COVID-19 Post-acute Care
Major Organ Damage: A Living Rapid Review

Prepared for:
Department of Veterans Affairs
Veterans Health Administration
Health Services Research & Development Service
Washington, DC 20420

Prepared by:
Evidence Synthesis Program (ESP) Center
Minneapolis VA Health Care System
Minneapolis, MN
Timothy J. Wilt, MD, MPH, Director
Wei Duan-Porter, MD, PhD, Associate Director

Authors:
Nancy Greer, PhD
Bradley Bart, MD
Charles Billington, MD
Susan J. Diem, MD, MPH
Kristine E. Ensrud, MD, MPH
Anjum Kaka, MD
Mark Klein, MD
Anne Melzer, MD, MS
Scott Reule, MD
Aasma Shaukat, MD, MPH
Kerry Sheets, MD
Jamie Starks, MD
Orly Vardeny, PharmD, MS
Lauren McKenzie, MPH
Benjamin Stroebel, MPH
Wei Duan-Porter, MD, PhD
Timothy J. Wilt, MD, MPH

WHAT’S NEW
Updated June 7, 2021
Search current as of January 12, 2021
Next update expected September 2021
Prevalence estimates have been updated to include 51 new studies. Conclusions are largely unchanged due to limitations of the available evidence, notably poorly described study populations, lack of patient-centered clinical outcomes, and few control groups or pre-COVID-19 data.
PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program comprises three ESP Centers across the US and a Coordinating Center located in Portland, Oregon. Center Directors are VA clinicians and recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Center Program. The Coordinating Center was created to manage program operations, ensure methodological consistency and quality of products, and interface with stakeholders. To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee composed of health system leadership and researchers. The program solicits nominations for review topics several times a year via the program website.

Comments on this report are welcome and can be sent to Nicole Floyd, Deputy Director, ESP Coordinating Center at Nicole.Floyd@va.gov.


This report is based on research conducted by the Evidence Synthesis Program (ESP) Center located at the Minneapolis VA Health Care System, Minneapolis, MN, funded by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.
# TABLE OF CONTENTS

Preface .............................................................................................................................................. i  
Background ..................................................................................................................................... 1  
Key Questions and Scope ............................................................................................................... 2  
Methods........................................................................................................................................... 3  
Results ............................................................................................................................................. 5  
  
  Key Findings ............................................................................................................................... 5  
  PRISMA Flow Diagram ............................................................................................................. 5  
  Overview of Included Studies ..................................................................................................... 7  
  Pulmonary Outcomes ................................................................................................................... 9  
    Key Findings ........................................................................................................................... 9  
    Overview of Studies ................................................................................................................ 9  
    Radiographic Fibrosis ............................................................................................................. 9  
    Other Computed Tomography Findings .............................................................................. 10  
    Other Imaging ....................................................................................................................... 11  
    Pulmonary Function .............................................................................................................. 12  
    Dyspnea ................................................................................................................................. 13  
    Other Pulmonary Outcomes ................................................................................................. 14  
  Cardiovascular Outcomes .......................................................................................................... 14  
    Key Findings .......................................................................................................................... 14  
    Overview of Studies .............................................................................................................. 14  
    Ejection Fraction ................................................................................................................... 14  
    Fibrosis and/or Inflammation by Cardiovascular Magnetic Resonance Imaging (cMRI) .... 14  
    Pericardial Effusion ............................................................................................................... 15  
    High Sensitivity Troponin T (hsTNT) .................................................................................. 15  
    Other Findings ...................................................................................................................... 16  
  Neurological Outcomes ............................................................................................................. 16  
    Key Findings .......................................................................................................................... 16  
    Overview of Studies .............................................................................................................. 16  
    Modified Rankin Scale ......................................................................................................... 16  
    NIH Stroke Scale ............................................................................................................... 18  
    Other Neurological Outcomes .............................................................................................. 18  
  Renal Outcomes ....................................................................................................................... 19  
    Key Findings .......................................................................................................................... 19  
    Overview of Studies .............................................................................................................. 19
Acute Kidney Disease (AKD) and Need for Renal Replacement Therapy (RRT) ...................................................... 19
Imaging Findings ......................................................................................................................................................... 20
Gastrointestinal Outcomes ..................................................................................................................................... 20
Hematologic Outcomes ......................................................................................................................................... 21
Key Findings ......................................................................................................................................................... 21
Overview of Studies ............................................................................................................................................. 21
Thromboembolism ................................................................................................................................................ 21
Bleeding Events .................................................................................................................................................... 22
Healthcare/Resource Utilization Outcomes ........................................................................................................ 23
Key Findings ......................................................................................................................................................... 23
Overview of Studies ............................................................................................................................................. 23
Discharge Disposition ........................................................................................................................................ 23
Hospital Readmission ........................................................................................................................................ 26
Post-discharge Treatment ................................................................................................................................. 28
Discussion .......................................................................................................................................................... 30
Key Findings ......................................................................................................................................................... 30
Limitations .......................................................................................................................................................... 31
Future Research ................................................................................................................................................ 32
Ongoing Data Collection ..................................................................................................................................... 33
Conclusions ........................................................................................................................................................ 34
Acknowledgments ............................................................................................................................................... 35
References .......................................................................................................................................................... 36

FIGURES
Figure 1. Analytic Framework ............................................................................................................................. 2
Figure 2. PRISMA Flow Diagram ....................................................................................................................... 6
Figure 3. Radiographic Pulmonary Fibrosis ....................................................................................................... 10
Figure 4. Modified Rankin Scale (mRS) ≤2 (“Good Outcome”) at Discharge .................................................. 17
Figure 5. Discharge Other Than Home ............................................................................................................. 24
Figure 6. Readmission Rate ............................................................................................................................... 27

TABLES
Table 1. Study Eligibility Criteria .................................................................................................................... 4
Table 2. Overview of Included Studies ............................................................................................................ 8
Table 3. Radiographic Pulmonary Fibrosis ........................................................................................................ 10
Table 4. Chest CT Findings .............................................................................................................................. 11
Table 5. Pulmonary Function Test Findings
Table 6. Modified Rankin Scale (mRS) at Discharge – ‘Good’ Prognosis
Table 7. Need for Renal Replacement Therapy
Table 8. Post-discharge Thromboembolism
Table 9. DischargeDisposition
Table 10. Hospital Readmission

Appendix A. Search Strategies
Appendix B. Peer Reviewer Comments and Responses
Appendix C. Evidence Tables
  Table 1. Study Characteristics
  Table 2. Study Quality Appraisal
  Table 3. Pulmonary Outcomes
  Table 4. Cardiovascular Outcomes
  Table 5. Neurological Outcomes
  Table 6. Renal Outcomes
  Table 7. Gastrointestinal Outcomes
  Table 8. Hematologic Outcomes
  Table 9. Healthcare/Resource Utilization Outcomes
Appendix D. PRISMA Checklist
BACKGROUND

Coronavirus disease-2019 (COVID-19) is a viral illness that, as of June 7, 2021, was identified in over 173 million individuals (over 33 million in the US) in over 220 countries, areas, or territories (https://www.who.int/emergencies/diseases/novel-coronavirus-2019, https://coronavirus.jhu.edu/, https://covid.cdc.gov/covid-data-tracker/#cases_casesper100klast7days). Over 3.7 million deaths worldwide (over 597,000 in the US) are attributed to COVID-19. Within the VA, as of June 7, 2021, 12,253 deaths and 262,805 convalescent cases have been reported based on publicly available data (https://www.accesstocare.va.gov/Healthcare/COVID19NationalSummary), though these figures likely underestimate the number of Veterans receiving VA healthcare infected with and dying from COVID-19. COVID-19 is caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) and was declared a pandemic by the World Health Organization on March 11, 2020. In addition to the potential for severe pulmonary disease, there have been numerous reports of other major organ system manifestations and complications in patients hospitalized with COVID-19 including cardiovascular, renal, neurological, hematologic, endocrine, and gastrointestinal.

Persistent symptoms have been reported in patients following recovery from acute COVID-19, with fatigue, shortness of breath, muscle or body pain, and difficulty concentrating being most common. Multi-organ damage and long-term clinical outcomes following other coronavirus outbreaks – severe acute respiratory syndrome (SARS) and Middle East Respiratory syndrome (MERS) – have been reported, suggesting the potential for similar multi-organ damage and adverse long-term clinical outcomes with COVID-19 infections. In addition, because many COVID-19 patients are admitted to intensive care units, outcomes similar to those observed in post-intensive care syndrome or post-sepsis syndrome have also been suggested as possible long-term consequences of COVID-19 infections.

The purpose of this living rapid review is to determine the prevalence of post-acute care major organ damage and healthcare or service use needs associated with major organ damage in adults who were hospitalized with or for COVID-19. Our review is limited to post-hospital major organ damage or healthcare/service use needs – a subset of post-acute sequelae of SARS-CoV-2 infection (PASC) as described by the National Institutes of Health. The topic was nominated by the VA Evidence Synthesis Program Coordinating Center in collaboration with VHA clinical and operations partners in order to guide future clinical care decisions and resource needs related to COVID-19. It is 1 in a series of 3 living rapid reviews conducted across VA ESP sites addressing post-acute care prevalence related to: 1) mental health, 2) rehabilitation/functional status, and 3) major organ damage in patients hospitalized with or for COVID-19. Our analytic framework is shown in Figure 1.
KEY QUESTIONS AND SCOPE

Key Question 1: What is the post-acute care prevalence of major organ damage among adults hospitalized with or for proven COVID-19 disease?

Key Question 2: Does the post-acute care prevalence of major organ damage among adults with or for COVID-19 disease vary by patient characteristics (eg, age, sex, race/ethnicity, preexisting co-morbidities/frailty, place of residence), COVID-19 disease severity, or other factors (eg, treatment for COVID-19)?

Key Question 3: What are the short- (< 3 months) and long-term (≥ 3 months) healthcare or service use needs of adults surviving COVID-19 disease with major organ damage?

In consultation with VA Central Office operational partners, we included studies of adults hospitalized for COVID-19 and studies of adults hospitalized for another indication who have a positive COVID-19 test. Additionally, in collaboration with our local clinical content experts we prioritized conditions likely of greatest clinical relevance and included criteria for determining definitions and measures of symptomatic versus asymptomatic as well as acute versus chronic major organ damage. All patients had laboratory-confirmed COVID-19. We defined post-acute to include major organ damage or healthcare/service use needs reported on the day of hospital discharge or any time post-discharge. We included studies reporting “surrogate measures” (eg, a radiologic or laboratory measure consistent with a definition of a disease such as pulmonary...
function tests, radiographic pulmonary abnormalities, laboratory liver function tests or imaging studies, creatinine, glucose or hemoglobin A1c values, cardiac imaging defined as abnormal, or imaging studies for venous thromboembolism). We excluded studies reporting only mean or median values for these tests, as mean or median values do not provide a reliable measure of organ damage prevalence or healthcare/service use. We also excluded studies reporting only general symptoms (eg, fatigue, pain), and did not extract these data from included studies, because symptoms are not specific to a disease or organ damage. We included studies reporting on dyspnea as we determined dyspnea to be most consistent with pulmonary or cardiac damage. As noted above, post-acute mental health and functional status are addressed in separate ESP reviews. We excluded studies of children and studies of adults who had COVID-19 but were not hospitalized. We also excluded studies that did not provide information at the time of or after hospital discharge even if they included patient information during hospitalization.

