It is important to plumb the depths of pathways implicated in LAM pathogenesis to determine druggable targets. The data on the LAMCORE cell, its gene expression pattern, and its effect on its microenvironment were generated with the input of only three LAM lungs owing to the difficulty of obtaining fresh tissue samples. However, many of the pathways and processes proposed here fit with data already available about LAM pathogenesis. It is interesting to note that LAMCORE cells could not be detected in the lung from a patient who had been taking sirolimus, the only approved drug for LAM that was tested in a double-blind clinical trial (14), suggesting that the LAMCORE cell is sensitive to sirolimus and is indeed involved in disease pathogenesis. It would be interesting to see the expression pattern of the metastatic, circulating LAM cells and if they differ from the LAMCORE cell. And although the theorized uterine origin of the LAM cell is promising and deserves further investigation, it does not explain the rare occurrence of LAM in males (15). LAM cells in the lung may arise from another site, which would, of necessity, be the case in males. Nevertheless, this study has given the LAM scientific community opportunities for future studies and represents a major advance in our understanding of this disease.

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Supporting a Precious Resource: Healthcare Clinicians

The well-being of frontline clinicians has received attention over the years (1). But the coronavirus disease (COVID-19) pandemic and its impact on clinicians smacked us all in the face with this reality—images of nurses with brushes on their faces wearing personal protective equipment, stories of clinicians succumbing to suicide, and a seemingly never-ending surge of patients. Although evidence is building to show the impact of COVID-19 on clinicians, the essentialness of clinicians as one of the most, if not the greatest, precious resource in health care has never been clearer.

In this issue of the Journal, Azoulay and colleagues (pp. 1388–1398) examined symptoms of anxiety, depression, and peritraumatic dissociation in clinicians from 21 ICUs in France during spring 2020 (2). Nearly half of respondents reported anxiety, and a third reported depression and peritraumatic dissociation; these data are consistent with reports from other countries (3, 4). The sheer prevalence of anxiety, depression, and peritraumatic dissociation is staggering. The authors also identified six individual and organizational modifiable factors. Four factors associated with increased depression, anxiety, and dissociation were related to clinicians’ emotions and circumstances. Fear was associated with increased odds of anxiety (odds ratio, 1.21; 95% confidence
Emerging research suggests that anxiety can be spread by social contagion (11, 12). Increasing uncertainty related to COVID-19 has led to overall increases in anxiety. It is plausible that the high prevalence of anxiety in this study may be due to social contagion, that is, by an increase in anxiety among peers. Unfortunately, the current study design prevents further investigation, but future studies could examine this. Doing so would inform interventions to minimize poor mental health outcomes by leveraging peer support commonly found in groups of nurses and healthcare clinicians, especially in light of Azoulay and colleagues’ results that collegial support was paramount. It is also important to note that 10% of clinicians reported euphoria, exaltation, hyperactivity, and high self-esteem. These symptoms may be an indicator of mood instability as described by Azoulay and colleagues, but they could also be coping mechanisms; ICU clinicians may be attempting to find joy at work and reframe their part in the pandemic to give them purpose (13).

Based on these findings and our prior work, support for clinicians must take a three-pronged approach at the national, organizational, and individual levels (14). At the national level, transparency of the situation, communication, and adequate personal protective equipment is a must. At the hospital level, policies for proper time off by conscious scheduling and additional work–life support for primary family caregivers are mandatory to avoid excessive overtime and limit hazardous work hours (15). Most importantly, because clinicians were negatively affected regardless of COVID-19 caseload, all hospitals and units should prioritize clinician well-being by promoting self-care but also by building policy and infrastructures to support clinicians in balancing work and life.

In summary, this study highlights the vulnerability of clinicians during an unprecedented time. Every ICU personnel is at risk for psychological stress. As a society, and professional community, we must come together to preserve the well-being of our most precious human resource—healthcare clinicians.

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Watchful Waiting in the ICU? Considerations for the Allocation of ICU Resources

The emergence of value-based health care—a reckoning of the benefits and costs of clinical and organizational interventions—has included an interest in the optimal use of critical care resources. Understanding the ideal allocation of costly and often limited resources, such as ICU beds, is essential to a hospital’s daily operation and sustainability (1). When faced with uncertainty about the best triage decision for a sick patient, clinicians must ask: Does this patient benefit from ICU admission? They may also ask: What is my hospital’s ICU bed availability at present? Conversely, toward the end of a patient’s ICU course, clinicians must routinely consider: Is this recovering ICU patient ready for transfer to the medical ward (i.e., does this patient no longer benefit from the ICU)? They may also, and often do, ask: Is there another patient who needs this ICU bed more?

These latter questions, related to the timing of ICU discharge, are informed by 1) a clinical assessment of “readiness for discharge” and 2) the availability of ICU and ward beds at that time. High ward occupancy is a common source of healthcare capacity strain (2, 3). When present, this strain can delay both ICU discharge and, in turn, likely delay upstream new ICU admissions to those still-occupied beds. Thus, some typical ICU patients may instead be admitted to the ward or may “board” in the emergency department or in a specialty ICU that is not ideally matched with their needs. These scenarios may be associated with higher mortality relative to timely, appropriate ICU admission (4, 5).

In this issue of the Journal, Forster and colleagues (pp. 1399–1406) shed new light on the timing of ICU discharge as an explicit component of ICU resource allocation (6). The authors sought to understand the impact of an unintended delay in ICU discharge on patient outcomes. ICU discharge delay was defined as time between a patient being deemed “ready” for ICU discharge by the clinical team and actually leaving the ICU. Implicit in this definition is that the delay was driven by system-level factors, such as high ward occupancy or infection control needs, and not patient-level factors, and the patient remained ready and awaiting discharge during this delay. The authors performed a thoughtful retrospective cohort study using the Australian and New Zealand Intensive Care Society Adult Patient Database. They studied over 1 million patients from 190 ICUs who were discharged alive from the ICU to the ward after their first ICU admission. The authors developed a hierarchical model to estimate the association between discharge delay and mortality or ICU readmission. In sensitivity analyses, the investigators examined outcomes among three prespecified subgroups stratified by predicted risk of death upon ICU admission.

Forster and colleagues report that 75% of patients were discharged within 6 hours of being deemed ready, 13% were discharged after a 6- to 12-hour delay, and 2% were delayed 48–72 hours. Relative to discharge within 6 hours, risk-adjusted mortality was lower, with a discharge delay of 24–48 hours (adjusted odds ratio, 0.94; 95% confidence interval, 0.90–0.99), and reached its lowest estimated value at 48–72 hours of delay (adjusted odds ratio, 0.87; 95% confidence interval, 0.79–0.94). However, mortality was not significantly lower than the reference group when discharge