Highlights in the Medicine Literature from 2016-2017:

Should any results change our practice?

Kelly Evans, MD
“We are constantly misled by the ease with which our minds fall into the ruts of one or two experiences.”

“No human being is constituted to know the truth, the whole truth, and nothing but the truth; and even the best of men must be content with fragments, with partial glimpses, never the full fruition.”

-Sir William Osler
I have no conflicts of interest to disclose.
Objectives

• Derive clinical meaning from 3 recently published articles- RCT and other data types

• Discuss the merits and flaws of each trial

• Decide if each trial is meaningful enough to affect or change one’s current practice in regards to the relevant condition
Prevalence of Pulmonary Embolism among Patients Hospitalized for Syncope

Paolo Prandoni, M.D., Ph.D., Anthonie W.A. Lensing, M.D., Ph.D.,
Martin H. Prins, M.D., Ph.D., Maurizio Ciammaichella, M.D., Marica Perlati, M.D.,
Nicola Mumoli, M.D., Eugenio Bucherini, M.D., Adriana Visonà, M.D.,
Carlo Bova, M.D., Davide Imberti, M.D., Stefano Campostrini, Ph.D.,
and Sofia Barbar, M.D., for the PESIT Investigators*

NEJM 2016 375:16
Background

• Syncope... Ugh.

• Current AHA guidelines for w/u do not include guidance for whether we should r/o PE

• Should non-massive PE physiologically cause syncope?
The Study

- Cross-sectional study to determine prevalence
- Patients enrolled 2012-2014
- Patients: Adults admitted to 11 Italian hospitals for a first episode of syncope
  - NOT: Outpatients, patients discharged from ED, recurrent/previous episodes syncope, pts on anticoag, pregnant pts
The Study: Protocol

- PE ruled out or in within 48 hrs of admission in all eligible patients

Wells Score
- <4 (low prob)
- >4 (high prob)

D-dimer*
- Negative – RULED OUT
- Positive

CT PE or V/Q scan

*Used lab cutoff at each center (250-500 mcg/ml)
Results

• 717 admitted patients; 157 excluded (on anticoag or recurrent syncope) → 560 patients enrolled

• Of the 560 patients included, 97 (17.3%) had pulmonary embolism confirmed with imaging
2584 Patients visited the emergency departments for syncope

- 1867 Were discharged
  - 829 Had vasovagal syncope
  - 465 Had situational syncope (e.g., after urination or after a meal)
  - 380 Had drug-induced hypotension
  - 112 Had volume depletion
  - 81 Declined hospitalization

- 717 Patients were admitted to the hospitals

- 157 Were excluded
  - 118 Were receiving anticoagulation therapy
  - 82 Had atrial fibrillation
  - 36 Had other reasons
  - 35 Had recurrent syncope
  - 4 Declined to participate

- 560 Patients were included in the study

- 330 Had low pretest probability for pulmonary embolism and negative D-dimer assay
- 230 Had high pretest probability for pulmonary embolism, positive D-dimer assay, or both

- 180 Underwent computed tomographic scanning
  - 49 Underwent ventilation-perfusion scanning
  - 1 Died and an autopsy was performed

