Neurological diagnoses in hospitalized COVID-19 patients associated with adverse outcomes: a multinational cohort study

COVID Predictions: New Methods and Applications

S06

Meghan R. Hutch

Northwestern University

Twitter: @meghan_hutch

#IS23

Disclosure

I have no relevant relationships with commercial interests to disclose

Learning Objectives

After participating in this session the learner should be better able to:

- **Recognize** the utility of federated learning for COVID-19 research
- **Review** a random-effects meta-analysis approach for conducting studies within federated networks
- **Consider** the risk for poor health outcomes in hospitalized COVID-19 patients with concurrent neurological manifestations

4CE: Consortium for Clinical Characterization of COVID-19 by EHR

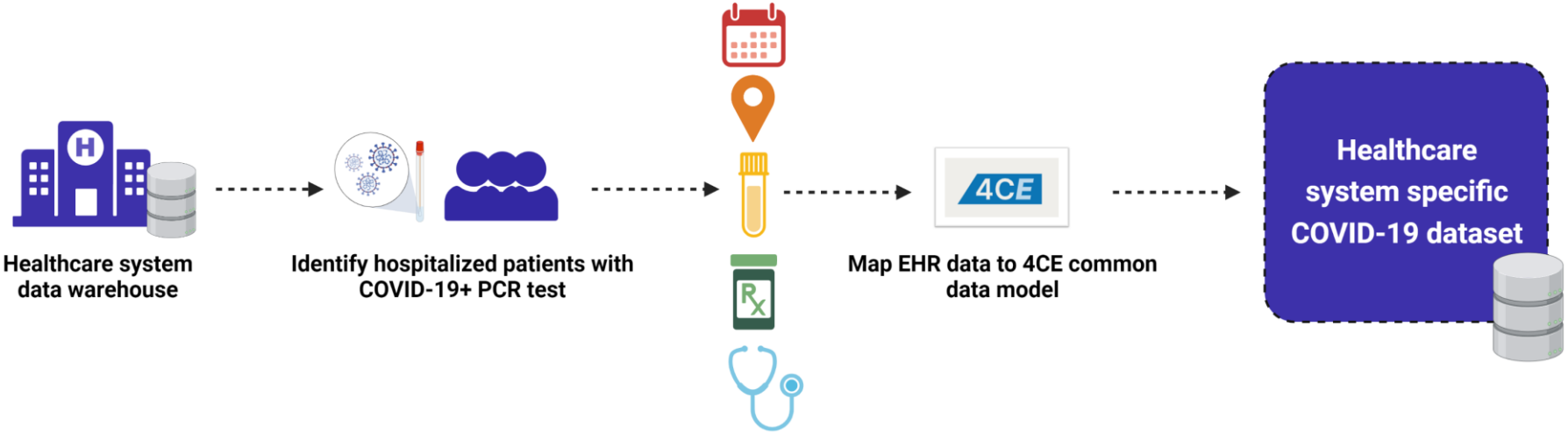
Rapidly leverage data from multiple healthcare systems

