

Infection-Associated Chronic Conditions and Illnesses (IACCI)

A Primer

Multi-systemic chronic conditions and illnesses can develop after the cumulative effect of one or more disruptors to the immune system.



While various factors may precipitate symptoms, infections are almost always present and often play a major, if not pivotal, role. Common viral, bacterial, fungal, or parasitic acute infectious diseases such as strep throat, mononucleosis, or vector borne diseases, have all been associated with chronic conditions. Other factors of concern include challenges to the immune system such as vaccines, environmental exposures, pregnancy, concussions and other severe physical injuries.

Tens of millions of Americans suffer from IACCI



Examples of IACCI include: myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), Chronic Lyme/Post-Treatment Lyme Disease Syndrome (PTLDS), pediatric acute-onset neuropsychiatric syndrome (PANS), postural orthostatic tachycardia syndrome (POTS) and other infection-triggered dysautonomias, and more recently, Long COVID.

Like cancer, IACCI is a category of diseases



While IACCI arise from different etiologies, they often share similar symptoms and may share underlying mechanisms in the body. At a core level, patients commonly experience immune system alterations, chronic inflammation, changes in their gut microbiomes, mitochondrial and metabolic dysfunction, antigen persistence, latent virus reactivation, and damage to connective tissue and endothelium.

IACCI should be studied in conjunction with one another



Interest in solving the puzzle of IACCI is emerging in the research community. In June 2023, the National Academies developed a unifying framework for these illnesses, highlighting the need for a coordinated research agenda capable of identifying commonalities and differences across IACCI.

Responsive and accountable public research infrastructure is needed



IACCI have historically been underfunded relative to their prevalence and burden. Understanding the big picture for why some people develop chronic illness after an acute infection will require new kinds of studies with multiple disease cohorts. Unfortunately, the siloed structure of the National Institutes for Health (NIH) doesn't support such studies at this time.



IACCI by the numbers

Prevalence

In the United States alone, tens of millions of people experience an array of infection-associated chronic conditions and illnesses.

	Infection Source	Impacted Population
ME/CFS	Myalgic Encephalomyelitis/Chronic Fatigue Syndrome often follows viral or bacterial infections, including COVID-19 ¹ and Epstein-Barr virus ² .	3.4 million Americans (1.3% of the adult population) were living with ME/CFS in 2021 ³ . With half of Long COVID patients meeting the ME/CFS diagnosis, that number is now estimated to 6 millions ⁴ .
Lyme	Chronic Lyme, also known as Post-Treatment Lyme Disease Syndrome (PTLDS), follows a <i>Borrelia burgdorferi</i> bacterial infection often combined with other tick-borne co-infections such as babesiosis and bartonellosis.	2 million Americans were living with Lyme-infection associated chronic illness in 2020 ⁵ with approximately 476,000 cases of acute Lyme disease diagnosed annually in the U.S. ⁶
POTS	Postural Orthostatic Tachycardia Syndrome and other forms of dysautonomias can onset after multiple infections, including by COVID-19, EBV, Influenza, H1N1, mycoplasma pneumoniae, and tick-borne infections.	Experts estimate the POTS population to be at least 6 million Americans , double pre-pandemic numbers ⁷ . Data on the prevalence of other infection-associated dysautonomias is less clear.
PANDAS PANS	Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) are, as stated in the name, associated with streptococcal infections. Other infections, including SARS-CoV-2, influenza, mycoplasma pneumonia, Lyme, and many more, can trigger Pediatric Acute-onset Neuropsychiatric Syndrome (PANS).	The prevalence of PANS and PANDAS in the US is unknown. Available estimates of the incidence, or new cases, of PANS and PANDAS vary widely. ⁸ Further epidemiological study is needed.
Long COVID	Long COVID, also known as Post-Acute Sequelae of SARS-CoV-2 infection (PASC) or Post COVID Condition, follows a SARS-CoV-2 viral infection.	6.9% of U.S. adults, or nearly 18 million adults , were experiencing Long COVID symptoms in March of 2024. ⁹

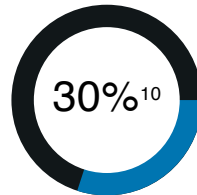


IACCI by the numbers

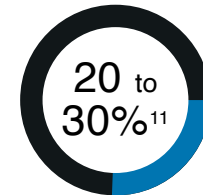
Demographic and Economic Impacts

Infection-associated chronic conditions and illnesses disproportionately impact women and minority populations and keep people out of the workforce.

IACCI affect a subset of those experiencing an infection. In what proportions and why is not well understood and requires further research.

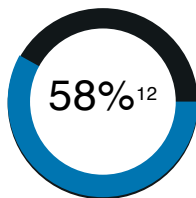


Long COVID

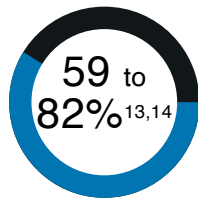


Lyme

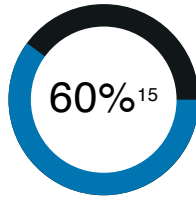
Female predominance in IACCI is generally recognized but is not uniformly documented. More studies are necessary to understand this phenomenon.