- 463 Had pulmonary embolism ruled out
- 97 Had pulmonary embolism confirmed
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (N = 560)</th>
<th>Pulmonary Embolism Confirmed (N = 97)</th>
<th>Pulmonary Embolism Ruled Out (N = 463)</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean — yr</td>
<td>76±14</td>
<td>77±13</td>
<td>76±14</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td>Median (interquartile range) — yr</td>
<td>80 (72–85)</td>
<td>78 (73–85)</td>
<td>80 (72–85)</td>
<td>0.68</td>
<td></td>
</tr>
<tr>
<td>≥70 yr — no. (%)</td>
<td>435 (77.7)</td>
<td>78 (80.4)</td>
<td>357 (77.1)</td>
<td>1.22 (0.71–2.11)</td>
<td>0.48</td>
</tr>
<tr>
<td>≥80 yr — no. (%)</td>
<td>294 (52.5)</td>
<td>45 (46.4)</td>
<td>249 (53.8)</td>
<td>0.74 (0.48–1.15)</td>
<td>0.19</td>
</tr>
<tr>
<td>Male sex — no. (%)</td>
<td>223 (39.8)</td>
<td>37 (38.1)</td>
<td>186 (40.2)</td>
<td>1.09 (0.69–1.71)</td>
<td>0.71</td>
</tr>
<tr>
<td>Obese — no. (%)</td>
<td>34 (6.1)</td>
<td>6 (6.2)</td>
<td>28 (6.0)</td>
<td>1.02 (0.41–2.55)</td>
<td>0.96</td>
</tr>
<tr>
<td>Previous venous thromboembolism — no. (%)</td>
<td>31 (5.5)</td>
<td>11 (11.3)</td>
<td>20 (4.3)</td>
<td>2.83 (1.31–6.13)</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>Potential explanations for syncope — no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurally mediated†</td>
<td>149 (26.6)</td>
<td>20 (20.6)</td>
<td>129 (27.9)</td>
<td>0.67 (0.39–1.15)</td>
<td>0.14</td>
</tr>
<tr>
<td>Orthostatic hypotension‡</td>
<td>112 (20.0)</td>
<td>14 (14.4)</td>
<td>98 (21.2)</td>
<td>0.63 (0.34–1.15)</td>
<td>0.13</td>
</tr>
<tr>
<td>Cardiac disorders§</td>
<td>94 (16.8)</td>
<td>11 (11.3)</td>
<td>83 (17.9)</td>
<td>0.59 (0.30–1.15)</td>
<td>0.12</td>
</tr>
<tr>
<td>Undetermined</td>
<td>205 (36.6)</td>
<td>52 (53.6)</td>
<td>153 (33.0)</td>
<td>2.34 (1.50–3.65)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Clinical features — no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prodromal symptoms</td>
<td>227 (40.5)</td>
<td>41 (42.3)</td>
<td>186 (40.2)</td>
<td>1.09 (0.70–1.69)</td>
<td>0.70</td>
</tr>
<tr>
<td>Respiratory rate &gt;20 breaths/min</td>
<td>77 (13.8)</td>
<td>44 (45.4)</td>
<td>33 (7.1)</td>
<td>10.80 (6.34–18.45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart rate &gt;100 beats/min</td>
<td>107 (19.1)</td>
<td>32 (33.0)</td>
<td>75 (16.2)</td>
<td>2.55 (1.56–4.19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure &lt;110 mm Hg</td>
<td>141 (25.2)</td>
<td>35 (36.1)</td>
<td>106 (22.9)</td>
<td>1.90 (1.19–3.04)</td>
<td>0.006</td>
</tr>
<tr>
<td>Clinical signs of deep-vein thrombosis</td>
<td>60 (10.7)</td>
<td>39 (40.2)</td>
<td>21 (4.5)</td>
<td>14.20 (7.79–25.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Risk factors for venous thrombosis — no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prolonged immobility</td>
<td>38 (6.8)</td>
<td>10 (10.3)</td>
<td>28 (6.0)</td>
<td>1.79 (0.84–3.81)</td>
<td>0.13</td>
</tr>
<tr>
<td>Recent trauma or surgery</td>
<td>27 (4.8)</td>
<td>7 (7.2)</td>
<td>20 (4.3)</td>
<td>1.72 (0.71–4.20)</td>
<td>0.23</td>
</tr>
<tr>
<td>Active cancer</td>
<td>65 (11.6)</td>
<td>19 (19.6)</td>
<td>46 (9.9)</td>
<td>2.21 (1.23–3.97)</td>
<td>0.007</td>
</tr>
<tr>
<td>Infectious disease</td>
<td>49 (8.8)</td>
<td>12 (12.4)</td>
<td>37 (8.0)</td>
<td>1.63 (0.81–3.25)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

*Values in each column are mean ± SD. The row encompassing data for active cancer is highlighted in green.*
Discussion

• Could some of these PE’s be incidentalomas?

• Is there a good pathophysiologic explanation for non-massive PE causing cerebral hypoperfusion?

