DIAGNOSTIC JOURNEYS OF PATIENTS WITH LONG COVID

NASEM Workshop: Toward a Common Research Agenda in Infection-Associated Chronic Illnesses
June 30, 2023

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Clinical Associate Professor of Medicine
Co-Director, Stanford Long COVID Program
Director, Stanford Consultative Medicine

Stanford MEDICINE

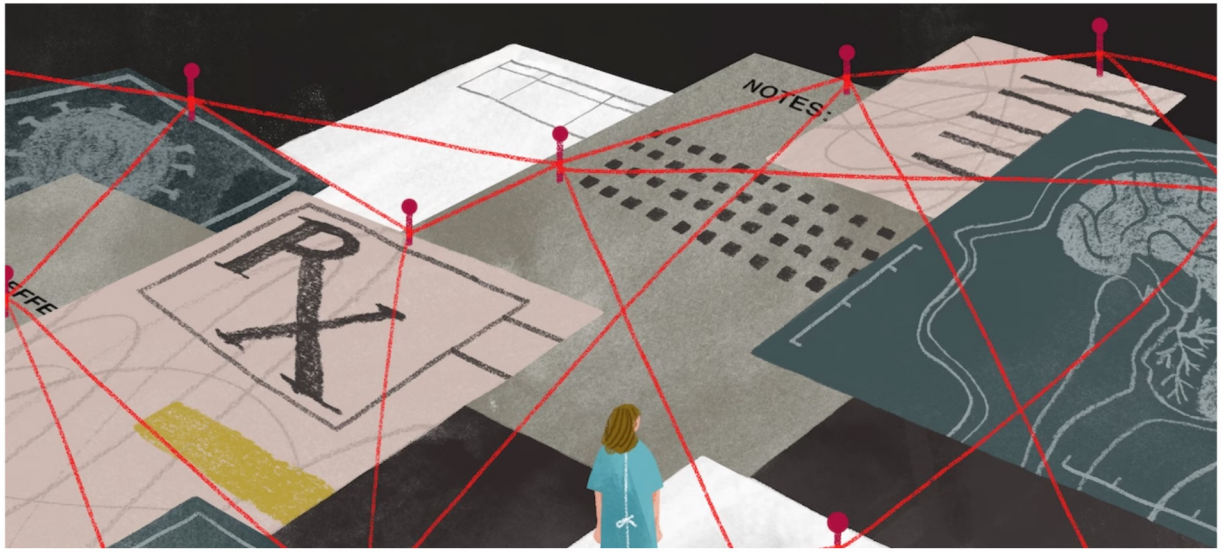
The Washington Post
Democracy Dies in Darkness

She went to one doctor, then another and another

Lindsay Polega's two-year odyssey with long covid shows how the medical system fails many patients

By Ariana Eunjung Cha

April 18, 2022 at 2:30 p.m. EDT



MEDICINE AND SOCIETY

Consultative Medicine — An Emerging Specialty for Patients with Perplexing Conditions

Linda N. Geng, M.D., Ph.D., Abraham Verghese, M.D., and Jon C. Tilburt, M.D.

The emerging specialty of consultative medicine is rooted in generalism and aims to integrate the best of the Oslerian diagnostic tradition with the multidisciplinary collaboration and modern technologies needed to tackle uncertain, difficult, or complex diagnoses.

December 23, 2021
N Engl J Med 2021; 385:2478-2484
DOI: 10.1056/NEJMms2111017

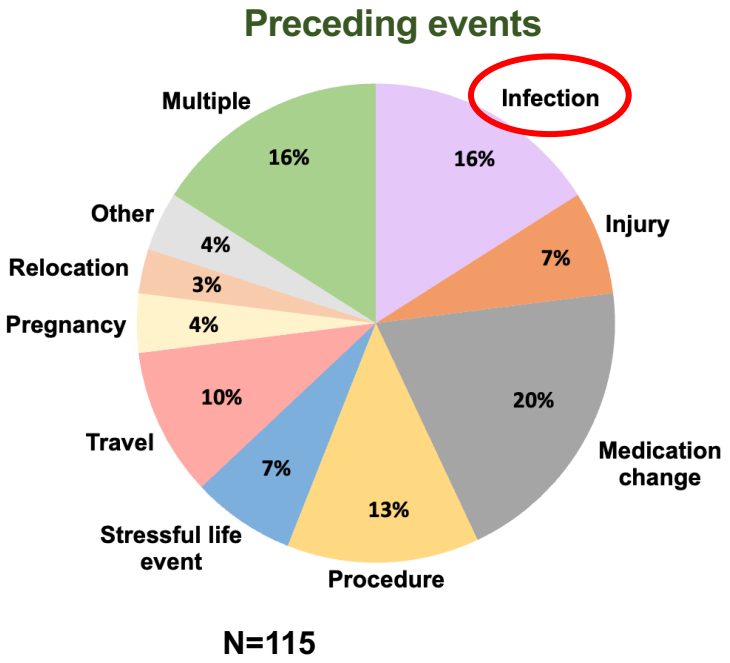
Types of conditions for which patients endure long diagnostic and healthcare journeys:

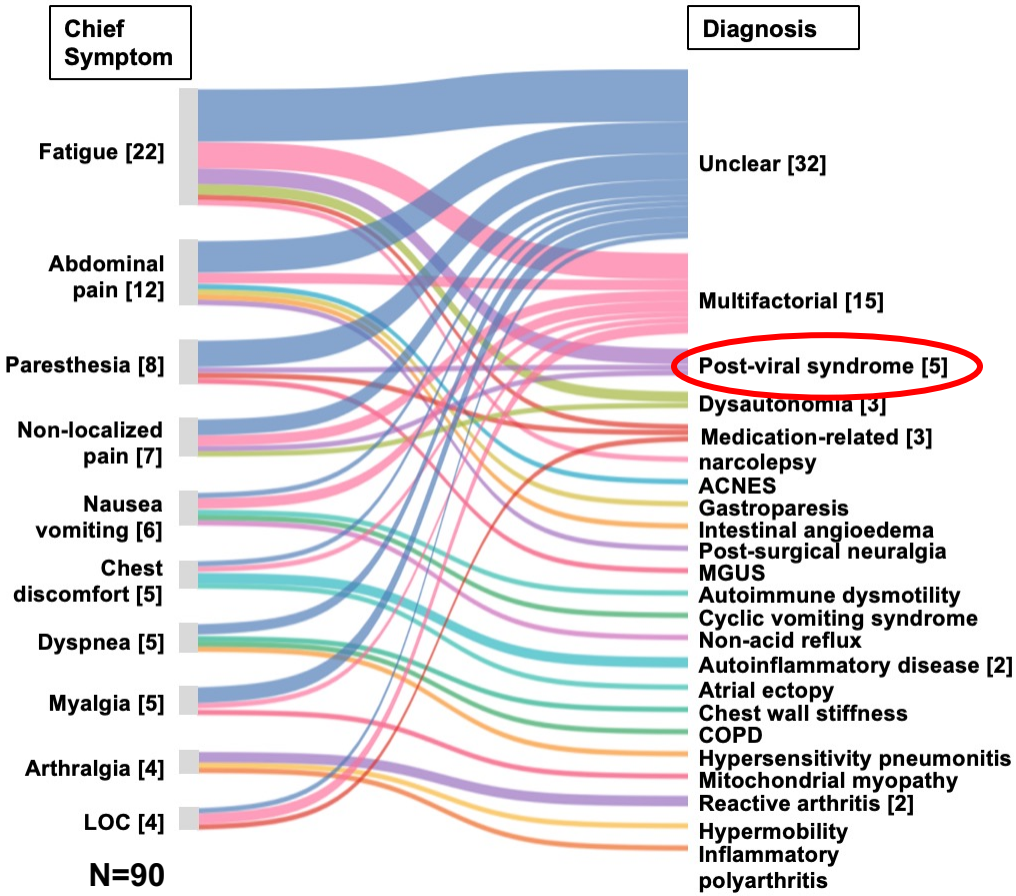
- Rare conditions
- Atypical presentations of common conditions
- Complex conditions with multiple systems involved
- Novel or poorly understood conditions

Long COVID

Other infection-associated chronic illnesses

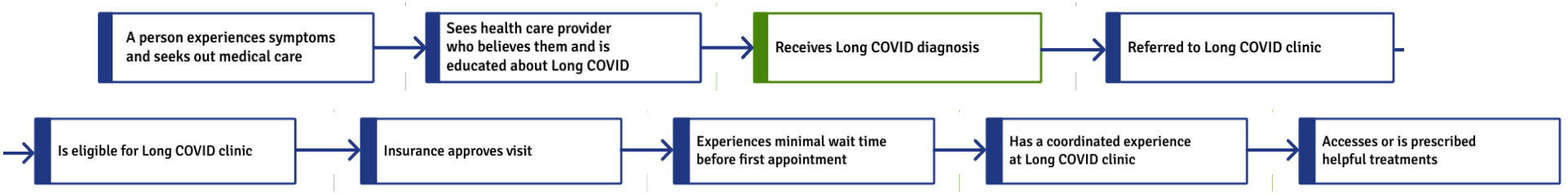
Post-infectious syndromes are commonly seen in diagnostic second opinion clinic





Chao et al. (2022) *Diagnosis (Berl)*

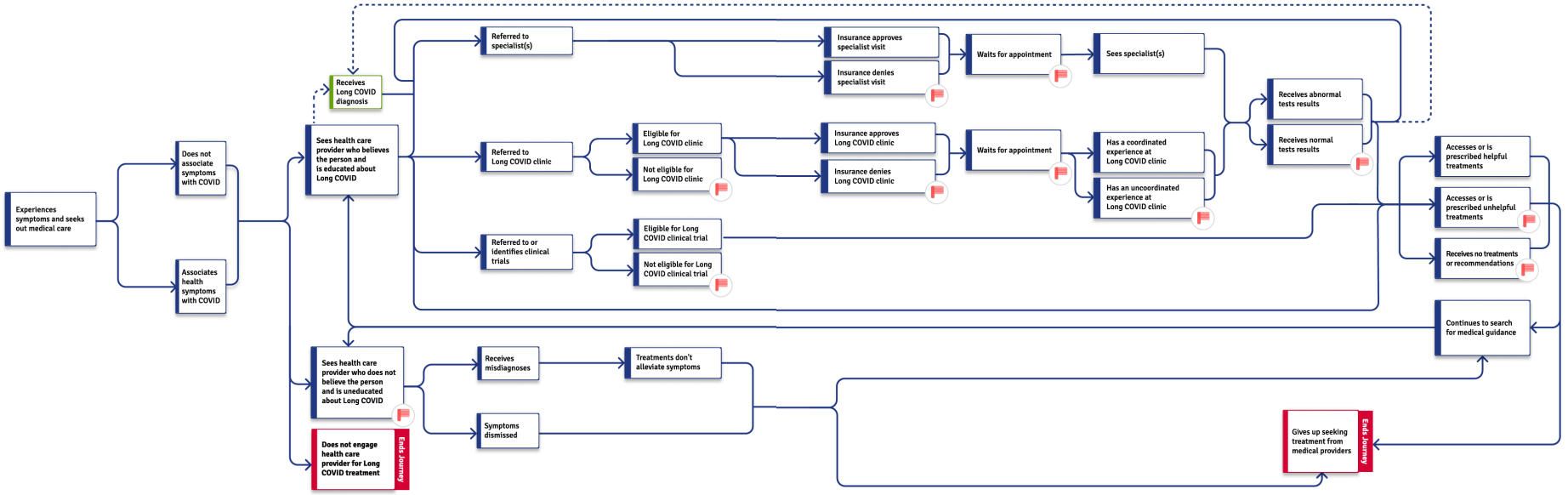
Ideal Journey for Patient with Long COVID



