Brief Summary of Findings on the Association Between Disabilities and Severe COVID-19 Outcomes

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Summary

Overall, intellectual and developmental disabilities, disability (composite), learning disability, Down syndrome, spinal cord injuries, dependence, and activities of daily living are associated with an increase in mortality among people with COVID-19. Intellectual and developmental disabilities, learning disability, Down syndrome, cerebral palsy, and congenital malformations, and attention-deficit/hyperactivity disorder are associated with an increase in hospitalization in people with COVID-19. The literature search retrieved data on 48 disabilities or disability categories, however the data for most disabilities were limited to case reports, case series, one study, or a combination of studies with no comparative data, each of which were insufficient to determine an association between most of the exposures and severe COVID-19 outcomes.

Below is a summary table of major findings:

	Hospitalization	ICU	Intubation	Ventilation	Mortality	Strength and Direction Table
Disabilities (composite)	NR	NR	NR	NR	✓+	Table 6
Intellectual and Developmental Disabilities (IDD)*	✓+	I	NR	O	✓+	Table 2
Down Syndrome*	✓+	O	O	O	✓+	Table 9
Dependence for basic activities of daily living*	O	O	NR	O	✓+	Table 13
Learning Disabilities (composite)*	✓+	O	NR	NR	✓+	Table 16
Activities of Daily Living (ADL) Impairments	NR	NR	NR	NR	✓+	Table 18
Neuromuscular Disease	O	O	O	NR	I	Table 19
Spinal Cord Injuries	O	NR	NR	NR	✓+	Table 20
Cerebral Palsy*	✓+	O	NR	O	O	Table 21
Congenital Malformations	NR	NR	NR	NR	✓+	Table 23
Cognitive Impairment*	NR	O	NR	NR	I	Table 24
Neurodevelopmental Disorders	O	NR	NR	NR	O	Table 26
Neuromyelitis Optica Spectrum Disorder (NMOSD)*	NR	O	O	O	O	Table 28
Severe and complex disability (Polyhandicap Disability) *	O	O	NR	NR	O	Table 31
Mobility Impairment	NR	NR	NR	NR	O	Table 33
Immobilization (Movement Disorders)	O	O	NR	NR	O	Table 34
Disability Severity as Indicated by Barthel Index*	NR	NR	NR	NR	O	Table 35
Attention-Deficit/ Hyperactivity Disorder (ADHD)*	✓+	NR	NR	NR	O	Table 37
Traumatic Brain Injury	O	NR	NR	NR	O	Table 40
Movement Disorders	O	O	O	NR	O	Table 41
Autism	O	NR	NR	NR	NR	Table 42

	Hospitalization	ICU	Intubation	Ventilation	Mortality	Strength and Direction Table
Wheelchair Use	NR	NR	NR	NR	O	Table 43
Chromosomal Disorders	O	NR	NR	NR	O	Table 44
Neuropathy, Ataxia, and Retinitis Pigmentosa (NARP)	NR	NR	NR	NR	O	Table 45
Primary Mitochondrial Myopathy (PMM)	O	NR	NR	NR	O	Table 46
Spina Bifida and Other Nervous System Anomalies	NR	NR	NR	NR	O	Table 47
Leber's Hereditary Optic Neuropathy (LHON) or Autosomal Dominant Optic Atrophy (ADOA)	O	NR	NR	NR	NR	Table 48
Multiple Disability (or Bedridden Disability)	NR	NR	NR	NR	O	Table 49
Fragile X Syndrome	O	O	O	O	NR	Table 50
Gaucher Disease	O	NR	NR	NR	O	Table 51
Hearing Impairment (Deafness/Hearing Loss)	O	NR	NR	NR	NR	Table 52
The Association between Maternal Inherited Diabetes and Deafness (MIDD)	O	NR	NR	NR	NR	Table 53
Leigh Syndrome	O	NR	NR	NR	NR	Table 54
Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-Like Episodes (MELAS)*	O	NR	NR	NR	NR	Table 55
Multisystem Disease	O	NR	NR	NR	NR	Table 57
Myoclonic Epilepsy with Ragged Red Fibers (MERRF)	O	NR	NR	NR	NR	Table 58
Perinatal Spastic Hemiparesis	O	O	NR	NR	NR	Table 59
Charcot Foot	O	O	NR	NR	NR	Table 60
Tourette Syndrome	O	NR	NR	NR	O	Table 61
Chromosome 18q Deletion	O	O	O	NR	NR	Table 62
Chromosome 17 and 19 Deletion	O	NR	NR	NR	NR	Table 63
Congenital Hydrocephalus	O	NR	NR	NR	NR	Table 64
Fahr's Syndrome	O	O	O	O	O	Table 65
Hands and Feet Disorder (Birth Defect)	O	O	O	NR	NR	Table 66
Myotonic Dystrophy	O	NR	O	O	O	Table 67
Progressive Supranuclear Palsy	O	NR	NR	NR	O	Table 68
Senior-Loken Syndrome	O	NR	NR	NR	NR	Table 69
Visual Impairment/Blindness	O	O	NR	O	O	Table 70

O Limited evidence including case reports, case series, one study, or a combination of studies with no comparative data.

✓+ High Risk (conclusive and high risk)
*Severity and Comorbidity tables available
I = inconsistent results between available studies preclude the ability to draw a conclusion
NR Not Reported

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A. Methods

The aim of this review is to identify and synthesize the best available evidence on the association between underlying disabilities and severe COVID-19 to update the Centers for Disease Control and Prevention (CDC) website on underlying conditions and add to the provider-specific website.

The methods for underlying conditions and risk factors are outlined in the webpage, https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/systematic-review-process.html. These methods were established in May 2021 and are used for conditions and risk factors where CDC conducted the review.

Below are methodologic highlights and additional methods unique to this review. For more information, please visit https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/systematic-review-process.html.

A.1. Literature Search

A list of search terms was developed to identify the literature most relevant to the population, exposure, comparator, outcomes (PECO) question. Clinical experts and library scientists were consulted to develop a robust list of search terms. These terms were then incorporated into search strategies, and these searches were performed in OVID using the COVID-19 filter for all articles from the beginning of each data base until May 24, 2021. The detailed search strategies for identifying primary literature and the search results are provided in PartB. References were included if retrieved by the literature search and reported exposures and outcomes relevant to this review.

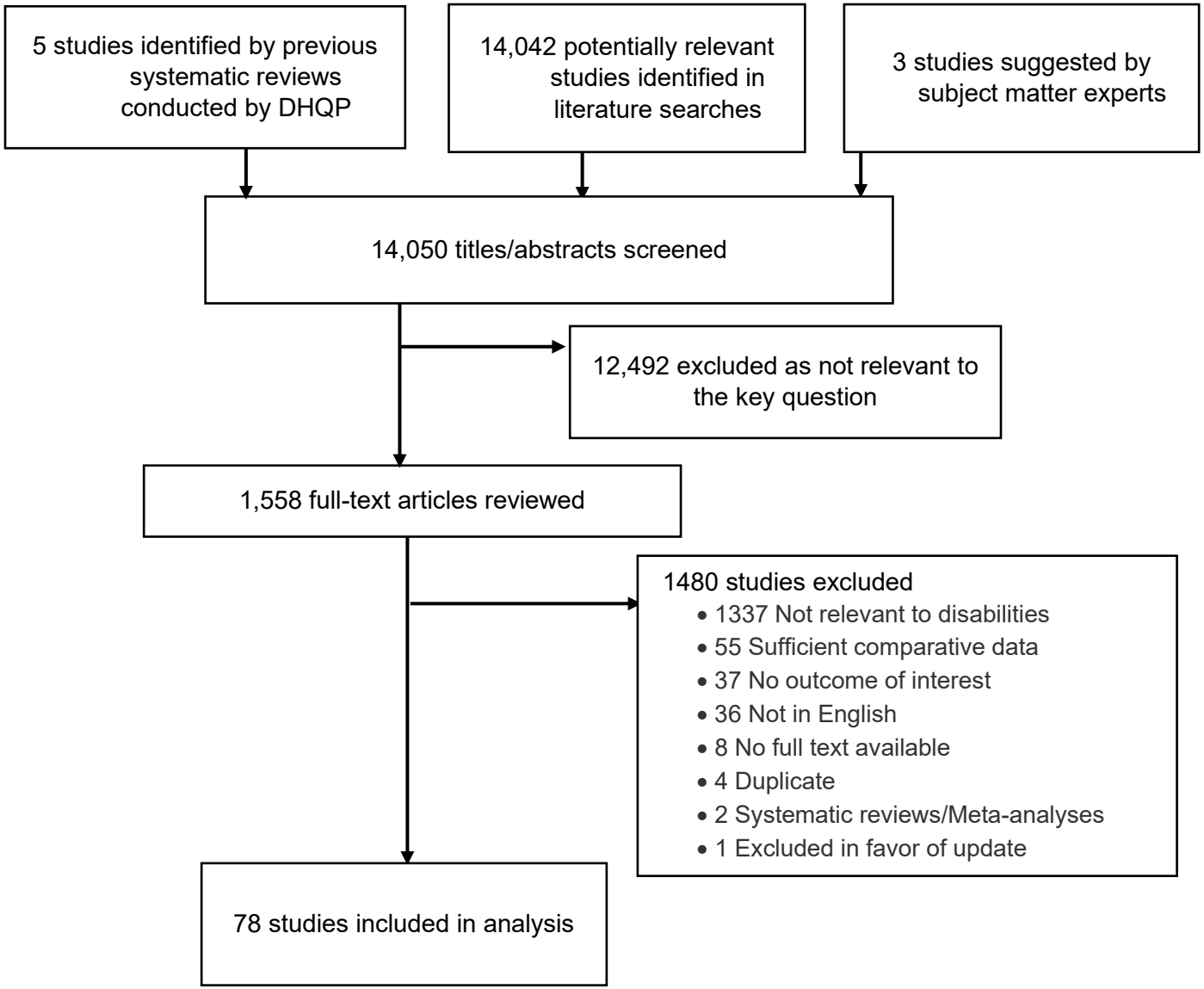
A.2. Study Selection

Titles and abstracts from references were screened by dual review (C.N.S., M.W., T.R., D.O.S., J.K., M.C., M.M., or E.C.S.). Full-text articles were retrieved if they were:

1. relevant to the PECO question;
2. primary research;
3. humans only;
4. in healthcare settings; and
3. written in English.

Part B presents the full list of exclusion criteria. The full texts of selected articles were then screened by two independent reviewers, and disagreements were resolved by discussion (C.N.S., M.W., T.R., D.O.S., J.K., M.C., M.M., or E.C.S.). After the full-text screening was complete, a bibliography of the articles selected for inclusion was vetted with subject matter experts. Additional studies suggested by the subject matter experts were screened for inclusion as described above. The results of the study selection process are depicted in Figure 1.

Figure 1. Results of the Study Selection Process



A.4. Data Extraction and Synthesis

Methodologic data and results of relevant outcomes from the studies meeting inclusion criteria were extracted into standardized evidence tables. Data and analyses were extracted as presented in the studies. For the purposes of this review, statistical significance was defined as $p < 0.05$.

A.5. Internal Validity Assessment

The internal validity associated with each study was assessed using scales developed by the Division of Healthcare Quality Promotion and scores were recorded in the evidence tables. Part B includes the questions used to assess the quality of each study design. The strength, magnitude, precision, consistency, and applicability of results were assessed for all comparators. The overall confidence in the evidence base is reported in the aggregation tables in Part B. The denominators used in the aggregation tables are of people diagnosed with COVID-19. If the number was not given, the denominator was listed as "not reported" (NR).

A.6. Reviewing and Finalizing the Systematic Review

Draft findings, aggregation tables, and evidence tables are presented to CDC subject matter experts for review and input. Following further revisions, the summary will be published on the CDC website.

B. Systematic Literature Review Search Strategy

B.1. Search Strategy

Table 1 Disabilities search conducted May 2021

#	Search History
1	Disabilit* OR disabled OR disorder* OR (impair* ADJ2 physical*) OR (impair* ADJ2 visual*) OR (impair* ADJ2 vision*) OR (impair* ADJ2 hear*) OR (sensory ADJ2 impair*) OR blind OR deaf OR handicap* OR cerebral palsy OR autism OR autistic OR asperger* OR ADHD OR Down Syndrome OR Trisomy OR Fragile X OR Muscular Dystroph* OR Tourette*
2	Limit 1 to covid-19
3	(2020* or 2021*).dt
4	(2020* or 2021*).dc
5	3 or 4
6	2 and 5
7	Deduplicate 6

B.2. Study Inclusion and Exclusion Criteria

Inclusion Criteria: Studies were included at the title and abstract screen if they:

- were relevant to the key question "What is the association between underlying disabilities and severe COVID-19?";
    - exposures: underlying intellectual, developmental, and physical disabilities
    - outcomes: mortality, ICU admission, intubation, ventilation, and hospitalization
- were primary research;
- were written in English (can be seen as [language] in title);
- examined humans only; and
- were in healthcare settings.

Exclusion Criteria: Studies were excluded at full text review if they:

- were not available as full-text;
- were autopsy studies;
- reported only composite outcome measures for "severe COVID-19";
- were replies and response papers; and
- notably, descriptive data or comparative data where n < 5 with the exposure of interest were included only when comparative data was unavailable for an exposure of interest.

B.3. Evidence Review: Underlying Disabilities and Severe COVID-19

B.3.a. Strength & Direction of Evidence

Table 2 The Association between Intellectual and Developmental Disabilities (IDD) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence from six studies[1-6] (Landes 2020, Landes 2021, Dobre 2021, Gleason 2021, Makary 2020, Turk 2020) (N =2,249,674) indicates intellectual and developmental disabilities (IDD) are associated with an increase in mortality in COVID-19 patients. Four studies[1,2,5,6] were found to have a moderate threat to internal validity, and two[3,4] had a high threat to internal validity. • Strength of Association: Three studies reported adjusted measures of association ranging from aHR of 1.32-5.91. • Precision of Association: Of the three studies reporting confidence intervals, two were wide and one of these wide confidence intervals cross the null. • Consistency of Association: Five studies reported an increased risk of mortality, and one reported no association. • Applicability of Association: Four studies were conducted in the U.S., one was conducted in France, and one was multi-national. Summary of Evidence • Five cohort studies[1-5] (N= 2,219,392) indicated that IDD is associated with an increase in mortality among people with COVID-19. Three of these cohort studies[1,2,5] (N=1,026,795) reported effect measures ranging from aHR 1.32 (95% CI 1.17 - 1.51) to 5.91 (95% CI: 5.28 - 6.62) among 3,909 people with IDD; two of these studies reported adjusted effect measures[2,5]. Two additional cohort studies[3,4] (N= 1,192,597) of 4,550 people with IDD and COVID-19 reported prevalence rates suggesting that IDD is associated with an increase in mortality (p = NR). ▪ Two studies[1,5] reported wide confidence intervals. One of these studies[1], reported a low prevalence of IDD in the study population, which may have resulted in wide confidence intervals that crossed the null. The other study[5] did not report on the prevalence of IDD in the study population, decreasing confidence in the results. Two studies[3,4] did not conduct statistical analyses. • One cohort study[6] (N= 30,282) reported data suggesting no association between mortality and cognitive impairment in COVID-19 patients. ▪ One cohort study[6] (N= 30,282) of international patients suggested no difference in mortality among patients with developmental disabilities compared to those without developmental disabilities (5.1% [24/474] vs. 5.4% [1,614/29,808], p = NR). No statistical analyses were conducted, decreasing confidence in the results.
ICU admission	Overall, the evidence from two studies[2,7] (Chow 2020, Gleason 2021) is inconclusive to determine an association between IDD and ICU admission in COVID-19 patients. Both studies were found to have a moderate threat to internal validity. • Strength of Association: One study reported an adjusted measure of association of 1.04. • Precision of Association: One study reported a narrow confidence interval that crossed the null. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: Two studies were conducted in the U.S.

	Summary of Evidence • One cohort study[7] (N= 7,162) reported prevalence rates suggesting IDD is associated with an increase in ICU admission. ▪ One cohort study[7] (= 7,162) of persons repatriated to the U.S. from Wuhan, China and the Diamond Princess cruise ship reported an increase in ICU admission among 52 COVID-19 patients with intellectual disabilities compared to those without intellectual disabilities [13.5% (7/52) vs. 2.2% (99/4,470), p = NR]. This study reported a low number of hospitalizations, decreasing confidence in the results. • One cohort study[2] (N= 558,672) reported no association between ICU admission and IDD. ▪ One cohort study[2] (N = 558,672) of U.S. patients reported no difference in the odds of ICU admission among 3,897 COVID-19 patients with intellectual disabilities compared to those without intellectual disabilities when adjusting for common comorbidities [aOR 1.04 (95% CI: 0.94-1.15)].
Ventilation	Overall, limited data from only one study[8] is insufficient to determine an association between IDD and ventilation in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[8] (n= 66) reported data on ventilation and IDD in COVID-19 patients. As this study did not have a comparison group, it is not possible to determine an association between IDD and ICU admission. ▪ One cohort study[8] (N= 66) reported that 3.0% (2/66) of the COVID-19 patients with IDD who were living in residential or community settings or intermediate care facilities were mechanically ventilated.
Hospitalization	Overall, the evidence from three studies[2,7,9] (N= 566,288) indicates IDD is associated with an increase in hospitalization in COVID-19 patients. All three studies were found to have a moderate threat to internal validity. • Strength of Association: Two studies reported effect measures ranging from an unadjusted measure of OR= 1.85 to an adjusted measure of aOR=2.74. • Precision of Association: One study reported a narrow confidence interval for an adjusted odds ratio and the other study reported a wide confidence interval that crossed the null for an unadjusted odds ratio. • Consistency of Association: Overall, the evidence is consistent. • Applicability of Association: Three studies were conducted in the U.S. Summary of Evidence • Three cohort studies[2,7,9] (N= 566,288) reported that IDD is associated with an increase in hospitalization. ▪ One cohort study[2] (n= 558,672) comprised of U.S. patients reported an increase in the odds of hospitalization among 3,897 COVID-19 patients with intellectual disabilities compared to those without intellectual disabilities when adjusting for common comorbidities [aOR 2.74 (95% CI: 2.49-3.01)]. ▪ One cohort study[9] (n= 454) of pediatric patients in the US with Laboratory confirmed (positive SARS-CoV-2 PCR) COVID-19 suggested an increase in hospitalization among 38 patients with a developmental/behavioral comorbidity compared to those without a developmental/behavioral comorbidity [OR 1.85 (95% CI: 0.8-4.1), p = 0.13]. The study, which did

	not provide a definition for developmental/behavioral, reported a wide confidence interval that crossed the null, decreasing confidence in the result. ▪ One cohort study[7] (n= 7,162) of persons repatriated to the U.S. from Wuhan, China and the Diamond Princess cruise ship reported an increase in hospitalization among 52 COVID-19 patients with intellectual disabilities compared to those without intellectual disabilities [61.5% (32/52) vs. 9.0% (404/4,470), p = NR]. This study reported a low number of hospitalizations, decreasing confidence in the results.

Table 3 The Association between Intellectual and Developmental Disabilities (IDD), Risk Markers and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, evidence from four studies[2,4-6] (N= 1,876,163) indicates younger age and living in a nursing intermediate care facility for the developmentally disabled (ICF/DD) or skilled nursing facility are associated with an increase in mortality in COVID-19 patients. Three studies[2,5,6] were found to have a moderate threat to internal validity, and one[4] had a high threat to internal validity. • Strength of Association: One study reported adjusted measures of association ranging from 3.06-4.76. • Precision of Association: One study reported wide confidence intervals that do not cross the null. • Consistency of Association: Overall, the evidence is consistent. • Applicability of Association: Three studies were conducted in the U.S., and one study was multi-national. Summary of Evidence • Three cohort studies[2,5,6] (N= 1,056,727) suggested that being a younger adult with IDD and COVID-19 is associated with an increase in mortality. ▪ One cohort study[5] (N= 467,773) of U.S. patients reported an increase in the odds of mortality in patients of all ages with developmental disorders (aOR 3.06 [95% CI: 1.55-6.01] p = 0.01) when compared to those without developmental disorders, and for patients younger than 70 years old with developmental disorders (aOR 4.76 [95% CI: 1.86-12.22], p < 0.01) when compared to those without developmental disorders when adjusting for age and sex. The increase in mortality was larger when the analysis was restricted to patients under the age 70. This study did not report on the prevalence of IDD in the study population, decreasing confidence in the results. ▪ One cohort study[2] (n= 558,672) of U.S. patients reported no difference in mortality for admitted patients with intellectual disabilities under the age of 20 (0.82% [1/122] vs. 0.65% [22/3,385], p = NR) and those aged 60-79 years (16.67% [158/948] vs. 16.06% [10,528/65,554], p = NR) and 80 years or older (25.0% [22/88] vs. 24.36% [7,023/28,830], p = NR) when compared to admitted patients without intellectual disability. However, there was an increase in mortality for admitted patients with intellectual disability aged 20-39 years [5.24% (25/458) vs. 1.76% (387/21,989), p = NR] and 40-59 years (12.10% (102/843) vs. 6.65% [2,758/41,474] p = NR) when compared to those without intellectual disability. This study did not report on significance for these comparisons, decreasing confidence in the results. ▪ One cohort study[6] (n= 30,282) of patients in a global database of 42 healthcare organizations suggested an increase in mortality among patients aged 0-17 years with developmental disability (1.6% [2/125] vs. 0.1% [1/791], p = NR) and among patients aged 18-74 with developmental disability [4.5% (14/311) vs. 2.7% (671/24,456), p = NR] when compared to those without developmental disability, however there was no difference among patients aged 75 and

	older [21.1% (8/38) vs. 20.7% (942/4,561), p = NR]. This study reported a low number of deaths, decreasing confidence in the results. • One cohort study[4] (n= 819,436) reported that mortality rates were higher in patients in a nursing (ICF/DD) and skilled nursing facility than in their own home, community care facility, habilitative ICF/DD, or ICF/DD. ▪ One study[4] (n= 819,436) of 2,948 individuals living in California and receiving IDD services reported 2.8% (47/1,651) of the patients who received IDD services in their own home or family home, 4.3% (23/538) of the patients in a community care facility, 6.2% (13/209) of the patients in a habilitative ICF/DD, 15.8% (15/95) of the patients in a nursing ICF/DD, 4.7% (5/106) of the patients in an ICF/DD, and 20.4% (58/284) of the patients in a skilled nursing facility died. The study did not report any measures of association for this outcome.
Hospitalization	Overall, limited data from only one study[8] is insufficient to determine an association between IDD, sex, and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[8] (N=66) reported that an increase in hospitalization was associated with male sex in COVID-19 patients with IDD. ▪ One cohort study[8] (N=66) of 66 individuals with intellectual and developmental disabilities who tested positive for COVID-19 and lived in residential or community settings and intermediate care facilities in the US reported that hospitalization was more likely among individuals with IDD who were male. This study did not report a measure of effect.

Table 4 The Association between IDD and Other Comorbidities and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[8] is insufficient to determine an association between IDD, other comorbidities, and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[8] (N=66) reported that hospitalization increased in COVID-19 patients with IDD as the number of chronic medical conditions increased. ▪ One cohort study[8] (N=66) of 66 US patients with intellectual and developmental disabilities who tested positive for COVID-19 and lived in residential or community settings and intermediate care facilities reported that hospitalization was more likely among individuals with IDD who had a higher number of chronic medical conditions. This study did not report a measure of effect.

Table 5 The Association between Disability (Composite) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence from four studies[11-14] (N=10,753) suggests disability (composite) is associated with an increase in mortality in COVID-19 patients. All four studies were found to have a moderate threat to internal validity. • Strength of Association: Three studies reported measures of association ranging from 0.27 - 1.32. • Precision of Association: Of the three studies reporting confidence intervals, two were wide, crossing the null and one was narrow, crossing the null. • Consistency of Association: The evidence is consistent in the direction of increased mortality • Applicability of Association: Two studies were conducted in the US, one was conducted in South Korea, and one was conducted in Italy. Summary of Evidence • Three studies[11,12,14] (N=10,753) reported effect measures and proportions suggesting an increase in mortality in patients with disability and COVID-19. ▪ One cohort study[14] (N=516) of geriatric patients hospitalized with COVID-19 in Italy suggested an increased hazard of mortality among 171 patients with functional disability compared to patients without disability when adjusting for sex, age, functional disability, dementia, number of chronic diseases, use of CPAP, nutritional status, chest X-ray or CT findings, and serum CRP [aHR 1.32 (95% CI: 0.89 - 1.96), p < 0.17]. Functional disability was measured by the presence of a dependence in bathing or dressing or a Barthel Index score of 90 or more or 100 one month before hospitalization. This study reported a confidence interval crossing the null, and the p-value was not significant, decreasing confidence in the results. ▪ One cross-sectional ecological study[11] (n = NR) of US counties reported an increase in the odds of mortality in counties with higher disability rates compared to counties with lower disability rates [estimate 0.27 (95% CI: 0.09 - 0.45), p < 0.02]. The number of people with disabilities and COVID-19 was unknown in this study. ▪ One cohort study[12] (n = 10,237) of people in South Korea with COVID-19 reported a higher proportion of mortality among those with disabilities compared to those with no disabilities [8.2% (62/760) vs. 1.8% (166/9,477), p = NR]. The study did not conduct statistical analyses. • One study[13] (n = NR) reported effect measures suggesting no association in mortality between disabled and non-disabled patients. ▪ One cross-sectional study[13] (N= NR) reported no association between mortality and disabled patients compared to non-disabled patients [IRR: 0.99 (95% CI: 0.98 - 1.01), p = 0.35]. Disability was measured by the Social Vulnerability Index (SVI) which was developed by the Centers for Disease Control and Prevention to provide a composite measure of community susceptibility to adversities in the face of health shocks, including disease outbreaks. This study did not report on prevalence of underlying disability among the sample population.

Table 6 The Association between Severity of Disability (Composite) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence from three studies[12,15,16] (N=16,069) suggests severity of disability is associated with an increase in mortality in COVID-19 patients. All three studies were found to have a moderate threat to internal validity. • Strength of Association: Three studies reported adjusted measures of association (for the highest severity of disability) from 1.63 to 3.60. • Precision of Association: Of the three studies reporting confidence intervals, all three were wide. • Consistency of Association: The evidence is consistent in the direction of increased mortality • Applicability of Association: One study was conducted in South Korea, one was conducted in Europe, and one was conducted in the U.S. Summary of Evidence • Three studies[12,15,16] (N=16,069) reported adjusted effect measures indicating that severity of disability is associated with an increase in mortality in COVID-19 patients. ▪ One cohort study[12] (N=10,237) of patients with confirmed COVID-19 reported an increase in mortality among 760 patients with all severity levels of disability when compared to those without disabilities in univariable analysis. When analyses were adjusted by age, sex, income level, residence, household type, disability, symptom, and infection route, the increase in risk remained significant only among 244 patients with moderate to severe disabilities [aHR: 1.63 (95% CI: 1.01 - 2.63), $p < 0.05$]. This study had a low number of deaths, decreasing confidence in the results. ▪ One study[15] (N=5,256) of symptomatic nursing home residents with COVID-19 reported an increased odds of mortality among 1,410 patients with ADL impairment scores in the highest quartile (21-28), which is the most severe dependence for ADL [aOR: 1.64 (95% CI: 1.30-2.08), p = NR], and 1,179 patients with scores in the third quartile (19-20) [aOR: 1.49 (95% CI: 1.18-1.88), p = NR] compared to patients with scores in the lowest quartile (0-13) when adjusting for age, sex, race/ethnicity, comorbidities, symptoms, ADL score, and cognitive function. When comparing 1,320 patients with scores in the second quartile (14-18) to patients with scores in the lowest quartile, the study suggested no difference in the odds of mortality after adjustment [aOR: 0.98 (95% CI: 0.77-1.25), p = NR] ▪ One cohort study[16] (N=576) of hospitalized COVID-19 patients 18 years and older in Spain reported an increased odd of mortality in patients with mRS≥3 when compared to patients with modified Rankin scale scores (mRS)<3 when adjusting for age, sex, hypertension, diabetes, cardiological disorders, pulmonary disorders, cancer, chronic neurological disorders, smoking, anosmia, prior mRS≥3, and time from clinical onset to the emergency department [aOR: 3.60 (95% CI: 1.79 – 7.20), $p < 0.01$]. A higher mRS score indicated a greater degree of disability/dependence prior to hospitalization. This study reported wide confidence intervals and only included hospitalized patients, decreasing confidence in the results.
ICU Admission	Overall, limited data from only one study[16] is insufficient to determine an association between prior mRS ≥3 and ICU admission in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study.

	• One cohort study[16] reported effect measures suggesting that mRS≥3 is associated with a decrease in ICU admission in COVID-19 patients. ▪ One cohort study[16] (N=576) of hospitalized COVID-19 patients 18 years and older in Spain reported a decreased odds of ICU admission in patients with mRS≥3 when compared to patients with mRS<3 adjusting for time from clinical onset to the emergency departments, mRS, age, sex, diabetes, and smoking [aOR: 0.07 (95% CI: 0.01 – 0.55), p = 0.01]. A higher prior mRS score indicated a greater degree of disability/dependence prior to hospitalization. This study reported wide confidence intervals and only included hospitalized patients, decreasing confidence in the results.

Table 7 The Association between Risk Markers in Disability (Composite) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited evidence from two studies[11,17] is inconclusive on the association between sex, poverty, disability, and mortality in COVID-19 patients. Both studies were found to have a moderate threat to internal validity. • Strength of Association: One study reported measures of association ranging from 1.21-1.55. • Precision of Association: Of the one study reporting confidence intervals, none were wide, and none reported confidence intervals crossed the null. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: Settings were applicable. One study was conducted in the U.S. and one was conducted in the UK. Summary of Evidence • One study[17] (N=NR) reported measures of association suggesting an increase in mortality for both men and women with disability. ▪ One cohort study[17] (N=NR) of adult patients over 30 years in England suggests a higher hazard of mortality in women than in men, regardless of severity of disability [less-disabled: aHR: 1.28 (95% CI: 1.25 - 1.31), p = NR; more-disabled: aHR: 1.55 (95% CI: 1.51 - 1.59), p = NR] [less-disabled: aHR: 1.21 (95% CI: 1.18 - 1.23), p = NR; more-disabled: aHR: 1.35 (95% CI: 1.32 - 1.38), p = NR] when adjusting for age, residence type, local authority district, population density, area deprivation, socioeconomic status, ethnicity, household composition, occupational exposure, and pre-existing conditions. Disability status was self-reported. • One study[11] (N=NR) reported estimates suggesting that poverty in disabled patients is not associated with mortality. ▪ One cross-sectional ecological study[11] (N=NR) reported that including poverty as an interaction term with disability in the linear regression model analyzing death rate did not result in a significant result (p < 0.47) and suggested these two variables could be independent in their contribution to the risk of mortality. The number of people with disabilities and COVID-19 was unknown in this study.

Table 8 The Association between Down Syndrome and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence from five studies[10,18-21] (N=14,386,205) indicates Down syndrome is associated with an increase in mortality in COVID-19 patients. All five studies were found to have a moderate threat to internal validity. • Strength of Association: Four studies reported measures of association ranging from 1.51 - 24.37. • Precision of Association: Of the four studies reporting confidence intervals, all four were wide, but none included the null. • Consistency of Association: The evidence is consistent in the direction of increased mortality • Applicability of Association: Two studies were conducted in Europe, one in Latin America, one in the Middle East, and one was an international survey. Summary of Evidence • Five studies[10,18-21] (N= 14,386,205) suggested that Down syndrome is associated with an increase in mortality among people with COVID-19. Three cohorts[10,19,21] (n=8,303,031) and one case-control[20] (n=72) reported effect measures ranging from 1.51 (95% CI: 1.2 - 1.9) to 24.37 (95% CI: 2.39 - 247.94) among 4,459 COVID-19 patients with Down syndrome, of which three[10,19,20] reported adjusted measures ranging from 2.49 (95% CI: 1.51 - 3.69) to 24.37 (95% CI: 2.39 - 247.94). One cohort study[18] reported prevalence rates suggesting that Down syndrome is associated with an increase in mortality (p = NR). ○ Four studies[10,19-21] reported wide confidence intervals, however none included the null. Two[18,19] reported a low prevalence of Down syndrome in the study population, and one[20] included few patients with Down syndrome, decreasing confidence in the results. Two studies[20,21] were conducted in middle-income countries. Adjusted measures controlled for chronic cardiac disease, chronic pulmonary disease, chronic kidney disease, liver disease, obesity, chronic neurological disorder, dementia, malignant neoplasm, age, sex, data source (caregiver vs. Clinician survey), country of residence, BMI, Townsend score, ethnic group, domicile, comorbid conditions, treatments, respiratory distress, headache, intubation, death, smoking status, alcohol intake, ethnicity, dementia diagnosis, care home residency, and congenital heart disease.
ICU Admission	Overall, limited data from only one study[22] is insufficient to determine an association between Down syndrome and ICU admission in COVID-19 patients. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One study[22] (N=502,656) suggested that Down syndrome is associated with an increase in ICU admission among people with Down syndrome and COVID-19. ▪ One case-control[22] (N=502,656) using data from Swedish nationwide registries reported an increase in the odds of ICU admission among 57 COVID-19 patients with Down syndrome compared to those without Down syndrome when adjusting for demographic variables, comorbidities, and prescription medications [aOR: 4.26 (95% CI: 1.01-17.90), p = NR]. This study reported a wide confidence interval and a low prevalence of Down syndrome in the study population, decreasing confidence in the result.

Intubation	Overall, limited data from only one study[20] is insufficient to determine an association between Down syndrome and intubation in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One study[20] (N=72) reported proportions suggesting that Down syndrome is associated with an increase in intubation among people with Down syndrome and COVID-19. ▪ One case-control[20] (N=72) of patients admitted to healthcare facilities with confirmed, probable, or possible COVID-19 reported a higher proportion of intubation among patients with Down syndrome and COVID-19 compared to patients without Down syndrome (39% [7/18] vs. 6% [3/54], p < 0.01). The directionality of increased risk was no longer statistically significant in the logistic regression model when adjusting for respiratory distress, headache, and death (p = 0.24). The study reported few patients with Down syndrome, decreasing confidence in the results.
Ventilation	Overall, limited data from only one study[23] is insufficient to determine an association between Down syndrome and ventilation in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Down syndrome, and aggregation indices are not assessed for outcomes reported by only one study. • One study[23] (N= 205) reported on ventilation in COVID-19 patients with Down syndrome, and due to the small number of patients with Down syndrome, limited conclusions can be drawn from the study. ▪ One cohort study[23] (N=100) of pediatric patients admitted to an Iranian hospital included a patient with Down syndrome who was ventilated and compared that to 61/99 patients without Down syndrome who were ventilated [100% (1/1) vs. 61.6% (61/99), p = NR]. This study included only one patient with Down syndrome, limiting the ability to assess the association between Down syndrome and ventilation.
Hospitalization	Overall, the evidence from three studies[18,19,22] (N=539,189) indicates Down syndrome is associated with an increase in hospitalization in COVID-19 patients. One study[22] was found to have a low threat to internal validity, and two studies[18,19] had a moderate threat to internal validity. • Strength of Association: Two studies reported measures of association (aOR) ranging from 3.24 – 4.94. • Precision of Association: Of the two studies reporting confidence intervals, both were wide. • Consistency of Association: The evidence is consistent in the direction of increased hospitalization • Applicability of Association: Two studies were conducted among primary care practices in England and one among a national Swedish registry. Summary of Evidence • Three studies[18,19,22] (N= 539,189) suggested that Down syndrome is associated with an increase in hospitalization among patients with COVID-19. ▪ One case-control[22] (N=502,656) using data from Swedish nationwide registries reported an increase in the odds of hospitalization among 57 COVID-19 patients with Down syndrome compared to those without Down syndrome when adjusting for demographic variables, comorbidities, and prescription medications [aOR: 3.24 (95% CI: 1.55-6.78), p = NR]. This study reported a wide confidence interval and a low prevalence of Down syndrome in the study population, decreasing confidence in the result.

	▪ One cohort study[19] (N=36,428) using a national primary care database of adult English patients reported an increase in the hazard of hospitalization among 4,053 COVID-19 patients with Down syndrome compared to those without Down syndrome when adjusting for age, sex, ethnicity, BMI, dementia diagnosis, care home residency, congenital heart disease, and a range of other comorbid conditions and treatments [aHR 4.94 (95% CI: 3.63-6.73), p = NR]. This study reported a wide confidence interval and a low prevalence of Down syndrome in the study population, decreasing confidence in the findings. ▪ One cohort study[18] (N=NR) using a national primary care database of adult English patients reported an increase in hospitalization in COVID-19 patients with Down syndrome when compared to those without Down syndrome [0.90% (27/3,013) vs. 0.18% (10,749/6,080,089), p = NR]. This study did not report on significance and the study population had a low prevalence of Down syndrome, decreasing confidence in the result.

Table 9 Severity of Underlying Down Syndrome and Intellectual Disability Examined for Association with Severe COVID-19 Outcomes

Mortality	Overall, limited data from only one study[10] is insufficient to determine an association between mortality and severity of Down syndrome in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One study[10] (N=588) reported an increase in mortality among Down syndrome patients with more severe intellectual and developmental disabilities (IDD). ▪ One cohort[10] (N=588) suggested an increase in mortality among 184 symptomatic COVID-19 patients with Down syndrome who have severe or profound IDD when compared to those who have borderline, normal, or mild IDD when adjusting for age, sex, data source and country of residence [aOR: 1.33 (95% CI: 0.47-3.77), p = 0.59]. However, there was a decrease in mortality among 580 symptomatic COVID-19 patients with Down syndrome who have moderate IDD [aOR: 0.81 (95% CI: 0.30-2.17), p = 0.68]. This study reported confidence intervals that included the null, decrease confidence in the findings.
Hospitalization	Overall, limited data from only one study[10] is insufficient to determine an association between hospitalization and severity of Down syndrome in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One study[10] (N=588) reported an increase in hospitalization among Down syndrome patients with more severe intellectual and developmental disabilities (IDD). ▪ One cohort[10] (N= 588) suggested an increase in hospitalization among 184 symptomatic COVID-19 patients with Down syndrome who have severe or profound IDD [aOR: 1.19 (95% CI: 0.67-2.09), p = 0.55] and 580 patients who have moderate IDD [aOR: 1.21 (95% CI: 0.78-1.89), p = 0.40] when compared to those who have borderline, normal, or mild IDD when adjusting for age, sex, data source and country of residence. This study reported confidence intervals that included the null, decreasing confidence in the findings.

