Antibiotic Stewardship at WRMC

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WASHINGTON

Disclosures

- I do not have any financial or commercial disclosures
- I have prescribed and taken antibiotics

Famous ABX quotes

- "On the whole, the position of antimicrobial agents in medical therapy is highly satisfactory. The majority of bacterial infections can be cured simply, effectively, and cheaply. The mortality and morbidity from bacterial diseases has fallen so low that they are no longer among the important unsolved problems of medicine. These accomplishments are widely known and appreciated…"

Ernest Jawetz, noted microbiologist. 1956

Famous ABX quotes

- “The war against infectious disease has been won”

Dr. Willam Stuart, US Surgeon General. 1969

Statistics on ABX Usage

- **80%** of all ABX in the USA are used in animal/food industry
- 25 million pounds of ABX are produced for human consumption annually
- 160 million courses of ABX in NONhospitalized pts annually
- **30%-50%** of all hospitalized pts receive a course of ABX
- 50%-99% of antimicrobial use is inappropriate

Reasons for Inappropriate Use

- Treatment duration too long
- Treatment of noninfectious entities
  - Colonization
  - "Lasix-responsive" pneumonia
  - "CYA"
- Ineffective therapy when pathogen is ID'd
  - Wrong choice
  - Wrong dose

Goals of ABX Stewardship

- Improve patient care
- Reduce unwanted consequences of ABX overuse or misuse
- Reduction in emergence of MDROs
- Preservation of antimicrobial activity for future use
- Reduction in healthcare costs

ABX Stewardship as a CoP

- **By the end of 2017**, CMS should have Federal regulations (Conditions of Participation) in place that will require **U.S. hospitals, critical access hospitals, and long-term care and nursing home facilities** to have in place **robust antibiotic stewardship programs that adhere to best practices, such as those contained in the CDC Core Elements for Hospital Antibiotic Stewardship Program recommendations.** Similar requirements should be phased in rapidly for other settings including long-term acute care hospitals, other post-acute facilities, ambulatory, surgery centers, and dialysis centers.

How do we know what these new ASP measures will be?

We don’t but there are some clues based on currently available data

Summary of Core Elements of Hospital Antibiotic Stewardship Programs

Leadership Commitment: Dedicating necessary human, financial and information technology resources
Accountability: Appointing a single leader responsible for program outcomes. Experience with successful programs show 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, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. “antibiotic time out” after 48 hours)
Tracking: Monitoring antibiotic prescribing and resistance patterns
Reporting: Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff
Education: Educating clinicians about resistance and optimal prescribing

http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html

Checklist for Core Elements of Hospital Antibiotic Stewardship Programs

The following checklist is a companion to *Core Elements of Hospital Antibiotic Stewardship Programs.*

This checklist should be used to systematically assess key elements and actions to ensure optimal antibiotic prescribing and limit overuse and misuse of antibiotics in hospitals. CDC recommends that all hospitals implement an Antibiotic Stewardship Program. Facilities using this checklist should involve one or more knowledgeable staff to determine if the following principles and actions to improve antibiotic use are in place. The elements in this checklist have been shown in previous studies to be helpful in improving antibiotic use though not all of the elements might be feasible in all hospitals.

http://www.cdc.gov/nhsn/forms/57.103_PSHospSurv_BLANK.pdf

LEADERSHIP SUPPORT ESTABLISHED AT FACILITY

A. Does your facility have a formal, written statement of support from leadership that supports efforts to improve antibiotic use (antibiotic stewardship)?

❑ Yes ❑ No

B. Does your facility receive any budgeted financial support for antibiotic stewardship activities (e.g., support for salary, training, or IT support)?

❑ Yes ❑ No

ACCOUNTABILITY

A. Is there a physician leader responsible for program outcomes of stewardship activities at your facility?

❑ Yes ❑ No

DRUG EXPERTISE

A. Is there a pharmacist leader responsible for working to improve antibiotic use at your facility?

❑ Yes ❑ No

KEY SUPPORT FOR THE ANTIBIOTIC STEWARDSHIP PROGRAM

Does any of the staff below work with the stewardship leaders to improve antibiotic use?

B. Clinicians

❑ Yes ❑ No

C. Infection Prevention and Healthcare Epidemiology

❑ Yes ❑ No

D. Quality Improvement

❑ Yes ❑ No

E. Microbiology (Laboratory)

❑ Yes ❑ No

F. Information Technology (IT)

❑ Yes ❑ No

G. Nursing

❑ Yes ❑ No

ACTIONS TO SUPPORT OPTIMAL ANTIBIOTIC USE

POLICIES POLICY ESTABLISHED

A. Does your facility have a policy that requires prescribers to document in the medical record or during order entry a dose, duration, and indication for all antibiotic prescriptions?

❑ Yes ❑ No

B. Does your facility have facility-specific treatment recommendations, based on national guidelines and local susceptibility, to assist with antibiotic selection for common clinical conditions?

❑ Yes ❑ No

SPECIFIC INTERVENTIONS TO IMPROVE ANTIBIOTIC USE

Are the following actions to improve antibiotic prescribing conducted in your facility?

BROAD INTERVENTIONS

C. Is there a formal procedure for all clinicians to review the appropriateness of all antibiotics 48 hours after the initial orders (e.g. antibiotic time out)?

❑ Yes ❑ No

D. Do specified antibiotic agents need to be approved by a physician or pharmacist prior to dispensing (i.e., pre-authorization) at your facility?

❑ Yes ❑ No

E. Does a physician or pharmacist review courses of therapy for specified antibiotic agents (i.e., prospective audit with feedback) at your facility?

❑ Yes ❑ No

PHARMACY-DRIVEN INTERVENTIONS

Are the following actions implemented in your facility?

F. Automatic changes from intravenous to oral antibiotic therapy in appropriate situations?

❑ Yes ❑ No

G. Dose adjustments in cases of organ dysfunction?

❑ Yes ❑ No

H. Dose optimization (pharmacokinetics/pharmacodynamics) to optimize the treatment of organisms with reduced susceptibility?

❑ Yes ❑ No

I. Automatic alerts in situations where therapy might be unnecessarily duplicative?

❑ Yes ❑ No

J. Time-sensitive automatic stop orders for specified antibiotic prescriptions?

❑ Yes ❑ No

DIAGNOSIS AND INFECTIONS SPECIFIC INTERVENTIONS

Does your facility have specific interventions in place to ensure optimal use of antibiotics to treat the following common infections?

K. Community-acquired pneumonia

❑ Yes ❑ No

L. Urinary tract infection

❑ Yes ❑ No

M. Skin and soft tissue infections

❑ Yes ❑ No

N. Surgical prophylaxis

❑ Yes ❑ No

O. Empiric treatment of Methicillin-resistant Staphylococcus aureus (MRSA)

❑ Yes ❑ No

DIAGNOSIS AND INFECTIONS SPECIFIC INTERVENTIONS (con't)

P. Non-C. Difficile infection (CDI) antibiotics in new cases of CDI

❑ Yes ❑ No

Q. Culture-proven invasive (e.g., blood stream) infections

❑ Yes ❑ No

TRACKING: MONITORING ANTIBIOTIC PRESCRIBING, USE, AND RESISTANCE

PROCESS MEASURES

A. Does your stewardship program monitor adherence to a documentation policy (dose, duration, and indication)?

❑ Yes ❑ No

B. Does your stewardship program monitor adherence to facility-specific treatment recommendations?

❑ Yes ❑ No

C. Does your stewardship program monitor compliance with one of more of the specific interventions in place?

❑ Yes ❑ No

ANTIBIOTIC USE AND OUTCOME MEASURES

D. Does your facility track rates of C. difficile infection?

❑ Yes ❑ No

E. Does your facility produce an antibiogram (cumulative antibiotic susceptibility report?

❑ Yes ❑ No

Does your facility monitor antibiotic use (consumption) at the unit and/or facility wide level by one of the following metrics:

F. By counts of antibiotic(s) administered to patients per day (Days of Therapy; DOT)?

❑ Yes ❑ No

G. By number of grams of antibiotics used (Defined Daily Dose, DDD)?

❑ Yes ❑ No

H. By direct expenditure for antibiotics (purchasing costs)?

❑ Yes ❑ No

REPORTING INFORMATION TO STAFF ON IMPROVING ANTIBIOTIC USE AND RESISTANCE

A. Does you stewardship program share facility-specific reports on antibiotic use with prescribers?

❑ Yes ❑ No

B. Has a current antibiogram been distributed to prescribers at your facility?

❑ Yes ❑ No

C. Do prescribers ever receive direct, personalized communication about how they can improve their antibiotic prescribing?

❑ Yes ❑ No

EDUCATION

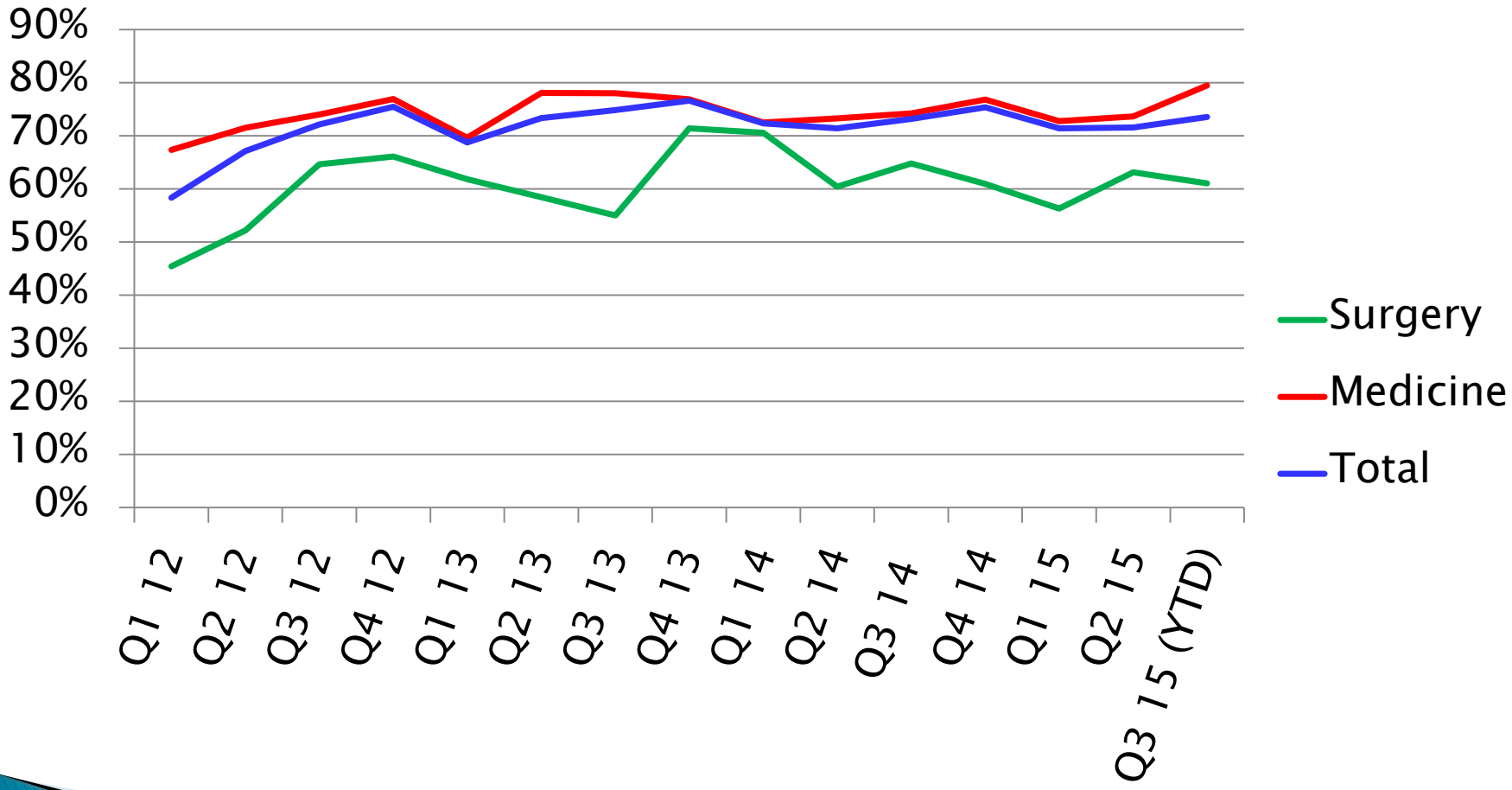
A. Does your stewardship program provide education to clinicians and other relevant staff on improving antibiotic prescribing?