Department of Health and Human Services (2022)

health+ Long COVID
Human-Centered Design Report

Actual Journey for patient with Long COVID

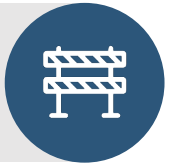


Department of Health and Human Services (2022)

health+ Long COVID
Human-Centered Design Report

CHALLENGES AND BARRIERS

FACTORS THAT PROLONG THE JOURNEY



Patient and clinician awareness

Limited care access

Complex care navigation

Misdiagnosis/missed diagnosis

Condition not well defined

Lack of treatments

Stigma

CHALLENGES AND BARRIERS

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Cannot diagnose it if people do not seek care and if clinicians do not think of it.

- Health literacy barriers
- Vulnerable communities

Current definitions depend on knowledge of acute COVID-19 infection.

- Acute testing limitations
- Lack of biomarker

CHALLENGES AND BARRIERS

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Demand >>> Capacity

Specialized Long COVID clinics are concentrated in urban areas and academic centers.

Long waits for appointments at Long COVID clinics.

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Care coordination across different clinics and institutions.

Even after entering a Long COVID program, patients are often referred to and seen by multiple specialists.

Long waits for appointments continues…

CHALLENGES AND BARRIERS

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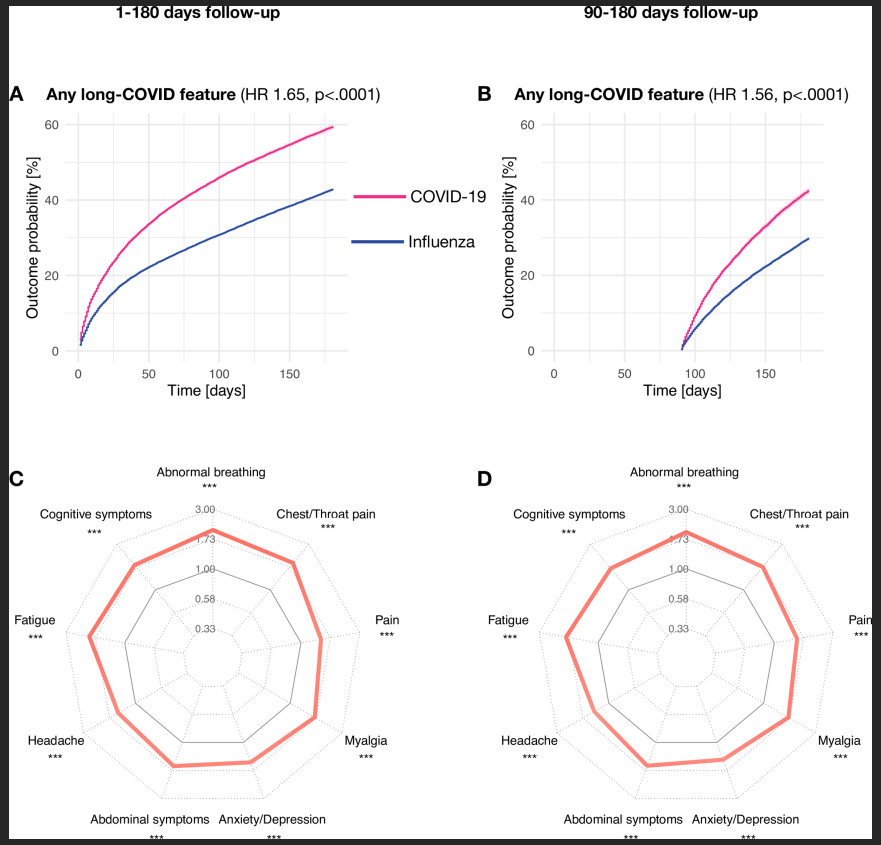
Long COVID can be misdiagnosed as something else or missed completely.

- *"aging"*
- *"depression"*
- *"perimenopause"*

Other conditions can be misdiagnosed as Long COVID.

Multiple things can be going on at the same time, adding to the complexity.