Table 10 The Association between Down syndrome and Other Comorbidities and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[10] is insufficient to determine an association between Down syndrome, comorbidities, and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[10] (N=588) reported an increase in mortality in COVID-19 patients with Down syndrome and obesity and Alzheimer's disease or dementia, and a decrease in mortality among those with Down syndrome and obstructive sleep apnea, congenital heart defect, behavioral and psychiatric conditions, chronic lung disease, or diabetes. ▪ One study[10] (N=588) reported an increase in the odds of mortality in COVID-19 patients with Down syndrome and obesity [aOR: 1.33 (95% CI: 0.75-2.35), p = 0.32] and Alzheimer's disease or dementia [aOR: 2.13 (95% CI: 1.10-4.12), p < 0.03] when adjusting for age, sex, data source, and country of residence. As the number of comorbidities increased, so did the odds of mortality in COVID-19 patients with Down syndrome [aOR: 1.26 (95% CI: 0.89-1.77), p < 0.19]. The study suggested a decrease in the odds of mortality in COVID-19 patients with Down syndrome and obstructive sleep apnea [aOR: 0.68 (95% CI: 0.37-1.26), p = 0.22], congenital heart defect [aOR: 0.89 (95% CI: 0.47-1.66), p = 0.70], behavioral and psychiatric condition [aOR: 0.85 (95% CI: 0.48-1.49), p = 0.56], chronic lung disease [aOR: 0.80 (95% CI: 0.38-1.70), p = 0.56], or diabetes [aOR: 0.54 (95% CI: 0.24-1.21), p < 0.14]. The study reported wide confidence intervals, and many included the null, decreasing confidence in these findings.
Hospitalization	Overall, limited data from only one study[10] is insufficient to determine an association between Down syndrome, comorbidities, and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[10] (N=588) reported an increase in hospitalization in COVID-19 patients with Down syndrome and other comorbidities. ▪ One cohort study[10] (N=588) reported an increase in the odds of hospitalization among COVID-19 patients with Down syndrome and obesity [aOR: 2.03 (95% CI: 1.44-2.87), p < 0.01], obstructive sleep apnea [aOR: 1.17 (95% CI: 0.84-1.65), p = 0.35], congenital heart defect [aOR: 1.46 (95% CI: 1.05-2.03), p < 0.03], diabetes [aOR: 1.93 (95% CI: 1.20-3.12), p < 0.01] when adjusting for age, sex, data source, and country of residence. As the number of comorbidities increased, so did the odds of hospitalization in COVID-19 patients with Down syndrome [aOR: 1.12 (95% CI: 0.90-1.41), p < 0.32]. The study reported a decrease in the odds of hospitalization in COVID-19 patients with Down syndrome and Alzheimer's disease or dementia [aOR: 0.77 (95% CI: 0.44-1.36), p = 0.37] or chronic lung disease [aOR: 0.89 (95% CI: 0.60-1.31), p = 0.55]. The study reported wide confidence intervals, and many included the null, decreasing confidence in these findings.

Table 11 The Association between Down Syndrome and Risk Markers and Severe COVID-19 Outcomes

Mortality	Overall, the evidence from two studies[10,18] (N=588) indicates female sex and older age are associated with an increase in mortality in COVID-19 patients with Down syndrome. Both studies were found to have a moderate threat to internal validity. • Strength of Association: Two studies reported adjusted measures of association ranging from 2.42 - 32.55. • Precision of Association: Of the two studies reporting confidence intervals, one reported a wide confidence interval. • Consistency of Association: The evidence is consistent in the direction of increased mortality. • Applicability of Association: Two studies were conducted, one of primary care patients in England, and one was an international survey. Summary of Evidence • Two studies[10,18] (N=588) reported effect measures suggesting that mortality in COVID-19 patients with Down syndrome was greater among females and older patients. ▪ One cohort study[18] (N=NR) reported an increase in mortality in COVID-19 patients with Down syndrome compared to those without Down syndrome regardless of sex, however a larger increase was observed for female patients [aHR 32.55 (95% CI: 18.13-58.42), p = NR] than for male patients [aHR 9.80 (95% CI: 4.62-20.78), p = NR] when adjusting for age, BMI, Townsend score, ethnic group, domicile, and comorbid conditions and treatments. This study reported wide confidence intervals, decreasing confidence in the findings. ▪ One cohort study[10] (N=588) reported an increase in mortality in COVID-19 patients with Down syndrome compared to those without Down syndrome regardless of age, however a larger increase was observed for 147 patients aged 40 and older [aRR: 2.73 (95% CI: 1.71-3.84), p < 0.01] than for 41 patients aged younger than 40 [aOR: 2.42 (95% CI: 0.12-12.88), p = 0.44] when adjusting for chronic cardiac disease, chronic pulmonary disease, chronic kidney disease, liver disease, obesity, chronic neurological disorder, dementia, and malignant neoplasm. This study reported wide confidence intervals, one of which included the null, decreasing confidence in the results.
Hospitalization	Overall, limited data from only one study[18] is insufficient to determine an association between sex and hospitalization in COVID-19 patients with Down syndrome. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One study[18] reported effect measures suggesting that hospitalization in COVID-19 patients with Down syndrome was greater among females. ▪ One cohort study[18] (N=NR) reported an increase in hospitalization in COVID-19 patients with Down syndrome compared to those without Down syndrome regardless of sex, however a larger increase was observed for female patients [aHR 8.84 (95% CI: 5.37-14.55)] than for male patients [aHR 4.36 (95% CI: 2.39-7.94)] when adjusting for age, BMI, Townsend score, ethnic group, domicile, and comorbid conditions and treatments. This study reported wide confidence intervals, decreasing confidence in the findings.

Table 12 The Association between Dependence and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence from five studies[24-28] (N=1,879) indicates dependence is associated with an increase in mortality in COVID-19 patients. Four studies[25-28] were found to have a moderate threat to internal validity, and one[24] had a high threat to internal validity. • Strength of Association: Three studies reported measures of association ranging from 0.64-2.51. • Precision of Association: Of the three studies reporting confidence intervals, two were wide. • Consistency of Association: The evidence is consistent in the direction of increased mortality among patients with some level of dependence. • Applicability of Association: Two studies were conducted in Europe, one in the US, and one in the Middle East. Summary of Evidence • Five studies[24-28] (N= 1,879) reported data suggesting that dependence is associated with an increase in mortality among hospitalized COVID-19 patients. Two cohort studies[26,27] that included 136 patients with exposures reported an adjusted odds of 2.51 (95% CI: 1.02 - 6.15) and an adjusted hazard of 2.51 (95% CI: 1.38-3.94) suggesting severe functional dependency[26] or dependence for basic activities of daily living[27] were associated with an increase in mortality. One cohort study reported complete autonomy[28] was associated with a decrease in mortality [0.64 (95%CI: 0.42-0.98)]. One cohort study[24] suggested an increase in mortality among patients with high or mild to moderate dependence compared to those with no dependence (53% vs. 27% vs. 19%, $p < 0.01$). And one ecological study[25] (n = 369 counties) using county-level data in the US suggested that counties with a higher population of independent living difficulty had a higher rate of COVID-19 mortality, but not significant, when adjusting for total population, median income, and state [estimate: 0.16 (95% CI: 0-0.32), $p > 0.50$]. ▪ Two studies[26,27] reported wide confidence intervals that did not cross the null, three[24,26,27] had small sample sizes, and one[27] did not define dependence for basic activities of daily living, decreasing confidence in these findings. One study[25] used county-level data to assess the association between mortality and independent living difficulty. Dependence was heterogeneously defined across studies, however this did not contribute to differences in the magnitude of effect.
ICU admission	Overall, limited data from only one study[28] is insufficient to determine an association between dependence and ICU admission in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[28] reported an adjusted effect measure suggesting that dependence is associated with a decrease in ICU admission among hospitalized COVID-19 patients. ▪ One study[28] (N=1,264) of adults in Italy with symptoms and chest findings compatible with COVID-19 interstitial pneumonia suggested an increase in ICU admission among 784 patients with complete autonomy in daily activities compared to 470 patients with complete or partial dependence when adjusting for age, sex, and period of admission [aOR 41.6 (95% CI: 2.8-615), $p < 0.01$]. Complete or partial dependence was defined as total or partial dependency in performing daily activities as retrieved from the medical history and were considered as a proxy of disability and frailty. As the median age of the study population was 71 during the first wave and 79 in the second, there is likely

	confounding due to age. This study reported a low number of ICU admissions among those with complete or partial dependence in daily activities, leading to a wide confidence interval and decreased confidence in the finding.
Ventilation	Overall, limited data from only one study[28] is insufficient to determine an association between dependence and ventilation in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[28] reported an adjusted effect measure suggesting that dependence is associated with a decrease in non-invasive ventilation among hospitalized COVID-19 patients. ▪ One study[28] (N=1,264) of adults in Italy with symptoms and chest findings compatible with COVID-19 interstitial pneumonia suggested an increase in ventilation among 784 patients with complete autonomy in daily activities compare to 470 patients with complete or partial dependence when adjusting for age, sex, and period of admission [aOR 13.50 (95% CI: 4.34-41.92), p < 0.01]. Complete or partial dependence was defined as total or partial dependency in performing daily activities as retrieved from the medical history and were considered as a proxy of disability and frailty. As the median age of the study population was 71 during the first wave and 79 in the second, there is likely confounding due to age. This study reported a low number of ventilations among those with complete or partial dependence in daily activities, leading to a wide confidence interval and decreasing confidence in the finding.
Hospitalization	Overall, limited data from only one study[29] is insufficient to determine an association between dependence and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[29] reported an effect measure suggesting a decrease in the odds of hospitalization for people with COVID-19 who were dependent. ▪ One study[29] (N=10,454) of people with COVID-19 in Spain suggested a decrease in hospitalization among 132 people who were dependent compared to those who were not dependent [aOR 0.62 (95% CI: 0.42-0.93)]. The study had a low number of hospitalization events in those who were dependent (n = 42), reducing confidence in the results.

Table 13 The Association between the Severity of Dependence and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence from two studies[24,28] (N=1,455) suggests the level of dependence is associated with an increase in mortality in COVID-19 patients. One study[28] was found to have a moderate threat to internal validity, and one[24] had a high threat to internal validity.

	• Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: The evidence is consistent in the direction of increased mortality. • Applicability of Association: One study was conducted in the US and one in Europe. Summary of Evidence • Two cohort studies[24,28] (N=1,455) suggested that more severe dependence is associated with an increase in mortality in COVID-19 patients with some level of dependence. ▪ One study[24] (N=191) of hospitalized adults with COVID-19 over the age of 60 years in the US reported an increase in mortality among patients with high dependence compared to those with mild to moderate dependence (53.0% vs. 27.0%, p = NR). High and mild to moderate dependence were classified based on functional state prior to hospitalization using ADL dependence, use of walking aids, and living situation as document in the medical record by case managers. This study had a small sample size and did not report on significance for this comparison, decreasing confidence in the finding. ▪ One study[28] (N=1,264) of adults in Italy with symptoms and chest findings compatible with COVID-19 interstitial pneumonia reported an increase in mortality among patients with complete dependence in daily activities compared to those with partial dependence [43% (90/210) vs. 34% (87/257), p = NR]. Complete or partial dependence was defined as total or partial dependency in performing daily activities as retrieved from the medical history and were considered as a proxy of disability and frailty. This study did not report on significance for this comparison, decreasing confidence in the finding.
ICU admission	Overall, limited data from only one study[28] is insufficient to determine an association between the level of dependence and ICU admission in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One study[28] suggested no association between severity of dependence and ICU admission among hospitalized COVID-19 patients with some level of dependence in daily activities. ▪ One study[28] (N=1,264) of adults in Italy with symptoms and chest findings compatible with COVID-19 interstitial pneumonia reported no difference in ICU admissions among patients with complete dependency in daily activities compared to those with partial dependence [0% (0/210) vs. 1% (3/257), p = NR]. This study reported a low number of ICU admissions among patients with either complete or partial dependency in daily activities, decreasing confidence in the finding.
Ventilation	Overall, limited data from only one study[28] is insufficient to determine an association between the level of dependence and ventilation in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study.

	• One study[28] suggested complete dependency in daily activities is associated with a decrease in non-invasive ventilation in COVID-19 patients with some level of dependence in daily activities. ▪ One study[28] (N=1,264) of adults in Italy with symptoms and chest findings compatible with COVID-19 interstitial pneumonia reported a decrease in non-invasive ventilation among patients with complete dependence in daily activities compared to those with partial dependence [0% (0/210) vs. 5% (13/257), p = NR]. This study reported a low number of non-invasive ventilations among patients with either complete or partial dependency in daily activities and the study did not report on significance for this comparison, decreasing confidence in the finding.
Hospitalization	Overall, limited data from only one study[30] is insufficient to determine an association between the level of dependence and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort[30] reported on the level of dependence among hospitalized COVID-19 patients. As this study did not have a comparison group, it is not possible to determine an association between dependence and hospitalization. ▪ One study[30] (N=254) of hospitalized COVID-19 patients in Spain reported 6.7% (17/254) were dependent, 3.5% (9/254) were semi-dependent, and 81.1% (206/254) were independent (p < 0.01). The levels of dependence were not defined, and the study had no comparison group and included a small number of patients who were dependent.

Table 14 The Association between Dependence and Risk Factors and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence from two studies[25,26] (N=NA – different units of measurement) suggests age and White race modifies the association between dependence and mortality in COVID-19 patients. Both studies were found to have a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: One study reported wide confidence intervals. • Consistency of Association: The evidence is consistent in the direction of increased mortality. • Applicability of Association: One study was conducted in the US and one in the Middle East. Summary of Evidence • One ecological study[25] (N=369 countries) suggested an increase in the risk of mortality among White disabled populations and younger adults living with disabilities. ▪ One ecological study[25] (N=369 countries) reporting bivariate regression analysis estimates using county-level data in the US suggested that counties with a higher prevalence of disability among White persons (parameter estimate: 0.19

	(95% CI: 0.01-0.37] p < 0.04) and those aged 18-34 [estimate: 0.17 (95% CI: 0.02-0.31), p = 0.02] had a higher rate of SARS-CoV-2 mortality when adjusting for total population, median income, and state. • One cohort study[26] reported proportions suggested mortality increased for patients with severe functional dependency regardless of age. ▪ One study[26] (N=186) suggested an increase in the prevalence of mortality for COVID-19 patients with severe functional dependency compared to patients without severe functional dependency for those aged 65-79 years [18.3% (6/32) vs. 8.7% (6/69), p = NR] and those aged 80 years and older [45.6% (26/57) vs. 17.9% (5/28), p < 0.05], and this increase was slightly larger among older patients. Severe functional dependency was evaluated by the Katz Index of Independence in Activities of Daily Living such as bathing, dressing, toileting, transfer, continence, and feeding, and were defined as scores 0-3. This study had a small sample size with a low number of deaths for each group and did not report on significance for some of these comparisons, decreasing confidence in the findings.
ICU admission	Overall, limited data from only one study[26] is insufficient to determine whether age modifies the association between dependence and ICU admission in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[26] suggested ICU admission increased for patients with severe functional dependency regardless of age. ▪ One study[26] (N=186) suggested an increase in the prevalence of ICU admission for COVID-19 patients with severe functional dependency compared to patients without severe functional dependency for those aged 65-79 years [31.3% (10/32) vs. 11.6% (8/69), p < 0.05] and those aged 80 years and older [21.1% (12/57) vs. 14.3% (4/28), p = NR], however this increase was larger among younger patients. Severe functional dependency was evaluated by the Katz Index of Independence in Activities of Daily Living such as bathing, dressing, toileting, transfer, continence, and feeding, and were defined as scores 0-3. This study had a small sample size with a low number of ICU admissions for each group , decreasing confidence in the findings.
Ventilation	Overall, limited data from only one study[26] is insufficient to determine whether age modifies the association between dependence and ventilation in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[26] suggested mechanical ventilation increased for patients aged 65-79 with severe functional dependency, but not for patients aged 80 and older. ▪ One study[26] (N=186) suggested an increase in the prevalence of mechanical ventilation for COVID-19 patients aged 65-79 years with severe functional dependency compared to those without severe functional dependency [18.8% (6/32) vs. 5.8% (4/69), p < 0.05], however, there was no difference among those aged 80 years and older [14.0% (8/57) vs. 14.3% (4/28), p = NR]. Severe functional dependency was evaluated by the Katz Index of Independence in Activities of Daily Living such as bathing, dressing, toileting, transfer, continence, and feeding, and were defined as scores 0-3. This study had a small sample size with a low number of ventilations for each group, decreasing confidence in the findings.

Table 15 The Association between Learning Disabilities (Composite) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence from four studies[18,19,31,32] (N=88,051) indicates that learning disabilities (composite) are associated with an increase in mortality in COVID-19 patients. All four studies were found to have a moderate threat to internal validity. • Strength of Association: Three studies reported adjusted measures of association ranging from 1.27 to 4.75. • Precision of Association: Of the three studies reporting confidence intervals, two were wide and one was narrow. • Consistency of Association: Overall, the evidence is consistent. • Applicability of Association: All four studies were conducted in the United Kingdom. Summary of Evidence • Four cohort studies[18,19,31,32] (N=88,051) suggested that learning disabilities are associated with an increase in mortality in COVID-19 patients in the United Kingdom. Three cohort studies[19,31,32] (N=88,051) reported adjusted odds ratios ranging from 1.27 (95% CI: 1.16-1.40) to 4.75 (95% CI: 1.91-11.84) among 629 COVID-19 patients with learning disabilities. One cohort study[18] (N=NR) reported prevalence rates suggesting that learning disabilities are associated with an increase in mortality. All four studies were conducted in high income countries. ▪ Two studies[31,32] (N=51,623) indicated wide confidence intervals, and neither crossed the null. One study[31] included only 28 patients with an underlying learning disability and one study[19] did not report the prevalence of underlying learning disabilities in the study sample, reducing confidence in the results.
ICU admission	Overall, limited data from only one study[31] is insufficient to determine an association between learning disability and ICU admission in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[31] (N=1,781) reported an effect measure suggesting that learning disability is associated with an increase in ICU admission. ▪ One cohort study[31] (N=1,781) of English patients aged 16 years or older suggested an increase in the odds of ICU admission among 28 COVID-19 patients with learning disabilities compared to those without learning disabilities when adjusting for demographic and socioeconomic factors, obesity, smoking status, and 17 individual clinical factors [aOR 1.22 (95% CI: 0.26-5.79), p = 0.80]. The confidence interval is wide and crosses the null, decreasing confidence in the result.
Hospitalization	Overall, the evidence from two studies[18,31] (N=1,781) suggests learning disabilities are associated with an increase in hospitalization in COVID-19 patients. Both studies were found to have a moderate threat to internal validity. • Strength of Association: One study reported an adjusted odds ratio of 2.07.

	• Precision of Association: One study reported a wide confidence interval. • Consistency of Association: Overall, the evidence is consistent. • Applicability of Association: Both studies were conducted in England. Summary of Evidence • Two cohort studies[18,31] (N=1,781) suggested that learning disability is associated with an increase in hospitalization. ▪ One cohort study[31] (N=1,781) of English patients aged 16 years or older suggested an increase in the odds of hospitalization among 28 COVID-19 patients with a learning disability compared to those without a learning disability when adjusting for demographic and socioeconomic factors, obesity, smoking status, and 17 individual clinical factors [aOR 2.07 (95% CI: 0.78-5.45), p = 0.14]. The confidence interval is wide and crosses the null, decreasing confidence in the result. ▪ One cohort study[18] (N=NR) of English adults suggested a higher prevalence of hospitalization in COVID-19 patients with learning disabilities compared to those without learning disabilities [0.46% (498/107,107) vs. 0.17% (10,251/5,972,982), p = NR]. As this study did not report the number of patients with COVID-19 infection, the prevalence of hospitalization was calculated among the entire study population of those with and without COVID-19. The study also did not report on significance for this comparison, decreasing confidence in the result.

Table 16 The Association between Learning Disability and Risk Markers and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[18] is insufficient to determine an association between learning disability, sex, and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[18] (N=NR) reported mortality increased in COVID-19 patients with learning disabilities regardless of sex. ▪ One cohort study[18] (N=NR) of English adults with COVID-19 reported similar increases in the hazard of mortality for both men [aHR 1.36 (95% CI: 1.14 -1.60)] and women with learning disabilities [aHR 1.36 (95% CI: 1.11-1.65)].
Hospitalization	Overall, limited data from only one study[18] is insufficient to determine an association between IDD, sex, and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[18] (N=NR) reported an increase in hospitalization in COVID-19 patients with learning disabilities was greater among females than males.

	▪ One cohort study[18] (N=NR) of English adults reported an increase in the hazard of hospitalization in both men [aHR 1.38 (95% CI: 1.22 -1.56)] and women [aHR 1.53 (95% CI: 1.34-1.76)] with learning disabilities compared to those without learning disabilities, however the increase in hospitalization was greater among women.

Table 17 The Association between Activities of Daily Living (ADL) Impairments and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence from three studies[15,33,34] (N=5,828) indicates activities of daily living (ADL) impairments are associated with an increase in mortality in COVID-19 patients. Two studies[15,34] were found to have a moderate threat to internal validity, and one study[33] had a high threat to internal validity. • Strength of Association: Two studies reported measures of association ranging from 3.8-8.89. • Precision of Association: One study reported confidence intervals that were wide. • Consistency of Association: The evidence is consistent in the direction of increased mortality. • Applicability of Association: One study was conducted in the US, one was conducted in Asia, and one did not report where the study was conducted. Summary of Evidence • Three cohort studies[15,33,34] (N=5,828) reported data suggesting that ADL impairments are associated with an increase in mortality among patients with COVID-19. ▪ One study[34] (N=340) of hospitalized patients with COVID-19 aged 65 and older in South Korea reported increased mortality among 84 patients with ADL impairments compared to patients with no ADL impairments when adjusting for age, sex, comorbidity, fever, initial chest X-ray, and initial C-reactive protein [aOR: 8.89 (95% CI: 4.37-18.10), p < 0.01]. This study reported wide confidence intervals. ▪ One study[33] (N=232) of patients with COVID-19 aged 60 and older admitted to the ICU reported increased mortality among 49 patients with ADL impairments compared to patients with no impairments [OR: 3.8 (95% CI: NR), p <0.01]. This study also reported increased mortality among 70 patients with Instrumental Activities of Daily Living (IADL) impairment compared to patients with no impairment [OR: 6.1 (95% CI: NR), p < 0.01]. There is concern over confounding by indication because the population examined patients who were already admitted to the ICU, and confidence intervals and study location were not reported, decreasing confidence in these measures of effect. ▪ One study[15] (N=5,256) of symptomatic nursing home residents with COVID-19 reported a higher prevalence of mortality in 3,909 patients with ADL impairments compared to 1,327 patients with no impairments [23% (913/3,909) vs. 16% (209/1,327), p = NR]; however, no statistical analysis was conducted.

Table 18 The Association between Neuromuscular Disease and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited evidence from three studies[35-37] (N=30,249) is inconclusive on the association between neuromuscular disease and mortality in COVID-19 patients. Two studies[36,37] were found to have a moderate threat to internal validity. Internal validity assessments are not completed for studies with less than 10 people with neuromuscular disease[35]. • Strength of Association: Two studies reported measures of association ranging from 0.86-1.70. • Precision of Association: Of the two studies reporting confidence intervals, the confidence interval was wide in both studies. • Consistency of Association: The evidence is inconsistent and inconclusive. • Applicability of Association: One study was conducted in a hospital in the U.S. and two were conducted in Europe using national registries. Summary of Evidence • One cohort study[37] suggested an increase, but not statistically significant, in mortality in COVID-19 patients with neuromuscular disorders. ▪ One cohort study[37] (N=2,354) of Swedish intensive care patients reported an increase in the hazard of mortality among 34 patients with neuromuscular diseases compared to patients without neuromuscular diseases when adjusting for sex, age, comorbidities, hospital level, and admission month [aHR 1.42 (95% CI: 0.81 - 2.48), p = 0.22]. This study also reported an increase in the odds of 90-day all-cause mortality from first admission to the ICU [aOR 1.7 (95% CI: 0.74 - 3.80), p = 0.2]. • One cohort study[35] (N=1,563) suggested no difference in mortality between patients with and without chronic neuromuscular disease. ▪ One study[35] (N=1,563) of adult COVID-19 patients admitted to the ICU in Sweden reported no difference in the odds of mortality in patients with neuromuscular disease when compared to patients without neuromuscular diseases [30.0% (6/20) vs. 27.0% (417/1,543, p = NR]. Only 20 people had neuromuscular disease, and there was a low number of deaths, decreasing confidence in these results. • One cohort study[36] (N=26,332) suggested a decrease in mortality in COVID-19 patients with neuromuscular disorders. ▪ One cohort study[36] (N=26,332) of COVID-19 patients in the U.S. reported a decrease in the odds of mortality among 3,627 patients with neuromuscular disorder compared to patients without a neuromuscular disorder [OR 0.86 (95% CI: 0.71–1.05)]. However, the confidence interval crossed the null, decreasing confidence in this result.
ICU admission	Overall, limited data from only one study[36] is insufficient to determine an association between neuromuscular disorders and ICU admission in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[36] (N=26,332) reported an effect measure suggesting no association between neuromuscular disease and ICU admission among people with neuromuscular diseases.

	▪ One cohort study[36] (N=26,332) of COVID-19 patients in the U.S. reported no difference in the odds of being admitted to the ICU among 3,627 patients with neuromuscular disorder when compared to patients without a neuromuscular disorder [OR 1.1 (95% CI: 0.91–1.33)].
Intubation	Overall, limited data from only one study[36] is insufficient to determine an association between neuromuscular disorders and intubation in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[36] (N=26,332) suggested that neuromuscular disease is associated with an increase in the odds of intubation in COVID-19 patients. ▪ One cohort study[36] (N=26,332) of COVID-19 patients in the U.S. reported increased intubation among 3,627 patients with a neuromuscular disorder when compared to patients without a neuromuscular disorder [OR 1.88 (95% CI: 1.49–2.37)].
Hospitalization	Overall, limited data from only one study[36] is insufficient to determine an association between neuromuscular disorders and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[36] (N=26,332) suggested that neuromuscular disease is associated with an increase in hospitalization in COVID-19 patients. ▪ One cohort study[36] (N=26,332) of COVID-19 patients in the U.S. reported increased hospitalization among 3,627 patients with a neuromuscular disorder when compared to patients without a neuromuscular disorder [OR 1.24 (95% CI: 1.09–1.39)].

Table 19 The Association between Spinal Cord Injuries and Disorders and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence from two studies[5,38] (N=488,282) indicates spinal cord injuries and disorders are associated with an increase in mortality in COVID-19 patients. Both studies were found to have a moderate threat to internal validity. • Strength of Association: One study reported a measure of association of 1.56. • Precision of Association: The confidence interval was wide in the one study reporting a confidence interval. • Consistency of Association: The evidence is consistent in the direction of increased mortality. • Applicability of Association: Two studies were conducted in the US. Summary of Evidence • Two cohort studies[5,38] (N=488,282) indicate that spinal cord injuries and disorders are associated with an increase in mortality in COVID-19 patients.

	▪ One study[5] (N=467,773) using data from a private healthcare claims database of COVID-19 inpatients and outpatients in the US reported an increase in mortality among patients with spinal cord injury compared to those without spinal cord injury when adjusting for age and sex [aOR: 1.56 (95% CI: 1.16-2.10), p < 0.01]. This study reported a wide confidence interval and did not report on the prevalence of spinal cord injuries in the study population nor the number of deaths among those with or without spinal cord injuries, decreasing confidence in the results. ▪ One study[38] (N=20,509) of veterans with COVID-19 who received care through the Veterans Health Administration system in the US suggested an increase in mortality among veterans with spinal cord injuries and disorders compared to those without [19.0% (26/140) vs. 7.7% (1,564/20,369), p < 0.01]. The study included spinal cord injuries and disorders of traumatic or nontraumatic etiology and reported a prevalence of 0.7% in the study population.
Hospitalization	Overall, limited data from only one study[38] is insufficient to determine an association between spinal cord injuries and disorders and hospitalizations in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[38] reported hospitalizations among veterans with spinal cord injuries and disorders and COVID-19. As this study did not have a comparison group, it is not possible to determine an association between spinal cord injuries and disorders and hospitalization. ▪ One study[38] (N=20,509) of veterans with COVID-19 who received care through the Veterans Health Administration system in the US reported 48.0% (67/140) patients with spinal cord injuries and disorders were hospitalized. Hospitalization data for those without spinal cord injuries and disorders was not reported. The study included spinal cord injuries and disorders of traumatic or nontraumatic etiology.

Table 20 The Association between Cerebral Palsy and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[19] is insufficient to determine an association between cerebral palsy and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One study[19] (N=36,428) reported effect measures suggesting cerebral palsy is associated with an increase in mortality in COVID-19 patients. ▪ One cohort study[19] using a national primary care database of adult English patients reported an increase in the hazard of mortality in patients with cerebral palsy compared to those without cerebral palsy when adjusting for age, sex, ethnicity, BMI, dementia diagnosis, care home residency, congenital heart disease, and other comorbid conditions and treatments [aHR 2.66 (95% CI: 1.62-4.36), p = NR]. This study did not report the prevalence of patients with cerebral palsy or their vital status.

ICU admission	Overall, limited data from only one study[39] is insufficient to determine an association between cerebral palsy and ICU admission in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with cerebral palsy, and aggregation indices are not assessed for outcomes reported by only one study. • One study[39] (N= 5) reported data on cerebral palsy and ICU admission in hospitalized pediatric patients with COVID-19. ▪ One cohort study[39] (n = 5) of pediatric patients with confirmed COVID-19 in the UK reported that the percentage of ICU admissions in patients with cerebral palsy was higher than patients without cerebral palsy [100.0% (1/1) vs. 25.0% (1/4), p = NR]. This study had a small sample size and only one patient with cerebral palsy.
Ventilation	Overall, limited data from only one study[39] is insufficient to determine an association between cerebral palsy and ventilation in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with cerebral palsy, and aggregation indices are not assessed for outcomes reported by only one study. • One study[39] (N=5) reported data on cerebral palsy and mechanical and non-invasive ventilation in hospitalized pediatric patients with COVID-19. ▪ One cohort study[39] (N=5) of pediatric patients with confirmed COVID-19 in the UK reported that the percentage of ventilations in patients with cerebral palsy was higher compared to patients without cerebral palsy [100.0% (1/1) vs. 25.0% (1/4), p = NR]. This study had a small sample size and only one patient with cerebral palsy.
Hospitalization	Overall, the evidence from two studies[18,40] (N=7,632) suggests cerebral palsy is associated with an increase in hospitalization in COVID-19 patients. Both studies were found to have a moderate threat to internal validity. • Strength of Association: No measures of association were reported. • Precision of Association: No confidence intervals were reported. • Consistency of Association: The evidence is consistent in the direction of increased hospitalization. • Applicability of Association: One study was conducted in the United Kingdom and one study was conducted in Norway. Summary of Evidence • Two studies[18,40] (N=7,632) reported proportions suggesting that cerebral palsy is associated with an increase in hospitalization among patients with COVID-19. ▪ One cohort study[18] (N=NR) of adult English people with COVID-19 reported a higher proportion of hospitalization in people with cerebral palsy compared to those without cerebral palsy [0.42% (27/6,481) vs. 0.18% (10,749/6,076,621), p = NR]. ▪ One cohort study[40] (N=7,632) of Norwegian adults with COVID-19 reported an increase in the proportion of hospitalizations in people with and cerebral palsy compared to those without cerebral palsy [38.46% (5/13) vs. 13.39% (1,020/7,619), p = NR]. This study reported a low number of hospitalizations.

Table 21 The Association between Risk Markers in Cerebral Palsy and Severe COVID-19 Outcomes

Outcome	Results

Mortality	Overall, limited data from only one study[18] is insufficient to determine whether sex modifies the association between cerebral palsy and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One study[18] (N=NR) reported effect measures suggesting that among people with COVID-19 and cerebral palsy, mortality among women with COVID-19 increased more than among men. ▪ One cohort study[18] (N=NR) of English adults with COVID-19 reported an increase in the hazard of mortality among patients with cerebral palsy compared to those without cerebral palsy regardless of sex, and this increase was larger among women [aHR 3.45 (95% CI: 1.10 - 10.78)] than men [aHR 2.77 (95% CI: 1.23 - 6.23)] when adjusting for age, BMI, Townsend score, ethnic group, domicile, and comorbid conditions and treatments.
Hospitalization	Overall, limited data from only one study[18] is insufficient to determine an association between sex, cerebral palsy, and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One study[18] (N=NR) reported effect measures suggesting that male sex is associated with hospitalization in COVID-19 patients. ▪ One cohort study[18] (N =NR) of English adults reported an increase in the hazard of hospitalization among patients with cerebral palsy compared to those without cerebral palsy, and this increase was larger among men [aHR 2.85 (95% CI: 1.76 - 4.62)] than women [aHR 2.66 (95% CI: 1.42 - 4.98)] when adjusting for age, BMI, Townsend score, ethnic group, domicile, and comorbid conditions and treatments.

Table 22 The Association between Congenital Malformations and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, the evidence from two studies[41,42] (N=20,019) suggests congenital malformations is associated with an increase in hospitalization in COVID-19 patients. Both studies were found to have a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported • Consistency of Association: The evidence is consistent in the direction of increased hospitalization. • Applicability of Association: One study was conducted in Italy and one study was conducted in the US. Summary of Evidence • Two studies[41,42] (N=20,019) reported proportions suggesting that congenital malformations are associated with an increase in hospitalization among COVID-19 patients. ▪ One cohort[41] (N=19,260) including electronic health record data on 5,639 US pediatric patients with COVID-19, reported an increased prevalence of congenital malformations among patients hospitalized with COVID-19 compared to those diagnosed with COVID-19 [13.5% (54/399) vs. 4.7% (265/5,639), p = NR].

	▪ One cohort study[42] (N=759) of pediatric COVID-19 patients in Italy reported a higher proportion of hospital admissions among patients with congenital malformations compared to patients without congenital malformations [85% (17/20) vs. 47% (344/739), p = NR]. This study reported a low number of hospitalizations.

Table 23 The Association between Cognitive Impairment and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited evidence from three studies[15,43,44] (N=5,494) is inconclusive on the association between cognitive impairment and mortality in COVID-19 patients. All three studies were found to have a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconsistent. • Applicability of Association: One study was conducted in the U.S and two in Europe. Summary of Evidence • One study[15] (N=5,256) reported a proportion suggesting that cognitive impairment is associated with an increase in mortality. ▪ One cohort study[15] (N=5,256) of nursing home residents with laboratory-confirmed COVID-19 reported a higher proportion of mortality among patients with cognitive impairment compared to those with no cognitive impairment [26.2% (836/3,189) vs. 14.2% (275/2,023), p = NR]. • One cohort study[43] (N=113) reported data suggesting no association between mortality and cognitive impairment. ▪ One cohort study[43] (N=113) of patients admitted to a Spanish hospital with laboratory-confirmed COVID-19 reported no difference in mortality between patients with cognitive impairment compared to those with no cognitive impairment ($p < 0.02$); however, this study had a small sample size and reported a low number of deaths. • One cohort study[44] (N=125) reported the prevalence of mortality among COVID-19 patients with unspecified cognitive impairment. As this study did not have comparison groups, it is not possible to determine the association between unspecified cognitive impairment and mortality. ▪ One cohort study[44] (N= 125) of hospitalized patients over 65 years old with dementia reported that 22.67% (17/75) of patients with unspecified cognitive impairment and COVID-19 died.
ICU admission	Overall, limited data from only one study[43] is insufficient to determine an association between cognitive impairment and ICU admission in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[43] (n = 113) reported data suggesting no association between ICU admission and cognitive impairment.

	▪ One cohort study[43] (N= 113) of patients admitted to a Spanish hospital with laboratory-confirmed COVID-19 reported no difference in ICU admission between patients with cognitive impairment compared to those with no cognitive impairment (p = 0.99); however, this study had a small sample size and reported a low number of ICU admissions.

Table 24 Severity of Underlying Cognitive Impairment Examined for Association with Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[15] is insufficient to determine an association between severity of cognitive impairment and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[15] (N= 5,256) reported increasing severity of cognitive impairment is associated with an increase mortality in COVID-19 patients in nursing homes. ▪ One cohort study[15] (N= 5,256) of individuals with laboratory-confirmed COVID-19 residing in nursing homes suggested an increasing odds of mortality among 1,179 patients with mild cognitive impairment [aOR: 1.11 (95% CI: 0.89-1.39)], 1,547 patients with moderate cognitive impairment [aOR: 2.09 (95% CI: 1.68-2.59)], and 463 patients with severe cognitive impairment [aOR: 2.79 (95% CI: 2.14-3.66)] compared to those with no cognitive impairment when adjusting for age, sex, race/ethnicity, comorbidities, symptoms, ADL score, and cognitive function.

Table 25 The Association between Neurodevelopmental Disorders and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[45] is insufficient to determine an association between neurodevelopmental disorders and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cross-sectional study[45] (N=4,020) reported the prevalence of mortality in COVID-19 patients with neurodevelopmental disorders. As this study did not have comparison groups, it is not possible to determine an association between neurodevelopmental disorders and mortality. ▪ One study[45] (N=4,020) of patients within an Italian National Institute of Health and COVID-19 Integrated Surveillance System reported 1.34% (54/4,020) of COVID-19 patients with a neurodevelopmental disability died.

Hospitalization	Overall, limited data from only one study[41] is insufficient to determine an association between neurodevelopmental disorders and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[41] (N=19,260) suggested an increase in hospitalization in COVID-19 patients with neurodevelopmental disorders. ▪ One cohort study[41] (N=19,260) including electronic health record data of 5,639 US pediatric patients with COVID-19, reported an increased prevalence of neurodevelopmental disorders among patients hospitalized with COVID-19 compared to those diagnosed with COVID-19 [20.6% (82/399) vs. 8.2% (462/5,639), p = NR].

Table 26 The Association between Neurodevelopmental Disorder and Other Comorbidities and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[45] is insufficient to determine an association between neurodevelopmental disorders, other comorbidities, and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cross-sectional study[45] (N=4,020) suggested a decrease in hospitalization in COVID-19 patients with neurodevelopmental disorders and severe psychiatric disorder. ▪ One cross-sectional study[45] (N=4,020) of Italian patients suggested that COVID-19 patients with neurodevelopmental disorders and psychiatric disorders had a lower proportion of in-hospital mortality than those with neurodevelopmental disorders and no psychiatric disorder [18.5% (10/54) vs. 79.6% (43/54), p = NR]. This study included 1.34% (54/4,020) patients with neurodevelopmental disorder and had a low number of deaths among those who also have severe psychiatric disorders, reducing confidence in the finding.

Table 27 The Association between Neuromyelitis Optica Spectrum Disorder (NMOSD) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited evidence from three studies[46-48] (N=195) is inconclusive on the association between NMOSD and mortality in COVID-19 pa One study[46] was found to have a moderate threat to internal validity, and one[47] had a high threat to internal validity. Internal validity assessments are not completed for studies with less than 10 people with NMOSD[48].

	• Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: Two studies were conducted in Latin America and one in the Netherlands. Summary of Evidence • One cohort study[48] (N=16) reported proportions on mortality among patients with NMOSD and COVID-19. ▪ One cohort study[48] (N=16) in the Netherlands reported that among the patients who were COVID-19 positive, the one patient with underlying NMOSD did not die compared to two of the 15 without NMOSD who died [0% (0/1) vs. 13.3% (2/15), p = NR]. However, this study had a small sample size with only one patient with NMOSD and reported a low number of deaths, reducing confidence in the finding. • Two cohort studies[46,47] (N=179) reported the prevalence of mortality in COVID-19 patients with NMOSD. As these studies did not have comparison groups, it is not possible to determine an association between NMOSD and mortality. ▪ One cohort study[47] (N=34) of COVID-19 patients with NMOSD in Brazil reported that 2.9% (1/34) of the patients had died. This study had a small sample size with a low number of deaths. ▪ One cohort study[46] (N=145) conducted across medical centers in 15 Latin American countries included COVID-19 patients from a multiple sclerosis and NMOSD registry and reported that 31.3% (5/16) of the patients with NMOSD died from COVID-19. This study had a small sample size with a low number of deaths and was conducted in low to middle-income countries.
ICU admission	Overall, limited evidence from four studies[46-49] (N=194) is inconclusive on the association between NMOSD and ICU admission in COVID-19 patients. One study[46] was found to have a moderate threat to internal validity, and two studies[47,49] had a high threat to internal validity. Internal validity assessments are not completed for studies with less than 10 people with NMOSD[48]. • Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: The four studies were conducted in Europe, and Latin America. Summary of Evidence • One cohort study[48] (N=16) reported that the one COVID-19 patient with NMOSD was admitted to the ICU. ▪ One cohort study[48] (N=16) in the Netherlands reported that among the patients who were COVID-19 positive, the one patient with underlying NMOSD was admitted to the ICU compared to two of the 15 patients without NMOSD [100% (1/1) vs. 33% (2/15), p = NR]. However, this study had a small sample size with only one patient with NMOSD and reported a low number of ICU admissions, reducing confidence in the results. • Three cohort studies[46,47,49] (N=194) reported the prevalence of ICU admission in COVID-19 patients with NMOSD. ▪ One study[46] (N=145) reported that 43.8% (7/16) of Latin American patients with NMOSD were hospitalized. This study had a small sample size, a low prevalence of underlying NMOSD, and a low number of ICU admissions.

