The learning healthcare system describes a vision of US healthcare that capitalizes on science, information technology, incentives, and care culture to drive improvements in the quality of health care. The inpatient setting, one of the most costly and impactful domains of healthcare, is an ideal setting in which to use data and information technology to foster continuous learning and quality improvement. The rapid digitization of inpatient medicine offers incredible new opportunities to use data from routine care to generate new discovery and thus close the virtuous cycle of learning. We use an object lesson—sepsis care within the 21 hospitals of the Kaiser Permanente Northern California integrated healthcare delivery system—to offer insight into the critical elements necessary for developing a learning hospital system. We then describe how a hospital-wide data-driven approach to inpatient care can facilitate improvements in the quality of hospital care.

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could be recovered, however, the quality of healthcare could be improved dramatically.8 The pursuit of continuous learning is aided by rapid changes in the quality and quantity of biomedical data available over the past decade, especially through the use of electronic health records, novel biomolecular tools, and digital sensors.2,7,9 The Internet has ushered in a new era of data connectivity, for example, allowing for highly engaged communication between patients and providers as well as collaboration between professional or citizen scientists on data of unprecedented scale.10 New methodologic approaches, including data mining and machine learning, increasingly leverage commodity hardware to conduct previously computationally intractable analyses.9 Moreover, the development of domain ontologies fosters the discovery of meaningful insights from data of heterogeneous types.11 Ultimately, however, improvements in data alone are inadequate to achieve continuous learning. As shown in Figure 1, whereas data form the channels that allow for transitions from science to evidence to care, novel insights need to be steeped within the right culture, motivated by the right incentives, and supported by the right leaders.1,12 Within the sustainable learning healthcare system, knowledge generation feeds practice change with the support and guidance of system leadership; improved practice, in turn, generates new knowledge and completes the virtuous cycle of learning.

THE PROMISE OF CONTINUOUS LEARNING IN HOSPITAL SETTINGS

The hospital is an ideal setting in which to foster continuous learning because advances in inpatient care have the potential to substantially improve healthcare quality and value.8 Americans were hospitalized roughly 37 million times in 2012; in total, these episodes cost $378 billion.3 Over 700,000 patients die in US hospitals annually, with reports showing that many patients utilize greatly increased inpatient and critical care services near the end of their lives in a manner that appears misaligned with their preferences.11,13 Hospital care is also highly variable in quality and cost; this heterogeneity is not closely associated with improved outcomes.14,15 Preventable harm and medical injury occur commonly in hospitals and are now recognized to be a leading cause of inpatient death.16 Finally, emerging research illuminates the substantial toll that acute care has on patients and families resulting in new comorbidity, functional or neuropsychiatric impairment, rehospitalization, and financial burden that persist long after patients are discharged.17

Fortunately, inpatient care also exhibits several qualities that improve the likelihood that continuous learning can be achieved. Although it is clear that hospitalizations occur within the arc of a patient’s larger health trajectory, these distinct episodes offer the potential to observe patient trajectories and treatments evolving within relatively compressed time intervals; over that same interval, a large volume of data are produced. Stored within comprehensive electronic health records, these granular data now allow inpatient episodes to be digitally recapitulated with high fidelity, bolstering their use in driving care improvements.18
that sepsis had a major impact on hospital outcomes. For example, even though sepsis patients were still relatively under-recognized at the time, accounting for fewer than 3% of hospitalizations, they contributed to one-quarter of hospital deaths. In light of these compelling data, senior regional leadership identified reducing sepsis mortality as a key performance improvement goal (Figure 2, step 2).

Based on the principles of performance improvement methodology, clinical and operational leaders established an environment with aligned culture, incentives, and leadership around sepsis care. The effort was launched in late 2008 at a Sepsis Summit, bringing together a multidisciplinary group of stakeholders (eg, hospitalist, emergency department, and intensive care chiefs of staff and nursing managers; medical center and nursing executive and operational leadership) and providing sepsis care pathways based on the best available evidence. Regional investments in the digital infrastructure to support implementation resulted in the provision of granular data within monthly sepsis scorecards quantifying each medical center’s performance and trends for a diverse set of sepsis bundle metrics.

The resulting changes in sepsis care were substantial. For example, improved early recognition of infected patients meeting the criteria for sepsis resulted in large changes in the standardized diagnostic criteria used to label patients (Figure 3A). Implementing screening strategies using serum lactate testing for any patient receiving blood cultures resulted in a roughly 10-fold increase in the use of lactate testing in the emergency department (Figure 3B). Earlier recognition of sepsis also increased the number of patients receiving early antibiotics and receiving central venous catheters for quantitative resuscitation.

CLOSING THE LOOP TOWARD CONTINUOUS LEARNING IN SEPSIS
Leveraging timely and actionable data steeped within an aligned organizational milieu resulted in large-scale changes across a heterogeneous set of hospitals. However, to realize the true vision of a learning hospital system, a looming question remained: Could the data generated as the byproduct of routine care now be used to complete the virtuous cycle and drive new scientific discovery (Figure 2, step 3)?