• Should we change our practice???
Gradual Versus Abrupt Smoking Cessation
A Randomized, Controlled Noninferiority Trial
Nicola Lindson-Hawley, PhD; Miriam Banting, MSc; Robert West, PhD; Susan Michie, DPhil; Bethany Shinkins, DPhil; and Paul Aveyard, PhD
Background

• Quitting smoking is HARD

• 6 month quit rates in clinical trials

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Quit Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>10-12%</td>
</tr>
<tr>
<td>Nicotine replacement therapy</td>
<td>17-20%</td>
</tr>
<tr>
<td>Bupropion</td>
<td>14-20%</td>
</tr>
<tr>
<td>Varenicline</td>
<td>21-28%</td>
</tr>
</tbody>
</table>

Cahill et al. *JAMA* 2014 311:193
The Study

Randomization to abrupt or gradual cessation (spouses were paired in randomization)

Patients asked to set a quit day 2 weeks out
*Gradual*: asked to halve smoking week 1, quarter week 2
*Abrupt*: No reduction prior to quit date

**NRT**: Gradual got patches + short-acting prior to quit date; Abrupt just patches prior; Both got patches + short-acting after QD

Both got behavioral support from 2 weeks prior to 8 weeks after quit date

**Primary outcome**: 4-week abstinence (ITT)
Secondary: 8-week and 6-month abstinence
*All validated by exhaled CO

Exclusion crit:
*Current cessation tx Contraind to NRT*
Table 1. Baseline Participant Characteristics*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All (n = 697)</th>
<th>Gradual-Cessation Group (n = 342)</th>
<th>Abrupt-Cessation Group (n = 355)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (IQR), y</td>
<td>49.0 (40.0-57.0)</td>
<td>49.0 (39.8-57.0)</td>
<td>49.0 (40.0-57.0)</td>
</tr>
<tr>
<td>Male</td>
<td>350/697 (50.2)</td>
<td>175/342 (51.2)</td>
<td>175/355 (49.3)</td>
</tr>
<tr>
<td>White ethnicity</td>
<td>648/692 (93.6)</td>
<td>319/341 (93.5)</td>
<td>329/351 (93.7)</td>
</tr>
<tr>
<td>Postsecondary school (aged 15-16 y) educational qualification</td>
<td>345/678 (50.9)</td>
<td>160/330 (48.5)</td>
<td>185/348 (53.2)</td>
</tr>
<tr>
<td>In paid employment</td>
<td>382/691 (55.3)</td>
<td>190/340 (55.9)</td>
<td>192/351 (54.7)</td>
</tr>
<tr>
<td>Median age started smoking (IQR), y</td>
<td>16.0 (14.0-18.0)</td>
<td>16.0 (15.0-18.0)</td>
<td>16.0 (14.0-18.0)</td>
</tr>
<tr>
<td>Lives with smoker</td>
<td>266/688 (38.7)</td>
<td>116/335 (34.6)</td>
<td>150/353 (42.5)</td>
</tr>
<tr>
<td>Median previous quit attempts (IQR), n</td>
<td>2.0 (1.0-3.0)</td>
<td>2.0 (1.0-3.0)</td>
<td>2.0 (1.0-4.0)</td>
</tr>
<tr>
<td>Type of cigarettes smoked</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manufactured</td>
<td>530/697 (76.0)</td>
<td>266/342 (77.8)</td>
<td>264/355 (74.4)</td>
</tr>
<tr>
<td>Hand-rolled</td>
<td>137/697 (19.7)</td>
<td>61/342 (17.8)</td>
<td>76/355 (21.4)</td>
</tr>
<tr>
<td>Both</td>
<td>30/697 (4.3)</td>
<td>15/342 (4.4)</td>
<td>15/355 (4.2)</td>
</tr>
<tr>
<td>Median cigarettes per day (IQR), n</td>
<td>20.0 (15.0-25.0)</td>
<td>20.0 (15.0-25.0)</td>
<td>20.0 (16.0-25.0)</td>
</tr>
<tr>
<td>Median expired CO concentration (IQR), ppm</td>
<td>24.0 (17.0-31.0)</td>
<td>24.0 (17.0-31.0)</td>
<td>24.0 (17.0-31.0)</td>
</tr>
<tr>
<td>Median salivary cotinine concentration (IQR), nmol/L</td>
<td>2036.3 (1475.2-2659.9)</td>
<td>2074.9 (1452.1-2807.5)</td>
<td>1985.2 (1441.0-2564.0)</td>
</tr>
<tr>
<td>Median FTCD score (IQR)†</td>
<td>6.0 (4.0-7.0)</td>
<td>6.0 (4.0-7.0)</td>
<td>6.0 (4.0-7.0)</td>
</tr>
<tr>
<td>Preference</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abrupt-cessation group</td>
<td>224/697 (32.1)</td>
<td>107/342 (31.3)</td>
<td>117/355 (33.0)</td>
</tr>
<tr>
<td>Gradual-cessation group</td>
<td>355/697 (50.9)</td>
<td>179/342 (52.3)</td>
<td>176/355 (49.6)</td>
</tr>
<tr>
<td>No preference</td>
<td>118/697 (16.9)</td>
<td>56/342 (16.4)</td>
<td>62/355 (17.5)</td>
</tr>
<tr>
<td>Median confidence in quitting (IQR)‡</td>
<td>4.0 (4.0-5.0)</td>
<td>4.0 (4.0-5.0)</td>
<td>4.0 (4.0-5.0)</td>
</tr>
</tbody>
</table>