351 hospitals and **43 healthcare systems**

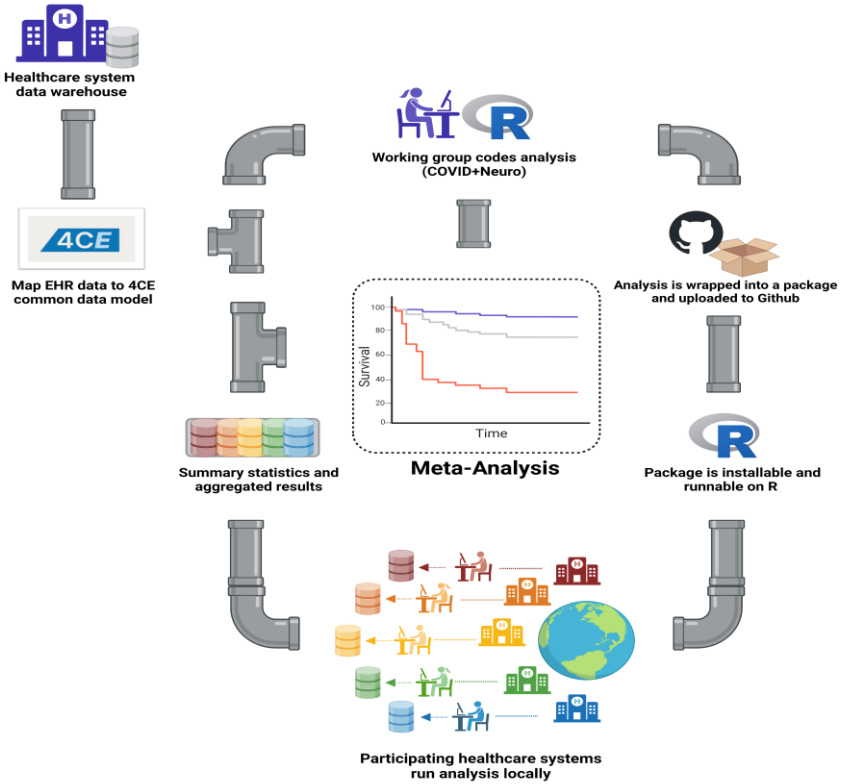
Participating healthcare systems map electronic health records (EHR) to a common data model

In the 4CE model, patient level data does not leave the respective healthcare system

Data is Mapped to the 4CE Common Data Model



Federated Learning Pipeline Facilitates Analysis



Benefits of a Federated Approach

- Better protections of **patient confidentiality**
- **“Why doesn’t my R code work?”**
- Faster identification of QC issues at the local hospital ***and*** the analysis level
- Network of clinicians, statisticians, informaticians, and analysts who can quickly resolve QC issues

COVID-19 has been widely reported to be associated with new neurological manifestations

- Studies have reported that COVID-19 patients with **concurrent** or **new** onset neurological manifestations are at an **increased risk** for prolonged hospital stay, disease severity, and mortality

- Comorbidities have also been associated with the manifestation of neurologic illness

- Mixed findings regarding risk and time of poor health outcomes:
  - Differences in study design (CNS vs PNS diagnoses)
  - Single-centered studies and small sample size
  - Non-diverse geographic locations

Objective

Leverage the 4CE's large, multinational, and geographically diverse dataset to evaluate the risk of adverse clinical health outcomes (e.g., longer hospital stay and mortality) in hospitalized COVID-19 patients with concurrent neurological manifestations

