Abstract
Measuring brain and cognitive variables in COVID-19 survivors is highly significant to public health because of the enormous number of recovered patients (many millions) and the high incidence of cognitive complaints among survivors (up to 50% report “brain fog”). In this project, we will recruit a group of COVID-19 survivors who were treated at UNMC and a comparison group of non-COVID-19 patients with similar symptoms for a study of cognitive deficits and brain structure/function. This will provide preliminary data describing cognitive and brain changes associated with COVID-19 as well as the relationship between cognitive, brain, and disease variables.

Introduction
The lasting health consequences of COVID-19 remain unknown — including for brain health and cognition. Early evidence suggests that:
1) SARS-CoV-2 can be found in brain tissue post mortem
2) Significant pathology is often evident in the brains of COVID-19 patients
3) Neuroimaging (including in vivo) can reveal pathology such as white matter abnormalities, ischemic infarcts, and cranial nerve changes
4) Neurological findings are frequently observed in COVID-19 patients
5) Subjective and objective cognitive changes have been observed in many COVID-19 survivors
These neurological effects of COVID-19 highlight brain and cognitive challenges related to recovery from the disease. Further, recovery time is highly variable.

Methods
Inclusion/Recruitment
We will be enrolling COVID-19 survivors with no prior cognitive complaints who were treated at UNMC for moderately severe COVID-19 (hospitalization, supplemental O₂, NOT intubated/ventilated).

We will use the opt-in registry managed by UNMC’s Health Record Data Access Core to identify two cohorts:
1) Patients treated for COVID-19 at our institution who experienced moderately severe disease
2) Patients treated at our institution for non-COVID-19 respiratory complaints

Expectations
We predict that cognitive and brain measures in COVID-19 survivors will differ from normative expectations for age, sex, etc., and further that cognitive and brain outcomes will be correlated with disease variables (time in hospital, time on supplemental O₂, symptom severity).

Measures to be Collected
Questionnaires:
- Questionnaire data assessing subjective cognitive complaints, subjective symptoms post-COVID-19, and factors related to mood

Cognitive Assessments:
Table 1. NIH Toolbox: constructs addressed, measures included, and time required.

<table>
<thead>
<tr>
<th>Construct</th>
<th>Measure</th>
<th>Test Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention &amp; Exec. Functions</td>
<td>Flanker Inhibitory Control and Attention</td>
<td>3 min.</td>
</tr>
<tr>
<td>Episodic Memory</td>
<td>Picture Sequence Memory</td>
<td>7 min.</td>
</tr>
<tr>
<td>Working Memory</td>
<td>List Sorting Working Memory</td>
<td>7 min.</td>
</tr>
<tr>
<td>Language</td>
<td>Picture Vocabulary</td>
<td>4 min.</td>
</tr>
<tr>
<td>Language</td>
<td>Oral Reading Recognition</td>
<td>3 min.</td>
</tr>
<tr>
<td>Executive Function</td>
<td>Dimensional Change Card Sort</td>
<td>4 min.</td>
</tr>
<tr>
<td>Processing Speed</td>
<td>Pattern Comparison Processing Speed</td>
<td>3 min.</td>
</tr>
<tr>
<td>Total</td>
<td>—</td>
<td>31 min.</td>
</tr>
</tbody>
</table>

Brain Variables:
Manual:
- Derived from clinical over-read of brain data and assigned a score from 0-3
- Include WM abnormalities, ischemic infarcts, and involvement of cranial nerves

Automated:
- HCP’s automated processing pipeline will give us regional brain volume, cortical thickness, WM abnormalities, perfusion, and functional brain network status

Disease Variables:
- Information will be extracted from the participant’s EMR with her/his consent
- Variables include: duration of hospitalization, time on supplemental O₂, duration of fever >100.3°F, degree of lung involvement on CT imaging, and development/duration of delirium

Conclusion
By assessing brain structure/function, cognitive abilities, and disease variables in a cohort of patients treated at UNMC, this study will make a novel contribution to the literature of COVID-19 by providing an unprecedented opportunity to test associations between brain, cognitive, and disease variables simultaneously.