

Today

- What is long COVID?
 - Definition, Coding, Symptoms
 - History
 - Epidemiology
 - Risk factors
- Updates on treatment
- Long COVID and other sequelae of infectious diseases





Long COVID

Also known as...

- Long-haul COVID
- Post-acute COVID
- Chronic COVID, etc.

What all these terms have in common is persistence of COVID-19 <u>symptoms</u> for days, months, years after the initial infection.

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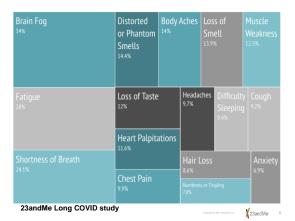
How Long is "Long"?

WHO: symptoms must persist for 3+ months

CDC: symptoms must persist for 4+ weeks

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As of 2023, No Consistent Definition Exists

But there is an ICD-10-CM code: U09.9, "Post COVID-19 condition, unspecified"

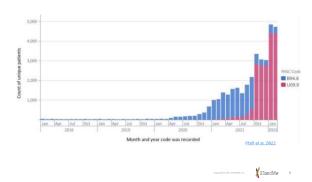
This code was created 1+ year after initial patient reports (October 2021)

Previously, code B94.8 was used instead: "Sequelae of other specified infectious and parasitic diseases"



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ICD-10-CM Code Use



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The Problem With The ICD-10-CM Definition

It necessarily only captures the experiences of patients who have sought contact with the medical system.

May exclude:

- milder cases
- experiences of individuals without access to healthcare
- experiences of individuals trying to avoid stigma

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Long COVID

History worth reviewing: it was patients who created the term "long COVID" (or "long-haul COVID").

Possibly the first disease to be defined via patients finding each other on social media.

Just like COVID-19, it was a new disease.



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The Newness of New Diseases

"In the 1960s and 1970s, most physicians were aware of the possibility of pandemics... However, the emergence of **a truly new infectious disease** that could dramatically affect society was still a purely hypothetical concept.

That all changed in the summer of 1981 with the recognition of the first cases of what would become known as AIDS."

Fauci 2022		
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Why	Did	The	Patients	Need	to	Define
Long	CO	VID:	?			

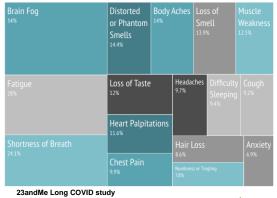
COVID-19 itself was also a new disease but with a clear etiologic agent (SARS-CoV2)

Long COVID:

- no definitive diagnostic tests (or even a definition) exist
- symptoms (subjective, self-reported):
 - are widely heterogeneous
 - overlap with other conditions



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Why Did The Patients Need to Define Long COVID?

COVID-19 itself was also a new disease but with a clear etiologic agent (SARS-CoV2)

Long COVID:

- no definitive diagnostic tests (or even a definition) exist
- symptoms (subjective, self-reported):
 - are widely heterogeneous
 - overlap with other conditions
- Often gets dismissed as a 'all in your head' condition

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Why Did The Patients Need to Define	
Long COVID? Prior to May 2020: long-term effects were not	
considered; most patients believed to have mild	
disease and fast recovery	
Inconsistent with people's actual experiences→	
social media groups like <u>Body Politic</u> emerged	
(later \rightarrow Patient-Led Research for COVID-19)	
May 2020: survey of 640 patients revealed first	
clues into comorbidities and epidemiology of long COVID	
Citizen science project	
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Multiple Forms of Patient Advocacy	
05/05/2020: Dr. Garner's op-ed in the British Medical Journal	
Paul Garner: For 7 weeks I have been through a roller coaster of ill health,	
extreme emotions, and utter exhaustion May 5, 2020	
Paul Garner, professor of infectious diseases at Liverpool School of Tropical Medicine, discusses his	
experience of having covid-19	
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Patient-Led Research for COVID-19 Survey (May 2020)	
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Featured in the NIH Director's Blog in September 2020 https://patientresearch.co/d19.com/research/report//	
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And Yet	-
Since July 2021: considered a disability under the ADA.	
4 million full-time equivalent workers are believed to be	
unable to work due to long COVID.	
That's 2.4% of the US working population.	
(Brookings Institution/ Lancet/ Federal Reserve/ NPR, 07/31/2022)	
19	
And Yet	
7.11.0 1.01.11	
August 2022: the US has set up the National Research Actional Plan on Long	
COVID #RESEARCHLONGCOVID	
→ NIH Researching COVID to Enhance Recovery (RECOVER) initiative (\$1.15B)	
Image credit: The Guardian	
Compared the contraction, so. 22 Sand May 20	
20	
2023 Updates	
Public health emergency set to expire on 05/11/2023	
However:	
Currently ~65 million people worldwide are estimated to have long COVID symptoms.	
Lancet Editorial Baset 2/8/23	
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23andMe Long COVID Study

- In 2020, we sent out surveys to capture COVID-19 (not yet long COVID at that time) diagnoses in our US customer population
- ~1.1 million responses
- Identified genetic markers of COVID-19 risk and loss of smell/taste

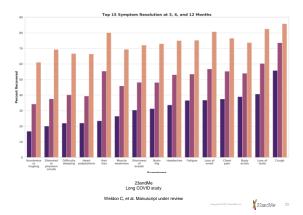


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23andMe Long COVID Study

- In 2021, we contacted the initial COVID-19 cases and deployed surveys to better understand their long-term experience
- Of ~100,000 respondents, almost half reported symptoms lasting for a month or longer
 - Estimates widely vary across studies
 - Sample comprised many early cases

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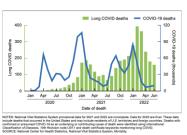
Long COVID Epidemiology: Take Home Messages

- Long COVID affects a substantial proportion of all acute COVID-19 cases, although estimates of both prevalence and system resolution vary widely
 - ~60% of hospitalized cases
 - ~20% of non-hospitalized cases
 - ~11% of vaccinated cases
- Emerging <u>body of evidence</u> supports persistence of symptoms beyond 2 years



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Long COVID Mentioned on 3,500+ U.S. Death Certificates

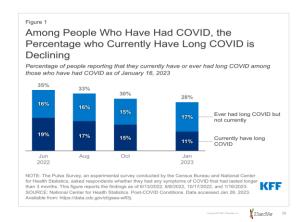


Peak in long COVID deaths occurred in February 2022.