Confirming Concordance in the Impact of Sepsis Nationally
The heightened identification of sepsis patients through program implementation revealed that the impact of sepsis on hospital mortality was greater than originally estimated; based on improved patient identification, sepsis now accounted for upward of 1 in 2 hospital deaths. This sobering statistic confirmed that the investments in standardizing best sepsis care following the mortality diagnostic were critical. However, were similar estimates of sepsis-attributable mortality consistent outside of the KPNC system? To study this, we examined US hospitalizations occurring across >1000 hospitals and involving >6 million hospital stays to estimate corresponding prevalence. In this national sample, sepsis contributed to as many as half of hospital deaths in the United States in 2010, lending strong support to ongoing international and state-based efforts to improve sepsis care. These studies also paved the way to use these data drawn from our large sepsis population to inform updated international consensus definitions for sepsis and septic shock.

Identifying New Avenues for Reducing the Toll of Sepsis
A major concern of sepsis program leaders was the prior findings that sepsis hospitalizations among Medicare

FIG. 2. Closing the continuous learning loop in sepsis care. Schematic representation of the continuous learning hospital system generating new discovery in sepsis care.
survivorship care.32,33

predictions outside of KPNC have confirmed these concerning facility-based care. Subsequent studies in other populations have confirmed that the sepsis impact is at least 20- to 100-fold larger than that reported in prior studies.12

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AHSN’s sepsis leadership group was able to rapidly assemble a “sepsis cart.” Multidisciplinary teams included ED physician “champion,” ED nurse “champion,” improvement advisor, hospitalists, intensivists, quality improvement personnel, nurse educators, and even resident physicians.

beneficiaries were associated with substantial new cognitive and functional disability.29 This lingering toll of sepsis has been termed a “hidden public health disaster.”30 To further understand the posthospital impact of sepsis and to begin investigating new avenues to reduce this impact, a cohort of patients was followed for 1 year following sepsis hospitalization.31 Over that period, nearly half of sepsis survivors were rehospitalized. When compared with their presepsis levels of healthcare utilization, middle-aged and elderly sepsis patients experienced a 3-fold increase in their days using facility-based care. Subsequent studies in other populations outside of KPNC have confirmed these concerning findings, resulting in new efforts to address postsepsis survivorship care.22,23

Phenotyping New Targets for Standardized Sepsis Care

At its outset, the sepsis improvement program applied the best available evidence to treat patients with the most severe forms of sepsis—septic shock. However, once the initial implementation phase had succeeded, clinicians and operational leaders quickly realized from the emerging data that there was a far larger group of sepsis patients for whom treatment guidelines were poorly defined.25,34,35 These were severe sepsis patients with so-called intermediate lactate values between 2 mmol/L and 4 mmol/L; they comprised a substantial proportion of all sepsis patients dying in the hospital. Using data generated from the routine care of sepsis patients treated across 21 hospitals, the sepsis leadership group was able to rapidly assemble a cohort of intermediate lactate sepsis patients up to 20- to 100-fold larger than that reported in prior studies and evaluate their outcomes.34,35

The data used to evaluate these intermediate lactate sepsis patients now spurred a new implementation program in 2013 for a group of patients in whom there was essentially no existing evidence to guide care. Rapidly implemented within a mature sepsis performance improvement program, evaluations at the 6-month and 1-year intervals demonstrated significant decreases in...
Importantly, to allay the justified concerns of clinicians, these evaluations also clearly showed no evidence of harm from more aggressive fluid resuscitation (eg, increased transfer to intensive care, increased rates of mechanical ventilation). Again, driven by clinician input, subgroup analyses further revealed that the implementation program was only associated with reduced mortality in patients who could be at risk for iatrogenic fluid overload (ie, those with a history of congestive heart failure or chronic kidney disease). Spurred by these provocative findings, operational and clinical leaders are currently considering how to guide future care in these patients, especially with the emerging use of noninvasive methods to quantify patients’ fluid responsiveness.

**PRINCIPLES FOR LEVERAGING DATA IN THE LEARNING HOSPITAL SYSTEM**

The object lesson of using data to drive improved sepsis care and further new scientific discovery offers some important insights for continuous learning.

**Building a Digital Infrastructure for Utilizing Granular Hospital Data**

As described above, current transitions between the nodes of the learning framework are rife with missed opportunities. Perhaps one of the most glaring is the inability to use highly granular data already collected within the electronic health record (eg, trajectories and trends across vital signs or laboratory results, large-scale medication administration records to evaluate multidrug interactions). An essential starting point for continuous learning is investing in the digital infrastructure to improve the use of data beyond traditional claims (administrative data–admission source codes, disposition codes, diagnoses, and procedures). As shown in Table 2, the first key step is incorporating laboratory data into the quality assessment/improvement process. In addition, using these data to automate severity of illness and risk adjustment metrics fosters use of similar comparison cohorts across time or disease types.

