Welcome!

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What’s Happening in Non-COVID Sepsis

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President-elect CHEST
Professor of Medicine
Division of Pulmonary, Critical Care, and Sleep Medicine
University of Kansas
• I have nothing to disclose
Epidemiology
Sepsis Among Medicare Beneficiaries: Manuscript Trilogy

The Burdens of Sepsis 2012-2018

The Trajectories of Sepsis 2012-2018

The Methods, Models and Forecasts of Sepsis 2012-2018

Critical Care Medicine 2020; 48(3), 276-318

Timothy G. Buchman, PhD, MD1,2; Steven Q. Simpson, MD1,3; Kimberly L. Sciarretta, PhD1; Kristen P. Finne, BA4; Nicole Sowers, MPP5; Michael Collier, BA6; Saurabh Chavan, MBBS, MPH5; Ibijoke Oke, MPA5; Meghan E. Pennini, PhD1; Aathira Santhosh, MA5; Marie Wax, MBA1; Robyn Woodbury, PhD6; Steve Chu, JD6; Tyler G. Merkeley, MS, MBA1; Gary L. Disbrow, PhD1; Rick A. Bright, PhD1; Thomas E. Macurdy, PhD6,7,8,9; Jeffrey A. Kelman, MD, MMSc6

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Objectives

- Evaluate the burden of sepsis in the Medicare population
- Estimate contemporary national sepsis costs
- Forecast future Medicare costs for sepsis care

Healthcare quality improvement study
Medicare Data Analyzed
January 1, 2012 – December 31, 2018

Total Sepsis Inpatient Admissions
(Acute, Long Term, Psychiatric, Rehabilitation)

9,587,636

6,998,888
Fee For Service
Medicare Part A/B
(Paid Claims)

2,588,748
Medicare Advantage
Medicare Part C
(Encounter data)

6,731,828
Acute Hospital Sepsis Admissions

267,060
Other Inpatient Hospital Sepsis Admissions

1. Sepsis Present on Admission
2. Sepsis Not Present on Admission
   (Hospital Acquired)

DataLink Project
Pre-adjudicated administrative claims for real-time monitoring and research;
Inpatients and SNF

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Sepsis Dataset

Accounted for ICD-9 to 10 transition: crosswalk similar, no discontinuity

Used Generalized Equivalence Mapping to provide a 1:1 crosswalk of ICD-9 and ICD-10

ICD-9/ICD-10 Transition

ICD-9: 038, 995.91, 995.92, 785.52
ICD-10 crosswalk:

Severity Stratification

Septic Shock:
ICD-9: 785.52 or ICD-10: R6521
Severe Sepsis without Shock:
ICD-9 995.92 or ICD-10: R6520
Non-Severe Sepsis, Unspecified:
ICD-9: 0389 or 995.91 or ICD-10: A419

6,731,828
Acute Hospital Sepsis Admissions

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Virtual Congress
26 June 2020

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Sepsis Incidence Trends

Exploring rates and counts of sepsis severity

Sepsis claims increased steadily
• Rate *per capita* (of Medicare beneficiaries) increased ~40%
• Medicare beneficiary total population increased ~22%

Seasonal variation during winter months (≈ respiratory Illness)
Could this be due to “over-coding”?

Not a major contributor, difficult to “overcode” severe sepsis and septic shock

However, proportions of septic shock and severe sepsis stay similar
- Might expect disproportionate fall in severe sepsis and septic shock if coding effect

 Increased across all severities
- Sepsis is more common
- Rate of increase ~40% / 7 years

![Graph showing fractional severity by month from Jan-12 to Jan-18.](image)

6,731,828 Acute Hospital Sepsis Admissions

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Sepsis Incidence Trends

Exploring onset setting

Rise seen in admissions is exclusively in the present on admission (POA) group:
- Increased fraction: 87% (2012) to 93% (2018)
- Continues to rise in community

