first-line treatment and the presence of diabetes, cancer, or treatment with an oral corticosteroid or another immunosuppressant drug. To the contrary, initiation of systemic antifungal therapy as first-line treatment was associated with a lower age and a lower Charlson comorbidity index (results not shown), suggesting an association with a diagnosis of asthma rather than COPD.

We used prescription sequence symmetry analysis, which limits unmeasured confounding encountered in cohort- and case-control studies. This analysis is increasingly used as a signal detection method for adverse drug events because of ease of application and consistent risk estimates and temporal analyses across different data sets in different health systems (10).

The main limitation of our analysis is the lack of information on indications for drug use in the prescription registry we used. Systemic antifungal therapy could have been used by some patients for other infections (such as fungal vaginitis, as suggested by the sex distribution). However, when stratifying for type of antifungal treatment, we found similar sex distributions among systemic and topical antifungal drug initiators (72.3% females initiating systemic therapy and 66.3% initiating topical therapy).

In summary, we found an increase in prescriptions for systemic antifungal drugs after initiation of ICS therapy. Contrary to current guidelines, one in four patients received a prescription for a systemic antifungal formulation as first-line treatment, presumably for oral candidiasis. The risk increased with ICS inhaler type and higher ICS dose, as well among males and with older age. Larger ICS particle size might also be a risk factor, but additional research is desirable to confirm this observation.

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Validity of the Posttraumatic Stress Symptoms-14 Instrument in Acute Respiratory Failure Survivors

To the Editor:

We read with interest the recent publication by Sjoding and colleagues (1) describing how the power to detect a secondary endpoint (i.e., posttraumatic stress disorder [PTSD] symptoms)

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might guide selection of an instrument to assess that outcome within the context of a randomized controlled trial.

Clinicians and researchers agree that mental health outcomes, such as PTSD symptoms, should be included in studies evaluating survivors of critical illness (2). Given that “gold standard” clinician-administered, semistructured psychiatric interviews to diagnose PTSD symptoms are often not feasible for assessing a secondary outcome measure after a critical illness, most trials use validated patient-reported outcome instruments to assess symptoms of PTSD. However, there is a great deal of heterogeneity in the use of such instruments within critical care research (3), and attempting to more consistently use a single measure would help advance the field.

In their publication (1), the authors compared two PTSD instruments that rely on patient-reported symptoms: the Posttraumatic Stress Symptoms-14 (PTSS-14) and the Impact of Event Scale-Revised (IES-R), both of which have had their measurement properties evaluated in acute respiratory failure survivors.

Notably, only the IES-R was evaluated against a “gold standard” PTSD assessment (i.e., the Clinician-Administered PTSD Scale) in this patient population (4). In contrast, the PTSS-14 was evaluated against the Post-traumatic Stress Diagnostic Scale (PDS), which is another patient-reported outcome measure (5). Hence, the measurement properties of the PTSS-14 have not been as rigorously evaluated as the IES-R, and thus the internal validity of the PTSS-14 in acute respiratory failure survivors remains uncertain. Moreover, although the PTSS-14 was administered at three points (4–14 days, 2 months, and 3 months post-ICU discharge) in the validation study, the PDS was administered only at 3 months post-ICU discharge (5). Despite this, the area under the receiver operating characteristics curve for the PTSS-14 was calculated for all three points, with the authors recommending a PTSS-14 threshold of 45 based on the highest area under the receiver operating characteristics curve from the 2-month assessment (5).

This recommendation may be problematic, given that the PTSS-14 and PDS were not administered at the same point. Notably, Sjoding and colleagues only used the sensitivity/specificity (86%/97%) of the PTSS-14 (vs. PDS) at the 2-month assessment. However, at the 3-month assessment, which is when the PDS and PTSS-14 were both administered in the validation study, the PTSS-14 sensitivity/specificity (100%/84%) were very similar to those of the IES-R at the recommended threshold of 1.6 (100%/85%). Had Sjoding and colleagues used the 3-month sensitivity/specificity estimates for the PTSS-14, their results and conclusions would have changed, given very little difference in the measurement properties of the PTSS-14 versus IES-R.

Several other aspects of the PTSS-14 and its validation study are noteworthy, given a goal of measuring PTSD symptoms. First, the validation study was conducted in the United Kingdom and did not include any patients from ethnic minorities (5), potentially limiting its external validity. In addition, of the 14 questions included in the PTSS-14, only two (14%) focus on the mandatory *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, PTSD symptom criterion of intrusion/re-experiencing, whereas two (14%) focus on symptoms not relevant for PTSD (i.e., mood swings and muscle tension). Hence, there may be limitations in the ability of the PTSS-14 for measuring PTSD symptoms.

Finally, as opposed to the IES-R (which does prompt patients to respond to its questions specifically with respect to their ICU experience), the PTSS-14 does not anchor patient respondents to any specific traumatic event when answering each item,

which could give rise to PTSD symptoms being reported from a pre-ICU event, as recently highlighted in the critical care literature (6).

Hence, we believe that these issues regarding the PTSS-14, and its evaluation by Sjoding and colleagues, are valuable considerations when reviewing their recent publication.

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Reply

We thank Dr. Parker and colleagues for their comments regarding the validation study of the Posttraumatic Stress Symptoms-14 instrument we cited in our manuscript examining the power of

instruments to measure differences in clinical outcomes. We agree there are many issues to consider when choosing a specific instrument to measure an outcome for a clinical trial. Issues stressed in their letter included the importance of considering how rigorously the validation of the instrument was performed in similar populations.

Our manuscript examined how the power of two instruments can be compared for their ability to detect statistically significant differences in outcome rates between trial arms. Our results show that in general, specificity is more important than sensitivity for statistical power to detect a difference between the arms when the outcome has a low prevalence, a result potentially counterintuitive to clinicians.

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