METHODS

Our protocol was registered in PROSPERO: CRD42020204788.

SEARCH STRATEGY

We searched MEDLINE, Embase, and the Cochrane Library. Our initial report (December 2020) included studies identified in a search from January 1, 2019 to October 6, 2020. The updated report (June 2021) includes studies identified in a search through January 12, 2021. The search strategy (Appendix A) was developed with input from expert medical librarians. We also reviewed non-peer-reviewed public postings about post-COVID-19 complications for links to peer-reviewed data reports.

SCREENING PROCESS

Consistent with established rapid review methods, abstracts were reviewed by 1 investigator. A subset of 200 abstracts underwent dual independent review with substantial agreement between the 2 investigators. All articles identified as potentially eligible based on abstract review were independently reviewed by 2 investigators at the full-text level. Reasons for exclusion were noted. Conflicts were resolved by discussion. Our inclusion and exclusion criteria are reported in Table 1. We did not require studies to include a comparison group nor did we require that studies provide information about “preCOVID-19” health status/conditions or the primary reason for hospitalization (ie, due to COVID-19 compared to for other conditions where COVID-19 may be a contributing factor or identified incidentally on screening).

DATA ABSTRACTION

Study characteristics (location, design, funding), study inclusion and exclusion criteria, baseline demographic data (age, sex, race, comorbidities), hospitalization characteristics (COVID-19 severity, ICU admission, mechanical ventilation, length of hospital stay), length of time post-hospital, and outcomes data were abstracted by 1 investigator and verified by a second. Discrepancies were resolved by discussion.
**RISK OF BIAS ASSESSMENT**

We did not formally rate risk of bias of individual studies. We assessed study quality characteristics using the Joanna Briggs Critical Appraisal Tool for case series taking into account clarity of inclusion criteria and completeness of inclusion, use of standard methods for identification and assessment of the condition, and inclusion of adequate information about the subjects and setting.

**SYNTHESIS**

Due to heterogeneity in study populations, study designs, and methods of outcome assessment, we were unable to pool outcomes data. We narratively synthesized the evidence.

**Table 1. Study Eligibility Criteria**

<table>
<thead>
<tr>
<th>Study Characteristic</th>
<th>Include</th>
<th>Exclude</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Adults (age 18 and older)</td>
<td>Children or adolescents, age &lt;18; MERS; SARS</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Discharge (or ready for discharge) from hospitalization after admission with or for proven COVID-19</td>
<td>Data only collected from patients during ongoing hospital acute-care admission with or for proven COVID-19</td>
</tr>
<tr>
<td><strong>Comparator</strong></td>
<td>Discharge from hospitalization for individuals without COVID-19 (ideally another respiratory condition); a comparator was not required</td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Prevalence and severity of major organ damage (respiratory, renal, cardiovascular, hematologic, neurologic, metabolic/endocrine, gastrointestinal, and rheumatologic/musculoskeletal); healthcare or service use needs related to major organ damage*</td>
<td>No outcomes of interest</td>
</tr>
<tr>
<td><strong>Timing</strong></td>
<td>Short-term (&lt; 3 months) and long-term (≥ 3 months) post-discharge</td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>Any post-discharge setting (eg, home, rehabilitation or long-term care facility); may include re-hospitalization</td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Study Designs</strong></td>
<td>Cohort, case series, other observational; may prioritize articles using a best-evidence approach</td>
<td>Case report, narrative review, descriptive/opinion article with no data</td>
</tr>
</tbody>
</table>

*In the original report, we included studies reporting “re-positive” RT-PCR test results following discharge. For the May 2021 update, we excluded studies only reporting “re-positive” test results and removed those studies from the original set of included studies. As more information about the natural history of SARS-CoV-2 has become available, it has been recognized that virus levels fluctuate and are not informative for post-acute COVID-19.
LIVING REVIEW

We plan to update our review approximately every 3 months through December 2021, using the literature search strategy outlined above to identify evidence related to post-acute major organ damage and associated healthcare/service use needs. Study eligibility criteria, procedures for data abstraction, and risk of bias assessment will remain the same. Our data synthesis plan may change if future evidence allows. New evidence that does not substantially change review conclusions will be summarized. New evidence that changes review conclusions or certainty of evidence will be incorporated into a major update.

PEER REVIEW

A draft version of each update of this report will undergo peer review by content experts and clinical leadership. Reviewer comments and our responses will be presented in Appendix B and the final report will incorporate the comments.

RESULTS

KEY FINDINGS

Key Question 1: Post-hospital data provides wide-ranging prevalence estimates based mainly on physiologic outcomes for pulmonary, neurologic, cardiac, renal, and hematologic conditions from convenience samples without controls; most not conducted in US and none in the VA.

Key Question 2: Information is insufficient to assess if prevalence varies by patient, disease, and comorbidity factors.

Key Question 3: Post-hospitalization resource use including discharge disposition and readmission varies by outcome definition and timing. Results are limited by use of convenience samples and lack of controls.

PRISMA FLOW DIAGRAM

The results of our literature search and study selection process are depicted in Figure 2.
Figure 2. PRISMA Flow Diagram

**Identification**
- MEDLINE: k=4173
- Embase: k=8218
- Cochrane: k=111

**Screening**
- Total identified records: k=12502
  - Duplicates removed: k=3057

**Eligibility**
- Records screened after duplicates removed: k=9445
  - Hand search: k=17
  - Records excluded: k=8840

**Included**
- Full-text studies assessed for eligibility: k=622
  - Full text studies excluded: k=532
    - No study population of interest (k=62)
    - No post acute care data (k=257)
    - No major organ condition of interest (k=33)
    - No outcomes of interest (k=160)
    - No study design of interest (k=17)
    - Non-English publication (k=3)

- Included references: k=90
  - Pulmonary: k=27
  - Cardiac: k=9
  - Neurologic: k=15
  - Renal: k=11
  - Musculo-skeletal and Endocrine: k=0
  - Gastro-Intestinal: k=2
  - Hematologic: k=11
  - Resource Use: k=44

*Studies may have reported more than one category of outcomes*
OVERVIEW OF INCLUDED STUDIES

Our December 2020 report included 42 studies. After removing 3 of those studies only reporting “re-positive” results (see Table 1 footnote) and adding 51 studies identified in the literature search through January 2021, we include 90 studies reporting outcomes data (Table 2) at the time of hospital discharge (k=36), post-discharge (24 studies at 30 days or fewer follow-up) (k=46), or both (k=7). One study did not report time post-hospitalization. Twenty-seven studies reported pulmonary outcomes, 15 reported neurological outcomes, 9 studies reported cardiovascular outcomes, 11 reported renal outcomes, 11 reported hematologic outcomes, 2 reported gastrointestinal outcomes, and 44 reported healthcare or resource utilization outcomes. We found no studies reporting musculoskeletal or endocrine outcomes. Studies were typically described as retrospective, case series, or cross-sectional, although 20 reported that data were collected prospectively. Study inclusion and exclusion criteria, patient demographics, and hospitalization characteristics are reported in Appendix C, Table 1.

Study quality assessments are reported in Appendix C, Table 2. In 42% (38/90) of the studies, it was unclear whether all patients were assessed for eligibility or whether consecutive patients were enrolled. Fifty-three percent (48/90) were conducted at a single site. In 43% (39/90), fewer than 100 patients were enrolled. Training and experience of individuals abstracting data from medical records, administering tests, or interpreting imaging results was rarely reported. Although many studies obtained data from electronic medical records, it was often unclear what data were abstracted (e.g., ICD codes). Many studies did not report COVID-19 severity; among those that did, different criteria were used. Pre-existing comorbidities and COVID-19 severity were rarely linked to outcomes.
Table 2. Overview of Included Studies

<table>
<thead>
<tr>
<th>Outcomes Frequently Reported</th>
<th>Pulmonary</th>
<th>Cardiac</th>
<th>Neurologic</th>
<th>Renal</th>
<th>Musculo-skeletal/Endocrine</th>
<th>Gastro-intestinal</th>
<th>Hematologic</th>
<th>Resource Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrosis CT Abnormalities</td>
<td>27</td>
<td>9</td>
<td>15</td>
<td>11</td>
<td>0</td>
<td>2</td>
<td>11</td>
<td>44</td>
</tr>
<tr>
<td>Pulmonary Function Dyspnea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impaired or Reduced EF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evidence of Fibrosis and/or Inflammation (by cMRI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pericardial Effusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated hsTNT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Modified Rankin Scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Need for RRT AKD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal Liver Imaging</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thromboembolism Bleeding Events</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Readmission Discharge Other than Home</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AKD=acute kidney disease; cMRI=cardiovascular magnetic resonance imaging; EF=ejection fraction; hsTNT=high-sensitivity Troponin T; RRT=renal replacement therapy

*Studies may have reported more than one category of outcomes
PULMONARY OUTCOMES

Key Findings

Main reported pulmonary outcomes were radiographically defined fibrosis at varying time intervals (k=5) with estimates ranging from 7% to 61% of enrolled patients, lung CT abnormalities in 0% to 88% (k=8), abnormal diffusing capacity of the lung for carbon monoxide (DLCO) in 21% to 84% (k=7), and dyspnea in 2% to 22% (k=9).

Interpretation of the findings is limited by varying degrees of COVID-19 severity and different outcome definitions, assessment methods, and follow-up lengths.

Overview of Studies

Of the 27 studies reporting pulmonary outcomes (Appendix C, Tables 1 and 3), 12 were from China,35,46,56,64,72,74,75,86,89,101,102,108 8 were from Europe,28,30,31,61,62,82,83,97 2 were from the UK,58,110 3 were from the Middle East,24,76,95 and 1 each was from the US92 and Canada.96 Sample sizes ranged from 18 to 1733 with only 1 study enrolling over 1000 individuals and 15 studies enrolling 100 or fewer individuals. Mean or median ages ranged from 37 to 73 years and the percentage of males enrolled ranged from 38% to 84%. Only 2 studies reported race. A history of chronic obstructive pulmonary disease (COPD) was reported in 0% to 19% of participants (14 studies) and a history of smoking in 3% to 28% (10 studies). Thirteen studies reported the percentage of study participants with severe or critical COVID-19. Two studies enrolled only patients with severe COVID-19.24,76 Of the remaining 11 studies, 53% or fewer were classified as severe. Two studies excluded patients who received mechanical ventilation.35,82 None of the studies included a comparison to non-COVID-19 patients. Reported outcomes varied across the studies with most reporting surrogate measures of health outcomes.