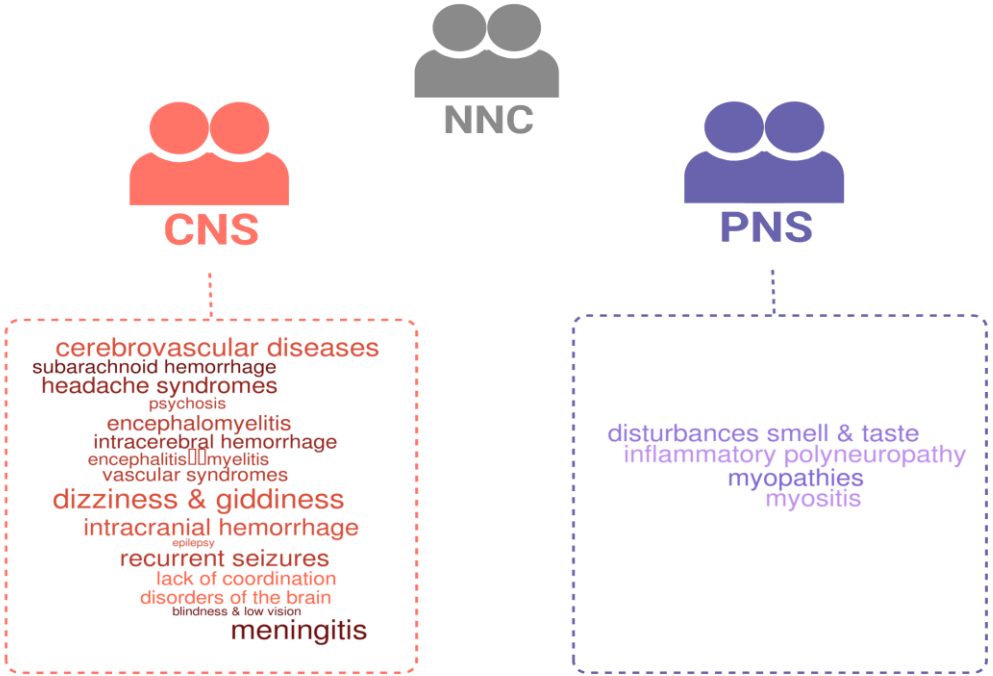
Data Collection

- We included **21 healthcare systems (293 hospitals)** from the 4CE that contained patient-level data

- Healthcare systems spanned **6 countries** (United States, France, Italy, Spain, United Kingdom, Germany, and Singapore)

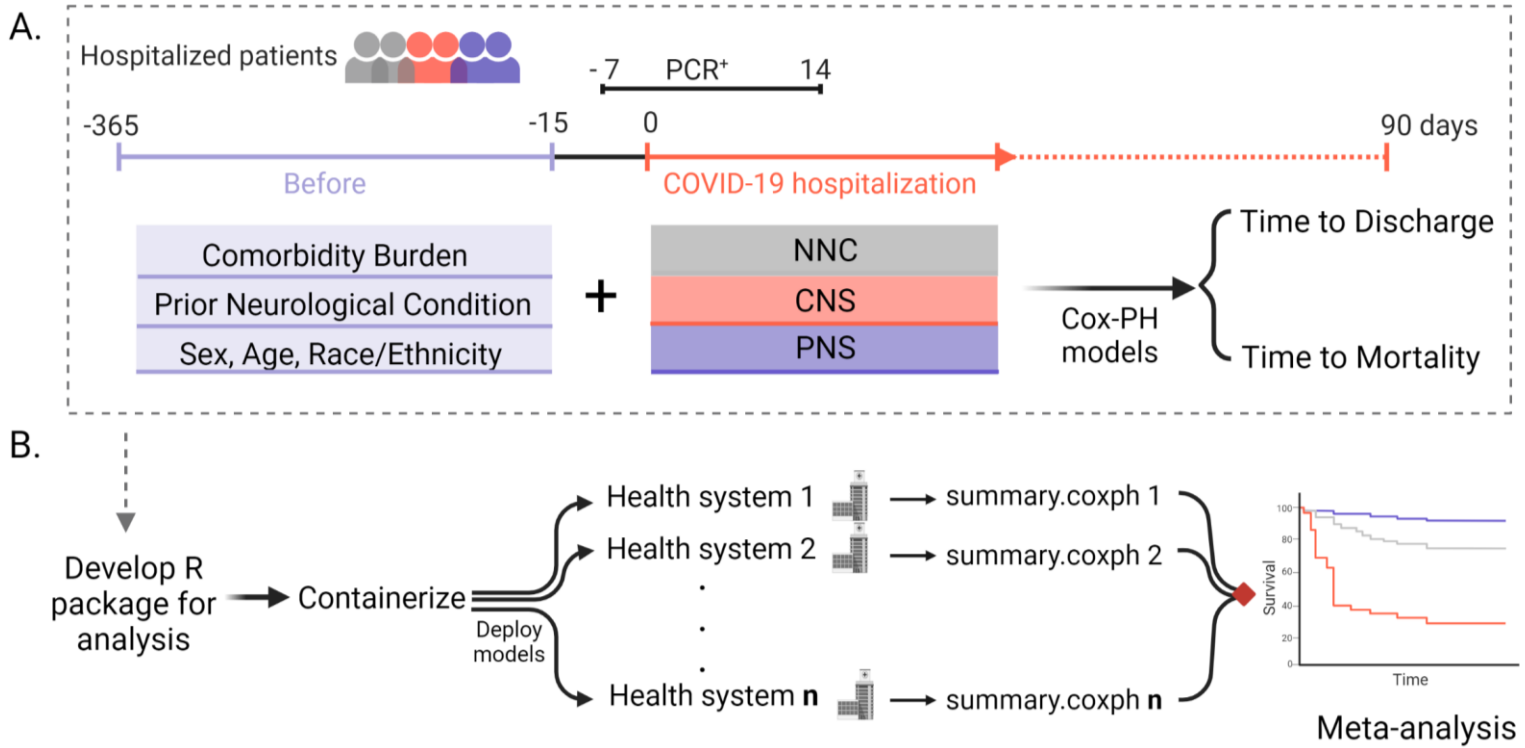
- All hospitalized COVID-19 patients were included in the study (ages 0-80+)

