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Virtual Congress

26 June 2020

Welcome!

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What's Happening in Non-COVID Sepsis

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Steven Q Simpson, MD, FCCP

President-elect CHEST

Professor of Medicine

Division of Pulmonary, Critical Care, and Sleep Medicine

University of Kansas

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- I have nothing to disclose

Epidemiology

Sepsis Among Medicare Beneficiaries: Manuscript Trilogy

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The Burdens of Sepsis 2012-2018

The Trajectories of Sepsis 2012-2018

The Methods, Models and Forecasts of Sepsis 2012-2018

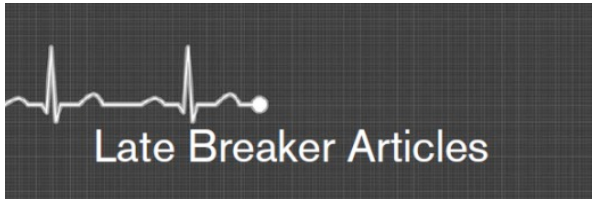
ASPR ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

BARDA BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY

CMS CENTERS FOR MEDICARE & MEDICAID SERVICES

ACUMEN

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



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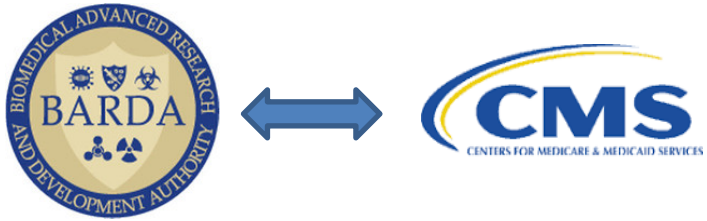
Objectives



Healthcare quality improvement study

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

Medicare Data Analyzed

January 1, 2012 – December 31, 2018

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

DataLink Project

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

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)

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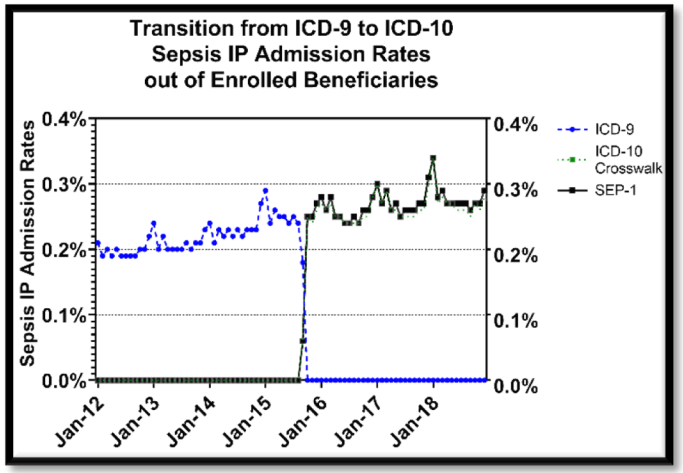
Sepsis Dataset

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



ICD-9 to ICD-10

2012 ⟵ **2015** ⟶ 2018

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:
A409, A412, A4101 A4102, A411, A403, A414, A4150, A413, A4151, A4152, A4153, A4159, A4189, A419, A419, R6520, R6521

ICD-10 SEP-1 Metric: A021, A227, A267, A327, A400, A401, A403, A408, A409, A4101, A4102, A411, A412, A413, A414, A4150, A4151, A4152, A4153, A4159, A4181, A4189, A419, A427, A5486, B377, R6520, R6521

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, Organism-Specific ICD-9: 0380, 03810, 03811, 03812,03819, 0382, 03840, 03841, 03842, 03843, 03844, 03849, 0388
and ICD-10: A409, A412, A4101, A4102, A411, A403, A414, A4150, A413, A4151, A4152, A4153, A4159, A4189, A021, A227, A267, A327, A400, A401, A408, A4181, A427, A5486, B377

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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Sepsis Incidence Trends

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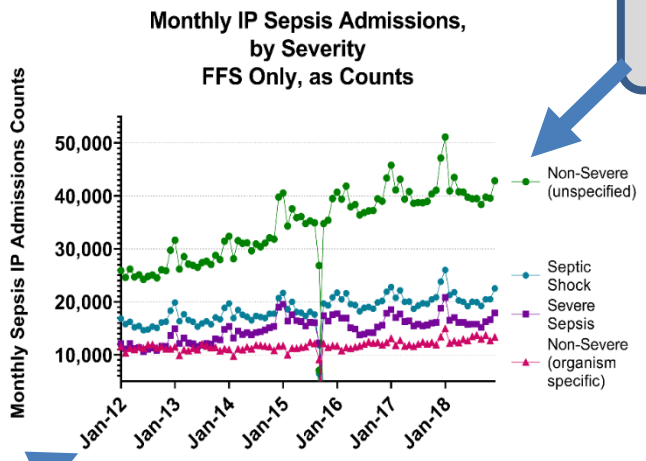
Exploring rates and counts of sepsis severity

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)



Total: 1,104,683 (FFS,2018)

Total: 770,834 (FFS,2012)

6,731,828 Acute Hospital Sepsis Admissions

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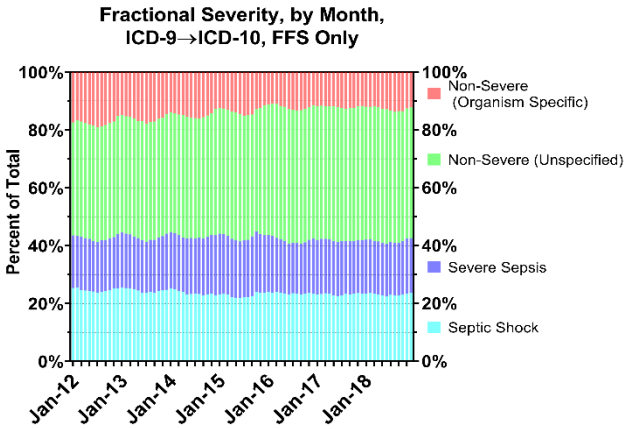
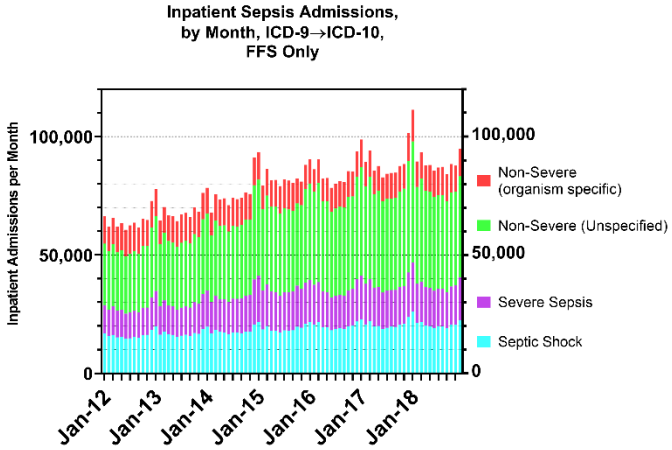
Could this be due to “over-coding”?