CO = carbon monoxide; FTCD = Fagerström Test for Cigarette Dependence; IQR = interquartile range.
* Values are numbers/total (percentages) unless otherwise indicated. Numbers of participants used to calculate statistics for each variable vary slightly in some cases because of missing data (denominators provided). Percentages may not sum to 100 due to rounding.
† From 0-10, where 10 indicates the highest level of dependence.
‡ Measured on a scale from 1-6, where 1 indicates very low and 6 indicates extremely high.

No difference in groups

Median age: 49
50/50 M/F
93% white
35-38% lived with smoker
Median cigs/day: 20
Confidence in quitting: 4 (scale 1-6)
### Results

<table>
<thead>
<tr>
<th>Abstinence Outcome</th>
<th>Abstinence, n (%)</th>
<th>Absolute Difference (95% CI), percentage points</th>
<th>Relative Risk (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gradual-Cessation Group (n = 342)</td>
<td>Abrupt-Cessation Group (n = 355)</td>
<td></td>
</tr>
<tr>
<td>Prolonged CO-validated Russell Standard abstinence†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 wk after quitting</td>
<td>134 (39.2)</td>
<td>174 (49.0)</td>
<td>9.8 (2.5-17.1)</td>
</tr>
<tr>
<td>8 wk after quitting</td>
<td>100 (29.2)</td>
<td>130 (36.6)</td>
<td>7.4 (0.4-14.3)</td>
</tr>
<tr>
<td>6 mo after quitting</td>
<td>53 (15.5)</td>
<td>78 (22.0)</td>
<td>6.5 (0.7-12.2)</td>
</tr>
<tr>
<td>7-d point prevalence‡, CO-validated†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 wk</td>
<td>146 (42.7)</td>
<td>191 (53.8)</td>
<td>9.1 (1.8-16.5)</td>
</tr>
<tr>
<td>8 wk</td>
<td>106 (31.0)</td>
<td>136 (38.3)</td>
<td>7.3 (0.3-14.3)</td>
</tr>
<tr>
<td>6 mo</td>
<td>63 (18.4)</td>
<td>94 (26.5)</td>
<td>8.1 (1.9-14.2)</td>
</tr>
<tr>
<td>Self-reported</td>
<td>210 (61.4)</td>
<td>252 (71.0)</td>
<td>9.6 (2.6-16.5)</td>
</tr>
</tbody>
</table>

* CO = carbon monoxide. Adjusted for nurses.
† Validated by a CO reading <10 ppm.
‡ No smoking 7 d before assessment.

**Abstinence rates:**

- **Abrupt cessation**
  - 4 weeks: 49%
  - 8 weeks: 36%
  - 6 months: 22%

- **Gradual cessation**
  - 4 weeks: 39%
  - 8 weeks: 29%
  - 6 months: 15%

**NNT:** 10 (4 weeks); 14 (6 months)
Discussion

• What do you tell your patients? Is this surprising to you?

• Physiologic or psychologic explanation?

