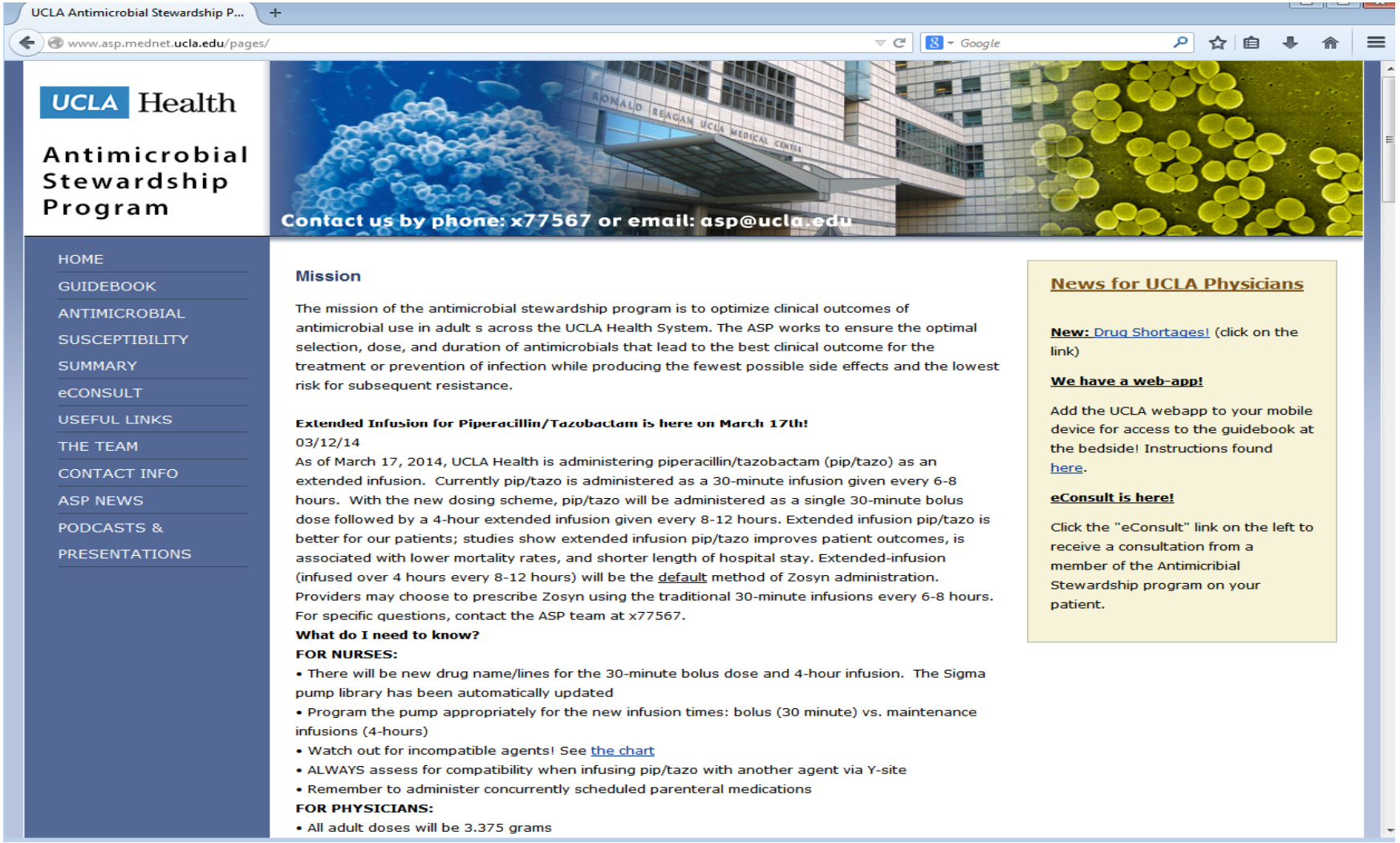
- Physicians champions
  - Dan Uslan, MD, Program Director
  - Lynn Ramirez, MD (Pediatrics)
- Clinical pharmacists
  - Jennifer Curello, PharmD (RRUMC)
  - Meganne Kanatani, PharmD (RRUMC)
  - Zahra Kassamali, PharmD (Santa Monica)
- Project manager
  - Brandy Bryant, MPH (Quality)
- Clinical Microbiology
  - Romney Humphries, PhD

From left to right: Daniel Uslan, MD, Director; Brandy Bryant, MPH, Project Manager; Meganne Kanatani, PharmD, ID Pharmacist.
Not Pictured: Zahra Kassamali, PharmD; Jen Curello, PharmD, Romney Humphries, PhD