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

6,731,828
Acute Hospital Sepsis Admissions

Sepsis Incidence Trends

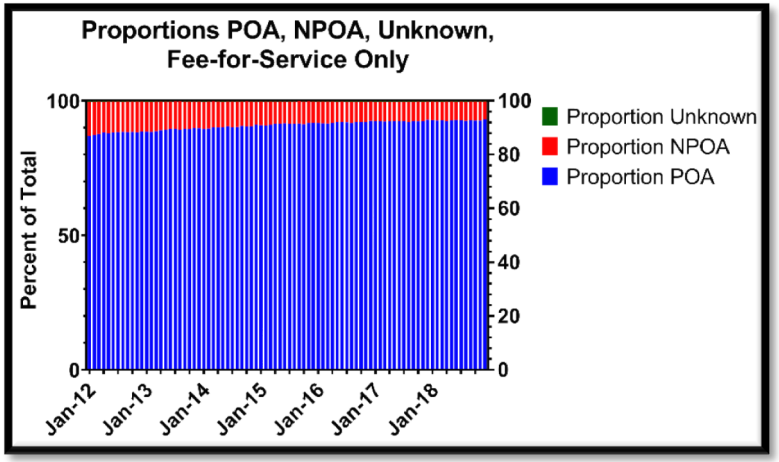
Exploring onset setting

Rise seen in admissions is exclusively in the present on admission (POA) group:

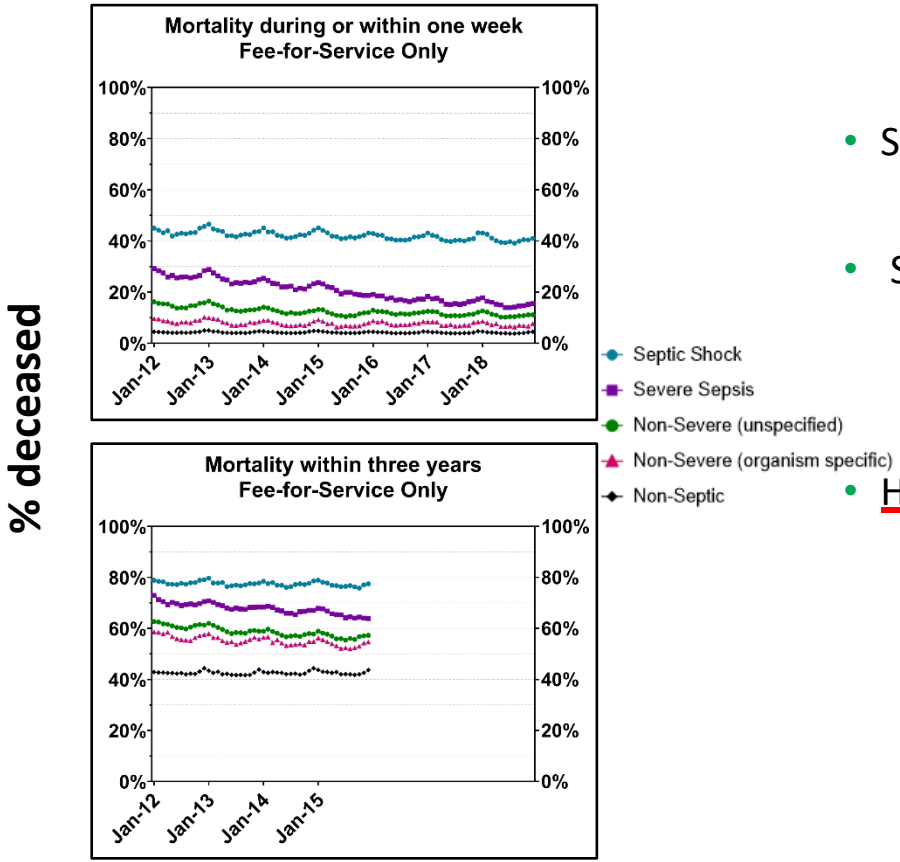
- Increased fraction: 87% (2012) to 93% (2018)
- Continues to rise in community

Hospital acquired sepsis (NPOA):

- Decreased fraction: 13% (2012) to 7.5% (2018)
- Decreased counts: 88,321 to 77,089
- Suggests hospital practices are improving



6,731,828
Acute Hospital Sepsis Admissions



- 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

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

Economic Burden of Sepsis

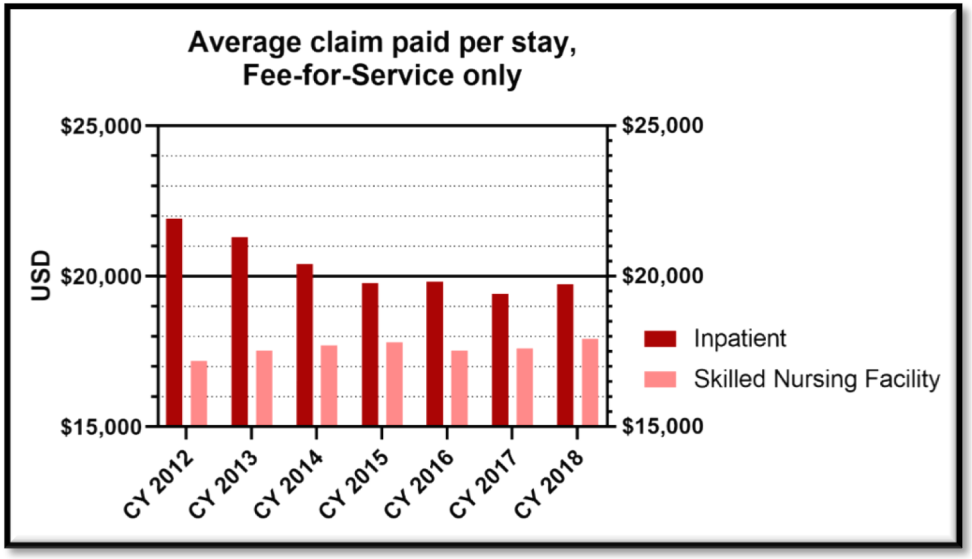
Contemporary Costs

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)

Torio C and Moore B. National Inpatient Hospital Costs: The Most Expensive Conditions by Payer, 2013. HCUP Statistical Brief #204. May 2016.

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)

6,731,828
Acute Hospital Sepsis Admissions

1,963,238
SNF admissions

2018 Medicare Beneficiary Sepsis Spend

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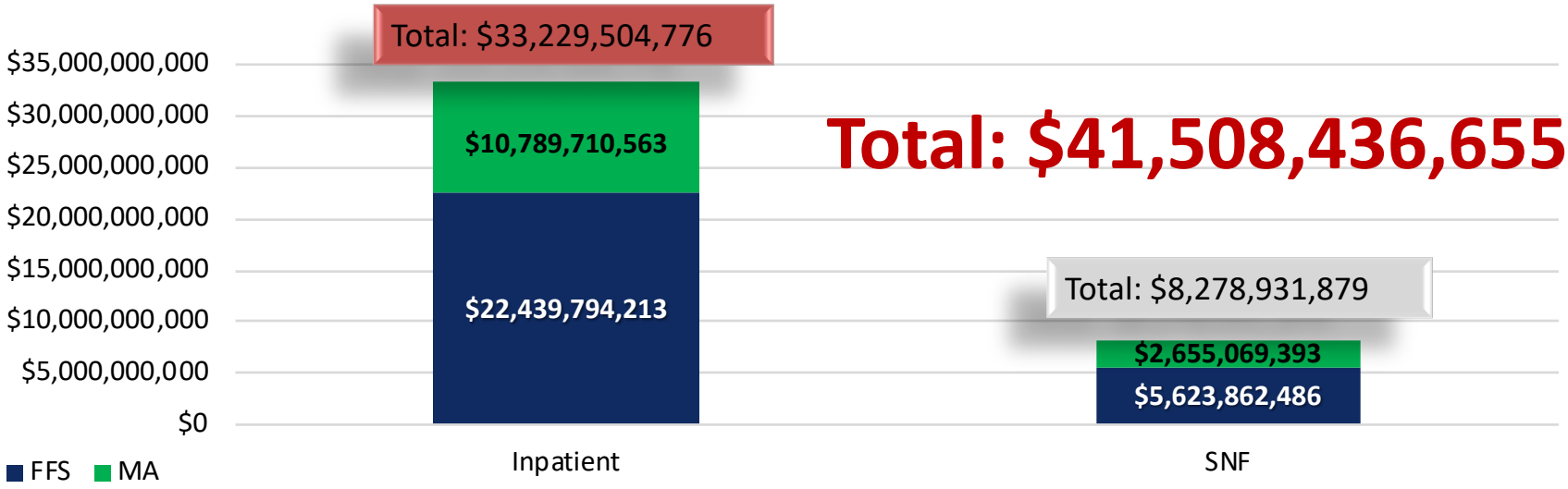