Patient Stratification



ICD codes recorded during hospitalization were used to categorize patients into **one** of **three** groups: **No Neurological Condition (NNC)**, **Central Nervous System Condition (CNS)**, **Peripheral Nervous System Condition (PNS)**

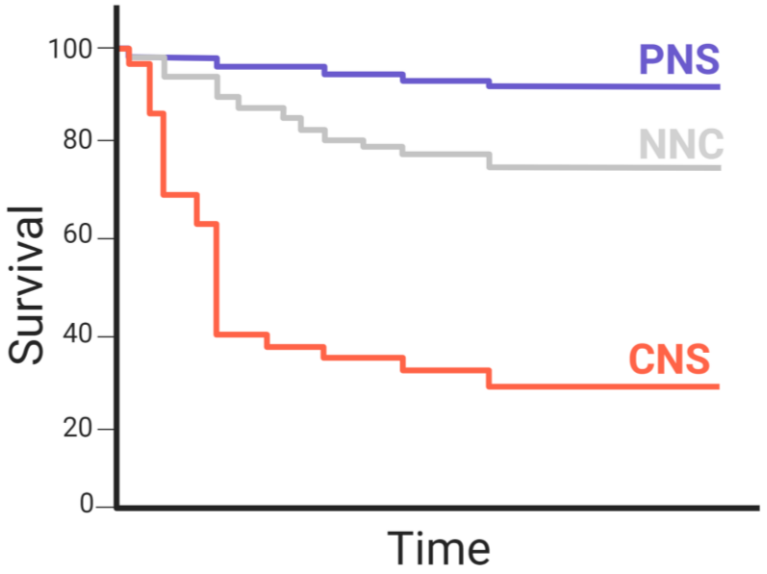
Study Design: Federated Network Approach