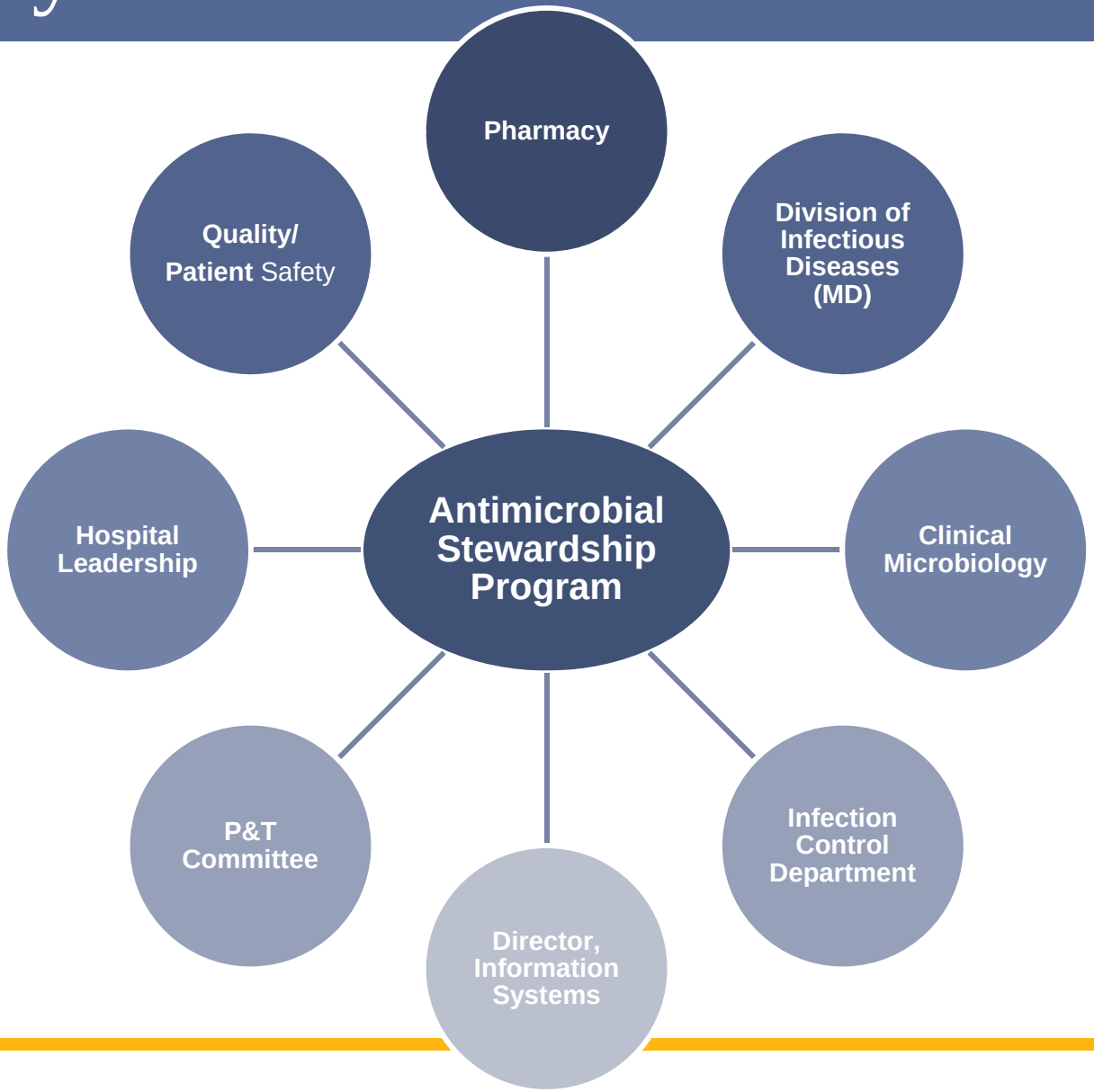
ASP website


Welcome to the UCLA Health Syst...
www.mednet.ucla.edu
Google
UCLA Health
Information Resources for Physicians & Staff
Wednesday, June 11, 2014
Flu Survey
Careers
Care Connect
Event Reporting
Wellness Initiative
UCLA Operating System
cicare
Paging
Directory
Change Password
Mednet E-Mail
News & Events
Disaster Information
Health Sciences Newsroom
Health Sciences Media Reports
Health System Employee News
Weekly Message Digest
Additional Resources
UCLA Health Resources
Medical References
PubMed Medline
Harrison's On-Line
MD Consult
STAT! Ref Medical Ref.
Lab and Formulary Manual
Micromedex (MDX)
Biomedical Library
Pain Management
UpToDate-CME (AD login required)
UpToDate
Zynx Health
Thieme ElectronicBook Library
DynaMed
VisualDX
Psychiatry Online
CDC Vaccine Information Statements
Clinical Systems
CareConnect Local
CareConnect Remote
Forms Portal
Krames Patient Engagement
Nursing - Staff Information
WW Transport / BedXpress
SM Transport / BedXpress
NPH BedXpress
Graduate Medical Education (GME)
PHI Tracking System
SCIP
Antimicrobial Stewardship Program
iCAP
Image Viewer
Signout
Historical Lab Results (pre 01/01/2006)
eReferral
Life Image
Business Systems
CareConnect Local
CareConnect Remote
Inpatient Census
UCLA Medical Group & Managed Care Operations
DGSOM OTR
DGSOM / FPG HBS Time Suite
DGSOM / FPG HBS Web Clock
EMPAC Requisitions & Approval
Ascend eInvoice
HBS TP TimeSuite
HBS TP WebClock
UCLA Financial Services
Transfer Center (New)
Equipment Search
Insight
ANSOS-OneStaff Web Scheduling
Hospital CDM Pricing
Hospital Research Clinical Trial Pricing
Supply Crosswalk