Total: $41,508,436,655

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

9,587,636 Sepsis Inpatient Admissions

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2019 Medicare Beneficiary Sepsis Spend (Projected)

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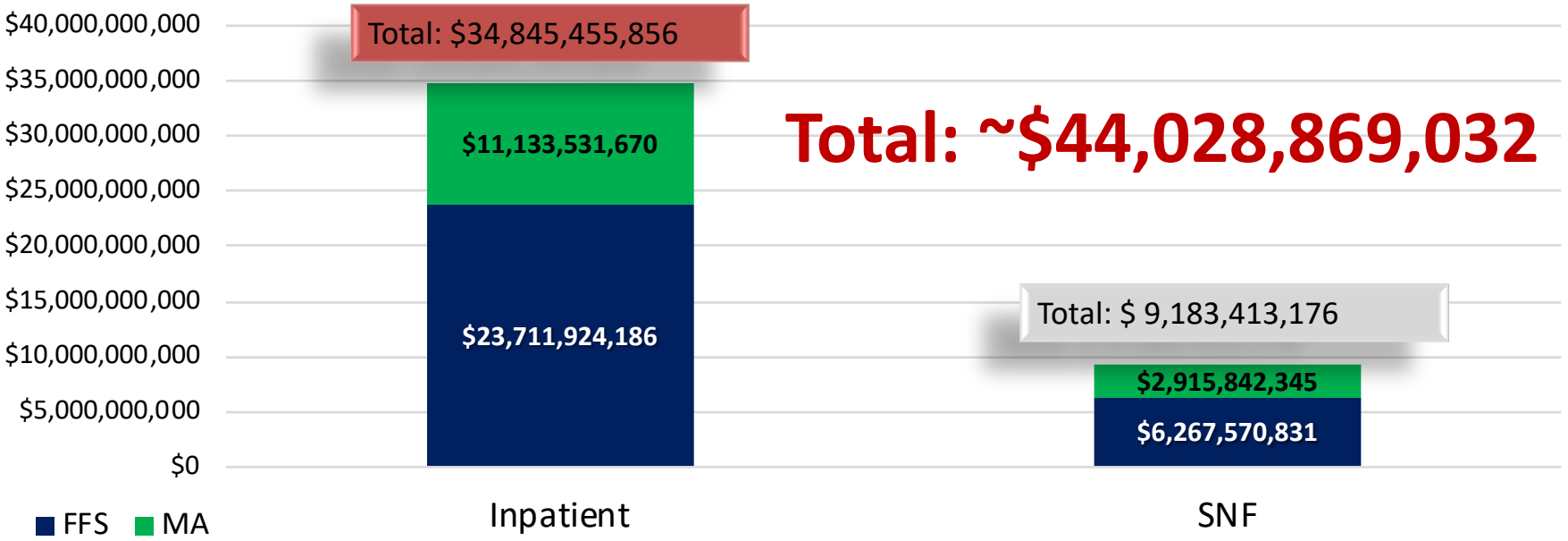

The numbers in **blue** are FFS and real payments
The numbers in **green** are MA and imputed.

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Total Sepsis Inpatient + SNF Estimated Costs

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From the AHRQ-HCUP study

$14.6 BILLION
of the $23.7 billion total
61.5% of the total

APPROXIMATION
$35 BILLION = 66.7%
2019 Inpatient Medicare cost — **Medicare total cost**

TOTAL INPATIENT COST
~$53 BILLION

Estimated SNF costs, Medicare only
+ ~$9 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

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$62 BILLION

…conservative rough order of magnitude lower bound

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Medicare Claims Data Analyzed

January 1, 2012 – December 31, 2018

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

CMS Centers for Medicare & Medicaid Services

ASPR Assistant Secretary for Preparedness and Response

DataLink Project

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

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

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

Largest in-patient epidemiological study

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

compare

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

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Lead-in to Admission:

Can we use chronic conditions to predict who is going to be septic?

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Chronic Conditions - Comparison

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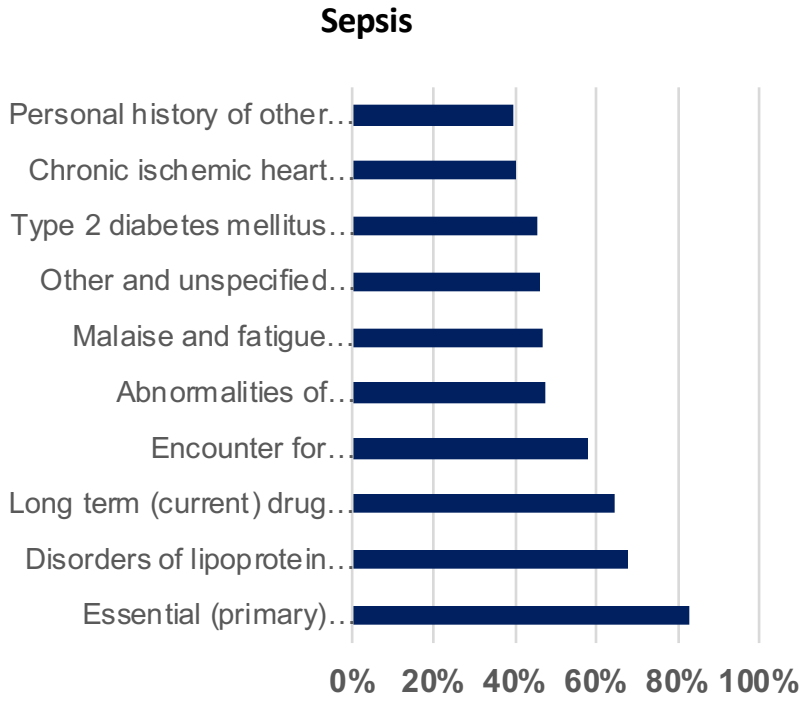

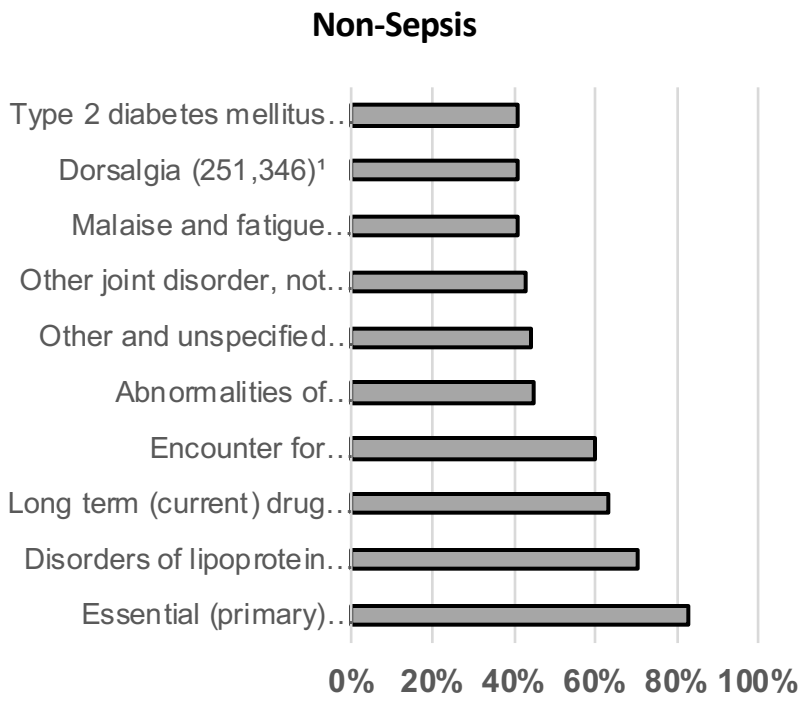

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Chronic Conditions - Comparison