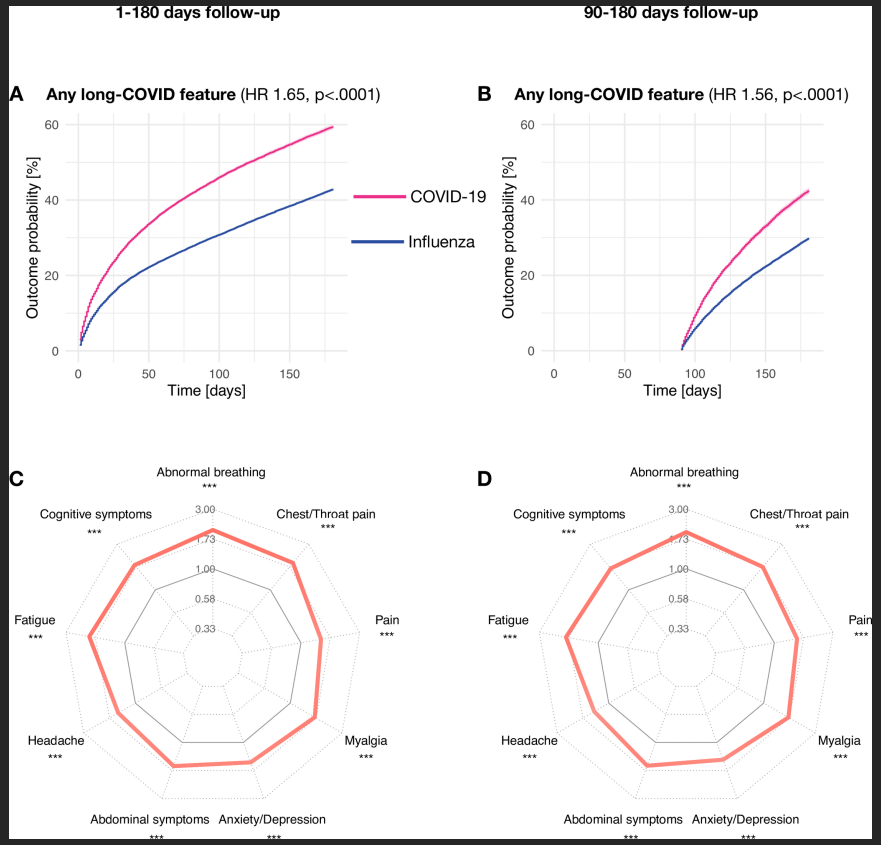
”Long COVID” symptoms also seen Post-Flu, but at lower rate than Post-COVID



Taquet M, et al. *PLoS Med*. 2021

89 million patients from 59 healthcare organizations

”Long COVID” symptoms also seen Post-Flu, but at lower rate than Post-COVID



Taquet M, et al. *PLoS Med*. 2021

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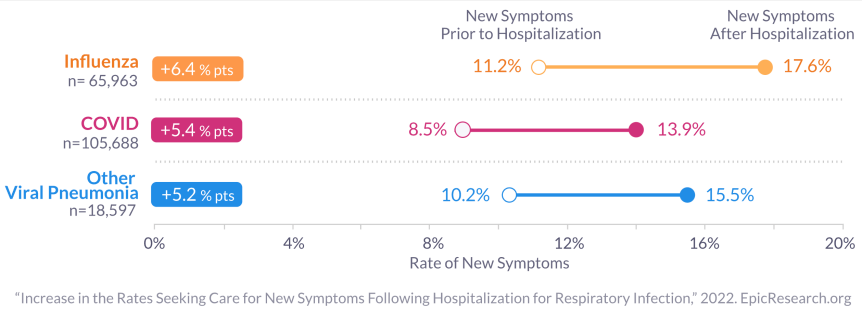
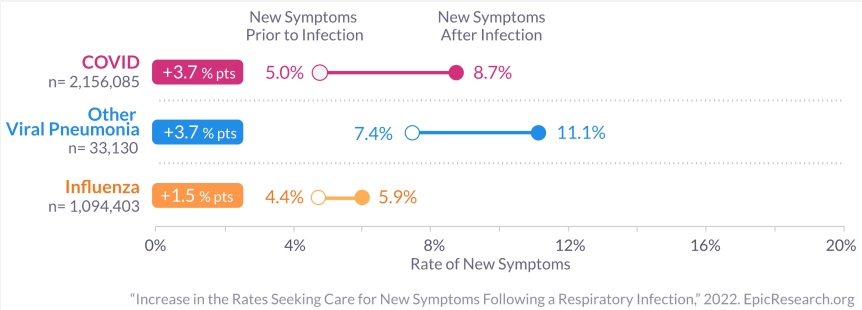
Patients also seek care for long-term symptoms after influenza and non-COVID viral pneumonias