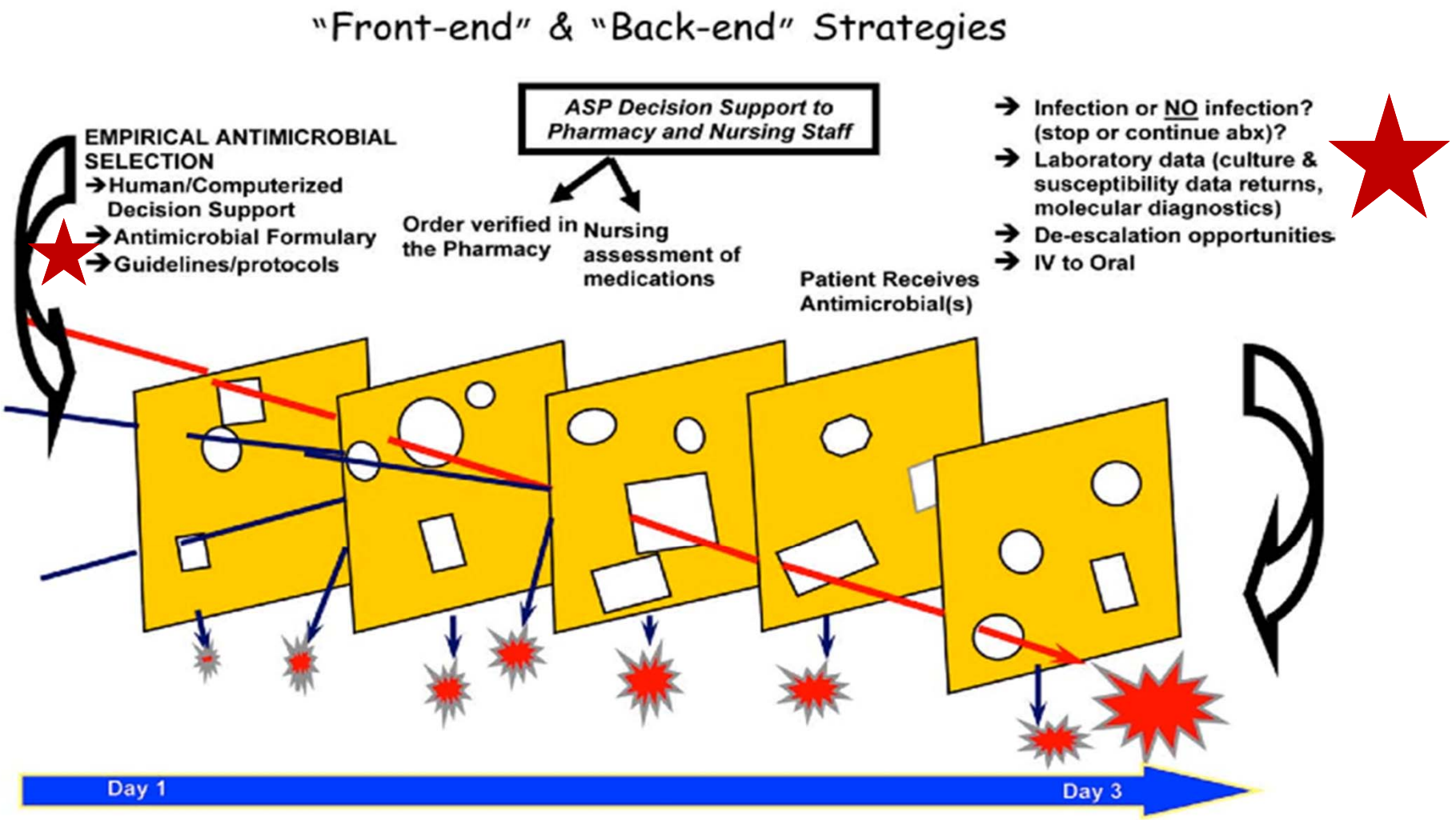
ASP Website


UCLA Antimicrobial Stewardship P...
www.asp.mednet.ucla.edu/pages/
Google
UCLA Health
Antimicrobial Stewardship Program
Contact us by phone: x77567 or email: asp@ucla.edu
HOME
GUIDEBOOK
ANTIMICROBIAL SUSCEPTIBILITY SUMMARY
eCONSULT
USEFUL LINKS
THE TEAM
CONTACT INFO
ASP NEWS
PODCASTS & PRESENTATIONS
Mission
The mission of the antimicrobial stewardship program is to optimize clinical outcomes of antimicrobial use in adult s across the UCLA Health System. The ASP works to ensure the optimal selection, dose, and duration of antimicrobials that lead to the best clinical outcome for the treatment or prevention of infection while producing the fewest possible side effects and the lowest risk for subsequent resistance.
Extended Infusion for Piperacillin/Tazobactam is here on March 17th!
03/12/14
As of March 17, 2014, UCLA Health is administering piperacillin/tazobactam (pip/tazo) as an extended infusion. Currently pip/tazo is administered as a 30-minute infusion given every 6-8 hours. With the new dosing scheme, pip/tazo will be administered as a single 30-minute bolus dose followed by a 4-hour extended infusion given every 8-12 hours. Extended infusion pip/tazo is better for our patients; studies show extended infusion pip/tazo improves patient outcomes, is associated with lower mortality rates, and shorter length of hospital stay. Extended-infusion (infused over 4 hours every 8-12 hours) will be the default method of Zosyn administration. Providers may choose to prescribe Zosyn using the traditional 30-minute infusions every 6-8 hours. For specific questions, contact the ASP team at x77567.
What do I need to know?
FOR NURSES:
• There will be new drug name/lines for the 30-minute bolus dose and 4-hour infusion. The Sigma pump library has been automatically updated
• Program the pump appropriately for the new infusion times: bolus (30 minute) vs. maintenance infusions (4-hours)
• Watch out for incompatible agents! See the chart
• ALWAYS assess for compatibility when infusing pip/tazo with another agent via Y-site
• Remember to administer concurrently scheduled parenteral medications
FOR PHYSICIANS:
• All adult doses will be 3.375 grams
News for UCLA Physicians
New: Drug Shortages! (click on the link)
We have a web-app!
Add the UCLA webapp to your mobile device for access to the guidebook at the bedside! Instructions found here.
eConsult is here!
Click the "eConsult" link on the left to receive a consultation from a member of the Antimicribial Stewardship program on your patient.