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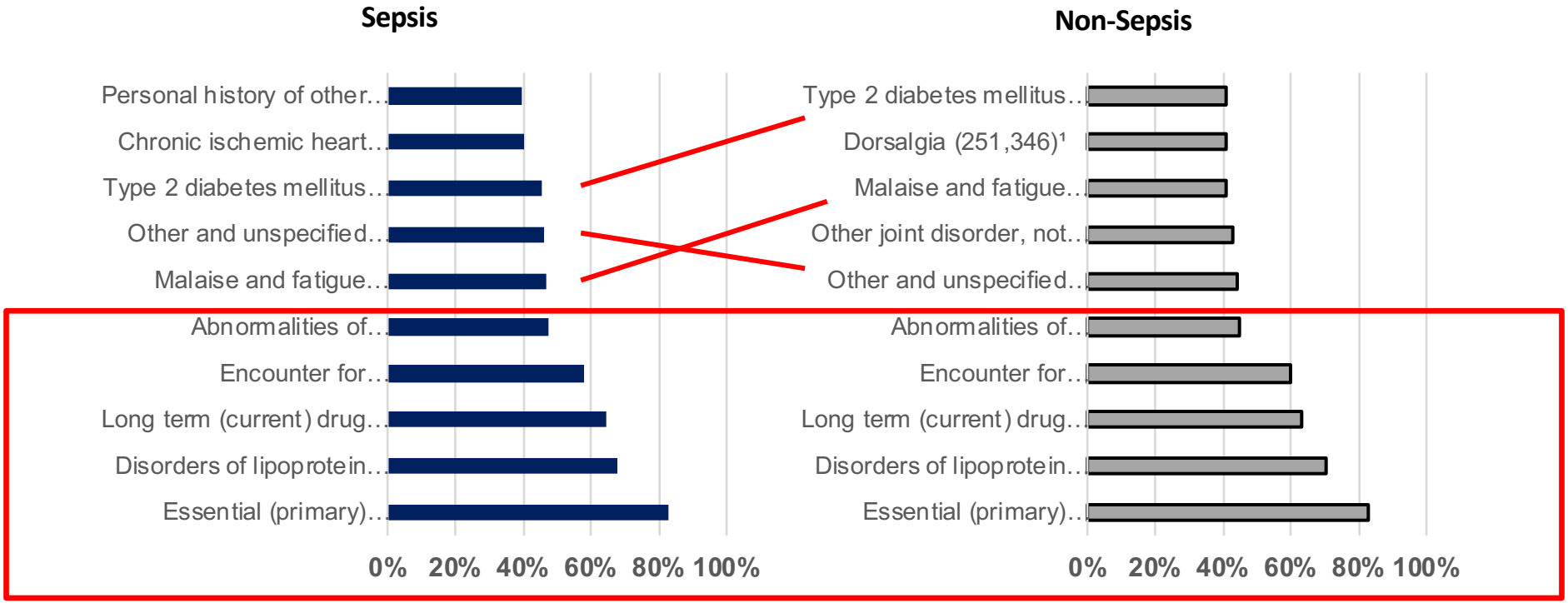

Sepsis versus Non-Sepsis Inpatient Admissions

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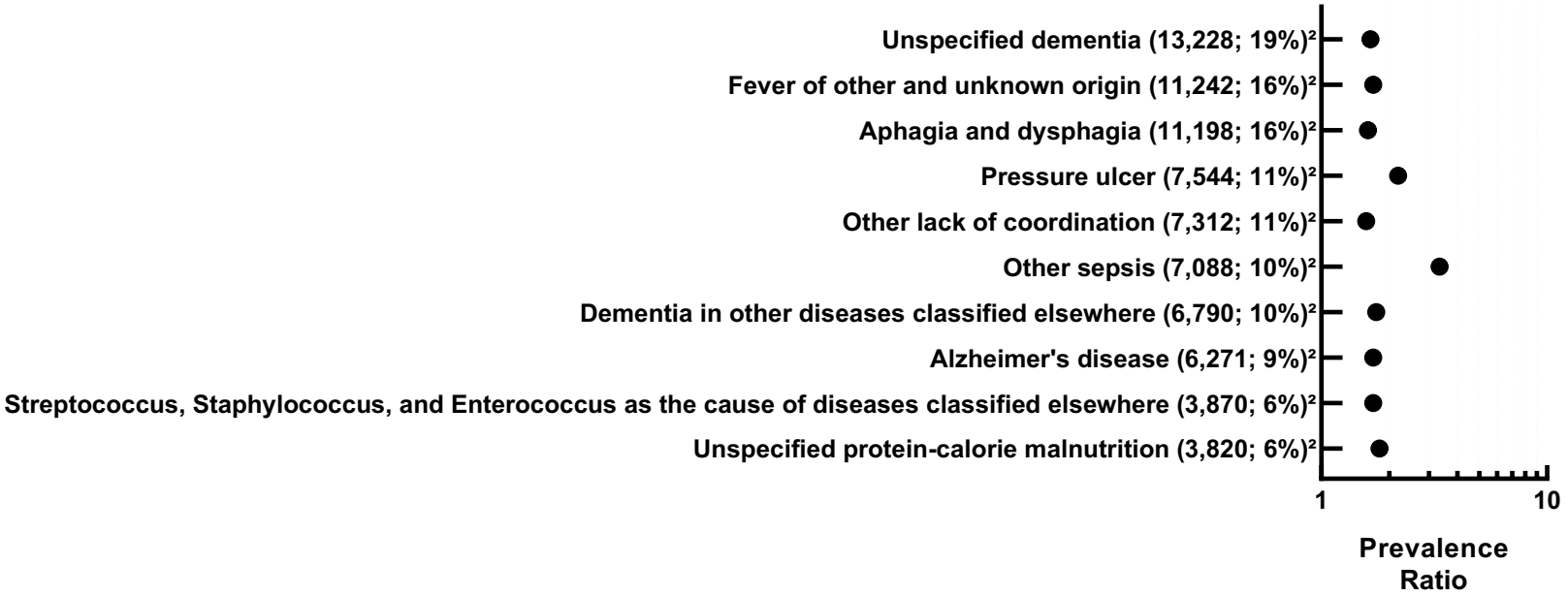
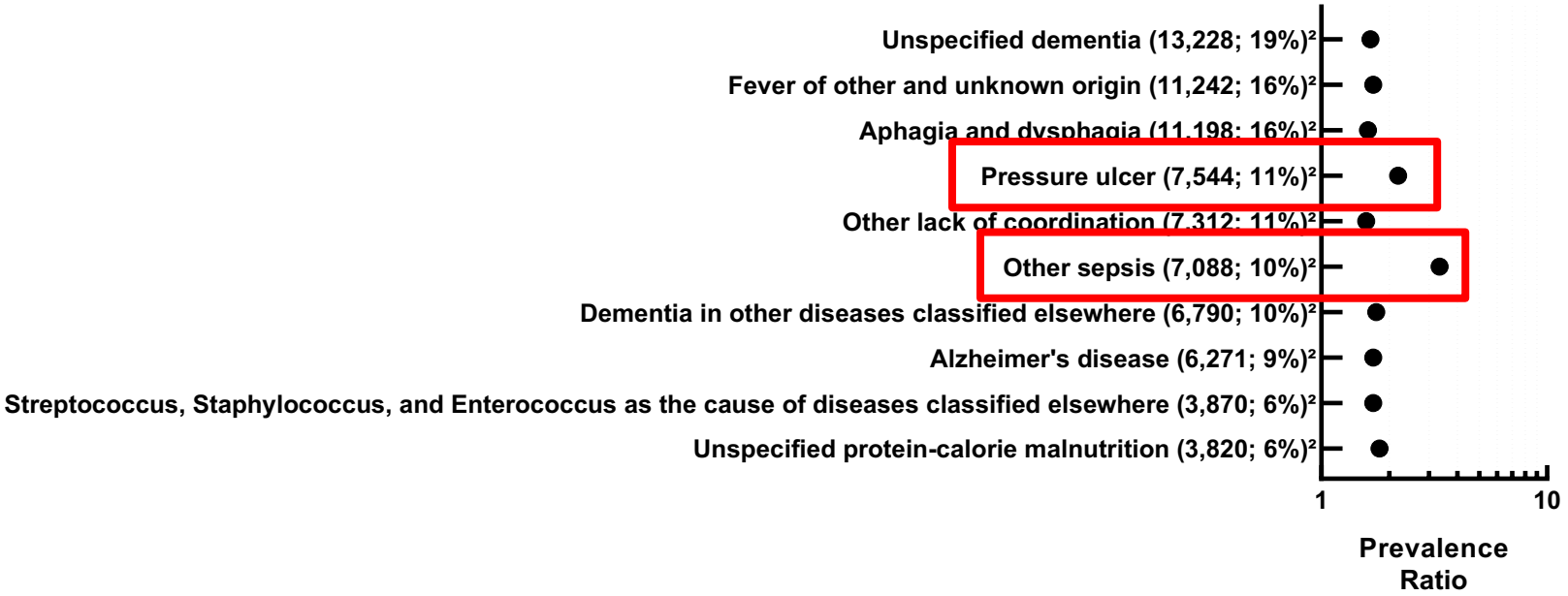
Top Prevalent Diagnoses Before a Sepsis Admission Relative to a Non-Sepsis Admission[1]