Allen et al. *EpicResearch.org* 2022

142 million patients from 166 Epic organizations

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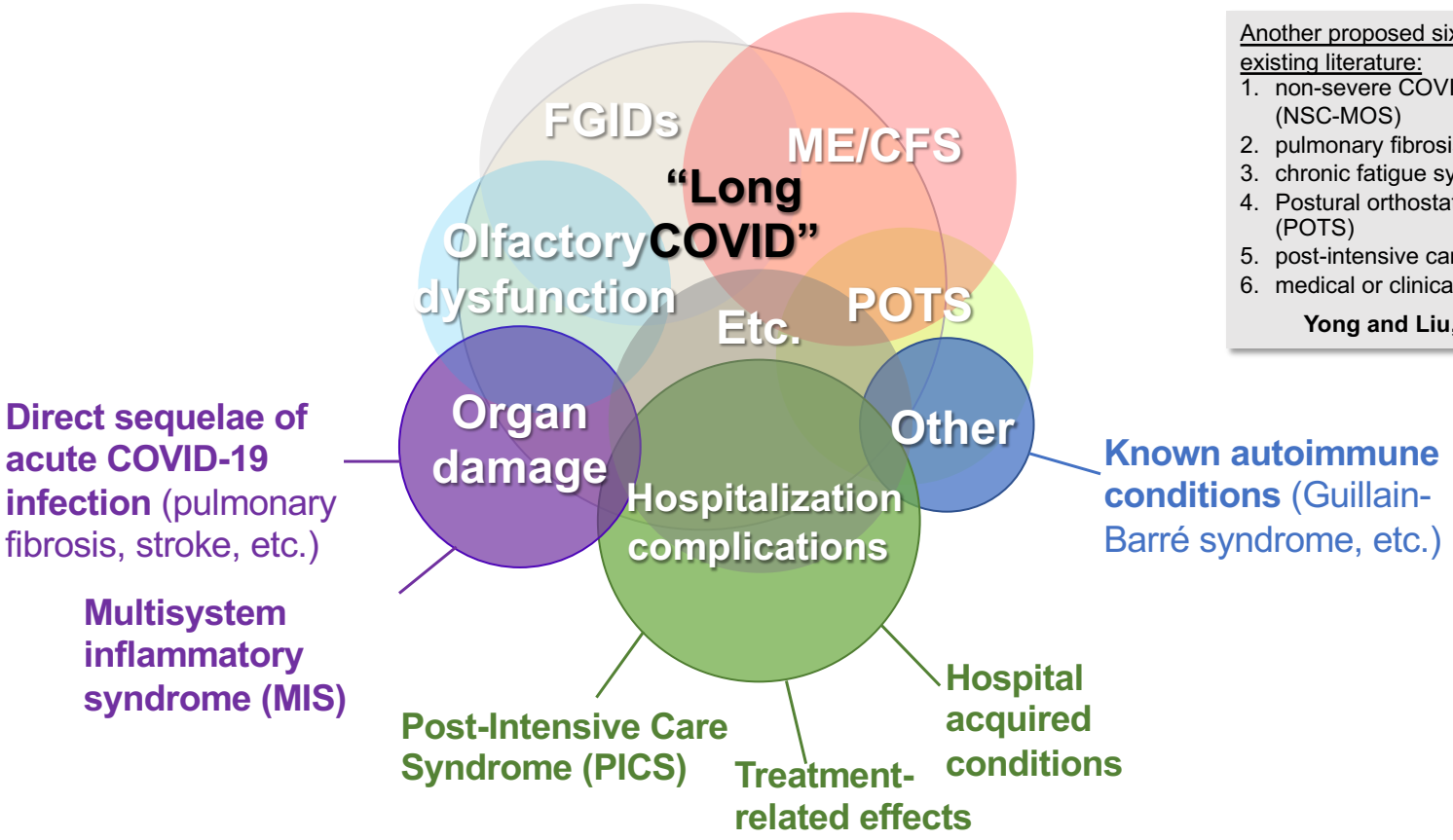
What exactly is Long COVID?

What symptoms? How long? Start time? How severe? Testing? Exclusion of other diagnoses? How certain? Etc.

NATIONAL ACADEMIES Sciences Engineering Medicine

"Examining the Working Definition for Long COVID" (2023, ongoing)

A Syndrome of Syndromes



Another proposed six subtypes based on the existing literature:

1. non-severe COVID-19 multi-organ sequelae (NSC-MOS)
2. pulmonary fibrosis sequelae (PFS)
3. chronic fatigue syndrome (ME/CFS)
4. Postural orthostatic tachycardia syndrome (POTS)
5. post-intensive care syndrome (PICS)
6. medical or clinical sequelae (MCS)

Yong and Liu, *Rev Med. Vir.* (Dec 2021)

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Currently no established evidence-based treatments for Long COVID

Difficult to empirically confirm diagnostic accuracy

Clinicians less likely to refer to specialists or Long COVID centers given “futility”