Radiographic Fibrosis

Five studies reported the percentage of patients with pulmonary fibrosis (Figure 3, Table 3). One study defined fibrosis on CT chest imaging as a combination of findings including parenchymal bands, irregular interfaces, coarse reticular pattern, and traction bronchiectasis.75 Another used an artificial intelligence program to identify fibrosis volume.46 The other 3 studies did not report how fibrosis was diagnosed. One of the studies also reported 61% (11/18) with ground-glass opacity plus pulmonary fibrosis.74
Figure 3. Radiographic Pulmonary Fibrosis

Table 3. Radiographic Pulmonary Fibrosis

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>COVID-19 Severitya</th>
<th>Time of Assessment</th>
<th>Definition/Assessment</th>
<th>Pulmonary Fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hu, 202046 China</td>
<td>17% severe</td>
<td>Discharge</td>
<td>Artificial intelligence to calculate fibrosis volume or % of fibrosis in entire lung</td>
<td>61% (46/76)</td>
</tr>
<tr>
<td>Yu, 202075 China</td>
<td>ICU admission: 16%</td>
<td>9 days post-discharge</td>
<td>Fibrosis: combination of parenchymal bands, irregular interfaces, course reticular pattern, and traction bronchiectasis</td>
<td>44% (14/32)</td>
</tr>
<tr>
<td>Zhang, 2020101 China</td>
<td>17% severe</td>
<td>14 days post-discharge</td>
<td>NR</td>
<td>31% (35/112)</td>
</tr>
<tr>
<td>Huang Y, 202064 China</td>
<td>30% severe</td>
<td>30 days post-discharge</td>
<td>NR</td>
<td>7% (4/57)</td>
</tr>
<tr>
<td>You, 202074 China</td>
<td>34% severe/critical</td>
<td>38 days post-discharge</td>
<td>NR</td>
<td>22% (4/18)</td>
</tr>
</tbody>
</table>

aSeverity (%) as defined by study authors; if severity not reported, maximum oxygen requirements or ICU admission used as markers of severity

Other Computed Tomography Findings

Several studies reported findings from computed tomography (CT) (Table 4).
Table 4. Chest CT Findings

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>COVID-19 Severity(^a)</th>
<th>Time of Assessment</th>
<th>Findings</th>
</tr>
</thead>
</table>
| Xia, 2020\(^66\) China | Mild or moderate | Discharge | Residual infiltrates without fibrosis: 82% (233/282)  
Residual infiltrates and consolidation fibrosis: 14% (39/282) |
| Liu, 2020\(^70\) China | Mild or moderate | Discharge  
14 days  
28 days | Consolidations  
D/C: 49% (25/51)  
14 d: 8% (4/51)  
28 d: 2% (1/51) |
| Wang, 2020\(^72\) China | 53% severe | 7-14 days  
21-28 days | Chest CT Deterioration\(^c\)  
7-14 d: 6% (2/36)  
21-28d: 0% (0/54) |
| Zhang, 2020\(^101\) China | 83% non-severe | 14 days | Normal CT  
40% (45/112) |
| Huang Y, 2020\(^64\) China | 30% severe | 30 days | Residual Abnormality  
54% (31/57)  
Severe: 94% (16/17)  
Non-severe: 38% (15/40) |
| Sonnweber, 2020\(^87\) Austria | ICU admission: 22% | 60 days  
100 days | Pathological CT  
60 d: 77% (112/145)  
100 d: 63% (84/133) |
| Shah, 2020\(^96\) Canada | 22% requiring mechanical ventilation | 84 days | Abnormal  
88% (53/60) |
| Huang C, 2021\(^86\) China | ICU admission: 4% | 153 days (median) | At least 1 Abnormal CT Pattern\(^b\)  
Scale 3: 52% (49/93)  
Scale 4: 54% (87/161)  
Scale 5-6: 54% (50/92) |
| Huang Y, 2020\(^64\) China | 30% severe | 30 days | Residual Abnormality  
54% (31/57)  
Severe: 94% (16/17)  
Non-severe: 38% (15/40) |

**Abbreviations:** CT=computed tomography; GGO=ground glass opacity  
\(^a\)Severity (%) as defined by study authors; if severity not reported, maximum oxygen requirements or ICU admission used as markers of severity  
\(^b\)Scale 3=no supplemental oxygen; Scale 4=requiring supplemental oxygen; Scale 5-6=requiring high flow nasal cannula, non-invasive ventilation, or invasive mechanical ventilation  
\(^c\)Outcomes did not differ by COVID-19 severity  

**Other Imaging**

One study reported “lung abnormalities” (worsening or appearance of X-ray pulmonary infiltrates) in 85% (6/7) at the time of hospital discharge.\(^31\) Patients in this study were all receiving maintenance hemodialysis at the time of hospitalization.

Another study measured lung impairment with MRI at a median of 105 days after a positive COVID-19 result.\(^58\) Deep breathing fractional area change of <31% was observed in 12% (4/34) evaluated.

Pleural effusions were detected using point-of-care ultrasound in 2% (1/64).\(^24\) At ICU admission, pleural effusions had been observed in 22.4% (20/89). A second study reported pleural effusions
in 19% (24/127) at 2 months and 12% (15/127) at 4 months post-discharge. Both studies enrolled patients admitted to the ICU, most of whom required invasive mechanical ventilation.

**Pulmonary Function**

Pulmonary function tests were reported by 10 studies (Table 5). Four studies provided more detail on the abnormal findings. One study reported a restrictive pattern in 8% (4/50 enrolled patients), restriction with altered diffusion capacity in 18% (9/50), and altered diffusion capacity only in 26% (13/50). The study by Huang further described the observed pulmonary dysfunction as obstructive in 11% (6/57), restrictive in 12% (7/57), and combined obstructive and restrictive in 4% (2/57). Ramani et al reported obstruction in 15% (4/26), restriction in 19% (5/26), and mixed obstruction and restriction in 4% (1/26). The fourth study reported 17% (3/18) with obstructive and 17% (3/18) with restrictive ventilatory impairment.

**Table 5. Pulmonary Function Test Findings**

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>Time of Assessment</th>
<th>COVID-19 Severitya</th>
<th>FEV1 &lt;80% Predicted</th>
<th>FVC &lt;80% Predicted</th>
<th>Abnormal DLCO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frija-Masson, 202061 France</td>
<td>30 days after symptom onset</td>
<td>50% severe</td>
<td>Abnormal lung function: 52% (26/50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Huang C, 202186 China</td>
<td>153 days post-discharge (median)</td>
<td>ICU admission: 4%</td>
<td>Scale 3: 8% (7/89)a Scale 4: 2% (4/172) Scale 5-6: 13% (11/88)</td>
<td>Scale 3: 3% (3/89)a Scale 4: 1% (1/172) Scale 5-6: 11% (10/88)</td>
<td>Scale 3: 22% (18/83)a Scale 4: 29% (48/165) Scale 5-6: 56% (48/88)</td>
</tr>
<tr>
<td>Huang Y, 202064 China</td>
<td>30 days post-discharge</td>
<td>30% severe</td>
<td>9% (5/57)c 11% (6/57)c</td>
<td>53% (30/57) Severe: 77% (13/17) Non-severe: 43% (17/40) P=.02</td>
<td></td>
</tr>
<tr>
<td>Lv, 202089 China</td>
<td>14 days post-discharge</td>
<td>20% severe</td>
<td>24% (33/137) Severe: 56% (15/27) Non-severe: 16% (18/110)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mo, 202035 China</td>
<td>Discharge</td>
<td>17% severe</td>
<td>14% (15/110)b 9% (10/110)b</td>
<td>47% (51/110) Mild: 30% (7/24) Pneumonia: 42% (28/67) Severe: 84% (16/19) P&lt;.01 Severe vs others</td>
<td></td>
</tr>
<tr>
<td>Ramani, 202192 US</td>
<td>40 days post-discharge (median)</td>
<td>86% requiring mechanical ventilation</td>
<td>Abnormal lung function: 39% (10/26)</td>
<td>Reduced diffusion capacity: 27% (7/26)</td>
<td></td>
</tr>
</tbody>
</table>
### Dyspnea

Measures of dyspnea were reported in 9 studies. Five used a modified Medical Research Council measure. Two assessed dyspnea within 30 days of discharge. One reported that all had functionally limiting dyspnea with 12% (4/32) having Grade 4 and 88% (28/32) having Grade 5 dyspnea at the time of admission to a rehabilitation unit.\(^{28}\) Grade 4 indicates a need to stop for breath after 100 meters or a few minutes on level ground while Grade 5 indicates too breathless to leave the house, or breathless after undressing (https://mrc.ukri.org/research/facilities-and-resources-for-researchers/mrc-scales/mrc-dyspnoea-scale-mrc-breathlessness-scale/). In contrast, another reported that 25% (31/126) were experiencing mild dyspnea while 3% (4/126) had moderate, 2.4% (3/126) had severe, and 1.5% (2/126) had very severe dyspnea at a median of 22 days post-discharge.\(^{83}\)

Three other studies reported longer follow-up times and generally noted that functionally limiting dyspnea was common. One study reported that 2% (3/145) experienced severe dyspnea (mMRC 3-4) at 60 days post-discharge and 4% (5/133) at 100 days post-discharge.\(^{97}\) Another reported 29% (35/120) were at Grade 2 or higher at a mean of 111 days post-discharge. Grade 2 is described as “walks slower than people of the same age because of dyspnea or has to stop for breath when walking at own pace”.\(^{62}\) The third reported the percentage of patients with mMRC scores greater than or equal to 1 assessed at a median of 153 days post-discharge.\(^{86}\) A score of 1 indicates an individual is “not troubled by breathless except on strenuous exercise.” Overall, a score of 1 or greater was reported by 26% (419/1615), including 24% (102/425) of patients not requiring supplemental oxygen, 26% (277/1079) of patients requiring supplemental oxygen, and 36% (40/111) of patients requiring either high flow nasal cannula, non-invasive ventilation, or invasive mechanical ventilation.

An additional study used the Borg scale and assessed dyspnea following the 6-minute walk test.\(^{30}\) Values were generally less than 3 (ie, “moderate” dyspnea) on a 10-point scale. This study also reported the presence of exercise-induced hypoxia (defined as SpO₂ <90%) in 50% (13/26).
Six of the patients underwent further testing and pulmonary embolism was confirmed in 67% (4/6).\textsuperscript{30}

The remaining 3 studies did not specify how dyspnea was assessed.\textsuperscript{82,95,96} At 1 to 12 weeks follow-up, dyspnea was reported for 15% to 33% of patients.