Sepsis versus Non-Sepsis Inpatient Admissions

Top Prevalent Diagnoses Before a Sepsis Admission Relative to a Non-Sepsis Admission[1]



Average Predicted Probability of Death Within 1 Week of Discharge

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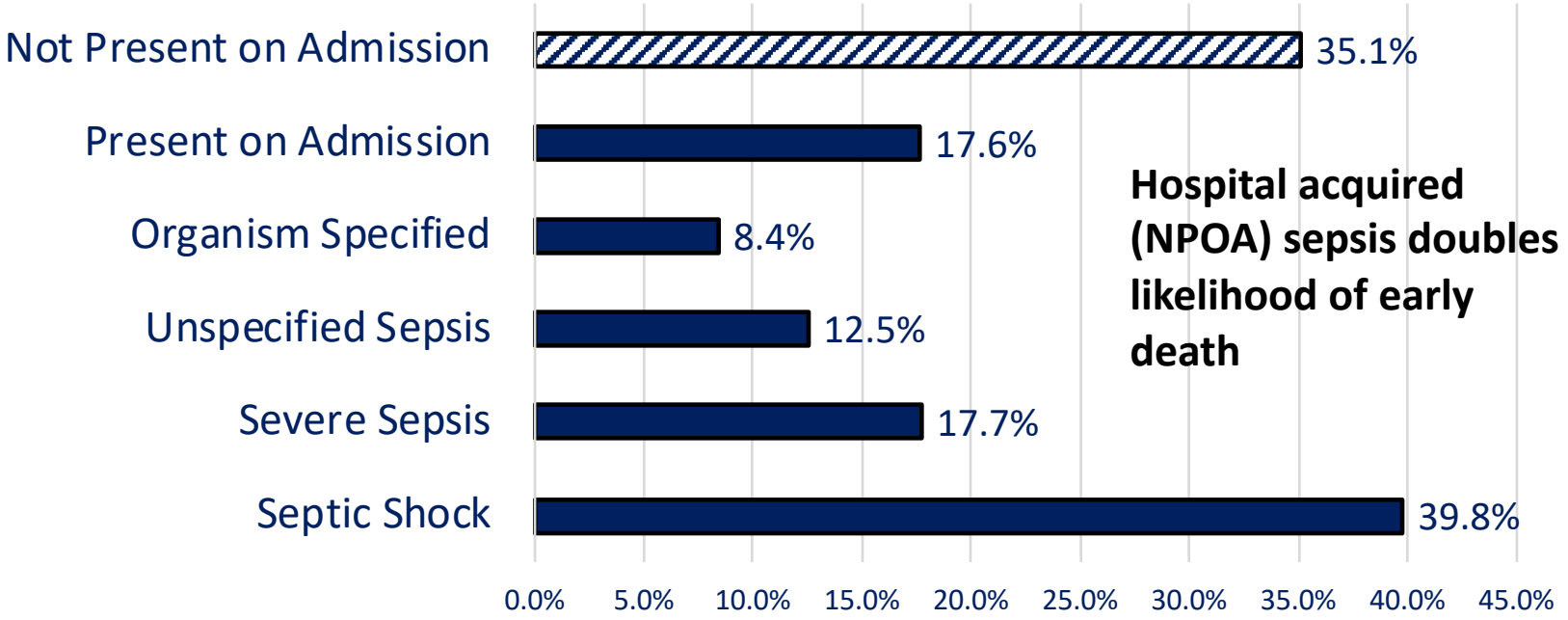

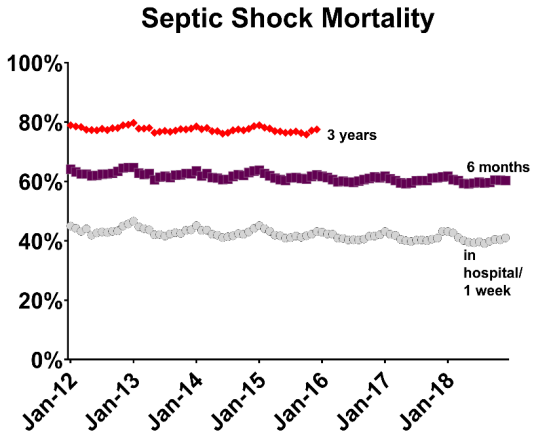

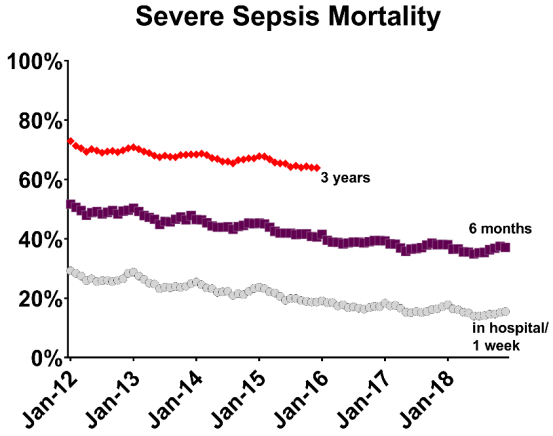

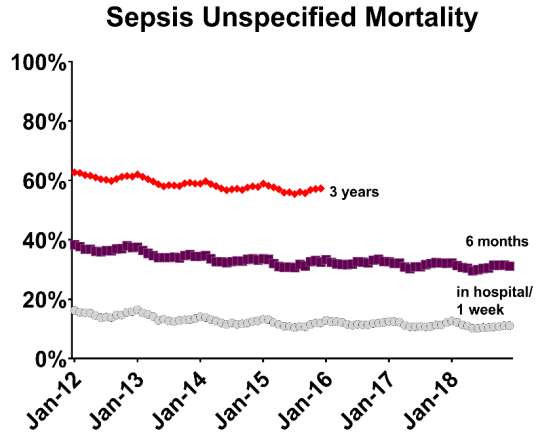

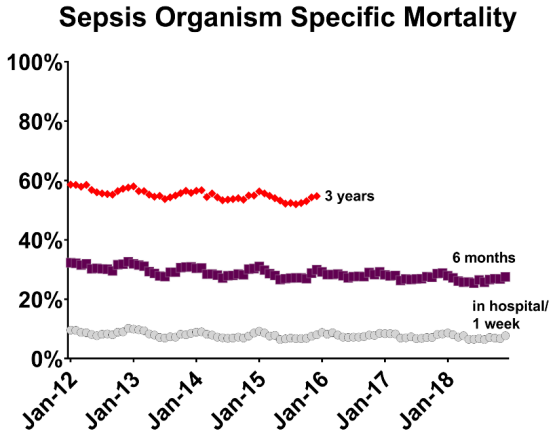

Regardless of Severity:

- 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?