Patients may also give up on seeking care

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Associated Stigma

Patients: *"No one believes me."*

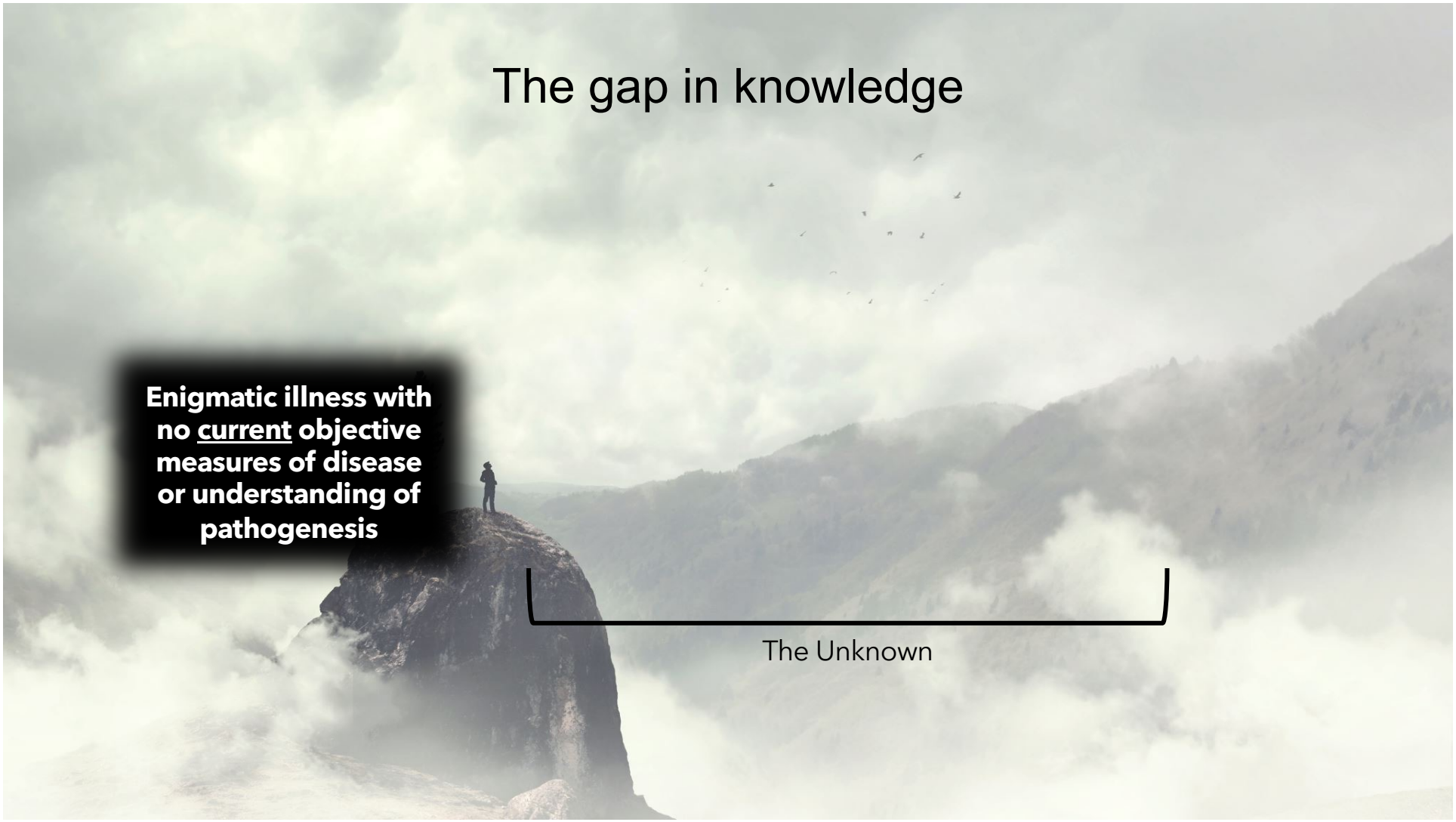
- Dismissed by friends, family, coworkers/employers
- Dismissed by healthcare providers

Some clinicians and researchers:
"Isn't it just a psychological illness?"

