Innovative Health System Approaches to Improving Sepsis Diagnosis

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Background

- Sepsis diagnosis is challenging
- Developments in biomarkers and predictive analytics will drive improved sepsis diagnosis and targeted treatments
- Ongoing performance improvement programs and public education campaigns will reinforce the need for timely diagnosis and treatment
- What other health system opportunities are available to mitigate the impact of sepsis?

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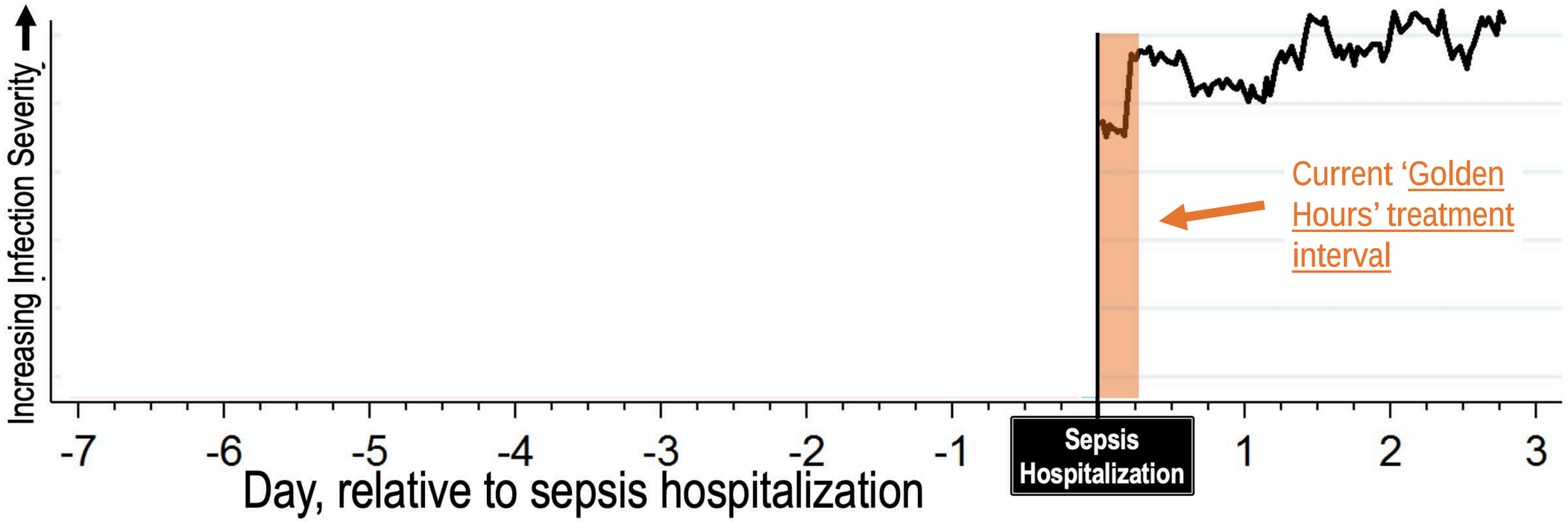
Nearly all diagnosis currently focuses on early hospital period

Are there opportunities for primary sepsis prevention?