**Other Pulmonary Outcomes**

A study of patients admitted to a rehabilitation unit following hospitalization (with ICU admission) for COVID-19 reported that 41% (13/32) required oxygen via nasal cannula, 13% (4/32) required an oxygen mask, and 25% (8/32) required a Venturi mask at admission.\textsuperscript{28} A study of patients referred for clinical signs of dysphagia during hospitalization for COVID-19 reported no new cases of aspiration pneumonia.\textsuperscript{110} Length of follow-up was not reported.

**CARDIOVASCULAR OUTCOMES**

**Key Findings**

Pericardial effusions, myocardial inflammation/fibrosis, and possibly mild reductions in ejection fraction were identified following COVID-19 hospitalization. Pericardial effusion was reported in 0% to 20% (k=5). Impairment in left ventricular ejection fraction (LVEF) was noted in 3% to 11% (k=3).

**Overview of Studies**

Cardiovascular outcomes were reported in 9 studies (Appendix C, Tables 1 and 4) – 4 from Europe,\textsuperscript{67,82,83,97} 2 from China,\textsuperscript{63,100} 2 from the Middle East,\textsuperscript{24,76} and 1 from the UK.\textsuperscript{58} Sample sizes range from 26 to 538, mean or median ages ranged from 38 to 64 years, and the percentage of males enrolled ranged from 38% to 84%. The study from the UK reported race, with 76% White. A history of CVD or CAD was reported in 0% to 40% (8 studies) with a history of hypertension in 5% to 59% (8 studies). Severity of COVID-19 was reported in 4 studies, with 2 enrolling only patients with severe or critical COVID-19. In the remaining 2 studies, 15% and 39% had severe or critical COVID-19. Three studies included comparison groups.\textsuperscript{63,67,100}

**Ejection Fraction**

Daher et al used echocardiography to assess left ventricular ejection fraction (LVEF) on admission and at 6 weeks follow-up.\textsuperscript{82} Findings were normal for 94% (17/18) with echocardiography on admission and 88% (29/33) at 6 weeks. Another study using echocardiography reported LVEF <53% for 3% (4/145) at both 60 days and 100 days post-discharge.\textsuperscript{97} A study from the United Kingdom reported LVEF, assessed with cMRI, for 37 previously hospitalized patients at a median of 105 days after COVID-19 diagnosis.\textsuperscript{58} Impairment (≤51%) was noted in 11% (4/37). Evidence of myocarditis was noted in 22% (8/37).

**Fibrosis and/or Inflammation by Cardiovascular Magnetic Resonance Imaging (cMRI)**

Two studies used cMRI to assess myocardial injury. In a study from Germany, 100 patients were assessed at a median of 71 days following diagnosis.\textsuperscript{67} Thirty-three had been hospitalized. The mean age of the patients was 49 years and 53% were male. Among the hospitalized patients, 2
underwent mechanical ventilation and 17 underwent non-invasive ventilation. The study also reported imaging findings for 50 healthy controls and 57 risk factor-matched controls. Late gadolinium enhancement (LGE), reflecting scarring, was observed in 32% (32/100) (myocardial) and 22% (22/100) (pericardial) of the COVID-19 group. Myocardial LGE was significantly more prevalent (P<.05) in the COVID-19 patients than in the healthy controls (0%) or the risk factor-matched controls (17% (9/57)). Pericardial LGE was significantly more prevalent (P<.05) in the COVID-19 patients than in the healthy controls (0%) but not compared with the risk factor-matched controls (14% (8/57)). Abnormal native T1 values were observed in 73% (73/100) of all COVID-19 patients, with significantly higher values (P=.008) in those who had required hospitalization, although the difference was characterized as small. Reporting of T1 and T2 abnormalities, which generally reflect myocardial inflammation, indicated that abnormal native T1 was reported in 12% (6/50) of the healthy controls and 58% (33/57) of the risk factor-matched controls (both P<.05 vs the COVID-19 group). Abnormal native T2 values were observed in 60% (60/100) of the COVID-19 group with no difference between hospitalized and non-hospitalized patients. Prevalences were 12% (6/50) and 26% (15/57) in the healthy controls and risk factor-matched groups, respectively (both P<.05 vs the COVID-19 group).

The second study, from China, evaluated 26 patients referred for CMR due to cardiac symptoms post-discharge.63 Patients with a history of coronary artery disease or myocarditis were excluded. COVID-19 was reported as severe for 15% (4/26) and moderate for 85% (22/26). The study reported data from healthy controls (similar age and gender with no cardiovascular disease or systemic inflammation) who underwent CMR at the same hospital. CMR for the COVID-19 patients was completed at a median of 47 days after the onset of cardiac symptoms. Myocardial edema was noted in 54% (14/26). Of the 14 with edema, 50% (7/14) had positive LGE and 50% (7/14) had a small pericardial effusion. A total of 8 patients (1 without myocardial edema) had positive LGE. Native T1, T2, and extracellular volume (ECV) were significantly elevated in the recovered COVID-19 patients with positive CMR findings compared with the healthy controls.

**Pericardial Effusion**

Five studies reported pericardial effusion. The study from Germany, described above, used CMR imaging and reported pericardial effusion (>10 mm) in 20% (20/100) of the COVID-19 patients, 0% of the healthy controls, and 7% (4/57) of the risk factor-matched controls.67 The difference between the COVID-19 group and the other groups was statistically significant (P<.05). Four studies used ultrasound to assess pericardial effusion. Two studies, both from Saudi Arabia, included only patients admitted to the ICU. One reported pericardial effusion at hospital discharge in 2% (1/64)24 while the second reported rates of 16% (20/127) at 2 months and 11% (14/127) at 4 months.76 The third study, from Austria, reported pericardial effusion at 60 days (6% [8/145]) and 100 days (1% [1/134]) in patients, the majority of whom did not require ICU admission.97 The fourth study, conducted in Germany, reported no pericardial effusion at 6 weeks in patients who did not require mechanical ventilation.82

**High Sensitivity Troponin T (hsTNT)**

The CMR study from Germany also reported blood test results.67 Detectable hsTNT (>3 pg/mL) was reported in 71% (71/100) of the COVID-19 group, with significantly elevated hsTNT (>13.9 pg/mL) in 5% (5/100). The mean hsTNT value was significantly lower (P=.002) in patients who recovered at home compared with those who were hospitalized; the difference was described as
small. The percentage of patients with detectable hsTNT was significantly higher (P<.05) in the COVID-19 group than the healthy controls (22% [11/50] or risk factor-matched controls (54% [31/57]).

Other Findings

Two studies reported outcomes related to hypertension. A study from Italy reported uncontrolled blood pressure requiring a change in medication in 21% (26/126) at a median of 22 days post-discharge. A study from China reported newly diagnosed hypertension in 1% (7/538) of the COVID-19 group and 0% (0/184) of a non-COVID-19 control group quarantined at home for greater than 3 months.

NEUROLOGICAL OUTCOMES

Key Findings

A “good” prognosis based on modified Rankin Scale scores at the time of discharge was reported in 17% to 60% of patients hospitalized for stroke and testing positive for COVID-19 (k=6). Cognitive impairment at 22 to 42 days post-discharge was observed in 18% to 57% (k=3).

Overview of Studies

Fifteen studies reported neurological outcomes (Appendix C, Tables 1 and 5). Five were conducted in Europe, 4 in the US, 3 in multiple nations, and 1 each in the Middle East, India, and the UK. Sample sizes ranged from 13 to 1409, mean or median ages ranged from 49 to 76 years, and between 39% and 88% were male. In 6 studies reporting race, 14% to 80% were White, 0% to 40% were Black, 6% to 57% were Hispanic, and 0% to 19% were Asian. Three studies reported on severity of COVID-19 with 8%, 25%, and 62% of enrollees with severe or critical COVID-19. Eight studies included a comparison group (either concurrent non-COVID-19 or pre-COVID-19 patients).

Modified Rankin Scale

Eight studies (7 in neurology patients) reported modified Rankin Scale (mRS) results at the time of hospital discharge (Figure 4, Table 6). Based on an mRS score of 0 to 2 being considered a good outcome – individuals are “able to look after their own affairs without assistance” – only 1 of the 7 studies of neurology patients reported that the majority had a good outcome at discharge.
Figure 4. Modified Rankin Scale (mRS) ≤2 (“Good Outcome”) at Discharge

Table 6. Modified Rankin Scale (mRS) at Discharge – ‘Good’ Prognosis

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>Population</th>
<th>COVID-19 Severitya</th>
<th>‘Good’ Prognosis at Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akhtar, 202140 Qatar</td>
<td>Hospitalized for stroke</td>
<td>31% requiring mechanical ventilation</td>
<td>28% (9/32) Concurrent Non-COVID group: 52% (112/216) Pre-COVID era group: 60% (348/585) P=.001</td>
</tr>
<tr>
<td>Al Kasab, 202023 Multi-national</td>
<td>Mechanical thrombectomy post-stroke; symptomatic patients tested for COVID-19</td>
<td>39% requiring mechanical ventilation</td>
<td>17% (2/12) Concurrent Non-COVID group: 30% (94/316) P=.52</td>
</tr>
<tr>
<td>Benussi, 202025 Italy</td>
<td>Admitted for acute cerebrovascular disease and tested positive for COVID-19</td>
<td>NR</td>
<td>26% (11/43) Non-COVID group: 71% (48/68) P&lt;.001</td>
</tr>
<tr>
<td>Grewal, 202032 US</td>
<td>COVID admission followed by stroke (n=6) or stroke admission followed by positive for COVID-19 (n=7)</td>
<td>62% severe/critical</td>
<td>23% (3/13) Concurrent Non-COVID group: 53% (28/53) P=.047</td>
</tr>
<tr>
<td>Liotta, 202034 US</td>
<td>With and without neurological manifestations during hospitalization with COVID-19</td>
<td>26% severe</td>
<td>71% (363/509) With neurological manifestations 71% (299/419) No neurological manifestation: 70% (63/90)</td>
</tr>
</tbody>
</table>
Another multi-nation study reported severe disability based on mRS scores in 51% (49 of 96 survivors). The median [IQR] scores for the COVID-19 group and a propensity-matched group were 4 [2-6] and 2 [1-4], respectively (P<.001).

**NIH Stroke Scale**

Two studies reported NIH Stroke Scale scores. Scores range from 0 (no symptoms) to 42 (severe symptoms) with scores between 1 and 4 indicating minor stroke symptoms and scores between 5 and 15 indicating moderate stroke symptoms. The study from Italy reported median [IQR] scores of 9.0 [1.0-19.0] in the COVID-19 group and 2.0 [0.0-6.8] in the non-COVID-19 group (P=.005). The study from the US reported median [IQR] scores of 11 [4-23] in the overall study group of 13 patients and 3 [2-13] in the non-COVID comparison group.