• Should this study change our practice?
Time to Treatment and Mortality during Mandated Emergency Care for Sepsis


NEJM 2017 376;23
Background: Sepsis and Protocols (EGDT)

Do early goal-directed therapy protocols make a difference?

• Rivers et al. 2001: YES!

• PROCESS 2014: Nope.
The Study: Background

• All NY hospitals required sepsis protocols, including a **3-hr bundle**
  – Blood culture prior to abx
  – Serum lactate measurement
  – Administration of *broad-spectrum abx*

• And a **6-hr bundle**
  – 30cc/kg bolus IVF if hypotension or lactate >4
  – Vasopressors for refractory hypotension
  – Remeasurement of serum lactate
The Study

• Retrospective study including patient-level data from 185 NY hospitals (2014-2016)
• Patients age >17; clinically defined *severe sepsis or septic shock* (according to Sepsis-2 2001)
• Patients had protocol initiated in ED (ignored hospital-acquired sepsis)
• Excluded patients:
  – 3-hr bundle took >12 hours
  – Advance directives limiting treatment or declined tx
  – Hospitals with fewer than 50 cases of sepsis
The Study

• Primary outcome: In-hospital mortality
• Primary exposure: Time to completion of 3-hr bundle

• Risk-adjustment model to determine association between exposure and mortality
  – Bivariate (yes/no completion in 3 hrs) and continuous analyses
### Table 1. Characteristics of the Patients.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (N = 49,331)</th>
<th>3-Hr Bundle Completed in 3 Hr</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Yes (N = 40,696)</td>
<td>No (N = 8635)</td>
</tr>
<tr>
<td>Percentage of patients</td>
<td>100.0</td>
<td>82.5</td>
<td>17.5</td>
</tr>
<tr>
<td>Age at admission — yr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>73</td>
<td>73</td>
<td>71</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>60–83</td>
<td>61–84</td>
<td>59–82</td>
</tr>
<tr>
<td>Female sex — no. (%)</td>
<td>23,634 (47.9)</td>
<td>19,157 (47.1)</td>
<td>4477 (51.8)</td>
</tr>
<tr>
<td>Race — no. (%)†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>33,075 (67.0)</td>
<td>27,605 (67.8)</td>
<td>5470 (63.3)</td>
</tr>
<tr>
<td>Black</td>
<td>8,269 (16.8)</td>
<td>6,487 (15.9)</td>
<td>1782 (20.6)</td>
</tr>
<tr>
<td>Asian</td>
<td>2,167 (4.4)</td>
<td>1,774 (4.4)</td>
<td>393 (4.6)</td>
</tr>
<tr>
<td>Other</td>
<td>5,820 (11.8)</td>
<td>4,830 (11.9)</td>
<td>990 (11.5)</td>
</tr>
<tr>
<td>Hispanic ethnic group — no. (%)†</td>
<td>4,851 (9.8)</td>
<td>4,022 (9.9)</td>
<td>829 (9.6)</td>
</tr>
<tr>
<td>Coexisting condition — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic respiratory failure</td>
<td>5,738 (11.6)</td>
<td>4,656 (11.4)</td>
<td>1082 (12.5)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>10,092 (20.5)</td>
<td>8,311 (20.4)</td>
<td>1781 (20.6)</td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td>5,207 (10.6)</td>
<td>4,109 (10.1)</td>
<td>1098 (12.7)</td>
</tr>
<tr>
<td>Admission source — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>33,464 (67.8)</td>
<td>27,306 (67.1)</td>
<td>6158 (71.3)</td>
</tr>
<tr>
<td>Skilled nursing facility</td>
<td>13,233 (26.8)</td>
<td>11,247 (27.6)</td>
<td>1986 (23.0)</td>
</tr>
<tr>
<td>Other‡</td>
<td>2,634 (5.3)</td>
<td>2,143 (5.3)</td>
<td>491 (5.7)</td>
</tr>
<tr>
<td>Site of infection — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary</td>
<td>13,439 (27.2)</td>
<td>10,963 (26.9)</td>
<td>2476 (28.7)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>19,839 (40.2)</td>
<td>16,806 (41.3)</td>
<td>3033 (35.1)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>4,649 (9.4)</td>
<td>3,580 (8.8)</td>
<td>1069 (12.4)</td>
</tr>
<tr>
<td>Other§</td>
<td>11,404 (23.1)</td>
<td>9,347 (23.0)</td>
<td>2057 (23.8)</td>
</tr>
<tr>
<td>Positive blood cultures — no. (%)</td>
<td>14,574 (29.5)</td>
<td>12,322 (30.3)</td>
<td>2252 (26.1)</td>
</tr>
<tr>
<td>Serum lactate — mmol/liter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>2.7</td>
<td>2.8</td>
<td>2.5</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>1.7–4.4</td>
<td>1.8–4.4</td>
<td>1.6–4.1</td>
</tr>
<tr>
<td>Septic shock — no. (%)</td>
<td>22,336 (45.3)</td>
<td>18,393 (45.2)</td>
<td>3943 (45.7)</td>
</tr>
<tr>
<td>Teaching facility — no. (%)</td>
<td>40,257 (81.6)</td>
<td>7,739 (19.0)</td>
<td>7300 (84.5)</td>
</tr>
<tr>
<td>In-hospital death — no. (%)</td>
<td>11,251 (22.8)</td>
<td>9,213 (22.6)</td>
<td>2038 (23.6)</td>
</tr>
</tbody>
</table>