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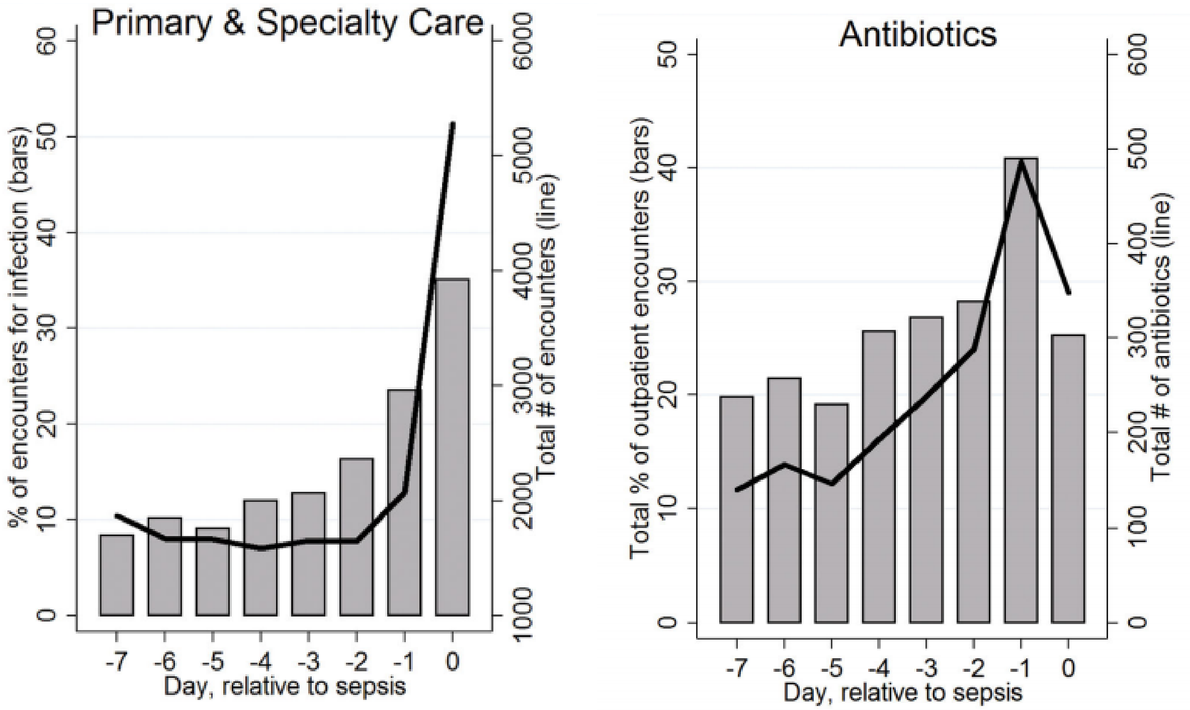
Half of sepsis patients are seen in the week prior to sepsis

Novel biomarkers and predictive analytics could accelerate pre-sepsis risk recognition

- Among 46K patients hospitalized for sepsis in KP and VA, nearly 50% were seen by physicians in the week prior to sepsis hospitalization[1]
- CDC sepsis data from 10 states confirmed that 61% had healthcare exposures in the week leading up to community-acquired sepsis[2]
- Infectious symptom onset was greatest 3-4 days prior to sepsis, although high-risk symptoms peaked closer to sepsis[3]

Increasing acute infectious diagnoses and antibiotic use in the 7 days before sepsis



[1]Liu, Prescott et al. CCM 2018. [2]Fay et al. JNO 2020. [3]Liu et al (under review)

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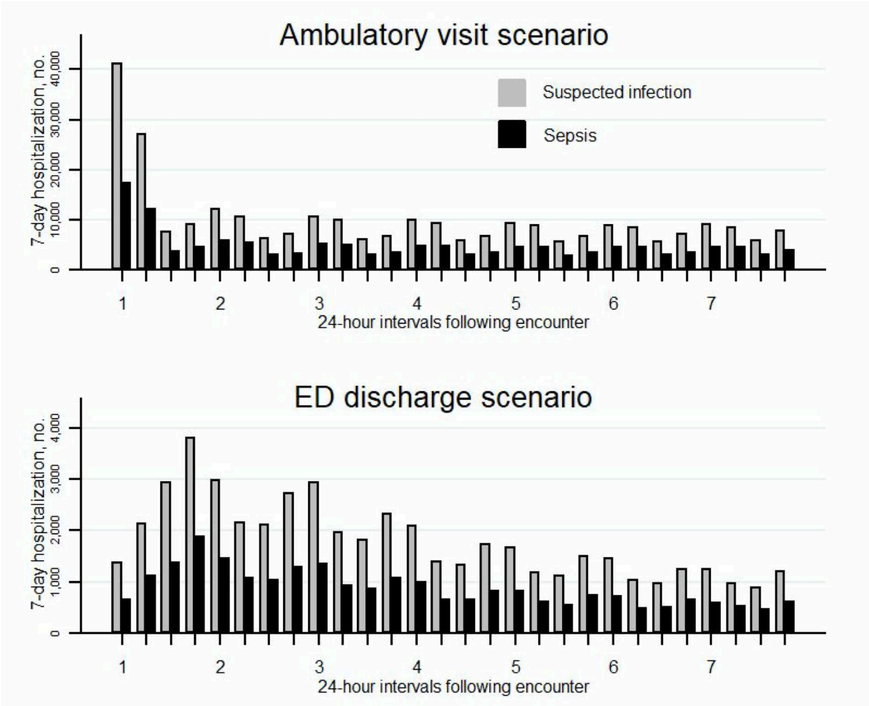
Risk and timing of impending sepsis varies by healthcare visit types