Hospital acquired sepsis (NPOA):
- Decreased fraction: 13% (2012) to 7.5% (2018)
- Decreased counts: 88,321 to 77,089
- Suggests hospital practices are improving
• Sepsis mortality reflected sepsis severity
  – Accumulates over 1 week, 6 months, 1 and 3 years

• Sepsis mortality steadily **decreased** in 7 year period
  – Non-sepsis mortality has no change
  – Suggests sepsis diagnosis and treatment is effective

• **High 3 year mortality**
  – 75% septic shock
  – 60% non-severe sepsis
  – 40% non-sepsis
Economic Burden of Sepsis

2013: Reported cost of sepsis, $23.7B
- Based on Agency for Healthcare Research and Quality (AHRQ) 2016 study on cost of septicemia
- Most expensive condition treated
- Medicare population ~$14.6B (61.5% of cost)

Contemporary Costs

Paid Claims per Admission

- Average claim payment decreases over time at all severities
  - $21,922 (2012)
  - $19,738 (2018)

- Average payment for SNF care rises slightly over time
  - $17,196 (2012)
  - $17,920 (2018)
2018 Medicare Beneficiary Sepsis Spend

The numbers in blue are FFS and real payments
The numbers in green are MA and imputed.

Total: $33,229,504,776

Total: $41,508,436,655

Total: $8,278,931,879

9,587,636 Sepsis Inpatient Admissions
2019 Medicare Beneficiary Sepsis Spend (Projected)

Inpatient

- FFS: $11,133,531,670
- MA: $23,711,924,186
- Total: $34,845,455,856

SNF

- FFS: $2,915,842,345
- MA: $6,267,570,831
- Total: $9,183,413,176

Total: ~$44,028,869,032

The numbers in **blue** are FFS and real payments.
The numbers in **green** are MA and imputed.
Total Sepsis Inpatient + SNF Estimated Costs

From the AHRQ-HCUP study

$14.6 \text{ BILLION} \quad \text{of the $23.7 billion total}

61.5\% \quad \text{of the total}

$35 \text{ BILLION} = 66.7\%

2019 Inpatient Medicare cost

Medicare total cost

TOTAL INPATIENT COST

$53 \text{ BILLION}

Estimated SNF costs, Medicare only

$9 \text{ BILLION}

Used a more conservative number to account for the aging of the US population

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Direct Costs of Sepsis in the US

$62 BILLION

...conservative rough order of magnitude
lower bound
Medicare Claims Data Analyzed
January 1, 2012 – December 31, 2018

9,587,636 Total Sepsis Inpatient Admissions
(Acute, Long Term, Psychiatric, Rehabilitation)

6,998,888 Fee For Service
Medicare Part A/B
(Paid Claims)

2,588,748 Medicare Advantage
Medicare Part C
(Encounter data)

736,189 Unique Sepsis Patients
CY 2017
NO Sepsis Admission 2016

6,803,165 Non-Sepsis Admission
NO Sepsis Admission 2016

DataLink Project
Pre-adjudicated administrative claims for real
time monitoring and research;
Inpatients and SNF

Largest in-patient epidemiological study
Lead-in to Admission:
Can we use chronic conditions to predict who is going to be septic?
Chronic Conditions - Comparison

### Sepsis

- Personal history of other...
- Chronic ischemic heart...
- Type 2 diabetes mellitus...
- Other and unspecified...
- Malaise and fatigue...
- Abnormalities of...
- Encounter for...
- Long term (current) drug...
- Disorders of lipoprotein...
- Essential (primary)...

### Non-Sepsis

- Type 2 diabetes mellitus...
- Dorsalgia (251,346)¹
- Malaise and fatigue...
- Other joint disorder, not...
- Other and unspecified...
- Abnormalities of...
- Encounter for...
- Long term (current) drug...
- Disorders of lipoprotein...
- Essential (primary)...

