Update in Hospital Medicine 2012

Brad Sharpe, MD, SFHM, FACP
UCSF Division of Hospital Medicine

Romsai Boonyasai, MD, MPH
Johns Hopkins Department of Medicine

Ethan Cumbler, MD, FACP
University of Colorado School of Medicine

Sponsored by the SGIM Academic Hospitalist Taskforce
Update in Hospital Medicine 2012

• Updated literature since March 2011

Process:
• CME collaborative review of journals
  ▪ Including ACP J. Club, J. Watch, etc.
• Five hospitalists ranked articles
  ▪ Definitely include, can include, don’t include
• Removed articles covered by others
Update in Hospital Medicine 2012

Chose articles based on 2 criteria:

1) Change, modify, or confirm your practice.
2) Change, modify, or confirm your teaching.

• Hope to limit our use of the words
  ▪ Markov model, Kaplan-Meier, Student’s t-test
• Focus on breadth, not depth
• Not all randomized-controlled trials

Update in Hospital Medicine
Update in Hospital Medicine 2012

- Major reviews/short takes
- Four cases, multiple choice questions
- Chance to ask questions
Syllabus/Bookkeeping

• Final presentation will be posted

• Can email me for copies:

  sharpeb@medicine.ucsf.edu
Case Presentation

On a busy on-call day your resident approaches you to present a case.

He describes a 63 year-old man with a history of HTN who presented with a few hours of shortness of breath and a new cough. At triage, he was afebrile, had a heart rate of 105, respiratory rate of 28, and a normal oxygen saturation.

The evaluation in the ED was negative - unremarkable exam, negative troponin x 2, normal EKG, normal CXR.
Case Presentation

The resident states “So, we thought about PE but he feels fine now – his shortness of breath has resolved and his heart rate is 60-70 and he is breathing at 14. If we use the normal vitals, his Wells and Geneva are basically negative. I was just going to have the ED discharge him.”

How do you respond to the resident?
How do you respond to the resident regarding this patient?

A. Why don’t we get a d-dimer, that could help us to rule out PE.
B. If the vitals have normalized, it is unlikely to be a PE – sounds like a plan.
C. You know, you can’t trust that the vitals have normalized – it still could be PE.
D. Great job using clinical prediction rules and evidence-based medicine, I like your plan.
E. You fist bump the resident, state “Block it baby! Yeah!” And then blow it up.
Vital Signs in PE

Question: Does normalization of vital signs in the ED help rule out PE?

Design: Prospective, obs study, 1 med center; Pts who got a CT scan for PE; vital signs at triage & per standard of care; Follow-up at 45 & 90 days

A total of 687 patients got a CT scan, 192 enrolled

Results

- Prevalence of PE was 18% (35/192)
- Most pts got 2, 3, or 4 sets of vitals

<table>
<thead>
<tr>
<th>Vital Sign</th>
<th>Prevalence of PE if vital normalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td></td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td></td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td></td>
</tr>
</tbody>
</table>

### Results

- Prevalence of PE was 18% (35/192)
- Most pts got 2, 3, or 4 sets of vitals

<table>
<thead>
<tr>
<th>Vital Sign</th>
<th>Prevalence of PE if vital normalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>18%</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td></td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td></td>
</tr>
</tbody>
</table>

Results

- Prevalence of PE was 18% (35/192)
- Most patients got 2, 3, or 4 sets of vitals

<table>
<thead>
<tr>
<th>Vital Sign</th>
<th>Prevalence of PE if vital normalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>18%</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>14%</td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td></td>
</tr>
</tbody>
</table>

## Results

- Prevalence of PE was 18% (35/192)
- Most patients got 2, 3, or 4 sets of vitals

<table>
<thead>
<tr>
<th>Vital Sign</th>
<th>Prevalence of PE if vital normalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>18%</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>14%</td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td>19%</td>
</tr>
</tbody>
</table>
Vital Signs in PE

Question: Does normalization of vital signs in the ED help rule out PE?

Design: Prospective, obs study, pts eval for PE in ED, vitals at triage & per protocol

Conclusion: Overall PE prevalence = 18%; no single vital predicted PE; normalization of vitals did not rule out PE in the ED

Comment: Small study, may be missing pts who didn’t get CT because of normalization of vitals

Many clinicians use vital sign normalization Prediction rules use most abnormal vital sign during evaluation

How do you respond to the resident regarding this patient?

A. Why don’t we get a d-dimer, that could help us to rule out PE.
B. If the vitals have normalized, it is unlikely to be a PE – sounds like a plan.
C. You know, you can’t trust that the vitals have normalized – it still could be PE.
D. Great job using clinical prediction rules and evidence-based medicine, I like your plan.
E. You fist bump the resident, state “Block it baby! Yeah!” And then blow it up.
Case Presentation

After reviewing this article, you decide to perform a CT scan and the patient has an acute subsegmental pulmonary embolism.

You find him ambulating around his room with normal vital signs including a heart rate of 65, respiratory rate of 16, and an oxygen saturation of 98% on room air.

His physical exam is normal and he asks you if he can take the blood thinners at home rather than staying in the hospital.
How do you know if he is safe to be treated as an outpatient?