❑ Yes ❑ No

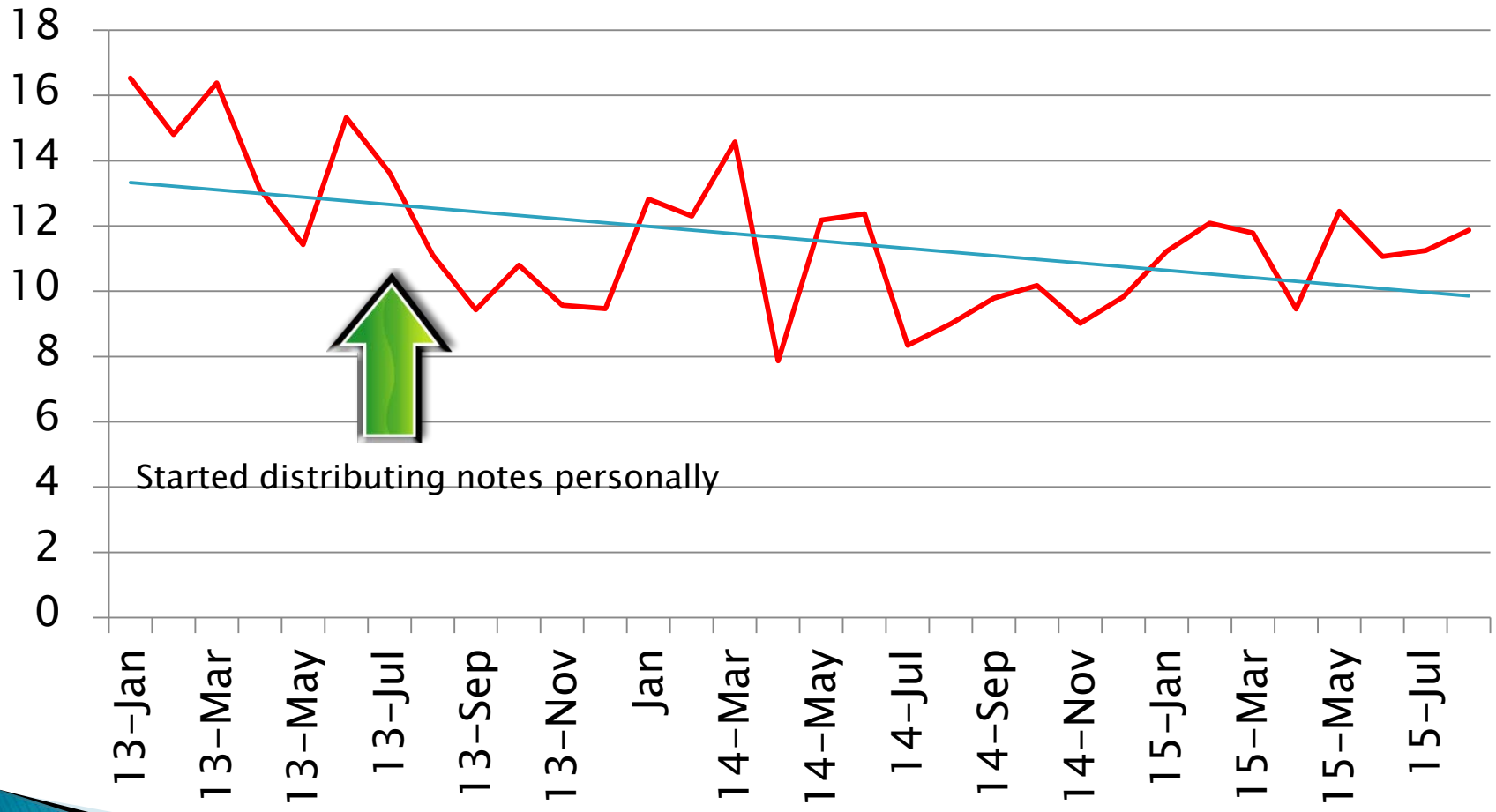
WRMC ASP Impact

Established- Jan 2012

Quarterly ASP Compliance



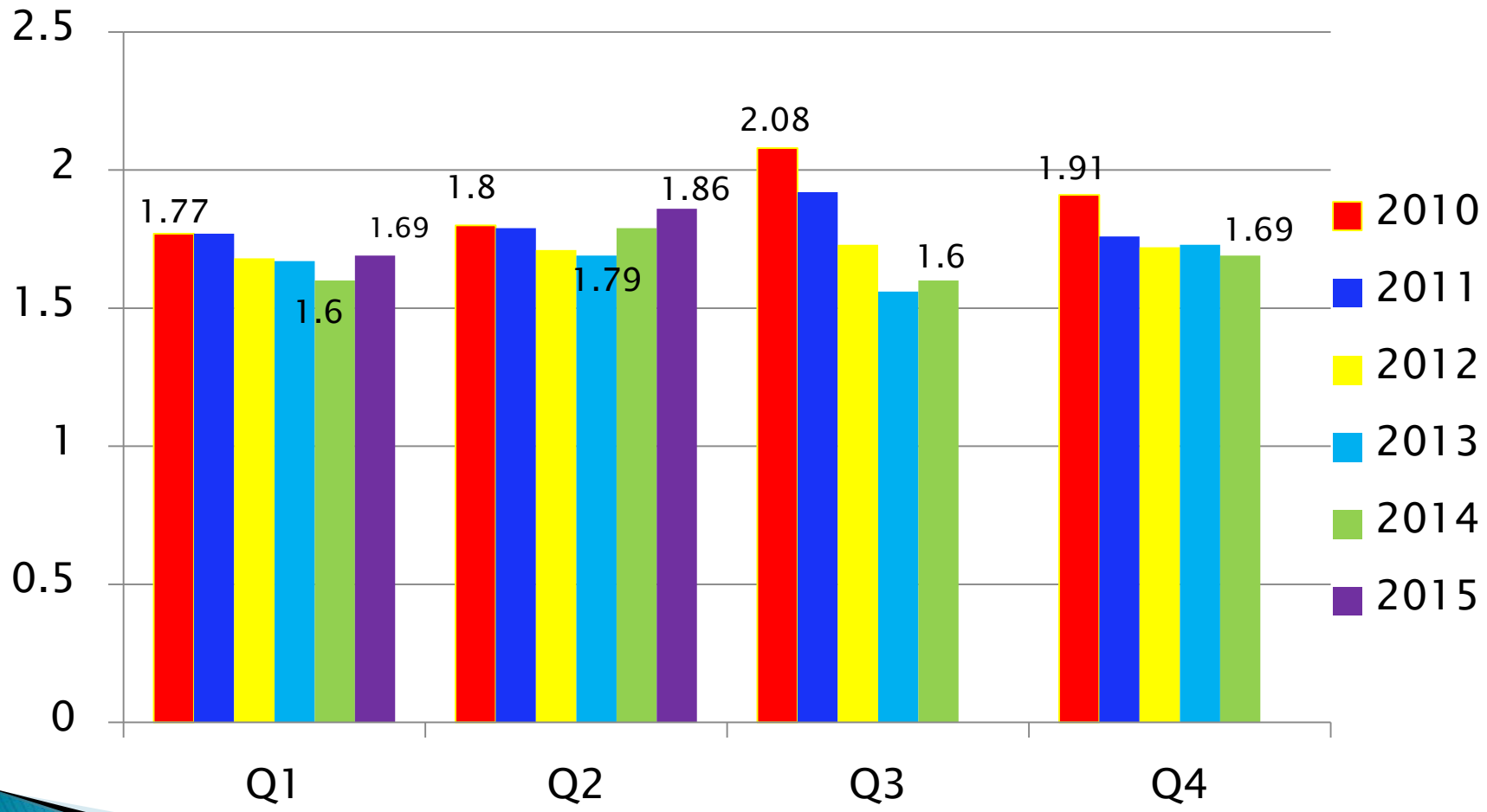
Hours until ABX Recs Initiated

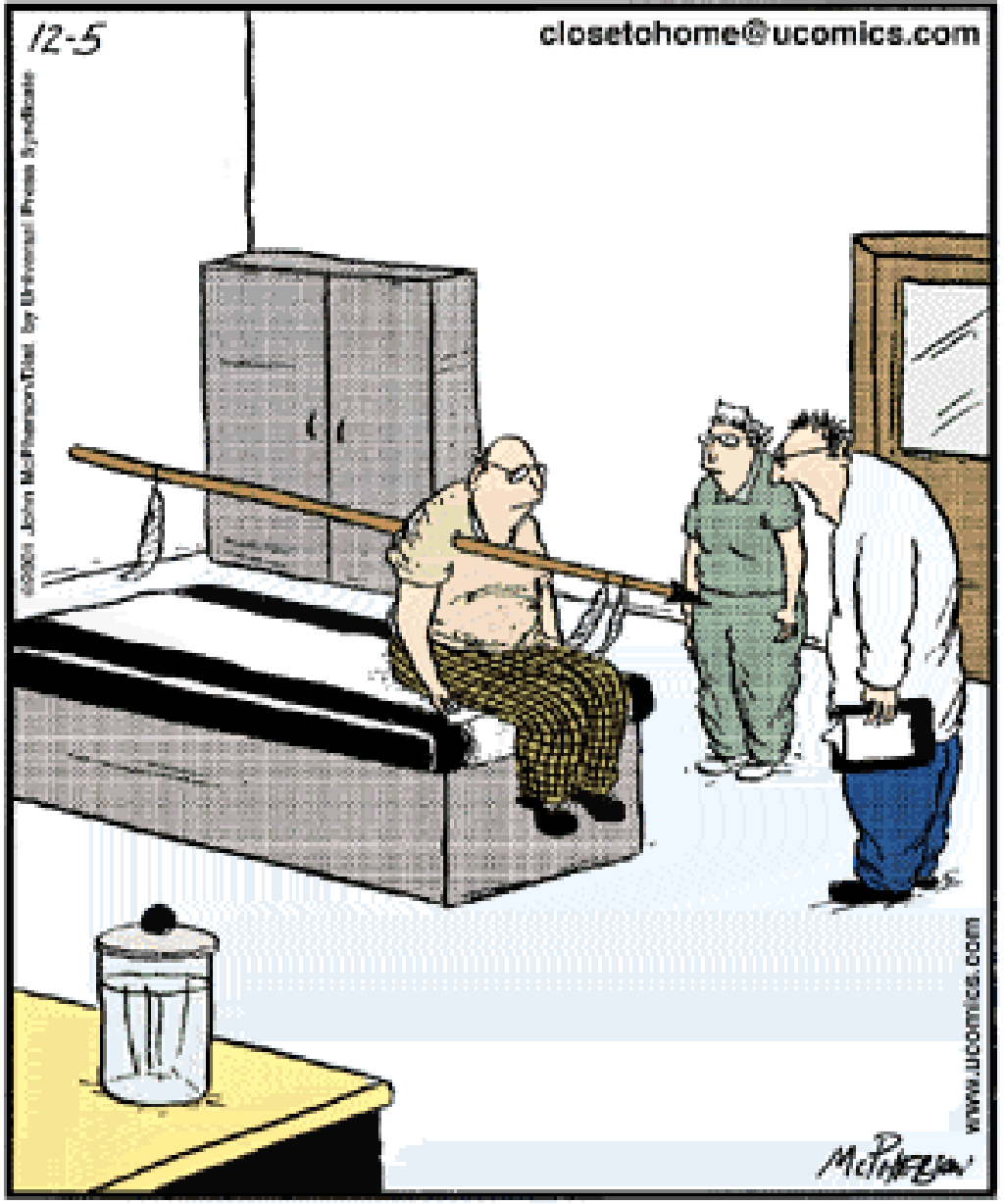


WRMC Impact on LOT (days)

	Recs taken	Recs not taken	LOT Reduction (d)	% reduction
Mean 2012	2.26	3.24	-0.98	-30.2%
Mean 2013	2.43	3.44	-1.01	-29.4%
Mean 2014	2.51	3.92	-1.41	-36.0%

WRMC ABX Usage (ABX doses/inpt days)



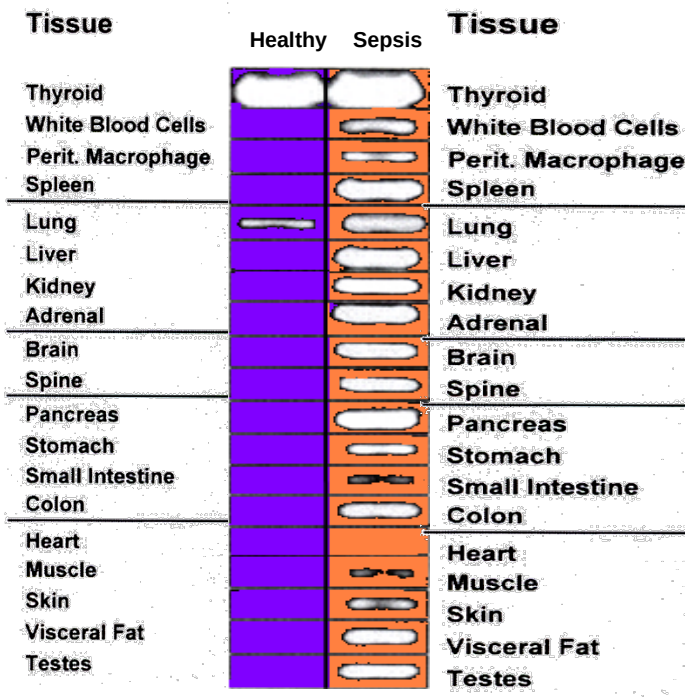


"We can't be absolutely certain until we run some tests, but your initial blood work indicates that you may have a large spear through your right shoulder."

Procalcitonin Facts

- **Simple blood test** specific for bacterial infection
- **In healthy people**, PCT concentration are found <0.05ng/ml