**Other Neurological Outcomes**

Several studies reported on cognitive function with most indicating some cognitive dysfunction in many individuals, though lack of pre-COVID cognitive status assessment or controls limits conclusions. Two studies used the Montreal Cognitive Assessment (MoCA) tool. A study from Italy reported cognitive impairment (MoCA <24) in 29% (36/126) at a median of 22 days post-discharge. A study from the US reported mild cognitive impairment (MoCA <26) in 57% (16/28) at a median of 40 days post-discharge. A study from Germany reported cognitive disorders in 18% (6/33) at 6 week follow-up but did not describe the measure used. A study of patients who were admitted to home health care following hospitalization for COVID-19 reported that 23% (297/1302) required prompting and 6% (76/1302) required assistance and direction at the time of admission. At discharge from home health care, the values were 10% (130/1302) and 3% (42/1302), respectively. This study also reported confusion in new and complex situations for 41% (536/1302) at admission and 19% (251/1302) at discharge.

A study from France reported attention disorder in 27% (32/120) and memory loss in 34% (41/120) when patients were assessed at a mean of 111 days post-discharge. No differences were reported for either measure when patients who were treated on the ward were compared to patients who required ICU admission.
RENAL OUTCOMES

Key Findings

Outcomes were typically assessed at the time of discharge, with acute kidney disease reported for 25% and 33% (k=2) and need for renal replacement therapy (RRT) in 4% to 31% of those who had required RRT during hospitalization (k=5).

Overview of Studies

Renal outcomes were reported by 11 studies (Appendix C, Tables 1 and 6): 6 from the US, 2 from the UK, and 1 each from Brazil, China, and Japan. Enrollments ranged from 37 to 3,993 with 6 including over 1000. Mean or median ages ranged from 50 to 71, with 38% to 73% male. Seven studies reported race with 11% to 76% White, 5% to 36% Black, and 4% to 43% Hispanic. A history of chronic kidney disease was reported in 2% to 67% (7 studies) and hypertension in 5% to 79% (10 studies). Only 2 reported COVID-19 severity with 32% and 100% severe. Three studies enrolled only patients admitted to an ICU.

Acute Kidney Disease (AKD) and Need for Renal Replacement Therapy (RRT)

Acute kidney disease (k=2) or need for renal replacement therapy (k=8) were commonly reported, though the lack of pre-COVID renal status or controls limits conclusions. A study from the US reported acute kidney disease (AKD) at discharge in 25% (291/832). Twenty-three percent were Stage 1, 6% Stage 2, and 6% Stage 3. AKD stages were defined according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria based on creatinine. At a median follow-up of 21 days, data were available for n=77 with AKD at discharge. Of those, 36% (29/77) had recovered, 33% (25/77) were Stage 1, 13% (10/77) were Stage 2, and 18% (14/77) were Stage 3. Data were also available for n=135 who had recovered kidney function at discharge. Of those, 86% (116/135) remained recovered, 10% (14/135) had new Stage 1 AKD, 2% (3/135) had new Stage 2 AKD, and 2% (3/135) had new Stage 3 AKD.

A second study from the US reported on 3,854 individuals who developed acute kidney injury while hospitalized for COVID-19. Among those who required RRT while hospitalized, 17% (108/638) survived. Of the survivors, 33% (36/108) had not recovered kidney function. Authors reported that 58% (19/33) had underlying chronic kidney disease at hospital admission. Among those who did not require RRT while hospitalized, 52% (1663/3216) survived and 26% (430/1663) of those had not recovered kidney function.

Several studies reported the need for RRT post-discharge (Table 7). Between 1% and 34% required RRT at the time of discharge (8 studies). Two of the studies reported post-discharge data with 7% and 18% continuing to require RRT.
### Table 7. Need for Renal Replacement Therapy

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>COVID-19 Severity*</th>
<th>Time of Assessment</th>
<th>Renal Replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doher, 2020</td>
<td>ICU admission: 100%</td>
<td>Discharge</td>
<td>11% (1/9)</td>
</tr>
<tr>
<td>Gupt, 2020</td>
<td>ICU admission: 100%</td>
<td>Discharge</td>
<td>34% (73/216 discharged; required RRT during hospitalization)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>18% (39/216 discharged; required RRT during hospitalization)</td>
</tr>
<tr>
<td>Hamilton, 2020</td>
<td>ICU admission: 16%</td>
<td>Discharge</td>
<td>6% (2/32 who required RRT during hospitalization)</td>
</tr>
<tr>
<td>Hittesdorf, 2020</td>
<td>100% severe</td>
<td>Discharge</td>
<td>4% (2/45 who required RRT during hospitalization)</td>
</tr>
<tr>
<td>Matsunaga 2020</td>
<td>32% severe</td>
<td>Discharge</td>
<td>1% (16/2,431)</td>
</tr>
<tr>
<td>Naar, 2020</td>
<td>ICU admission: 92%</td>
<td>Discharge</td>
<td>11% (5/46 who required RRT during hospitalization)</td>
</tr>
<tr>
<td>Ng, 2020</td>
<td>ICU admission: 100%</td>
<td>Discharge</td>
<td>31% (33/108 who required RRT during hospitalization)</td>
</tr>
<tr>
<td>Stevens, 2020</td>
<td>ICU admission: 100%</td>
<td>30 days (median) from RRT Initiation (in hospital)</td>
<td>8% (9/115) (NOTE: 2/9 had been discharged)</td>
</tr>
</tbody>
</table>

*Severity (%) as defined by study authors; if severity not reported, maximum oxygen requirements or ICU admission used as markers of severity

### Imaging Findings

A study from the UK reported an imaging finding at a median of 105 days post-COVID-19 diagnosis. Impairment on kidney cortex T1 was observed in 5% (2/37) with normal findings in 95% (35/37). A study from China reported no abnormal kidney morphology (on ultrasound) at a median of 153 days post-discharge.

### Gastrointestinal Outcomes

Two studies reported gastrointestinal outcomes defined by liver imaging abnormalities (Appendix C, Tables 1 and 7). The UK study, noted above, reported liver inflammation (cT1 in ms) was normal (<784 ms) in 76% (28/36 evaluated) and impaired (≥784 ms) in 24% (9/37). The study from China, reporting outcomes in 1733 patients at a median of 153 days post-discharge, observed no cases of abnormal liver morphology on ultrasound.
HEMATOLOGIC OUTCOMES

Key Findings

Post-discharge VTE was reported in 0% to 14% (k=10). Interpretation is limited by varying time points post-discharge (5 days to 153 days), little reporting on prophylactic anticoagulant use, and varying study inclusion criteria (ie, assessment of individuals with versus without signs or symptoms of VTE; follow-up of all patients via medical records, outpatient clinics, or telephone contact vs evaluation of patients with suspicion of VTE).

Overview of Studies

Eleven studies reported hematologic outcomes defined as venous thromboembolism or bleeding events (Appendix C, Tables 1 and 8). Three studies were from the UK, 3 from the Middle East, 3 from the US, and 1 each from Europe and China. Sample sizes ranged from 9 to 2,748 with 4 studies enrolling more than 1000. Mean or median ages of enrolled patients were 43 to 74 years and 48% to 84% were male. Only 1 study reported race, a UK study with 37% White. Two studies from the Middle East enrolled only patients with severe or critical COVID-19; other studies did not specify COVID-19 severity.

Thromboembolism

A study from Saudi Arabia reported the incidence of deep venous thrombosis (DVT) based on screening discharge ultrasound was 13% (8/64). All patients had been admitted to intensive care and received mechanical ventilation. None had DVT signs or symptoms.

The other 10 studies reported VTE outcomes post-discharge (Table 8). Follow-up ranged from a mean of 5 days to 4 months with VTE in 0% to 14.2%. In 5 of the 9 studies, the rate was less than 0.5%.

Table 8. Post-discharge Thromboembolism

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>COVID-19 Severitya</th>
<th>Anticoagulation at Discharge</th>
<th>Method of Assessment</th>
<th>Time Post-Discharge</th>
<th>Thromboembolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brosnahan, 202080 US</td>
<td>NR</td>
<td>NR</td>
<td>Re-presented to study hospital or ED with concern for a thrombotic event</td>
<td>5 days (mean)</td>
<td>Thrombotic eventb 0.46% (9/1,975)</td>
</tr>
<tr>
<td>Roberts, 202069 UK</td>
<td>ICU admission: 11%</td>
<td>0% (thromboprophylaxis withdrawn on hospital discharge)</td>
<td>Imaging if suspicion of VTE on re-presentation or primary care referral</td>
<td>8 days (median)</td>
<td>VTE 0.48% (9/1,877) Comparison cohort 0.31% (56/18,159 OR 1.6 (95%CI 0.77, 3.1)</td>
</tr>
<tr>
<td>Salisbury, 202094 UK</td>
<td>ICU admission: 16%</td>
<td>0%a</td>
<td>Medical records</td>
<td>14 days (median)</td>
<td>VTE 3% (4/152)c</td>
</tr>
<tr>
<td>Hill, 202055 US</td>
<td>Mechanical ventilation: 52%</td>
<td>No routine post-discharge VTE prophylaxis</td>
<td>Medical records</td>
<td>21 days (median)</td>
<td>VTE 0.14% (3/2,075)</td>
</tr>
<tr>
<td>Author, Year Country</td>
<td>COVID-19 Severity⁵</td>
<td>Anticoagulation at Discharge</td>
<td>Method of Assessment</td>
<td>Time Post-Discharge</td>
<td>Thromboembolism</td>
</tr>
<tr>
<td>---------------------------</td>
<td>--------------------</td>
<td>-----------------------------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>--------------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Patell, 2020⁶⁶ US</td>
<td>ICU admission: 26%</td>
<td>0% (excluded from primary analysis)</td>
<td>Medical records (at least 1 post-discharge contact)</td>
<td>23 days (median)</td>
<td>PE, intracardiac thrombus, thrombosed arteriovenous fistula, ischemic stroke (1 each) 2.5% (4/163)</td>
</tr>
<tr>
<td>Vlachou, 2021⁹⁹ UK</td>
<td>NR</td>
<td>100% “severe” (not defined)</td>
<td>Admissions post-discharge</td>
<td>28 days</td>
<td>PE 1% (4/370 enrolled)⁶</td>
</tr>
<tr>
<td>Daher, 2020⁸² Germany</td>
<td>Mechanical ventilation: 0%</td>
<td>None</td>
<td>Outpatient pulmonary clinic</td>
<td>42 days</td>
<td>Thromboembolic event 0% (0/33)</td>
</tr>
<tr>
<td>Rashidi, 2020⁹³ Iran</td>
<td>ICU admission: 8%</td>
<td>NR</td>
<td>Telephone follow-up with in-person evaluation of patients reporting symptoms and documentation from patients already evaluated</td>
<td>45 days</td>
<td>PE 0.2% (3/1,529)</td>
</tr>
<tr>
<td>Alharthy, 2020⁷⁶ Saudi Arabia</td>
<td>ICU admission: 100%; “Severe” COVID-19</td>
<td>NR</td>
<td>All surviving patients assessed at 2 and 4 months; 49% were symptomatic at 4 months</td>
<td>2 months 4 months</td>
<td>DVT 2 months: 14.2% (18/127) 4 months: 7.1% (9/127)</td>
</tr>
<tr>
<td>Huang C, 2021⁸⁶ China</td>
<td>ICU admission: 4%</td>
<td>NR</td>
<td>21% randomly selected for US and CT post-discharge; 76% of those selected were evaluated</td>
<td>153 days (median)</td>
<td>DVT or lower limbs (US) 0% (NOTE: post-discharge PE was an exclusion criteria [n=1])</td>
</tr>
</tbody>
</table>