	▪ One cohort study[47] (N=34) of COVID-19 patients with NMOSD in Brazil reported that 11.76% (4/34) of the patients had died. This study had a small sample size with a low number of ICU admissions. ▪ One study[49] (N=15) reported that 6.67% (1/15) French patients with NMOSD or myelin oligodendrocyte glycoprotein antibody disorders (MOGAD) were hospitalized. This study had a small sample size, a low prevalence of underlying NMOSD or MOGAD, and a low number of ICU admissions.
Intubation	Overall, limited data from only one study[49] is insufficient to determine an association between NMOSD and intubation in COVID-19 patients. The study was found to have a high threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[49] (N=15) reported data on intubation in COVID-19 patients with NMOSD or MOGAD. This study did not have a comparison group and it is not possible to determine the association between NMOSD or MOGAD and intubation. ▪ One cohort study[49] (N=15) of COVID-19 patients in France reported 6.7% (1/15) of patients with NMOSD or MOGAD were intubated. This study had a small sample size with a low number of intubations.
Ventilation	Overall, limited evidence from two studies[48,49] (N=31) is insufficient to determine an association between NMOSD and ventilation in COVID-19 patients. One study[49] was found to have a high threat to internal validity. Internal validity assessments are not completed for studies with less than 10 people with NMOSD[48]. • Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: Both studies were conducted in Europe. Summary of Evidence • One cohort study[48] (N=16) reported that the one COVID-19 patient with NMOSD was ventilated. ▪ One cohort study[48] (N=16) in the Netherlands reported that among the patients who were COVID-19 positive, the one patient with underlying NMOSD was mechanically ventilated and one of the 15 patients without NMOSD was mechanically ventilated [100% (1/1) vs. 6.6% (1/15), p = NR]. This study had a small sample size with only one patient with NMOSD and reported a low number of ventilations, reducing confidence in the results. • One cohort study[49] (n = 15) reported prevalence of ventilation in COVID-19 patients with NMOSD or MOGAD. As this study did not have comparison groups, it is not possible to determine an association between NMOSD and hospitalization. ▪ One cohort study[49] (n = 15) of COVID-19 patients in France reported 6.7% (1/15) of the patients with NMOSD or MOGAD were ventilated. This study had a small sample size with a low number of ventilations.
Hospitalization	Overall, limited evidence from four studies[46,48-50] (N=181) is inconclusive on the association between NMOSD and hospitalization in COVID-19 patients. One study[46] was found to have a moderate threat to internal validity, and one[49] had a high threat to internal validity. Internal validity assessments are not completed for studies with less than 10 people with NMOSD[48,50].

	• Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: The four studies were conducted in Europe, Latin America, and the Middle East. Summary of Evidence • One cohort study[48] (N=16) reported that the one COVID-19 patient with NMOSD was hospitalized. ▪ One study[48] (N=16) in the Netherlands reported that among the patients who were COVID-19 positive, the one patient with underlying NMOSD was hospitalized compared to seven of the 15 patients without NMOSD [100% (1/1) vs. 46.6% (7/15), p = NR]. However, this study had a small sample size with only one patient with NMOSD and reported a low number of hospitalizations, reducing confidence in the results. • Three cohort studies[46,49,50] (N=165) reported prevalence of hospitalization in patients with NMOSD and COVID-19. As these studies did not have comparison groups, it is not possible to determine an association between NMOSD and hospitalization. ▪ One study[50] (N=5) reported that 60.0% (3/5) of Iranian patients with NMOSD were hospitalized. This study had a small sample size, a low prevalence of underlying NMOSD, and a low number of hospitalizations. ▪ One study[49] (N=15) reported that 33.3% (5/15) French patients with NMOSD or MOGAD were hospitalized. This study had a small sample size, a low prevalence of underlying NMOSD or MOGAD, and a low number of hospitalizations. ▪ One study[46] (N=145) reported that 56.0% (9/16) of Latin American patients with NMOSD were hospitalized. This study had a small sample size, a low prevalence of underlying NMOSD, and a low number of hospitalizations.

Table 28 The Association between NMOSD and Other Comorbidities and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[46] is insufficient to determine an association between NMOSD, other comorbidities, and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[46] (N=125) reported prevalence rates suggesting that hospitalized NMOSD patients were more likely to be obese. ▪ One cohort study[46] (N=145) conducted across medical centers in 15 Latin American countries included COVID-19 patients from a multiple sclerosis and NMOSD registry reported that hospitalized patients were more likely to be obese than non-hospitalized patients [55.5% (5/9) vs. 14.3% (1/7), p = 0.09]. This study had a small sample size with a low number of hospitalizations, reducing confidence in the results.

Table 29 The Association between NMOSD and Risk Factors and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[46] is insufficient to determine an association between NMOSD, age, sex, and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[46] (N=125) reported data suggesting that hospitalized NMOSD patients were more likely to be older females. ▪ One cohort study[46] (N=145) conducted across medical centers in 15 Latin American countries included COVID-19 patients from a multiple sclerosis and NMOSD registry reported that hospitalized patients were more likely to be female [88.8% (8/9) vs. 85.7% (6/7), p = 0.87] and had a higher median age than non-hospitalized patients (54 years vs. 36 years, p < 0.01). The study did not include any current smokers. This study had a small sample size with a low number of hospitalizations, reducing confidence in the results.

Table 30 The Association between severe and complex disability (Polyhandicap Disability) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[51] is insufficient to determine an association between being severe and complex disability (polyhandicapped) and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[51] reported on mortality among severe and complex disability (polyhandicapped) patients with COVID-19. As this study did not have a comparison group, it is not possible to determine an association between spinal cord injuries and disorders and hospitalization. ▪ One study[51] (N=98) of severe and complex disability (polyhandicapped) patients with COVID-19 in France reported 4.1% (4/98) died. Severe and complex disability (polyhandicapped)was defined by the combination of motor deficiency and severe or profound mental impairment associated with everyday life dependence and restricted mobility with age at onset of cerebral lesion below 6 years. The study had no comparison group and included a small number of patients.
ICU admission	Overall, limited data from only one study[51] is insufficient to determine an association between being severe and complex disability (polyhandicapped) and ICU admission in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study.

	• One cohort study[51] reported on ICU admission among severe and complex disability (polyhandicapped) patients with COVID-19. As this study did not have a comparison group, it is not possible to determine an association between spinal cord injuries and disorders and hospitalization. ▪ One study[51] (N=98) of severe and complex disability (polyhandicapped) patients with COVID-19 in France reported 4.1% (4/98) were admitted to the ICU and 1.0% (1/98) declined admission to the ICU despite medical indication. The study had no comparison group and included a small number of patients.
Ventilation	Overall, limited data from only one study[51] is insufficient to determine an association between being severe and complex disability (polyhandicapped) and ventilation in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[51] reported on ventilation among severe and complex disability (polyhandicapped) patients with COVID-19. As this study did not have a comparison group, it is not possible to determine an association between spinal cord injuries and disorders and hospitalization. ▪ One study[51] (N=98) of severe and complex disability (polyhandicapped)patients with COVID-19 in France reported 2.0% (2/98) received non-invasive mechanical ventilation. The study had no comparison group and included a small number of patients.
Hospitalization	Overall, limited data from only one study[51] is insufficient to determine an association between being severe and complex disability (polyhandicapped) and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[51] reported on hospitalization among severe and complex disability (polyhandicapped) patients with COVID-19. As this study did not have a comparison group, it is not possible to determine an association between spinal cord injuries and disorders and hospitalization. ▪ One study[51] (N=98) of severe and complex disability (polyhandicapped) patients with COVID-19 in France reported 16.3% (16/98) were hospitalized and 2.0% (2/98) declined hospitalization despite medical indication. The study had no comparison group and included a small number of patients.

Table 31 The Association between severe and complex disability (Polyhandicap Disability) and Risk Factors and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[51] is insufficient to determine whether age or sex modifies the association between being severe and complex disability (polyhandicapped) and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study.

	• One cohort study[51] suggested an increase in mortality among adult and male severe and complex disability (polyhandicapped) patients with COVID-19. ▪ One study[51] (N=98) of severe and complex disability (polyhandicapped) patients with COVID-19 in France suggested an increase in mortality among males compared to females [6.4% (3/47) vs. 2.1% (1/48), p = NR]. This study also suggested an increase among adults compared to children [5.0% (4/80) vs. 0% (0/18), p = NR] and among individuals older than 50 years compared to those younger than 50 [5.9% (2/34) vs. 3.3% (2/61), p = NR]. Severe and complex disability (polyhandicapped) was defined by the combination of motor deficiency and severe or profound mental impairment associated with everyday life dependence and restricted mobility with age at onset of cerebral lesion below 6 years. This study had a small sample size with a low number of deaths and did not report on significance for this comparison, decreasing confidence in the results.
ICU admission	Overall, limited data from only one study[51] is insufficient to determine whether age or sex modifies the association between being severe and complex disability (polyhandicapped) and ICU admission in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[51] suggested an increase in ICU admission among pediatric severe and complex disability (polyhandicapped) patients. ▪ One study[51] (N=98) of severe and complex disability (polyhandicapped) patients with COVID-19 in France suggested no difference in ICU admission between males and females [6.4% (3/47) vs. 4.2% (2/48), p = 1.0]. The study did suggest an increase among children compared to adults [11.1% (2/18) vs. 3.8% (3/80), p = 0.5] and among individuals younger than 50 years compared to those older than 50 [6.6% (4/61) vs. 2.9% (1/34), p = 0.6]. This study had a small sample size with a low number of ICU admissions and the results were not statistically significant.
Hospitalization	Overall, limited data from only one study[51] is insufficient to determine whether age or sex modifies the association between being severe and complex disability (polyhandicapped) and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[51] suggested an increase in hospitalization among female severe and complex disability (polyhandicapped) patients and adult severe and complex disability (polyhandicapped) patients younger than 50 years old and with COVID-19. ▪ One study[51] (N=98) of polyhandicapped patients with COVID-19 in France suggested an increase in hospitalization among females compared to males [16.7% (8/48) vs. 12.8% (6/47), p = 0.6]. This study also suggested an increase among adults compared to children [17.5% (14/80) vs. 11.1% (2/18), p = 0.7], however there was an increase among individuals younger than 50 years compared to those older than 50 [18.0% (11/61) vs. 14.7% (5/34), p = 0.7], possibly indicating hospitalizations were more common among younger adults. This study had a small sample size with a low number of hospitalizations the results were not statistically significant.

Table 32 The Association between Mobility Impairments and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[5] is insufficient to determine an association between mobility impairments and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[5] reported effect measures suggesting mobility impairments are associated with an increase in mortality in COVID-19 patients. ▪ One study[5] (N= 467,773) using data from a private healthcare claims database of COVID-19 inpatients and outpatients in the US reported an increase in mortality among patients with mobility impairments compared to those without mobility impairments when adjusting for age and sex (aOR: 1.62, p = NR, but described as statistically significant). When the analysis was restricted to patients under the age of 70, the association between mobility impairments and mortality slightly increased (aOR: 1.88, p = NR, but described as statistically significant). This study did not report the prevalence of mobility impairments in the study population, confidence intervals, nor the number of deaths among those with or without mobility impairments, decreasing confidence in the results.

Table 33 The Association between Immobilization (Movement Disorders) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[29] is insufficient to determine an association between immobilization and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[29] reported on mortality among immobilized patients with COVID-19. As this study did not have a comparison group, it is not possible to determine an association between spinal cord injuries and disorders and hospitalization. ▪ One study[29] (N= 10,454) of COVID-19 patients in Spain reported 54.5% (12/22) of immobilized inpatients died. The study reported a low prevalence of immobilization in the study population, and a low number of deaths.
ICU admission	Overall, limited data from only one study[29] is insufficient to determine an association between immobilization and ICU admission in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[29] reported on ICU admission among immobilized patients with COVID-19. As this study did not have a comparison group, it is not possible to determine an association between spinal cord injuries and disorders and hospitalization.

	▪ One study[29] (N=10,454) of COVID-19 patients in Spain reported that none (0/22) of the 22 immobilized inpatients were admitted to the ICU. The study reported a low prevalence of immobilization in the study population, and a low number of ICU admissions.
Hospitalization	Overall, limited data from only one study[29] is insufficient to determine an association between immobilization and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[29] reported on hospitalization among people with COVID-19 who were immobilized. As this study did not have a comparison group, it is not possible to determine an association between spinal cord injuries and disorders and hospitalization. ▪ One study[29] (N=10,454) of COVID-19 inpatients and outpatients in Spain reported 41.5% (22/53) of immobilized patients were hospitalized. The study reported a low prevalence of immobilization in the study population, and a low number of hospitalizations.

Table 34 The Association between Disability Severity as Indicated by Barthel Index and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[52] is insufficient to determine an association between disability severity as indicated by Barthel Index and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[52] reported an effect measure suggesting no association between disability severity as indicated by Barthel Index and mortality among hospitalized patients with COVID-19. ▪ One study[52] (N=375) of hospitalized COVID-19 patients in Spain suggested an increase in mortality per 5-point decrease in Barthel Index score when adjusting for sex, age, Quick Sequential Organ Failure Assessment, polypharmacy, and whether patients had three or more comorbidities [aOR: 1.11 (95% CI: 1.03-1.20), $p < 0.01$]. The study used the Barthel Index to categorize patients as having a severe disability (0-60), a moderate disability (65-85), a mild disability (90-95), or no disability (100).

Table 35 The Association between Disability Indicated by Barthel Index, Comorbidities, Risk Factors and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[52] is insufficient to determine whether comorbidities or risk factors modify the association between disability indicated by Barthel Index and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[52] suggested the odds of mortality among hospitalized COVID-19 patients did not change as the number of comorbidities increased.

	▪ One study[52] (N=375) of hospitalized COVID-19 patients in Spain reported that the increase in the odds of mortality per 5-point decrease in Barthel index was similar regardless of comorbidities when adjusting for sex, age, Quick Sequential Organ Failure Assessment, polypharmacy, and whether patients had three or more comorbidities. However, stratified analyses suggest that for men, the risk of mortality doubled among those with three or more comorbidities, compared to those with less than three, across Barthel Index scores and age categories. For women over 50, the risk of mortality also doubled among those with three or more comorbidities regardless of Barthel Index scores.

Table 36 The Association between Attention-Deficit/ Hyperactivity Disorder (ADHD) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited evidence from two studies[53,54] is inconclusive on the association between ADHD and mortality in COVID-19 patients. One study[54] was found to have a moderate threat to internal validity, and one[53] had a high threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconsistent. • Applicability of Association: One study was conducted in the US and one in Europe. Summary of Evidence • One ecological study[53] suggested no difference in mortality between individuals with and without ADHD. ▪ One study[53] (N= 34 states) evaluated the association between the underlying prevalence of ADHD in the US at the state level and COVID-19 infection, mortality, and recovery rates. This study suggested no correlation between ADHD and population size, COVID-19 infection rate, and COVID-19 mortality rate (correlation coefficient: -0.03, p = 0.86). Recovery rates, however, rose with the prevalence of ADHD. This study used state-level data to evaluate the association between ADHD and mortality and only included data on 34 states, decreasing confidence in the findings. • One case series[54] reported the prevalence of ADHD among patients who died of COVID-19. ▪ One study[54] (N= 66) of deceased individuals with intellectual disability who died from COVID-19 in England and Ireland reported 2% (1/66) had ADHD. This study had a small sample size which included only one patient with ADHD and used snowball sampling to identify deceased individuals meeting the inclusion criteria.
Hospitalization	Overall, the evidence from two studies[41,55] (N= 21,130) suggests ADHD is associated with an increase in hospitalization in COVID-19 patients. Both studies were found to have a moderate threat to internal validity. • Strength of Association: One study reported a measure of association of 1.93. • Precision of Association: One study reported a wide confidence interval. • Consistency of Association: The evidence is consistent. • Applicability of Association: One study was conducted in the US and one in the Middle East. Summary of Evidence • Two cohort studies[41,55] reported data suggesting that ADHD is associated with an increase in hospitalization in COVID-19 patients.

	▪ One study[55] (N=1,870) of COVID-19 patients in Israel reported an increase in hospitalization among 231 patients with ADHD compared to those without ADHD when adjusting for age, sex, SES, depression/anxiety, schizophrenia, diabetes mellitus, hypertension, cardiovascular disease, chronic obstructive pulmonary disease, obesity, and smoking [aOR 1.93 (95% CI: 1.06-3.51), p = 0.03]. ADHD diagnosis was established by senior physicians specializing in ADHD. The study reported a wide confidence interval, decreasing confidence in the finding. ▪ One study[41] (N=19,260) including electronic health record data on 5,639 US pediatric patients with COVID-19, reported an higher prevalence of ADHD among patients hospitalized with COVID-19 compared to those diagnosed with COVID-19 [10.3% (41/399) vs. 5.4% (305/5,639), p = NR].

Table 37 The Association between the Severity of ADHD and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[54] is insufficient to determine an association between ADHD severity and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case series[54] reported on one patient with ADHD who died of COVID-19. ▪ One study[54] (N=66) of deceased individuals with intellectual disability who died from COVID-19 in England and Ireland reported that the one patient with ADHD had a moderate to profound intellectual disability. Moderate to profound intellectual disabilities were identified using ICD-10 codes for moderate (F71), severe (F72), and profound intellectual disability (F73). This study had a small sample size which included only one patient with ADHD and used snowball sampling to identify deceased individuals meeting the inclusion criteria.

Table 38 The Association between ADHD and Risk Factors and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[55] is insufficient to determine whether age modifies the association between ADHD and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[55] suggested hospitalization in COVID-19 patients with ADHD increased with age. ▪ One study[55] (N=1,870) of COVID-19 patients in Israel reported an increase in hospitalizations among those with ADHD compared to those without ADHD for patients aged 5-20 [OR 1.64 (95% CI: 0.37-5.67), p = NS], 21-40 [OR 2.96 (95% CI: 1.40-5.93), p = NR], and 41-60 [OR 2.56 (95% CI: 0.60-8.99), p = NR]. ADHD was associated with higher rates of hospitalization among the older age groups and the results were not significant for those age 5-20, however there was

	a small number of hospitalizations in this age group. This study reported wide confidence intervals, reducing confidence in the findings.

Table 39 The Association between Traumatic Brain Injury and Severe COVID-19 Outcomes

Outcome	Results
ICU admission	Overall, limited evidence from only one study[56] is insufficient to determine an association between traumatic brain injury and ICU admission in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with a traumatic brain injury, and aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[56] (N=135) reported data on traumatic brain injury and ICU admissions in patients with COVID-19. ▪ One cohort study[56] (N=135) of Austrian adult patients reported a lower proportion of ICU admissions in COVID-19 patients with traumatic brain injury compared to those without a traumatic brain injury [0% (0/3) vs. 23.5% (31/132), p = NR]. This study reported only three patients with a traumatic brain injury, none of whom were admitted to the ICU, reducing confidence in the finding.
Hospitalization	Overall, limited evidence from only one study[56] is insufficient to determine an association between traumatic brain injury and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with a traumatic brain injury, and aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[56] (N=135) suggested an increase in hospitalization in COVID-19 patients with a traumatic brain injury. ▪ One cohort study[56] (N=135) of Austrian adults reported a higher proportion of hospitalization among patients with traumatic brain injury compared to those without a traumatic brain injury [66.6% (2/3) vs. 53% (70/132), p = NR]. This study reported only three patients with a traumatic brain injury, reducing confidence in these findings.

Table 40 The Association between Movement Disorders and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[36] is insufficient to determine an association between movement disorders and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[36] reported an effect measure suggesting no association between movement disorders and mortality in patients with COVID-19. ▪ One cohort study[36] (N=26,332,166) of COVID-19 patients in the US reported no difference in the odds of mortality among 1,703 patients with movement disorder compared to patients without a movement disorder [OR 1.02 (95% CI: 0.81–1.29)]. However, the confidence interval crossed the null, reducing confidence in these findings.

ICU admission	Overall, limited data from only one study[36] is insufficient to determine an association between movement disorders and ICU admission in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[36] reported an effect measure suggesting no association between movement disorders and ICU admission in patients with COVID-19. ▪ One cohort study[36] (N=26,332) of COVID-19 patients in the US reported no difference in the odds of being admitted to the ICU among 1,703 patients with movement disorder compared to patients without a movement disorder [OR 0.99 (95% CI: 0.72–1.35)]. However, the confidence interval crossed the null, reducing confidence in these findings.
Intubation	Overall, limited data from only one study[36] is insufficient to determine an association between movement disorders and intubation in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[36] reported an effect measure suggesting that having movement disorders is associated with a decrease in intubation in patients with COVID-19. ▪ One cohort study[36] (N=26,332) of COVID-19 patients in the US reported a decrease in the odds of intubation among 1,703 patients with a movement disorder when compared to patients without a movement disorder [OR 0.79 (95% CI: 0.51–1.16)]. However, the confidence interval crossed the null, reducing confidence in these findings.
Hospitalization	Overall, limited data from only one study[36] is insufficient to determine an association between movement disorders and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[36] (N=26,332) reported no association between movement disorders and hospitalization in COVID-19 patients. ▪ One cohort study[36] (N=26,332) of COVID-19 patients in the U.S. reported no difference in the odds of hospitalization among 1,703 patients with a movement disorder compared to patients without a movement disorder [OR 1.09 (95% CI: 0.92–1.34)]. The confidence interval crosses the null, decreasing confidence in these findings..

Table 41 The Association between Autism and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited evidence from two studies[41,42] (N=20,019) is inconclusive on the association between autism and hospitalization in COVID-19 patients. Both studies were found to have a moderate threat to internal validity. • Strength of Association: No measures of association were reported. • Precision of Association: No study reported on confidence intervals.

	• Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: One study was conducted in USA and one in Italy. Summary of Evidence • One study[41] (N=19,260) suggested an increase in hospitalization among COVID-19 patients with autism. ▪ One cohort[41] (N=19,260) including electronic health record data on 5,639 US pediatric patients with COVID-19, reported an increased prevalence of autism among patients hospitalized with COVID-19 compared to those diagnosed with COVID-19 [3.5% (14/399) vs. 1.3% (73/5,639), p = NR]. • One study[42] (N=759) reported prevalence rates suggesting no association between autism and hospitalization among people with COVID-19. ▪ One cohort[42] of pediatric COVID-19 patients in Italy reported a higher proportion of hospitalization among patients with autism or neurological development impairment compared to patients without autism or neurological development impairment [50% (4/8) vs. 48% (357/751), p = NR]. This study reported a low prevalence of the exposure in the study population, and a low number of deaths.

Table 42 The Association between Being Wheelchair Use and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[57] is insufficient to determine an association between being wheelchair use and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One study[57] (N=88) reported proportions suggesting that being wheelchair use is associated with an increase in mortality in COVID-19 patients. ▪ One cohort study[57] (N=88) of nursing home residents with COVID-19 in the Netherlands reported a higher proportion of mortality among patients who were wheelchair use [41.4% (12/29) vs. 28.2% (11/39), p = NR] and or needed help walking compared to independent patients [47.4% (9/19) vs. 28.2% (11/39), p = NR]. However, mortality was lower among patients who were bedridden compared to independent patients [0.0% (0/1) vs. 28.2% (11/39)]. This study had a small sample size and reported a low number of deaths.

Table 43 The Association between Chromosomal Disorders and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[58] is insufficient to determine an association between chromosomal disorders and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study.

	• One cohort study[58] (N=3,896) reported data suggesting no difference in mortality among hospitalized COVID-19 patients with chromosomal disorders. ▪ One cohort study[58] (N=3,896) of hospitalized adult patients in Brazil reported no difference in the percentage of people with chromosomal disorders who died from or survived COVID-19 [1.1% (12/1,045) vs. 0.9% (27/2,851), p = 0.7]. This study was conducted in a middle-income country and reported a low number of deaths.
Hospitalization	Overall, limited data from only one study[41] is insufficient to determine an association between chromosomal disorders and hospitalization in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[41] (N=19,260) reported proportions suggesting that chromosomal disorders are associated with an increase in hospitalization among pediatric patients hospitalized with COVID-19 ▪ One cohort[41] (N=19,260) including electronic health record data on 5,639 US pediatric patients with COVID-19, reported an increased prevalence of chromosomal disorders among patients hospitalized with COVID-19 compared to those diagnosed with COVID-19 [3.5% (14/399) vs. 0.8% (45/5,639), p = NR].

Table 44 The Association between Neuropathy, Ataxia, and Retinitis Pigmentosa (NARP) and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited evidence from two studies[59,60] (N=28) is inconclusive on the association between NARP and hospitalization in COVID-19 patients. Internal validity is not assessed for case reports and studies with less than 10 people diagnosed with NARP. • Strength of Association: Zero studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: Both studies were conducted in Europe (Italy and the UK). Summary of Evidence • Two studies[59,60] (N=28) reported prevalence of hospitalization in patients with NARP. As these two studies did not have comparison groups, it is not possible to determine an association between NARP and hospitalization. ▪ One cohort study[59] (n = 27) of COVID-19 patients with primary mitochondrial diseases included in an Italian registry reported that none of the three people with NARP were hospitalized. This study did not report on measures of association nor significance value and had a small sample size with only three people diagnosed with NARP. ▪ One case report[60] (N= 1) of a 53-year-old man with COVID-19 in the UK with Retinitis pigmentosa reported that the patient was hospitalized.

Table 45 The Association between Primary Mitochondrial Myopathy (PMM) and Severe COVID-19 Outcomes

Outcome	Results

Mortality	Overall, limited data from only one study[59] (n = 27) is insufficient to determine an association between PMM and mortality in COVID-19 patients. Internal validity is not assessed for studies with less than 10 people diagnosed with PMM, and aggregation indices are not assessed for outcomes reported by only one study. • One study[59] (n = 27) reported data on mortality and PMM in COVID-19 patients. This study did not have a comparison group. ▪ One cohort study[59] (N= 27) of COVID-19 patients with primary mitochondrial diseases included in an Italian registry reported 25% (1/4) of people with PMM died. This study did not report on measures of association nor significance value and had a small sample size with only four people diagnosed with PMM.
Hospitalization	Overall, limited data from only one study[59] (N=27) is insufficient to determine an association between PMM and hospitalization in COVID-19 patients. Internal validity is not assessed for studies with less than 10 people diagnosed with PMM, and aggregation indices are not assessed for outcomes reported by only one study. • One study[59] (n = 27) reported data on hospitalization and PMM in COVID-19 patients. This study did not have a comparison group. ▪ One cohort study[59] (N= 27) of COVID-19 patients with primary mitochondrial diseases included in an Italian registry reported 50% (2/4) of people with PMM were hospitalized. This study reported a small number of hospitalizations and sample size.

Table 46 The Association between Spina Bifida and Other Nervous System Anomalies and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[5] is insufficient to determine an association between Spina Bifida and other nervous system anomalies and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One study[5] (N=467,773) reported effect measures suggesting that spina bifida is associated with an increase in mortality in patients with COVID-19. ▪ One cohort study[5] (N=467,773) of US patients of all ages diagnosed with COVID-19 reported an increase in the odds of mortality in patients with spina bifida and other nervous system anomalies compared to patients without spina bifida and other nervous system anomalies when adjusting for age and sex [aOR 2.48 (95% CI: 1.03 - 6.00, p = 0.03]. This study reported a wide confidence interval and the number of patients with Spina Bifida was not reported, decreasing confidence in the results.

Table 47 The Association between Leber's Hereditary Optic Neuropathy (LHON) or Autosomal Dominant Optic Atrophy (ADOA) and Severe COVID-19 Outcomes

Outcome	**Results**

Hospitalization	Overall, limited data from only one study[59] (N= 27) is insufficient to determine an association between Leber's hereditary optic neuropathy (LHON)/autosomal dominant optic atrophy (ADOA) and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with LHON/ADOA, and aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[59] reported data on hospitalization and LHON/ADOA in COVID-19 patients. This study did not have a comparison group. ▪ One cohort study[59] (N= 27) of COVID-19 patients with LHON/ADOA included in an Italian registry reported 0% (0/4) of people with LHON/ADOA were hospitalized. This study did not report on measures of association nor significance value and had a small sample size.

Table 48 The Association between Bedridden Disability (or Multiple Disability) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[57] (N= 88) is insufficient to determine an association between bedridden disability and mortality in COVID-19 patients. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[57] reported data on hospitalization and bedridden disability in COVID-19 patients. ▪ One cohort study[57] (N= 88) of people living in nursing homes with COVID-19 reported a lower proportion of mortality in people who were bedridden compared to independent people with or without mobility aids [0.0% (0/1) vs. 28.2% (11/39), p = NR]. However, only one of the individuals was bedridden prior to COVID-19, decreasing the generalizability of these results.

Table 49 The Association between Fragile X Syndrome and Severe COVID-19 Outcomes

Outcome	Results
ICU admission	Overall, limited evidence from two studies[61,62] (N= 4) is inconclusive on the association between Fragile X syndrome and ICU admission in COVID-19 patients. Internal validity assessments are not completed for case series / case reports. • Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: Both studies were conducted in a hospital setting in the US. Summary of Evidence • One case series[61] and one case report[62] reported ICU admission in patients with Fragile X syndrome and COVID-19.

	▪ One case series[61] (N= 3) of patients with COVID-19 in the U.S. reported that one 9-year-old patient was a person with Fragile X syndrome and admitted to the pediatric ICU. The patient had a history of intermittent asthma. ▪ One case report[62] (N= 1) of a 46-year-patient with Fragile X syndrome and COVID-19 in the U.S. reported that the patient was admitted to the medical ICU (MICU) on day five of hospitalization. The patient had a history of hypertension, morbid obesity, type II diabetes mellitus, asthma, and deep venous thrombosis in their left lower extremity.
Intubation	Overall, limited evidence from two studies[61,62] (n = 4) is inconclusive on the association between Fragile X syndrome and intubation in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Fragile X syndrome. • Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: Both studies were conducted in a hospital setting in the US. Summary of Evidence • One case series[61] and one case report[62] reported intubation in patients with Fragile X syndrome and COVID-19. ▪ One case series[61] (N= 3) of patients with COVID-19 in the U.S. reported that one 9-year-old patient with Fragile X syndrome was intubated [33.3% (1/3)]. The patient had a history of intermittent asthma. ▪ One case report[62] (n = 1) of a 46-year-patient with Fragile X syndrome and COVID-19 in the U.S. reported that the patient was intubated on day five of hospitalization. The patient had a history of hypertension, morbid obesity, type II diabetes mellitus, asthma, and deep venous thrombosis in their left lower extremity.
Ventilation	Overall, limited evidence from two studies[61,62] (n = 4) is inconclusive on the association between Fragile X syndrome and ventilation in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Fragile X syndrome. • Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association Both studies were conducted in a hospital setting in the US. Summary of Evidence • Two case series[61] and one case report[62] reported ventilation in patients with Fragile X syndrome and COVID-19. ▪ One case series[61] (N= 3) of patients with COVID-19 in the U.S. reported one 9-year-old child with Fragile X syndrome that was non-invasively ventilated with CPAP [33.3% (1/3)]. The patient had a history of intermittent asthma. ▪ One case report[62] (N= 1) of a 46-year-patient with Fragile-X syndrome and COVID-19 in the U.S. reported that the patient was mechanically ventilated. The patient had a history of hypertension, morbid obesity, type II diabetes mellitus, asthma, and deep venous thrombosis in their left lower extremity.
Hospitalization	Overall, limited evidence from three studies[61-63] (n = 6) is inconclusive on the association between Fragile X syndrome and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Fragile X syndrome. • Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported.

	• Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: Three studies were conducted in a hospital setting, two in the US and one in Europe. Summary of Evidence • Two case series[61,63] and one case report[62] reported hospitalization in patients with Fragile X syndrome and COVID-19. ▪ One case series[63] (N= 2) of patients with COVID-19 in Italy reported that one 11-year-old patient with Fragile X syndrome was hospitalized [50.0% (1/2)]. The patient had a history of recurrent status epilepticus (seizures) triggered by febrile episodes. ▪ One case series[61] (N= 3) of patients with COVID-19 in the U.S. reported that one 9-year-old child with Fragile X syndrome was admitted to the hospital [33.3% (1/3)]. The patient had a history of intermittent asthma. ▪ One case report[62] (n = 1) of a 46-year-patient with Fragile-X syndrome and COVID-19 in the U.S. reported that the one patient was admitted to the hospital. The patient had a history of hypertension, morbid obesity, type II diabetes mellitus, asthma, and deep venous thrombosis in their left lower extremity.

Table 50 The Association between Gaucher Disease and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from two studies[64,65] (n = 46) is inconclusive on the association between Gaucher disease and mortality in COVID-19 patients. One study[64] was found to have a moderate threat to internal validity while the other study[65] was found to have a high threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: Both studies were conducted in the US and did not report the age of patients or the setting of the study. Summary of Evidence • One cross-sectional study[64] and one case series[65] reported data on mortality in people with Gaucher disease and COVID-19. As these studies did not have a comparison group, it is not possible to determine an association between Gaucher disease and mortality. ▪ One cross-sectional study[64] (N= 16) of people with Gaucher disease and confirmed or suspected COVID-19 in the New York University (NYU) Langone Health Lysosomal Storage Disorders Program reported no deaths due to COVID-19. This study included a small number of people. ▪ One case series[65] (N= 30) of people with COVID-19 in the NYU Langone Health Lysosomal Storage Disorders Program reported that one patient with Gaucher disease died [3.8% (1/26)]. The patient had a history of morbid obesity, COPD, hypertension, and diabetes.

Hospitalization	Overall, limited data from two studies[64,65] (n = 46) is inconclusive on the association between Gaucher disease and hospitalization in COVID-19 patients. One study[64] was found to have a moderate threat to internal validity while the other study[65] was found to have a high threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: Both studies were conducted in the US and did not report the age of patients or the setting of the study. Summary of Evidence • One cross-sectional study[64] and one case series[65] reported data on hospitalization in people with Gaucher disease and COVID-19. As these studies did not have a comparison group, it is not possible to determine an association between Gaucher disease and hospitalization. ▪ One cross-sectional study[64] (N= 16) of people with confirmed or suspected COVID-19 in the NYU Langone Health Lysosomal Storage Disorders Program with Gaucher disease reported no hospitalizations due to COVID-19. This study included a small number of people. ▪ One case series[65] (N=30) of people with COVID-19 in the NYU Langone Health Lysosomal Storage Disorders Program reported that one patient with Gaucher disease was hospitalized [3.8% (1/26)]. The patient had a history of morbid obesity, COPD, hypertension, and diabetes.

Table 51 The Association between Hearing Impairment (Deafness/Hearing Loss) and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[66] (N= 1) is insufficient to determine an association between hearing impairment and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with hearing impairments, and aggregation indices are not assessed for outcomes reported by only one study. • One study[66] reported data on hospitalization and hearing impairment in a COVID-19 patient. ▪ One case report[66] (n = 1) reported that one patient with COVID-19 and a hearing impairment was hospitalized . The patient had a history of hypertension and hepatitis B.

Table 52 The Association between Maternal Inherited Diabetes and Deafness (MIDD) and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[59] (N= 27) is insufficient to determine an association between maternally inherited diabetes and deafness (MIDD) and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with MIDD, and aggregation indices are not assessed for outcomes reported by only one study.

	• One descriptive study[59] reported data on hospitalization and MIDD in COVID-19 patients. This study did not have a comparison group. ▪ One descriptive study[59] (N= 27) of people with COVID-19 and MIDD included in an Italian registry reported 0% (0/1) of people with MIDD were hospitalized. This study did not report on measures of association nor significance value and had a small sample size with only one person diagnosed with MIDD.

Table 53 The Association between Leigh Syndrome and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[59] (N= 27) is insufficient to determine an association between Leigh syndrome and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Leigh syndrome, and aggregation indices are not assessed for outcomes reported by only one study. • One descriptive study[59] reported data on hospitalization and Leigh syndrome in COVID-19 patients. This study did not have a comparison group. ▪ One descriptive study[59] (N= 27) of people with COVID-19 and Leigh syndrome in an Italian registry reported 0% (0/3) were hospitalized. This study did not report on measures of association nor significance value and had a small sample size with only three people diagnosed with Leigh syndrome.

Table 54 The Association between Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-Like Episodes (MELAS) and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[59] (N= 27) is insufficient to determine an association between mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with MELAS, and aggregation indices are not assessed for outcomes reported by only one study. • One descriptive study[59] reported data on hospitalization and MELAS in COVID-19 patients. This study did not have a comparison group. ▪ One descriptivestudy[59] (n = 27) of COVID-19 patients with primary mitochondrial diseases included in an Italian registry reported that 50% (2/4) of the patients with MELAS were hospitalized. This study did not report on measures of association nor significance value and had a small sample size with only four people diagnosed with MELAS.

Table 55 The Association between Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-Like Episodes (MELAS) and Risk Markers and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[59] (N=27) is insufficient to determine an association between mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS), sex, and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with MELAS, and aggregation indices are not assessed for outcomes reported by only one study. • One descriptive study[59] reported data on hospitalization and sex among MELAS people with COVID-19. • One descriptive study[59] (N= 27) of COVID-19 patients with primary mitochondrial diseases included in an Italian nationwide registry reported no difference in hospitalization due to sex [50% (1/2) vs. 50% (1/2), p = NR]. However, only four individuals had MELAS, decreasing the generalizability of the findings.

Table 56 The Association between Multisystem Disease and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[59] (n = 27) is insufficient to determine an association between multisystem disease and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with multisystem disease, and aggregation indices are not assessed for outcomes reported by only one study. • One descriptive study[59] reported data on hospitalization and multisystem disease in COVID-19 patients. This study did not have a comparison group. ▪ One descriptive study[59] (N= 27) of people with COVID-19 and multisystem disease in an Italian registry reported 0% (0/6) were hospitalized. This study did not report on measures of association nor significance value and had a small sample size with only six people diagnosed with multisystem disease.

Table 57 The Association between Myoclonic Epilepsy with Ragged Red Fibers (MERRF) and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[59] (N= 27) is insufficient to determine an association between myoclonic epilepsy with ragged red fibers (MERRF) and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with MERRF, and aggregation indices are not assessed for outcomes reported by only one study. • One descriptive study[59] reported data on hospitalization and MERFF in COVID-19 patients. This study did not have a comparison group. ▪ One descriptive study[59] (N= 27) of people with COVID-19 and MERFF in an Italian registry reported 0% (0/2) were hospitalized. This study did not report on measures of association nor significance value and had a small sample size with only two people diagnosed with MERFF.