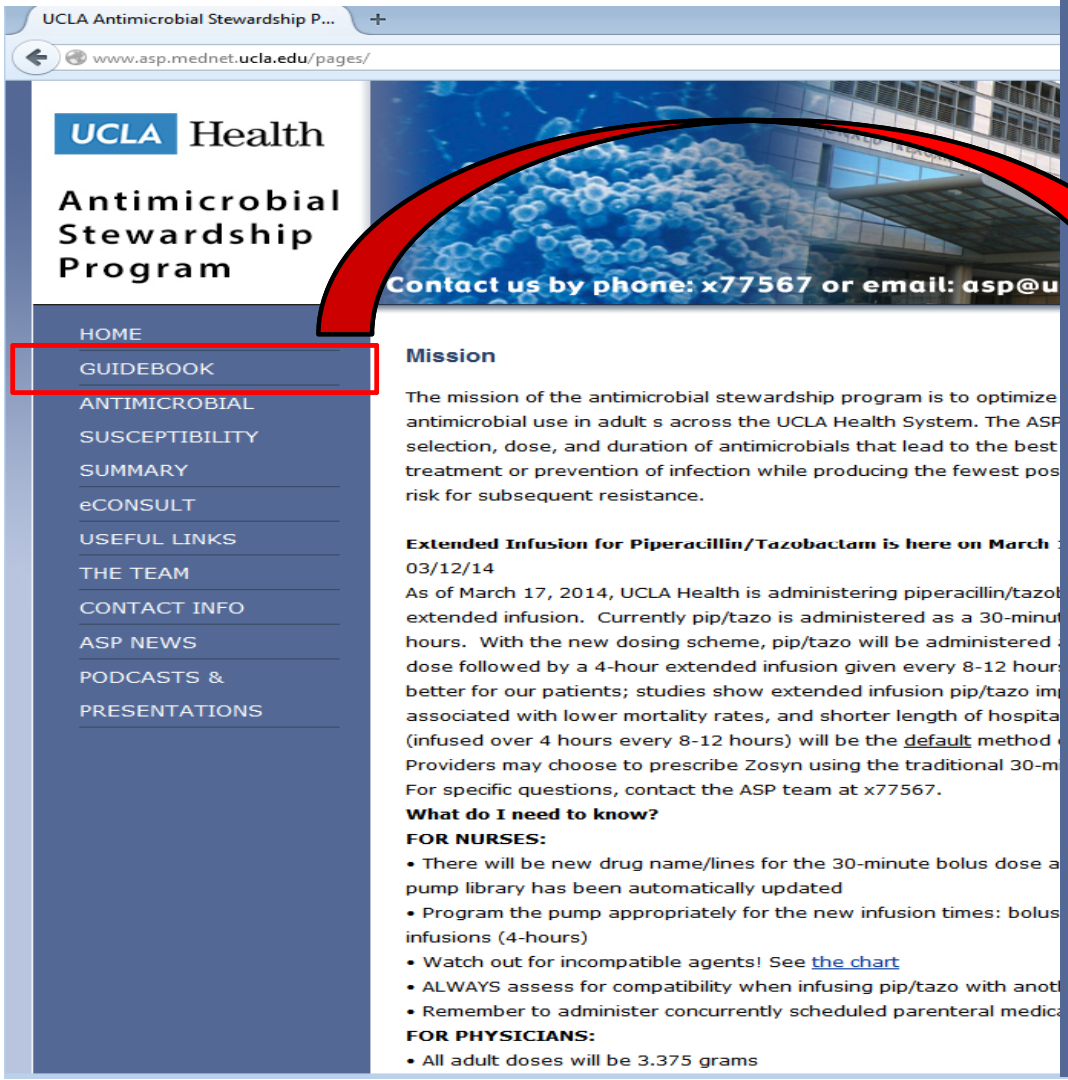
Key players


Pharmacy
Quality/ Patient Safety
Division of Infectious Diseases (MD)
Hospital Leadership
Antimicrobial Stewardship Program
Clinical Microbiology
P&T Committee
Director, Information Systems
Infection Control Department

Our strategies



Front-end strategies



Infectious Syndromes

Specific Treatment of Select Bacterial Organisms at UCLA

Clostridium Difficile

Central Nervous System Infections

Bloodstream Infections

- Central line-associated bloodstream infection (CLABSI)
- Coagulase-negative staphylococci (CoNS)
- Staphylococcus aureus
- Enterococcus faecalis
- Enterococcus faecium
- Gram-negative bacilli

Pulmonary Infections

- Community-acquired pneumonia in hospitalized patients
- Healthcare-associated Pneumonia (NOT ventilator-associated)
- Ventilator-associated Pneumonia (VAP)
- Seasonal Influenza Diagnosis and Management
- Tuberculosis (TB) Infection