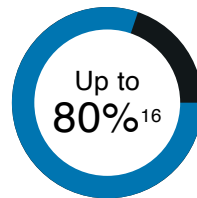
Lyme



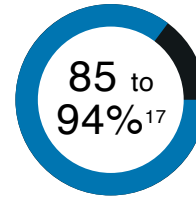
Long COVID



Dysautonomia example
Autoimmune Autonomic
Gangliopathy



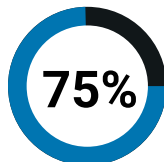
ME/CFS



POTS



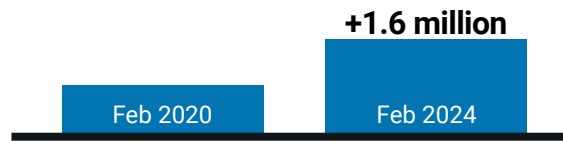
Youth IACCI patients can struggle to go to school. Working-age sufferers can be disabled for life. However, due to their relapsing and remitting nature, people are unable to qualify for disability even though they are too sick to work. Patients require assistance with daily activities, and full-time caregiving responsibilities often fall on family members.



Up to 75% of ME/CFS patients are unable to work¹⁸



About half of adult POTS patients cannot work¹⁹



Disabled working age U.S. population²⁰

Case Study: Long COVID

As of March 2024, Long COVID affects 30% of American adults who have ever had COVID-19¹⁰. People with Long COVID may receive additional diagnoses for Long COVID associated conditions, including other IACCI. Depending on the study, 58.7% to 81.7% of patients are women. The female reproductive health impacts of Long COVID and associated conditions include disruptions to the menstrual cycle, gonadal function, ovarian sufficiency, menopause, and fertility, as well as symptom exacerbation around menstruation, but research on these topics is currently lacking.²¹

A deeper analysis reveals that Long COVID is more prevalent in people without a four-year college degree, Hispanic people, and sexual and gender minorities, especially those who identify as transgender.¹³

Research Infrastructure

Underfunded Diseases

IACCI have historically been underfunded relative to their prevalence.

A review of the distribution of NIH-funded IACCI research over 10 years by nonprofit SOLVE ME shows that major IACCI – in total – receive an average of \$5.2 million in NIH research per year. This funding is spread across 21 different NIH institutes with little to no central coordination.

For 22 million Americans living with Long COVID in March 2024, the NIH dedicated \$1.5 billion so far through the RECOVER Initiative, \$70 million in NIH appropriations in 2022 and \$80 million in 2023.

For comparison, HIV/AIDS receives 3 billion annually in NIH appropriations for approximately 1.2 million people living with HIV in the U.S in 2021²⁴.

ME/CFS	\$12 million
Chronic Lyme	\$3.2 million (2023) \$1 million (pre-2023)
POTS	\$1.5 million ²³
PANS/PANDAS	\$1 million

Average NIH annual funding per IACCI 2014-2024²².

“As long as infectious agents exist, there will be ME/CFS, POTS, and other infection-associated chronic illnesses. A short temporary fix cannot comprehensively address the research and care needs of impacted people. This requires an ongoing and coordinated commitment – similar to what we have done for heart disease and cancer. Infection-associated chronic illnesses have been marginalized and ignored for far too long. It is time to change that.”

– Ziyad Al-Aly, MD, Director of the Clinical Epidemiology Center, and the Chief of Research and Development Service at Veterans Affairs St. Louis Health Care System.



A growing coalition of patient organizations advocate for responsive and accountable public research infrastructure for IACCI:

- Bay Area Lyme Foundation
- BIPOC Equity Agency
- Center for Lyme Action
- Dysautonomia International
- C19 LongHauler Advocacy
- Solve M.E.
- S4HI
- Patient Led Research Collaborative
- MassME
- MEAction
- Minnesota ME/CFS Alliance
- National Alliance for PANS/PANDAS Action (NAPPA)
- Neuroimmune Foundation
- The Louisa Adelynn Johnson Fund for Complex Disease
- Lymedisease.org
- Long Covid Moonshot
- San Diego Lyme Alliance
- The Alex Manfull Fund



Sources

Prevalence

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Demographic and Economic Impacts

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Research Infrastructure

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Recommended Reading

An emerging topic in public health

Understanding Infection-Associated Conditions and Illnesses and their Similarities

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Burden of IACCIs on Society

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Emerging Research Needs for IACCIs

- National Academies of Sciences, Engineering, and Medicine. (2024). Toward a common research agenda in infection-associated chronic illnesses: Proceedings of a workshop. *The National Academies Press*. <https://doi.org/10.17226/27462>
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A Campaign for a Research Coordination Office for IACCIs

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