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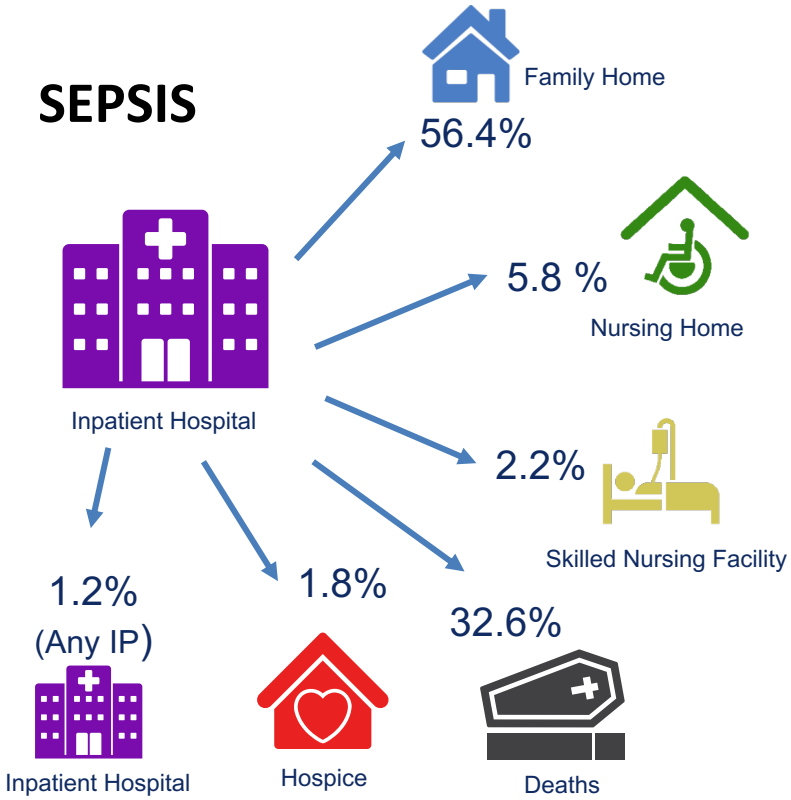

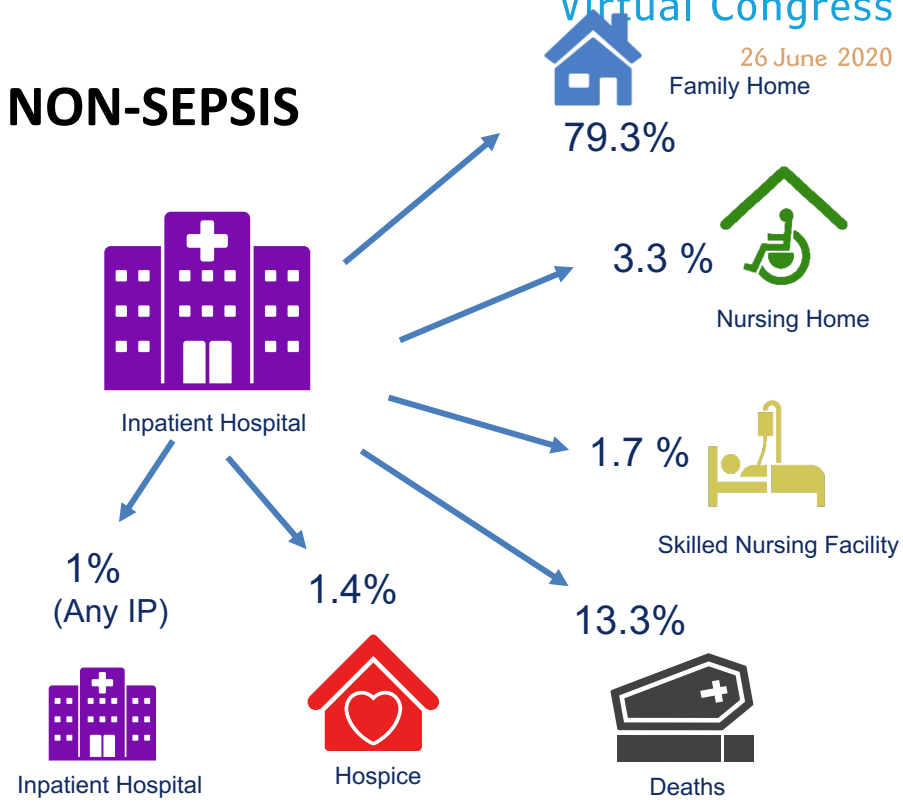

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If one goes first to a SNF, then what? (6 months)

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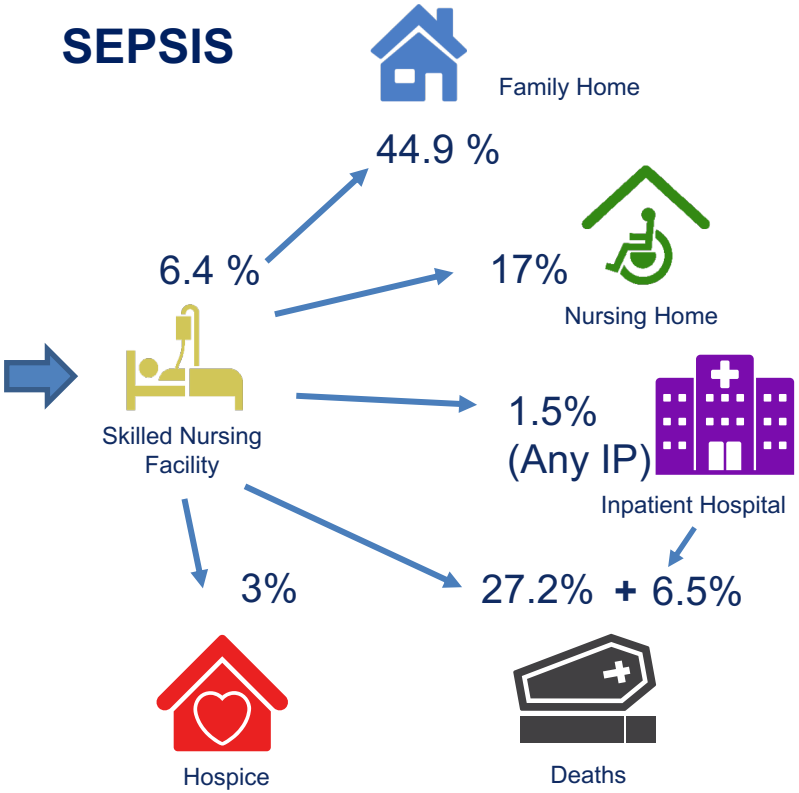