A. If he has a negative troponin and BNP <100.
B. He has a normal respiratory rate and oxygen saturation on room air.
C. No evidence of right heart strain on echocardiogram.
D. If he is low risk using a severity scoring system.
E. If he has said goodbye to his wife and kids and is ready to meet his maker.
Outpatient vs. Inpatient PE

Question: Can patients with acute pulmonary embolism be managed as outpatients?

Design: Randomized trial, 19 EDs; pts with acute PE, low risk; inpt vs. outpt

- Low risk defined by PESI Score

Pulmonary Embolism Severity Index

- Age >80
- Male Gender
- History of Cancer, HF, COPD
- Pulse >110 bpm
- Systolic BP <100
- Respiratory Rate >30 bpm
- Temperature <36
- Altered Mental Status
- Arterial oxygen sat <90%

- Low risk = 0-2 risk factors
Outpatient vs. Inpatient PE

Question: Can patients with acute pulmonary embolism be managed as outpatients?

Design: Randomized trial, 19 EDs; pts with acute PE, low risk; inpt vs. outpt

- Low risk defined by PESI Score
- All received ≥5 days of LMWH & 90 days of oral anticoagulation
- Excluded if hypoxic, hypotensive, etc. or patients unable to participate

Results

- A total of 344 pts randomized

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Outpatient (n=172)</th>
<th>Inpatient (n=172)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent VTE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major Bleeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LOS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


*Update in Hospital Medicine*
### Results

- A total of 344 patients randomized

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Outpatient (n=172)</th>
<th>Inpatient (n=172)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent VTE</td>
<td>1 (0.6%)</td>
<td>0</td>
<td>non-inferior</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>3 (1.8%)</td>
<td>0</td>
<td>non-inferior</td>
</tr>
<tr>
<td>Mortality</td>
<td>1 (0.6%)</td>
<td>1 (0.6%)</td>
<td>non-inferior</td>
</tr>
<tr>
<td>LOS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Results

- A total of 344 patients randomized

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Outpatient (n=172)</th>
<th>Inpatient (n=172)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent VTE</td>
<td>1 (0.6%)</td>
<td>0</td>
<td>non-inferior</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>3 (1.8%)</td>
<td>0</td>
<td>non-inferior</td>
</tr>
<tr>
<td>Mortality</td>
<td>1 (0.6%)</td>
<td>1 (0.6%)</td>
<td>non-inferior</td>
</tr>
<tr>
<td>LOS</td>
<td>0.5 days</td>
<td>3.9 days</td>
<td>p &lt;0.001</td>
</tr>
</tbody>
</table>

### Results

- A total of 344 patients randomized

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Outpatient (n=172)</th>
<th>Inpatient (n=172)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent VTE</td>
<td>1 (0.6%)</td>
<td>0</td>
<td>non-inferior</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>3 (1.8%)</td>
<td>0</td>
<td>non-inferior</td>
</tr>
<tr>
<td>Mortality</td>
<td>1 (0.6%)</td>
<td>1 (0.6%)</td>
<td>non-inferior</td>
</tr>
<tr>
<td>LOS</td>
<td>0.5 days</td>
<td>3.9 days</td>
<td>p &lt;0.001</td>
</tr>
</tbody>
</table>

- Patient satisfaction same between groups (92% vs. 95%)
- 14% of outpts preferred more time in the hospital
- 29% of inpts preferred to be treated at home.
Outpatient vs. Inpatient PE

Question: Can patients with acute pulmonary embolism be managed as outpatients?

Design: Randomized trial, 19 EDs; pts with acute PE, low risk; inpt vs. outpt

Conclusion: Outpt not inferior to inpt; similar rates of recurrent VTE & bleeding; LOS much shorter with outpt treatment

Comment: Small study, not real-life management; long LOS for hospitalized pts? Raises question of outpt management of PE Likely not ready for prime time But, use PESI to consider earlier discharge

How do you know if he is safe to be treated as an outpatient?

A. If he has a negative troponin and BNP <100.
B. He has a normal respiratory rate and oxygen saturation on room air.
C. No evidence of right heart strain on echocardiogram.
D. If he is low risk using a severity scoring system.
E. If he has said goodbye to his wife and kids and is ready to meet his maker.
Case Continued

The patient is low risk but you are (appropriately) anxious about discharging that day. He is started on LMWH and warfarin.

The following morning the medical student presents the case and at the end states, “So for GI prophylaxis, the patient was started on a proton pump inhibitor.”

What do you think about this choice for GI prophylaxis?
What do you think about this choice for GI prophylaxis in this patient?

A. A PPI is a good choice.
B. Should go with an H2 blocker
C. Tums tums tums tums tums tums.
D. This patient should not get GI prophylaxis.
E. You’re staring at your Nexium pen, your Wyeth badge holder, and your Pfizer breath mints (why breath mints?) with fond memories of that fancy Aciphex® dinner and wonder what to do…
Question: For non-ICU inpatients, do PPIs or H2 blockers lower the incidence of nosocomial GI bleeding?