[¹] Sepsis

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Chronic Conditions - Comparison

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sepsis</th>
<th>Non-Sepsis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal history of other disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic ischemic heart disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other and unspecified disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malaise and fatigue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormalities of lipoproteins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Encounter for malaise and fatigue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long term (current) drug use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disorders of lipoproteins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Essential (primary)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsalgia (251,346)¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malaise and fatigue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other joint disorder, not specified</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other and unspecified disorders</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Dorsalgia (251,346)¹ indicates a specific code or identifier relevant to the condition.
Sepsis versus Non-Sepsis Inpatient Admissions

Top Prevalent Diagnoses Before a Sepsis Admission Relative to a Non-Sepsis Admission\(^1\)

- Unspecified dementia (13,228; 19%)\(^2\)
- Fever of other and unknown origin (11,242; 16%)\(^2\)
- Aphagia and dysphagia (11,198; 16%)\(^2\)
- Pressure ulcer (7,544; 11%)\(^2\)
- Other lack of coordination (7,312; 11%)\(^2\)
- Other sepsis (7,088; 10%)\(^2\)
- Dementia in other diseases classified elsewhere (6,790; 10%)\(^2\)
- Alzheimer’s disease (6,271; 9%)\(^2\)
- Streptococcus, Staphylococcus, and Enterococcus as the cause of diseases classified elsewhere (3,870; 6%)\(^2\)
- Unspecified protein-calorie malnutrition (3,820; 6%)\(^2\)

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Sepsis versus Non-Sepsis Inpatient Admissions

Top Prevalent Diagnoses Before a Sepsis Admission Relative to a Non-Sepsis Admission

- Unspecified dementia (13,228; 19%)^2
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- Unspecified protein-calorie malnutrition (3,820; 6%)^2

Prevalence Ratio

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^1 In partnership with the CHEST Delegation Italy

^2 congress.chestnet.org
Average Predicted Probability of Death
Within 1 Week of Discharge

<table>
<thead>
<tr>
<th>Condition</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Present on Admission</td>
<td>35.1%</td>
</tr>
<tr>
<td>Present on Admission</td>
<td>17.6%</td>
</tr>
<tr>
<td>Organism Specified</td>
<td>8.4%</td>
</tr>
<tr>
<td>Unspecified Sepsis</td>
<td>12.5%</td>
</tr>
<tr>
<td>Severe Sepsis</td>
<td>17.7%</td>
</tr>
<tr>
<td>Septic Shock</td>
<td>39.8%</td>
</tr>
</tbody>
</table>

Hospital acquired (NPOA) sepsis doubles likelihood of early death.
Regardless of Severity:

- Mortality is high
- But decreased
- Why 6 months?

Of all the deaths that occur within 3 years of discharge
~ half occur by 6 months
Where are patients 6 months after discharge?

**SEPSIS**
- 56.4% in Family Home
- 5.8% in Nursing Home
- 2.2% in Skilled Nursing Facility
- 1.8% in Hospice
- 1.2% (Any IP)
- 32.6% in Inpatient Hospital
- 1.4% in Deaths

**NON-SEPSIS**
- 79.3% in Family Home
- 3.3% in Nursing Home
- 1.4% in Skilled Nursing Facility
- 1.8% in Hospice
- 1% (Any IP)
- 13.3% in Inpatient Hospital
- 1.7% in Deaths
If one goes first to a SNF, then what? (6 months)

**SEPSIS**
- 44.9% Family Home
- 6.4% Skilled Nursing Facility
- 17% Nursing Home
- 1.5% (Any IP) Inpatient Hospital
- 3% Hospice
- 27.2% + 6.5% Deaths

**NON-SEPSIS**
- 60.1% Family Home
- 5% Skilled Nursing Facility
- 1.2% (Any IP) Inpatient Hospital
- 2.5% Hospice
- 19.6% + 4.3% Deaths
Modeling 6-Month Mortality – Effect of Age