Even though men are less likely to get long COVID, they have a slightly higher fatality rate.

Racial/ethnic disparities exist and may reflect both risk and access to care.







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Epidemiology Holds Clues to Etiology

- Long COVID affects a substantial proportion of all acute COVID-19 cases, although estimates of both prevalence and system resolution vary widely
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- Emerging <u>body of evidence</u> supports persistence of symptoms beyond 2 years

Davis et al. 2	1023	
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22andMa Lang COVID Study	
23andMe Long COVID Study	
 We captured patients across the spectrum of disease severity (i.e. not only patients 	
who went to the doctor)	
who were to the doctory	
 Risk factors for long COVID in our data: 	
 Hospitalization (~10x) 	
 XX karyotype (~2x) 	
 Prior cardiometabolic disease (~1.9x) 	
 Prior autoimmune disease (~2.5x) 	
 Prior depression/anxiety (~2x) 	
Gayanger time transmit to 22 and May 31	
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23andMe Study Was Uniquely Timed To Study Vaccine Effects	
 Vaccination helps prevent long COVID, but likely not cure it: 	
The majority of our participants did not	
experience a change in their symptoms	
following vaccination	
3	
Approximately twice as many people in our	
cohort reported improvement vs. worsening	
of LC following vaccination	
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23andMe Long COVID Study	
Our findings were largely consistent with	
other reports in literature	
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Open questions:	
 Why are XX people more susceptible to 	
this condition?	
 What is the role of mental and physical 	
comorbidities?	
What is the role of genetics in	
determining susceptibility?	
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Effective Treatment Requires:

- Understanding of the underlying pathophysiology (challenging with a new disease)
- Proper diagnostic tools
- Actual treatments targeting the disease processes

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Understanding Long COVID Pathogenesis X23andMer 37 37 **Diagnosing Long COVID** • More than 200 symptoms have been identified to date When tested using standard of care diagnostic tools, long COVID patients often appear as 'normal' (similarly to ME/CFS) Multiple new tests in development 38 **From Understanding to Treatment** • From 200+ symptoms to clusters; a 2023 study used machine learning to identify 4 subtypes: Cardiorenal (more serious, likely to be acute complications like HF) Dyspnea Muskuloskeletal Digestive Tremendous heterogeneity between patients makes one-size-fits-all approaches ineffective • Subgroups are hard to establish prior to starting trials

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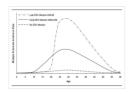
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• Treatment has historically been symptom-focused

An Incomplete List of Prope	oead Traatmonte*	
Paxlovid (for both preventing)		
and treatment)SSRIs		
 Exercise/quality of life interventions (controversia 	al)	
Pacing/cognitive pacing IV immunoglobulin for imit		
dysfunction Probiotics Low dose naltrexone	Long COVID exercise trials proposed by NIH raise alarm Abouters the US bloundful agency to rethink the deelige of th RECOVER indicative,	
*With ~evidence of succes	citing possible harm and funding waste. SS Davis et.al. 2623	
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What About Variants	and Repeated Infections?	
	ent variants impacting	
long COVID risk is mediated by sever		
	ong COVID after 2nd	
and 3rd infections vaccination status		
	,	
	Davis et al. 2023	
	Computing 20 2021 2 20 and No. 10. 23 and May 41	
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A Detour: We've Seen This Before

- $\bullet \ \ Initial \ infection \rightarrow \ chronic \\ symptoms$
- February 2022: Science publishes a compelling story about Epstein-Barr virus infection causing multiple sclerosis



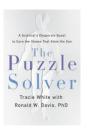
Immune or autoimmune?

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Ascherio et al. 2007

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A Detour: We've Seen This Before



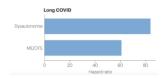
- Initial infection leads to chronic symptoms in a minority of cases
- Similarity to the world of Lyme disease and ME/CFS



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More on ME/CFS and Long COVID



 Extremely strong associations between long COVID and meeting diagnostic criteria for ME/CFS and dysautonomia (e.g. POTS)

Davis et al. 2023

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	Faces of ME/CFS: Whitney Dafoe Before and After	
	Affects -1M Americans Since 2016, NIH has been investing in ME/CFS understanding (not yet therapeutics) Lessons from ME/C/FS are likely to translate to long COVID	
	Consequence that the second law. \$\frac{1}{2}23andMe^- 40	
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	Long COVID: Take Home Messages	
	Long COVID: Take Home Messages Long COVID is a debilitating condition with diverse	
	manifestations.	
	Its heterogeneity and lack of biomarkers/biological	
	understanding so far have prevented effective universal treatments.	
	Take patient experiences seriously! They are the best	
	resource for understanding this emerging condition.	
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	Acknowledgments	
	23andMe Research participants	
	Companyon and Standards American Standards Add	
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