- **Concentrations** ≥0.5ng/ml can be interpreted as abnormal
- During severe bacterial infections and sepsis, **blood levels rise rapidly** (up to x100K) – no elevation from viral infections
- **Standard of Care** for much of Europe in the management of infection and sepsis

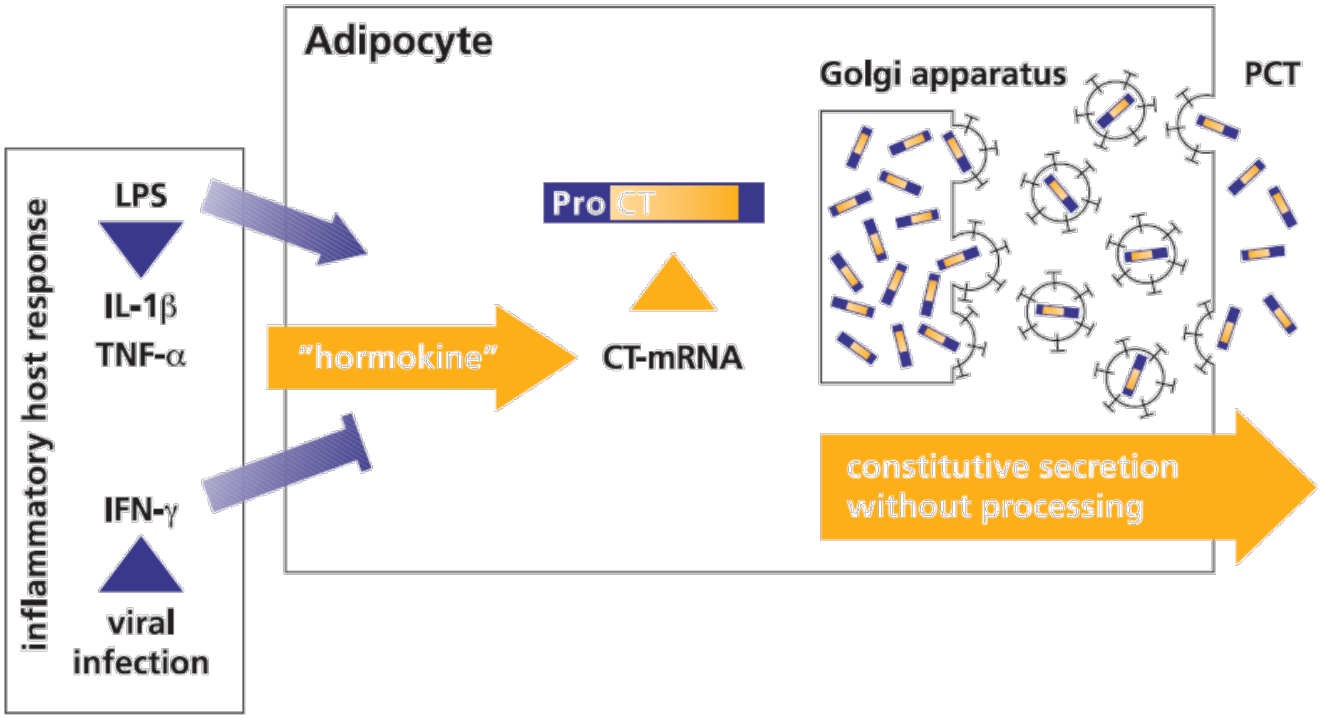
Highly specific induction – Produced all tissue



In relevant bacterial infection, PCT is produced and released into circulation from the entire body

Müller B. et al., JCEM 2001

Induction and release of PCT due to bacterial infection



Alternative synthesis of PCT

Bacterial toxins (gram+/−) and cytokines **stimulate production** of PCT in all parenchymal tissues

PCT is **immediately released** into bloodstream

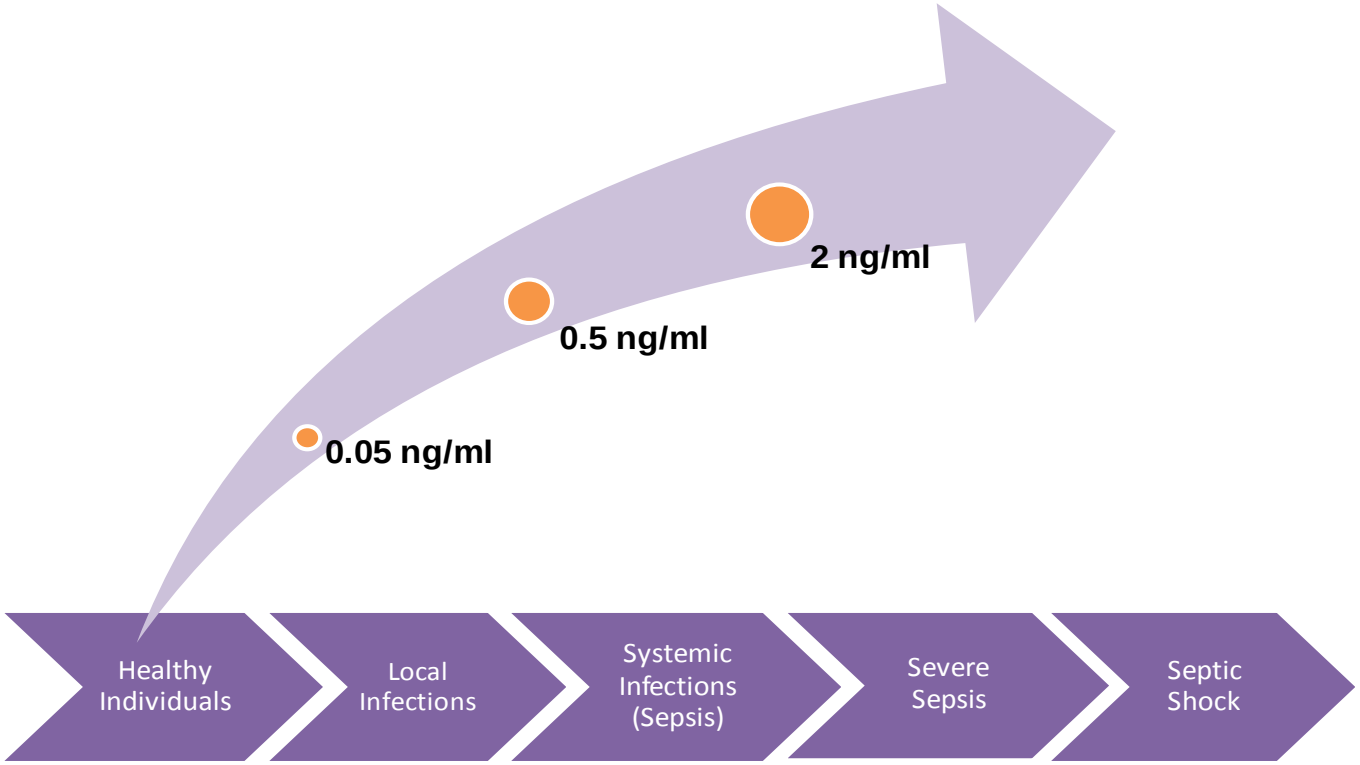
This process can be **blocked** during viral infections