Design: Observational cohort study; 78,394 adult inpatients; compared PPI or H2 blocker usage to no therapy; Standard definition for nosocomial GI bleeding

## Results

- Incidence of nosocomial UGI B: 0.29%
- Incidence of clinically significant UGI B: 0.22%

### Incidence of nosocomial UGI B:

<table>
<thead>
<tr>
<th>PPI or H2B</th>
<th>Adjusted OR* (95% CI)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nosocomial UGI B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clin Sig UGI B</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*With propensity scoring

Controlled for anticoagulation
Independent of DVT prophylaxis

Herzig, SJ et al. *Arch Int Med.* 2011;171:991
### Results

- Incidence of nosocomial UGI B: 0.29%
- Incidence of clinically significant UGI B: 0.22%

<table>
<thead>
<tr>
<th>PPI or H2B</th>
<th>Adjusted OR* (95% CI)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nosocomial UGI B</td>
<td>0.63 (0.42-0.93)</td>
<td>770</td>
</tr>
<tr>
<td>Clin Sig UGI B</td>
<td>0.58 (0.37-0.91)</td>
<td>834</td>
</tr>
</tbody>
</table>

Controlled for anticoagulation
Independent of DVT prophylaxis

*With propensity scoring

Herzig, SJ et al. *Arch Int Med.* 2011;171:991
Acid-Suppression & Nosocomial GI Bleeding

Question: For non-ICU inpatients, do PPIs or H2 blockers lower the incidence of nosocomial GI bleeding?

Design: Observational cohort study, 79,287 adult inpatients; compared PPI or H2 vs. nothing

Conclusion: Incidence of nosocomial UGIB out of the ICU very low; PPI or H2 blockers reduced bleeding; independent of DVT proph

Comments: Retrospective, administrative data

Beneficial, but rare event and meds have costs/side effects; OK to continue if on it

Not routinely use GI proph. in non-ICU pts

Herzig, SJ et al. Arch Int Med; 2011;171:991
What do you think about this choice for GI prophylaxis in this patient?

A. A PPI is a good choice.
B. Should go with an H2 blocker
C. Tums tums tums tums tums tums.
D. This patient should not get GI prophylaxis.
E. You’re staring at your Nexium pen, your Wyeth badge holder, and your Pfizer breath mints (why breath mints?) with fond memories of that fancy Aciphex® dinner and wonder what to do…
In a systematic review, proton pump inhibitors are associated with an increased susceptibility to:

- *Clostridium difficile*-associated diarrhea
- *Salmonella*
- *Campylobacter*

You quote this article to the medical student and the team and decide he does not need GI prophylaxis.

Not wanting to miss a “teachable moment” you decide to ask a question about DVT prophylaxis. You turn to the resident and ask, “What does the data suggest is the optimal strategy for DVT prophylaxis in non-ICU medical patients?”

How does the resident respond to your question?
How does the resident respond to your question about DVT prophylaxis?

A. Twice daily unfractionated heparin (UFH) is best.
B. Once daily LMWH is the best strategy.
C. We’ve been doing three-times daily UFH.
D. I think BID UFH, TID UFH, and once-daily LMWH are all the same.
E. I think there is some new evidence that daily Zumba works.
**Optimal DVT Prophylaxis Dosing**

**Question:** In non-ICU medical patients, what is the optimal strategy for pharmacologic DVT prophylaxis?

**Design:** Mixed-treatment comparison meta-analysis of RCTs; BID UFH, TID UFH, or LMWH vs. placebo or vs. each other;

Results

- Included 16 trials; 27,667 patients
- Data vs. controls below

<table>
<thead>
<tr>
<th></th>
<th>DVT</th>
<th>PE</th>
<th>Major Bleed</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>BID UFH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TID UFH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily LMWH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Results

- Included 16 trials; 27,667 patients
- Data vs. controls below

<table>
<thead>
<tr>
<th></th>
<th>DVT</th>
<th>PE</th>
<th>Major Bleed</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>BID UFH</td>
<td>0.28*</td>
<td>0.33</td>
<td>3.81</td>
<td>0.94</td>
</tr>
<tr>
<td>TID UFH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily LMWH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* p<0.05
## Results

- Included 16 trials; 27,667 patients
- Data vs. controls below

<table>
<thead>
<tr>
<th></th>
<th>DVT</th>
<th>PE</th>
<th>Major Bleed</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>BID UFH</td>
<td>0.28*</td>
<td>0.33</td>
<td>3.81</td>
<td>0.94</td>
</tr>
<tr>
<td>TID UFH</td>
<td>0.42*</td>
<td>0.54</td>
<td>3.39</td>
<td>1.10</td>
</tr>
<tr>
<td>Daily LMWH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* *p* < 0.05
Results

- Included 16 trials; 27,667 patients
- Data vs. controls below

<table>
<thead>
<tr>
<th></th>
<th>DVT</th>
<th>PE</th>
<th>Major Bleed</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>BID UFH</td>
<td>0.28*</td>
<td>0.33</td>
<td>3.81</td>
<td>0.94</td>
</tr>
<tr>
<td>TID UFH</td>
<td>0.42*</td>
<td>0.54</td>
<td>3.39</td>
<td>1.10</td>
</tr>
<tr>
<td>Daily LMWH</td>
<td>0.38*</td>
<td>0.47</td>
<td>1.16</td>
<td>0.97</td>
</tr>
</tbody>
</table>

* p<0.05
## Results

- Included 16 trials; 27,667 patients
- Data vs. controls below

<table>
<thead>
<tr>
<th></th>
<th>DVT</th>
<th>PE</th>
<th>Major Bleed</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>BID UFH</td>
<td>0.28*</td>
<td>0.33</td>
<td>3.81</td>
<td>0.94</td>
</tr>
<tr>
<td>TID UFH</td>
<td>0.42*</td>
<td>0.54</td>
<td>3.39</td>
<td>1.10</td>
</tr>
<tr>
<td>Daily LMWH</td>
<td>0.38*</td>
<td>0.47</td>
<td>1.16</td>
<td>0.97</td>
</tr>
</tbody>
</table>

- No difference between the 3 strategies.
Optimal DVT Prophylaxis Dosing

Question: In non-ICU medical patients, what is the optimal strategy for pharmacologic prophylaxis?