Simple measures of illness burden and severity risk-stratify routine patients

The timing of 7-day incident infection and sepsis hospitalization after encounters



- Health system review of 98M healthcare encounters highlighted heterogeneity in the incidence and timing of 7-day sepsis and infection hospitalization[1]
- Incidence of 7-day infection hospitalization was: 2.5% for hospital discharge, 1.1% for ED treat/release, and 0.3% for outpatient visit
- Chronic and acute severity of illness indices identified high-risk patient strata

Liu et al (under review)

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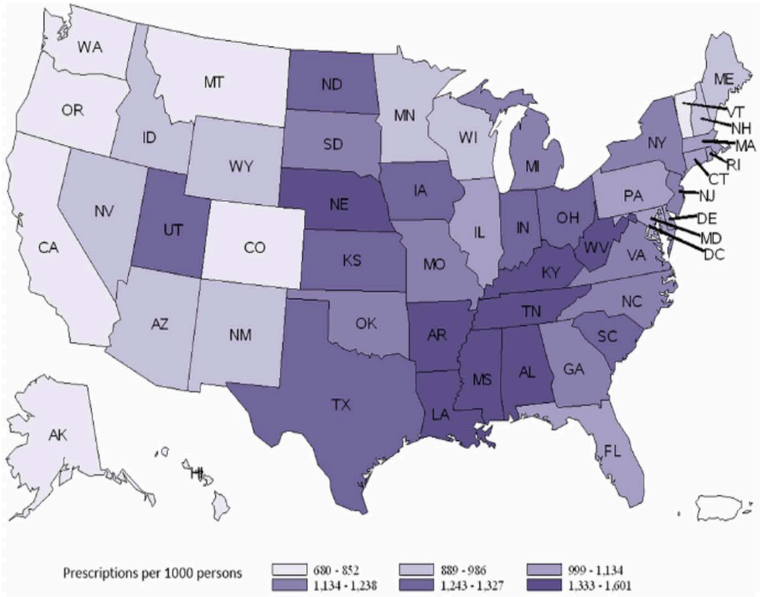
But, do we need more outpatient antibiotics?

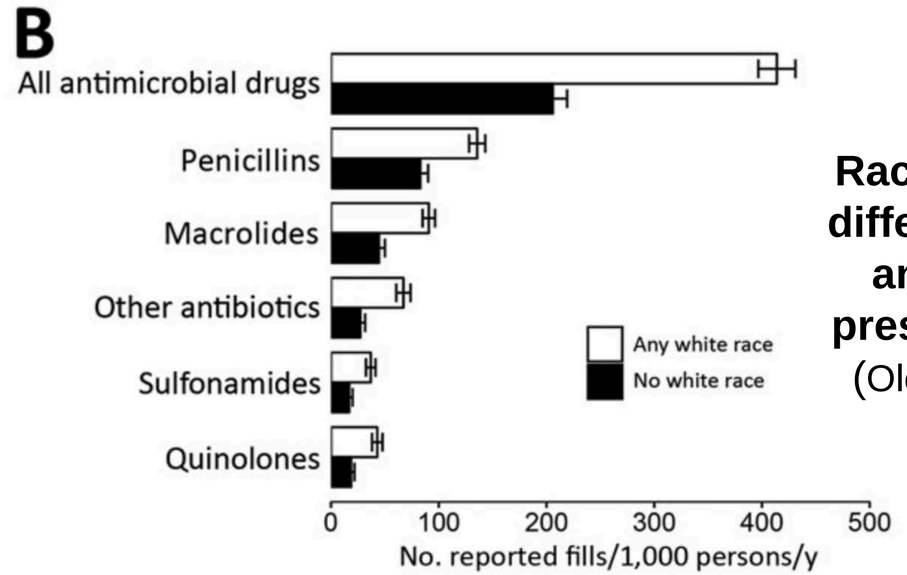
Excessive antibiotic use drives resistance, with likely limited patient-level benefit