Sepsis NOTE: For the Sepsis order set, click here

Skin and Soft Tissue Infections

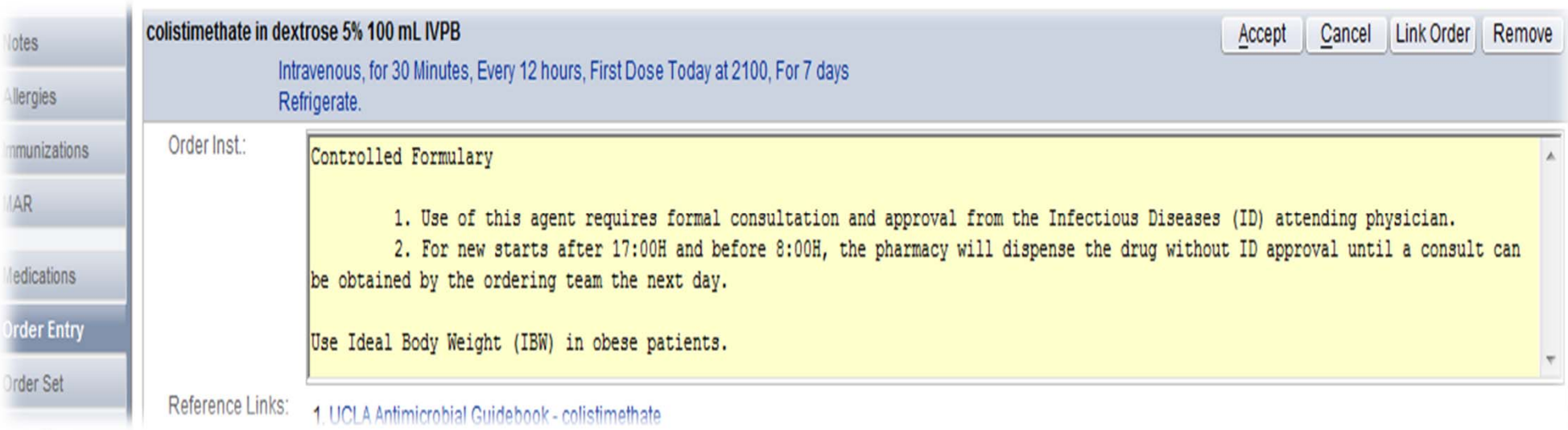
- Cellulitis
- Cutaneous Abscess
- Recurrent MRSA Skin Infections
- Diabetic Foot Infections
- Surgical Site Infections (SSI)
- Necrotizing Fasciitis

Urinary Tract Infections

- Non-catheter-associated UTI
- Catheter-associated UTI (CAUTI)

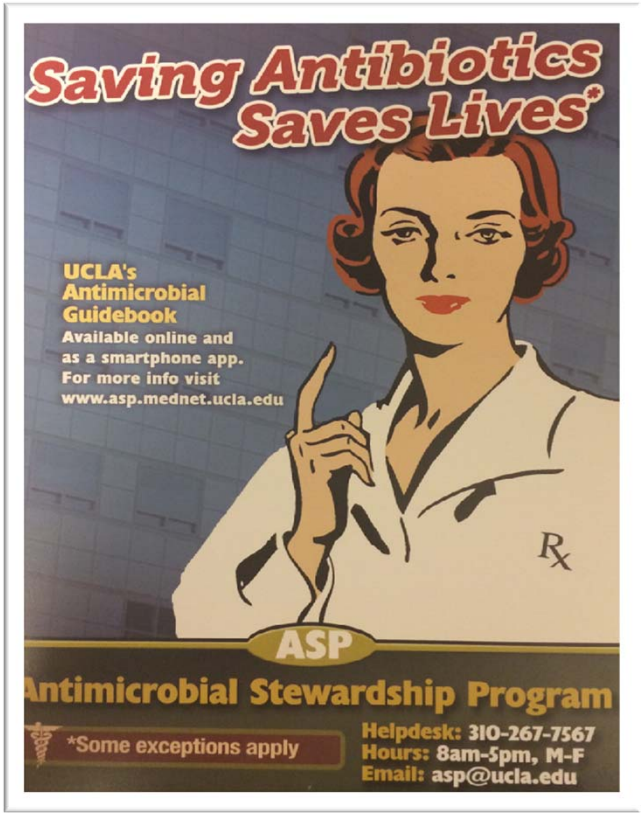
Front-end strategies

- Antimicrobial restriction
  - Colistin (Polymyxin E) now REQUIRES consultation by an infectious diseases specialist before it can be prescribed for any patient at UCLA (HS1444).