Design: Mixed-treatment meta-analysis of RCTs; BID UFH, TID UFH, or LMWH vs. placebo or vs. each other;

Conclusion: All 3 strategies decreased DVT but no impact on PE, bleed, death; No difference among the 3 strategies

Comments: Method dilutes data, allows for comparison Compared with prior meta-analyses; Unlikely to get a large definitive RCT; Base decisions on cost, availability, local

How does the resident respond to your question about DVT prophylaxis?

A. Twice daily unfractionated heparin (UFH) is best.
B. Once daily LMWH is the best strategy.
C. We’ve been doing three-times daily UFH.
D. I think BID UFH, TID UFH, and once-daily LMWH are all the same.
E. I think there is some new evidence that daily Zumba works.
Short Take: Voluntary Urinary Retention

In a prospective study, healthy volunteers drank 250ml of water every 15 minutes while doing cognitive tests (had to hold it).

Voluntary urinary retention reduced decision-making speed and delayed retrieval from working memory (like a BAL of 0.05%).

Performance on cognitive tests returned to normal after micturition.

Summary

Definitely

1) Don’t use normalization of vital signs in the ED to rule out pulmonary embolism.
2) Don’t routinely give GI prophylaxis to non-ICU medical inpatients.

Consider

1) Using the PESI score to determine low-risk in patients with PE.
2) Why patients are on PPIs as they can increase the risk for *C diff*.
3) Any of the 3 dosing strategies for DVT prophylaxis in non-ICU medical patients.
Update in Hospital Medicine
Case Presentation

A 67 year old nutritional epidemiologist is referred by his PCP for a 2 day history of fever, tachycardia, and weakness. Initial studies are notable for WBC 15K and CXR showing bilateral LL infiltrates. She is admitted for “pneumonia” but as you are writing admission orders, she tells you that she wants to avoid antibiotics if possible. She tells you she has heard something about “this Procalcitonin test” and wonders if it would help her avoid pharmaceuticals.
“What about this procalcitonin test?”

A. The test can distinguish between a bacterial infection and other inflammatory states, but there is a slightly higher risk of dying when it’s used to guide antibiotic treatment decisions

B. It can help us distinguish between a bacterial pneumonia and some other problem. There is no difference in mortality rates when it’s used to guide treatment decisions

C. I’m the doctor, you’re the patient. Take your antibiotics like a good girl….there you go!
Procalcitonin to guide abx prescribing

Question: What is the evidence for using procalcitonin levels to guide antibiotic prescribing?

Design: Systematic review of 14 RCTs

- Studies involved 4467 patients
- 2 studies in primary care setting
- 6 studies in emergency dept. setting
- 6 studies in intensive care unit setting

*Only 3 studies considered to be low-risk for bias*

### Results

<table>
<thead>
<tr>
<th>Setting</th>
<th>Studies</th>
<th>OR for death (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary care</td>
<td>2</td>
<td>0.13 (0-6.64)</td>
</tr>
<tr>
<td>ED</td>
<td>6</td>
<td>0.95 (0.67-1.36)</td>
</tr>
<tr>
<td>ICU</td>
<td>6</td>
<td>0.89 (0.66-1.20)</td>
</tr>
<tr>
<td>Overall</td>
<td>14</td>
<td>0.91 (0.73-1.14)</td>
</tr>
</tbody>
</table>

- Reduced abx prescribing in primary care and ED settings
- Reduced abx duration in high-acuity ED and ICU settings

Question: What is the evidence for using procalcitonin levels to guide antibiotic prescribing?

Design: Systematic review of 14 RCTs

Conclusion: Using procalcitonin algorithms to make antibiotic treatment decisions decreases overall antibiotic exposure without increasing mortality

Comments: Studies are heterogeneous and only 3 are considered low-risk for bias

“What about this procalcitonin test?”

A. The test can distinguish between a bacterial infection and other inflammatory states, but there is a slightly higher risk of dying when it’s used to guide antibiotic treatment decisions.

B. It can help us distinguish between a bacterial pneumonia and some other problem. There is no difference in mortality rates when it’s used to guide treatment decisions.

C. I’m the doctor, you’re the patient. Take your antibiotics like a good girl….there you go!
Case Presentation

The procalcitonin level is 1.1 mcg/L, consistent with bacterial pneumonia. You decide to treat. As you head down to the ED for your 6th admission, her nurse asks if your patient should receive steroids too.
Should your patients also be on steroids?