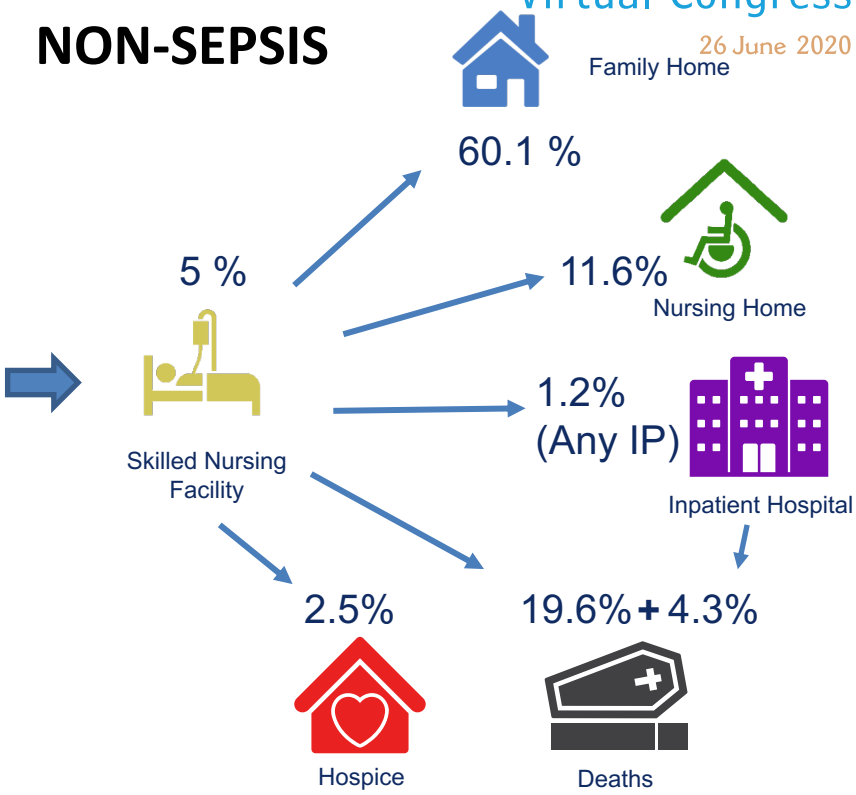

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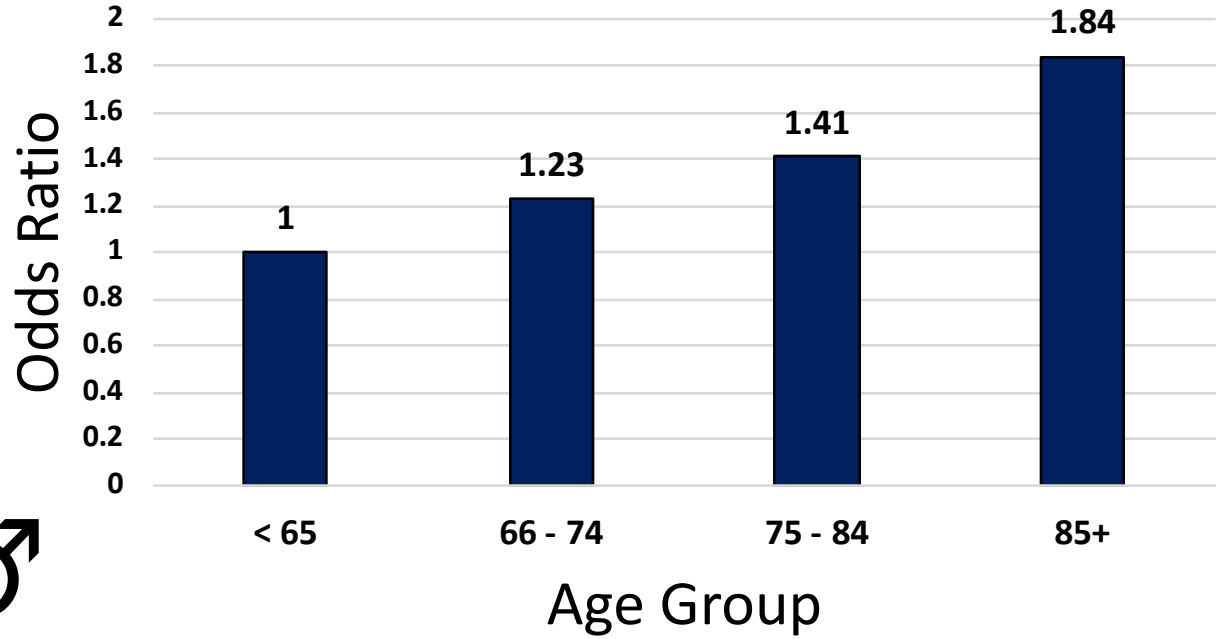
Modeling 6-Month Mortality – Effect of Age



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

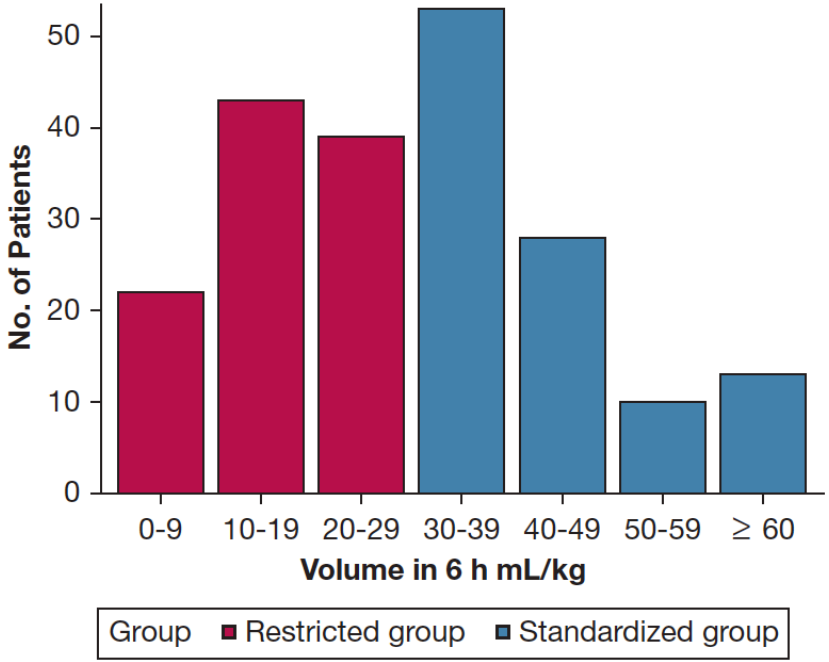
CHEST 2020; 157(2):286-292

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,


No. of Patients
50
40
30
20
10
0
0-9
10-19
20-29
30-39
40-49
50-59
≥ 60
Volume in 6 h mL/kg
Group
Restricted group
Standardized group

Demographics and Baseline Data

TABLE 1] Patient Characteristics and Clinical Variables of Both Groups

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

Outcomes

TABLE 2] Primary and Secondary Outcomes

Outcome	Restricted Group (< 30 mL/kg) (n = 104)	Standardized Group (> 30 mL/kg) (n = 104)	*P* Value
Intubation within 72 h	36 (35%)	33 (32%)	.64
Change in F_{IO_2}, %	6 ± 14	7 ± 12	.89
Time to intubation, h	14 ± 15	16 ± 19	.55
Alive ICU-free days at day 28	17 ± 10	17 ± 11	.64
Hospital mortality	19 (18%)	26 (25%)	.21
Ventilator days	11 ± 16	10 ± 12	.96

Fluid Response Evaluation in Sepsis Hypotension and Shock: A Randomized Clinical Trial