Table 58 The Association between Perinatal Spastic Hemiparesis and Severe COVID-19 Outcomes

Outcome	Results
ICU admission	Overall, limited data from only one study[56] (N=135) is insufficient to determine an association between perinatal spastic hemiparesis and ICU admission in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with perinatal spastic hemiparesis, and aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[56] reported data on perinatal spastic hemiparesis and ICU admission among people with COVID-19. ▪ One cohort study[56] (N=135) of COVID-19 patients in Austria reported a lower proportion of ICU admission among people with perinatal spastic hemiparesis when compared to people without perinatal spastic hemiparesis [0.0% (0/1) vs. 23.1% (31/134, p = NR]. However, only one patient had perinatal spastic hemiparesis, decreasing confidence in the findings.
Hospitalization	Overall, limited data from only one study[56] (N=135) is insufficient to determine an association between perinatal spastic hemiparesis and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with perinatal spastic hemiparesis, and aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[56] reported data on perinatal spastic hemiparesis and hospitalization among people with COVID-19. ▪ One cohort study[56] (N=135) of COVID-19 patients in Austria reported a higher proportion of hospitalization among people with perinatal spastic hemiparesis when compared to people without perinatal spastic hemiparesis [100.0% (1/1) vs. 53.0% (71/134), p = NR]. This study reported only one person with perinatal spastic hemiparesis, decreasing confidence in the results.

Table 59 The Association between Charcot Foot and Severe COVID-19 Outcomes

Outcome	Results
ICU admission	Overall, limited data from only one study[67] (N=1) is insufficient to determine an association between Charcot foot and ICU admission in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Charcot foot, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[67] (N=1) reported ICU admission in a COVID-19 patient with Charcot foot. ▪ One case report[67] (N=1) of a hospitalized 63-year-old female in the US with Charcot foot and COVID-19 reported that the patient was admitted to the intensive care unit. The patient had a history of type 2 diabetes mellitus (T2DM) complicated by peripheral neuropathy, hypertension, peripheral artery disease, and mild asthma.
Hospitalization	Overall, limited data from only one study[67] (N=1) is insufficient to determine an association between Charcot foot and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Charcot foot, and aggregation indices are not assessed for outcomes reported by only one study.

	• One case report[67] (N=1) reported hospitalization in a COVID-19 patient with Charcot foot. ▪ One case report[67] (N=1) of a 63-year-old female in the US with Charcot foot and COVID-19 reported that the patient was hospitalized. The patient had a history of type 2 diabetes complicated by peripheral neuropathy, hypertension, peripheral artery disease, and mild asthma.

Table 60 The Association between Tourette Syndrome and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[68] (N=36) is insufficient to determine an association between Tourette syndrome and mortality in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Tourette syndrome, and aggregation indices are not assessed for outcomes reported by only one study. • One case series[68] (N=36) reported on mortality in COVID-19 patients with Tourette syndrome. ▪ One case series[68] (N=36) of COVID-19 patients reported that neither patient with Tourette syndrome died 0% (0/2). The two patients with Tourette syndrome included in the study were a 55-year-old female with no comorbidities and a 65-year-old female with a history of sarcoidosis, asthma, and atrial fibrillation.
Hospitalization	Overall, limited data from only one study[68] (N=36) is insufficient to determine an association between Tourette syndrome and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Tourette syndrome, and aggregation indices are not assessed for outcomes reported by only one study. • One case series[68] (N=36) reported hospitalization of a patient with Tourette syndrome and COVID-19. ▪ One case series[68] (N=36) of COVID-19 patients reported that 50% (1/2) patients with Tourette syndrome were hospitalized. The hospitalized patient was a 55-year-old female with no comorbidities.

Table 61 The Association between Chromosome 18q Deletion and Severe COVID-19 Outcomes

Outcome	Results
ICU admission	Overall, limited evidence from one study[69] (N=1) is inconclusive on the association between chromosome 18q deletion and ICU admission in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with chromosome 18q deletion, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[69] (N=1) reported ICU admission in a patient with a chromosome 18q deletion and COVID-19.

	▪ One case report[69] (N=1) of a 16-year-old boy with a chromosome 18q deletion and COVID-19 in the US reported that the patient was admitted to the ICU. The patient had a history of epilepsy.
Intubation	Overall, limited evidence from one study[69] (N=1) is inconclusive on the association between chromosome 18q deletion and intubation in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with chromosome 18q deletion, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[69] (N=1) reported intubation in a patient with a chromosome 18q deletion and COVID-19. ▪ One case report[69] (N=1) of a 16-year-old boy with a chromosome 18q deletion and COVID-19 in the US reported that the patient was intubated. The patient had a history of epilepsy.
Hospitalization	Overall, limited evidence from one study[69] (N=1) is inconclusive on the association between chromosome 18q deletion and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with chromosome 18q deletion, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[69] (N=1) reported hospitalization in a patient with a chromosome 18q deletion and COVID-19. ▪ One case report[69] (N=1) of a 16-year-old boy with a chromosome 18q deletion and COVID-19 in the US reported that the patient was hospitalized. The patient had a history of epilepsy

Table 62 The Association between Chromosome 17 and 19 Deletion and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[70] (N=1) is insufficient to determine an association between chromosome 17 and 19 deletions and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with chromosome 17 and 19 deletion, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[70] (N=1) reported hospitalization in a patient with chromosome 17 and 19 deletions and COVID-19. ▪ One case report[70] (N=1) of a 6-year-old with chromosome 17 and 19 deletions and COVID-19 reported that the patient was hospitalized. The patient had a history of prematurity (born at 30 weeks), submucosal cleft palate, surgically repaired atrial and ventricular septal defects, agammaglobulinemia with hyper IgM, hypospadias, asthma, and moderate obstructive sleep apnea.

Table 63 The Association between Congenital Hydrocephalus and Severe COVID-19 Outcomes

Outcome	Results

Hospitalization	Overall, limited data from only one study[71] (N=51) is insufficient to determine an association between congenital hydrocephalus and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with congenital hydrocephalus, and aggregation indices are not assessed for outcomes reported by only one study. • One case series[71] (N=51) of COVID-19 patients reported hospitalization in one patient with congenital hydrocephalus. ▪ One case series[71] (N=51) of pediatric COVID-19 patients reported that one patient with congenital hydrocephalus was hospitalized. The patient was an infant with no other comorbidities.

Table 64 The Association between Fahr's Syndrome and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[72] (N=1) is insufficient to determine an association between Fahr's syndrome and mortality in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Fahr's syndrome, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[72] (N=1) reported mortality in a patient with Fahr's syndrome and COVID-19. ▪ One case report[72] (N=1) of a 68-year-old female patient in Turkey with Fahr's syndrome reported that the patient died. The patient had a history of hypoparathyroidism.
ICU Admission	Overall, limited data from only one study[72] (N=1) is insufficient to determine an association between Fahr's syndrome and ICU admission in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Fahr's syndrome, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[72] (N=1) reported ICU admission in a patient with Fahr's syndrome and COVID-19. ▪ One case report[72] (N=1) of a 68-year-old female patient in Turkey with Fahr's syndrome reported that the patient was admitted to the ICU. The patient had a history of hypoparathyroidism.
Intubation	Overall, limited data from only one study[72] (N=1) is insufficient to determine an association between Fahr's syndrome and intubation in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Fahr's syndrome, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[72] (N=1) reported intubation in a patient with Fahr's syndrome and COVID-19. ▪ One case report[72] (N=1) of a 68-year-old female patient in Turkey with Fahr's syndrome reported that the patient was intubated. The patient had a history of hypoparathyroidism.

Ventilation	Overall, limited data from only one study[72] (N=1) is insufficient to determine an association between Fahr's syndrome and ventilation in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Fahr's syndrome, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[72] (N=1) reported ventilation in a patient with Fahr's syndrome and COVID-19. ▪ One case report[72] (N=1) of a 68-year-old female patient in Turkey with Fahr's syndrome reported that the patient received ventilation. The patient had a history of hypoparathyroidism.
Hospitalization	Overall, limited data from only one study[72] (N=1) is insufficient to determine an association between Fahr's syndrome and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Fahr's syndrome, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[72] (N=1) reported hospitalization in a patient with Fahr's syndrome and COVID-19. ▪ One case report[72] (N=1) of a 68-year-old female patient in Turkey with Fahr's syndrome reported that the patient was hospitalized. The patient had a history of hypoparathyroidism and was diagnosed with Fahr's syndrome while hospitalized for COVID-19.

Table 65 The Association between Hands and Feet Disorder (Birth Defect) and Severe COVID-19 Outcomes

Outcome	Results
ICU admission	Overall, limited data from only one study[73] (N=7) is insufficient to determine an association between hands and feet birth defect and ICU admission in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with hands and feet birth defect, and aggregation indices are not assessed for outcomes reported by only one study. • One case series[73] (N=7) reported one patient with a hands and feet birth defect and COVID-19 was admitted to the ICU. ▪ One case series[73] (N=7) that included a 39-year-old Native American female with a hands and feet birth defect in the US reported that the patient was admitted to ICU. The patient had a history of diabetes.
Intubation	Overall, limited data from only one study[73] (N=7) is insufficient to determine an association between hands and feet birth defect and intubation in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with hands and feet birth defect, and aggregation indices are not assessed for outcomes reported by only one study. • One case series[73] (N=7) reported one patient with a hands and feet birth defect and COVID-19 was intubated. ▪ One case series[73] (N=7) that included a 39-year-old Native American female with a hands and feet birth defect in the US reported that the patient was intubated. The patient had a history of diabetes.

Hospitalization	Overall, limited data from only one study[73] is insufficient to determine an association between hands and feet birth defect and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with hands and feet birth defect, and aggregation indices are not assessed for outcomes reported by only one study. • One case series[73] (N=7) reported one patient with a hands and feet birth defect and COVID-19 was hospitalized. ▪ One case series[73] (N=7) that included a 39-year-old Native American female with a hands and feet birth defect in the US reported that the patient was hospitalized. The patient had a history of diabetes.

Table 66 The Association between Myotonic Dystrophy and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[74] (N= 3) is insufficient to determine an association between myotonic dystrophy and mortality in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with myotonic dystrophy, and aggregation indices are not assessed for outcomes reported by only one study. • One case series[74] (N=3) reported mortality in patients with myotic dystrophy and COVID-19. ▪ One case series[74] (N=3) of hospitalized COVID-19 patients with myotonic dystrophy in Belgium reported 100% (3/3) died. One patient tested negative by RT-PCR twice and was diagnosed with presumptive COVID-19 based on epidemiology, radiography, and biochemistry. Two patients had a history of obesity, one of which was also wheelchair-use. The third patient had a history of cardiovascular disease.
Intubation	Overall, limited data from only one study[74] (N= 3) is insufficient to determine an association between myotonic dystrophy and intubation in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with myotonic dystrophy, and aggregation indices are not assessed for outcomes reported by only one study. • One case series[74] (N=3) reported on intubation in patients with myotic dystrophy and COVID-19. ▪ One case series[74] (N=3) of hospitalized COVID-19 patients with myotonic dystrophy in Belgium reported none were intubated 0% (0/3). One patient tested negative by RT-PCR twice and was diagnosed with presumptive COVID-19 based on epidemiology, radiography, and biochemistry. Two patients had a history of obesity, one of which was also wheelchair-use. The third patient had a history of cardiovascular disease.
Ventilation	Overall, limited data from only one study[74] (N=3) is insufficient to determine an association between myotonic dystrophy and ventilation in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with myotonic dystrophy, and aggregation indices are not assessed for outcomes reported by only one study. • One case series[74] (N=3) reported non-invasive ventilation in patients with myotonic dystrophy and COVID-19. ▪ One case series[74] (N=3) of hospitalized COVID-19 patients with myotonic dystrophy in Belgium reported 100% (3/3) received non-invasive ventilation. One patient tested negative by RT-PCR twice and was diagnosed with presumptive

	COVID-19 based on epidemiology, radiography, and biochemistry. Two patients had a history of obesity, one of which was also wheelchair-use. The third patient had a history of cardiovascular disease.
Hospitalization	Overall, limited data from only one study[74] (N=3) is insufficient to determine an association between myotonic dystrophy and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with myotonic dystrophy, and aggregation indices are not assessed for outcomes reported by only one study. • One case series[74] (N=3) reported hospitalization in patients with myotic dystrophy and COVID-19. ▪ One case series[74] (N=3) of COVID-19 patients with myotonic dystrophy in Belgium reported 100% (3/3) were hospitalized. One patient tested negative by RT-PCR twice and was diagnosed with presumptive COVID-19 based on epidemiology, radiography, and biochemistry. Two patients had a history of obesity, one of which was also wheelchair-use. The third patient had a history of cardiovascular disease.

Table 67 The Association between Progressive Supranuclear Palsy and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[68] (N= 36) is insufficient to determine an association between progressive supranuclear palsy and mortality in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with progressive supranuclear palsy, and aggregation indices are not assessed for outcomes reported by only one study • One case series[68] (N=36) reported mortality in patients with progressive supranuclear palsy and COVID-19. ▪ One case series[68] (N=36) of COVID-19 patients reported that 100% (2/2) patients with progressive supranuclear palsy died. The patients with progressive supranuclear palsy included in the study were a 68-year-old female with a history of diabetes mellitus type 2, breast cancer, and renal cell carcinoma and a 72-year-old male with a history of cervical dystonia and dementia.
Hospitalization	Overall, limited data from only one study[68] (n = 36) is insufficient to determine an association between progressive supranuclear palsy and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with progressive supranuclear palsy, and aggregation indices are not assessed for outcomes reported by only one study. • One case series[68] (N=36) reported on hospitalization in patients with progressive supranuclear palsy and COVID-19. ▪ One case series[68] (N=36) of COVID-19 patients reported 0% (0/2) patients with progressive supranuclear palsy were hospitalized. The patients with progressive supranuclear palsy included in the study were a 68-year-old female with a history of diabetes mellitus type 2, breast cancer, and renal cell carcinoma and a 72-year-old male with a history of cervical dystonia and dementia.

Table 68 The Association between Senior-Loken Syndrome and Severe COVID-19 Outcomes

Outcome	Results
Hospitalization	Overall, limited data from only one study[75] (N=1) is insufficient to determine an association between Senior-Loken syndrome and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with Senior-Loken syndrome and aggregation indices are not assessed for outcomes reported by only one study. • One case report[75] (N=1) reported hospitalization in a patient with Senior-Loken syndrome and COVID-19. ▪ One case report[75] (N=1) of a 36-year-old woman with Senior-Loken syndrome and COVID-19 in Italy reported that the patient was hospitalized. The patient had a history of two kidney transplants.

Table 69 The Association between Visual Impairment/Blindness and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, limited data from only one study[76] (N= 1) is insufficient to determine an association between visual impairment and mortality in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with visual impairment, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[76] (N=1) reported data on mortality in a patient with a visual impairment and COVID-19. ▪ One case report[76] (N=1) of a 70-year-old man in China with a visual impairment reported that the patient died. Visual impairment was defined as bitemporal hemianopsia caused by pituitary adenoma. The patient had a history of hypertension, diabetes, and heart attack.
ICU admission	Overall, limited data from only one study[77] (N= 1) is insufficient to determine an association between visual impairment and ICU admission in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with visual impairment, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[77] (N=1) reported ICU admission in a patient with a visual impairment and COVID-19. ▪ One case report[77] (N=1) of a 90-year-old African American female with a visual impairment in the US reported that the patient was admitted to the ICU. Visual impairment was defined as right-eye blindness. The patient had a history of hypertension, osteoarthritis, type 2 diabetes mellitus, deep venous thrombosis, pulmonary embolism, stage 2 chronic kidney disease, atrial flutter, cataract, macular degeneration, pressure ulcer stage II, and mild dementia.
Ventilation	Overall, limited data from only one study[76] (N=1) is insufficient to determine an association between visual impairment and ventilation in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with visual impairment, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[76] (N=1) reported data on ventilation in a patient with a visual impairment and COVID-19.

	▪ One case report[76] (N=1) of a 70-year-old man in China with a visual impairment reported that the patient received non-invasive ventilation. Visual impairment was defined as bitemporal hemianopsia caused by pituitary adenoma. The patient had a history of hypertension, diabetes, and heart attack.
Hospitalization	Overall, limited data from two studies[76,77] (N=2) is insufficient to determine an association between visual impairment and hospitalization in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with visual impairment. • Strength of Association: No measures of association were reported. • Precision of Association: Confidence intervals were not calculated. • Consistency of Association: Overall, the evidence is inconclusive. • Applicability of Association: One study was conducted in China and one study was conducted in the US. Summary of Evidence • Two case reports[76,77] (N=2) reported hospitalization for both patients with visual impairments and COVID-19. ▪ One case report[76] (N=1) of a 70-year-old man in China with a visual impairment reported that the patient was hospitalized. Visual impairment was defined as bitemporal hemianopsia caused by pituitary adenoma. The patient had a history of hypertension, diabetes, and heart attack. ▪ One case report[77] (N=1) of a 90-year-old African American female with a visual impairment in the US reported that the patient was hospitalized. Visual impairment was defined as right-eye blindness. The patient had a history of hypertension, osteoarthritis, type 2 diabetes mellitus, deep venous thrombosis, pulmonary embolism, stage 2 chronic kidney disease, atrial flutter, cataract, macular degeneration, pressure ulcer stage II, and mild dementia.
Readmission	Overall, limited data from only one study[77] (N=1) is insufficient to determine an association between visual impairment and non-elective readmission in COVID-19 patients. Internal validity assessments are not completed for studies with less than 10 people with visual impairment, and aggregation indices are not assessed for outcomes reported by only one study. • One case report[77] (N=1) reported on readmission in a patient with a visual impairment and COVID-19. ▪ One case report[77] (N=1) of a 90-year-old female with a visual impairment in the US reported that the patient was hospitalized, later discharged after negative SARS-CoV-2 test, and was readmitted to the hospital with posterior reversible encephalopathy syndrome over 3 weeks after initial discharge. Visual impairment was defined as right-eye blindness. The patient had a history of hypertension, osteoarthritis, type 2 diabetes mellitus, deep venous thrombosis, pulmonary embolism, stage 2 chronic kidney disease, atrial flutter, cataract, macular degeneration, pressure ulcer stage II, and mild dementia.

B.3.b. Extracted Evidence

Table 70 Extracted Studies Reporting the Association between Disabilities and Severe COVID-19 Outcomes

Source	Population/Setting	Sample Size/ Comparison group	Outcomes	Results
Author: Abedi[11] **Publication:** 2021 **Data Extractor:** TR **Reviewer:** ES **Study Design:** Cross-sectional ecological study **Study Objective:** To explore racial and economic inequality associated with the infection rate and risk of mortality due to COVID-19 in the US. **IVA Score:** 23 (moderate)	**Population:** N= 102,178,117 N=369 counties in 7 states **Setting:** Hospitals, nursing homes, and other health facilities **Data Source:** 1) Publicly available data from USA facts and the US Census Bureau for COVID-19 cases and county-level demographic data, 2) COVID-19 data reported by each state on their department of health websites, 3) State Population by Race/Ethnicity data, and 4) mobility data extracted from Google. Mortality data reported by hospitals, nursing homes, and other health facilities **Location:** California, Michigan, New York, New Jersey, Louisiana, Pennsylvania, and Massachusetts, USA **Study Dates:** Up to April 2020 **Inclusion Criteria:** Only data provided by the	**Medical Condition, n/N (%):** County-level % persons with a disability: 15% (6.5% - 28.5%) **Control/Comparison Group, n/N (%):** NR	**Medical Condition(s):** Disability: ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *OR: Odds Ratio* *Mortality, n/N (%):* Disability: • OR: 0.27 (95% CI: 0.087-0.452), p = 0.004 *County-level median mortality rate:* Disability Rate Mean (SD) • Death rate ≤ 3.4 (N=109 counties): 12.92 (2.87) • Death rate >3.4 (N=109 counties): 14.26 (3.10) • ANOVA p-value: p = 0.001 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** Mortality • Authors included an interaction term for poverty and disability in the linear regression model and not observe a significant interaction (p = 0.469), and suggested these two variables could be independent in their contribution to the risk of mortality **Long-term Sequelae:** NR

	states on their official websites were included in this study **Exclusion Criteria:** NR			
Author: Alonso[46] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** CS **Study Design:** Prospective cohort **Study Objective:** To describe the clinical characteristics and outcomes of multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) patients included in RELACOEM (Registro Latino americano de Covid-19 y esclerosis múltiple). **IVA Score:** 20 (Moderate)	**Population:** N=145 **Setting:** Medical centers **Data Source:** RELACOEM (Registro Latino americano de Covid-19 y esclerosis múltiple), a LATAM registry of MS and NMOSD patients infected with COVID-19 **Location:** 15 Latin American countries **Study Dates:** March – August 30, 2020 **Inclusion Criteria:** MS and NMOSD patients with a biologically confirmed COVID-19 diagnosis based on a positive result of a COVID-19 polymerase chain reaction (PCR) test on a nasopharyngeal swab or suspected COVID-19 cases according to the WHO definition. **Exclusion Criteria:** MS and NMOSD patients with incomplete data during follow-up.	**Medical Condition, n/N (%):** Neuromyelitis optica spectrum disorder (NMOSD): 16/145 (11%) **Control/Comparison Group, n/N (%):** NA	**Medical Condition(s):** *NMOSD:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* hospitalized and/or ICU admitted *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality:* 5 out of 16 patients with NMOSD (31.2%) died from COVID-19 *ICU admission:* 7 out of 16 patients with NMOSD (43.8%) required ICU admission *Hospitalization:* 9 out of 16 patients with NMOSD (56.0%) required hospitalization **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** *Hospitalization, n/N (%) among patients with NMOSD:* Obese: • Hospitalized: 5/9 (55.5%) • Not hospitalized: 1/7 (14.3%) • p = 0.09 **Risk Markers:** *Hospitalization, n/N (%) or median (standard deviation) among patients with NMOSD:* Female: • Hospitalized: 8/9 (88.8%) • Not hospitalized: 6/7 (85.7%) • p = 0.87 Age: • Hospitalized: 54 (+/-3) • Not hospitalized: 36 (+/-3) • p<0.001 Current smoker: • Hospitalized: 0/9 (0%) • Not hospitalized: 0/7 (0%)

				Long-term Sequelae: NR
Author: An[12] **Publication:** 2020 **Data Extractor:** MW **Reviewer:** MC **Study Design:** Retrospective cohort **Study Objective:** To develop and validate machine learning models that predict the prognosis of COVID-19 patients based on sociodemographic information, infection route, and medical status and history, for the nationwide cohort of South Korea. **IVA Score:** 24 (Moderate)	**Population:** N =10,237 **Setting:** Hospital **Data Source:** Two data sources provided by the Korean National Health Insurance Service (KNHIS): the database of beneficiaries of national health insurance and the newly added database of patients with laboratory-confirmed diagnosis of COVID-19 **Location:** South Korea **Study Dates:** January 23 - April 16, 2020 **Inclusion Criteria:** Patients who had tested positive for COVID-19. **Exclusion Criteria:** Patients with missing values were excluded.	**Medical Condition, n/N (%):** Disability: 760/10,237 (7.4%) **Control/Comparison Group, n/N (%):** No disability: 9,477/10,237 (92.6%)	**Medical Condition(s):** *Disability:* ND **Severity Measure(s):** *Mild disability:* ND *Moderate or severe disability:* ND **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** The study included 10,237 Korean patients of these patients, 228 (2.2%) had died, 7772 (75.9%) had recovered, and 2237 (21.9%) were still in isolation or being treated.	**Severe COVID-19:** *aHR: Adjusted Hazard Ratio; Cox proportional hazards ratio; included model variables: age, sex, income level, residence, household type, disability, symptom, and infection route* *HR: Hazard Ratio* *Mortality, n/N (%):* • Disability: 62/760 (8.2%) • No disability: 166/9,477 (1.8%) **Severity of Condition:** *Mortality, n/N (%):* Mild disability: • aHR: 0.98 (95% CI: 0.67-1.42), p = 0.911 • HR: 4.76 (95% CI: 3.32-6.82), p<0.0001 • Mild disability: 40/516 (7.8%) • No disability: 166/9,477 (1.8%) Moderate or severe disability: • aHR: 1.63 (95% CI: 1.01-2.63), p = 0.047 • HR: 6.19 (95% CI: 3.96-9.68), p<0.0001 • Moderate or severe disability: 22/244 (9.0%) • No disability: 166/9,477 (1.8%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Andres-Esteban[30] **Publication:** 2021 **Data Extractor:** TR **Reviewer:** JKK **Study Design:** Cohort **Study Objective:** To explore the complications of	**Population:** N=254 **Setting:** Hospital **Data Source:** La Paz University Hospital database **Location:** Spain **Study Dates:** July 15 – July 31, 2020	**Medical Condition, n/N (%):** Dependent: 17/254 (6.7%) Semi dependent: 9/254 (3.5%) **Control/Comparison Group, n/N (%):** Independent: 206/254 (81.1%)	**Medical Condition(s):** NR **Severity Measure(s):** *Dependent:* ND *Semi dependent:* ND *Independent:* ND **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR	**Severe COVID-19:** NR **Severity of Condition:** *Hospitalization, n/N (%):* • Dependent: 17/254 (6.7%) • Semi dependent: 9/254 (3.5%) • Independent: 206/254 (81.1%) • p<0.001 **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR

COVID-19 in patients admitted to a third-level hospital and to evaluate the relationship between these complications and frailty. **IVA** **Score:** 20 (moderate)	**Inclusion Criteria:** Patients admitted with a respiratory infection by SARS-CoV-2 (determined by polymerase chain reaction) since the beginning of the current pandemic. **Exclusion Criteria:** NR		*Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Long-term Sequelae:** NR
Author: Arbel[53] **Publication:** 2020 **Data Extractor:** MM **Reviewer:** DOS **Study Design:** Ecological study using regression analysis **Study Objective:** To investigate the relationships between infection, mortality, and recovery rates from COVID-19 and the prevalence of ADHD at the US state level. **IVA Score:** 16 (High)	**Population:** N=34 states **Setting:** Nationwide **Data Source:** NR **Location:** US **Study Dates:** August 11, 2020 **Inclusion Criteria:** States with observations regarding recovery cases from coronavirus. Information on ADHD prevalence was also obtained. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** ADHD: 3%-13% **Control/Comparison Group, n/N (%):** No ADHD: 87%-97%	**Medical Condition(s):** *ADHD:* a common neurodevelopmental disorder of childhood typically presenting as trouble paying attention, controlling behavior, acting without fully considering expected results, or exhibit over-active behavior **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality:* • The study reports no correlations between ADHD and population size, and infection and mortality rates from coronavirus [-0.0251, p = 0.861]. Recovery rates rose with the prevalence of ADHD. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Balangue[24] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** MM/DOS	**Population:** N=191 **Setting:** Multicenter healthcare system **Data Source:** NR **Location:** Arizona, USA	**Medical Condition, n/N (%):** Mild to moderate dependence: 73/191 (38%) High dependence: 32/191 (17%) **Control/Comparison Group, n/N (%):** No dependence: 86/191 (45%)	**Medical Condition(s):** NA **Severity Measure(s):** *High dependence:* classified based on functional state prior to hospitalization using ADL dependence, use of walking aids and living situation as documented in the EHR by case managers	**Severe COVID-19:** NA **Severity of Condition:** *Mortality (%):* • High dependence: 53.0% • Mild to moderate dependence: 27.0% • No dependence: 19.0% • p = 0.001

Study Design: Retrospective cohort **Study Objective:** To classify hospitalized older adults based on their functional state prior to hospitalization and its association with adverse outcomes of COVID-19. **IVA Score:** 17 (High)	**Study Dates:** March – April 2020 **Inclusion Criteria:** Hospitalized adults older than 60 years with a positive PCR test for SARS-CoV-2. **Exclusion Criteria:** NR		*Mild to moderate dependence:* classified based on functional state prior to hospitalization using ADL dependence, use of walking aids and living situation as documented in the EHR by case managers *No dependence:* classified based on functional state prior to hospitalization using ADL dependence, use of walking aids and living situation as documented in the EHR by case managers **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Bartiromo[75] **Publication:** 2020 **Data Extractor:** AH **Reviewer:** CS **Study design:** Case report **Study Objective:** To present the case of a woman with Senior-Loken syndrome who underwent a 2nd kidney transplant and developed a pauci-symptomatic COVID-19 pneumonia. **IVA Score:** Internal validity was not conducted for case reports/case series.	**Population:** N= 1 **Setting:** Hospital **Location:** Italy **Study dates:** March 6-24, 2020 **Inclusion criteria:** NR **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Senior-Loken syndrome (SLS): 1/1 (100.0%)	**Medical Condition(s):** *Senior-Loken syndrome*: a rare genetic disorder characterized by nephronophthisis and retinal degeneration leading to blindness and end-stage kidney disease (ESKD). **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality:* No *ICU admission:* No *Intubation (or Invasive Ventilation):* No *Ventilation (mechanical, or non-invasive ventilation):* No *Hospitalization:* Yes *General Progression* • *Case 1:* A 36-year-old woman with SLS and two kidney transplants tested positive for COVID-19 by PCR test and hospitalized. She experienced fatigue, dry cough, coryza and subsequently developed COVID-19 pneumonia. She received antivirals / immunosuppressive therapy and on day 4, she started to experience abdominal pain, nausea, and vomit. The antivirals were discontinued; in the following days she recovered from her gastrointestinal symptoms and showed a general amelioration of her clinical condition. She was discharged on day 9 and put in home isolation until having two consecutive negative COVID-19 PCR tests on day 12 and 18 after discharge.

				Severity of Condition: NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** • *Case 1:* History of ESKD (2 Kidney Transplants in 1993 and 1995) caused by SLS **Risk Markers:** NR **Long-term Sequelae:** NA
Author: Bergman[22] **Publication:** 2021 **Data Extractor:** DOS **Reviewer:** CS **Study Design:** Case-control **Study Objective:** To investigate the importance of potential medical and demographic risk factors for COVID-19 diagnosis, hospitalization (with or without ICU admission), and subsequent all-cause mortality during the first wave of COVID-19. **IVA Score:** 26 (Low)	**Population:** N=502,656 **Setting:** Hospital **Data Source:** Swedish registries **Location:** Sweden **Study Dates:** NR - mid-September 2020 **Inclusion Criteria:** All cases of COVID-19 confirmed in Sweden until mid-September 2020. Reporting confirmed cases to is required by law. Control population comprised of random sample of 5 non-diagnosed individuals for each COVID-19 case. Each control was residing in Sweden on January 1, 2020 and was alive on January 31, 2020. **Exclusion Criteria:** Persons were excluded if they had missing data on at least one of the included variables.	**Medical Condition, n/N (%):** Down syndrome: 57/68,575 (0.1%) **Control/Comparison Group, n/N (%):** No down syndrome: 297/434,081 (0.1%)	**Medical Condition(s):** *Down syndrome:* ICD10 Q90 **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* All-cause mortality until October 1, 2020 *ICU admission:* ICU hospitalization for confirmed COVID-19 (ICD-10 U071) *Intubation:* NR *Ventilation:* NR *Hospitalization:* non-ICU hospitalization with confirmed COVID-19 (ICD-10 U071) *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aHR: Adjusted hazard ratio; cox regression; model included demographic variables, comorbidities, and prescription medications* *HR: Unadjusted hazard ratio* *aOR: Adjusted odds ratio; multinomial logistic regression; model included demographic variables, comorbidities, and prescription medications* *OR: Unadjusted odds ratio; univariable logistic regression* *Mortality, n/N (%):* Down syndrome: • aHR: 10.91 (95% CI: 5.41-22.02) • HR: 2.70 (95% CI: 1.62-4.47) *ICU admission, n/N (%):* Down syndrome: • aOR: 4.26 (95% CI: 1.01-17.90) • OR: 4.52 (95% CI: 2.21-9.25) • ICU admission: 8/2494 (0.3%) *Hospitalization, n/N (%):* Down syndrome: • aOR: 3.24 (95% CI: 1.55-6.78) • OR: 2.16 (95% CI:1.37-3.40) • Hospitalized: 20/13,589 (0.1%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NA **Long-term Sequelae:** NR

Author: Boaventura[47] **Publication:** 2020 **Data Extractor:** MW/CS **Reviewer:** TR **Study Design:** Retrospective cohort **Study Objective:** To describe the frequency and clinical characteristics of COVID-19 in neuromyelitis optica s pectrum disorder (NMOSD) patients in Brazil. **IVA Score:** 14 (High)	**Population:** N =2,061 N=34 COVID-19+ **Setting:** Neuroimmunology centers **Data Source:** REDONE.br platform **Location:** Brazil **Study Dates:** March 19 – July 31, 2020 **Inclusion Criteria:** NMOSD diagnosis according to 2015 International Panel and confirmed SARS-Cov-2 infection (RT-PCR or serology) or clinical suspicion of COVID-19 diagnosed according to CDC case definition. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** NMOSD & COVID-19: 34/34 (100%) **Control/Comparison Group, n/N (%):** NA	**Medical Condition(s):** *NMOSD*: ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality:* • One patient with NMOSD died while receiving treatment at the ICU *ICU admission:* • Four patients with NMOSD needed treatment at the ICU **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Bosworth[17] **Publication:** 2021 **Data Extractor:** DOS **Reviewer:** CS **Study Design:** Retrospective cohort **Study Objective:** To use population-level data from England containing detailing socio-demographic characteristics and information on pre-pandemic health status to estimate the association of death	**Population:** N=29,293,845 **Setting:** Community **Data Source:** Office for National Statistics Public Health Data Asset which comprises linked data from the 2011 Census, General Practice Extraction Service Data for Pandemic Planning and Research, Hospital Episode Statistics Admitted Patient Care, and death registrations **Location:** England	**Medical Condition, n*/N (%):** Disabled: 4,979,954/29,293,845 (17%) • More-disabled: 2,050,569/29,293,845 (7%) • Less-disabled: 2,929,385/29,293,845 (10%) **Control/Comparison Group, n*/N (%):** Non-disabled: 24,313,891/29,293,845 (83%) *Numerators calculated using overall population and reported percentages	**Medical Condition(s):** *Disabled:* self-reported disability status retrieved from the 2011 Census question, “Are your day-to-day activities limited because of a health problem or disability which has lasted, or is expected to last, at least 12 months? Include problems related to old age”; responses of “Yes, limited a lot” and “Yes, limited a little” were classified as disabled **Severity Measure(s):** *More-disabled:* response of "Yes, limited a lot” to the 2011 Census question *Less-disabled:* response of "Yes, limited a little” to the 2011 Census question **Clinical Marker:** NR	**Severe COVID-19:** *aHR1: Adjusted Hazard Ratio; Cox proportional hazards regression model adjusted for age, residence type, local authority district, population density, area deprivation, socioeconomic status, ethnicity, household composition, occupational exposure, and pre-existing conditions* *aHR2: Age-adjusted Hazard Ratio* **Severity of Condition:** *Deaths involving COVID-19 among males:* • More-disabled, aHR1: 1.35 (95% CI: 1.32-1.38) • Less-disabled, aHR1: 1.21 (95% CI: 1.18-1.23) • Non-disabled: ref *Deaths involving COVID-19 among females:* • More-disabled, aHR1: 1.55 (95% CI: 1.51-1.59) • Less-disabled, aHR1: 1.28 (95% CI: 1.25-1.31) • Non-disabled: ref *Cumulative mortality involving COVID-19 per 1,000, males:*

involving COVID-19 with self-reported disability. **IVA Score:** 24 (Moderate)	**Study Dates:** January 24, 2020 - February 28, 2021 **Inclusion Criteria:** Adults aged 30 to 100 years living in private households or communal establishments (including care homes) in England, who were enumerated at the 2011 Census, were alive on January 24, 2020, and could be linked to the 2011 to 2013 Patient Registers and General Practice Extraction Service Data for Pandemic Planning and Research dataset. **Exclusion Criteria:** Individuals aged less than 30 years in 2020 as their living circumstances are likely to have changed since 2011.		**Outcome Definitions:** *Mortality:* • All-cause mortality • Death involving COVID-19: COVID-19 ICD-10 code of U07.1 or U07.2 anywhere on death certificate during period January 24, 2020 - February 28, 2021 *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	• More-disabled: 9.39 (95% CI: 9.20-9.59) • Less-disabled: 5.55 (95% CI: 5.44-5.67) • Non-disabled: 2.99 (95% CI: 2.95-3.03) *Cumulative mortality involving COVID-19 per 1,000, females:* • More-disabled: 7.36 (95% CI: 7.20-7.52) • Less-disabled: 3.92 (95% CI: 3.84-4.00) • Non-disabled: 2.11 (95% CI: 2.08-2.15) *Deaths involving COVID-19, age-standardized mortality rate per 100,000 person-years at risk, males:* • More-disabled: 899 (95% CI: 883-915) • Less-disabled: 535 (95% CI: 526-545) • Non-disabled: 291 (95% CI: 287-295) *Deaths involving COVID-19, age-standardized mortality rate per 100,000 person-years at risk, females:* • More-disabled: 627 (95% CI: 616-639) • Less-disabled: 318 (95% CI: 312-324) • Non-disabled: 162 (95% CI: 159-164) *All-cause mortality, age-standardized mortality rate per 100,000 person-years at risk, males:* • More-disabled: 3931 (95% CI: 3897-3965) • Less-disabled: 2451 (95% CI: 2430-2472) • Non-disabled: 1413 (95% CI: 1405-1422) *All-cause mortality, age-standardized mortality rate per 100,000 person-years at risk, females:* • More-disabled: 2973 (95% CI: 2946-2999) • Less-disabled: 1681 (95% CI: 1666-1696) • Non-disabled: 980 (95% CI: 974-986) **Duration of Condition:** NR **Comorbid Conditions:** Compared with non-disabled people, disabled people tended to have a pre-existing health condition and have been admitted to the hospital in the past three years. **Risk Markers:** Compared with non-disabled people, disabled people tended to be older, and were more likely to have no qualifications. Disabled people were more likely to live in a care home, or in single-adult households, social rented accommodation, a household where the household reference person was in a non-managerial occupation, and in the most deprived areas. *Deaths involving COVID-19 among males aged 30 to 69 years old in 2020:*

				• More-disabled, aHR2: 5.42 (95% CI: 5.18-5.68) • Less-disabled, aHR2: 2.64 (95% CI: 2.50-2.79) • Non-disabled: ref *Deaths involving COVID-19 among females aged 30 to 69 years old in 2020:* • More-disabled, aHR2: 8.47 (95% CI: 8.01-8.95) • Less-disabled, aHR2: 3.35 (95% CI: 3.13-3.58) • Non-disabled: ref *Deaths involving COVID-19 among males aged 70 to 100 years old in 2020:* • More-disabled, aHR2: 2.68 (95% CI: 2.62-2.74) • Less-disabled, aHR2: 1.73 (95% CI: 1.69-1.77) • Non-disabled: ref *Deaths involving COVID-19 among females aged 70 to 100 years old in 2020:* • More-disabled, aHR2: 2.98 (95% CI: 2.91-3.05) • Less-disabled, aHR2: 1.82 (95% CI: 1.78-1.86) • Non-disabled: ref **Long-term Sequelae:** NR
Author: Brisca[63] **Publication:** 2021 **Data Extractor:** AH **Reviewer:** CS **Study design:** Case series **Study Objective:** To determine whether seizure exacerbation might be an issue for children with pre-existing epilepsy and SARS-CoV-2 infection by describing two children with a reappearance of seizures during a COVID-19 after a long seizure-free period. **IVA Score:** Internal validity was not conducted for case reports/case series.	**Population:** N= 2 **Setting:** Hospital **Location:** Italy **Study dates:** NR **Inclusion criteria:** NR **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Fragile X syndrome: 1/2 (50.0%)	**Medical Condition(s):** *Fragile X syndrome*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality:* No *report ICU admission:* No *Intubation (or Invasive Ventilation):* No *Ventilation (mechanical, or non-invasive ventilation):* No *Hospitalization:* Yes *General Progression* • *Case 1:* An 11-year-old girl with Fragile X syndrome and recurrent status epilepticus usually triggered by febrile episodes tested positive for COVID-19 by PCR test. She had a fever for 2 days and subsequently developed prolonged focal seizures that required intravenous midazolam. She also had transient respiratory acidosis. She was discharged after 6 days. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** • The patient had a history of recurrent status epilepticus (seizures) triggered by febrile episodes. **Risk Markers:** NR