A. This is pneumonia, not COPD. Steroids won’t help.

B. Hmmm...steroids have been associated with shorter lengths of stay when given to patients hospitalized with pneumonia.

C. Steroids would compromise her immune response and worsen her pneumonia, actually.

Dexamethasone for pts with CAP

**Question:** How does IV dexamethasone compare with placebo in reducing LOS in hospitalized patients with CAP?

**Design:** Triple-blind placebo-controlled RCT

304 non-immunocompromised patients with abnormal CXR and $\geq 2$ symptoms

- Dexamethasone 5 mg IV daily x 4 days vs. saline placebo
- Primary outcome: hospital length of stay
- Secondary outcomes: mortality, ICU admission, empyema, 30-day readmissions

## Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dexamethasone</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOS, days (IQR)</td>
<td>6.5 (5-9)</td>
<td>7.5 (5.3-11.5)</td>
<td>0.048</td>
</tr>
</tbody>
</table>

- No difference in hospital mortality, 30 day mortality, ICU admission, development of empyema, or 30-day readmission
- Patients in dexamethasone group reported higher social functioning at 30 days (P=0.009)
- Patients in dexamethasone group had higher rates of hyperglycemia (44% vs. 23%, P<0.001)

Dexamethasone for pts with CAP

**Question:** How does IV dexamethasone compare with placebo in reducing LOS in hospitalized patients with CAP?

**Design:** Triple-blind placebo-controlled RCT
- 304 non-immunocompromised patients with abnormal CXR and ≥2 symptoms

**Conclusion:** Dexamethasone can reduce hospital LOS when added to antibiotics in non-immunocompromised patients with community-acquired pneumonia

**Comment:** Study from Netherlands, where average LOS is longer than in U.S.

Should your patients also be on steroids?

A. This is pneumonia, not COPD. Steroids won’t help.
B. Hmmm... steroids have been associated with shorter lengths of stay when given to patients hospitalized with pneumonia.
C. Steroids would decrease her immune response and worsen her pneumonia, actually.
You go back to recommend adding steroids to your patient’s antibiotic regimen, but she expresses reluctance because steroids have so many side effects.

She tells you, “You doctors are always pushing treatments that you wouldn’t take yourself.”

Is she right?
A survey of 940 primary care physicians from AMA Masterfile presented respondents 1 of 2 scenarios, each involving 2 treatment alternatives. One alternative offered a better chance of survival from a fatal illness, the other offered a higher risk for unpleasant side effects. Respondents were randomly asked to select a treatment alternative either for themselves or as a recommendation to a hypothetical patient.

In both scenarios, more physicians chose the treatment with a higher death rate/fewer side-effects for themselves, but the one with lower mortality risk for their patients.

Case Continued

Four days into her hospitalization, you patient develops diarrhea. A *C. difficile* PCR confirms your suspicion. In discussing treatment options with a medical student, you learn that your patient had *C. difficile* two months ago. Your student wonders, “should we prescribe a ‘stronger’ antibiotic?”
Should we choose a stronger antibiotic?

A. Good pick-up, let’s go with Vancomycin

B. Studies have shown that adding rifampin to the metronidazole is beneficial. Let’s do that.

C. There really isn’t any difference in initial cure rates among the antibiotic option, so let’s go with the one that is least harmful and least costly.

D. Why don’t you fetch me a donut, one with sprinkles on top?
Comparing treatments for *C. difficile*

**Question:** What is the comparative effectiveness and harms of different antibiotic treatments for *C. difficile*?

**Design:** Systematic review of 11 RCTs

- Studies involved 1463 participants
- 3 compared metronidazole vs. vancomycin
- 8 compared another abx vs. metronidazole or vancomycin

- Strength of evidence *moderate* for:
  - Initial cure with metronidazole vs. vancomycin
  - Initial cure or recurrence with vancomycin vs. fidaxomicin

Vancomycin vs. metronidazole (3 studies, 335 patients)
- Initial cure with vancomycin: 84-94%
- Initial cure with metronidazole 73-94%
- Recurrence with vancomycin 7-17%
- Recurrence with metronidazole 5-21%

NS

NS

Results

Vancomycin vs.
- Fidaxomicin (1 study, 629 patients)**
- Nitazoxanide (1 study, 50 patients)
- Bacitracin (1 study, 81 patients)

Metronidazole vs.
- Nitazoxanide (1 study, 142 patients)
- Metronidazole plus rifampin (1 study, 39 patients)

** Subgroup analysis of comparing fidaxomicin vs. vancomycin found decreased recurrence with fidaxomicin (15% vs. 25%, $P = 0.005$)

Comparing treatments for *C. difficile*

**Question:** What is the comparative effectiveness and harms of different antibiotic treatments for *C. difficile*?

**Design:** Systematic review of RCTs

**Conclusion:** No antibiotic is superior for achieving initial cure with *C. difficile* infection. Recurrence occurs less often with fidaxomicin vs. vancomycin.

**Comment:** There was substantial variability in definitions for infection, cure and recurrence among all studies.

Should we choose a stronger antibiotic?

A. Good pick-up, let’s go with Vancomycin
B. Studies have shown that adding rifampin to the metronidazole is beneficial. Let’s do that.
C. There really isn’t any difference in initial cure rates among the antibiotic option, so let’s go with the one that is least harmful and least costly.
D. Why don’t you look that up and give me a report on Tuesday
Your patient confirm that she was recently treated for C. difficile. She asks is this a new infection or if perhaps she was inadequately treated the last time. She also wants to know if there are any “natural” remedies…
Investigators at a tertiary care cancer center identified 102 patients with C. difficile infection occurring ≥2 weeks apart. Time between infections was recorded and isolates were identified with PCR ribotyping to distinguish relapse vs. new infection.