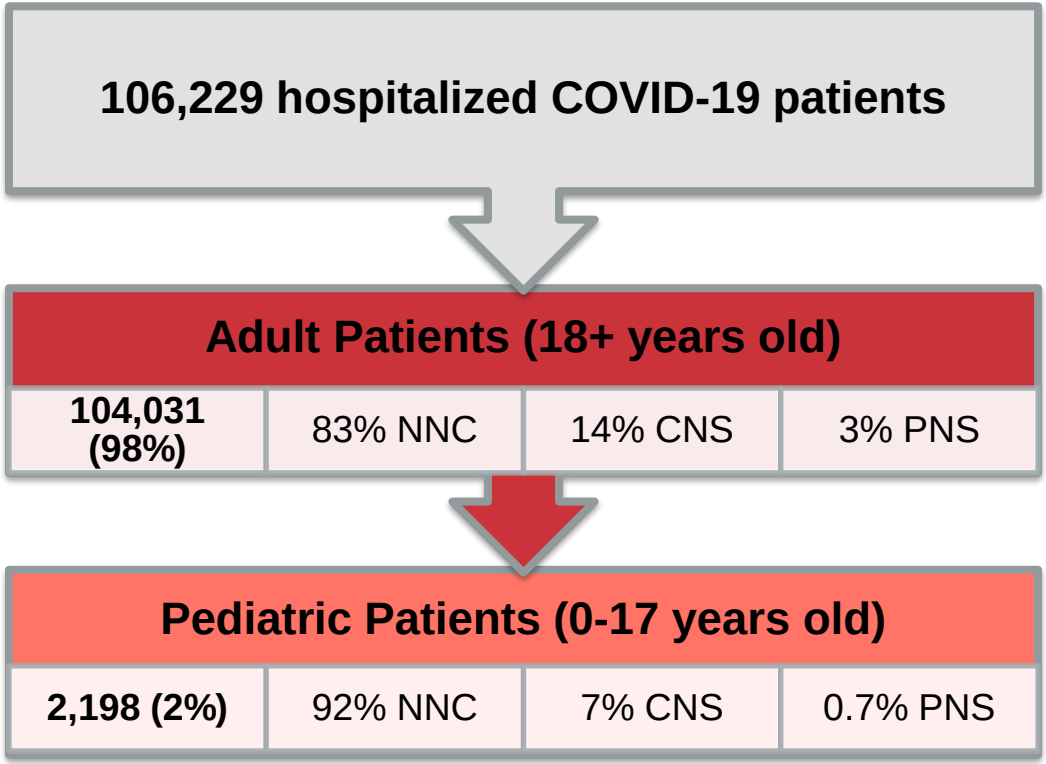
Random-effects meta-analysis was used to evaluate data from *all* healthcare systems

- **Random-effects meta-analysis** allowed us to compute a **pooled** effect size using the **local** effect size estimated at each participating healthcare system