				Long-term Sequelae: NA
Author: Burns[38] **Publication:** 2020 **Data Extractor:** MM **Reviewer:** MC **Study Design:** Retrospective cohort **Study Objective:** To describe case fatality of COVID-19 in veterans with spinal cord injuries and disorders (SCI/D) as determined using operational reports. **IVA Score:** 23 (Moderate)	**Population:** COVID-19+, N=20,509 **Setting:** Medical centers and outpatients care sites of the Veterans Health Administration (VHA) system **Data Source:** National operational reports **Location:** USA **Study Dates:** March 9 - June 30, 2020 **Inclusion Criteria:** Veterans with SCI/D of traumatic or nontraumatic etiology that tested positive for COVID-19. **Exclusion Criteria:** Veterans with SCI/D, multiple sclerosis, and amyotrophic lateral sclerosis that did not test positive for COVID-19.	**Medical Condition, n/N (%):** Spinal cord injuries and disorders (SCI/D): 140/17,452 (0.7%) **Control/Comparison Group, n/N (%):** No SCI/D: 20,369/N=NR (99.3%)	**Medical Condition(s):** *SCI/D:* American Spinal Injury Association Impairment Scale *(*AIS)-categories: C1-C4 tetraplegia AIS A–C, C5–C8 tetraplegia AIS A–C, paraplegia AIS A–C, AIS D **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%):* • SCI/D Veterans: 26/140 (19.0%) • Non-SCI/D Veterans: 1,564/20,369 (7.7%) The COVID-19 case fatality rate for SCI/D Veterans was 2.4 times the rate for non-SCI/D Veterans and the absolute rate is 11% greater (95% CI: 5%-19%), p<0.0002). *Hospitalization, n/N (%):* • SCI/D Veterans: 67/140 (48.0%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Chew[35] **Publication:** 2021 **Data Extractor:** DOS **Reviewer:** MW **Study Design:** Cohort **Study Objective:** To describe characteristics and outcomes among	**Population:** N=1563 **Setting:** ICU **Data Source:** Swedish databases; Swedish Intensive Care Registry (SIR) and Swedish Intensive Care Influenza and Viral Infections Registry	**Medical Condition, n/N (%):** Chronic neuromuscular disease: 20/1563 (1.3%) **Control/Comparison Group, n/N (%):** No chronic neuromuscular disease: 1543/1563 (98.7%)	**Medical Condition(s):** *Chronic neuromuscular disease*: ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* 30-day all-cause mortality *ICU admission:* NR *Intubation:* NR *Ventilation:* NR	**Severe COVID-19:** *Mortality, n/N (%):* Chronic neuromuscular disease: • Died: 6/417 (1.4%) • Survived: 14/1146 (1.2%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR

critically ill patients with COVID-19 admitted to Swedish ICUs during the first 2 months of the pandemic and to identify independent risk factors associated with increased mortality for these patients. **IVA Score:** 24 (Moderate)	**Location:** Sweden **Study Dates:** March 6 - May 6, 2020 **Inclusion Criteria:** All adult patients ≥18 years admitted to Swedish ICUs with PCR confirmed SARS-CoV-2 infection and COVID-19 disease (code U07.1) during study period. Patients were registered to Swedish Intensive Care Registry (SIR) and its supplementary database Swedish Intensive Care Influenza and Viral Infections Registry. **Exclusion Criteria:** Patients whose 30-day follow-up data was not available. This included persons without a Swedish personal identify number.		*Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Risk Markers:** NA **Long-term Sequelae:** NR
Author: Chow[7] **Publication:** 2020 **Data Extractor:** CS **Reviewer:** MW **Study Design:** Cohort **Study Objective:** To compare COVID-19 trends among people with and without Intellectual an Developmental Disabilities (IDD), overall and stratified by age.	**Population:** N=122,653 Complete information: N=7,162 **Setting:** Hospitals **Data Source:** data reported to CDC by states and territories **Location:** 50 states, 4 territories and affiliated islands, the District of Columbia, and New York City of the US	**Medical Condition, n/N (%):** Neurologic disorder, neurodevelopmental, intellectual disability: 52/7162 (0.7%) **Control/Comparison Group, n/N (%):** None of the above conditions: 4470/7162 (62.4%)	**Medical Condition(s):** *Neurologic disorder, neurodevelopmental, intellectual disability*: dementia, memory loss, or Alzheimer's disease; seizure disorder; Parkinson's disease; migraine/headache; stroke; autism; aneurysm; multiple sclerosis; neuropathy; hereditary spastic paraplegia; myasthenia gravis; intracranial hemorrhage; and altered mental status **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:**	**Severe COVID-19:** *ICU Admission, n/N (%):* Neurologic disorder, neurodevelopmental, intellectual disability: • Neurologic disorder, neurodevelopmental, intellectual disability: 7/52 (13.5%) • No conditions: 99/4470 (2.2%) *Hospitalization, n/N (%):* Neurologic disorder, neurodevelopmental, intellectual disability: • Neurologic disorder, neurodevelopmental, intellectual disability: 32/52 (61.5%) • No conditions: 404/4470 (9.0%) **Severity of Condition:** NR

IVA Score: 20 (Moderate)	**Study Dates:** February 12 – March 28, 2020 **Inclusion Criteria:** Laboratory-confirmed COVID-19 cases. **Exclusion Criteria:** Cases among persons repatriated to the US from Wuhan, China and the Diamond Princess cruise ship.		*Mortality:* NR *ICU admission:* estimated for persons aged ≥19 years because of the small sample size of cases in children with underlying health conditions *Intubation:* NR *Ventilation:* NR *Hospitalization:* estimated for persons aged ≥19 years because of the small sample size of cases in children with underlying health conditions *Non-elective readmissions*: NR **Comments:** None	**Duration of Condition:** NR **Comorbid Conditions:** NA **Risk Markers:** NA **Long-term Sequelae:** NR
Author: Clift[18] **Publication:** 2020 **Data Extractor:** MW **Reviewer:** TR/CS **Study Design:** Cohort **Study Objective:** To develop and validate population-based prediction models to estimate the risks of becoming infected with and subsequently dying from covid-19 and of becoming infected and subsequently admitted to hospital with covid-19. **IVA Score:** 25 (Moderate)	**Population:** N=6,083,102 COVID-19+, N=NR **Setting:** 1,205 General practices **Data Source:** QResearch database **Location:** England **Study Dates:** January 24 – June 30, 2020 **Inclusion Criteria:** People aged 19-100 years registered with participating general practices in England. **Exclusion Criteria:** People who did not have a valid National Health Service number.	**Medical Condition, n/N (%):** Learning disability: 107,107/6,083,102 (1.78%) Down syndrome: 3,013/6,083,102 (0.05%) Cerebral palsy: 6,481/6,083,102 (0.11%) **Control/Comparison Group, n/N (%):** No learning disability: 5,972,982/6,083,102 (98.19%) No down syndrome: 6,080,089/6083102 (99.95%) No cerebral palsy: 6,076,621/6,083,102 (99.89%)	**Medical Condition(s):** *Learning disability:* ND *Down syndrome:* ND *Cerebral palsy:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Death due to confirmed or suspected covid-19 as per the death certification or death occurring in a person with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the period 24 January to 30 April 2020 *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* Hospital admission with covid-19 defined as an ICD-10 (International Classification of Diseases, 10th revision) code for either confirmed or suspected covid-19 or new hospital admission associated with a confirmed SARS-CoV-2 infection in the study period *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aHR: Adjusted Hazard Ratio; adjusted age, BMI, Townsend score, ethnic group, domicile, and comorbid conditions and treatments* *Mortality, n/N (%):* • Learning disability: 255/107,107 (0.24%) • No learning disability: 4,110/5,972,982 (0.07%) • Down syndrome: 19/3,013 (0.63%) • No down syndrome: 4,365/6,080,089 (0.07%) *Hospitalization, n/N (%):* • Learning disability: 498/107,107 (0.46%) • No learning disability: 10,251/5,972,982 (0.17%) • Down syndrome: 27/3,013 (0.90%) • No down syndrome: 10,749/6,080,089 (0.18%) • Cerebral palsy: 27/6,481 (0.42%) • No cerebral palsy: 10,749/6,076,621 (0.18%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR

				Risk Markers: *Mortality in women:* Learning disability apart from down syndrome: • aHR: 1.36 (95% CI: 1.11-1.65) Down syndrome: • aHR: 32.55 (95% CI: 18.13-58.42) Cerebral palsy: • aHR: 3.45 (95% CI: 1.10-10.78) *Mortality in men:* Learning disability apart from down syndrome: • aHR: 1.36 (95% CI: 1.14-1.60) Down syndrome: • aHR: 9.80 (95% CI: 4.62-20.78) Cerebral palsy: • aHR: 2.77 (95% CI: 1.23-6.23) *Hospitalization in women:* Learning disability apart from down syndrome: • aHR: 1.53 (95% CI: 1.34-1.76) Down syndrome: • aHR: 8.84 (95% CI: 5.37-14.55) Cerebral palsy: • aHR: 2.66 (95% CI: 1.42-4.98) *Hospitalization in men:* Learning disability apart from down syndrome: • aHR: 1.38 (95% CI: 1.22-1.56) Down syndrome: • aHR: 4.36 (95% CI: 2.39-7.94) Cerebral palsy: • aHR: 2.85 (95% CI: 1.76-4.62) **Long-term Sequelae:** NR
Author: Clift[19] **Publication:** 2021 **Data Extractor:** JKK **Reviewer:** CS **Study Design:** Cohort	**Population:** N=8,256,158 COVID-19+, N=36,428 **Setting:** Primary care **Data Source:** QResearch, population-level primary care database in England	**Medical Condition, n/N (%):** Down syndrome: 4,053/8,256,158 (0.05%) Learning disability apart from Down syndrome: NR Cerebral palsy: NR **Control/Comparison Group, n/N (%):** No Down syndrome: 8,252,105/8,256,158 (99.95%)	**Medical Condition(s):** *Down syndrome*: ND *Learning disability apart from Down syndrome:* ND *Cerebral palsy*: ND **Severity Measure(s):** NR **Clinical Marker:** NR	**Severe COVID-19:** *aHR[1]: Adjusted Hazard Ratio; Cox proportional hazards ratio; included model variables: smoking status, alcohol intake, age, sex, ethnicity, BMI, dementia diagnosis, care home residency, congenital heart disease, and a range of other comorbid conditions and treatments* *aHR[2]: Adjusted Hazard Ratio; Cox proportional hazards ratio; included model variables: age, sex, ethnicity, BMI, dementia diagnosis, care home*

Study Objective: To evaluate Down syndrome as a risk factor for death from COVID-19 through a comprehensive analysis of individual-level data in a cohort study of 8.26 million adults (aged >19 years), as part of a wider COVID-19 risk prediction project commissioned by the UK government. **IVA** **Score:** 25 (moderate)	**Location:** England **Study Dates:** January 24 – June 30, 2020 **Inclusion Criteria:** Adults aged >19 years. **Exclusion Criteria:** NR	No learning disability apart from Down syndrome: NR No cerebral palsy: NR	**Outcome Definitions:** *Mortality:* COVID-19 mortality in or out of the hospital, defined as confirmed or suspected COVID-19 on the death certificate or death within 28 days of a confirmed SARS-CoV-2 infection in the study period *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* COVID-19 hospital admission during study period *Non-elective readmissions*: NR **Comments:** None	*residency, congenital heart disease, and a range of other comorbid conditions and treatments* *Mortality, n/N (%):* Down syndrome: • aHR[1]: 10.12 (95% CI: 6.90-14.84) • Down syndrome: 27/4,053 (0.67%) • No Down syndrome: 8457/8,252,105 (0.10%) Learning disability apart from Down syndrome: • aHR[2]: 1.27 (95% CI: 1.16-1.40) Cerebral palsy: • aHR[2]: 2.66 (95% CI: 1.62-4.36) *Hospitalization, n/N (%):* Down syndrome: • aHR[2]: 4.94 (95% CI: 3.63-6.73) • Down syndrome: 41/4,053 (1.01%) • No Down syndrome: 19,057/8,252,105 (0.23%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Cummins[31] **Publication:** 2021 **Data Extractor:** CS **Reviewer:** MW **Study Design:** Cohort study **Study Objective:** To identify risk factors associated with increased risk of hospitalization,	**Population:** N=1781 **Setting:** Hospital **Data Source:** Secondary Uses Service hospital inpatient data **Location:** England **Study Dates:** February 1-June 30, 2020 **Inclusion Criteria:** Patients ≥16 years old registered with a	**Medical Condition, n/N (%):** Learning disability: 28/1781 (1.6%) **Control/Comparison Group, n/N (%):** No learning disability: 1753/1781 (98.4%)	**Medical Condition(s):** *Learning disability:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression; included model variables: demographic and socioeconomic factors as well as obesity, smoking status and the 17 individual clinical factors as covariates* *Mortality, n/N (%):* Learning disability: • aOR: 4.75 (95% CI: 1.91-11.84); p = 0.001 • Died: 11/28 (39.3%) *ICU Admission, n/N (%):* Learning disability: • aOR: 1.22 (95% CI: 0.26-5.79); p = 0.801 • ICU: 2/28 (7.1%)

intensive care unit (ICU) admission and mortality in inner North East London during the first UK COVID-19 wave. **IVA Score:** 24 (moderate)	general practice in the North East London area (Newham, Tower Hamlets and City and Hackney) with a confirmed diagnosis of COVID-19 were included. **Exclusion Criteria:** NR			*Hospitalization, n/N (%):* Learning disability: • aOR: 2.07 (95% CI: 0.78-5.45); p = 0.142 • Hospitalized: 22/28 (78.6%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: De Marcaida[68] **Publication:** 2020 **Data Extractor:** MW **Reviewer:** MM **Study design:** Case series **Study Objective:** To describe the demographic characteristics, presentation, management, and outcome of these patients, with the intent of exploring factors that may influence the clinical course in this patient population. **IVA Score:** Internal validity was not conducted for case reports/case series.	**Population:** N=36 **Setting:** Hospital **Location:** Connecticut, USA **Study dates:** March 8 – June 6, 2020 **Inclusion criteria:** Patients with Parkinson disease and other movement disorders who contracted COVID-19 were included. **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Tourette syndrome: 2/36 (5.5%) Progressive Supranuclear Palsy: 2/36 (5.5%)	**Medical Condition(s):** *Tourette syndrome:* ND *Progressive Supranuclear Palsy:* ND **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Tourette syndrome:* *Mortality:* 0/2 *Hospitalization:* 1/2 (50.0%) *General Progression* • *Case 1:* A 55-year-old female patient was admitted to the hospital after showing generalized weakness symptoms but eventually recovered. • *Case 2:* A 65-year-old female patient did not require hospital admission, was put on Oseltamivir treatment, and eventually recovered. *Progressive Supranuclear Palsy:* *Mortality:* 2/2 *Hospitalization:* 0/2 *General progression* • *Case 1:* A 68-year-old female patient who lived in an extended care facility did not require a hospital admission but eventually died. • *Case 2:* A 72-year-old male patient living at home, was not admitted to the hospital but eventually died. **Severity of Condition:** NR **Duration of Condition:** NR

				Comorbid Conditions/ History of Disease: *Tourette syndrome:* • *Case 1:* No comorbidities • *Case 2*: History of Sarcoidosis, Asthma, and atrial fibrillation *Progressive Supranuclear Palsy:* • *Case 1:* History of diabetes mellitus type 2, Breast cancer, Renal Cell Carcinoma • *Case 2:* History of Cervical Dystonia and dementia **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: Not applicable for this study type
Author: Demir[72] **Publication:** 2020 **Data Extractor:** AH **Reviewer:** CS **Study design:** Case report **Study Objective:** To present an incidental diagnose of Fahr's syndrome in a patient with SARS-CoV-2 (COVID-19) infection. **IVA Score:** Internal validity was not conducted for case reports/case series.	**Population:** N= 1 **Setting:** Hospital **Location:** Turkey **Study dates:** NR **Inclusion criteria:** NR **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Fahr's Syndrome: 1/1 (100.0%)	**Medical Condition(s):** *Fahr's syndrome*: rare, neurological disorder characterized by bilateral calcification in the cerebellum, thalamus, basal ganglia, and cerebral cortex as a result of calcium and phosphorus metabolism disorder; disease with an autosomal dominant genetic transition, but autosomal recessive transition and sporadic development may occur **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* ND *Ventilation:* mechanical *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** The patient was diagnosed with Fahr's while hospitalized with COVID-19. Due to its genetic nature, the authors suggest that the patient may	**Severe COVID-19:** *Mortality:* Yes *ICU admission:* Yes *Intubation (or Invasive Ventilation):* Yes *Ventilation (mechanical, or non-invasive ventilation):* Yes *Hospitalization:* Yes *General Progression* • *Case 1:* A 68-year-old woman with cough and fatigue was admitted to the emergency department. She tested positive for COVID-19 by PCR test and was hospitalized. On day 2 she experienced respiratory distress and oxygen desaturation prompting her admission to the ICU. On the same day in the ICU, the patient had a tonic-clonic convulsion starting from the left arm and spreading to the whole body. A cranial CT image showed bilateral calcifications at the corona radiata, nucleus dentatus, basal ganglia, and cerebellum and she was diagnosed with Fahr's syndrome. On day 3, the patient was tracheally intubated and mechanically ventilated due to severe acute respiratory distress syndrome (ARDS). The ARDS caused by COVID-19 pneumonia became severe and the patient died on the 8th day in the ICU.

			have had Fahr's before contracting COVID-19.	**Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** Patient had a history of hypoparathyroidism **Risk Markers:** NR **Long-term Sequelae:** NA
Author: Dhont[74] **Publication:** 2020 **Data Extractor:** MM **Reviewer:** MW **Study design:** Case series **Study Objective:** To study the clinical course of COVID-19 in hospitalized patients with myotonic dystrophy. **IVA Score:** Internal validity was not conducted for case reports/case series.	**Population:** N=3 **Setting:** Hospital **Location:** Belgium **Study dates:** April 1-30, 2020 **Inclusion criteria:** Myotonic dystrophy patients diagnosed with COVID-19 were included. **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Myotonic dystrophy: 3/3 (100%)	**Medical Condition(s):** *Myotonic dystrophy:* an inherited neuromuscular disorder that primarily affects muscle function, characterized by progressive weakness and sustained muscle contraction **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* ND *Ventilation:* ND *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality:* 3/3 (100%) *Ventilation (non-invasive):* 3/3 (100%) No patients were intubated *General Progression* • *Case 1:* A 44-year-old female tested negative for COVID-19 twice via nasopharyngeal swabs. A presumptive diagnosis was made based on a CO-RADS score of 5. Patient was treated with non-invasive ventilation, empiric antimicrobial therapy and intensive respiratory physiotherapy. Patient died on day 6. • *Case 2:* A 47-year-old female diagnosed with COVID-19 from chest imaging and nasopharyngeal swab PCR testing. Patient treated with hydroxychloroquine, non-invasive ventilation, empiric antimicrobial therapy and intensive respiratory physiotherapy. Patient died on day 5. • *Case 3:* A 64-year-old male diagnosis of COVID-19 from chest imaging and nasopharyngeal swab PCR testing; treatment with non-invasive ventilation, empiric antimicrobial therapy and intensive respiratory physiotherapy. Patient died on day 8. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** • *Case 1:* wheelchair-use, obese • *Case 2:* obese • *Case 3:* history of cardiovascular disease **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: Not applicable for this study type

Author: Dobre[1] **Publication:** 2021 **Data Extractor:** MM **Reviewer:** MC/CS **Study Design:** Retrospective cohort **Study Objective:** To assess the clinical features of patients hospitalized in COVID/Psychiatric wards and the risk factors associated with their clinical aggravation and mortality. **IVA Score:** 22 (Moderate)	**Population:** N=350 **Setting:** 22 psychiatric hospitals **Data Source:** Medical records **Location:** France **Study Dates:** February 28- May 30, 2020 **Inclusion Criteria:** Patients with a psychiatric disorder requiring hospitalization and who presented a clinical diagnosis of COVID-19. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Intellectual disability: 12/350 (3.0%) Psychological development disorder: 25/350 (7.0%) **Control/Comparison Group, n/N (%):** No intellectual disability: 338/350 (97.0%) No psychological development disorder: 325/350 (93.0%)	**Medical Condition(s):** *Intellectual disability:* ND *Psychological development disorder:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *OR: Odds Ratio* *Mortality, n/N (%):* *Intellectual disability:* • OR: 5.0 (95% CI: 0.6-45.4), p = 0.1 *Hospitalization, n/N (%):* Intellectual disability: • 12/350 (3.0%) Psychological development disorder: • 25/350 (7.0%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Duarte-Salles[41] **Publication:** 2020 **Data Extractor:** MW **Reviewer:** JKK/DOS **Study Design:** Cohort **Study Objective:** To describe the demographics, comorbidities, symptoms, in-hospital treatments, and health outcomes of children/adolescents diagnosed or	**Population:** N =55,270 N (US) = 19,260 **Setting:** Hospital **Data Source:** 19 different databases **Location:** France, Germany, Spain, South Korea, and USA **Study Dates:** January – September 22, 2020 **Inclusion Criteria:** Only databases with data on patients below the age of 18 years with a clinical diagnosis of	**Medical Condition, n/N (%):** Autistic disorder: NR Neurodevelopmental disorder: NR Attention deficit hyperactivity disorder (ADHD): NR Chromosomal disorder: NR Congenital malformation: NR **Control/Comparison Group, n/N (%):** No autistic disorder: NR No neurodevelopmental disorder: NR No ADHD: NR No chromosomal disorder: NR No congenital malformation: NR	**Medical Condition(s):** *Autistic disorder:* ND *Neurodevelopmental disorder:* ND *ADHD:* ND *Chromosomal disorder:* ND *Congenital malformation:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Hospitalization data from IQVIA OpenClaims (US) and OPTUM EHR (US), n/N (%)*:* Autistic disorder: IQVIA OpenClaims (US) • Hospitalized: 44/1899 (2.3%) • Diagnosed: 191/13621 (1.4%) OPTUM EHR (US) • Hospitalized: 14/399 (3.5%) • Diagnosed: 73/5639 (1.3%) Neurodevelopmental disorder: IQVIA OpenClaims (US) • Hospitalized: 317/1899 (16.7%) • Diagnosed: 1199/13621 (8.8%) OPTUM EHR (US) • Hospitalized: 82/399 (20.6%) • Diagnosed: 462/5639 (8.2%)

hospitalized with COVID-19, using electronic health records (EHRs) and health claims databases across the US, Europe, and Asia. **IVA Score:** 20 (Moderate)	COVID-19 or a SARS-CoV-2 positive test between the study dates were included. A cohort of children/adolescents diagnosed with seasonal influenza in 2017-2018 was included for comparison. **Exclusion Criteria:** Chil dren below age one were excluded from the cohorts requiring 365 days of prior observation.			ADHD: IQVIA OpenClaims (US) • Hospitalized: 76/1899 (4.0%) • Diagnosed: 599/13621 (4.4%) OPTUM EHR (US) • Hospitalized: 41/399 (10.3%) • Diagnosed: 305/5639 (5.4%) Chromosomal disorder: IQVIA OpenClaims (US) • Hospitalized: 110/1899 (5.8%) • Diagnosed: 177/13621 (1.3%) OPTUM EHR (US) • Hospitalized: 14/399 (3.5%) • Diagnosed: 45/5639 (0.8%) Congenital malformation: IQVIA OpenClaims (US) • Hospitalized: 431/1899 (22.7%) • Diagnosed: 1076/13621 (7.9%) OPTUM EHR (US) • Hospitalized: 54/399 (13.5%) • Diagnosed: 265/5639 (4.7%) *Calculated by ERT **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Emami[20] **Publication:** 2020 **Data Extractor:** MM/AH **Reviewer:** MW **Study Design:** Case-control **Study Objective:** To determine whether COVID-19 is	**Population:** N=72 **Setting:** Hospital **Data Source:** electronic health records database **Location:** Iran	**Medical Condition, n/N (%):** Down syndrome: 18/72 (25%) **Control/Comparison Group, n/N (%):** No down syndrome: 54/72 (75%)	**Medical Condition(s):** *Down syndrome:* a genetic disorder with several congenital defects (e.g., cardiac, respiratory, immunological) **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:**	**Severe COVID-19:** *aOR: Adjusted Odds Ratio; Multivariable Logistic Regression model included respiratory distress, headache, intubation, and death* *Mortality, n/N (%):* • aOR: 24.37 (95% CI: 2.39-247.94), p = 0.007 • DS: 8/18 (44%) • No DS: 1/54 (1.9%) • p = 0.0001

associated with a different presenting clinical picture or a more severe course of illness (e.g., intubation and death) in people with Down syndrome. **IVA Score:** 25 (Moderate)	**Study Dates:** February 19 – November 20, 2020 **Inclusion Criteria:** Patients referred and admitted to healthcare facilities with confirmed, probable, or possible COVID-19 diagnosis. Patients had a COVID-19 diagnosis by a positive 1RT-PCR test of a nasopharyngeal or oropharyngeal sample, probable COVID-19 via positive CT scan, or possible COVID-19 diagnosis by clinical manifestations compatible with COVID-19. **Exclusion Criteria:** NR		*Mortality:* ND *ICU admission:* NR *Intubation:* ND *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	*Intubation, n/N (%):* • aOR: NR, p = 0.236 • DS: 7/18 (39%) • No DS: 3/54 (6%) • p = 0.002 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** *Hospitalization, n/N (%):* • DS & Cardiac problems: 3/18 (16.6%) • DS & Diabetes mellitus: 1/18 (5.5%) • DS & Cardio-pulmonary problems: 1/18 (5.5%) **Risk Markers:** *Hospitalization, n/N (%) or mean:* Age, mean (SD): • DS: 28.6 ± 14.5 • No DS: 28.0 ± 12.6 • p = 0.868 Sex: • Female DS: 7/18 (39%) • Female no DS: 21/54 (39%) • Male DS: 11/18 (61%) • Male no DS: 33/54 (61%) • p = 1.00 **Long-term Sequelae:** NR
Author: Falandry[33] **Publication:** 2020 **Data Extractor:** MW **Reviewer:** TR/DOS **Study Design:** Retrospective cohort **Study Objective:** To evaluate the risk and predictors of mortality in elderly patients admitted to the intensive care unit (ICU).	**Population:** N =232 **Setting:** 7 Hospitals **Data Source:** Senior-COVID-Rea **Location:** NR **Study Dates:** March – May 2020 **Inclusion Criteria:** Patients over 60 admitted in ICU for severe COVID-19 disease. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** ADL disability: 49/232 (21%) IADL disability: 70/232 (30%) **Control/Comparison Group, n/N (%):** No disability: 113/232 (48.7%)	**Medical Condition(s):** *ADL disability:* ND *IADL disability:* ND **Severity Measure(s):** *Frailty according to Fried's criteria:* ≥3 *Clinical frailty:* score ≥4 **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Mortality at 30 days of admission *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR	**Severe COVID-19:** *OR: Univariable (Univariate) Logistic Regression* *Mortality:* ADL disability: • OR: 3.8, p<0.001 IADL disability: • OR: 6.1, p<0.001 Severity of Condition: *Mortality:* Frailty according Fried's criteria: • OR: 3.6, p = 0.001 Clinical frailty: • OR: 3.5, p<0.001

IVA Score: 16 (High)			**Comments:** None	**Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Fierro[64] **Publication:** 2021 **Data Extractor:** TR **Reviewer:** CS **Study Design:** Cross-sectional **Study Objective:** To evaluate the determinants of SARS-CoV-2 infection in Gaucher disease (GD). **IVA Score:** 19 (Moderate)	**Population:** N=181 COVID-19 positive: 16 **Setting:** Tertiary care center **Data Source:** Lysosomal Storage Disease Program medical records/electronic database of Illinois Critical Access Hospital Network School of Medicine at Mount Sinai **Location:** New York, USA **Study Dates:** June-August 2020 **Inclusion Criteria:** Patients with a confirmed diagnosis of Gaucher disease (GD). **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Gaucher disease (GD): 181/181 (100%) **Control/Comparison Group, n/N (%):** NA	**Medical Condition(s):** *Gaucher disease (GD)*: an autosomal recessive lysosomal storage disorder, deficiency of the enzyme acid β-glucosidase leads to the accumulation of inflammatory glycosphingolipids, glucocerebroside and glucosylsphingosine **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** No patients were hospitalized and no deaths due to COVID-19 occurred. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Garazzino[42] **Publication:** 2021 **Data Extractor:** MM/CS **Reviewer:** MW **Study Design:** Cohort	**Population:** N=759 **Setting:** 11 pediatric hospitals, 51 pediatric units **Data Source:** Medical records **Location:** Italy	**Medical Condition, n/N (%):** Congenital malformations: 20/759 (14.7 %) Autism or neurological development impairment: 8/759 (5.9%) Complex genetic syndromes: 13/759 (9.6%) **Control/Comparison Group, n/N (%):** No congenital malformations: 739/759 (97.4%)	**Medical Condition(s):** *Congenital malformations:* ND *Autism or neurological development impairment:* ND *Complex genetic syndromes:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:**	**Severe COVID-19:** *Hospitalization, n/N (%):* • Congenital malformations: 17/20 (85%) • No congenital malformations: 344/739 (47.0%) • Autism or neurological development impairment: 4/8 (50.0%) • No autism: 357/751 (48.0%)

Study Objective: To investigate epidemiological, clinical, and therapeutic characteristics of pediatric SARS-CoV-2 infection, focusing on risk factors for complicated and critical disease. **IVA** **Score:** 24 (Moderate)	**Study Dates:** March 24- September 15, 2020 **Inclusion Criteria:** All patients under 18 years of age with documented COVID-19 infection and referred to the coordinating center. **Exclusion Criteria:** NR	No autism: 751/759 (99%) No complex genetic syndromes: 746/759 (98.3%)	*Mortality:* NR *ICU admission:* ND *Intubation:* NR *Ventilation:* ND *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	• Complex genetic syndromes: 9/13 (69.2%) • No complex genetic syndromes: 352/746 (47.2%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Garcia-Menaya[43] **Publication:** 2020 **Data Extractor:** TR **Reviewer:** MW **Study Design:** Retrospective cohort **Study Objective:** To compare the characteristics, clinical presentation, and outcome of Covid-19 patients with allergic disorders, patients with no allergic antecedents and overall patients. **IVA** **Score:** 23 (moderate)	**Population:** N=113 **Setting:** Hospital **Data Source:** Hospital records **Location:** Spain **Study Dates:** March 16-April 24, 2020 **Inclusion Criteria:** Patients admitted to the study hospital diagnosed with Covid-19 by RT-PCR and/or serological tests. **Exclusion Criteria:** Patients who remained in the hospital when the manuscript was written because the clinical outcome was still uncertain, and patients directly discharged from the emergency	**Medical Condition, n/N (%):** Cognitive impairment: 13/113 (11.5%) **Control/Comparison Group, n/N (%):** No cognitive impairment: 100/113 (88.5%)	**Medical Condition(s):** *Cognitive impairment*: ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Mortality risk *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality:* Cognitive impairment: There were no statistically significant differences between the death frequency for patients with cognitive impairment, p = 0.199 *ICU admission:* There were no statistically significant differences between the ICU admission frequency for patients with cognitive impairment, p = 0.999 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

	department with no hospital admittance.			
Author: Gleason[2] **Publication:** 2021 **Data Extractor:** CS **Reviewer:** TR/DOS **Study Design:** Cohort study **Study Objective:** To describe the impact of the population of established patients across 547 health systems. **IVA Score:** 24 (moderate)	**Population:** N=64,414,495 COVID+ N: 558,672 **Setting:** 547 health care organizations, health systems, community hospitals, and academic medical centers **Data Source:** National database; Vizient Clinical Database/Resource Manager **Location:** US **Study Dates:** March–November 2020 **Inclusion Criteria:** All patients with a medical record that predates an encounter with a COVID-19 diagnosis were included. Patients with intellectual disabilities were distinct patients seen by any member location between January 2019-November 2020, with a diagnosis code of F70-F79. Patients with no intellectual disabilities included all member system patients from January 2019-November 2020 that were not included in the patients with intellectual disabilities	**Medical Condition, n/N (%):** Intellectual disabilities: 3,897/558,672 (0.70%) **Control/Comparison Group, n/N (%):** No intellectual disabilities: 554,775/558,672 (99.30%)	**Medical Condition(s):** *Intellectual disabilities:* ICD-10 diagnosis code F70-F79 **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* • Admitted patients: death among admitted patients only • All established patients: death among admitted and ER patients *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* admission among established patients only *Non-elective readmissions*: NR **Comments:** Author's note: Behavioral health comorbidities were excluded, as was any comorbidity that did not affect at least 10% of the patient population, diagnoses, or deaths.	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression; model included common comorbidities* *Mortality, n/N (%):* Admitted patients: • aOR: 1.324 (95% CI: 1.165-1.505) • Intellectual disabilities: 321/3,897 (8.2%) • No intellectual disabilities: 21,277/554,775 (3.8%) • p<0.001 All established patients: • aOR: 5.909 (95% CI: 5.277-6.617) *ICU admission (among all), n/N (%):* • aOR: 1.039 (95% CI: 0.941-1.147) • Intellectual disabilities: 565/3,897 (14.5%) • No intellectual disabilities: 35,139/554,775 (6.3%) • p<0.001 *Hospitalization, n/N (%):* • aOR: 2.739 (95% CI: 2.490-3.014) • Intellectual disabilities: 2,459/3,897 (63.1%) • No intellectual disabilities: 165,163/554,775 (29.1%) • p<0.001 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** Patients with intellectual disabilities had higher rates of all comorbidities examined in this study except for cancer when compared to patients without intellectual disabilities. **Risk Markers:** **Denominators calculated by ERT using percentages and numerators provided in Table 2* *Mortality, n/N* (%):* Admitted patients: Age:

	group. COVID-19 was identified by a principal or secondary diagnosis code of U07.1 starting in April 2020, or in March 2020 with either a principal diagnosis of B97.29, or a secondary diagnosis of B97.29 with a principal diagnosis of J12.98 or J12.9, or a diagnosis-related group in the following list, representing respiratory diseases, infections, and sepsis: 177, 178, 179, 207, 208, 853, 854, 855, 870, 871, 872. **Exclusion Criteria:** Patients who were screened and treated at other institutions or those who had mild cases and did not present were excluded from analysis. New patients (patients with no record of care at the institution they presented to with COVID-19 prior to the COVID-19 diagnosis were excluded.			Under 20: • Intellectual disabilities: 1/122 (0.82%) • No intellectual disabilities: 22/3,385 (0.65%) 20-39: • Intellectual disabilities: 24/458 (5.24%) • No intellectual disabilities: 387/21,989 (1.76%) 40-59: • Intellectual disabilities: 102/843 (12.10%) • No intellectual disabilities: 2758/41,474 (6.65%) 60-79: • Intellectual disabilities: 158/948 (16.67%) • No intellectual disabilities: 10,528/65,554 (16.06%) ≥80: • Intellectual disabilities: 22/88 (25.00%) • No intellectual disabilities: 7023/28,830 (24.36%) Patients with intellectual disabilities were more likely to be males and of low socioeconomic status compared to patients without intellectual disabilities. **Long-term Sequelae:** NR
Author: Graff[9] **Publication:** 2021 **Data Extractor:** CS **Reviewer:** MW **Study Design:** Cohort	**Population:** N=454 **Setting:** Children's hospital, pediatric referral center in a 7-state region **Data Source:** electronic medical records **Location:** Colorado, US	**Medical Condition, n/N (%):** Develop/behavioral: 38/435 (8.7%) **Control/Comparison Group, n/N (%):** No develop/behavioral: 397/435 (91.3%)	**Medical Condition(s):** *Develop/behavioral:* ND **Severity Measure(s):** NA **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NA *Intubation:* NR *Ventilation:* NR	**Severe COVID-19:** *OR: Univariable (Univariate) Logistic Regression* *Hospitalization, n/N (%):* Develop/behavioral: • OR: 1.85 (95% CI: 0.8-4.1); p = 0.13 • Hospitalized: 9/66 (14%) • Not hospitalized: 29/369 (8%) **Severity of Condition:** NA

Study Objective: To evaluate the epidemiology and risk factors for severe disease among children with SARS-CoV-2 infection. **IVA** **Score:** 24 (moderate)	**Study Dates:** March 15 – July 8, 2020 **Inclusion Criteria:** Ever y pediatric patient <21 years of age with SARS-CoV-2, confirmed by molecular testing of nasopharyngeal swabs, nasopharyngeal washes/aspirates, tracheal aspirate, and bronchoalveolar lavage specimens using RT-PCR. Patients ≥21 years were included only if they were followed by the hospital for a chronic medical condition. **Exclusion Criteria:** Pati ents tested outside Colorado, parents/caregivers of pediatric patients, pregnant women, and healthcare workers.		*Hospitalization:* among symptomatic patients *Non-elective readmissions*: NA **Comments:** None	**Duration of Condition:** NR **Comorbid Conditions:** NA **Risk Markers:** NA **Long-term Sequelae:** NA
Author: Guchelaar[48] **Publication:** 2021 **Data Extractor:** MM **Reviewer:** MW **Study Design:** Cohort **Study Objective:** To delineate the effect of an underlying immunological condition and/or immunosuppression on the course of	**Population:** N=4497 COVID-19+, N=16 **Setting:** Outpatient clinic **Data Source:** Clinical records **Location:** Netherlands **Study Dates:** March – August 2020 **Inclusion Criteria:** Patients known at the Clinical Immunolog y clinic who	**Medical Condition, n/N (%):** Neuromyelitis optica (NMO): 1/16 (6.3%) **Control/Comparison Group, n/N (%):** No Neuromyelitis optica: 15/16 (93.7%)	**Medical Condition(s):** *Neuromyelitis optica:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* Mechanical ventilation *Hospitalization:* General ward *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%):* • NMO: 0/1 (0%) • No NMO: 2/15 (13.3%) *ICU Admission, n/N (%):* • NMO: 1/1 (100.0%) • No NMO: 2/15 (33%) *Ventilation, n/N (%):* • NMO: 1/1 (100.0%) • No NMO: 1/15 (6.6%) *Hospitalization, n/N (%):* • NMO: 1/1 (100.0%) • No NMO: 7/15 (46.6%)