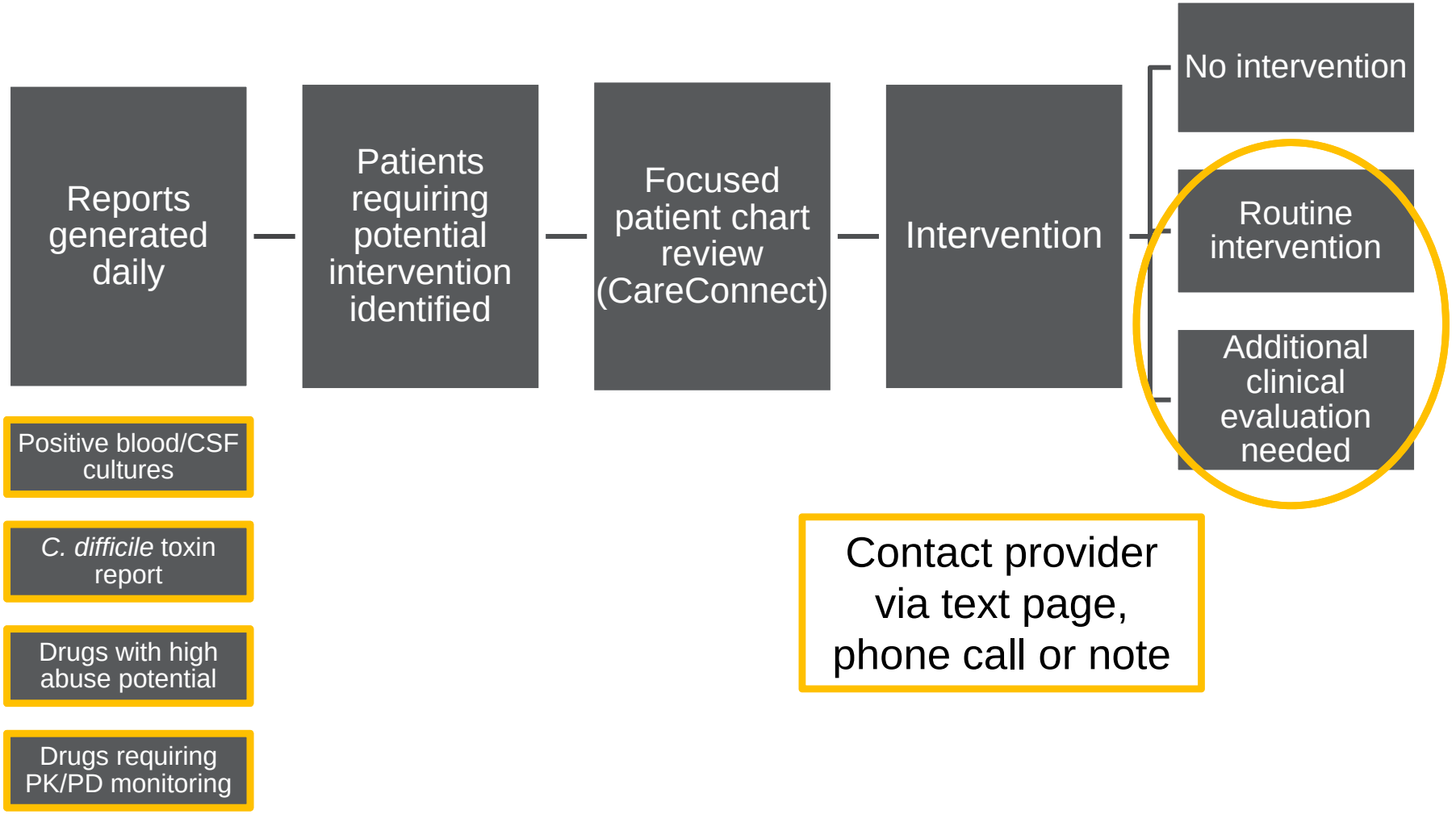


Back-end strategies

- **Targeted prospective audit with feedback**
  - Customized point-of-care feedback
    - Near real time
    - Non-putative
    - Educational opportunities
  - Education/marketing
  - Availability of expertise at the point of care
    - Antibiotic handbook/web app
    - Antibiotic hotline
  - Data monitoring and transparency

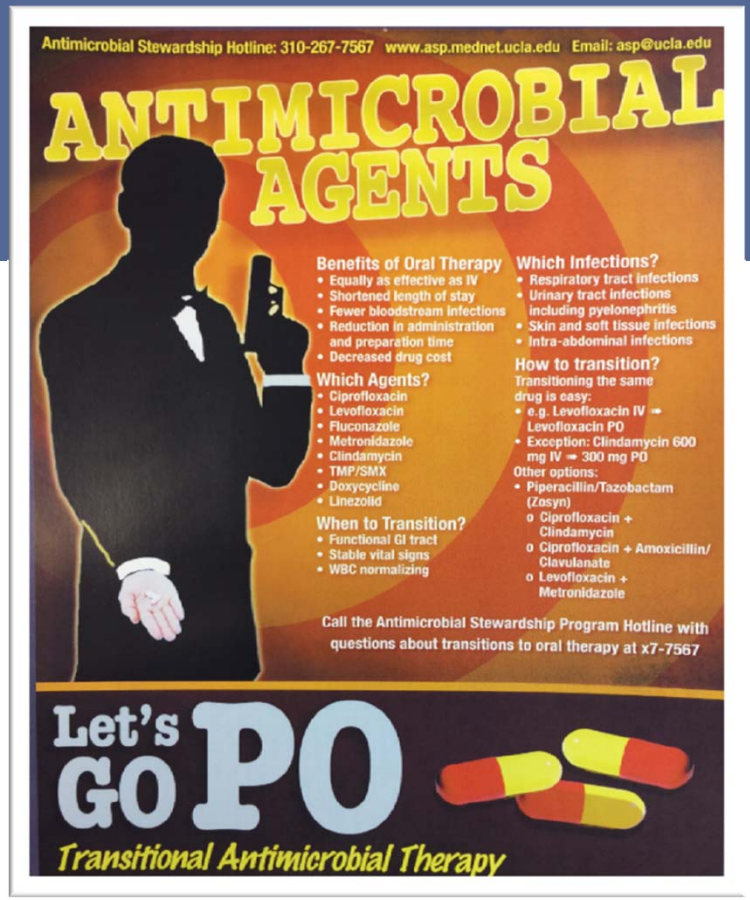


Daily audits



Interventions

- IV to PO conversion
- Antimicrobial regimen change
  - Streamline to avoid redundant coverage
  - Bug-drug mismatch
  - Assess appropriate duration
- Dose adjustments
  - Adjust for changes in renal or hepatic function
  - Optimization based on site of infection and pathogen MICs
- Drug-drug interaction modification
- Recommend obtaining infectious diseases consultation



MIC = minimum inhibitory concentration

Other endeavors

- Members of the ASP team are also members of the P&T Antimicrobial subcommittee, Infection Control committee, and Clinical Effectiveness committee
  - Enforce and develop policies of the institution sanctioned by the P&T committee
    - Formulary restriction
    - Pre-authorization policies
- Collaboration with Quality Management Program
  - Ensure compliance with the Surgical Care Improvement Project (SCIP)

SCIP Surgical Care Improvement Project
A National Quality Partnership

Other endeavors

- Collaboration with clinical microbiology
  - Antimicrobial susceptibility summary/antibiogram
    - http://www.asp.mednet.ucla.edu/pages/anti-suscep-summ