Adapted from Christ-Crain et al. 2005

Induction and elimination of PCT

- Three elements are required to the induction process
  - Stimulus – bacterial toxin or trauma
  - Differentiated parenchymal cells
  - Adhering monocytes
- PCT plasma concentrations
  - Significant after 6 hours
  - Peak values – 12 to 24 hours
  - Half-life – about 24 hours
  - Not impaired by neutropenia or other immunocomprised states

PCT values correlate directly with severity of bacterial load



- In critically ill patients, PCT levels elevate in correlation to the severity of bacterial infection. Also **excellent prognostic marker**.
- Integrating PCT in sepsis management can lead to improved patient outcomes

Clinical Situations where PCT may be useful

- Diagnosis of bacteremia/sepsis in adults and neonates (>72 hours old)
- Differentiating bacterial vs nonbacterial pneumonia
- Differentiating bacterial vs aseptic meningitis
- Diagnosis of bacterial infection in febrile neutropenia
- Diagnosis of septic arthritis

PCT release in the absence of infection

- Newborn <48hr-increased PCT values (physiological peak)
- Primary inflammation syndrome following extensive trauma: extensive burns, major surgery (cardiac, transplant, abdominal)
- Medullary C-cell cancers of the thyroid, pulmonary small-cell carcinoma
- Prolonged circulatory failure (cardiogenic shock, hemorrhagic shock, thermal shock)
- Malaria & some fungal infections

Key Considerations when Interpreting PCT Levels

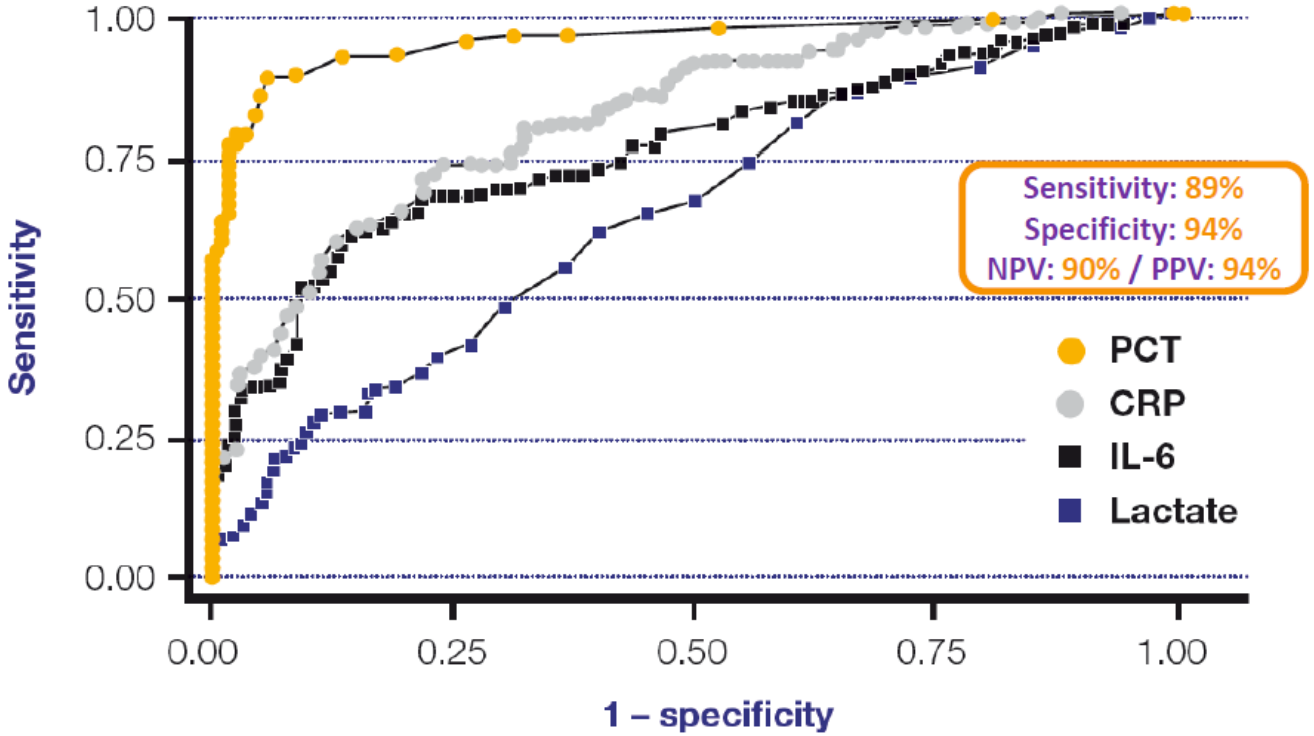
- **Consider the clinical context-**(pts in septic shock should not have ABX withheld if PCT is normal)
- **Serial measurements are preferred** and may be very helpful
- **Consider the dynamics of the disease-**(PCT levels fall after trauma if no infection present. If PCT levels are rising after ABX, consider changing ABX or looking for drainable source of infection)
- **Keep in mind conditions that will cause PCT levels to rise**

PCT evidence-based use for various ID conditions

Evidence-based Criterion	RCTs	Observational Studies
Strong evidence for PCT	URI COPD exacerbation Pneumonia Severe sepsis/septic shock	
Good evidence for PCT	VAP Postop infxns Meningitis	Bacteremia Pyelo/UTIs
Moderate evidence for PCT		Postop fever Septic arthritis Neutropenia
Weak evidence for PCT		Endocarditis Intra-abd abscess Pancreatitis

Riedel S. Diagn Microbiol Infect Dis. 73 (2012); 221-7.

Diagnostic accuracy of PCT compared to other biomarkers used in sepsis



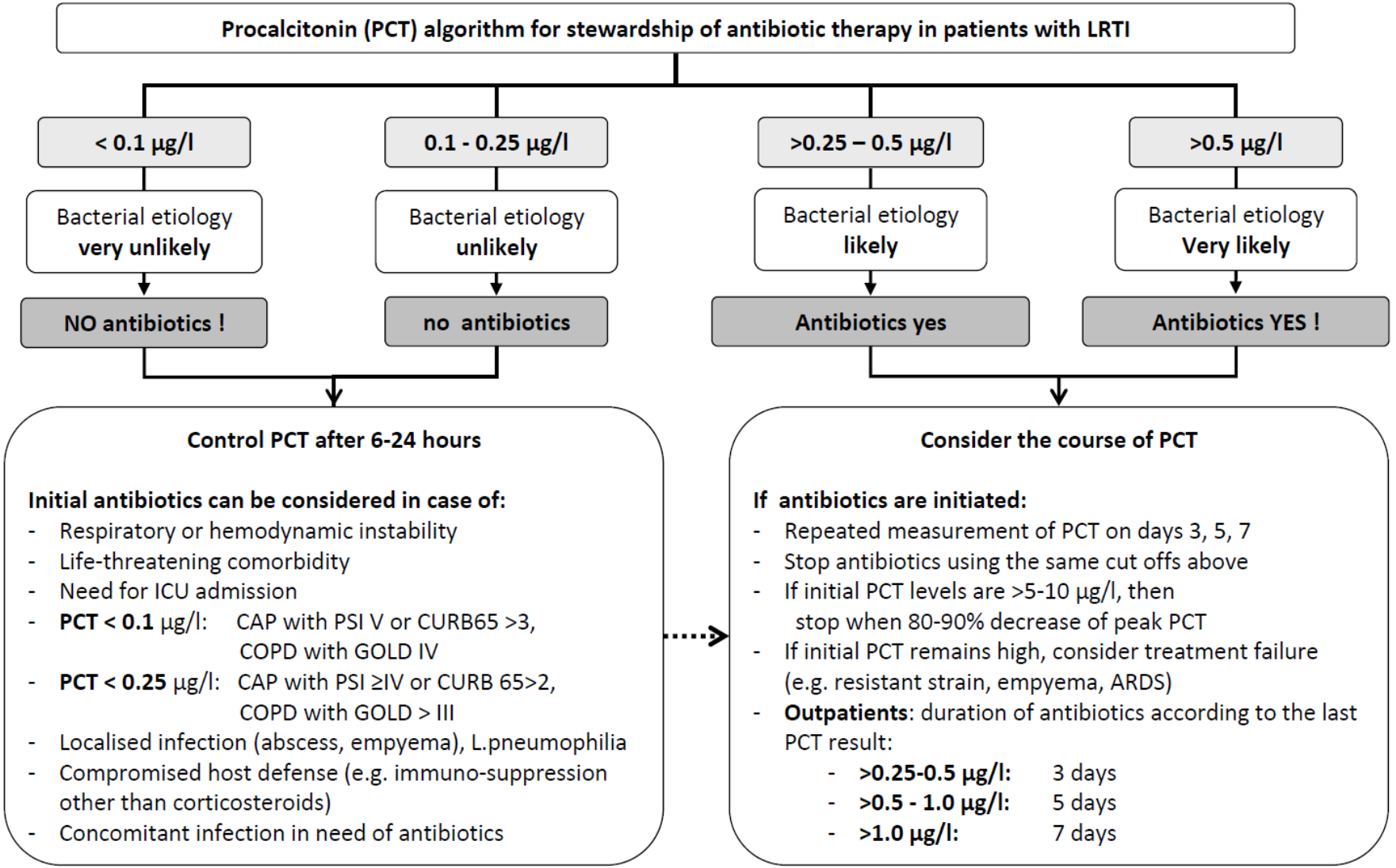
- **PCT levels accurately differentiate** sepsis from noninfectious inflammation*
- **PCT has been demonstrated** to be the best marker for **differentiating** patients with **sepsis** from those with systemic inflammatory reaction not related to infectious cause

Simon L. et al. Clin Infect Dis. 2004; 39:206-217.