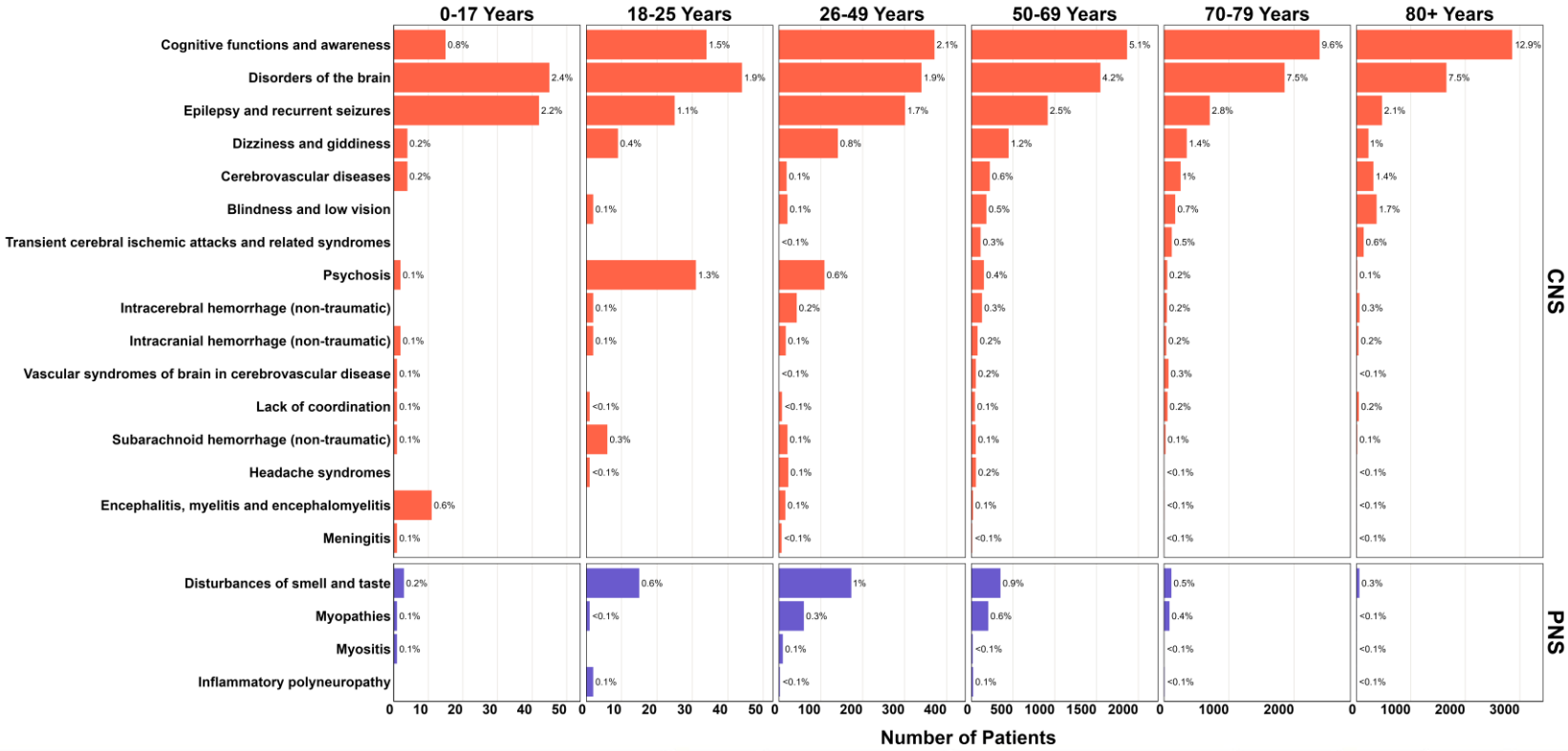
- **Inverse of the variance** was used to weight each study – this allows us to calculate the pooled effect size while accounting for heterogeneity between healthcare systems