<table>
<thead>
<tr>
<th>Time between episodes</th>
<th>Total</th>
<th>Relapse</th>
<th>2nd infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-4 weeks</td>
<td>48</td>
<td>43 (90%)</td>
<td>5 (10%)</td>
</tr>
<tr>
<td>4-8 weeks</td>
<td>37</td>
<td>32 (87%)</td>
<td>5 (14%)</td>
</tr>
<tr>
<td>&gt;8 weeks</td>
<td>49</td>
<td>32 (65%)</td>
<td>17 (35%)</td>
</tr>
</tbody>
</table>

A systematic review of 27 case series, involving 314 patients found fecal transplantation to be highly effective, resulting in disease resolution in 92% of cases overall.

Summary

Definitely

1) View metronidazole and vancomycin as interchangeable for treating *C. difficile* colitis

Consider

1) Prescribing intestinal microbiota transplantation for recurrent *C. difficile* infections
2) Using procalcitonin levels as an adjunct to other diagnostic information when there is uncertainty about a bacterial infection
3) Adding dexamethasone to standard therapies when treating community-acquired pneumonia in non-immunocompromised patients
Case Presentation

A 79 year old man “Mr Air Unger” with COPD, DMII, CAD, urge incontinence and insomnia presents with productive cough, and hypercarbic resp failure. This is his third exacerbation this year.

While writing admit orders your EMR helpfully alerts you to a drug interaction as you have ordered albuterol (beta agonist) and his home metoprolol (beta antagonist).
How should you respond to the EMR alert regarding beta-blockers in COPD?

A. Ignore it. Beta-blockers in COPD are safe.
B. Good catch EMR! this really could be a problem and you should stop the beta-blocker since COPD is most active issue.
C. Continue only metoprolol based on MI being most likely to cause mortality.
D. Complain to everyone within ear-shot about how you hate EMRs. Go on to reminisce about the good old days of bloodletting and tincture of arsenic to treat syphilis.
Question: What is the impact of long-term β-blocker use in patients with COPD?

Design: Scottish Retrospective cohort study of 5977 pts. Disease specific COPD database cross referenced with pharmacy utilization and hospitalization data.

Results

22% reduction in mortality in cases where beta-blockers were used

HR 0.78 [95% CI 0.67-0.92]

No harmful effect on FEV1

Interestingly a reduction in corticosteroids and hospitalization for respiratory problems and COPD

β-blockers & COPD

Question: What is the impact of long-term b-blocker use in patients with COPD?
Design: Scottish Retrospective cohort study of 5977 pts. Disease specific COPD database cross referenced with pharmacy utilization and hospitalization data

Comment: Retrospective- Confounding by indication? 88% cardioselective- may not apply to nonselective

Conclusion: Contrary to popular understanding, Beta-blockers do not worsen pulmonary function in COPD patients and improve overall outcomes.

“Half of what you’ll learn in medical school will be shown to be either dead wrong or out of date within five years of your graduation.....

the trouble is that nobody can tell you which half”

David Sackett
How should you respond to the EMR alert regarding beta-blockers in COPD?

A. Ignore it. Beta-blockers in COPD are safe.
B. Good catch EMR! this really could be a problem and you should stop the beta-blocker since COPD is most active issue.
C. Continue only metoprolol based on MI being most likely to cause mortality.
D. Complain to everyone within ear-shot about how you hate EMRs. Go on to reminisce about the good old days of bloodletting and tincture of arsenic to treat syphilis.
Short Take: Does your patient use his inhaler correctly…..or not so much?

A cross-sectional hospital-based study
(40 COPD, 60 Asthma)

Misuse of inhalers was common
- 86% for use of MDIs
- 71% with Disc inhalers

With training all were able to master inhaler use.

Bottom Line- Hospitalization is an opportunity for inhaler use training

Your patient is started on systemic steroids and initial BG is 330 mg/dl.

A first year student shadowing you for the day asks “I was taught that hyperglycemia is associated with adverse outcomes. How do you handle this issue in the hospital?”
How should you tell her to manage hyperglycemia in hospitalized patients?

A. Continue home sulfonylurea

B. Regular insulin sliding scale

C. Pre-meal anticipatory short acting plus long acting basal insulin to a goal of BG<180

D. Intensive insulin therapy to maintain normoglycemia

E. No therapy, glucosurea is a “natural” diuretic
Management of Hyperglycemia

Question: What is the role of intensive insulin therapy in hospitalized patients?

Design: Systematic Review and Meta-analysis
21 trials (ICU, periop, MI, CVA)

- No Impact on Short Term Mortality
- No Impact on Infection Rates
- No Impact on Length of Stay
- No Impact on Need for Dialysis
- Six fold increased risk of hypoglycemia

The Pendulum Swings
“Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true.”

How should you tell her to manage hyperglycemia in hospitalized patients?

A. Continue home sulfonylurea
B. Regular insulin sliding scale
C. Pre-meal anticipatory short acting plus long acting basal insulin to a goal of BG<180
D. Intensive insulin therapy to maintain normoglycemia
E. No therapy, glucosurea is a “natural” diuretic
An unbelievably bright and capable hospitalist has created an ACE unit in the hospital.