Algorithm-based or rule-guided decisions

- May be general or disease specific
- Simple or more involved
- Assist in:
  - Should antibiotic therapy be initiated
  - Initial antibiotic intensity
  - Repeat PCT
  - Course adjustment
  - De-escalation of therapy
  - Discontinuation of therapy

eFigure 1. PCT Algorithm for Antibiotic Stewardship



Abbreviations: PCT *procalcitonin*, CAP *community-acquired pneumonia*, PSI *pneumonia severity index*, COPD *chronic obstructive pulmonary disease,* GOLD *global initiative for obstructive lung disease*,

Philipp Schuetz, MD, MPH; Victor Chiappa, MD; Matthias Briel, MD, MSc; Jeffrey L. Greenwald, MD
ARCH INTERN MED/ VOL 171 (NO. 15), AUG 8/22, 2011 WWW.ARCHINTERNMED.COM

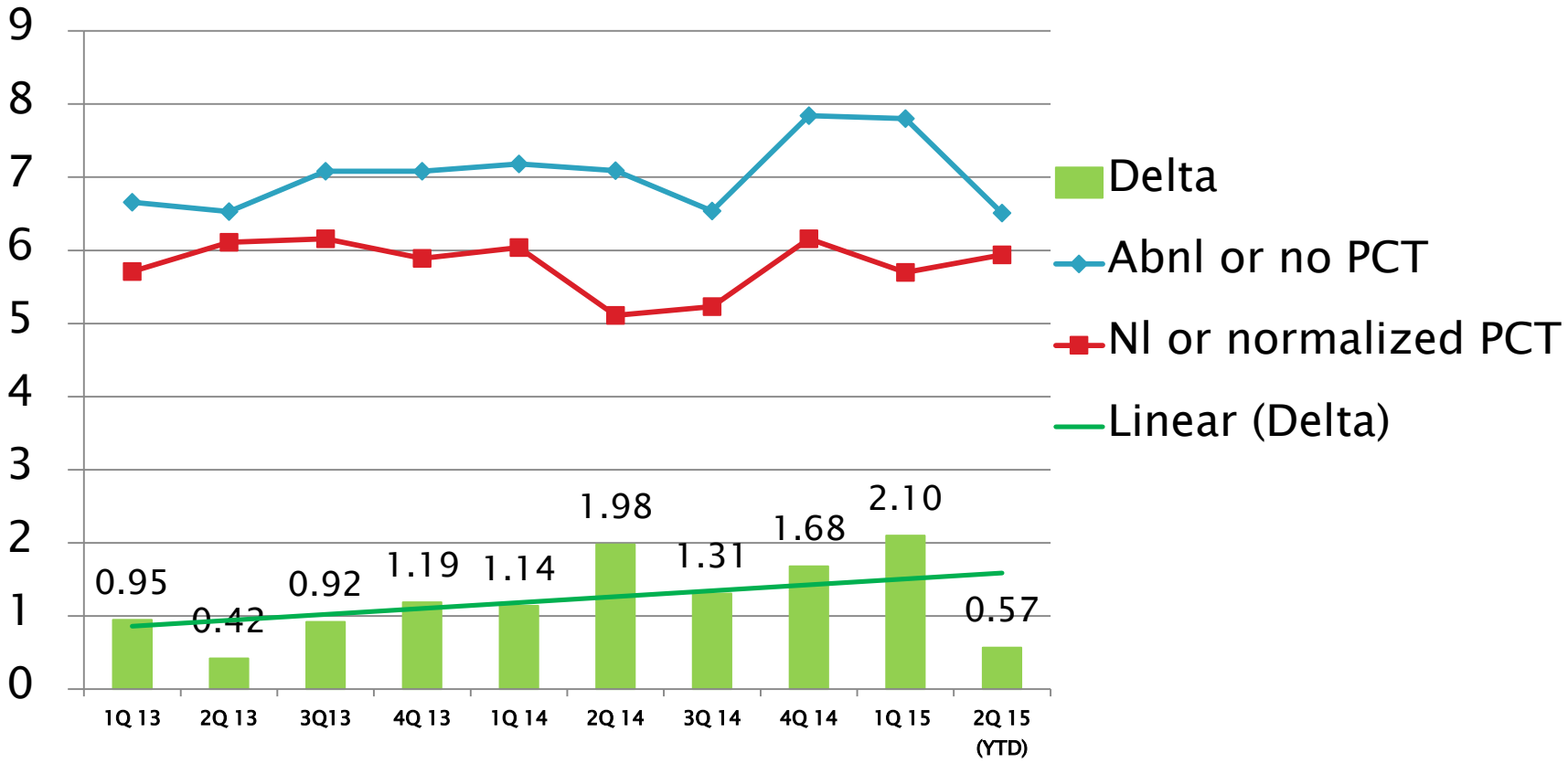
PCT Clinical Data

- Meta-analysis (4221 pts, 14 RCTs)
- PCT-guided vs standard Rx (control)
  - **No change in mortality** (5.7% vs 6.3%) **or in Rx failure** (19.1% vs 21.9%) in any clinical setting
  - Total ABX exposure reduced by **3.47 days** across all clinical settings [outpt (-3.06), ED (-2.96), ICU (-3.21)]
  - PC setting-lower prescription rates for resp illness
  - ED & ICU settings-shorter duration of ABX therapy

Schuetz P, Briel M, Christ-Cain M, et al. Clin Infect Dis 2012;55:651-62.

WRMC PCT Experience

Impact of PCT on LOS



PCT Impact on LOT (days)

	Total LOT (all WRASP pts)	Total LOT-PCT not checked	LOT (nl PCT)-on ABX	Rx Saved (on ABX) (days)	LOT (nl PCT)	Total Rx Saved (days)	ABX avoided	% avoided
Mean/ Totals 2013	5.24	4.78	3.27	1.97/1.51	2.07	3.18/2.71	715/1981	36.09%
Mean/ Totals 2014	5.29	5.10	3.35	1.94/1.75	2.17	3.12/2.93	722/2167	33.32%

PCT Impact on LOT (days)

	Total LOT (all WRASP pts)	Total LOT-PCT not checked	LOT (nl PCT)-on ABX	Rx Saved (on ABX) (days)	LOT (nl PCT)	Total Rx Saved (days)	ABX avoided	% avoided
Mean/ Totals 2014	5.29	5.10	3.35	1.94/1.75	2.17	3.12/2.93	722/2167	33.32%
Jan 15	6.14	5.79	3.49	2.65/2.30	2.37	3.72/3.42	73/223	32.74%
Feb 15	5.81	6.03	3.71	2.10/2.32	2.27	3.49/3.76	81/205	39.51%
Mar 15	6.10	5.62	3.95	2.15/1.67	2.53	3.50/3.09	72/196	36.73%
Apr 15	4.53	4.15	3.31	1.22/0.84	2.31	2.21/1.84	61/200	30.50%
May 15	5.18	4.76	3.76	1.42/1.00	2.29	2.80/2.47	75/183	40.98%
Jun 15								
Jul 15								
Aug 15								
Sep 15								
Oct 15								
Nov 15								
Dec 15								

WRMC PCT-guided ASP Experience

- 857 cases from 5/13-4/14
- Compared LOS and LOT in all ASP patients with PCT data
  - Total LOS (nl PCT vs abnl PCT)-8.5d vs 8.2d; p=0.2001
  - LOT after ASP advice (compliers vs noncompliers)- 2.5d vs 3.9d, P<0.0001
  - Total LOT (compliers vs noncompliers)-5.1d vs 6.6d, P<0.001

-No difference in any clinical outcomes

PCT-guided ASP can result in a significant reduction in antibiotic use

ID Week 2015-Poster #1507

PCT Summary

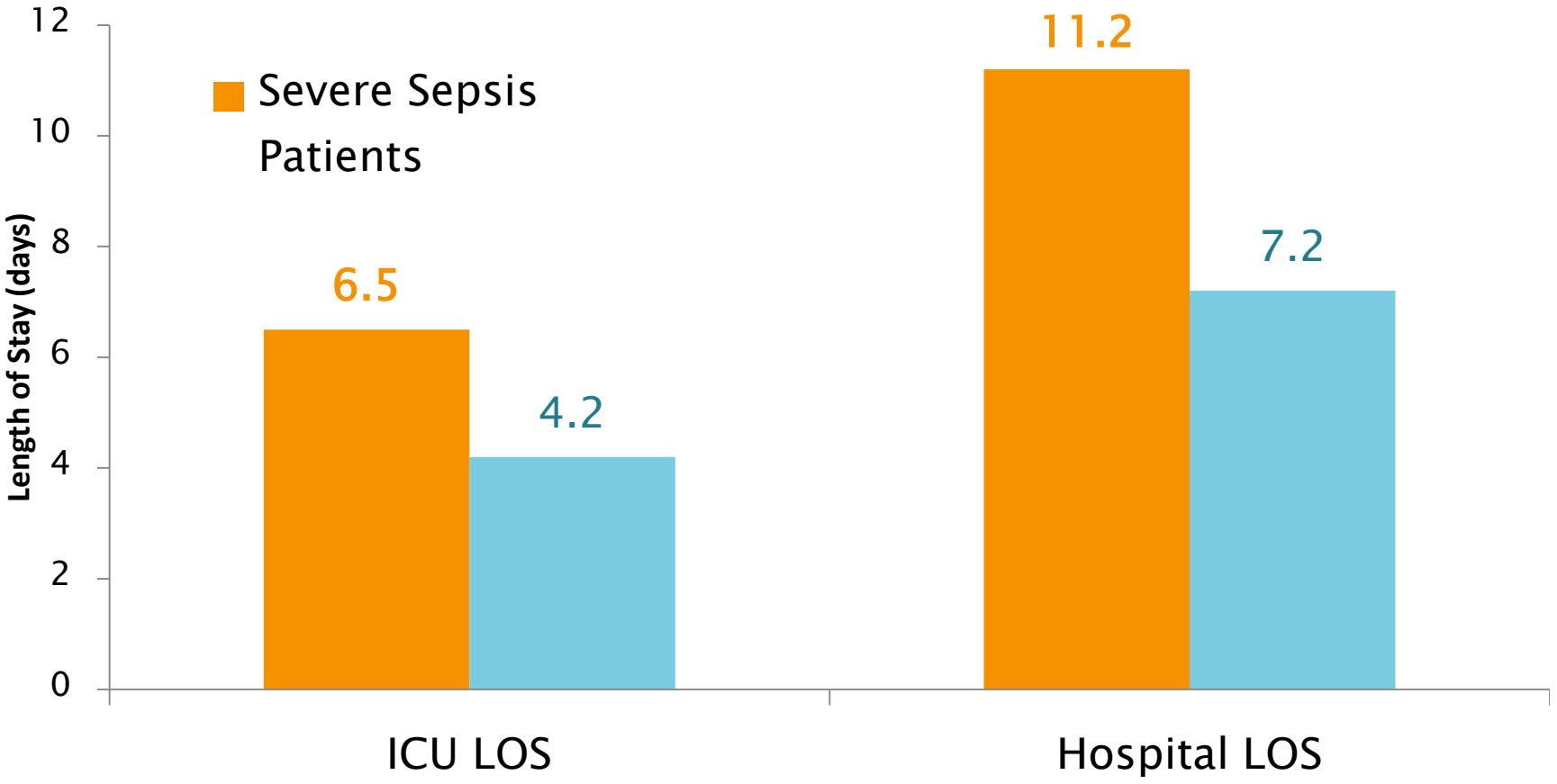
- Highly specific biomarker for bacterial infxn (best data is in resp infxn & sepsis)
- Excellent correlation with severity of illness thus an excellent prognostic marker
- Excellent decision tool for initiating ABX and de-escalation/discontinuation of therapy
- Serial measures are key to clinical success for inpatients.