Multivariate Logistic Regression

OR 1.16
Overall Conclusions

- Sepsis is extremely costly in lives and financially
- Incidence of sepsis actually is increasing – not an artifact of coding or billing
- Mortality rate is decreasing
- Cannot predict sepsis vs. non-sepsis admissions
- Sepsis markedly worsens outcomes and quality of life even in the mildest cases
Treatment
Association Between Volume of Fluid Resuscitation and Intubation in High-Risk Patients With Sepsis, Heart Failure, End-Stage Renal Disease, and Cirrhosis

Rizwan A. Khan, MD; Nauman A. Khan, MD; Seth R. Bauer, PharmD; Manshi Li, MS; Abhijit Duggal, MD, MPH; Xiaofeng Wang, PhD; and Anita J. Reddy, MD

CHEST 2020; 157(2):286-292
Background

• Fluids are mainstays of sepsis resuscitation
• Surviving Sepsis Guidelines recommend an initial 30 mL/kg crystalloid fluid for hypotensive patients
• Concern for increased intubation rate and mortality
Methods

• Retrospective analysis
• Sepsis patients – modification of eSOFA (CDC)
• Patients with pre-existing CHF, cirrhosis, end-stage renal disease
• LVEF < 40% or > 40%
• Propensity matching
• Primary outcome – intubation within 72 hours
• Secondary outcomes - time to intubation,
### Demographics and Baseline Data

**TABLE 1**  Patient Characteristics and Clinical Variables of Both Groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (N = 208)</th>
<th>Restricted Group (&lt; 30 ml/kg (n = 104)</th>
<th>Standardized Group (&gt; 30 ml/kg (n = 104)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>63 ± 14</td>
<td>62 ± 15</td>
<td>63 ± 14</td>
<td>.85</td>
</tr>
<tr>
<td>Male sex, No. (%)</td>
<td>119 (57%)</td>
<td>60 (58%)</td>
<td>59 (57%)</td>
<td>.89</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>84.6 ± 25</td>
<td>86.6 ± 25</td>
<td>82.7 ± 25</td>
<td>.11</td>
</tr>
<tr>
<td>Comorbid condition</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>147 (71%)</td>
<td>72 (69%)</td>
<td>75 (72%)</td>
<td>.65</td>
</tr>
<tr>
<td>HFrEF (≤ 40%)</td>
<td>32 (22%)</td>
<td>20 (28%)</td>
<td>12 (16%)</td>
<td>.65</td>
</tr>
<tr>
<td>HFrEF (&gt; 40%)</td>
<td>115 (78%)</td>
<td>52 (72%)</td>
<td>63 (84%)</td>
<td>.65</td>
</tr>
<tr>
<td>ESRD</td>
<td>57 (27%)</td>
<td>30 (29%)</td>
<td>27 (26%)</td>
<td>.65</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>60 (28%)</td>
<td>30 (29%)</td>
<td>30 (29%)</td>
<td>.99</td>
</tr>
<tr>
<td>Sepsis level, %</td>
<td></td>
<td></td>
<td></td>
<td>.70</td>
</tr>
<tr>
<td>Sepsis</td>
<td>93 (45%)</td>
<td>45 (43%)</td>
<td>48 (46%)</td>
<td>.70</td>
</tr>
<tr>
<td>Septic shock</td>
<td>115 (55%)</td>
<td>59 (57%)</td>
<td>56 (54%)</td>
<td>.92</td>
</tr>
<tr>
<td>APACHE III score</td>
<td>88 ± 30</td>
<td>88 ± 25</td>
<td>88 ± 34</td>
<td>.75</td>
</tr>
<tr>
<td>MAP at diagnosis</td>
<td>69 ± 14</td>
<td>70 ± 16</td>
<td>69 ± 12</td>
<td>.75</td>
</tr>
<tr>
<td>Mean MAP over 24 h</td>
<td>73 ± 10</td>
<td>73 ± 10</td>
<td>74 ± 9</td>
<td>.66</td>
</tr>
<tr>
<td>Lactate at diagnosis, mmol/L</td>
<td>3.0 ± 2.2</td>
<td>3.0 ± 2.7</td>
<td>3.1 ± 1.7</td>
<td>.67</td>
</tr>
</tbody>
</table>
# Table 2: Primary and Secondary Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Restricted Group (&lt; 30 mL/kg)</th>
<th>Standardized Group (&gt; 30 mL/kg)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubation within 72 h</td>
<td>36 (35%)</td>
<td>33 (32%)</td>
<td>.64</td>
</tr>
<tr>
<td>Change in $\text{FiO}_2$, %</td>
<td>6 ± 14</td>
<td>7 ± 12</td>
<td>.89</td>
</tr>
<tr>
<td>Time to intubation, h</td>
<td>14 ± 15</td>
<td>16 ± 19</td>
<td>.55</td>
</tr>
<tr>
<td>Alive ICU-free days at day 28</td>
<td>17 ± 10</td>
<td>17 ± 11</td>
<td>.64</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>19 (18%)</td>
<td>26 (25%)</td>
<td>.21</td>
</tr>
<tr>
<td>Ventilator days</td>
<td>11 ± 16</td>
<td>10 ± 12</td>
<td>.96</td>
</tr>
</tbody>
</table>
Fluid Response Evaluation in Sepsis Hypotension and Shock: A Randomized Clinical Trial