**Employing Novel Methods to Address the Limitations of Using Real-World Data**

The rapid digitization of medicine through the use of electronic medical records offers tremendous opportunities to facilitate continuous learning. However, these opportunities are accompanied by important limitations. Data collected as a byproduct of real-world care can be vulnerable to many forms of bias and confounding, potentially clouding the validity and robustness of corresponding analytic results. Fortunately, advanced methods including causal inference are now used routinely to address some limitations. In the context of a learning healthcare system, other opportunities for improved study design including cluster randomized trials or stepped wedge implementation can also be employed to preserve the statistical rigor of subsequent analyses. Finally, emerging methods employing randomization through the electronic medical record alongside adaptive trial design offer great potential to increase the efficiency of continuous learning.
Evaluating the Hospital as a Single System
Advances in contemporary hospital care require seamless transitions of patient care, screening strategies, and therapeutic approaches across multiple hospital domains and with diverse providers; these interventions also need to happen rapidly. Many traditional approaches to inpatient care have taken a bottom-up approach (e.g., studying a specific disease within a specific hospital ward like the intensive care unit) that have proven useful but may limit generalizability when applied to a real-world hospital operating with Pareto optimality (i.e., the trade-off scenario where new resource allocation to 1 area also requires resource withdrawal from another area). In certain cases, an empiric approach, without initial preference for any specific ward or disease, can aid decision making by hospital operational and clinical leaders by providing a global picture of impact and value.

Focusing on Early Detection in Hospital Settings as Secondary Prevention
Once patients have been admitted to the hospital, a race against the clock begins. Each additional hour of hospitalization increases the risks of iatrogenic injury or medical harm manifested by immobility, disorientation and delirium, nosocomial infections, or medication errors, among others. In this context, detection systems that use granular hospital data to focus on the earliest detection of risk can aid critical approaches to secondary prevention (although the hospitalization for sepsis cannot be avoided, careful attention to mobility can limit the risk of developing delirium. In turn, preventing delirium can limit the risk of new functional disability).

Contextualizing Hospital Care Within a Longitudinal Trajectory
Although we described the benefit of hospital episodes having well-demarcated beginning and ending points, it remains essential to recognize that the harms associated with hospitalization extend well beyond discharge. In this context, hospitalizations can serve as waypoints in patients’ health trajectories as well as an opportunity to achieve patient-centered care including discussing and aligning goals of care with actual care provision. Furthermore, although we have seen steady declines in hospital mortality over time, it is highly likely that we will reach a nadir in mortality where additional metrics of hospital outcomes will need to include postdischarge events like readmission, long-term mortality, quality of life, and the prevention of disability or decline.

CONCLUSION
Hospitalizations in the United States are costly and associated with high mortality and morbidity; the toll of hospitalization also extends well beyond hospital discharge. The promise of the learning hospital system has marked improvements in the quality of hospital care, especially where healthcare systems can steep critical investments in data and digital infrastructure within the right culture, incentives, and leadership. Where continuous learning is achieved, data generated during routine care offer the potential to yield new scientific discovery and drive further improvements in hospital care.

Disclosures
As part of our agreement with the Gordon and Betty Moore Foundation, we made a commitment to disseminate our findings in articles such as this one. However, the Foundation and its staff played no role in how we actually structured our articles, nor did they review or preapprove any of the manuscripts submitted as part of the dissemination component. None of the authors has any conflicts of interest to declare.

References

TABLE 2. Data Types Necessary to Actualize the Learning Hospital System Graded by Contents and the Degree of Difficulty Necessary to Access and Analyze the Data

<table>
<thead>
<tr>
<th>Data Type</th>
<th>Contents</th>
<th>Degree of Difficulty in Accessing</th>
<th>Degree of Difficulty in Analyzing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administrative</td>
<td>Traditional claims data, diagnostic or procedural codes</td>
<td>Low</td>
<td>Low to moderate</td>
</tr>
<tr>
<td>Standard cohort profiling</td>
<td>Limited instances of vital signs, laboratory, diagnostic testing, or treatment data</td>
<td>Low to moderate</td>
<td>Low to moderate</td>
</tr>
<tr>
<td>Metrics reporting for care improvement</td>
<td>Standard cohort identification, aggregated achievement of treatment targets, scorecard dissemination</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Advanced cohort profiling</td>
<td>Time series of physiologic data, inpatient triage and treatment data within short temporal intervals</td>
<td>Moderate to high</td>
<td>High</td>
</tr>
<tr>
<td>Research-grade discovery</td>
<td>Data with breadth (representative sample size) and depth</td>
<td>High</td>
<td>Very high</td>
</tr>
<tr>
<td>Patient-reported outcomes</td>
<td>Quality of life, functional and cognitive disability</td>
<td>Very high</td>
<td>High</td>
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