Abbreviations: ICU=intensive care unit; NR=not reported; OR=odds ratio; VTE=venous thromboembolism
⁵Severity (%) as defined by study authors; if severity not reported, maximum oxygen requirements or ICU admission used as markers of severity
⁶DVT, PE, limb ischemia due to coronary thrombosis, acute stroke, rapidly evolving hemodynamic instability with elevated D-dimer at time of presentation
⁷Subgroup of patients discharged without an indication for therapeutic anticoagulation and followed for 42 days although 5 (3%) received 7 days of standard dose low molecular weight heparin after a change in local COVID-19 guidelines
⁸Number discharged alive not reported

**Bleeding Events**

Two studies also reported bleeding events.⁶⁶,⁹⁴ In a study from the US, at a median of 27 days post-discharge, 3.7% (6/163) experienced hemorrhagic events. Two were considered ‘major bleeds”; both followed falls. Four were considered ‘clinically relevant non-major bleeding’. The patients experiencing thrombotic or hemorrhagic events had been discharged without anticoagulant therapy; among 13 patients discharged on thromboprophylaxis, there were no observed thrombotic or hemorrhagic complications. A study from the UK reported no bleeding events in the subgroup of patients discharged without an indication for therapeutic anticoagulation.⁹⁴
HEALTHCARE/RESOURCE UTILIZATION OUTCOMES

Key Findings

Frequently reported outcomes included discharge to a location other than home (3% to 47%, k=15) and hospital readmission (0% to 15%; k=20); 2-14% within 30 days of discharge (k=11) and 0-15% at greater than 30 days (k=9).

Few studies reported post-discharge oxygen or follow-up healthcare requirements.

Overview of Studies

Forty-four studies – 24 from the US, 6 from Europe, 6 from the UK, 3 from China, 2 from Iran, and 1 each from the Democratic Republic of the Congo, Japan, and multiple nations – reported measures of healthcare and/or resource utilization (Appendix C, Tables 1 and 9). Sample sizes ranged from 7 to 15,111 with 16 studies enrolling more than 1000 and 9 studies enrolling 100 or fewer. Mean or median ages ranged from 35 to 82. Between 0% and 94% were male. Race was reported in 27 studies with 5% to 90% White, 0% to 90% Black, 4% to 45% Hispanic, and 0% to 15% Asian. Diabetes was the most frequently reported comorbidity (40 studies), present in 2% to 71% of the study populations. COVID-19 severity was reported in 9 studies with 19% to 100% severe or critical. Need for invasive mechanical ventilation was reported in 30 studies. One study excluded patients requiring mechanical ventilation; in the remaining studies 1% to 86% received mechanical ventilation.

Discharge Disposition

Twenty-four studies reported on discharge disposition. Five studies enrolled patients with stroke or neurological conditions and 4 enrolled other, specific populations are described below. Findings from the remaining studies are reported in Table 9. Studies reporting discharge other than to home are depicted in Figure 5.
Figure 5. Discharge Other Than Home

Table 9. Discharge Disposition

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>COVID-19 Severitya</th>
<th>Home</th>
<th>Other Disposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atalla, 2020103 US</td>
<td>ICU admission: 33%</td>
<td>74% (14/19)b Home: 11; Hotel for Homeless with COVID-19: 3</td>
<td>Skilled nursing facility: 26% (5/19)b</td>
</tr>
<tr>
<td>Barbaro, 202042 Multi-national</td>
<td>ECMO support: 100%</td>
<td>Home or acute rehabilitation center: 53% (311/588)</td>
<td>Long-term acute care center or unspecified: 17% (101/588) Another hospital: 30% (176/588)</td>
</tr>
<tr>
<td>Chopra, 202081 US</td>
<td>ICU admission: 13%</td>
<td>81% (13/16)</td>
<td>Nursing facility (permanent residence): 6% (1/16) Hotel for those with confirmed COVID-19: 13% (2/16)</td>
</tr>
<tr>
<td>Fisher, 202029 US</td>
<td>ICU admission: 13%</td>
<td>77% (1,650/2,142) COVID-19 negative control group: 83% (788/950)</td>
<td>Nursing home: 23% (492/2142) COVID-19 negative control group: 17% (162/950)</td>
</tr>
<tr>
<td>Knights, 2020104 UK</td>
<td>Invasive mechanical ventilation: 8%</td>
<td>81% (56/69)</td>
<td>Care home: 14% (10/69) Other not specified: 5% (3/69)</td>
</tr>
<tr>
<td>Loerinc, 202038 US</td>
<td>ICU admission: 22%</td>
<td>91% (281/310)</td>
<td>Skilled nursing facility: 8% (25/310) Public health quarantine facility: 1% (4/310)</td>
</tr>
<tr>
<td>Author, Year Country</td>
<td>COVID-19 Severity$^a$</td>
<td>Home</td>
<td>Other Disposition</td>
</tr>
<tr>
<td>----------------------</td>
<td>------------------------</td>
<td>------</td>
<td>------------------</td>
</tr>
</tbody>
</table>
| Matsunaga, 2020$^{48}$ Japan | 32% severe | 72% (1,762/2,437) | Long-term care facility: 2% (44/2,437)  
Another hospital: 18% (437/2,437)  
Non-medical (isolation) facility: 8% (194/2,437) |
| Nachega, 2020$^{51}$ Democratic Republic of the Congo | 25% severe or critical | 97% (645/665) | Home care: 3% (20/665) |
| Nemer, 2021$^{52}$ US | ICU admission: 14% | 85% (278/328) | Subacute facility: 12% (40/328)  
Hospice: 2% (8/328) |
| Overstad, 2020$^{53}$ Norway | 19% critically ill | 83% (52/63)  
ICU patients: 63% (5/8)  
Ward patients: 89% (49/55) | 24-hour care: 17% (11/63)  
ICU patients: 38% (3/8)  
Ward patients: 13% (7/55) |
| Richardson, 2020$^{68}$ US | ICU admission: 4% | 94% (1,959/2,081) | Facility (eg, nursing home, rehabilitation): 6% (122/2,081) |
| Rodriguez, 2020$^{55}$ US | ICU admission: 29% | 74% (4,746/6,421) | Nursing facility: 17% (1,097/6,421)  
Another hospital: 5% (317/6,421)  
Hospice: 3% (192/6,421) |
| Suleyman, 2020$^{105}$ US | ICU admission: 40% | 92% (232/253)  
ICU patients: 79% (49/62)  
General practice unit: 96% (183/191) | Rehabilitation center: 8% (21/253)  
ICU patients: 21% (13/62)  
General practice unit: 4% (8/191) |
| Vizcaychipi, 2020$^{39}$ UK | ICU admission: 14% | 92.5% (614/664) | Temporary home: 2% (16/664)  
Residential care home: 5% (34/664) |
| Wang, 2020$^{72}$ China | 53% severe | 87% (114/131) | Community quarantine: 9% (12/131)  
Designated hospital: 4% (5/131) |

Abbreviation: ECMO=extracorporeal membrane oxygenation

$^a$Severity (%) as defined by study authors; if severity not reported, maximum oxygen requirements or ICU admission used as markers of severity

$^b$Discharge disposition for 19 patients readmitted at a median of 5 days post-discharge

$^c$Pregnant women admitted to hospital for COVID-19

**Patients with Stroke or Neurological Conditions**

Five studies enrolled patients with stroke or other neurological conditions.$^{32,33,38,41,112}$ Four studies were from the US.

One US study of patients who experienced a stroke reported that 30% (3/10) were discharged home (including 2 of 6 hospitalized for COVID-19 who subsequently experienced a stroke [‘COVID’] and 1 of 4 hospitalized for stroke symptoms who subsequently tested positive for COVID-19 [‘Neuro’]), 50% (5/10) were discharged to acute rehabilitation (3 of 6 in ‘COVID’ group, 2 of 4 in ‘Neuro’ group), and 20% (2/10) were discharged to long-term acute care (1 of 6 in ‘COVID’ group and 1 of 4 in ‘Neuro’ group).$^{32}$ Another US study of stroke patients (some had stroke onset during COVID-19 hospitalization and some had COVID-19 onset within 14 days of stroke onset) reported that 45% (25/56 discharged) were discharged home and 55% (31/56) to rehabilitation.$^{33}$ An additional 30 patients had died or were in hospice care (data not reported separately for deaths and hospice). In a comparison group of non-COVID-19 stroke...
patients, 52% (228/438 discharged) were discharged home and 48% (210/438) to rehabilitation. An additional 61 patients had died or were in hospice care. A third US study enrolled patients who received a neurologic or neurocritical care admission or consultation. Of the 64 patients discharged, 34% (22/64) went home without services, 32% (20/64) went to a skilled nursing facility, 14% (9/64) went to acute rehabilitation, 8% (5/64) when home with services, 6% (4/64) were in inpatient hospice, 5% (3/64) were in a long-term acute care hospital, and 2% (1/64) was home with hospice. Another US study of patients with ICD-10 codes at discharge for ischemic stroke and COVID-19 reported a favorable discharge (home or acute rehabilitation) for 34% (707/2086). The same outcome was reported for 66% (110,546/166,586) of a historical control group.

The fifth study, from the United Kingdom, reported that, of COVID-19 neurological patients discharged, 56% (9/16) went home and 31% (5/16) went to a rehabilitation or stroke unit; the location of 13% (2/16) was not reported.

Other Populations

One US study enrolled 20 patients with HIV who were hospitalized for COVID-19; 4 patients (20%) were from a VA Medical Center. Of patients discharged, 81% (13/16) were discharged home, 6% (1/16) to a nursing facility (permanent residence), and 13% (2/16) to a hotel for those with confirmed COVID-19. Five of the 20 patients enrolled had been living in a group living situation prior to hospitalization (3 in nursing homes, 1 incarcerated, 1 in a substance abuse recovery home).