Table 5. RRUMC: Adults (>21 y.o.) Gram-negative Bacteria – Excludes Urine Isolates, % Susceptible

Organism	No. Isolates	Penicillins			Cephalosporins				Carbapenems			Aminoglycosides			Fluoroquin-olone	Other
		Ampicillin	Ampicillin-sulbactam	Piperacillin-tazobactam	Cefazolin	Cefepime	Ceftazidime	Ceftriaxone	Ertapenem	Imipenem	Meropenem	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin	Trimethoprim – sulfamethoxazole
Citrobacter freundii	43	R[1]	R[1]	65	R[1]	86	—	—	86	88	88	98	81	81	81	70
Enterobacter aerogenes	68	R[1]	R[1]	85	R[1]	99	—	—	97	91	99	100	100	100	100	99
Enterobacter cloacae	144	R[1]	R[1]	87	R[1]	97	—	—	92	99	99	99	97	97	97	89
Escherichia coli	368	36	41	89	70	81	80	80	99	99	99	99	79	82	56	58
Klebsiella oxytoca	76	R[1]	63	96	72	97	97	97	98	99	99	100	99	97	97	95
Klebsiella pneumoniae	235	R[1]	63	83	79	83	82	83	92	93	93	94	91	86	83	77
Morganella morganii[2]	28	R[1]	R[1]	99	R[1]	100	—	—	97	11	99	100	75	86	75	68
Proteus mirabilis	86	71	84	99	80	88	88	88	99	47	99	99	77	81	57	61
Serratia marcescens	102	R[1]	R[1]	97	R[1]	99	—	—	97	85	99	99	99	98	92	98
Acinetobacter baumannii	61	R[1]	48	36	R[1]	43	36	—	R[1]	51	48	62	51	56	43	48
Pseudomonas aeruginosa	452	R[1]	R[1]	83	R[1]	85	83	R[1]	R[1]	76	82	96	89	92	75	R[1]
Stenotrophomonas maltophilia	61	R[1]	R[1]	R[1]	R[1]		31	R[1]	R[1]	R[1]	R[1]	R[1]	R[1]	R[1]	—	97

12

Other endeavors

- Evidence-based review and implementation of novel antimicrobial dosing strategies
  - Extended infusion piperacillin/tazobactam (Zosyn®)

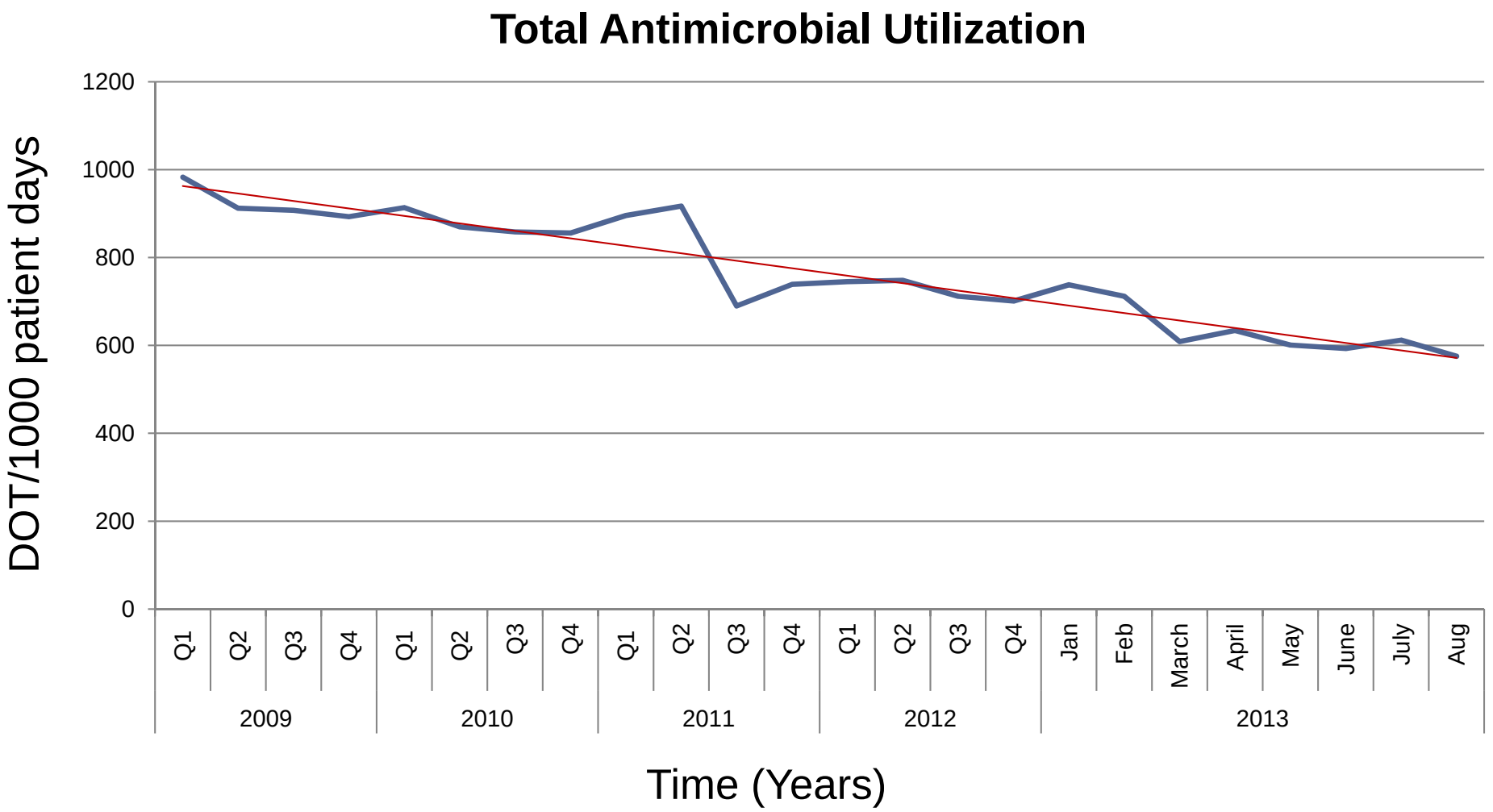
		L1	piperacillin-tazobactam 3.375g in dextrose 5% 50 ml IVPB	3.375 g	Intravenous	Every 8 hours @ 12.5 mL/hr over 4 Hours	6/12/2014 1000