- Lack of objective findings
- Lack of mechanistic understanding

Therapies may also be stigmatized

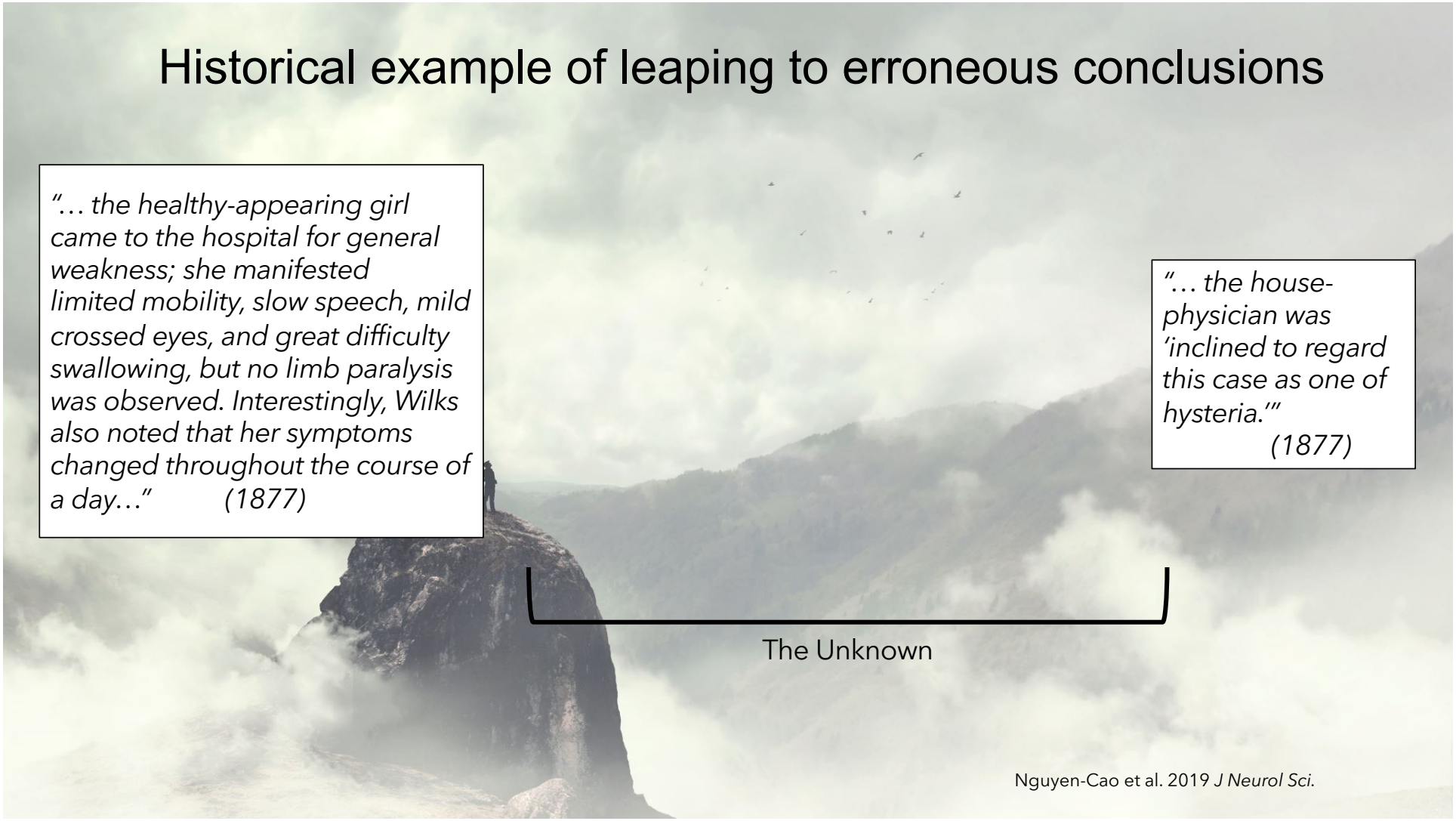
The gap in knowledge



Historical example of leaping to erroneous conclusions

"… the healthy-appearing girl came to the hospital for general weakness; she manifested limited mobility, slow speech, mild crossed eyes, and great difficulty swallowing, but no limb paralysis was observed. Interestingly, Wilks also noted that her symptoms changed throughout the course of a day…" *(1877)*

"… the house-physician was 'inclined to regard this case as one of hysteria.'" *(1877)*



Nguyen-Cao et al. 2019 *J Neurol Sci.*

Filling the knowledge gap

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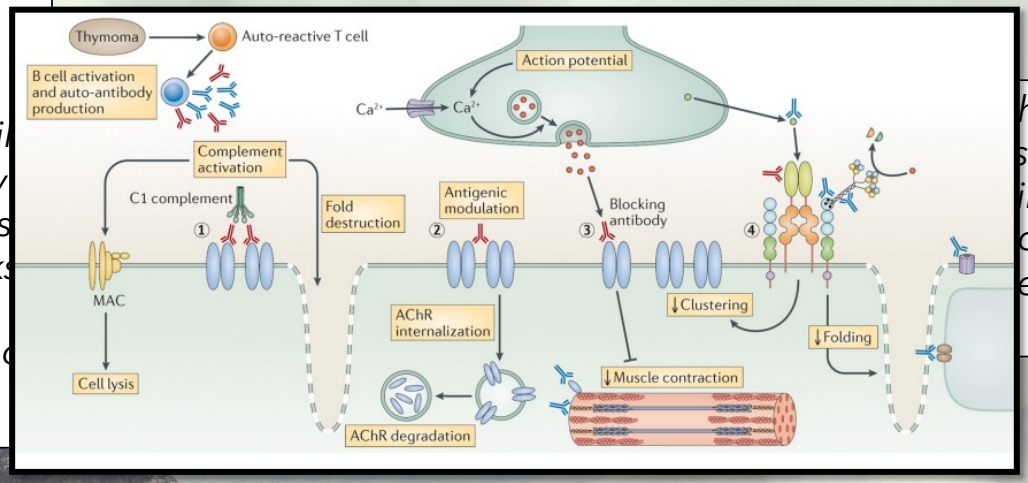