SUPPORT BACTERIA
It's the only culture
some people have
1285 ©2012 Bad Habits

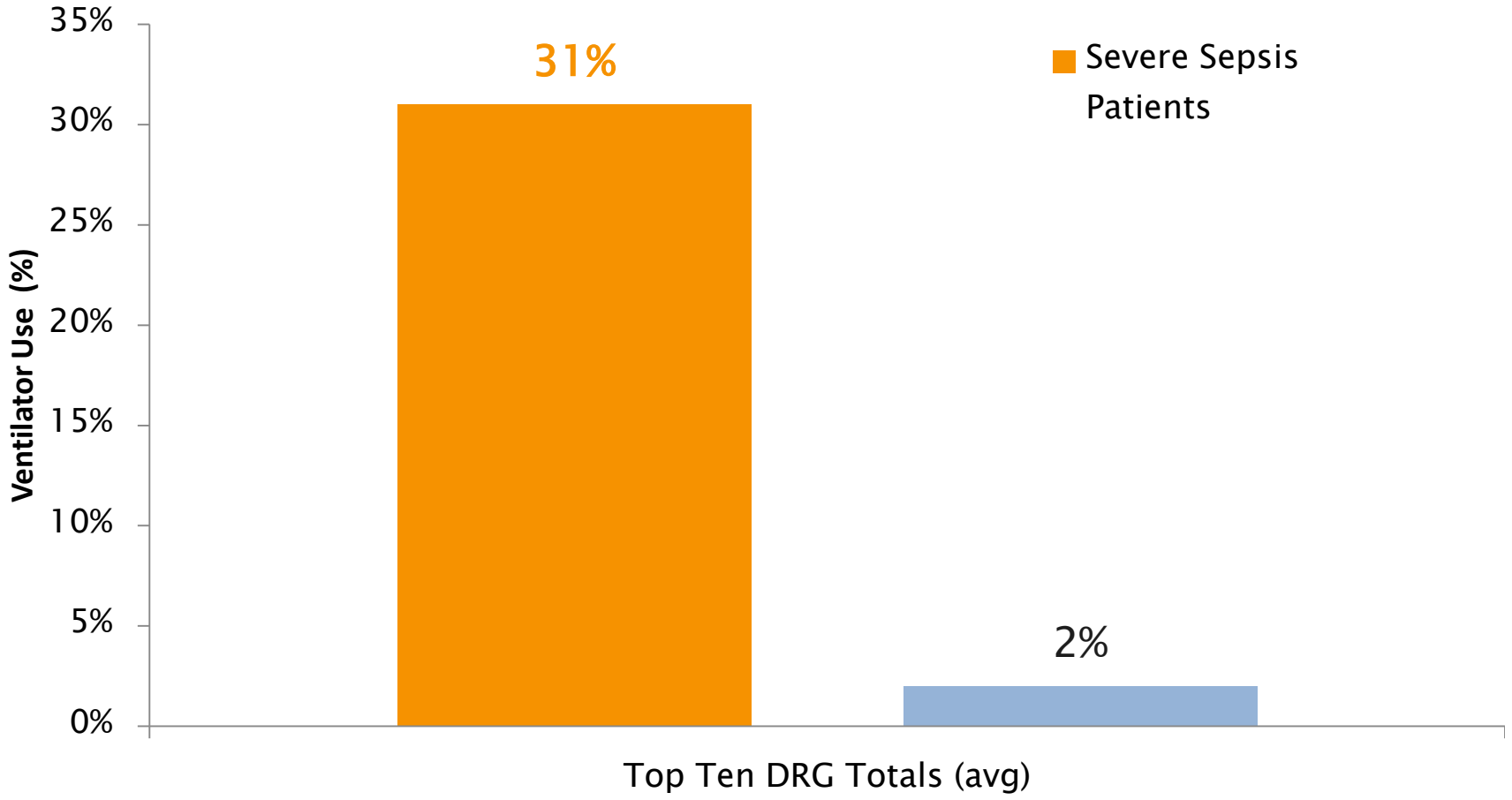
Severe sepsis is costly and life-threatening

- Strikes more than 750,000 people annually in the United States
- Mortality remains at 18% or higher
- Clinical diagnosis remains challenging
- Severe sepsis accounts for $16 billion hospital inpatient costs

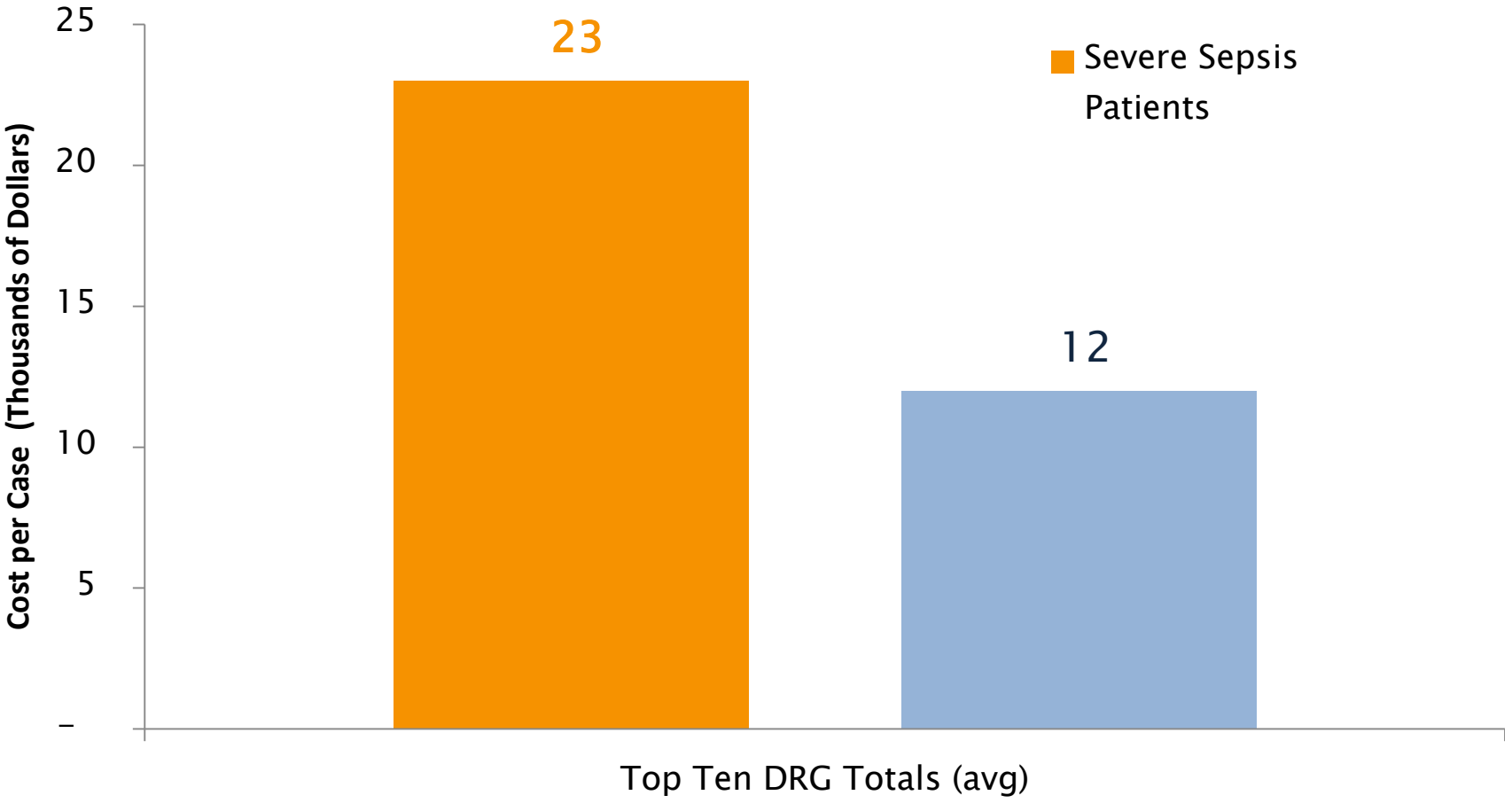
Severe Sepsis prolongs ICU LOS and hospital LOS by more than half