- Collaboration with the sepsis work group & department of pharmaceutical services
  - Improve efficiency in delivery and administration of first dose antibiotics in patients with sepsis and septic shock
    - ALL first dose antibiotics are STAT!

Other endeavors

- Education
  - Housestaff lectures
  - Infectious disease fellows core curriculum
  - Daily rounds with the infectious disease consult service and critical care team
- Research
- Future directions
  - Bringing stewardship into the outpatient setting
    - Transition of care
      - Outpatient parenteral antibiotic therapy (OPAT) program
    - Skilled nursing facilities
  - Collaboration with clinical microbiology on rapid diagnostics

The impact of our ASP over time



DOT = days of therapy

What can I do to help?...

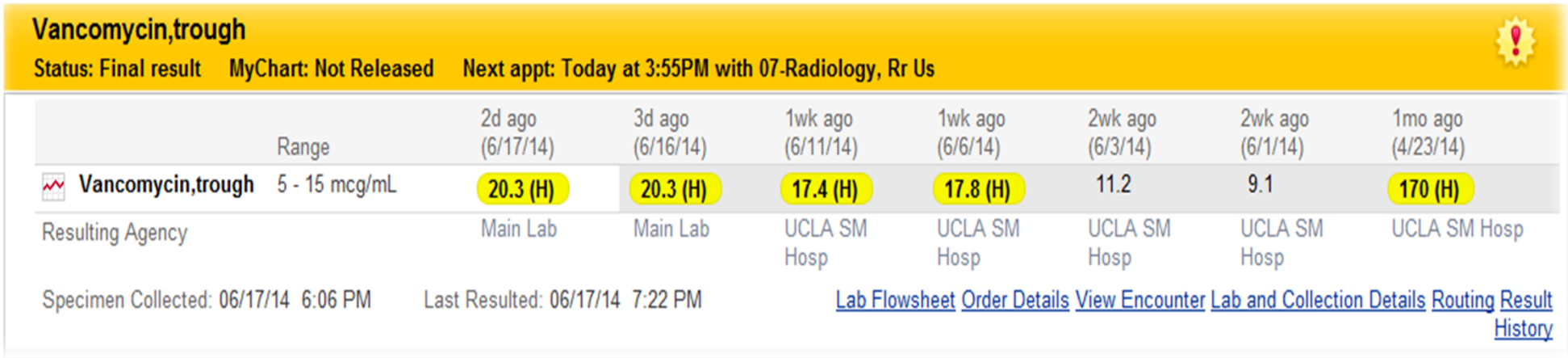
What can nurses do?

- Practice good hand hygiene
  - Gel in-Gel out
  - Wash your hands
- Elevate the head of the bead to prevent aspiration
- Reassess need for invasive devices
  - Does the patient still need:
    - IV catheters
      - Do antibiotics need to be IV or can the patient take PO instead?
    - Foley catheters

Let's go PO!

What can nurses do?

- Assist with appropriate antimicrobial dosing
  - Changes in renal function, initiating or stopping dialysis
  - Ensure drug levels are drawn accurately!
    - **Troughs**: drawn no sooner than 30 minutes prior to next dose
    - **Peaks**: usually drawn 1 hour after a dose is given



Vancomycin,trough

Status: Final result **MyChart: Not Released** **Next appt: Today at 3:55PM with 07-Radiology, Rr Us**

	Range	2d ago (6/17/14)	3d ago (6/16/14)	1wk ago (6/11/14)	1wk ago (6/6/14)	2wk ago (6/3/14)	2wk ago (6/1/14)	1mo ago (4/23/14)
Vancomycin,trough	5 - 15 mcg/mL	20.3 (H)	20.3 (H)	17.4 (H)	17.8 (H)	11.2	9.1	170 (H)
Resulting Agency		Main Lab	Main Lab	UCLA SM Hosp	UCLA SM Hosp	UCLA SM Hosp	UCLA SM Hosp	UCLA SM Hosp

Specimen Collected: 06/17/14 6:06 PM Last Resulted: 06/17/14 7:22 PM Lab Flowsheet | Order Details | View Encounter | Lab and Collection Details | Routing | Result History

Prescribers will respond to levels, even if they're drawn incorrectly!

What nurses can do?

- Know why your patients are on antibiotics, and ask MDs if they are necessary
  - Antibiotic "Time Out"
    - Ensure all orders for antimicrobials include:
      - Dose
      - Duration (stop date)
      - Indication

      } **CareConnect**

  - Obtain cultures
    - Ideally before starting or changing antibiotics
    - Once the culture data comes back, take an antibiotic "time out" and *re-assess therapy*

What can I do?

- Lead by example!
  - Avoid seeking antibiotics for viral URI's

Questions?