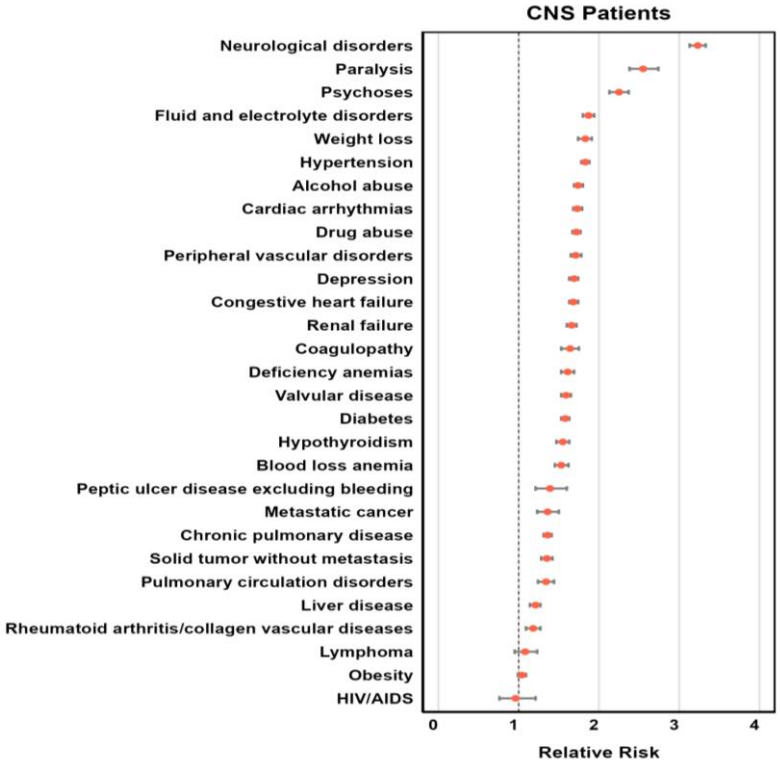
Demographic Characteristics



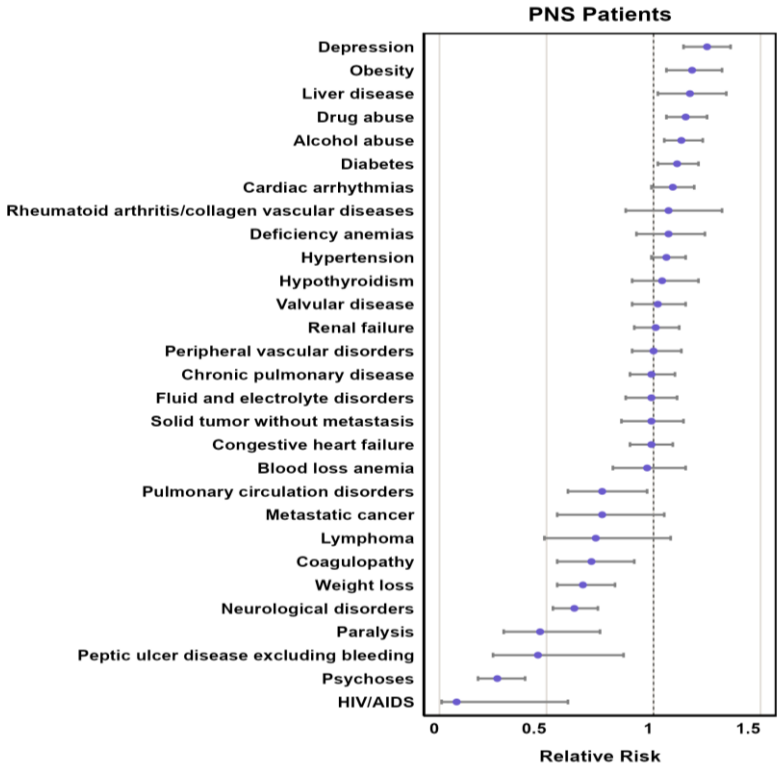
Most common neurological diagnoses were similar across age groups



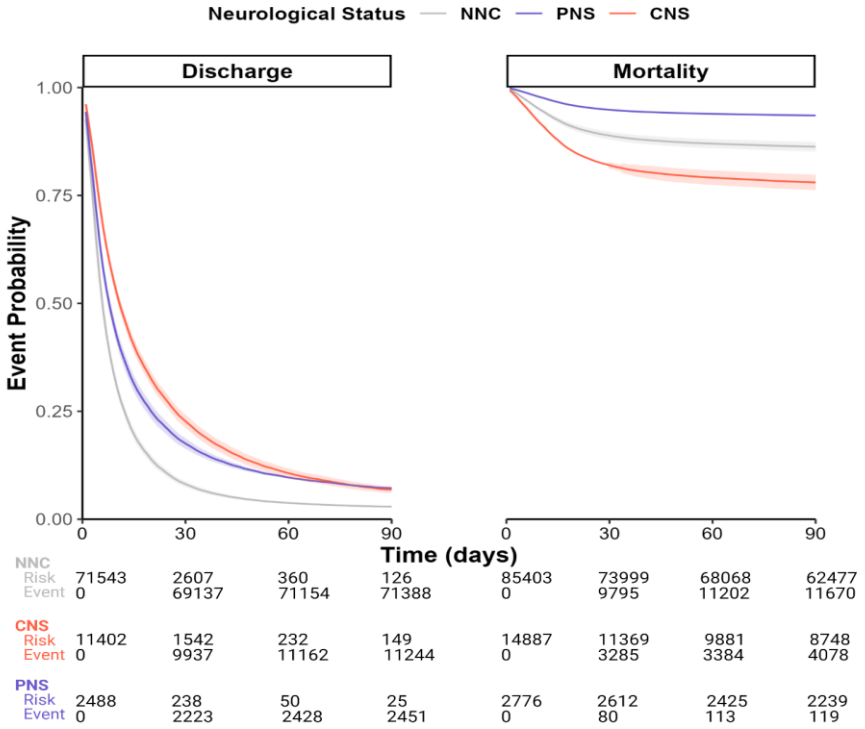
Comorbidities associated with increased risk of a CNS diagnosis during acute COVID-19 hospitalization



Comorbidities associated with both an increased and decreased risk of a PNS diagnosis during acute COVID-19 hospitalization



Patients with a neurological diagnosis during acute COVID-19 hospitalization differed in clinical outcomes compared to those without.