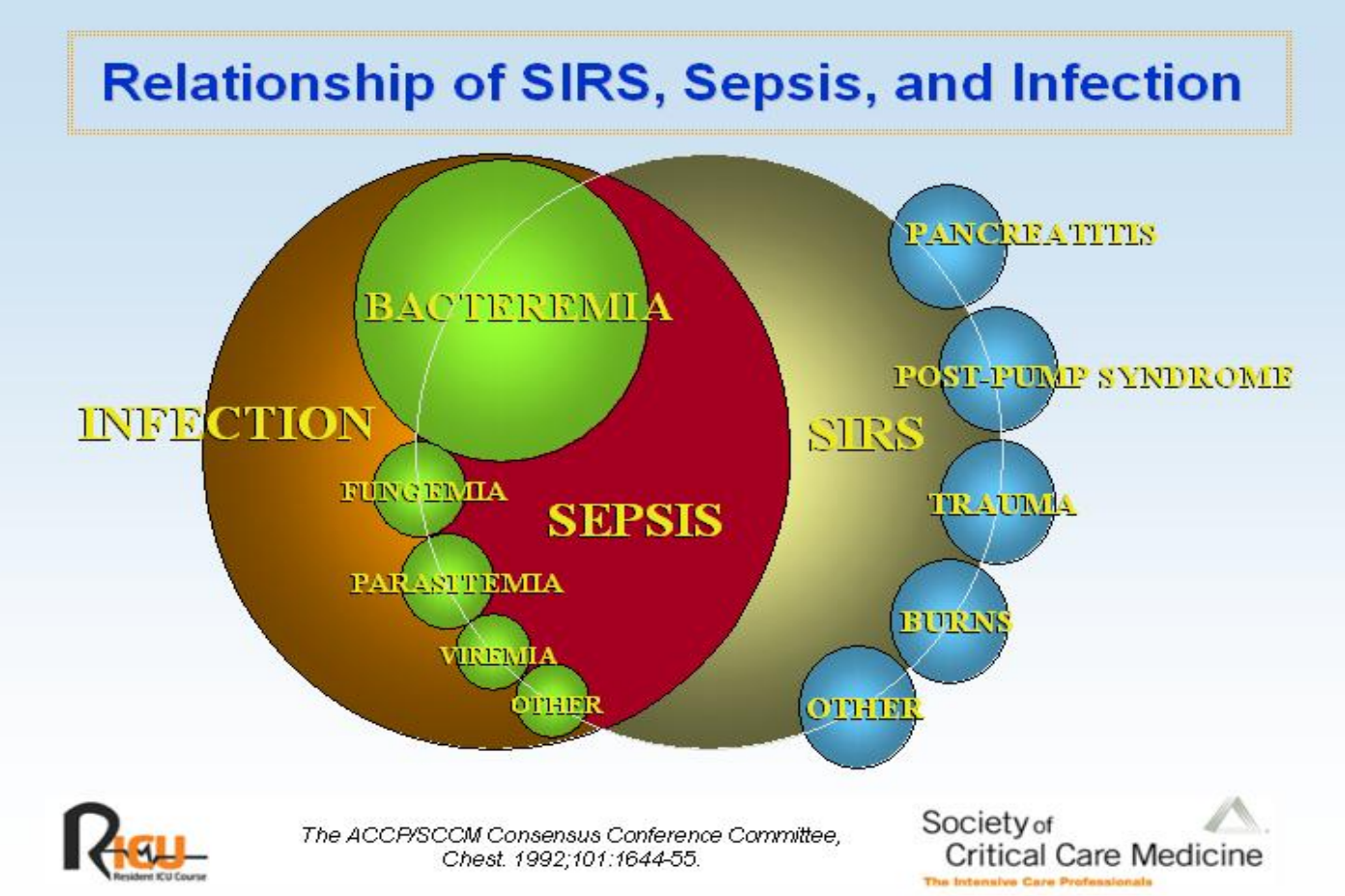
Ventilator use in severe sepsis patients with an ICU stay is more than 15 times that of other patients



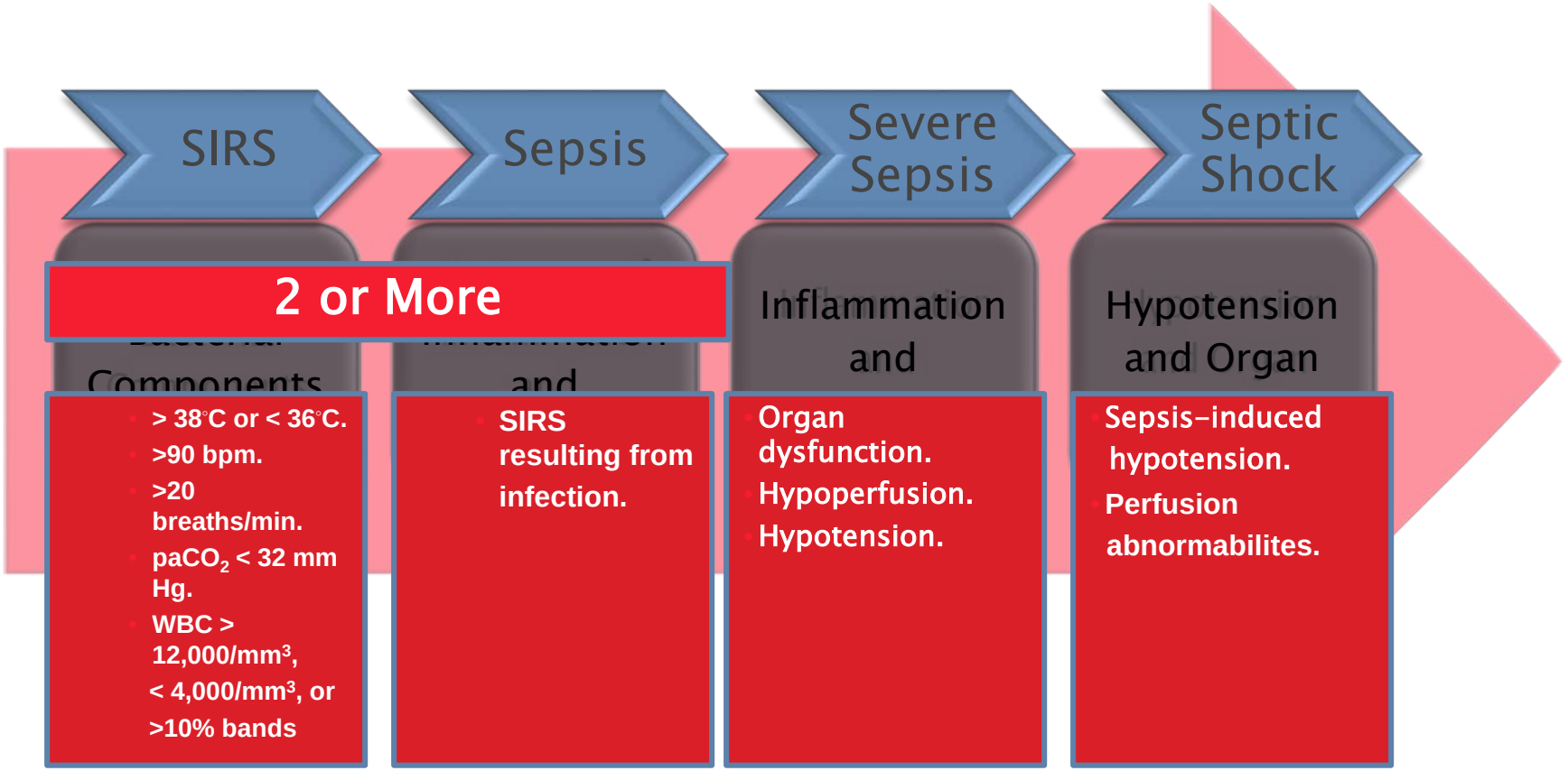
Hospital costs for severe sepsis patients with an ICU is nearly twice that of other patients



Sepsis: Systemic Inflammatory Response To Infection



SIRS/Sepsis/Severe Sepsis/Septic Shock



Determinants of mortality from sepsis

- Ist step is **RECOGNITION** of SEPSIS!!
- Early intervention is critical
- Appropriate antibiotic therapy within one hour of hypotension
- Resuscitation/re-establish perfusion within six hours

It is hard to treat something that you do not know exists….

Early Goal-Directed Therapy (EGDT)

- Algorithmic approach within the 1st 6h that increases O2 content, cardiac contractility, and O2 delivery.
  - Aggressive fluid resuscitation to achieve CVP 8-12
  - Vasopressors to achieve MAP of >65
  - Transfusion to keep Hct $\geq$30%
  - Inotropes if necessary
  - ETT, sedation, paralysis to achieve SvO2$\geq$70%

16% reduction in-house mortality!

Rivers E, Nguyen B, Havstad S, et al. N Engl J Med 2001;345:1368-77.

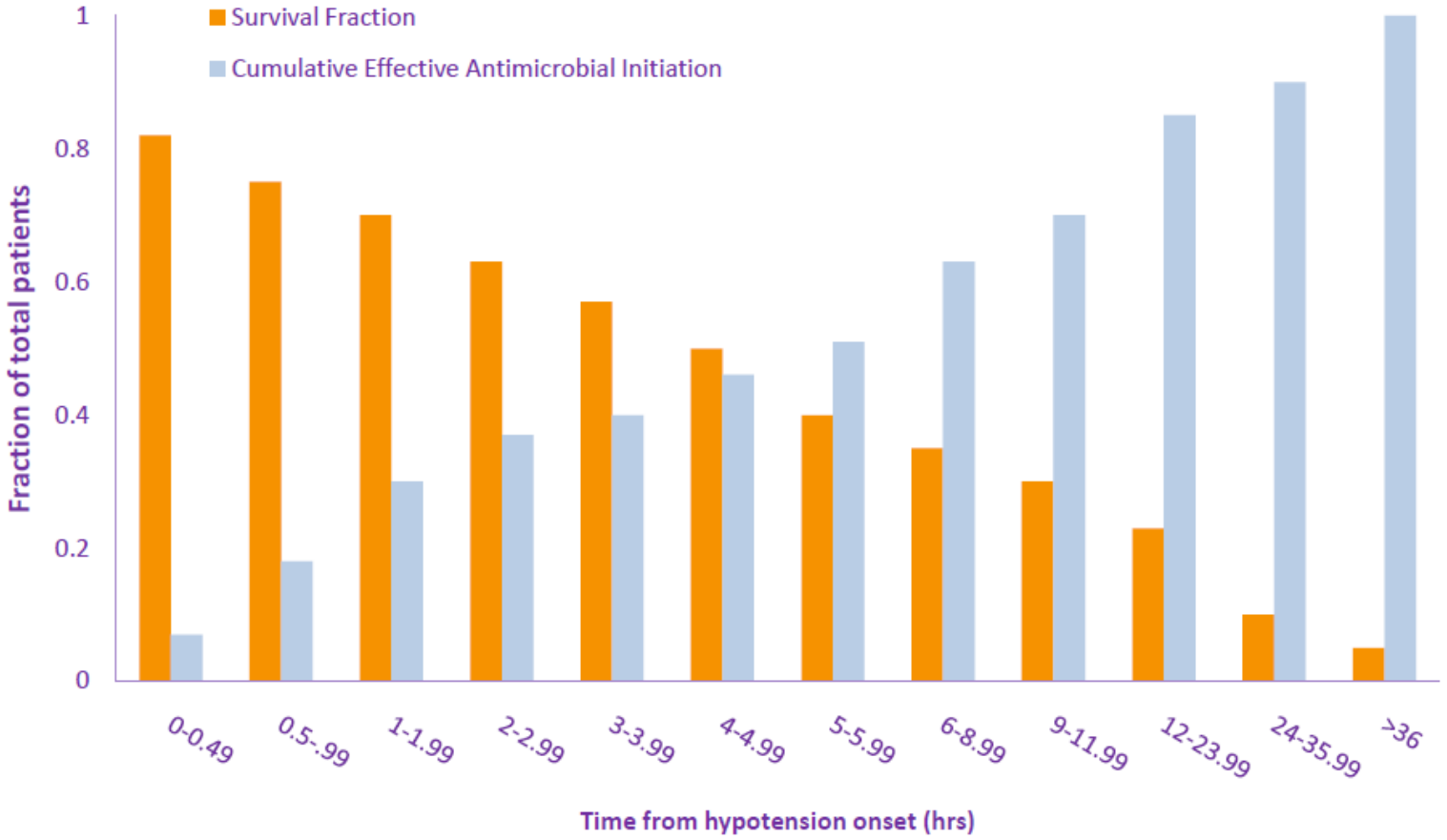
EGDT initiated in ED

- Decreases mortality (23% vs 43%)
- Decreases ICU LOS (5d vs 8 d)
- Decreases time in ED (thus increases throughput)-(201 mins vs 180 mins)

- Only initiated in 57% of eligible patients
  - Lack of recognition
  - Inexperience in junior medical staff
  - Lack of senior nursing staff

Sivayoham N, Rhodes A, Jaiganesh T, et al. Eur J Emerg Med. 2012;19:235-40.