Median age 73
67% White

Admitted from:
Home 67%
SNF 27%

Site of infection:
40% Respiratory
27% Urinary
Results

82% of patients had 3-hr bundle completed within 3 hrs
- Median time 1.3 hrs

In primary analysis (top graph), each hour of time to completion of 3-hr bundle was associated with higher mortality
- OR 1.04 per hr (95% CI 1.02-1.05)
- P<0.001

Comparing pts who had completion 3-12hrs to <3hrs, mortality OR 1.14 (95% CI 1.07-1.21, P<0.001)
Results

82% of patients had the 3-hr bundle completed within 3 hrs - Median time 1.3 hrs

No differences in characteristic of pts in whom completed within 3 hrs and those in whom completed between 3-12 hrs

In primary analysis (top graph), each hour of time to completion of 3-hr bundle was associated with higher mortality - OR 1.04 per hr (95% CI 1.02 - 1.05) - P<0.001

Comparing pts who had completion 3-12 hrs to <3 hrs, mortality OR 1.14 (95% CI 1.07 - 1.21, P<0.001)
Results

• “Our results would be robust unless an unmeasured confounder was at least twice as prevalent among pts who had the 3-hr bundle completed 1 hr later”

• Hospitals with higher rate of bundle completion within 3 hrs – more likely to be smaller, less likely teaching hospitals
Discussion

• Conflicting data in the literature
  – This one NOT a RCT- confounding?

• “Analysis of time to completion of IVF bolus is most prone to confounding by indication”

• Downsides to early admin of broad spectrum abx?

• Are certain elements of EGDT/bundles more important than others?
  – Recall, *Rivers* protocol included ScvO2 monitoring, PRBC transfusion, inotropes)
One Slide Summaries
• Review of studies investigating methods and outcomes of reduction/discontinuation of LTOT

• 67 studies met criteria (11 RCT’s; only 5 studies in primary care settings)
  – Only 3 met USPSTF criteria for good quality, 13 fair; review focused on these 16
Conclusions:

• Findings suggest that pain, function, QOL may **improve** during/after opioid dose reduction

Caveats:

• Maybe reverse causation?
• Most studies included willing participants
A Randomized Trial of Long-Term Oxygen for COPD with Moderate Desaturation

NEJM 2016 375;17

The Long-Term Oxygen Treatment Trial Research Group*

• RCT looking at $O_2$ vs no $O_2$ for patients with COPD and resting sats of 89-93%

• Found **no difference** in time to death or hospitalization, rate of hospitalization, exacerbations, or other measures
Retrospective cohort of pts (n=28,266) with EMR doc’d AR to statin (15-20% had CAD/stroke history)

Compared CV outcomes/death in patients who had statin continued/reinitiated vs those who didn’t.

70% did have reinitiated/continued statin rx

MI/stroke/death occurred in 12.2% of pts who had continued statin, 13.9% of those who didn’t

NNT= 59
Final thoughts?

Thanks!