Cited in Scopus: 0

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

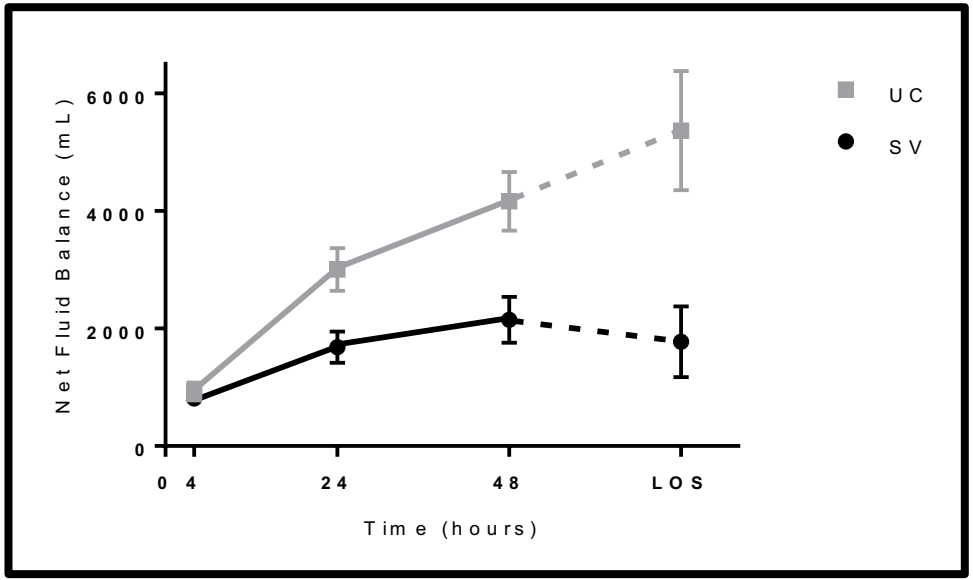
Publication stage: In Press Journal Pre-Proof
CHEST
Published online: April 27, 2020
Open Access

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



J. Crit Care 2017; 42:42 – 46.

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

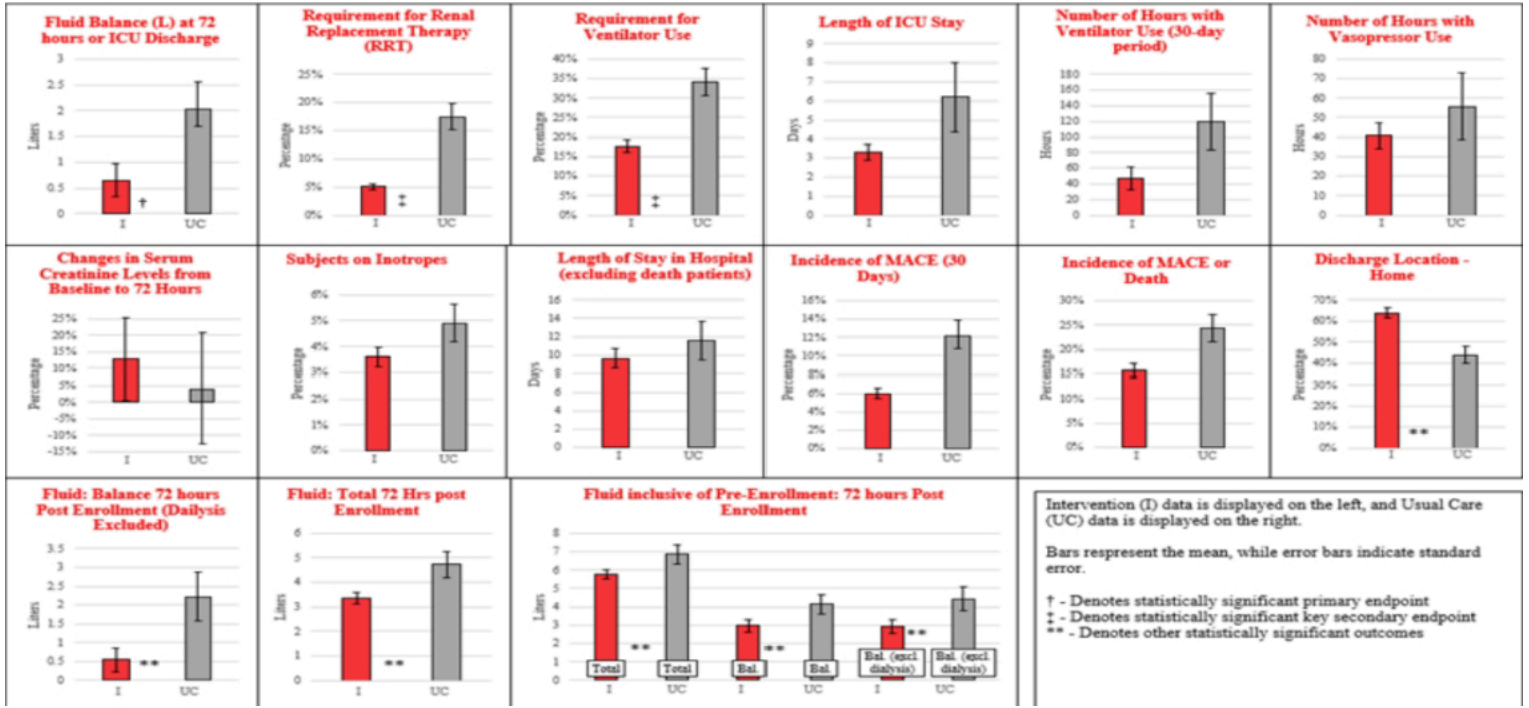
Table 1. Study Demographics

	mITT (124)	
	Intervention N=83	**Usual Care N=41**
Age (yrs)		
Mean ± SD (N)	61.8 ± 16.9 (83)	62.7 ± 15.0 (41)
Median (Q1, Q3)	65.0 (48.0, 75.0)	63.0 (55.0, 74.0)
Sex[b]		
Female	61.4% (51/83)	31.7% (13/41)
Male	38.6% (32/83)	68.3% (28/41)

Results

Parameter	mITT (124)			
	Intervention N = 83	Usual Care N = 41	Treatment Difference in Mean or Percentage, and 95% CI	p-value[a,b]
Primary Efficacy Endpoint				
Fluid Balance (L) at 72 hours or ICU Discharge				
Mean ± SD (N)	0.65 ± 2.85 (83)	2.02 ± 3.44 (41)	-1.37 (-2.53, -0.21)	0.021
Median (Q1, Q3)	0.53 (-0.84, 2.53)	1.22 (-0.03, 3.73)		

Results


Fluid Balance (L) at 72 hours or ICU Discharge
Liters
I
UC
†
Requirement for Renal Replacement Therapy (RRT)
Percentage
‡
Requirement for Ventilator Use
Length of ICU Stay
Days
Number of Hours with Ventilator Use (30-day period)
Hours
Number of Hours with Vasopressor Use
Changes in Serum Creatinine Levels from Baseline to 72 Hours
Subjects on Inotropes
Length of Stay in Hospital (excluding death patients)
Incidence of MACE (30 Days)
Incidence of MACE or Death
Discharge Location - Home
**
Fluid: Balance 72 hours Post Enrollment (Dailysis Excluded)
Fluid: Total 72 Hrs post Enrollment
Fluid inclusive of Pre-Enrollment: 72 hours Post Enrollment
Total
Bal.
Bal. (excl. dialysis)
Intervention (I) data is displayed on the left, and Usual Care (UC) data is displayed on the right.
Bars respresent the mean, while error bars indicate standard error.
† - Denotes statistically significant primary endpoint
‡ - Denotes statistically significant key secondary endpoint
** - Denotes other statistically significant outcomes

Thank You!

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