For an elderly patient such as this would it make a difference if he were admitted there versus to the general wards.
Meta-analysis of RCTs--22 Trials of 10,351 pts
“comprehensive geriatric assessment”- Interdisciplinary care

- ACE care increases chance of living in the community after d/c
  - OR 1.16 [95% CI 1.05-1.28; p=0.003]
  - NNT 33
  - Effect was seen for units not mobile teams
- No difference in mortality or readmissions
- Impact on cost difficult to analyze

Bottom Line-ACE model improves functional outcomes for elderly patients

Short Take: On D/C Which Medicine is Most Likely to Cause Him to Be Readmitted?

- **Design**: Retrospective sample of adverse event database

  **Results**
  Two medication classes caused 2/3rd of all ADEs causing hospitalization
  - Hypoglycemics
  - Antithrombotics
  Classically defined “High Risk Meds in the Elderly”
  Caused a small minority of hospitalizations
  - Beers List meds in 6.6%
  - HEDIS meds in 1.2%

- **Limitations**: Drugs with most obvious connections to presenting problems likely overrepresented (“Detection bias”) compared to more complex, subtle, or multidrug reactions which contribute to geriatric syndromes

This patient has been hospitalized for COPD every 4 months….are there any new options to keep him out of the hospital longer?
Which of the following is true about long term Azithromycin for COPD Hospitalizations?

A. Chronic Azithromycin is ineffective in reducing COPD exacerbations
B. It is unclear if it reduces exacerbations but with no side effects it can’t hurt
C. Azithromycin reduces exacerbations but not re-hospitalizations over one year
D. The government put Azithromycin in the water in 2009 as a mind control agent to get the public to accept the MMR Vaccine so additional antibiotics are unnecessary.

Update in Hospital Medicine
Chronic Azithromycin for COPD

Question: Can long term antibiotics improve COPD outcomes?

Design: Randomized Controlled Study
1142 Patients with normal hearing and Qtc
Azithromycin 250mg po qd or Placebo for 1 year

Primary Outcome- Time to first exacerbation
Defined as new or increased cough, sputum, wheezing, dyspnea, or chest tightness requiring treatment with steroids or antibiotics

## Results

### Exacerbation Rate per Year

<table>
<thead>
<tr>
<th></th>
<th>Azithromycin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED Visits</td>
<td>0.43</td>
<td>0.47</td>
</tr>
<tr>
<td>COPD Hospitalizations</td>
<td>0.34</td>
<td>0.49</td>
</tr>
</tbody>
</table>

### Median Time to First Exacerbation

- **Azithromycin**: 266 days [95% CI 227-313]
- **Placebo**: 174 days [95% CI 143-215]

**HR 0.73 p<0.001**

**Results**

- Hearing loss more common with azithromycin
  - 25% vs. 20%
  - P = 0.04

- New colonization with resp pathogens was with organisms resistant to Azithromycin 81% of the time compared to 41% in placebo group.

- ? clinically significant change in quality of life

Chronic Antibiotics for COPD

Question: Can long term Azithromycin improve COPD outcomes?

Design: Randomized Controlled Study. 1142 Patients with normal hearing and Qtc. Azithromycin 250mg po qday or Placebo for 1 year

Comments:
1. Study was plagued by protocol errors
2. Lasted only one year
   -(for a life-long disease)
3. Long term impact on hearing loss unknown
4. Antimicrobial selection pressure may have unintended consequences at population level

Conclusion:
Interesting….but not ready to apply to practice

Lindenauer PK, et al. JAMA;2010;303:2359.
Which of the following is true about long term Azithromycin for COPD Hospitalizations?

A. Chronic Azithromycin is ineffective in reducing COPD exacerbations
B. It is unclear if it reduces exacerbations but with no side effects it can’t hurt
C. Azithromycin reduces exacerbations but not re-hospitalizations over one year
D. The government put Azithromycin in the water in 2009 as a mind control agent to get the public to accept the MMR Vaccine so additional antibiotics are unnecessary.
On his way out the door you notice your patient methodically cracking the knuckles of his left hand. “Best give up that habit if you don’t want to get arthritis” you say.

**Design:** For 50 yrs the author cracked the knuckles of his left hand 2x/day, 36500 times total. The right hand “control” was not cracked—“Self Control.” No arthritis developed in either hand.

Summary

**Definitely**

1) Do not be afraid to use beta-blockers in COPD.
2) Recognize that intensive insulin therapy to achieve normoglycemia has harm and no clear benefit.
3) Do not use Azithromycin to prevent COPD exacerbations until we have longer follow-up.

**Consider**

1) ACE units are effective at keeping patients out of nursing homes.
Case Presentation

You are rounding on-call with your team and the intern presents a 48 year-old woman with metastatic breast cancer who was admitted with fever and confusion. Based on the evaluation, the team is concerned about a line infection.

She has borderline blood pressures despite an appropriate fluid resuscitation.

The intern states, “You know, we need to leave now to make our duty hours and we think she might need a pressor. Can you look up which is the best one in septic shock and start it if she continues to tank her pressures?”
How do you respond to the interns question about pressors in septic shock?

A. Dopamine is the best agent.
B. I’d go with phenylephrine (Neosynephrine®).
C. Definitely norepinephrine (Levophed®=“Leave ’em-dead”).
D. I like vasopressin.
E. You’re about to start in with a statement that begins with “Listen squirt” and references “when I was a resident . . .” But, instead you pause, sigh, ever-so-gently shake your head . . . and go to write the order.
Dopamine vs. Norepinephrine

Question: In patients with **septic** shock, what is the optimal first-line vasopressor agent, dopamine or norepinephrine?