Initiation of Antibiotic Therapy is critical:



7.6% increase in mortality for every hour that ABX not given!
You do the math!!

Kumar A, Roberts D, Wood KE, et al. Crit Care Med 2006;34:1589-96.

Impact of Time to ABX in the ED on Survival

- 261 patients undergoing EGDT
- Triage to ABX <1h (mortality 19.5% vs 33.2%)
- Qualification for EGDT to ABX <1h (mortality 25.0% vs 38.5%)

Gaieski DF, Mikkelsen ME, Band RA, et al. Crit Care Med 2010;38:1045-53.

How will we combat severe sepsis/septic shock at WRMC?

- Recognition
  - Automated sepsis alerts in Cerner and PICIS
  - Immediate evaluation followed by 2L fluid bolus (within 1h)
  - POC lactate
  - STAT procalcitonin (TAT <1h)

If lactate $\geq$4.0; PCT$\geq$1.0 or MAP<65 or SBP<90 after above fluid bolus then proceed to Phase 1 of the Sepsis Powerplan.

Phase 1 Sepsis Powerplan

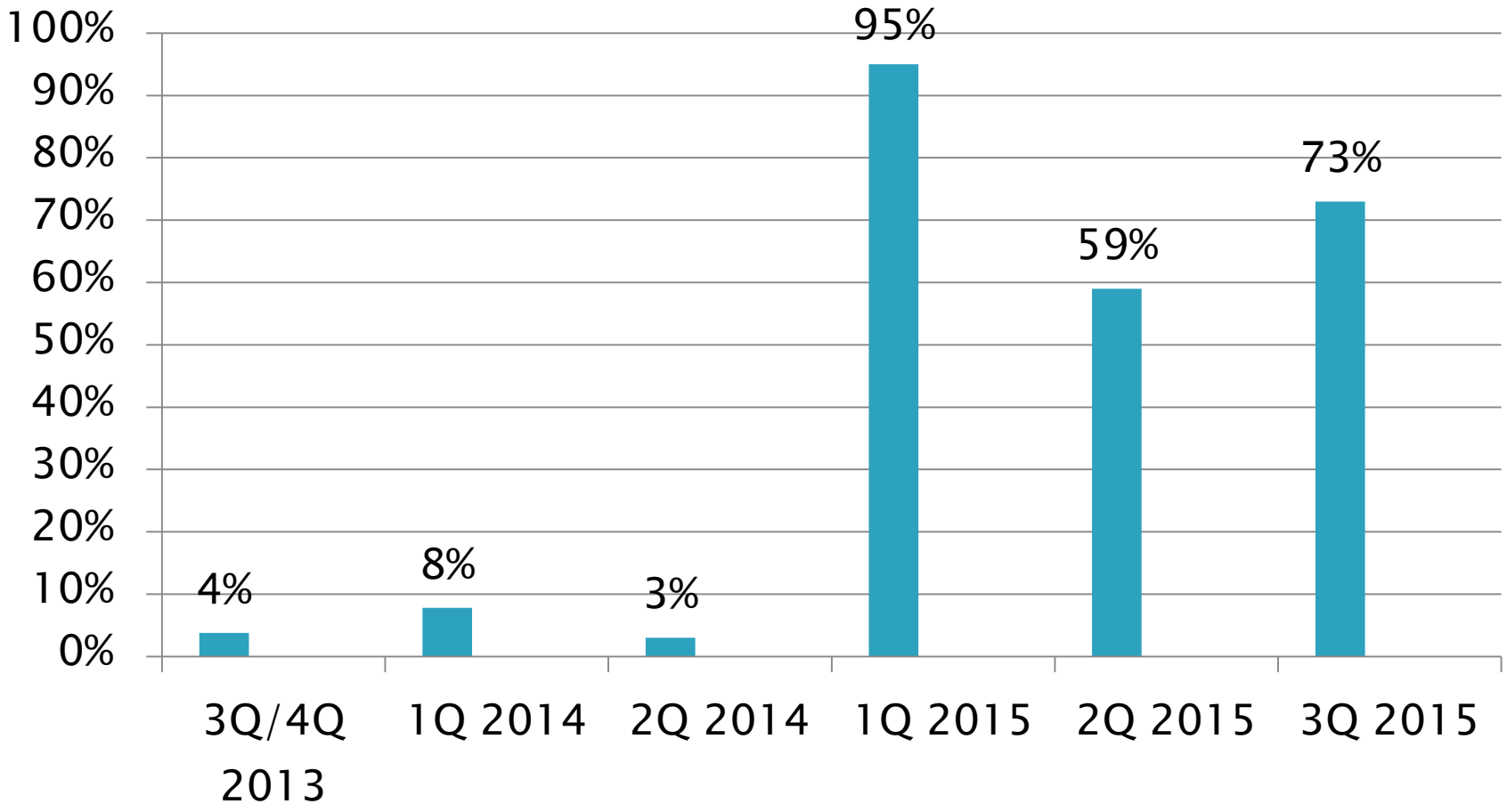
- Continue fluid boluses until MAP>65 or SBP>90
- Draw BCx's (always 2 sets)
- Meropenem-1 gm IVP over 3-5 mins
- Levaquin-750 mg IV over 0.5-1h
- Vancomycin-1 g IVPB over 45mins-1h

Place CVL if possible

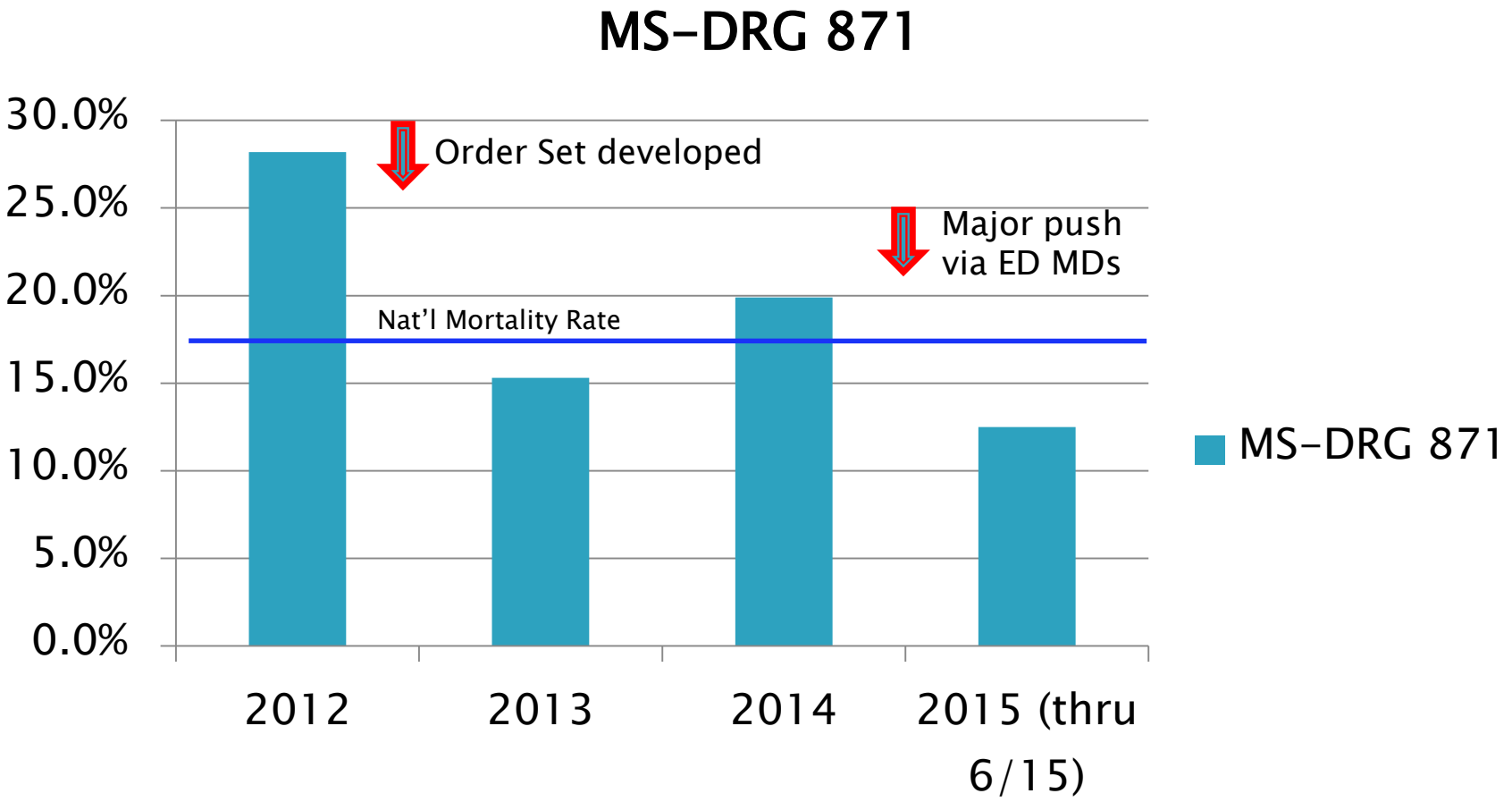
Phase 2 Sepsis Powerplan

- CVL must be in place
- Fluid management per defined CVP criteria
- Vasopressors dictated by MAP criteria
- Transfusions dictated by SvO2 criteria
- Predefined empiric antibiotic management directed by presumed source of infection
- CMS Core Measures addressed in powerplan.

Phase 1 PP Use (since launch)



Sepsis Mortality Rate



Sepsis/EGDT Summary

- Huge impact on society, financially, and patient outcomes (mortality, LOS, etc)
- **Must recognize and initiate treatment severe sepsis very early to impact survival**
- Modifiable determinants of mortality are aggressive fluid resuscitation and ABX initiation
- EGDT has the most significant impact on patient outcomes for sepsis in the last 25 years


WASHINGTON REGIONAL MEDICAL CENTER

"If you ask me the right questions,
I know some good answers."