COVID-19 and to investigate the incidence, disease course, and SARS-CoV-2 antibody production in a cohort of patients with a primary or secondary immunodeficiency. **IVA Score:** Internal validity was not conducted for studies with less than 10 people with neuromyelitis optica.	were referred to the emergency department and/or being admitted at the ward or ICU because of (a suspicion of) COVID-19, and patients at the outpatient clinic with auto-immune, auto-inflammatory, and primary immunodeficiency diseases that have symptoms of infection and are referred to the Clinical Immunology department. **Exclusion Criteria:** Patients attending the outpatient clinic that were not tested, did not present with symptoms, did not test positive for COVID-19, or were not referred to the ED or ICU.			**Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Gude-Sampedro[29] **Publication:** 2020 **Data Extractor:** CO **Reviewer:** ECS/MW/DOS **Study Design:** Retrospective cohort **Study Objective:** To develop and validate a prognostic model to identify patients with Covid-19 at a higher risk of hospitalization, ICU admission and death, based on their age, sex,	**Population:** N =10,454 **Setting:** NR **Data Source:** NR **Location:** Spain **Study Dates:** March 6, 2020-May 7, 2020 **Inclusion Criteria:** Patients with COVID-19 infection confirmed by RT-PCR on nasal or throat swab samples; data were collected from the Galician Health Service database (SERGAS), a	**Medical Condition, n/N (%):** Immobilized: 53/10,454 (0.5%) Dependence: 132/10,454 (1.3%) **Control/Comparison Group, n/N (%):** Not immobilized: 10,401/10,454 (99.5%) No dependence: 10,322/10,454 (98.7%)	**Medical Condition(s):** *Immobilized*: A28.01 *Dependence*: Z62.01 **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Death of any cause after RT-PCR diagnosis *ICU admission:* The patient was a candidate for ICU admission if they required mechanical ventilation or had a fraction of inspired oxygen of≥60% *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression* *Mortality (among hospitalized), n/N (%):* • Immobilized: 12/22 (54.5%) • Dependence: 22/42 (52.4%) *ICU Admission (among hospitalized), n/N (%):* • Immobilized: 0/22 (0%) • Dependence: 0/42 (0%) *Hospitalized (among all), n/N (%):* • Immobilized: 22/53 (41.5%) • Dependence: 42/132 (31.8%), aOR: 0.62 (95% CI: 0.42-0.93) **Severity of Condition:** NR **Duration of Condition:** NR

comorbidities and geographic place of residence. **IVA Score:** 25 (Moderate)	longitudinal Galicia dat a of the population. **Exclusion Criteria:** NR		**Comments:** None	**Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Harman[39] **Publication:** 2020 **Data Extractor:** MW **Reviewer:** CS **Study Design:** Cohort **Study Objective:** To describe the effect of COVID-19 on pediatric patients with comorbidities and aim to facilitate rapid sharing of information in this dynamic and evolving situation. **IVA Score:** Internal validity was not conducted for studies with less than 10 people with cerebral palsy.	**Population:** N =5 **Setting:** Hospital **Data Source:** Electronic patient records or the clinical information system of the pediatric intensive care unit, or both **Location:** United Kingdom **Study Dates:** February 25 - April 28, 2020 **Inclusion Criteria:** Children (aged 0–16 years) with confirmed COVID-19 by RT-PCR and comorbidities who required admission to hospital. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Cerebral palsy: 1/5 (20%) **Control/Comparison Group, n/N (%):** No cerebral palsy: 4/5 (80%)	**Medical Condition(s):** *Cerebral palsy:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* ND *Intubation:* NR *Ventilation:* Mechanical and non-invasive ventilation *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *ICU admission, n/N (%):* • Cerebral palsy: 1/1 (100%) • No cerebral palsy: 1/4 (25.0%) *Ventilation, n/N (%):* • Cerebral palsy: 1/1 (100%) • No cerebral palsy: 1/4 (25.0%) *Hospitalization, n/N (%):* • Cerebral palsy: 1/1 (100%) • No cerebral palsy: 4/4 (100%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Huang[66] **Publication:** 2020 **Data Extractor:** JKK **Reviewer:** AH **Study design:** Case report **Study Objective:** To describe a COVID-19 patient co-infected	**Population:** N=1 **Setting:** Hospital **Location:** Taiwan **Study dates:** March 15 – April 8, 2020 **Inclusion criteria:** NR **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Hearing impairment: 1/1 (100%)	**Medical Condition(s):** Hearing impairment: ND **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR	**Severe COVID-19:** *Hospitalization:* yes *General Progression* • A 61-year-old Taiwanese man presented with 2-day history of dry cough and general malaise. Chest radiography indicated mildly increased infiltrations in both lungs. Patient tested positive for SARS-CoV-2 by RT-PCR. His mycoplasma IgM was also positive with an unequivocal level of IgG. On day 3 of symptom onset, he developed fever, diarrhea, and respiratory distress requiring oxygen cannula. His high-

with *Mycoplasma pneumoniae*. **IVA Score:** Internal validity was not conducted for case reports/case series.			**Comments:** None	resolution CT revealed multiple patches of ground-glass opacity, crazy-paving pattern, and peribronchial consolidation. Patient was prescribed azithromycin and hydroxychloroquine for 8 days. His mycoplasma IgM and IgG levels returned to normal on March 30th and RT-PCR was negative for SARS-CoV-2 on April 8th. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** • History of hypertension and hepatitis B **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: Not applicable for this study type
Author: Huls[10] **Publication:** 2021 **Data Extractor:** DOS/AH **Reviewer:** CS/AH **Study Design:** Cohort **Study Objective:** To obtain large scale information on specific vulnerabilities, clinical presentation, and outcomes of COVID-19 in individuals with Down syndrome. **IVA Score:** 21 (moderate)	**Population:** N=60,071 T21RS DS, n = 1,046 ISARIC4C, n = 59,025 Analysis, n = 588 **Setting:** NR **Data Source:** T21RS DS survey; UK ISARIC4C survey **Location:** Worldwide **Study Dates:** February - October 22, 2020 **Inclusion Criteria:** Individuals with Down syndrome of all ages who tested positive for SARS-CoV-2 or reported signs or symptoms of COVID-19 were identified via the T21RS survey	**Medical Condition, n/N (%):** Down syndrome: 188/588 (32.0%) **Control/Comparison Group, n/N (%):** No Down syndrome: 400/588 (68.0%)	**Medical Condition(s):** *Down syndrome:* result of trisomy of chromosome 21 **Severity Measure(s):** *Level of intellectual and developmental disabilities (IDD):* categorized as borderline/normal/mild, moderate, or severe/profound **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* mortality among hospitalized individuals *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** Author's note: Samples for matched comparison were from the UK while the	**Severe COVID-19:** *aRR: Adjusted risk ratio among ISARIC4C samples and matched ISARIC4C controls; logistic regression model adjusted for chronic cardiac disease, chronic pulmonary disease, chronic kidney disease, liver disease, obesity, chronic neurological disorder, dementia, malignant neoplasm* *aOR: Adjusted odds ratio; logistic regression adjusted for age, sex, data source (caregiver vs. Clinician survey), and country of residence* *RR1: Risk ratio; univariable logistic regression among ISARIC4C samples and ISARIC4C controls matched on age, sex, and ethnicity* *RR2: Risk ratio; univariable logistic regression among T21RS samples and ISARIC4C controls matched on age, sex, and ethnicity* *Mortality, n/N (%):* • aRR: 2.49 (95% CI: 1.51-3.69), p = 0.0006 • RR1: 2.91 (95% CI: 2.11-3.79), p<0.0001 • RR2: 3.47 (95% CI: 2.58-4.39), p<0.0001 • Down syndrome: 82/188 (43.6%) • No Down syndrome: 55/400 (13.8%) **Severity of Condition:**

	completed by caregivers/family members or clinicians from April 9 - October 22, 2020. Only individuals with information on age and sex were included in the analyses. Hospitalized patients with COVID-19 from the UK ISARIC4C survey, a prospective observational cohort study engaging acute-care hospitals in England, Wales, and Scotland, who were entered between February - July 09, 2020. Patients with Down syndrome were matched 1:4 on age, sex, and ethnicity with patients without Down syndrome. Hospitalized patients from the T21RS survey were matched 1:1 with ISARIC4C patients with Down syndrome. **Exclusion Criteria:** T21RS duplicates based on age, sex, country, and other specific demographics, and UK ISARIC4C individuals with Down syndrome with incomplete data on age, sex, or ethnicity.		T21RS study samples came from many different countries. Author's note: It could not be determined whether the matched hospitalized T21RS cases from the UK were also part of ISARIC4C survey.	*Mortality, n/N (%):* Moderate IDD: • aOR: 0.81 (95% CI: 0.30-2.17); p = 0.676 • Moderate IDD: 54/580 (9.3%) • Borderline/normal/mild: 7/169 (4.1%) Severe/Profound IDD: • aOR: 1.33 (95% CI: 0.47-3.77); p = 0.591 • Severe/profound IDD: 46/184 (25.0%) • Borderline/normal/mild: 7/169 (4.1%) *Hospitalization, n/N (%):* Moderate IDD: • aOR: 1.21 (95% CI: 0.78-1.89); p = 0.400 Severe/profound IDD: • aOR: 1.19 (95% CI: 0.67-2.09); p = 0.552 **Duration of Condition:** NR **Comorbid Conditions:** *Mortality, n/N (%):* Obesity: • aOR: 1.33 (95% CI: 0.75-2.35); p = 0.323 • Died: 43/131 (32.8%) • Survived: 224/728 (30.8%) Alzheimer's disease/dementia: • aOR: 2.13 (95% CI: 1.10-4.12), p = 0.025 Obstructive sleep apnea: • aOR: 0.68 (95% CI: 0.37-1.26), p = 0.224 Congenital heart defect: • aOR: 0.89 (95% CI: 0.47-1.66); p = 0.704 • Died: 29/131 (22.1%) • Survived: 276/728 (37.9%) Behavioral and psychiatric condition: • aOR: 0.85 (95% CI: 0.48-1.49), p = 0.563 Chronic lung disease: • aOR: 0.80 (95% CI: 0.38-1.70); p = 0.562 • Died: 30/131 (22.9%) • Survived: 174/728 (23.9%) Diabetes: • aOR: 0.54 (95% CI: 0.24-1.21); p = 0.136 • Died: 26/131 (19.8%) • Survived: 107/728 (14.7%) Number of comorbidities: • aOR: 1.26 (95% CI: 0.89-1.77), p = 0.189 *Hospitalization, n/N (%):* Obesity:

				• aOR: 2.03 (95%: 1.44-2.87); p<0.001 Alzheimer's disease/ dementia: • aOR: 0.77 (95% CI: 0.44-1.36), p = 0.372 Obstructive sleep apnea: • aOR: 1.17 (95% CI: 0.84-1.65), p = 0.351 Congenital heart defect: • aOR: 1.46 (95%: 1.05-2.03); p = 0.026 Chronic lung disease: • aOR: 0.89 (95%: 0.60-1.31); p = 0.546 Diabetes: • aOR: 1.93 (95%: 1.20-3.12); p = 0.007 Number of comorbidities: • aOR: 1.12 (95% 0.90-1.41), p = 0.319 **Risk Markers:** *Mortality, n/N (%):* Age <40 years: • aRR: 2.42 (95% CI: 0.12-12.88), p = 0.4370 • RR1: 4.0 (95% CI: 0.78-14.62), p = 0.0809 • RR2: 4.17 (95% CI: 0.58-16.13), p = 0.11 • Down syndrome: 5/41 (12.2%) • No Down syndrome: 3/100 (3.0%) Age 40+ years: • aRR: 2.73 (95% CI: 1.71-3.84), p = 0.0001 • RR1: 2.85 (95% CI: 2.09-3.62), p<0.0001 • RR2: 3.21 (95% CI: 2.42-3.96), p<0.0001 • Down syndrome: 77/147 (52.4%) • No Down syndrome: 52/300 (17.3%) **Long-term Sequelae:** NR
Author: Hwang[34] **Publication:** 2020 **Data Extractor:** MM **Reviewer:** MW **Study Design:** Cohort **Study Objective:** To investigate the prognostic factors in elderly patients with COVID-19.	**Population:** N =340 **Setting:** 3 hospitals **Data Source:** Electronic medical records **Location:** South Korea **Study Dates:** February 17- June 5, 2020 **Inclusion Criteria:** Patients aged ≥65 with COVID-19 who were admitted between	**Medical Condition, n/N (%):** Activities of daily living impairment (ADL): 84/340 (24.7%) **Control/Comparison Group, n/N (%):** No activities of daily living impairment: 256/340 (75.3%)	**Medical Condition(s):** *Activities of daily living impairment:* Baseline impairment was classified according to whether the patient could independently perform daily activities before being diagnosed with COVID-19 **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression; model included age, sex, ADL impairment, comorbidity, fever, initial chest X-ray, initial C-reactive protein* *OR: Univariable (Univariate) Logistic Regression* *Mortality, n/N (%):* • aOR: 8.89 (95% CI: 4.37-18.10), p<0.001 • OR: 7.13 (95% CI: 2.93-17.40), p<0.001 • Deceased: 35/51 (68.6%) • Survived: 49/289 (17.0%) • p<0.001 **Severity of Condition:** NR

IVA **Score:** 24 (Moderate)	February 17 – May 31, 2020 and who were discharged or deceased by the end of the study date. COVID-19 was diagnosed using real-time RT-PCR. **Exclusion Criteria:** NR		*Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Janus[57] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** MM/JKK **Study Design:** Cohort **Study Objective:** To gain insight into the broad spectrum of signs/symptoms, disease course, and outcome in nursing home residents with COVID-19. **IVA Score:** 20 (Moderate)	**Population:** N=88 **Setting:** Care organizations **Data Source:** Electronic health records **Location:** Netherlands **Study Dates:** March – April 2020 **Inclusion Criteria:** Nurs ing home residents who stayed at a ward for long-term stay or geriatric rehabilitation during the study period and had confirmed COVID-19 by RT-PCR. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Bedridden: 1/88 (1.1%) Wheelchair: 29/88 (33%) Walking with physical help: 19/88 (21.6%) **Control/Comparison Group, n/N (%):** Independent with or without mobility aid: 39/88 (44.3%)	**Medical Condition(s):** *Bedridden:* ND *Wheelchair:* ND *Walking with physical help:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%):* • Bedridden: 0/1 (0.0%) • Independent: 11/39 (28.2%) • Wheelchair: 12/29 (41.4%) • Independent: 11/39 (28.2%) • Walking with physical help: 9/19 (47.4%) • Independent: 11/39 (28.2%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Joy[32] **Year:** 2020 **Data Extractor:** MC **Reviewer:** MW/CS **Study Design:** Cohort **Study Objective:** To describe the rate of all-	**Population:** N =56,628 COVID-19+, N=49,842 **Setting:** Research and Surveillance Centre (RSC) sentinel network **Data Source:** Primary h ealth care electronic records **Location:** United Kingdom	**Medical Condition, n/N (%):** Learning disability: 601/49,842 (1.2%) **Control/Comparison Group, n/N (%):** No learning disability: 49,241 /49,842 (98.8%)	**Medical Condition(s):** *Learning disability*: ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* all-cause mortality *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR	**Severe COVID-19:** *aOR: Multivariable adjusted Odds Ratio; models adjusted for age, sex, SARS-CoV-2 status, household size, ethnicity, socioeconomic status, smoking status, and underlying health conditions* *Mortality:* Learning disability: • aOR: 1.9682 (95% CI: 1.2186-3.1788), p = 0.0056 **Severity of Condition:** NR

cause mortality throug hout the first peak of COVID-19 in England and its association with SARS-CoV-2 status and other demographic and risk factors. **IVA** **Score:** 24 (moderate)	**Study Dates:** January 7 - May 19, 2019, and January 6 - May 18, 2020 **Inclusion Criteria:** All patients registered at general practices in the Oxford RCGP RSC network on 11 May 2020 and having ≥1 year of health records in the network (n = 4 413 734). **Exclusion Criteria:** NR		*Non-elective readmissions*: NR **Comments:** None	**Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Karmakar[13] **Publication:** 2021 **Data Extractor:** TR **Reviewer:** MM/CS **Study Design:** Ecological **Study Objective:** To examine the association between county-level sociodemographic risk factors and US COVID-19 incidence and mortality using the social vulnerability index (SVI). **IVA Score:** 24 (moderate)	**Population:** N= 4,289,283 **Setting:** Hospitals **Data Source:** Johns Hopkins University Center for Systems Science and Engineering data repository **Location:** 50 US states and Washington, District of Columbia **Study Dates:** January-July 2020 **Inclusion Criteria:** NR **Exclusion Criteria:** US territories, 52 observations with unassigned counties, and the 5 counties of New York City.	**Medical Condition, n/N (%):** Disability: NR **Control/Comparison Group, n/N (%):** NR	**Medical Condition(s):** *Disability:* Percentages of persons aged ≥ 65 years or ≤17 years, civilian noninstitutionalized population with disability, and single parent households with children aged <18 years **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Death *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** Social Vulnerability Index: developed by the CDC as a composite measure of community susceptibility to adversities in the face of health shocks. SVI is comprised of 4 subindices using American Community Survey data (2014-2018) on socioeconomic status, household composition and disability, racial/ethnic minority status and	**Severe COVID-19:** *IRR: incidence ratio rate, adjusted for population density, urbanicity, and COVID-19 testing rate* *Mortality, n/N (%):* People with disability (noninstitutionalized): • IRR: 0.99 (95% CI: 0.98-1.01), p = 0.35 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

			language, and housing and transportation type.	
Author: Kennedy[61] **Publication:** 2020 **Data Extractor:** JKK **Reviewer:** CS **Study design:** Case series **Study Objective:** To describe sonographic pulmonary features in patients with severe COVID-19 across a spectrum of ages. **IVA Score:** Internal validity was not conducted for case reports/case series.	**Population:** N=3 **Setting:** Hospital **Location:** NY, US **Study dates:** NR **Inclusion criteria:** NR **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Fragile X syndrome: 1/3 (33.3%)	**Medical Condition(s):** *Fragile X syndrome*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* pediatric intensive care unit (PICU) admission *Intubation:* ND *Ventilation:* non-invasive ventilation with CPAP *Hospitalization:* emergency department admission *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *ICU admission: Yes* *Intubation (or Invasive Ventilation): Yes* *Ventilation (mechanical, or non-invasive ventilation): Yes* *Hospitalization: Yes* *General Progression* • *Case 1:* A 9-year-old girl presented with fever, cough, increased respiratory effort, diarrhea, and posttussive vomiting. She was diagnosed with acute otitis media 2 days prior to admission to the ED for respiratory distress. Based on point-of-care ultrasound (POCUS), she was diagnosed with pneumonia and started noninvasive ventilation with CPAP. Due to worsening respiratory distress, the patient was admitted to the PICU and intubated. She was treated with antibiotics and hydroxychloroquine. She was intubated for 10 days and discharged on day 16 of hospitalization. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** • *Case 1:* overweight and history of intermittent asthma **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: Not applicable for this study type
Author: Kleiman[62] **Publication:** 2020 **Data Extractor:** JKK **Reviewer:** CS **Study design:** Case report	**Population:** N=1 **Setting:** Hospital **Location:** New York, USA **Study dates:** NR **Inclusion criteria:** NR	**Medical Condition, n/N (%):** Fragile-X Syndrome: 1/1 (100%)	**Medical Condition(s):** *Fragile-X Syndrome*: trinucleotide repeat disorder; may present with behavioral features and poor language development **Severity Measure(s):** NR **Clinical marker:** NR	**Severe COVID-19:** *ICU admission:* Yes *Intubation (or Invasive Ventilation):* Yes *Ventilation (mechanical, or non-invasive ventilation):* Yes *Hospitalization:* Yes *General Progression* • A 46-year-old female patient was admitted to the emergency department due

Study Objective: To document a case of COVID-19 in a female patient with Fragile-X Syndrome (FXS) and examine any role this genetic disorder may have had in her clinical course and outcome. **IVA Score:** Internal validity was not conducted for case reports/case series.	**Exclusion criteria:** NR		**Outcome Definitions:** *Mortality:* NR *ICU admission:* admission to the medical intensive care unit (MICU) *Intubation:* ND *Ventilation:* mechanical ventilation *Hospitalization:* admission to the general medicine ward *Non-elective readmissions*: NR **Comments:** None	to dyspnea with chest tightness and fatigue. She was admitted to the general medicine ward on assumption of community-acquired pneumonia and possible pulmonary embolism. The patient tested positive for SARS-CoV-2 by PCR and began treatment with ceftriaxone, doxycycline, and hydroxychloroquine. On day 5 of hospitalization, she was admitted to the MICU due to worsening tachypnea and oxygenation needs where she underwent intubation and mechanical ventilation. The patient was administered tocilizumab, steroids, and convalescent plasma infusion due to worsening chest x-ray and Coronavirus-associated pneumonia. Her condition was complicated by shock, ventilator-associated pneumonia with multi-drug resistance, acute kidney injury, and gluteal hematoma. She underwent tracheostomy on day 17 of MICU admission and was transferred to a step-down unit. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** • Hypertension, morbid obesity, type II diabetes mellitus, asthma, and history of deep venous thrombosis in left lower extremity **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: Not applicable for this study type
Author: Kobaidze[77] **Publication:** 2021 **Data Extractor:** JKK **Reviewer:** MM	**Population:** N=1 **Setting:** Hospital **Location:** GA, US **Study dates:** NR	**Medical Condition, n/N (%):** Right eye blindness: 1/1 (100%)	**Medical Condition(s):** Right eye blindness: ND **Severity Measure(s):** NR **Clinical marker:** NR	**Severe COVID-19:** *ICU admission:* Yes *Hospitalization:* Yes *General Progression* • A 90-year-old African American female presented to the emergency department with general tonic-

Study design: Case report **Study Objective:** To present a case of an elderly patient who developed seizures and posterior reversible encephalopathy syndrome (PRES) after recovering from the acute phase of COVID-19 infection. **IVA Score:** Internal validity was not conducted for case reports/case series.	**Inclusion criteria:** NR **Exclusion criteria:** NR		**Outcome Definitions:** *Mortality:* NR *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: ND **Comments:** None	clonic seizures; her blood pressure was elevated, and CT and basic laboratory work were unremarkable; the patient's EEG showed generalized slowing in bilateral temporal regions and her brain MRI reflected patterns compatible with PRES; patient experienced no more seizures after treatment with levetiracetam; her mental state returned to normal, and she was discharged 6 days after admission. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** • History of hypertension, osteoarthritis, type 2 diabetes mellitus, deep venous thrombosis, pulmonary embolism, stage 2 chronic kidney disease, atrial flutter, cataract, macular degeneration, pressure ulcer stage II, mild dementia **Risk Markers:** NR **Long-term Sequelae:** *Non-elective readmissions*: Patient was hospitalized and admitted to the ICU for COVID-19 pneumonia and later discharged after negative SARS-CoV-2 test. She was readmitted to the hospital with posterior reversible encephalopathy syndrome over 3 weeks after discharge.
Author: Landes[3] **Publication:** 2020 **Data Extractor:** AH **Reviewer:** DOS **Study Design:** Cohort **Study Objective:** To describe COVID-19 outcomes among people with IDD living in residential groups homes in the state of New York and the general population of New York State.	**Population:** N=373,161 **Setting:** Residential group homes **Data Source:** New York Disability Advocates (NYDA), New York Department of Health (NYDoH), New York City (NYC) COVID-19 Trackers, 2019 US Census Bureau **Location:** New York, US	**Medical Condition, n/N (%):** Intellectual and developmental disabilities (IDD): 1,602/20,431 (7.8%) **Control/Comparison Group, n/N (%):** No IDD (General New York State population): 371,559/19,453,291 (1.9%)	**Medical Condition(s):** *IDD*: lifelong disability that manifests before age 18 and involves functional limitations in the areas of learning, language, and behavior **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* • *Mortality rate*: deaths among total population • *Case fatality rate*: deaths among COVID-19 cases	**Severe COVID-19:** *Mortality rate per 100,000:* All regions: • IDD: 1175 • General population: 151 New York City: • IDD: 2,007 • General population: 251 Long-Island: • IDD: 1,939 • General population: 195 Mid-Hudson: • IDD: 1,821 • General population: 91 Rest of NY regions: • IDD: 95

IVA Score: 17 (High)	**Study Dates:** Beginning of pandemic - May 28, 2020 **Inclusion Criteria:** Individuals with IDD age 18 and over, living in residential group homes, and had COVID-19 at some point. **Exclusion Criteria:** NR		*ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** Author's note: Cannot guarantee exclusivity between the NYDA data and NYDoH data, so individuals with IDD might be included in the general population comparison group.	• General population: 24 *Case fatality rate, n/N (%):* All regions: • IDD: 240/1,602 (15.0%) • General population: 29,438/371,559 (7.9%) New York City: • IDD: 112/712 (15.7%) • General population: 20,895/205,854 (10.2%) Long-Island: • IDD: 60/318 (18.9%) • General population: 4,528/79,499 (5.7%) Mid-Hudson: • IDD: 60/425 (14.1%) • General population: 2,589/64,820 (4.0%) Rest of NY regions: • IDD: 8/147 (5.4%) • General population: 1,426/21,386 (6.7%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Landes[4] **Publication:** 2021 **Data Extractor:** MC **Reviewer:** TR **Study Design:** Cohort study **Study Objective:** To compare COVID-19 outcomes among people who were/were not receiving IDD services, and to examine whether differentials	**Population:** N =819,436 **Setting:** Residential group homes **Data Source:** The California Department of Developmental Disabilities Services (DDS), California Open Data Portal **Location:** California, USA **Study Dates:** early May- October 2, 2020	**Medical Condition, n/N (%):** Intellectual and developmental disabilities (IDD), receiving services: 2,948/354,640 (0.8%) **Control/Comparison Group, n/N (%):** Not receiving IDD services: 816,488/39,157,583 (2.1%)	***Medical Condition(s):*** *IDD: ND* ***Severity Measure(s):*** *NR* ***Clinical Marker:*** *NR* ***Outcome Definitions:*** *Mortality:* • *Mortality rate: deaths among the population* • *Case fatality rate: deaths among COVID-19 cases* *ICU admission: NR* *Intubation: NR* *Ventilation: NR* *Hospitalization: NR* *Non-elective readmissions: NR*	**Severe COVID-19:** *Mortality rate per 100,000:* • Receiving IDD services: 46 • Not receiving IDD services: 41 *Case fatality rate, n/N (%)*: • Receiving IDD services: 162/2,948 (5.5%) • Not receiving IDD services: 15,912/816,488 (1.9%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality, n/N (%):*

in outcomes varied by type of residence for people who were receiving IDD services. **IVA Score:** 16 (High)	**Inclusion Criteria:** People with IDD and COVID-19 outcomes living in residential groups homes in the state of California and the general population of California with COVID-19 outcomes. **Exclusion Criteria:** NR		***Comments:*** *It is possible that the primary characteristics determining COVID-19 outcomes among Californians receiving IDD services are age and pre-existing health conditions, and that type of residence simply appropriates these indicators. The California DDS COVID-19 data does provide the age distribution of those served, but it does not detail the age distribution by type of service. Thus, we are not able to account for the possible effect of age on COVID-19 outcomes by types of residence.*	Type of residence among those receiving IDD services: • Own home or family home: 47/1,651 (2.8%) • Community care facility: 23/538 (4.3%) • Intermediate Care Facility for the Developmentally Disabled (ICF/DD)-Habilitative: 13/209 (6.2%) • ICF/DD-Nursing: 15/95 (15.8%) • ICF for the Developmentally Disabled: 5/106 (4.7%) • Skilled nursing facility: 58/284 (20.4%) • Other: 1/65 (1.5%) **Long-term Sequelae:** NR
Author: Laosa[52] **Publication:** 2020 **Data Extractor:** MM **Reviewer:** MW/DOS **Study Design:** Cohort **Study Objective:** To evaluate the role of functional status along with other used clinical factors on the occurrence of death in patients hospitalized with COVID-19. **IVA Score:** 24 (Moderate)	**Population:** N =375 **Setting:** Hospital **Data Source:** Health care clinical records **Location:** Spain **Study Dates:** March 1 – June 18, 2020 **Inclusion Criteria:** Patients hospitalized during a one-month time period, selected consecutively according to the date of admission to hospital, and with a confirmed positive COVID-19 PCR test. **Exclusion Criteria:** Patients that were still in the hospital on June 18th were excluded from the analyses.	**Medical Condition, n/N (%):** Low Barthel index (Disability): 64/375 (17.0%) **Control/Comparison Group, n/N (%):** High Barthel index (No disability): 306/375 (82.0%)	**Medical Condition(s):** *Barthel index:* Assessed by the Barthel Index of Activities of Daily Living (ADL) **Severity Measure(s):** Barthel Index score: *0-60:* severe disability *65-85:* moderate disability *90-95:* mild disability *100:* no disability **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Mortality during hospitalization *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aOR4: model included sex, age, Barthel index, Quick Sequential Organ Failure Assessment (qSOFA), and polypharmacy, and ≥3 morbidities* *aOR3: model included sex, age, Barthel index, Quick Sequential Organ Failure Assessment (qSOFA), and polypharmacy* *aOR2: model included sex, age, Barthel index, Quick Sequential Organ Failure Assessment (qSOFA)* *aOR1: model included sex, age, Barthel index* *Mortality, n/N (%):* Barthel Index: • aOR4: 1.11 (95% CI: 1.03-1.20), p = 0.008 • aOR3: 1.12 (95% CI: 1.04-1.21), p = 0.005 • aOR2: 1.12 (95% CI: 1.04-1.21), p = 0.004 • aOR1: 1.13 (95% CI: 1.05-1.22), p = 0.002 • Disability (Barthel score 0-95): 29/64 (45.3%) • No disability (Barthel score 100): 43/306 (14%) **Severity of Condition:** *Mortality, n/N (%):* Barthel Index 0-60: 10/18 (55.5%) No disability: 43/306 (14%) Barthel Index 65-85: 8/19 (42.1%) No disability: 43/306 (14%)

				Barthel Index 90-95: 11/27 (40.7%) No disability: 43/306 (14%) **Duration of Condition:** NR **Comorbid Conditions:** *Mortality:* Number of comorbidities, aOR per 5-point decrease in Barthel Index: • ≥1 comorbidity, aOR4: 1.13 (95% CI: 1.04-1.22), p = 0.002 • ≥2 comorbidities, aOR4: 1.12 (95% CI: 1.04-1.21), p = 0.004 • ≥3 comorbidities, aOR4: 1.11 (95% CI: 1.03-1.21), p = 0.007 • ≥4 comorbidities, aOR4: 1.11 (95% CI: 1.02-1.20), p = 0.014 • ≥5 comorbidities, aOR4: 1.11 (95% CI: 1.03-1.21), p = 0.008 **Risk Markers:** Barthel Index remained associated with the risk of death in all the models in the study, with a mean increase of 10% to 15% in the risk of death by each decrease of 5 points. Age was the strongest predictor of death, with a very well-defined dose-dependent relationship. The study reported that functional status seems to modulate the effect of age on mortality. **Long-term Sequelae:** NR
Author: Latimer[69] **Publication:** 2020 **Data Extractor:** JKK **Reviewer:** AH **Study design:** Case report **Study Objective:** N To compare COVID-19	**Population:** N=1 **Setting:** Hospital **Location:** DC, US **Study dates:** NR **Inclusion criteria:** NR **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Chromosome 18q deletion: 1/1 (100%)	**Medical Condition(s):** *Chromosome 18q deletion*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* ND *Intubation:* ND *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR	**Severe COVID-19:** *ICU admission:* Yes *Intubation (or Invasive Ventilation):* Yes *Hospitalization:* Yes *General Progression* • A 16-year-old male presented with hemodynamic shock after 4 days of fever and one generalized seizure; he was intubated and resuscitated; his second test for SARS-CoV-2 on day 3 of admission was positive; the patient met criteria for mild pediatric acute respiratory distress syndrome and showed signs of kidney injury, liver injury, coagulopathy, and significant myocardial injury;

trends among people with and without IDD, overall and stratified by age **IVA Score:** Internal validity was not conducted for case reports/case series.			**Comments:** None	his presentation met criteria for thrombocytopenia-associated multiple organ failure (TAMOF) inflammation phenotype; patient was prescribed plasma exchange on days 2-3 and hydroxychloroquine was initiated on day 4 but discontinued; coagulopathy resolved and cardiac function recovered on day 9; renal failure improved with minimal dialysis on days 16 and 17; he developed bacterial tracheitis on day 23 and underwent tracheostomy on day 38; he was discharged to a rehabilitation facility on day 46 of ICU admission and he returned to behavioral baseline. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** • History of epilepsy **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: Not applicable for this study type
Author: Lau[65] **Publication:** 2020 **Data Extractor:** TR **Reviewer:** ES/JKK **Study Design:** Case series **Study Objective:** To describe the impact of COVID19 on 30 patients with LSDs with details of symptomatology, duration of illness, and treatment. **IVA Score:** Internal validity was not	**Population:** N=30 **Setting:** NR **Location:** New York, USA **Study Dates:** March – June 2020 **Inclusion Criteria:** Pati ents with lysosomal storage disorders in the NYU Langone Health Lysosomal Storage Disorders (LSD) Program who had 2 or more COVID-19 symptoms and/or were RT-PCR positive for SARS-CoV-2	**Medical Condition, n/N (%):** Gaucher disease (GD): 26/30 (86.7%)	**Medical Condition(s):** *Gaucher disease*: ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality:* 1/26 (3.8%) *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization* 1/26 (3.8%) *General Progression* • *Case 1*: One 55-year-old woman with Gaucher disease on enzyme replacement therapy progressed to acute respiratory distress syndrome, hospitalization, and death. GD burden was minimal. • *Other cases*: Had mild to moderate illness. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:**

conducted for case reports/case series.	RNA or positive for antibodies. **Exclusion Criteria:** NR			• *Case 1:* history of morbid obesity, COPD, hypertension, and diabetes • *Other cases:* NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: Not applicable for this study type
Author: Lega[45] **Publication:** 2021 **Data Extractor:** MC **Reviewer:** MM/CS **Study Design:** Cross-sectional **Study Objective:** To describe the clinical presentation, course, management, and care pathway of patients dying with COVID-19 and a prior psychiatric diagnosis compared to those with no previous psychiatric history. **IVA Score:** 18 (Moderate)	**Population:** N=4,020 **Setting:** 365 hospitals **Data Source:** Italian National Institute of Health; COVID-19 Integrated Surveillance System **Location:** Italy **Study Dates:** February 21 - August 3, 2020 **Inclusion Criteria:** Medical charts of COVID-19 related in-hospital deaths, that completed the review from February 22-September 1, 2020, representing 11.2% of all deaths occurred in Italy by that date. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Neurodevelopmental disorder: 54/4,020 (1.4%) **Control/Comparison Group, n/N (%):** No neurodevelopmental disorder: 3,966/4,020 (98.7%)	**Medical Condition(s):** *Neurodevelopmental disorder*: ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* in-hospital death with COVID-19 *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%):* Neurodevelopmental disorder: • Neurodevelopmental disorder: 54/4,020 (1.4%) • No neurodevelopmental disorder: 3,966/4,020 (98.7%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** *Mortality, n/N (%):* Neurodevelopmental disorder: • With severe psychiatric disorder: 10/54 (18.5%) • Without psychiatric disorder: 43/54 (79.6%) **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Louapre[49] **Publication:** 2020 **Data Extractor:** MW **Reviewer:** JKK **Study Design:** Cohort **Study Objective:** To describe outcomes of COVID-19 and to	**Population:** N=15 **Setting:** Multicenters **Data Source:** Covisep registry **Location:** France **Study Dates:** March 1 - June 30, 2020	**Medical Condition, n/N (%):** NMOSD or MOGAD: 15/15 (100%) **Control/Comparison Group, n/N (%):** NA	**Medical Condition(s):** *NMOSD:* ND *MOGAD:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR	**Severe COVID-19:** *ICU admission, n/N (%):* • NMOSD or MOGAD: 1/15 (6.6%) *Intubation, n/N (%):* • NMOSD or MOGAD: 1/15 (6.6%) *Ventilation, n/N (%):* • NMOSD or MOGAD: 1/15 (6.6%)

identify risk factors associated with COVID-19 severity in the neuromyelitis optica spectrum disorders (NMOSD) and antibody-associated disease (MOGAD) patients. **IVA Score:** 17 (High)	**Inclusion Criteria:** Patients with NMOSD or MOGAD and at least one of the following four criteria: (i) biologically confirmed COVID-19 diagnosis based on SARS-CoV-2 polymerase chain reaction (PCR) positivity in nasopharyngeal swab; (ii) typical thoracic computerized tomography (CT) abnormalities (ground glass opacities) in epidemic areas; (iii) anosmia or ageusia of sudden onset in the absence of rhinitis or nasal obstruction or (iv) typical symptoms (triad associating cough, fever, asthenia) in epidemic zone of COVID-19. **Exclusion Criteria:** Patient's opposition to the use of their medical data.		*ICU admission:* ND *Intubation:* ND *Ventilation:* Non-invasive ventilation or invasive mechanical ventilation *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	*Hospitalization, n/N (%):* • NMOSD or MOGAD: 5/15 (33.3%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Macedo[58] **Publication:** 2020 **Data Extractor:** MM **Reviewer:** DOS **Study Design:** Retrospective cohort **Study Objective:** To correlate patient's demographics,	**Population:** N=3,896 **Setting:** Hospitals **Data Source:** Health Secretary of the State of Bahia (SESAB) **Location:** Brazil **Study Dates:** March 3, 2020 - July 29, 2020 **Inclusion Criteria:** Hospitalized COVID-	**Medical Condition, n/N (%):** Chromosomal Disorder: 39/3,896 (1%) **Control/Comparison Group, n/N (%):** No Chromosomal Disorder: 3,857/3,896 (99%)	**Medical Condition(s):** Chromosomal Disorder: ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR	**Severe COVID-19:** *Mortality, n/N (%):* • Died: 12/1045 (1.1%) • Survived: 27/2851 (0.9%) • p = 0.7 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR

symptoms, and comorbidities, with the risk of mortality from COVID-19, length of hospital stays, and time from diagnosis to definitive outcome. **IVA Score:** 23 (Moderate)	19+ patients living in Bahia who were included in the SESAB dataset. COVID-19 diagnosis based on WHO guidance. **Exclusion Criteria:** Non-hospitalized COVID-19+ patients and patients with invalid registration in the SESAB dataset.		**Comments:** None	**Long-term Sequelae:** NR
Author: Makary[5] **Publication:** 2020 **Data Extractor:** CS **Reviewer:** DOS **Study Design:** Cohort study **Study Objective:** To study the risk factors (patient age, sex, and preexisting comorbidities) for COVID-19 mortality among privately insured patients. **IVA Score:** 23 (moderate)	**Population:** N=467,773 **Setting:** Any healthcare setting including hospitals **Data Source:** Nation's largest private healthcare claims database; FAIR Health National Private Insurance Claims database **Location:** US **Study Dates:** April 1-August 31, 2020 **Inclusion Criteria:** All privately insured patients in the dataset with a diagnosis of COVID-19 on the earliest claim record in any healthcare setting (including hospitals) were included. COVID-19 patients were identified as those who	**Medical Condition, n/N (%):** Developmental disorders: NR Intellectual disabilities and related conditions: NR Mobility impairments: NR Spina bifida and other nervous system anomalies: NR Spinal cord injury: NR **Control/Comparison Group, n/N (%):** No developmental disorders: NR No intellectual disabilities and related conditions: NR No mobility impairments: NR No spina bifida and other nervous system anomalies: NR No spinal cord injury: NR	**Medical Condition(s):** *≥3 claim lines with any one of the ICD-10-CM diagnosis codes found within the 67 Chronic Conditions Data Warehouse categories from April 1, 2017 - March 31, 2020* *Developmental disorders:* Developmental disorders of speech and language, developmental disorders of scholastic skills, central auditory processing disorders; does not include autism *Intellectual disabilities and related conditions:* Down syndrome and other chromosomal anomalies; mild, moderate, severe and profound intellectual disabilities; congenital malformations, such as certain disorders that cause microcephaly; does not include autism *Mobility impairments:* ND *Spina Bifida and other nervous system anomalies:* may overlap with intellectual/developmental disabilities and other conditions *Spinal cord injury:* ND **Severity Measure(s):** NR **Clinical Marker:** NR	**Severe COVID-19:** *aOR: Adjusted odds ratio; stepwise regression and a binary logit model with Fisher's scoring optimization; included model variables: age, sex* **Numerators calculated by ERT* *Mortality for all age groups:* Developmental disorders: • aOR: 3.06 (95% CI: 1.554-6.008); p = 0.0105 Intellectual disabilities and related conditions: • aOR: 2.75 (95% CI: 1.657-4.558); p = 0.0005 Mobility impairments: • aOR: 1.62; p = statistically significant Spina Bifida and other nervous system anomalies: • aOR: 2.48 (95% CI: 1.027-5.969); p = 0.0283 Spinal cord injury: • aOR: 1.56 (95% CI: 1.157-2.097); p = 0.0061 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality for patients under age 70:* Developmental disorders: • aOR: 4.76 (95% CI: 1.858-12.216); p = 0.0003 Intellectual disabilities and related conditions: • aOR: 3.61 (95% CI: 1.878-6.930); p = 0.0007