- As much as 30-45% of outpatient antibiotic prescriptions are likely to be inappropriate, with disparities by age and race/ethnicity[1-4]

Geographic differences in antibiotic prescriptions in elderly patients
(Kabbani et al)



Antibiotic prescribing per 1,000 persons according to state in 2014 for adults aged ≥65.



Racial/ethnic differences in antibiotic prescriptions
(Olesen et al)

[1]Fleming-Dutra et al, JAMA 2016. [2]Ray et al, BMJ 2019. [3]Kabbani et al, JAGS 2018. [4]Olesen, EID 2018

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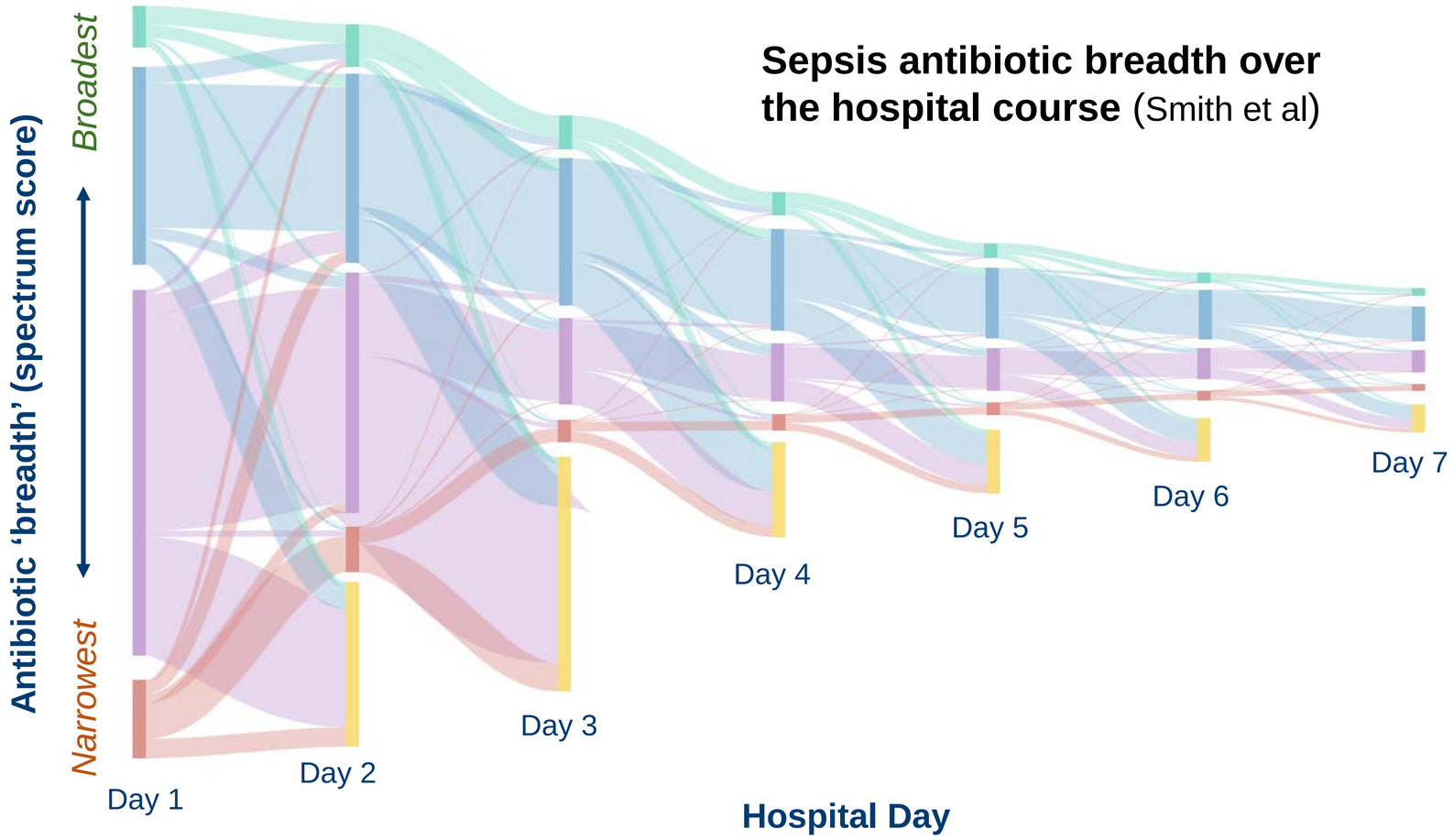
The risks of antibiotic use in sepsis are poorly understood