Design: Meta-analysis of observational studies and RCTs; dopamine vs. norepinephrine

- Five observational studies, 1360 patients
- Six RCTs, 1408 patients

### Results

- Calculated relative risk for dopamine vs. norepi

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Observational</th>
<th>RCTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (28 d)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results

- Calculated relative risk for dopamine vs. norepi

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Observational</th>
<th>RCTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (28 d)</td>
<td>1.23* (1.05-1.43)</td>
<td>1.12* (1.01-1.20)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results

- Calculated relative risk for dopamine vs. norepi

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Observational</th>
<th>RCTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (28 d)</td>
<td>1.23* (1.05-1.43)</td>
<td>1.12* (1.01-1.20)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>N/A</td>
<td>2.34* (1.46-3.77)</td>
</tr>
</tbody>
</table>

- No difference in ICU LOS or hospital LOS
- Absolute risk reduction: ~ 3.5%

## Dopamine vs. Norepinephrine

**Question:** In pts with septic shock, what is the optimal first-line pressor agent, dopamine or norepinephrine?

**Design:** Meta-analysis of observational studies and RCTs; dopamine vs. norepinephrine

**Conclusion:** Increased mortality with dopamine in septic shock in observational and RCTs; arrhythmias more common with dopamine

**Comments:** Well done, good methodology; use norepi as first-line agent in septic shock; likely should be first-line in other shock; work with ED/ICU providers.

How do you respond to the interns question about pressors in septic shock?

A. Dopamine is the best agent.
B. I’d go with phenylephrine (Neosynephrine®).
C. Definitely norepinephrine (Levophed®=“Leave-’em-dead”).
D. I like vasopressin.
E. You’re about to start in with a statement that begins with “Listen squirt” and references “when I was a resident . . .” But, instead you pause, sigh, ever-so-gently shake your head . . . and go to write the order.
**Short Take: Early v Late TPN**

In a randomized, multi-center trial comparing early (day 2) to late (day 8) initiation of TPN in critically ill patients, late TPN was associated with:

- Better ICU and hospital survival
- Fewer infections
- Less time on the ventilator
- Lower healthcare costs

Case Presentation

You do not start TPN but continue the enteral feeding.

Unfortunately the patient does not do well. She is intubated, stays on norepinephrine and develops multi-organ system failure.

You meet with her husband (DPOA) describe her condition and state clearly “It is unlikely she will survive. That means she is likely to die.”

What do you think his estimated percent chance of survival is for her based on this statement?
What is his estimated percent chance of survival for her based on this statement?

A. 0%
B. 5%
C. 50%
D. 30%
E. It is not effective to be quantitative with patients or surrogates as they may not understand.
F. It was hard to come up with an appropriate "joke" answer for this one. But, if you’re the one person that has to answer F, go right ahead.
Interpretation of Prognostic Information

Question: How do surrogates interpret prognostic statements and why?

Design: Mixed qualitative/quantitative; 3 ICUs; Approached surrogates of critically ill patients; Asked to interpret 16 prognostic statements, estimate % survival

- Using a numeric probability scale (0-100%)
- Ranging from “he will definitely survive” to “definitely not”
- If discordant, asked why estimate was different

Total of 80 surrogates included

Results

- Surrogates over-estimated prognosis when given survival estimates of < 50%;
- Some unaware of over-estimation
- Four main explanations:

1) Need to express optimism
2) Belief in patient’s fortitude
3) Disbelief in physician ability to prognosticate
4) Interpretation of prognosis as a “gist” and not a precise estimate

## Interpretation of Prognostic Information

**Question:** How do surrogates interpret prognostic statements and why?

**Design:** Mixed qualitative/quantitative; surrogates of critically ill pts; interpreted prognostic statements;

**Conclusion:** Surrogates inaccurately interpret poor prognostic statements; accurate with better prognoses; many complex reasons for this

**Comments:** Small study, hypotheticals on paper; Surrogates may be overly optimistic, be aware
Not just about the misunderstanding; May need to address reasons for optimism

What is his estimated percent chance of survival for her based on this statement?

A. 0%
B. 5%
C. 50%
D. 30%
E. It is not effective to be quantitative with patients or surrogates as they may not understand.
F. It was hard to come up with an appropriate “joke” answer for this one. But, if you’re the one person that has to answer E, go right ahead.
You have a good discussion with the husband and after a few more days everyone agrees to withdraw care. She dies peacefully with her husband and two kids at her bedside.

The husband says very clearly that he wants an autopsy, “So you all can learn from taking care of her – she would have wanted that.”

What is the chance that an autopsy will find a major diagnosis which could have impacted treatment?
In a prospective single-center study of 834 autopsies in ICU patients revealed 7.5% had a major error which could have impacted treatment and 11.4% had major unexpected findings which would not have changed treatment.

The most common major diagnoses discovered were pulmonary embolism, pneumonia, secondary peritonitis, invasive aspergillus, endocarditis, and MI.

Summary

Definitely

1) Use norepinephrine as your first-line agent in patients with septic shock.
2) Understand how surrogates may be overly optimistic if presented with poor prognostic information.

Consider

1) Delaying TPN until after at least a week in the ICU.
2) Other major diagnoses that might be found at autopsy in critically ill patients.