	had the ICD-10 diagnosis code U07.1 (COVID-19) in any of the 24 diagnosis positions on the claim or claim line using ICD-10-CM codes. **Exclusion Criteria:** Clai ms data from February to March 2020 to account for the variation in COVID-19 coding and treatment, and subsequent variance in mortality rates, prior to April 2020.		**Outcome Definitions:** *Mortality:* claim line for a patient with a discharge status of "expired" (admitted to morgue or autopsied) *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** Author's note: Mortality was defined by a claim line for a patient with a discharge status of "expired," possibly resulting in an undercounting in the number of deaths as it required the patient be admitted to the morgue or autopsied, which was not routinely done at the height of the COVID pandemic.	Mobility impairments: • aOR: 1.88; p = statistically significant **Long-term Sequelae:** NR
Author: Mancuso[59] **Publication:** 2021 **Data Extractor:** TR **Reviewer:** DOS **Study Design:** Retrosp ective cohort **Study Objective:** To analyze the clinical features, prognosis, and outcomes of COVID-19 in patients with primary mitochondrial diseases. **IVA Score:** Internal validity was not conducted for studies with less than 10 people with the given medical conditions.	**Population:** N= 27 **Setting:** Nationwide **Data Source:** National registry of the Nation-wide Italian Collaborative Network of Mitochondrial Diseases **Location:** Italy **Study Dates:** March 1, 2020-January 30, 2021 **Inclusion Criteria:** PCR confirmed COVID-19 patients with primary mitochondrial diseases included in the Nation-wide Network registry. All Italian pediatric and adulthood centers with expertise in	**Medical Condition, n/N (%):** Primary mitochondrial myopathy (PMM): 4/27 (14.8%) Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS): 4/27 (14.8%) Myoclonic epilepsy with ragged red fibers (MERRF): 2/27 (7.4%) Multisystem disease: 6/27 (22.2%) Leber's hereditary optic neuropathy (LHON)/ autosomal dominant optic atrophy (ADOA): 4/27 (14.8%) Neuropathy, ataxia, and retinitis pigmentosa (NARP): 3/27 (11.1%) Leigh: 3/27 (11.1%) Maternally inherited diabetes and deafness (MIDD): 1/27 (3.7%) **Control/Comparison Group, n/N (%):** NA	**Medical Condition(s):** *PMM:* ND *MELAS:* ND *MERRF:* ND *Multisystem disease:* NR *LHON/ADOA:* ND *NARP:* ND *Leigh:* ND *MIDD:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Death *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* Infective ward or COVID ward *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%):* PMM: 1/4 (25%) *Hospitalization, n/N (%):* PMM: 2/4 (50%) MELAS: 2/4 (50%) MERRF: 0/2 (0%) Multisystem disease: 0/6 (0%) LHON /ADOA: 0/4 (0%) NARP: 0/3 (0%) Leigh: 0/3 (0%) MIDD: 0/1 (0%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality, n/N (%):* PMM: Female: 0/2 (0%) Male: 1/2 (50%)

	mitochondrial disorders are enrolled in the network. **Exclusion Criteria:** Patients presenting with suggestive symptoms without any objective test confirming COVID-19 (possible cases), and patients in whom the results of the diagnostic tests were not available/reachable.			*Hospitalization, n/N (%):* PMM: Female: 1/2 (50%) Male: 1/2 (50%) MELAS: Female: 1/2 (50%) Male: 1/2 (50%) **Long-term Sequelae:** NR
Author: Merzon[55] **Publication:** 2021 **Data Extractor:** MM/DOS **Reviewer:** CS **Study Design:** Cohort **Study Objective:** To d etermine if ADHD is an independent risk factor for symptomatology and hospitalization with COVID-19. **IVA score:** 24 (moderate)	**Population:** N=1870 **Setting:** NR **Data Source:** 1) Database of Leumit Health Services patients 2) Electronic health record **Location:** Israel **Study Dates:** February 1 - June 30, 2020 **Inclusion Criteria:** All COVID-19 positive patients aged 5 to 60 years serviced by Leumit Health Services were included. Referral for COVID-19 testing was made at the discretion of the primary care physician according to	**Medical Condition, n/N (%):** Attention deficit hyperactivity disorder (ADHD): 231/1870 (12.4%) **Control/Comparison Group, n/N (%):** No ADHD: 1639/1870 (87.6%)	**Medical Condition(s):** *ADHD:* diagnosis based on the American Psychiatric Association's Diagnostic and Statistical Manuals 4th or 5th edition; diagnosis established by senior physicians specializing in ADHD **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression; included model variables: age, sex, SES, depression/anxiety, schizophrenia, diabetes mellitus, hypertension, cardiovascular disease, chronic obstructive pulmonary disease, obesity, smoking* *OR: Univariable Logistic Regression* *Hospitalization, n/N (%):* ADHD: • aOR: 1.93 (95% CI: 1.06-3.51), p = 0.030 • OR: 1.71 (95% CI: 1.05-2.78), p = 0.030 • Hospitalized: 22/117 (18.8%) • Not hospitalized: 209/1753 (11.9%) • p<0.05 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *Hospitalization in ADHD patients, n/N (%):* Age categories: • Age 5-20, OR: 1.64 (95% CI: 0.37-5.67), p = not significant • Age 21-40, OR: 2.96 (95% CI: 1.40-5.93) • Age 41-60, OR: 2.56 (95% CI: 0.60-8.99)

	the Israeli Ministry of Health's criteria (direct, close unprotected exposure to a confirmed COVID-19 positive patient and/or presenting symptoms suggesting COVID-19 infection). Testing was performed with nasopharyngeal swabs evaluated for COVID-19 by an RT-PCR assay. **Exclusion Criteria:** NR			• p<0.001 **Long-term Sequelae:** NR
Author: Mills[8] **Publication:** 2020 **Data Extractor:** MM **Reviewer:** CS **Study Design:** Cohort **Study Objective:** To describe how individuals with intellectual and developmental disabilities (IDD) have been affected in the first 100 days of the COVID-19 pandemic. **IVA Score:** 23 (Moderate)	**Population:** N=11,540 Analyzed: N=66 **Setting:** Residential/community settings, intermediate care facilities, and hospitals **Data Source:** Electronic medical records **Location:** National; US **Study Dates:** January 20- April 30, 2020 **Inclusion Criteria:** Individuals with IDD who are provided support by BrightSpring Health Services and tested positive for COVID-19 by nucleic acid test. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** IDD: 66/66 (100.0%) **Control/Comparison Group, n/N (%):** No IDD: 0/66 (0.0%)	**Medical Condition(s):** *Intellectual and Developmental Disability:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* mechanical ventilation *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%):* • Death: 3/66 (4.5%) • No death: 63/66 (95.5%) *ICU Admission, n/N (%):* • ICU admitted: 2/66 (3.0%) • Not ICU admitted: 64/66 (97.0%) *Ventilation, n/N (%):* • Ventilated: 2/66 (3.0%) • Not ventilated: 64/66 (97.0%) *Hospitalization, n/N (%)* • Hospitalized: 15/66 (22.7%) • Not hospitalized: 51/66 (77.2%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** Among COVID-19-positive individuals with IDD, a higher number of chronic medical conditions and male sex were characteristics associated with a greater likelihood of hospitalization. **Long-term Sequelae:**

				Non-elective readmissions: NR
Author: Nystad[40] **Publication:** 2020 **Data Extractor:** TR **Reviewer:** DOS **Study Design:** Retrospective cohort **Study Objective:** To describe the distribution of various conditions among persons with a confirmed COVID-19 infection and among patients hospitalized for COVID-19 compared to the general population. **IVA Score:** 21 (Moderate)	**Population:** N= 4,118,831 COVID-19+, N=7,632 **Setting:** Hospital **Data Source:** Norwegian Patient Registry (NPR); Norwegian Registry for Primary Health Care (KPR); Norwegian Surveillance System for Communicable Diseases (MSIS) in the Norwegian Institute of Public Health; Person Registry (Norwegian Health Network's version of the National Population Registry) **Location:** Norway **Study Dates:** March 1, 2020 - May 13, 2020 **Inclusion Criteria:** All Norwegians aged 20 years or older who were residents of Norway as of March 1, 2020. Patients with COVID-19 tested positive for SARS-CoV-2 in a PCR test. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Cerebral palsy & COVID-19: 13/7,632 (0.17%) **Control/Comparison Group, n/N (%):** No cerebral palsy & COVID-19: 7,619/7632 (99.83%)	**Medical Condition(s):** *Cerebral palsy:* ICD-10 diagnosis code G80-G83 **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* hospitalization at a government-funded hospital *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Proportions are age-adjusted* *Hospitalized, n/N (%):* • Cerebral palsy: 5/13 (38.46%) • No cerebral palsy: 1,020/7,619 (13.39%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Olulana[25] **Publication:** 2020 **Data Extractor:** MW **Reviewer:** JKK/DOS **Study Design:** Ecological	**Population:** N=369 counties **Setting:** NA **Data Source:** USAFacts for SARS-CoV-2 cases estimated for the year 2020, mobility data	**Medical Condition, n/N (%):** High death rate: states with SARS-CoV-2 death rate ≥3.4 Disability: 14.3% Hearing difficulty: 3.5% Vision difficulty: 2.3% Cognitive difficulty: 5.5% Ambulatory difficulty: 7.1%	**Medical Condition(s):** *Disability:* Individuals who cannot engage in substantial productive activity due to medically diagnosable physical or mental impairment which is expected to lead to death or last for over twelve months *Hearing difficulty:* ND *Vision difficulty:* ND	**Severe COVID-19:** **Estimates from Bivariate regression analysis controlled for median income, state, and total population* ***Estimates from Bivariate regression analysis controlled for median income and state* *Mortality:* Disability:

Study Objective: To determine the association between county-level non-institutionalized disability rates, socioeconomic factors, and SARS-CoV-2 infection and death. **IVA Score:** 19 (Moderate)	provided by Google, and publicly available data from US Census Bureau data estimated for 2018 for demographic data per county as of April 5th, 2020 **Location:** California, Michigan, New York, New Jersey, Louisiana, Pennsylvania, and Massachusetts, USA **Study Dates:** NR - April 9, 2020 **Inclusion Criteria:** Counties with the highest number of SARS-CoV-2 infections in the US as of April 9th, 2020. **Exclusion Criteria:** NR	Self-care difficulty: 2.8% Independent living difficulty: 6.1% **Control/Comparison Group, n/N (%):** Low death rate: states with SARS-CoV-2 death rate <3.4 Disability: 12.9% Hearing difficulty: 3.5% Vision difficulty: 2.1% Cognitive difficulty: 5.2% Ambulatory difficulty: 6.6% Self-care difficulty: 2.7% Independent living difficulty: 5.9%	*Cognitive difficulty:* ND *Ambulatory difficulty:* ND *Self-care difficulty:* ND *Independent living difficulty:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* County-level SARS-CoV-2 mortality rates for the non-institutionalized disabled population *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	• *Est: 0.148 (95% CI: -0.045-0.34), p = 0.1312 • **Est: 0.094 (95% CI: -0.101-0.288), p = 0.3426 Hearing difficulty: • *Est: 0.09 (95% CI: -0.08-0.259), p = 0.2974 • **Est: 0.088 (95% CI: -0.053-0.228), p = 0.2201 Vision difficulty: • *Est: 0.074 (95% CI: -0.088-0.236), p = 0.3700 • **Est: 0.067 (95% CI: -0.089-0.223), p = 0.3960 Cognitive difficulty: • *Est: 0.104 (95% CI: -0.083-0.292), p = 0.2726 • **Est: 0.09 (95% CI: -0.083-0.264), p = 0.3056 Ambulatory difficulty: • *Est: 0.117 (95% CI: -0.071-0.305), p = 0.2213 • **Est: 0.119 (95% CI: -0.059-0.297), p = 0.1871 Self-care difficulty: • *Est: 0.077 (95% CI: -0.078-0.232), p = 0.3267 • **Est: 0.061 (95% CI: -0.087-0.209), p = 0.4513 Independent living difficulty: • *Est: 0.162 (95% CI: 0-0.324), p = 0.05039 • **Est: 0.149 (95% CI: -0.006-0.304), p = 0.06023 Counties with a higher population of independent living difficulty showed a higher rate of SARS-CoV-2 related mortality when controlling for median income and state. The same trend is observed when controlling for the total population, median income, and state. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality:* Disability Male: • *Est: 0.098 (95% CI: -0.116-0.312), p = 0.3660 • **Est: 0.137 (95% CI: -0.031-0.306), p = 0.1093 Disability Female: • *Est: 0.159 (95% CI: -0.038-0.356), p = 0.1118 • **Est: 0.143 (95% CI: -0.035-0.321), p = 0.1144 Disability Black: • *Est: 0.053 (95% CI: -0.154-0.259), p = 0.6156 • **Est: 0.095 (95% CI: -0.04-0.231), p = 0.1671 Disability Asian: • *Est: 0.111 (95% CI: -0.033-0.255), p = 0.1296

				• **Est: -0.07 (95% CI: -0.212-0.072), p = 0.3302 Disability White: • *Est: -0.06 (95% CI: -0.21-0.091), p = 0.4321 • **Est: 0.189 (95% CI: 0.012-0.366), p = 0.03672 Disability Hispanic: • *Est: 0.208 (95% CI: 0.012-0.405), p = 0.03772 • **Est: -0.03 (95% CI: -0.187-0.126), p = 0.7022 Disability 5 to 17 years old: • *Est: 0.008 (95% CI: -0.13-0.146), p = 0.9090 • **Est: -0.051 (95% CI: -0.202-0.1), p = 0.5054 Disability 18 to 34 years old: • *Est: -0.057 (95% CI: -0.217-0.103), p = 0.4829 • **Est: 0.166 (95% CI: 0.022-0.31), p = 0.02434 Disability 35 to 64 years old: • *Est: 0.195 (95% CI: 0.033-0.357), p = 0.01886 • **Est: 0.131 (95% CI: -0.063-0.325), p = 0.1838 Disability 65 to 74 years old: • *Est: 0.146 (95% CI: -0.064-0.356), p = 0.1722 • **Est: 0.067 (95% CI: -0.112-0.246), p = 0.4615 Disability 75 and over: • *Est: 0.075 (95% CI: -0.112-0.262), p = 0.4303 • **Est: -0.044 (95% CI: -0.191-0.102), p = 0.5510 Counties with a higher percentage of White disabled population and higher disability in the age group 18-34 years showed a higher rate of SARS-CoV-2 related mortality when controlling for median income and state. The same trend is observed when controlling for the total population, median income, and state. **Long-term Sequelae:** NR
Author: Onteddu[36] **Publication:** 2020 **Data Extractor:** MW **Reviewer:** MC/DOS **Study Design:** Cohort **Study Objective:** To evaluate if patients with neurological disorders are more vulnerable to COVID-19.	**Population:** N =26,332 COVID-19+ **Setting:** NR **Data Source:** TriNetX, electronical medical records **Location:** Arkansas, USA **Study Dates:** Up to July 4, 2020	**Medical Condition, n/N (%):** Movement disorder: 1703/13,116 (13%) Neuromuscular disorder: 3627/13,116 (27.6%) **Control/Comparison Group, n/N (%):** No neurological disorder: 13,166/13,166 (100%)	**Medical Condition(s):** *Movement disorder:* G20-26 *Neuromuscular:* G12.2, G60-65, G70-73, M60.8 and M60.9 **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* was obtained using deceased code *ICU admission:* was obtained using critical care services codes	**Severe COVID-19:** *OR: Odds Ratio* *Mortality:* • Movement disorder: 1.02 (95% CI: 0.81–1.29) • Neuromuscular disorder: 0.86 (95% CI: 0.71–1.05) *ICU admission:* • Movement disorder: 0.99 (95% CI: 0.72–1.35) • Neuromuscular disorder: 1.1 (95% CI: 0.91–1.33)

IVA **Score:** 23 (Moderate)	**Inclusion Criteria:** Population ≥ 18 years, any sex, and diagnostic ICD-10 Codes for prior neurological disorders with a matched control cohort, without a known neurological disorder, who were diagnosed with COVID-19 after January 20th, 2020, was used for comparisons. One-to-one propensity score matching was done for baseline characteristics and other comorbid conditions **Exclusion Criteria:** NR		*Intubation:* was obtained by using endotracheal insertion codes and invasive ventilation codes *Ventilation:* *Hospitalization:* was ascertained by using standard hospital admission codes, visit types, critical care service codes and consultation codes *Non-elective readmissions*: NR **Comments:** None	*Intubation:* • Movement disorder: 0.79 (95% CI: 0.51–1.16) • Neuromuscular disorder: 1.88 (95% CI: 1.49–2.37) *Hospitalization:* • Movement disorder: 1.09 (95% CI: 0.92–1.34) • Neuromuscular disorder: 1.24 (95% CI: 1.09–1.39) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Panagiotou[15] **Publication:** 2021 **Data Extractor:** MM **Reviewer:** MW/DOS **Study Design:** Cohort **Study Objective:** To identify risk factors for 30-day all-cause mortality among US nursing home residents with COVID-19. **IVA Score:** 25 (Moderate)	**Population:** N=5,256 **Setting:** 351 nursing homes **Data Source:** Electronic medical records, daily nursing home infection logs, and Minimum Data Set (MDS) resident assessments **Location:** US **Study Dates:** March 16 – September 15, 2020 **Inclusion Criteria:** All residents with PCR–confirmed SARS-CoV-2 infection and also had COVID-19–related symptoms starting in a time window ranging	**Medical Condition, n/N (%):** Cognitive impairment: 3,189/5,256 (60.7%) Activities of daily living impairment: 3,909/5,256 (74.4%) **Control/Comparison Group, n/N (%):** No cognitive impairment: 2,023/5,256 (38.5%) No activities of daily living impairment: 1,347/5,256 (26.0%)	**Medical Condition(s):** *Cognitive impairment:* Assessed with the Cognitive Function Scale, a hierarchical 4-level scale derived from a resident's Brief Interview for Mental Status assessment and/or Cognitive Performance Scale (CPS) and integrates findings into one score; CPS is calculated using an algorithm assigning residents a score between 0-6 based on daily decision-making, eating self-performance, ability to make self-understood, short-term memory, and whether the resident is comatose *Activities of daily living (ADL) impairment:* Physical function was measured with a validated 28-point composite score of ADL, including dressing, personal hygiene, toilet use, loco-motion on unit, transfer, bed mobility, and eating; ADL scores range from 0 to 28 and describes a patient's range from substantial to very severe	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression; model included age, sex, race/ethnicity, comorbidities, symptoms, ADL score, and cognitive function* *OR: Univariable (Univariate) Logistic Regression* *Mortality, n/N (%):* Cognitive impairment: 836/3189 (26%) No cognitive impairment: 275/2023 (14%) ADL impairment: 913/3,909 (23%) No ADL impairment: 209/1,327 (16%) **Severity of Condition:** *Mortality, n/N (%):* Mild cognitive impairment: • aOR: 1.11 (95% CI: 0.89-1.39) • OR: 1.28 (95% CI: 1.04-1.59) • Mild: 202/1,179 (17%) • No cognitive impairment: 275/2,023 (14%) Moderate cognitive impairment: • aOR: 2.09 (95% CI: 1.68-2.59)

	from 5 days prior to and up to 14 days after testing .Resident was classified as symptomatic if a change in condition was documented indicating any of the following symptoms: cough, fever (temperature ≥37.8°C), hypoxia (oxygen saturation <92% or a 3% decline from baseline), shortness of breath, chest congestion, nausea, vomiting, diarrhea, confusion, malaise, tachycardia, anosmia, rhinorrhea, sore throat, or nasal congestion. **Exclusion Criteria:** NR		impairment, with higher values indicating higher ADL impairment **Severity Measure(s):** *Severe cognitive impairment:* Individuals not able to complete the BIMS by themselves or have a CPS score of 5 or 6 *Moderate cognitive impairment:* BIMS score of ≤7 or a CPS score of 3-4 *Mild cognitive impairment:* BIMS score of 8-12 or a CPS score of ≤2 *No cognitive impairment:* Individuals able to complete the BIMS and scored between 13 and 15 *Activities of daily living impairment:* ADL 0-13: no ADL impairment ADL 14-18: NR ADL 19-20: NR ADL 21-28: most severe dependence for activities of daily living **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Death due to any cause within 30 days of a resident's first positive SARS-CoV-2 PCR test result *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	• OR: 2.61 (95% CI: 2.41-3.19) • Moderate: 469/1,547 (30.3%) • No cognitive impairment: 275/2,023 (14%) Severe cognitive impairment: • aOR: 2.79 (95% CI: 2.14-3.66) • OR: 3.36 (95% CI: 2.58-4.39) • Severe: 165/463 (36%) • No cognitive impairment: 275/2,023 (14%) ADL impairment score 21-28: • aOR: 1.64 (95% CI: 1.30-2.08) • OR: 2.15 (95% CI: 1.71-2.70) • ADL score 21-28: 404/1,410 (29%) • ADL score 0-13: 209/1,327 (16%) ADL impairment score 19-20: • aOR: 1.49 (95% CI: 1.18-1.88) • OR: 1.77 (95% CI: 1.41-2.23) • ADL score 19-20: 288/1,179 (24%) • ADL score 0-13: 209/1,327 (16%) ADL impairment score 14-18: • aOR: 0.98 (95% CI: 0.77-1.25) • OR: 1.05 (95% CI: 0.84-1.32) • ADL score 14-18: 221/1,320 (17%) • ADL score 0-13: 209/1,327 (16%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Perera[54] **Publication:** 2020 **Data Extractor:** TR **Reviewer:** MC **Study Design:** Observational descriptive	**Population:** N=66 **Setting:** NR **Data Source:** Various networks **Location:** England and Ireland	**Medical Condition, n/N (%):** Down syndrome: 20/66 (30%) Autism: 6/66 (9%) Attention-deficit hyperactivity disorder (ADHD): 1/66 (2%) **Control/Comparison Group, n/N (%):** No down syndrome: 46/66 (70%) No autism: 58/66 (91%) No ADHD: 65/66 (98%)	**Medical Condition(s):** *Down syndrome:* ND *Autism:* ND *ADHD:* ND **Severity Measure(s):** Each of the three subgroups of ICD-10 moderate (F71), severe (F72) and profound intellectual disability (F73) have a low prevalence (9% moderate intellectual disability, 4%	**Severe COVID-19:** *Mortality, n/N (%):* Down syndrome: 20/20 (100%) No down syndrome: 46/66 (69.7%) Autism: 6/6 (100%) No autism: 58/64 (91%) ADHD: 1/1 (100%) No ADHD: 65/66 (98.5%)

Study Objective: To identify comorbidities, demographic, and clinical factors of those individuals with intellectual disability who have died from COVID-19. **IVA Score:** 19 (Moderate)	**Study Dates:** March 1-June 19, 2020 **Inclusion Criteria:** People with intellectual disability who died from COVID-19. **Exclusion Criteria:** NR		severe intellectual disability, and about 2% profound) and together they would comprise 15% of the total intellectual disability population **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Deaths in intellectual disability *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** All patients in this cohort died.	**Severity of Condition:** *Mild intellectual disability, n/N (%)*: Down syndrome: • 6/22 (27%) Autism: • 1/22 (5%), p = 0.65 ADHD: • 0/22 (0%), p = 1.00 *Moderate to profound intellectual disability, n/N (%)*: Down syndrome: • 14/44 (32%) Autism: • 5/44 (12%), p = 0.65 ADHD: • 1/44 (2%), p = 1.00 **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality, n/N (%):* Sex: • Men: 39/66 (59.1%) • Women: 27/66 (40.9%) **Long-term Sequelae:** NR
Author: Perez-Gaxiola[71] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** JKK **Study design:** Case series **Study Objective:** To describe the clinical and epidemiological characteristics of the confirmed COVID-19 pediatric cases and to describe the characteristics of the	**Population:** N= 51 **Setting:** Hospital **Location:** Mexico **Study dates:** March 1 - May 31, 2020 **Inclusion criteria:** Pediatric patients, under 18 years old with SARS-CoV-2 infection. **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Down syndrome: 1/51 (2.0%) Congenital hydrocephalus: 1/51 (2.0%)	**Medical Condition(s):** *Down syndrome:* ND *Congenital hydrocephalus:* ND **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality:* 1/2 *ICU admission:* 1/2 *Hospitalization:* 2/2 *General Progression* • *Case 1:* A 4-month-old male with Down syndrome was admitted to the hospital and required treatment at the intensive care unit and eventually died. • *Case 2:* A female infant with congenital hydrocephalus was admitted to the hospital and was discharged for improvement. **Severity of Condition:** NR **Duration of Condition:** NR

patients admitted to the study Hospital. **IVA Score:** Internal validity was not conducted for case reports/case series.				**Comorbid Conditions/ History of Disease:** • Case 1: Ventricular septal defect and hypothyroidism • Case 2: None **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: Not applicable for this study type
Author: Plotnikov[26] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** MM/DOS **Study Design:** Cohort **Study Objective:** To compare demographic, clinical and laboratory characteristics, and short-term mortality among patients hospitalized for COVID-19, grouped according to age 65–79 and ≥ 80 years, with and without severe functional dependency. **IVA Score:** 24 (Moderate)	**Population:** N=186 **Setting:** COVID-19 facility in a tertiary university hospital **Data Source:** Electronic medical records **Location:** Israel **Study Dates:** March–August 2020 **Inclusion Criteria:** Patients hospitalized with symptomatic COVID-19 aged ≥ 65 years were included. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Severe functional dependency: 89/186 (47.8%) **Control/Comparison Group, n/N (%):** No severe functional dependency: 97/186 (52.2%)	**Medical Condition(s):** *Severe functional dependency*: Evaluated by the Katz Index of Independence in Activities of Daily Living (ADL) such as bathing, dressing, toileting, transfer, continence and feeding, and were defined according to the respective ADL scores 0-3 and 4-6 **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* composite of all-cause death during the current hospitalization *ICU admission:* ND *Intubation:* NR *Ventilation:* mechanical ventilation *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** The numbers for mortality in patients with severe functional dependency are inconsistent between tables 1 and 2.	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression; included model variables: patient sex, comorbidities (hypertension, diabetes mellitus, cerebrovascular disease, renal failure, heart failure, obesity, coronary artery disease, pressure sores, chronic lung disease, malignant disorders, and pneumonia), serum albumin and C-reactive protein (CRP) levels, and nursing-home residence* *Mortality, n/N (%):* Severe functional dependency: • aOR: 2.51 (95% CI: 1.02-6.15), p = 0.044 • Non-survivors: 21/43 (48.8%) • Survivors: 33/143 (23.1) • p<0.001 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality, n/N (%):* Age 65-79 years with severe functional dependency: • aOR: 1.46 (95% CI: 0.38−5.59), p = 0.58 • Age 65-79 with severe functional dependency: 6/32 (18.3%) • Age 65-79 without severe functional dependency: 6/69 (8.7%) Age ≥80 years with severe functional dependency: • aOR: 10.42 (95% CI: 3.27−33.24), p<0.001 • Age ≥80 with severe functional dependency: 26/57 (45.6%)

				• Age 65-79 without severe functional dependency: 6/69 (8.7%) Age ≥80 years without severe functional dependency: • aOR: 2.63 (95% CI: 0.60−11.42), p = 0.20 • Age ≥80 without severe functional dependency: 5/28 (17.9%) • Age 65-79 without severe functional dependency: 6/69 (8.7%) *ICU admission, n/N (%):* Age: • Age 65-79 years with severe functional dependency: 10/32 (31.3%) • Age 65-79 years without severe functional dependency: 8/69 (11.6%) • Age ≥80 years with severe functional dependency: 12/57 (21.1%) • Age ≥80 years without severe functional dependency: 4/28 (14.3%) • p = 0.10 *Mechanical ventilation, n/N (%):* Age: • Age 65-79 years with severe functional dependency: 6/32 (18.8%) • Age 65-79 years without severe functional dependency: 4/69 (5.8%) • Age ≥80 years with severe functional dependency: 8/57 (14.0%) • Age ≥80 years without severe functional dependency: 4/28 (14.3%) • p = 0.23 **Long-term Sequelae:** NR
Author: Rass[56] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** MM/DOS **Study Design:** Prospective cohort	**Population:** N=135 **Setting:** Three participating clinical trial sites **Data Source:** NA **Location:** Austria	**Medical Condition, n/N (%):** Traumatic brain injury: 3/135 (2.2%) Perinatal spastic hemiparesis: 1/135 (0.7%) Neuromuscular disease: 1/135 (0.7%) **Control/Comparison Group, n/N (%):** No traumatic brain injury: 132/135 (97.7%)	**Medical Condition(s):** *Traumatic brain injury:* ND *Perinatal spastic hemiparesis:* ND *Neuromuscular disease:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:**	**Severe COVID-19:** *ICU admission, n/N (%):* • Traumatic brain injury: 0/3 (0.0%) • No traumatic brain injury: 31/132 (23.5%) • Perinatal spastic hemiparesis: 0/1 (0.0%) • No perinatal spastic hemiparesis: 31/134 (23.1%)

Study Objective: To assess neurological manifestations and health-related quality of life (QoL) 3 months after COVID-19. **IVA Score:** Internal validity was not conducted for studies with less than 10 people with traumatic brain injury, perinatal spastic hemiparesis, and neuromuscular disease.	**Study Dates:** April – September 2020 **Inclusion Criteria:** Patients age ≥18 years with confirmed SARS-CoV-2 infection, and either hospitalization or outpatient management. Diagnosis of COVID-19 was based on a typical clinical presentation with a positive RT-PCR test from a nasopharyngeal or oropharyngeal swab. **Exclusion Criteria:** Patients who died during the acute phase.	No perinatal spastic hemiparesis: 134/135 (99.3%) No neuromuscular disease: 134/135 (99.3%)	*Mortality:* NR *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	• Neuromuscular disease: 1/1 (100.0%) • No neuromuscular disease: 30/134 (22.4%) *Hospitalization, n/N (%):* • Traumatic brain injury: 2/3 (66.6%) • No traumatic brain injury: 70/132 (53%) • Perinatal spastic hemiparesis: 1/1 (100.0%) • No perinatal spastic hemiparesis: 71/134 (53.0%) • Neuromuscular disease: 1/1 (100.0%) • No neuromuscular disease: 71/134 (53.0%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Rebora[14] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** TR/CS **Study Design:** Cohort **Study Objective:** To report the prevalence of delirium on admission to the units, identify the factors associated with delirium occurrence, and evaluate the association between delirium and in-hospital mortality.	**Population:** N =516 **Setting:** One tertiary hospital, two private hospitals, and one rehabilitation hospital **Data Source:** Electronic database **Location:** Italy **Study Dates:** February 22 – June 16, 2020 **Inclusion Criteria:** Consecutive geriatric patients admitted between February 22, 2020 and May 17, 2020 with	**Medical Condition, n/N (%):** Functional disability: 171/516 (33.1%) **Control/Comparison Group, n/N (%):** No functional disability: 345/516 (66.9%)	**Medical Condition(s):** *Functional disability:* The presence of a dependence in bathing or dressing or a Barthel Index score of 90 or more/100 one month before hospitalization **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* All-cause in-hospital mortality *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR	**Severe COVID-19:** *aHR: Adjusted Hazard Ratio, multivariable Cox regression model adjusted for sex, age, functional disability, dementia, number of chronic diseases, use of CPAP, nutritional status, chest X-ray or CT findings, and serum CRP* *Mortality:* Functional disability: • aHR: 1.32 (95% CI: 0.89-1.96), p = 0.167 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

IVA Score: 24 (Moderate)	positive polymerase chain reaction nasopharyngeal swab tests for SARS-CoV-2. **Exclusion Criteria:** Patients aged less than 65 years and/or were initially admitted to an intensive care unit (ICU).		**Comments:** None	
Author: Rivera-Izquierdo[27] **Publication:** 2020 **Data Extractor:** MM **Reviewer:** DOS **Study Design:** Retrospective cohort **Study Objective:** To identify and quantify the associations between baseline characteristics on hospital admission in patients with COVID-19 infection and mortality at a tertiary hospital. **IVA Score:** 24 (Moderate)	**Population:** N=238 **Setting:** Hospital **Data Source:** Electronic medical records **Location:** Spain **Study Dates:** March 16 – April 10, 2020 **Inclusion Criteria:** Patients admitted for COVID-19 who tested positive via PCR and either died or were discharged during study dates. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Dependence for basic activities of daily living (BADL): 47/238 (19.8%) **Control/Comparison Group, n/N (%):** No dependence for BADL: 191/238 (80.2%)	**Medical Condition(s):** *Dependence for BADL:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aHR: Adjusted Hazard Ratio; Cox proportional hazards ratio model included age, BADL dependence, diabetes mellitus, ageusia, $SatO_2/FiO_2$, and interstitial opacities* *Mortality, n/N (%):* • aHR: 2.51 (95% CI: 1.38–3.94) • Dependence for BADL: 37/47 = (78.7%) • No dependence for BADL: 24/191 = (12.6%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Rousseau[51] **Publication:** 2021 **Data Extractor:** MM **Reviewer:** CS	**Population:** N=98 **Setting:** Specialized institutions, rehabilitation centers, home, and pediatric/neurologic university hospitals	**Medical Condition, n/N (%):** Polyhandicap: 98/98 (100%) **Control/Comparison Group, n/N (%):** NA	**Medical Condition(s):** Polyhandicap: defined by the combination of motor deficiency (quadriplegia, hemiparesis as a predominant hemibody motor impairment, diplegia, extrapyramidal syndrome, cerebellar syndrome, and/or neuromuscular problems) and	**Severe COVID-19:** *Mortality, n/N (%):* • Death: 4/98 (4.1%) • Survive: 94/98 (95.9%) *ICU admission, n/N (%):* • ICU Admission: 4/98 (4.1%)

Study Design: Cohort **Study Objective:** To describe the characteristics of the COVID-19 infection among individuals with polyhandicap. **IVA Score:** 20 (Moderate)	**Data Source:** Practitioner questionnaire **Location:** France **Study Dates:** April 1-July 1, 2020 **Inclusion Criteria:** Polyhandicapped individuals were included if they tested COVID-19 positive by RT-PCR or if the patient had compatible symptoms for COVID-19 and lived in an institution where at least 2 patients had COVID-19 infection confirmed by laboratory tests, or if a patient with compatible symptoms for COVID-19 lived with relatives who had a diagnosis of laboratory confirmed COVID-19. **Exclusion Criteria:** NR		severe/profound mental impairment (intelligence quotient < 40; for patients older than 5 years: IQ= developmental age below 2 years old; for children 3–5 years old: IQ= developmental quotient < 40% or not assessable) associated with everyday life dependence (Functional Independence Measure < 55) and restricted mobility (Gross Motor Function Scale [GMFCS and GMFCS-ER], III, IV and V) with age at onset of cerebral lesion below 6 years **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* those admitted to the ICU and those where admission was required but patient denied *Intubation:* NR *Ventilation:* non-invasive mechanical ventilation *Hospitalization:* those admitted to the hospital and those where hospitalization was required by patient denied *Non-elective readmissions*: NR **Comments:** None	• ICU admission required but declined: 1/98 (1.0%) • No ICU Admission: 93/98 (94.9%) *Ventilation, n/N (%):* • Ventilation: 2/98 (2.0%) • No ventilation: 96/98 (98.0%) *Hospitalization, n/N (%):* • Hospitalized: 16/98 (16.3%) • Hospitalization required but declined: 2/98 (2.0%) • Not hospitalized: 80/98 (81.6%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality, n/N (%)* Sex: • Females died: 1/48 (2.1%) • Males died: 3/47 (6.4%) • p = NR Age: • Children Died: 0/18 (0%) • Adults Died: 4/80 (5.0%) • p = NR • <50 years old: 2/61 (3.3%) • >50 years old: 2/34 (5.9%) • p = NR *ICU admission required, n/N (%)* Sex: • Female ICU Admission: 2/48 (4.2%) • Male ICU Admission: 3/47 (6.4%) • p = 1.0 Age: • Children ICU Admission: 2/18 (11.1%) • Adults ICU Admission: 3/80 (3.8%) • p = 0.5

				• <50 years old: 4/61 (6.6%) • >50 years old: 1/34 (2.9%) • p = 0.6 *Hospitalization, n/N (%)* Sex: • Females Hospitalized: 8/48 (16.7%) • Males hospitalized: 6/47 (12.8%) • p = 0.6 Age: • Children Hospitalized: 2/18 (11.1%) • Adults hospitalized: 14/80 (17.5%) • p = 0.7 • <50 years old: 11/61 (18.0%) • >50 years old: 5/34 (14.7%) • p = 0.7 **Long-term Sequelae:** NR
Author: Sahraian[50] **Publication:** 2020 **Data Extractor:** MW **Reviewer:** MM **Study Design:** Cohort **Study Objective:** To investigate the prevalence of COVID-19 among patients with Neuromyelitis Optica Spectrum Disorder (NMOSD), who were referred to NMOSD Clinic at the study hospital. **IVA Score:** Internal validity was not conducted for studies with less than 10 people with NMOSD.	**Population:** N=130 N=5 COVID-19+ **Setting:** Hospital **Data Source:** Telephone calls **Location:** Iran **Study Dates:** May 2 – May 9, 2020 **Inclusion Criteria:** Patients with NMOSD, who were referred to the NMOSD Clinic at the study hospital. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** NMOSD: 5/5 (100%) **Control/Comparison Group, n/N (%):** NA	**Medical Condition(s):** *NMOSD:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Hospitalization:* • Hospitalized: 3/5 (60.0%) Three patients with NMOSD and COVID-19 required hospitalization. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Author: Santos[21] **Publication:** 2020 **Data Extractor:** MW **Reviewer:** CS **Study Design:** Retrospective cohort **Study Objective:** To analyze the survival of patients admitted to Brazilian hospitals due to the COVID-19 and estimate prognostic factors. **IVA Score:** 23 (Moderate)	**Population:** N =46,285 **Setting:** Hospitals **Data Source:** Public national epidemiological surveillance system **Location:** Brazil **Study Dates:** February 20 – June 2, 2020 **Inclusion Criteria:** All hospitalized patients and those confirmed with COVID-19 through the reverse transcription polymerase chain reaction (RT-PCR) exam were included in the study. **Exclusion Criteria:** Records of patients with missing hospitalization dates or inconsistencies in their diagnostic record and patients who were still hospitalized at the end of the study period were excluded from the study.	**Medical Condition, n/N (%):** Down syndrome: 200/46,285 (0.4%) **Control/Comparison Group, n/N (%):** No Down syndrome: 25,911/46,285 (56.0%)	**Medical Condition(s):** *Down syndrome:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *HR: Hazard Ratio* *Mortality, n/N (%):* Down syndrome: • HR: 1.51 (95% CI: 1.2-1.9), p<0.001 • Down syndrome: 73/200 (36.5%) • No down syndrome: 8,512/25,911 (32.9%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Shahbaznejad [23] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** CS **Study Design:** Cohort	**Population:** N =100 **Setting:** Hospital **Data Source:** Hospital records, hospital information sy stem software, and telephone contact **Location:** Iran	**Medical Condition, n/N (%):** Down syndrome & cerebral palsy: 1/100 (1%) **Control/Comparison Group, n/N (%):** No Down syndrome & cerebral palsy: 99/100 (99%)	**Medical Condition(s):** *Down syndrome:* ND *Cerebral palsy:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Mortality during admission *ICU admission:* NR	**Severe COVID-19:** *Mortality, n/N (%):* • Down syndrome & cerebral palsy: 1/1 (100.0%) • No down syndrome & cerebral palsy: 3/99 (3.0%) *Intubation, n/N (%):* • Down syndrome & cerebral palsy: 1/1 (100.0%)

Study Objective: To describe the characteristics and clinical manifestations of children with COVID-19 admitted to hospitals of Iran, and to investigate pre valence of clinical symptoms, laboratory and radiological findings, and clinical outcomes as well as to identify factors associated with pediatric COVID-19 infection. **IVA Score:** Internal validity was not conducted for studies with less than 10 people with Down syndrome & cerebral palsy.	**Study Dates:** February 12 – July 28, 2020 **Inclusion Criteria:** Pedi atric patients 1 day to 18 years of age admitted to 1 of 21 hospitals of Northern Iran with SARS-CoV-2 confirmed by RT-PCR using a nasopharyngeal swab or positive serology or pediatric patients with suspected SARS-CoV-2 with clinical signs or symptoms, COVID-19 compatible chest CT, and clinical symptoms with known sick contact. **Exclusion Criteria:** Pati ents with duplicate admission, inadequate data, or misdiagnosis with COVID-19.		*Intubation:* Endotracheal intubation *Ventilation:* Non-invasive ventilation (mask, nasal cannula, and oxyhood) *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	• No down syndrome & cerebral palsy: 5/99 (5.1%) *Ventilation, n/N (%):* • Down syndrome & cerebral palsy: 1/1 (100%) • No down syndrome & cerebral palsy: 61/99 (61.6%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Sharrack[60] **Publication:** 2020 **Data Extractor:** JKK **Reviewer:** AH **Study design:** Case report **Study Objective:** To present a case demonstrating a rare complication of COVID-19 infection. **IVA Score:** Internal validity was not conducted for case reports/case series.	**Population:** N=1 **Setting:** Hospital **Location:** UK **Study dates:** NR **Inclusion criteria:** NR **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Retinitis pigmentosa: 1/1 (100%)	**Medical Condition(s):** *Retinitis pigmentosa:* ND **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Hospitalization:* yes *General Progression* • A 53-year-old Caucasian man presented with pleuritic chest pain, shortness of breath and fever; he was negative for SARS-CoV-2 and was discharged 4 days later on amoxicillin; patient represented to the emergency department 8 days later with worsening shortness of breath and fever; his chest radiograph showed COVID-19 pneumonia and he tested positive for COVID-19; imaging suggested pulmonary embol and unilateral AH; the patient was treated with intravenous heparin infusion for 5 days then switched to apixaban; patient was discharged two days after intravenous heparin was discontinued and made a full recovery.