Sepsis misdiagnosis likely alters risk-benefit profile of antibiotic use

- Among >4 million sepsis episodes, antibiotics are frequently started and discontinued, highlighting challenges in the diagnosis of sepsis
- Quantitative tools like the Spectrum Score, which describes antibiotic breadth, help reveal how prescribing patterns change over time



Smith/Prescott/Liu et al (data in preparation)

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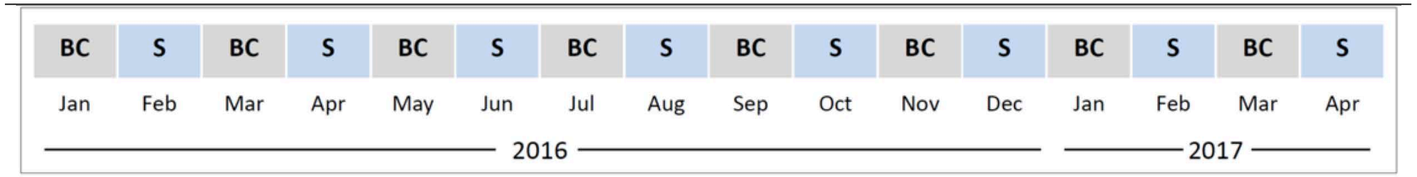
Health systems can play a critical role in designing experiments

Fusing clinical care and clinical research maximizes learning opportunities

- The SMART and SALT-ED trials embedded clinical trials of fluid management strategies leveraged modest practice changes. However, they produced tremendous clinical insight.[1,2]

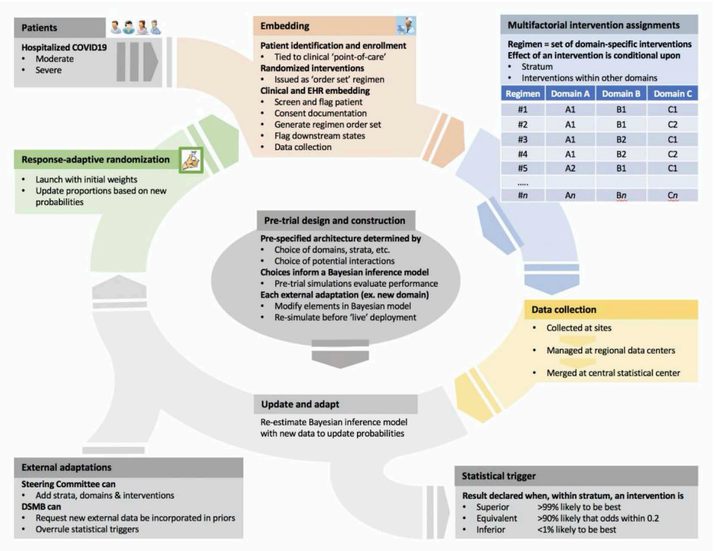
- REMAP (Randomized, Embedded, Multifactorial, Adaptive, Platform) trials offer similar opportunities across systems or hospitals[3,4]