Another US study enrolled patients with a history of heart failure. Among patients with COVID-19, 7% (428/6,357) were discharge to hospice and 41% (2,605/6,357) to skilled nursing or rehabilitative care. In a comparison group of non-COVID patients, 4% (4,068/95,556) were discharged to hospice and 21% (20,352/95,556) to skilled nursing or rehabilitative care.

A US study of pregnant women admitted for severe or critical COVID-19 reported that 92% (35/38) were discharged home without oxygen required and 8% (3/38) were discharged to either a skilled nursing facility, long-term acute care, or home with oxygen required. In a comparison group of non-pregnant women with severe or critical COVID-19, 85% (77/91) were discharged home without oxygen required and 15% (14/91) to another facility or home with oxygen required.

Patients with COVID-19 and Takotsubu cardiomyopathy were included in a study from the US. Three of 7 patients were discharged alive, 1 (33%) to a skilled nursing facility, and 2 (67%) to long-term acute care.

Hospital Readmission

Hospital readmission for any reason was reported by 22 studies. One study from the US enrolled individuals who were hospitalized for a hip fracture and tested positive for COVID-19 either before, during, or after hospitalization. Twenty-nine percent had been admitted to the ICU. Within 30 days of follow-up, 12% (2/17) of the COVID-19 confirmed positive patients, 7% (1/14) of the COVID-19 suspected positive patients, and 3% (3/107) of the COVID-19 confirmed negative patients were readmitted.
The remaining studies are summarized in Table 10. Figure 6 includes the study described above; 1 study is not included on Figure 6\textsuperscript{109} (see Table 10 footnote).

**Figure 6. Readmission Rate**

![Figure 6. Readmission Rate](image)

**Table 10. Hospital Readmission**

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>COVID-19 Severity\textsuperscript{a}</th>
<th>Length of Follow-up</th>
<th>Readmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Richardson, 2020\textsuperscript{68} US</td>
<td>ICU admission: 4%</td>
<td>3 days (median to readmission)</td>
<td>2% (45/2,081)</td>
</tr>
<tr>
<td>Atalla, 2020\textsuperscript{103} US</td>
<td>ICU admission: 33%</td>
<td>5 days (median to readmission)</td>
<td>6% (19/339)</td>
</tr>
<tr>
<td>Parra, 2020\textsuperscript{91} Spain</td>
<td>ICU admission: 5%</td>
<td>6 days (median to readmission)</td>
<td>4% (61/1,368)</td>
</tr>
<tr>
<td>Wang, 2020\textsuperscript{72} China</td>
<td>23% severe</td>
<td>7-14 days</td>
<td>4% (5/131)</td>
</tr>
<tr>
<td>Somani, 2020\textsuperscript{71} US</td>
<td>ICU admission: 19%</td>
<td>14 days</td>
<td>2% (56/2,864)</td>
</tr>
<tr>
<td>Brendish, 2020\textsuperscript{73} UK</td>
<td>ICU admission: 10%</td>
<td>30 days</td>
<td>11% (30/352) COVID-19 negative control group: 18% (105/702)</td>
</tr>
<tr>
<td>Hamilton, 2020\textsuperscript{84} UK</td>
<td>ICU admission: 16%</td>
<td>30 days</td>
<td>8% (86/1,032)</td>
</tr>
<tr>
<td>Loerinc, 2020\textsuperscript{88} US</td>
<td>ICU admission: 22%</td>
<td>30 days</td>
<td>5% (16/310) (69% [11/16] attributed to COVID-19)</td>
</tr>
<tr>
<td>Monday, 2020\textsuperscript{90} US (Veterans)</td>
<td>ICU admission: 34%</td>
<td>30 days (from admission)</td>
<td>14% (8/57)</td>
</tr>
<tr>
<td>Author, Year Country</td>
<td>COVID-19 Severity a</td>
<td>Length of Follow-up</td>
<td>Readmission</td>
</tr>
<tr>
<td>----------------------</td>
<td>---------------------</td>
<td>---------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Patell, 2020 US</td>
<td>ICU admission: 26%</td>
<td>30 days</td>
<td>7% (12/163)</td>
</tr>
<tr>
<td>Suleyman, 2020 US</td>
<td>ICU admission: 40%</td>
<td>30 days</td>
<td>11% (29/253) ICU: 3% (2/62) General practice unit: 14% (27/191)</td>
</tr>
<tr>
<td>Bowles, 2020 US</td>
<td>NR</td>
<td>32 days (mean)</td>
<td>10% (137/1,409) while in home healthcare</td>
</tr>
<tr>
<td>Knights, 2020 UK</td>
<td>Invasive mechanical ventilation: 8%</td>
<td>36 days (median) (from admission)</td>
<td>5% (3/56)</td>
</tr>
<tr>
<td>Casas-Rojo, 2020 Spain</td>
<td>ICU admission: 8%</td>
<td>40 days (median)</td>
<td>5% (573/11,928)</td>
</tr>
<tr>
<td>Chopra, 2020 US</td>
<td>ICU admission: 13%</td>
<td>60 days</td>
<td>15% (189/1,250)</td>
</tr>
<tr>
<td>Khalili, 2020 Iran</td>
<td>Invasive mechanical ventilation: 11%</td>
<td>90 days (from initial admission)</td>
<td>4% (10/254)</td>
</tr>
<tr>
<td>Nersesjan, 2021 Denmark</td>
<td>ICU admission: 47%</td>
<td>90 days</td>
<td>38% (17/45) b</td>
</tr>
<tr>
<td>Dawson, 2020 UK</td>
<td>ICU admission: 49%</td>
<td>NR</td>
<td>0% (0/208)</td>
</tr>
<tr>
<td>El Moheb, 2020 US</td>
<td>ICU admission: 100% (inclusion criteria)</td>
<td>NR</td>
<td>11% (10/92) Matched COVID-19 negative: 11% (10/92)</td>
</tr>
<tr>
<td>Lovinsky-Desir, 2020 US</td>
<td>Invasive mechanical ventilation: 21%</td>
<td>NR</td>
<td>5% (40/832) in 40-65 age group without asthma 5% (5/111) in 40-65 age group with asthma</td>
</tr>
<tr>
<td>Sachdeva, 2020 US</td>
<td>ICU admission: 27%</td>
<td>NR</td>
<td>9% (1/9)</td>
</tr>
</tbody>
</table>

aSeverity (%) as defined by study authors; if severity not reported, maximum oxygen requirements or ICU admission used as markers of severity

bPatients were discharged to a tertiary referral center following hospitalization

Post-discharge Treatment

Oxygen Therapy

Use of oxygen therapy was reported in 7 studies. A US study of Veterans reported home oxygen was required in 39% (22/57). Follow-up was 30 days. New home oxygen therapy was required for 13% (41/310) of patients in another US study (30 day follow-up). A third US study reported 7% (32/488) required oxygen at home and 7% (34/488) required new use of CPAP or other assistance when sleeping. A study from China reported that 6% (5/85) were receiving oxygen therapy via nasal cannula at home (time post-discharge not specified). Wang et al, also from China, reported that at 1-2 weeks after discharge 7% (9/131) were treated with oxygen therapy. At 3-4 weeks, the percentage decreased to 1% (1/131). Corticosteroid use was 4% (5/131) at 1-2 weeks and 2% (2/131) at 3-4 weeks. A study from Japan reported that 8% (182/2,430) required oxygen therapy.
at discharge. A study from Germany reported that 82% (27/33) of patients required oxygen therapy at admission; at 6 week follow-up, only 1 patient required oxygen therapy.

**Post-acute Care**

A US study reported need for post-acute rehabilitation in patients undergoing surgery for hip fracture. Ninety percent (9/17) of the COVID-19 group was receiving rehabilitation compared with 78.3% (83/107) of patients negative for COVID-19. The difference was not statistically significant (P=.61). Another US study reported the need for physical or occupational therapy in 14% (42/310) and home nursing service in 5% (16/310).

Several studies reported on self-care ability post-discharge. In a study from Iran, where 18% of patients were admitted to the ICU, 88% (370/420) reported no problems with self-care at a mean of 22 days post-discharge. A study from China reported that 1% (11/1,622) had personal care problems. Among patients from a study in Japan, 32% with severe COVID-19, 84% (2,045/2,4245) rated their self-care ability the same as before COVID-19, 10% (237/2,425) rated it worsened, and 4% (106/2,425) rated it improved.

Follow-up health care was also reported in several studies. “Need for follow-up” was reported for 60% (75/126) of patients enrolled in a study from Italy. Need was determined based on elevated respiratory rate, uncontrolled blood pressure, moderate to very severe dyspnea, malnutrition, or new-onset cognitive impairment. Recommended follow-up care was identified in a study from the US. Primary care appointments were recommended for 83% (258/310) and specialist appointments (including nephrology and cardiology) for 28% (90/310). Follow-up bloodwork was ordered for 10% (31/310) and follow-up radiology for 7% (21/310). A study from the US reported primary care follow-up within 60 days of discharge for 78% (382/488) of patients who completed a follow-up telephone survey. Total enrollment was 1,250. As with most other outcomes, the lack of controls hospitalized without COVID-19 limits conclusions.

A study from the US reported new short-term medications were required by 67% (207/310) of patients with an average of 2.2 new prescriptions per patient. New long-term medications were required for 23% (72/310) with an average of 1.6 new prescriptions per patient.

In a study from the United Kingdom, new “packages of care” were required for 2.9% (2/69) of patients discharged and an increase in mobility aids was noted for 11.6% (8/69).
DISCUSSION

Our review identified 90 reports of post-acute major organ damage or healthcare/service use outcomes in patients who were hospitalized with or for COVID-19. Thirty-three studies were from the US including 1 study exclusively of Veterans and 1 multisite US study that included patients from a VA Medical Center. The amount of data is increasing rapidly. We identified an additional 51 studies in the 3-month interval from our October search date. Future updates are likely to identify relevant new data. We provide “Key Findings”, “Limitation”, and “Suggestions for Future Research”.

KEY FINDINGS

Key Question 1

Post-hospital data provides wide ranging prevalence estimates based mainly on physiologic outcomes for pulmonary, neurologic, cardiac, renal, and hematologic conditions from convenience samples without controls. Most studies were not conducted in US and no studies were identified with prevalence of major organ damage among Veterans.

Available evidence suggests:

- Radiographically defined pulmonary fibrosis was reported at varying time intervals (k=5) with estimates ranging from 7% to 61%; lung CT abnormalities were noted in 0% to 88% (k=8), abnormal DLCO in 21% to 84% (k=7), and dyspnea in 2% to 22% (k=9).