Ivor S. Douglas, Philip M. Alapat, Keith A. Corl, Matthew C. Exline, Lui G. Forni, Andre L. Holder, David A. Kaufman, Akram Khan, and others

Publication stage: In Press Journal Pre-Proof

CHEST

Published online: April 27, 2020

Open Access
Background

- Fluids are mainstays of sepsis resuscitation
- Excess fluid associated with edema, organ dysfunction, respiratory and renal failure, and mortality
- Surviving Sepsis Guidelines recommend that fluid administration is guided by dynamic measures
- No recommendations are given for how to achieve this
Previous Work

- Retrospective
- Sepsis patients managed by SV measurement
- Reduced
  - Volume
  - LOS
  - Mechanical ventilation
  - Dialysis
  - Cost of care by $18,000/case

Methods

• Randomized, controlled trial
• Adult patients with sepsis and refractory hypotension
• Intervention arm vs usual care (2:1 randomization)
  – Non-Invasive Cardiac Output Monitor (NICOM)
  – Passive leg raise, SV response > 10%
  – 500 mL crystalloid bolus
  – Repeat process until SV < 10%; stop boluses, no maintenance fluids
• Primary Outcome – net fluid balance at 72 hours
• Secondary outcomes – mech vent, dialysis, LOS, mortality, vent hours, vasopressor hours, Δ creatinine, adverse events
## Results

### Table 1. Study Demographics

<table>
<thead>
<tr>
<th></th>
<th>mITT (124)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention N=83</td>
<td>Usual Care N=41</td>
<td></td>
</tr>
<tr>
<td><strong>Age (yrs)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD (N)</td>
<td>61.8 ± 16.9 (83)</td>
<td>62.7 ± 15.0 (41)</td>
<td></td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>65.0 (48.0, 75.0)</td>
<td>63.0 (55.0, 74.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>61.4% (51/83)</td>
<td>31.7% (13/41)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>38.6% (32/83)</td>
<td>68.3% (28/41)</td>
<td></td>
</tr>
</tbody>
</table>
### Results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>mITT (124)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention N = 83</td>
<td>Usual Care N = 41</td>
<td>Treatment Difference in Mean or Percentage, and 95% CI</td>
</tr>
<tr>
<td><strong>Primary Efficacy Endpoint</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluid Balance (L) at 72 hours or ICU Discharge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD (N)</td>
<td>0.65 ± 2.85 (83)</td>
<td>2.02 ± 3.44 (41)</td>
<td>-1.37 (-2.53, -0.21)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>0.53 (-0.84, 2.53)</td>
<td>1.22 (-0.03, 3.73)</td>
<td></td>
</tr>
</tbody>
</table>
Results
Thank You!