- Patients with a CNS diagnosis had worse outcomes than NNC
- Patients with a PNS diagnosis had better survival outcomes than NNC

Random-Effects Meta-Analysis of Locally run Cox-Proportional Hazard Models

Analysis	Status	Hazard Ratio (95% CI)	P-value
Discharge	CNS	0.54 (0.48, 0.6)	< .001*
	PNS	0.7 (0.6, 0.82)	< .001*
Mortality	CNS	1.78 (1.5, 2.11)	< .001*
	PNS	0.46 (0.38, 0.56)	< .001*

Conclusions

Demonstrated an approach for using federated learning on a large, multinational, and geographically diverse dataset to more definitively evaluate the association between **acute** COVID-19 and neurological manifestations

Our approach enabled the evaluation of clinical outcomes in patients with COVID-19 at each **local** healthcare system and **globally** across the 4CE network

Our multinational study provided a **generalizable** estimate of the risk of poor clinical outcomes in hospitalized patients with acute COVID-19 and concurrent neurological manifestations, distinguishing **CNS v. PNS involvement**

Limitations & Future Directions

Limitations

- Incomplete past medical history for some patients
- Vaccine data is challenging to incorporate
- Unsure if patient admitted “**for**” vs “**with**” COVID

Future Directions

- Evaluate whether acute COVID-19 patients with concurrent CNS diagnoses may be at higher risk for post-acute sequelae of COVID-19

Acknowledgements and many thanks to:

Co-first authors:

- Meghan R Hutch BS
- Jiyeon Son MD
- Trang T Le PhD
- Chuan Hong PhD
- Xuan Wang PhD
- Zahra Shakeri Hossein Abad PhD

Co-senior authors:

- Shyam Visweswaran MD, PhD
- Tianxi Cai ScD
- Yuan Luo PhD
- Zongqi Xia MD, PhD

- Michele Morris BA
- Alba Gutiérrez-Sacristán PhD
- Jeffrey G Klann MEng, PhD
- Anastasia Spiridou PhD
- Ashley Batugo BS
- Riccardo Bellazzi MS, PhD
- Vincent Benoit PhD
- Clara-Lea Bonzel MSc
- William A Bryant PhD
- Lorenzo Chiudinelli PhD
- Kelly Cho PhD, MPH
- Priyam Das PhD
- Tomás González MD
- David A Hanauer MD, MS
- Darren W Henderson BS
- Yuk-Lam Ho MPH
- Ne Hooi Will Loh MBBS
- Adeline Makoudjou MD
- Simran Makwana MS
- Alberto Malovini PhD
- Bertrand Moal MD, PhD
- Danielle L Mowery PhD
- Antoine Neuraz MD, PhD
- Malarkodi Jebathilagam Samayamuthu MD
- Fernando J Sanz Vidorreta BS
- Emily R Schriver MS
- Petra Schubert MPH
- Jeffery Talbert PhD
- Amelia LM Tan BSc, PhD
- Byorn W.L. Tan MBBS
- Bryce W.Q. Tan MBBS
- Valentina Tibollo MS
- Guillaume Verdy MSc
- William Yuan PhD
- Paul Avillach MD, PhD
- Nils Gehlenborg PhD
- Gilbert S Omenn MD, PhD
- Margaret Vella, BS

All members of The Consortium for Clinical Characterization of COVID-19 by EHR (4CE)

Figures created with BioRender.com

Thank you!

meghan.hutch@northwestern.edu

Twitter: @meghan_hutch