- Pericardial effusions, myocardial inflammation/fibrosis, and possibly mild reductions in ejection fraction were identified following COVID-19 hospitalization; pericardial effusion was reported in 0% to 20% (k=5); impairment in LVEF was noted in 3% to 11% (k=3).

- A “good” prognosis based on modified Rankin Scale scores at the time of discharge was reported in 17% to 60% of patients hospitalized for stroke and testing positive for COVID-19 (k=6); cognitive impairment at 22 to 42 days post-discharge was observed in 18% to 57% (k=3).

- Acute kidney disease at time of discharge was reported for 25% and 33% (k=2) and need for RRT was reported in 4% to 31% of those who had required RRT during hospitalization (k=5).

- Post-discharge VTE was reported in 0% to 14% (k=10); interpretation is limited by varying time points post-discharge (5 days to 153 days), little reporting on prophylactic anticoagulant use, and study inclusion criteria (ie, assessment of individuals with versus without signs or symptoms of VTE; follow-up of all patients via medical records, outpatient clinics, or telephone contact vs evaluation of patients with suspicion of VTE).

We found only 2 studies of gastrointestinal outcomes and both used imaging to assess for liver abnormalities. We found no published post-hospital information for metabolic/endocrine or rheumatologic/musculoskeletal conditions.
Key Question 2
We are unable to determine if post-acute care prevalence of major organ damage varies by patient characteristics (e.g., age, sex, race/ethnicity, pre-existing comorbidities/frailty, type of residence), COVID-19 disease severity, or other factors (e.g., treatment for COVID-19). Few studies reported outcomes for subgroups of patients.

Key Question 3
Frequently reported outcomes included discharge to a location other than home (3% to 47%; k=15) and hospital readmission (0% to 15%; k=20); 2-14% within 30 days of discharge (k=11) and 0-15% at greater than 30 days (k=9). Few studies reported post-discharge oxygen or follow-up health care requirements including post-hospital need for ambulatory care, imaging or laboratory monitoring needed, or treatments (i.e., medications, devices, procedures, surgery) required.

LIMITATIONS
Additional limitations of the available evidence include:

- Available data are from studies of small, convenience samples (often from a single hospital site) with poorly described study populations or measures of major organ damage; 18 studies included control groups for comparison of COVID-19 and non-COVID-19 patients. Most studies were not conducted in the US and only 1, reporting readmission and need for home oxygen, enrolled exclusively Veterans.

- Major organ damage measures were not standardized and varied considerably across studies. Reported prevalence rates are likely highly dependent on the measures used to assess and define major organ damage, the population being evaluated, and the timing of assessment relative to hospital discharge.

- Most studies assessed outcomes at discharge or had short follow-up post-discharge; long-term major organ damage prevalence and healthcare/service use needs are unknown.

- The contribution of comorbidities (prior to COVID-19 infection) to post-acute prevalence cannot be determined.

- There are no data reporting on outcomes based on patient living situation prior to COVID-19 infection (i.e., community dwelling versus nursing home or assisted care centers)

Limitations of our review methods include:

- We defined “post-acute COVID” as patients being post-hospital discharge. The applicability of these findings to non-hospitalized patients with acute COVID symptoms is unknown; this was out of our scope.

- Our literature search was through January 12, 2021 and would not have included information published after that date. Ongoing living review rapid review methods are needed to capture additional information.
FUTURE RESEARCH

Given the gaps in, and limitations of, the existing evidence,113 we suggest the following as a guide for future research to better inform healthcare systems as they plan for on-going care of patients recovering from COVID-19.

Population

We chose to define post-acute as post-hospitalization but other definitions may be appropriate.3,113 For example, patients with acute COVID-19 who are not hospitalized may have “post-acute” major organ damage. Limiting the scope of this review to patients hospitalized for acute COVID likely underestimates the total burden of post-acute major organ damage. This should be acknowledged for resource allocation planning in the future. Furthermore, we did not identify studies that assessed “long-haulers” or “long COVID” (ie, people who have either recovered from COVID-19 but still report lasting effects or who have had the usual symptoms for longer than might be expected).114 This is a poorly defined entity and no published data were available. Additionally, there are likely important difference in patients hospitalized for COVID-19 versus patients hospitalized for another indication who have a positive COVID-19 test. We chose to include both but this could influence prevalence, severity, and causality of findings. We also limited eligibility to studies that assessed patients with “confirmed” COVID-19. While this increases the specificity and accuracy of our review it also underestimates the burden of post-acute complications when also including patients with suspected COVID-19. Future studies should include all patients or consecutive patients rather than convenience samples. Study populations should be carefully described including severity of disease and treatments received. Results should be reported for subgroups based on age, gender, race/ethnicity, pre-existing conditions/frailty, type of residence (eg, independent living, assisted living, nursing home), COVID-19 severity, and treatment received. Ideally, researchers would be able to link pre-COVID-19 data with post-COVID-19 data. Without pre- and post- data, it is difficult to isolate the effects of COVID-19.

Comparator

The use of matched non-COVID-19 control groups would allow for a better understanding of the effects of COVID-19. Without appropriate comparators and information on pre-COVID conditions it is not possible to accurately determine the effect that COVID-19 has on post-acute health outcomes or the incremental effects versus controls without COVID-19. Nonetheless, given ongoing health and health care concerns associated with COVID-19, uncontrolled reports among patients with COVID-19 are still informative for care planning.

Outcomes

Many studies, excluded from our review, reported mean and median values of laboratory, radiologic, or physiologic measures. These data do not provide prevalence outcomes. Future research should include measures that will reflect prevalence of major organ damage or disease based on accepted definitions of disease, even if defined as asymptomatic laboratory, radiologic, or physiologic measures. Although many conditions have been reported to be associated with COVID-19 while patients are hospitalized, there has been little or no published post-hospital data for most of those conditions. Many reports were convenience samples and used testing measures available at that facility or selected for reporting for unclear reasons. Criteria for outcome
assessment, reporting and definition will have important implications on major organ damage
prevalence and severity.

**Timing**

Future research should include standardized and longer follow-up.

**Setting**

Information on major organ damage prevalence and healthcare/service use needs of non-
hospitalized patients is also needed.

**ONGOING DATA COLLECTION**

We are aware of a recent publication of Veterans Health Administration data from 13,654
Veterans with COVID-19 who survived at least 30 days after hospital admission.115 We are also
aware of several ongoing studies:

- A study of COVID-19 sequelae among Veterans treated in the VA
  (https://www.hsrdr.ephs.va.gov/research/abstracts.cfm?Project_ID=2141707422),

- A natural history study of COVID-19 titled “Epidemiology, Immunology and Clinical
  Characteristics of Emerging Infectious Diseases with Pandemic Potential” (EPICC-EID); a
  collaboration between the VA and the Department of Defense to better understand the

- A study sponsored by UK-based Perspectum Diagnostics
  (https://www.bioworld.com/articles/434620-perspectum-launches-study-of-post-covid-19-
  organ-damage),

- The Post-hospital COVID (PHOSP-COVID) study,114

- A multicenter observational registry, the North American COVID-19 ST-Segment-Elevation
  Myocardial Infarction (NACMI) registry, to collect data on ST elevation in COVID-19
  patients to determine the etiology and associated clinical outcomes,116

- An initiative from the NIH: Post-Acute Sequelae of SARS-CoV-2 infection (PASC) (NIH
  launches new initiative to study “Long COVID” | National Institutes of Health (NIH)).

- The Johns Hopkins COVID Long Study (Johns Hopkins COVID Long Study (covid-
  long.com),

- The Collaborative Cohort of Cohorts for COVID-19 Research (CoC) Study; a nationwide
  study of more than 50,000 individuals jointly funded by the National Heart, Lung, and Blood
  Institute, the National Institute of Neurological Disorders and Stroke, and the National
  Institute on Aging of the National Institutes of Health
effects-underway-37-academic-medical-centers)
Several major healthcare systems have established multidisciplinary post-COVID care clinics including the Mount Sinai (New York) Center for Post-COVID Care, the Penn Medicine Post-COVID Recovery Clinic, University of California San Francisco’s OPTIMAL Clinic, the University of Michigan’s Post ICU Longitudinal Survivor Experience (PULSE) Clinic (now focused on post-COVID-19), the Columbia University Irving Medical Center COVID-19 Rehabilitation Program, and the Mayo Clinic COVID Activity Rehabilitation Program (CARP). Anticipated post-acute care rehabilitation needs of patients and guidance on how to address those needs have been reported.117-126 There is an emphasis on multi-disciplinary programs to address respiratory, cardiovascular, thromboembolism, and neurological sequelae along with physical function and mental health needs. Patient groups have also been organized with a focus on long-term symptoms. These include Survivor Corps (https://www.survivorcorps.com/) and the COVID-19 “Long Hauler” Symptoms Survey,16 the Body Politic COVID-19 support group (https://www.wearebodypolitic.com/covid19), Long Covid SOS in the UK (www.longcovidso.org), and the COVID Symptom Study with an app to study symptoms and track the spread of the virus (https://covid.joinzoe.com/us-2).

CONCLUSIONS

Our systematic review of the literature yielded early published data on post-acute COVID-19 major organ damage and healthcare/service use needs. The majority of studies were from outside the United States; only 2 studies enrolled patients from a VA Medical Center. There was little information on patient-centered, clinical health outcomes. Available data are from studies of convenience samples with poorly described study populations and primarily physiologic outcomes. Few included control groups for comparison of COVID-19 and non-COVID-19 patients and interpretation is difficult due to the absence of pre-COVID-19 data. Future research should attempt to include clear descriptions of the patient populations and the timing of outcome assessment with respect to hospitalization, link pre-COVID-19 data with post-COVID-19 data, and assess outcomes that allow for determination of prevalence of major organ damage and healthcare/service use needs.
ACKNOWLEDGMENTS

This topic was developed in response to a nomination by Joe Francis MD, Chief Improvement and Analytics Officer for the Office of the Under Secretary for Health for the purpose of informing national VA planning efforts to support Veterans after hospital discharge for COVID-19. The scope was further developed with input from the Operational Partners, the ESP Coordinating Center, and the review team.

In designing the study questions and methodology at the outset of this report, the ESP consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

The authors gratefully acknowledge Julia Haskin for editorial support, and the following individuals for their contributions to this project:

**Operational Partners**

Operational partners are system-level stakeholders who have requested the report to inform decision-making. They recommend Technical Expert Panel (TEP) participants; assure VA relevance; help develop and approve final project scope and timeframe for completion; provide feedback on draft report; and provide consultation on strategies for dissemination of the report to field and relevant groups.

David Atkins, MD, MPH  
*Director, Health Services Research & Development*

Joseph Francis, MD  
*Chief Improvement & Analytics Officer, Office of Performance Measurement*
REFERENCES