Cluster randomized cross-over fluid design (Semler et al)



BC: balanced crystalloids; S: saline

REMAP-COVID Trial Design
(Angus et al)



[1]Semler MW et al, NEJM 2018. [2]Self WH et al, NEJM 2018. [3]Angus, JAMA 2015. [4]RECOVERY, NEJM 2020

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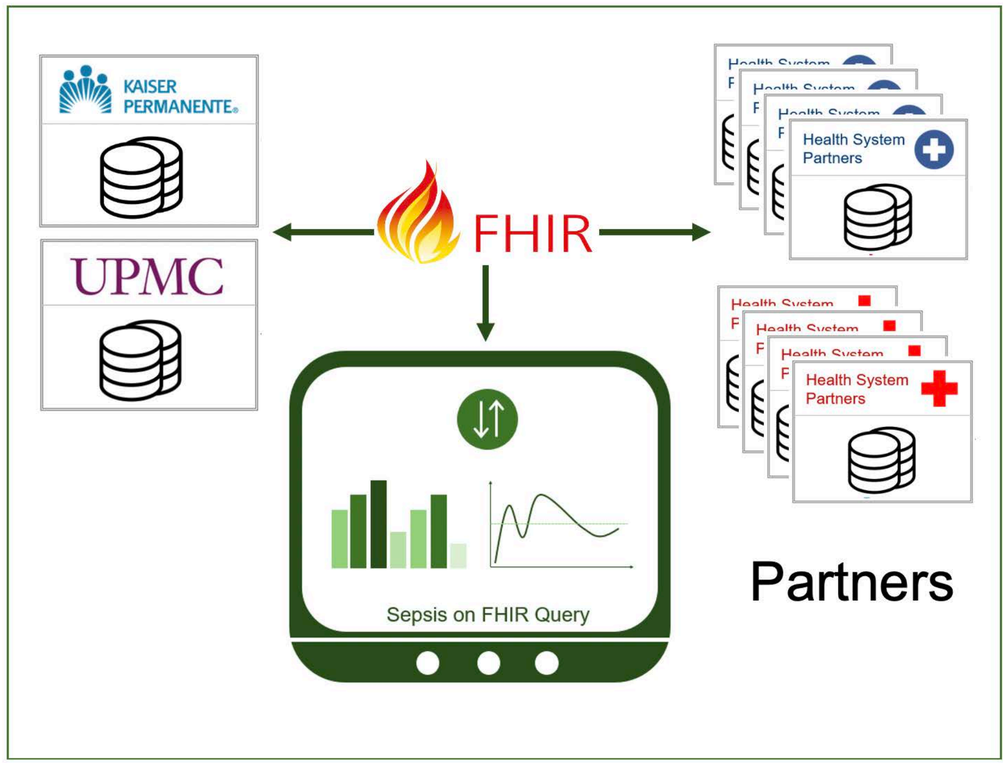
Data interoperability is key for a sepsis learning system

Millions of data elements are collected each day in the US, yet they remain siloed



Sepsis on FHIR schema (Liu/Seymour et al)

- Innovations in healthcare data interoperability have set the stage for technical implementation of standards which can improve sepsis diagnosis and treatment
- However, significant challenges remain in governance, privacy, security, and uptake to enable larger-scale and real-time sharing of sepsis data

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Summary

- Sepsis diagnosis is challenging, but will improve with innovation in biomarkers and predictive analytics, along with performance improvement and public education

- Health systems play a key role in identifying potent opportunities for improvement, by:

    - Expanding our treatment of sepsis ‘across its lifecycle’;
    - Understanding the real-world risks and benefits of key treatments;
    - Leveraging embedded research approaches to identify novel interventions;
    - Ensuring data interoperability technology that improves sepsis diagnosis.

- Collaborative infrastructure to achieve these aims should be designed and supported by health systems to ensure lasting value

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