				Severity of Condition: NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** • History of smoking **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: Not applicable for this study type
Author: Shekhar[73] **Publication:** 2020 **Data Extractor:** JKK **Reviewer:** AH **Study design:** Case series **Study Objective:** To study the central nervous system complications in patients with COVID-19 infection especially among Native American population in the current pandemic of severe acute respiratory syndrome virus (COVID-19). **IVA Score:** Internal validity was not conducted for case reports/case series.	**Population:** N=7 **Setting:** Hospital **Location:** New Mexico, US **Study dates:** February 1 - April 29, 2020 **Inclusion criteria:** Patients diagnosed with COVID-19 by RT-PCR from nasal swab with development of neurological complications (ischemic stroke intracerebral hemorrhage, sub-arachnoid hemorrhage, seizure, and encephalitis). **Exclusion criteria:** Patients with peripheral neurological symptoms such as nerve pain, tingling and/or minor CNS symptoms like headache, mild dizziness, altered mental status without focal neurological	**Medical Condition, n/N (%):** Hands and feet birth defect: 1/7 (14.3%) Traumatic brain injury: 1/7 (14.3%)	**Medical Condition(s):** *Hands and feet birth defect*: ND *Traumatic brain injury*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* ND *Intubation:* ND *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *ICU admission:* 2/2 *Intubation (or Invasive Ventilation):* 2/2 *Hospitalization:* 2/2 *General Progression* • *Case 1:* A 39-year-old Native American female presented with fever, cough, shortness of breath, chills, and fatigue; chest imagining found multifocal pneumonia and she was intubated; on day 5 of COVID symptom onset, she developed altered mental state and seizures; MRI revealed right cerebellar hemisphere infarct; she was treated with antiepileptic, anticoagulation, and high intensity statin; the patient was still admitted at the time of this report. • *Case 2:* A 53-year-old Native American male presented with fever; chest screening found bibasilar atelectasis and he was intubated; he developed altered mental state and status epilepticus on day 16 of COVID symptom onset; the patient was treated with antiepileptic and sedation; he was discharged after 6 days, 2 of which were spent in the ICU. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** • *Case 1:* history of diabetes • *Case 2:* history of alcohol use disorder in remission **Risk Markers:** NR **Long-term Sequelae:**

	signs, or metabolic encephalopathy.			Non-elective readmissions: Not applicable for this study type
Author: Showers[67] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** MM **Study design:** Case report **Study Objective:** To describe a patient with severe Covid-19-associated thrombosis in whom tissue analysis revealed direct viral-induced and complement-mediated mechanisms. **IVA Score:** Internal validity was not conducted for case reports/case series.	**Population:** N=1 **Setting:** Hospital **Location:** New York, USA **Study dates:** NR **Inclusion criteria:** NA **Exclusion criteria:** NA	**Medical Condition, n/N (%):** Charcot foot: 1/1 (100%)	**Medical Condition(s):** *Charcot foot:* ND **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *ICU admission:* Yes *Hospitalization:* Yes *General Progression* • *Case 1:* A 63-year-old woman with Charcot foot with chronic osteomyelitis requiring hallux amputation was admitted to the hospital following 2 days of progressive shortness of breath and lethargy. She was diagnosed with diabetic ketoacidosis and lactic acidosis and was admitted to an intensive care unit. She tested positive for SARS-CoV-2 infection by reverse transcriptase-polymerase chain reaction (RT-PCR) performed on a nasopharyngeal swab specimen. She underwent bilateral below-the-knee amputations (BKA) on hospital day 12. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** Patient also had history of type 2 diabetes mellitus (T2DM) complicated by peripheral neuropathy, hypertension, peripheral artery disease, and mild asthma **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: Not applicable for this study type
Author: Talavera[16] **Publication:** 2020 **Data Extractor:** MM **Reviewer:** DOS/JKK **Study Design:** Retrospective cohort **Study Objective:**	**Population:** N=576 **Setting:** Hospital **Data Source:** Electronic medical records **Location:** Spain **Study Dates:** March 8, 2020 – April 11, 2020	**Medical Condition, n/N:** Prior Modified Rankin Scale (mRS) ≥3: N=NR/576 **Control/Comparison Group, n/N:** Prior mRS <3: N=NR/576	**Medical Condition(s):** *mRS:* scale measuring the degree of disability/dependence prior to admission to hospital **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* in-hospital mortality of Covid-19 patients with anosmia *ICU admission:* ND	**Severe COVID-19:** *aOR1: Adjusted odds ratio; multivariate regression analysis included age, sex, hypertension, diabetes, cardiological disorders, pulmonary disorders, cancer, chronic neurological disorders, smoking, anosmia, prior mRS ≥3, and time from clinical onset to ED* *aOR2: Adjusted odds ratio; multivariate regression analysis included time from clinical onset to ED, mRS, age, sex, diabetes, and smoking* *OR: Odds ratio, univariate regression* *Mortality, n/N (%)*

To evaluate whether the presence of anosmia influences the prognosis of Covid-19 in hospitalized patients. **IVA Score:** 24 (Moderate)	**Inclusion Criteria:** All consecutive patients >18 years with confirmed case of COVID-19 that were hospitalized. COVID-19 was diagnosed with either a real-time RT-PCR assay, oropharyngeal-nasopharyngeal swab, sputum, lower respiratory tract sample, or serological tests with anti-SARS-CoV-2 IgM + IgA antibodies. **Exclusion Criteria:** Patients with no clinical records available or patients with hospitalization for a different serious condition prior to COVID-19.		*Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	Prior mRS ≥3: • aOR1: 3.595 (95% CI: 1.794-7.204), p<0.001 • OR: 11.371 (95% CI: 6.376-20.278), p<0.001 *ICU Admission, n/N (%)* Prior mRS ≥3: • aOR2: 0.072 (95% CI: 0.009-0.548), p = 0.011 • OR: 0.082 (95% CI: 0.011-0.600), p = 0.014 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Theophanous[70] **Publication:** 2021 **Data Extractor:** MC **Reviewer:** CS **Study design:** Case report **Study Objective:** To report on the association between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and Bell's palsy.	**Population:** N=1 **Setting:** Pediatric emergency room **Location:** NR **Study dates:** NR **Inclusion criteria:** NR **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Chromosome 17 deletion: 1/1 (100%) Chromosome 19 deletion: 1/1 (100%)	**Medical Condition(s):** *Chromosome 17 deletion*: ND *Chromosome 19 deletion*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality:* No *ICU admission:* No *Intubation (or Invasive Ventilation):* No *Ventilation (mechanical, or non-invasive ventilation):* No *Hospitalization:* Yes *General Progression* • *Case 1:* A 6-year-old boy presented to the emergency room with one day history of right sided facial droop due to Bell's palsy (HouseBrackmann grade: IV). The patient's nasopharyngeal swab sample tested positive for SARS-CoV-2 by RT-CR and was started on intravenous acyclovir every 8 hours. Once stable, the patient was discharged on a five-day course of prednisolone and acyclovir. At 3 weeks follow-up, the symptoms had improved. **Severity of Condition:** NR

IVA Score: Internal validity was not conducted for case reports/case series.				**Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** • History of prematurity (born at 30 weeks), submucosal cleft palate surgically repaired atrial and ventricular septal defects, agammaglobulinemia with hyper IgM, hypospadias, asthma, and moderate obstructive sleep apnea **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: Not applicable for this study type
Author: Ticinesi[28] **Publication:** 2021 **Data Extractor:** MM **Reviewer:** MW/DOS **Study Design:** Cohort **Study Objective:** To compare the clinical features and outcomes of patients admitted in different phases of the outbreak in a COVID-19 hospital hub, with particular focus on age, multimorbidity, and functional dependency and their association with hospital mortality. **IVA Score:** 24 (Moderate)	**Population:** N=1,264 **Setting:** Hospital **Data Source:** Clinical records **Location:** Italy **Study Dates:** February-June 2020 **Inclusion Criteria:** Patients age ≥18 years old with the presence of symptoms and high resolution chest tomography (HRCT) findings compatible with COVID-19 interstitial pneumonia. **Exclusion Criteria:** Patients who did not undergo chest HRCT on admission and patients lacking any clinical or radiological sign of interstitial pneumonia.	**Medical Condition, n/N (%):** Complete dependency in daily activities: 210/1,251 (16.8%) Partial dependency in daily activities: 257/1,251 (20.6%) **Control/Comparison Group, n/N (%):** Complete autonomy in daily activities: 784/1,251 (62.6%)	**Medical Condition(s):** NR **Severity Measure(s):** *Complete dependency in daily activities:* total dependency in performing daily activities as retrieved from the medical history, and considered as a proxy of disability *Partial Dependency in daily activities:* partial dependency in performing daily activities as retrieved from the medical history, and considered as a proxy of frailty *Complete autonomy in daily activities:* patients with complete autonomy in daily activities **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* Non-invasive *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression; included model variables: age, sex, period of admission* **Severity of Condition:** *Mortality, n/N (%):* Dependency in daily activities: • aOR for autonomy: 0.64 (95% CI: 0.42 - 0.98) • Complete dependency in daily activities: 90/210 (43%) • Partial dependency in daily activities: 87/257 (34%) • Complete autonomy in daily activities: 133/784 (17%) • p = 0.040 *ICU admission, n/N (%):* Dependency in daily activities: • aOR for autonomy: 41.6 (95% CI: 2.8 - 615) • Complete dependency in daily activities: 0/210 (0%) • Partial dependency in daily activities: 3/257 (1%) • Complete autonomy in daily activities: 55/784 (7%) • p = 0.007 *Non-invasive ventilation, n/N (%):*

				• aOR for autonomy: 13.50 (95% CI: 4.34 - 41.92) • Complete dependency in daily activities: 0/210 (0%) • Partial Dependency in daily activities: Ventilated: 13/257 (5.0%) • Complete autonomy in daily activities: 110/784 (14.0%) • p<0.001 **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Tse[78] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** MC/CS **Study Design:** Prospective cohort **Study Objective:** To characterize the incidence of presumed and confirmed COVID-19 illness, hospitalization, and death in congregate and non-congregate cohorts composed of more than 8,000 people served by a NYC not-for-profit behavioral health system. **IVA Score:** 17 (High)	**Population:** N =8,256 N=218 COVID-19 positive **Setting:** 29 congregate and non-congregate settings **Data Source:** NA **Location:** NY, USA **Study Dates:** March 9 - May 3, 2020 **Inclusion Criteria:** Total population of individuals served one citywide not-for-profit behavioral health agency. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Intellectual/developmental disabilities (IDD): NR **Control/Comparison Group, n/N (%):** NA	**Medical Condition(s):** *IDD:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality:* • IDD: 25% of death cases were found among the IDD congregate group (N=3) *Hospitalization:* • IDD: 42% of hospitalized cases were found among the IDD congregate group (N=5) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** Age: • People with intellectual/developmental disabilities and people age 45 or older were significantly more likely to be hospitalized or to have died **Long-term Sequelae:** NR

Author: Turk[6] **Publication:** 2020 **Data Extractor:** CS **Reviewer:** MC **Study Design:** Cohort study **Study Objective:** To compare COVID-19 trends among people with and without intellectual/developmental disabilities (IDD), overall and stratified by age. **IVA Score:** 19 (Moderate)	**Population:** N=30,282 **Setting:** 42 health care organizations representing hospitals, primary care, and specialty treatment providers designed to facilitate research related to COVID-19 **Data Source:** Global federated database of real-time electronic medical records; TriNetX COVID-19 Research Network **Location:** International **Study Dates:** January 20-May 14, 2020 **Inclusion Criteria:** EMR data on all COVID-19 patients included in the database during the study dates were included. COVID-19 patients were defined as those with either a COVID-19 diagnosis code (ICD-10 codes: B34.2, B97.29, J12.81, U07.1, U07.2) or a positive SARS-CoV-2 laboratory test result (LOINC codes: 94500-6, 94315-9, 94309-2, 94533-7, 94534-5, 94559-2). **Exclusion Criteria:** Patients with diagnosis codes of other specified viral infection (ICD-9 code: 097.89) or suspected exposure to other biologic agents (ICD-10 code: Z03.818) during the same	**Medical Condition, n/N (%):** Developmental disability: 474/30,282 (1.6%) • 33% had an intellectual disability, 56% had a pervasive and specific developmental disorder, 18% had cerebral palsy, and 21% had a chromosomal abnormality, including 5% with Down syndrome **Control/Comparison Group, n/N (%):** No developmental disability: 29,808/30,282 (98.4%)	**Medical Condition(s):** *Developmental disability:* intellectual disability (F70-79), pervasive and specific developmental disorder (F80-89), cerebral palsy (G80), and chromosomal abnormality (Q90-99), including Down syndrome (Q90) **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Deaths occurring within 30 days of the date of first COVID-19 documentation in the EMR were identified *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%):* Developmental disability: • Developmental disability: 24/474 (5.1%) • No developmental disability: 1614/29,808 (5.4%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** People with a positive diagnosis for COVID-19 and had an IDD diagnosis demonstrated higher rates for all pre-existing conditions (circulatory, endocrine, pulmonary) associated with COVID-19 disease severity and mortality across all age groups. **Risk Markers:** *Mortality, n/N (%):* Age: 0-17 years: • Developmental disability: 2/125 (1.6%) • No developmental disability: 1/791 (0.1%) 18-74 years: • Developmental disability: 14/311 (4.5%) • No developmental disability: 671/24,456 (2.7%) ≥75 years: • Developmental disability: 8/38 (21.1%) • No developmental disability: 942/4,561 (20.7%) **Long-term Sequelae:** NR

	timeframe were excluded.			
Author: Vrillon[44] **Year:** 2021 **Data Extractor:** MW **Reviewer:** MM **Study Design:** Prospective cohort **Study Objective:** To identify specific features and risk factors of death among patients with dementia and COVID-19. **IVA Score:** 22 (Moderate)	**Population:** N =125 **Setting:** Hospital **Data Source:** NA **Location:** France **Study Dates:** March 14 - May 7, 2020 **Inclusion Criteria:** Patients over 65 with dementia hospitalized for COVID-19 . **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Unspecified cognitive impairment: 75/125 (60%) **Control/Comparison Group, n/N (%):** No unspecified cognitive impairment: 50/125 (40%)	**Medical Condition(s):** *Unspecified cognitive impairment:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Death at 21 days *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%):* Unspecified cognitive impairment: • Died: 17/28 (60.7%) • Survived: 58/97 (59.8%) • p = 1.000 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Zettersten[37] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** CS **Study Design:** Retrospective cohort **Study Objective:** To analyze outcome beyond 90 days in ICU patients with COVID-19, with special focus on differences betwee n men and women. **IVA Score:** 24 (Moderate)	**Population:** N =2354 **Setting:** Hospital **Data Source:** National Swedish Intensive Care Registry (SIR) **Location:** Sweden **Study Dates:** March 6 - October 22, 2020 **Inclusion Criteria:** All patients ≥18 years of age with confirmed SARS-CoV-2 by polymerase chain reaction admitted to an ICU between March 6-June 30, 2020 in SIR were included. **Exclusion Criteria:** SARS-CoV-2-RNA	**Medical Condition, n/N (%):** Neuromuscular disease: 34/2354 (1.4%) **Control/Comparison Group, n/N (%):** No neuromuscular disease: 2320/2354 (98.6%)	**Medical Condition(s):** *Neuromuscular disease:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* 90-day all-cause mortality within 90 days from first admission to ICU *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aHR: Adjusted Hazard Ratio; Cox proportional hazards ratio* *HR: Hazard Ratio* *aOR: Adjusted odds ratio; multivariable logistic regression* *OR: Univariable (Univariate) Logistic Regression* *Crude mortality:* Neuromuscular disease: • aHR: 1.42 (95% CI: 0.81-2.48), p = 0.22 • HR: 1.59 (95% CI: 0.92 - 2.75), p = 0.098 *Mortality (90 days):* Neuromuscular disease: • aOR: 1.70 (95% CI: 0.74 - 3.80), p = 0.20 • OR: 1.69 (95% CI: 0.82 - 3.36), p = 0.14 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

	positive patients with reasons for admission other than COVID-19 and patients with temporary or invalid Swedish personal identification number were excluded.			
Author: Zhu[76] **Publication:** 2020 **Data Extractor:** MC **Reviewer:** CS **Study design:** Case report **Study Objective:** To prevent potential misinformation that could lead to unnecessary psychological burden upon medical service providers about a pituitary adenoma patient that was the first diagnosed COVID-19 case in a department where 14 medical staff were confirmed infected later. **IVA Score:** Internal validity was not conducted for case reports/case series.	**Population:** N=1 **Setting:** Hospital **Location:** China **Study dates:** December 2019-January 20, 2020 **Inclusion criteria:** NR **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Visual impairment, 1/1 (100%)	**Medical Condition(s):** Visual impairment: bitemporal hemianopsia caused by pituitary adenoma **Severity Measure(s):** NR **Clinical marker:** **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* non-invasive ventilation *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality: Yes* *ICU admission: No* *Intubation (or Invasive Ventilation): No* *Ventilation (mechanical, or non-invasive ventilation): Yes* *Hospitalization: Yes* *General Progression* • 70-yr-old male patient with a 2-mo history of visual impairment was admitted and then diagnosed with pituitary adenoma in late December 2019. Physical exam revealed bitemporal hemianopsia. Endonasal endoscopic pituitary adenoma resection was performed in a regular operating room on January 6th. Cerebrospinal fluid leakage occurred during resection process. Three days later he had a fever until January 14th and intravenous meropenem administration was initiated on January 10th for potential intracranial infection. On January 13th, he began to experience severe cough, fatigue, sputum production, shortness of breath, and low peripheral capillary oxygen saturation. He was put on non-invasive ventilation to maintain oxygen saturation. On January 18th an oral swab was taken and was positive for SARS-CoV-2 the next day. The patient was later transferred to a designated hospital and died of respiratory failure 4 weeks after surgery. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions/ History of Disease:** • *History of hypertension, diabetes, and heart attack* **Risk Markers:** NR

				Long-term Sequelae: Non-elective readmissions: Not applicable for this study type

B.3.c. Internal Validity Assessments of Extracted Studies

Table 71 Internal Validity Assessments of Extracted Studies reporting the Association between Underlying Disabilities and Severe COVID-19 Outcomes

	Author Publication	**Abedi 2021[11]**	**Alonso 2021[46]**	**An 2020[12]**	**Andres-Esteban 2021[30]**	**Arbel 2020[53]**	**Balangue 2021[24]**	**Bergman 2021[22]**	**Boaventura 2020[47]**
	Outcome(s)	Mortality	Mortality, ICU admission, Hospitalization	Mortality	Hospitalization	Mortality	Mortality	Mortality, ICU admission, hospitalization	Mortality, ICU admission
Domain	**Signaling question**								
Study Elements	Design appropriate to research question	1	1	1	1	1	1	1	1
	Well described population	1	1	1	1	1	1	1	0
	Well described setting	1	1	1	1	0	1	1	0
	Well described intervention/ exposure	1	1	1	1	0	1	1	1
	Well described control/ comparator	0	1	1	1	0	1	1	0
	Well described outcome	1	1	1	1	0	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1	1	1	0

Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1	1	1	1	1
	Attrition <10-15% of population	1	1	1	1	1	1	1	1
	Attrition appropriately analyzed	1	1	1	1	1	1	1	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	1	1	1	0	1	1	1
	Measure of outcome is valid	1	1	1	1	1	1	1	1
	Fidelity to intervention is measured	0	0	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0	0	0
	Prospective study	1	1	1	1	1	1	1	1
	Adequately powered to detect result	0	0	0	0	0	0	1	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	1	1	0	0	1	0
	Data collection methods appropriate	1	1	1	1	0	0	1	1

	Sufficient follow up to detect outcome	1	1	1	0	0	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	0	1	0	1	0	1	0
	Appropriate statistical analyses are conducted correctly	1	0	1	0	1	0	1	0
	Confidence interval is narrow	0	0	0	0	0	0	1	0
Confounding	Potential confounders identified	1	0	1	1	1	0	1	0
	Adjustment for confounders in study design phase	0	0	0	0	0	0	0	0
	Adjustment for confounders in data analysis phase	1	0	1	0	1	0	1	0
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1	1	0	1	0
SCORE	Threat to internal validity	23	20	24	20	16	17	26	14
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	High	High	Low	High

	Author Publication	**Bosworth 2021[17]**	**Burns 2020[38]**	**Chew 2021[35]**	**Chow 2020[7]**	**Clift 2020[18]**	**Clift 2021[19]**	**Cummins 2021[31]**	**Dobre 2021[1]**

	Outcome(s)	Mortality	Hospitalization, mortality	Mortality	ICU admission, hospitalization	Mortality, Hospitalization	Mortality, Hospitalization	Mortality, ICU Admission, Hospitalization	Mortality and ICU admission
Domain	**Signaling question**					data extracted from database			psychiatric hospital records
Study Elements	Design appropriate to research question	1	1	1	1	1	1	1	0
	Well described population	1	1	1	1	1	1	1	1
	Well described setting	1	1	1	1	1	1	1	1
	Well described intervention/ exposure	1	1	1	1	1	1	1	1
	Well described control/ comparator	1	1	1	1	1	1	1	1
	Well described outcome	1	1	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1	1	1	1	1

	Attrition <10-15% of population	1	1	1	1	1	1	1	1
	Attrition appropriately analyzed	1	1	1	1	1	1	1	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	0	1	1	1	1	1	1	1
	Measure of outcome is valid	1	1	1	1	1	1	1	1
	Fidelity to intervention is measured	0	0	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0	0	0
	Prospective study	1	1	1	1	1	1	1	1
	Adequately powered to detect result	1	0	0	0	1	1	0	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	1	1	1	1	1	1
	Data collection methods appropriate	0	1	1	1	1	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	0	1	1	1	1

	Appropriate statistical analyses are conducted correctly	1	1	1	0	1	1	1	1
	Confidence interval is narrow	1	0	0	0	0	0	0	0
Confounding	Potential confounders identified	1	1	1	0	1	1	1	1
	Adjustment for confounders in study design phase	0	0	0	0	0	0	0	0
	Adjustment for confounders in data analysis phase	1	0	1	0	1	1	1	0
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1	1	1	1	1
SCORE	Threat to internal validity	24	23	24	20	25	25	24	22
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate

	Author Publication	**Duarte-Salles 2020[41]**	**Emami 2021[20]**	**Falandry 2020[33]**	**Fierro 2021[64]**	**Garazzino 2021[42]**	**Garcia-Menaya 2020[43]**	**Gleason 2021[2]**	**Graff 2021[9]**
	Outcome(s)	Hospitalization	Hospitalization, intubation, mortality	Mortality	Mortality, hospitalization	ICU admission, ventilation, hospitalization	Mortality, ICU admission	Mortality, ICU Admission, Hospitalization	ICU admission, Hospitalization, re-admission

Domain	Signaling question	data extracted from multiple databases							
Study Elements	Design appropriate to research question	1	1	1	1	1	1	1	1
	Well described population	0	1	0	1	1	1	1	1
	Well described setting	1	1	1	1	1	1	1	1
	Well described intervention/ exposure	1	1	1	1	1	1	1	1
	Well described control/ comparator	1	1	0	0	1	1	1	1
	Well described outcome	1	1	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	0	1	1	1	1
	Attrition <10-15% of population	1	1	1	1	1	1	1	1
	Attrition appropriately analyzed	1	1	1	1	1	1	1	1

Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	1	0	1	1	1	1	1
	Measure of outcome is valid	1	1	1	1	1	1	1	1
	Fidelity to intervention is measured	0	0	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0	0	0
	Prospective study	1	1	1	1	1	1	1	1
	Adequately powered to detect result	1	0	0	0	0	0	0	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	0	1	1	1	1	1
	Data collection methods appropriate	1	1	0	1	1	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	0	1	1	0	1	1	1	1
	Appropriate statistical analyses are conducted correctly	0	1	1	0	1	1	1	1

	Confidence interval is narrow	0	0	0	0	0	0	0	0
Confounding	Potential confounders identified	0	1	0	1	1	1	1	1
	Adjustment for confounders in study design phase	0	1	0	0	0	0	0	0
	Adjustment for confounders in data analysis phase	0	1	0	0	1	0	1	1
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	0	1	1	1	1	1
SCORE	Threat to internal validity	20	25	16	19	24	23	24	24
	Low, Moderate, High	Moderate	Moderate	High	Moderate	Moderate	Moderate	Moderate	Moderate

	Author Publication	**Gude-Sampedro 2020[29]**	**Huls 2021[10]**	**Hwang 2020[34]**	**Janus 2021[57]**	**Joy 2020[32]**	**Karmakar 2021[13]**	**Landes 2020[3]**	**Landes 2021[4]**
	Outcome(s)	Mortality; ICU admission; hospitalization	Mortality	Mortality	Mortality	Mortality	Mortality	Mortality	Mortality
Domain	**Signaling question**	data extracted from electronic	survey data	electronic medical records	data from electronic health records	Data extracted from electronic	data extracted from data repository		Cohort

		medical records				health records			
Study Elements	Design appropriate to research question	1	1	1	1	1	1	1	1
	Well described population	1	0	1	1	1	1	1	1
	Well described setting	1	0	1	1	1	1	1	1
	Well described intervention/ exposure	1	1	1	1	1	1	1	1
	Well described control/ comparator	1	1	1	1	1	1	1	1
	Well described outcome	1	1	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1	1	1	1	0
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1	1	1	0	0
	Attrition <10-15% of population	1	1	1	1	1	1	0	0
	Attrition appropriately analyzed	1	1	1	1	1	1	0	0
Information Bias:	Measure of intervention/	1	1	1	1	1	1	1	1

Measurement and Misclassification	exposure is valid								
	Measure of outcome is valid	1	1	1	1	1	1	1	1
	Fidelity to intervention is measured	0	0	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0	0	0
	Prospective study	1	1	1	1	1	1	1	1
	Adequately powered to detect result	1	0	0	0	0	1	0	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	1	1	1	1	1	1
	Data collection methods appropriate	1	1	1	1	1	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	0	1	1	0	0
	Appropriate statistical analyses are conducted correctly	1	1	1	0	1	1	0	0
	Confidence interval is narrow	0	0	0	0	0	0	0	0

Confounding	Potential confounders identified	1	1	1	0	1	1	0	0
	Adjustment for confounders in study design phase	0	0	0	0	0	0	0	0
	Adjustment for confounders in data analysis phase	1	1	1	0	1	0	0	0
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1	1	1	1
Other Bias	No other sources of bias	1	0	1	1	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1	1	1	1	1
SCORE	Threat to internal validity	25	21	24	20	24	24	17	16
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	High	High

	Author Publication	**Laosa 2020[52]**	**Lega 2021[45]**	**Louapre 2020[49]**	**Macedo 2020[58]**	**Makary 2020[5]**	**Merzon 2021[55]**	**Mills 2020[8]**	**Nystad 2020[40]**
	Outcome(s)	Mortality	Mortality	ICU admission, Intubation, Ventilation, Hospitalization	Mortality	Mortality	Hospitalization	Hospitalization, Mortality	Hospitalization
Domain	**Signaling question**	clinical records	Surveillance system		data from national database		EMR & health insurance dataset	EMR	data extracted from national registry
Study Elements	Design appropriate to	1	1	1	1	1	1	1	1

	research question								
	Well described population	1	0	0	1	1	1	1	1
	Well described setting	1	1	1	1	1	0	1	1
	Well described intervention/ exposure	1	1	1	1	0	1	1	1
	Well described control/ comparator	1	1	0	1	0	1	1	1
	Well described outcome	1	1	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	0	1	1	1	1	1	1
	Attrition <10-15% of population	1	0	1	1	1	1	1	1
	Attrition appropriately analyzed	1	0	1	1	1	1	1	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	1	1	1	1	1	1	1
	Measure of outcome is valid	1	1	1	1	1	1	1	1

	Fidelity to intervention is measured	0	0	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0	0	0
	Prospective study	1	0	1	1	1	1	1	1
	Adequately powered to detect result	0	0	0	0	1	1	0	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	0	0	1	1	1	1	1
	Data collection methods appropriate	1	1	1	1	1	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	0	1	1	1	1	0
	Appropriate statistical analyses are conducted correctly	1	1	0	1	1	1	1	0
	Confidence interval is narrow	0	0	0	0	0	0	0	0
Confounding	Potential confounders identified	1	1	0	1	1	1	1	1
	Adjustment for confounders in	0	0	0	0	0	0	0	0

	study design phase								
	Adjustment for confounders in data analysis phase	1	1	0	0	1	1	0	0
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1	1	1	1	1
SCORE	Threat to internal validity	24	18	17	23	23	24	23	21
	Low, Moderate, High	Moderate	Moderate	High	Moderate	Moderate	Moderate	Moderate	Moderate

	Author Publication	**Olulana 2020[25]**	**Onteddu 2020[36]**	**Panagiotou[15]**	**Plotnikov 2021[26]**	**Rebora 2021[14]**	**Rivera-Izquierdo 2020[27]**	**Rousseau 2021[51]**	**Santos 2020[21]**
	Outcome(s)	Mortality	Mortality, ICU admission, Intubation, Hospitalization	Mortality	Mortality, ICU admission, Ventilation	Mortality	Hospitalized, mortality	Hospitalization, ICU admission, ventilation, mortality	Mortality
Domain	**Signaling question**	Data extracted from database	Data extracted from electronic records	electronic medical records, daily nursing home infection logs, and Minimum Data Set	data extracted from medical records	Electronic database	Medical records	data extracted from practitioner questionnaires	data extracted from database

				(MDS) assessments					
Study Elements	Design appropriate to research question	0	1	1	1	1	1	1	1
	Well described population	0	1	1	1	1	1	1	1
	Well described setting	0	1	1	1	1	1	1	1
	Well described intervention/ exposure	1	1	1	1	1	1	1	1
	Well described control/ comparator	0	1	1	1	1	1	0	1
	Well described outcome	1	1	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	0	1	1	1	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1	1	1	1	1
	Attrition <10-15% of population	1	1	1	1	1	1	1	1
	Attrition appropriately analyzed	1	1	1	1	1	1	1	1
Information Bias:	Measure of intervention/	1	1	1	1	1	1	1	0

Measurement and Misclassification	exposure is valid								
	Measure of outcome is valid	1	1	1	1	1	1	1	1
	Fidelity to intervention is measured	0	0	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0	0	0
	Prospective study	1	1	1	1	1	1	1	1
	Adequately powered to detect result	0	0	0	0	0	0	0	1
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	1	1	1	1	0	1
	Data collection methods appropriate	1	1	1	1	1	1	0	1
	Sufficient follow up to detect outcome	1	1	1	1	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	1	1	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1	1	1	1	1	1
	Confidence interval is narrow	0	0	1	0	0	0	0	0

Confounding	Potential confounders identified	1	0	1	1	1	1	1	1
	Adjustment for confounders in study design phase	0	1	0	0	0	0	0	0
	Adjustment for confounders in data analysis phase	1	0	1	1	1	1	0	0
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1	1	1	1	1
SCORE	Threat to internal validity	19	23	25	24	24	24	20	23
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate

	Author Publication	**Talavera 2020[16]**	**Ticinesi 2021[28]**	**Tse 2021[78]**	**Turk 2020[6]**	**Vrillon 2021[44]**	**Zettersten 2021[37]**
	Outcome(s)	Hospitalized, mortality	Hospitalization, Mortality	Mortality, Hospitalization	Mortality	Mortality	Mortality, ventilation, readmission
Domain	**Signaling question**	medical records	clinical records	data collected prospectively			data was extracted from national registry
Study Elements	Study Element: Design appropriate to research question	1	1	1	1	1	1

	Study Element: Well described population	1	1	0	1	1	1
	Well described setting	1	1	1	1	1	1
	Well described intervention/ exposure	1	1	0	1	0	1
	Well described control/ comparator	1	1	1	1	1	1
	Well described outcome	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1	1	1
	Attrition <10-15% of population	1	1	1	1	1	1
	Attrition appropriately analyzed	1	1	1	1	1	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	1	0	1	0	1
	Measure of outcome is valid	1	1	1	1	1	1

	Fidelity to intervention is measured	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0
	Prospective study	1	1	1	1	1	1
	Adequately powered to detect result	0	0	0	0	0	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	1	1	1	1
	Data collection methods appropriate	1	1	1	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	0	0	1	1
	Appropriate statistical analyses are conducted correctly	1	1	0	0	1	1
	Confidence interval is narrow	0	0	0	0	0	0
Confounding	Potential confounders identified	1	1	0	0	1	1
	Adjustment for confounders in	0	0	0	0	0	0

	study design phase						
	Adjustment for confounders in data analysis phase	1	1	0	0	1	1
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	0	1	1
SCORE	Threat to internal validity	24	24	17	19	22	24
	Low, Moderate, High	Moderate	Moderate	High	Moderate	Moderate	Moderate

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D. Abbreviations

Acronym	Description
*	Finds variant word endings (in a search of the literature)

95% CI	95% confidence interval
ADHD	attention-deficit/hyperactivity disorder
ADJ1	Word next to each other, in any order (in a search of the literature)
ADL	activities of daily living
ADOA	autosomal dominant optic atrophy
AHR	adjusted hazards ratio
AIS	American Spinal Injury Association impairment scale
ANOVA	analysis of variance
AOR	adjusted odds ratio
ARDS	acute respiratory distress syndrome
ARR	absolute risk reduction
BADL	basic activities of daily living
BIMS	brief interview for mental status
BKA	below-the-knee amputations
BMI	body mass index
CDC	centers for disease control and prevention
CI	Confidence interval
CM	clinical modification
COI	conflict of interest
COPD	chronic obstructive pulmonary disease
COVID-19	coronavirus SARS-CoV-2
CPAP	continuous positive airway pressure
CPS	cognitive performance scale
CRP	C-reactive protein
CT	computed tomography
ED	emergency department
EEG	electroencephalogram
EHR	electronic health records
EMR	electronic medical records
ER	emergency room
ERT	evidence review team
ESKD	end stage kidney disease
FXS	Fragile-X syndrome
GD	Gaucher disease
GMFCS	gross motor function scale

HR	hazard ratio
HRCT	high resolution chest tomography
IADL	instrumental activities of daily living
ICD	International Statistical Classification of Diseases and Related Health Problems
ICF	intermediate care facility
ICU	intensive care unit
IDD	intellectual and developmental disability
IRR	incidence ratio rate
IVA	internal validity assessment
KNHIS	Korean National Health Insurance Service
KPR	Norwegian Registry for primary health care
LHON	Leber's Hereditary Optic Neuropathy
LOINC	logical observation identifiers names and codes
LSD	lysosomal storage disorders
MDS	minimum data set
MELAS	mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes
MERFF	myoclonic epilepsy with ragged red fibers
MICU	medical intensive care unit
MIDD	maternal inherited diabetes and deafness
MOGAD	Myelin oligodendrocyte glycoprotein antibody disorders
MRI	magnetic resonance imaging
mRS	Modified Rankin Scale (for neurologic disability)
MS	multiple sclerosis
MSIS	Norwegian surveillance system for communicable diseases
n	number of individuals or observations
NA	not applicable
NARP	neuropathy, ataxia, and retinitis pigmentosa
ND	not defined
NMO	neuromyelitis optica
NMOSD	neuromyelitis optica spectrum disorders
NPR	Norwegian patient registry
NR	not reported
NY	New York
NYC	New York City
NYDA	New York disability advocates

NYU	New York University
OR	odds ratio
PCR	polymerase chain reaction
PECO	population, exposure, comparator, outcomes
PICU	pediatric intensive care unit
PMM	primary mitochondrial myopathy
POCUS	point-of-care ultrasound
RELACOEM	registro latino americano de COVID-19 y esclerosis multiple
RNA	ribonucleic acid
RR	risk ratio
RSC	research and surveillance center
RT	real time
SARS	severe acute respiratory syndrome
SCI/D	spinal cord injuries/disorders
SERGAS	Galician health service database
SESAB	Secretary of the State of Bahia
SIR	National Swedish intensive care registry
SLS	Senior-Loken syndrome
SOFA	sequential organ failure assessment
SVI	social vulnerability index
TAMOF	thrombocytopenia-associated multiple organ failure
TF	task force
UK	United Kingdom
US	US
USA	United State of America
VHA	Veterans' Health Administration
WHO	World Health Organization