Myasthenia Gravis

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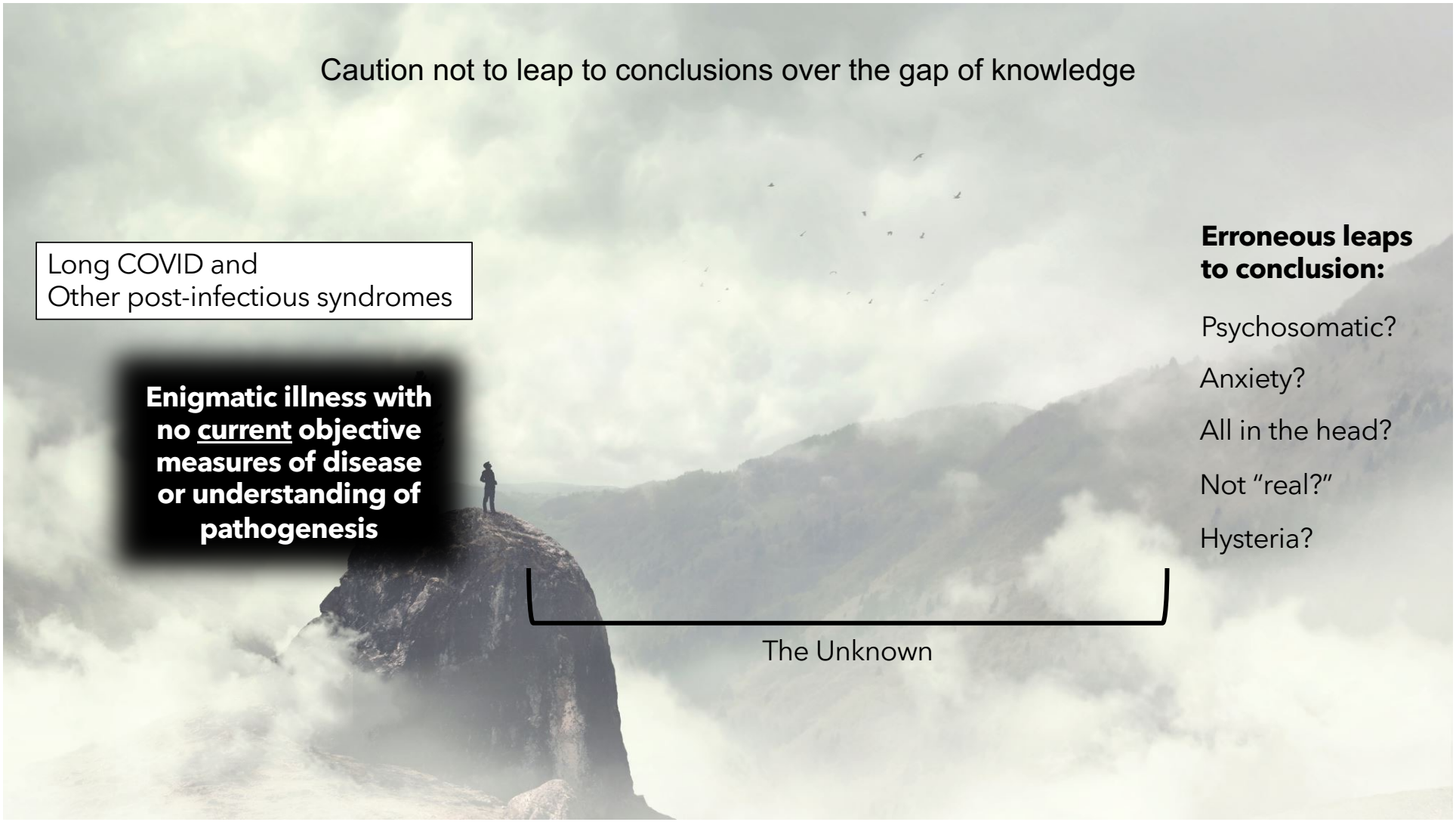
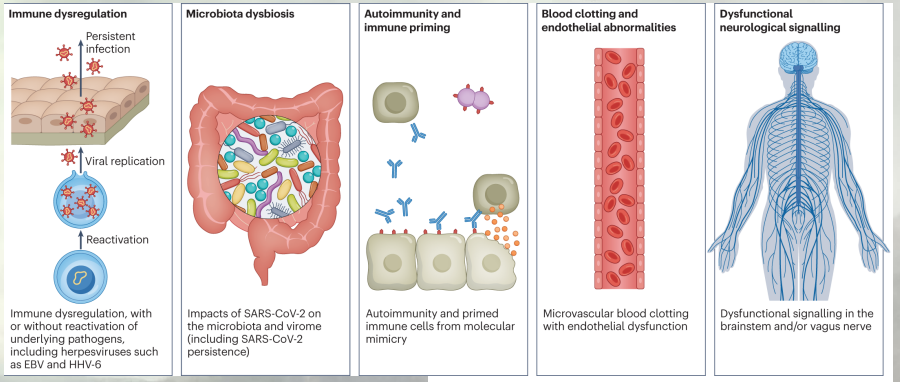
Nguyen-Cao et al. 2019 *J Neurol Sci.*


Caution not to leap to conclusions over the gap of knowledge
Long COVID and
Other post-infectious syndromes
Enigmatic illness with no current objective measures of disease or understanding of pathogenesis
Erroneous leaps to conclusion:
Psychosomatic?
Anxiety?
All in the head?
Not "real?"
Hysteria?
The Unknown

Long COVID and
Other post-infectious syndromes

Enigmatic illness with no <u>current</u> objective measures of disease or understanding of pathogenesis

Potential Mechanisms of Long COVID Pathogenesis



Davis et al. 2023 *Nat Rev Microbiol.*

We as a collective village are building the knowledge base

To lead to:

Treatments

Better care

Improved lives

Validating patients

CHALLENGES AND BARRIERS

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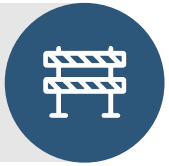

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SHORTENING THE JOURNEY

ADVANCING THE CARE

Improve awareness and education

Expand care access and coordination

Support primary care

Refine diagnosis and phenotyping

Define mechanisms

Identify treatments

Shift cultural perceptions

Future Directions

- Building the multi-disciplinary team and harnessing collective intellect
- Engaging patients, family, advocates
- Studying models of care
- Reimbursement and finance factors
- Considering equity and community
- Integrating education and training
- Advancing knowledge and research
- Intersections and broad applications across post-infectious syndromes

ACKNOWLEDGMENTS

Our patients

Multidisciplinary Clinical Team

Hector Bonilla
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Lauren Eggert
Husham Sharifi
Audra Horomanski
Beth Martin
Houssam Halawi
Oliver Sum-Ping
Norah Simpson
Leon Moskatel
Jacob Ballon
Tyler Prestwood
Shelby Lazarow
Zara Patel
Sarah Stranberg

Long COVID clinic and ME/CFS clinic staff and leadership

Research Teams
STOP-PASC trial
RECOVER initiative
IMPACC/LTI studies

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