

State of Knowledge, Emerging Research Needs & Canadian Research Landscape for Post COVID-19 Condition

**Dr. Jane Rylett, Scientific Director
CIHR Institute of Aging**



Discoveries for life / Découvertes pour la vie



Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

Canada

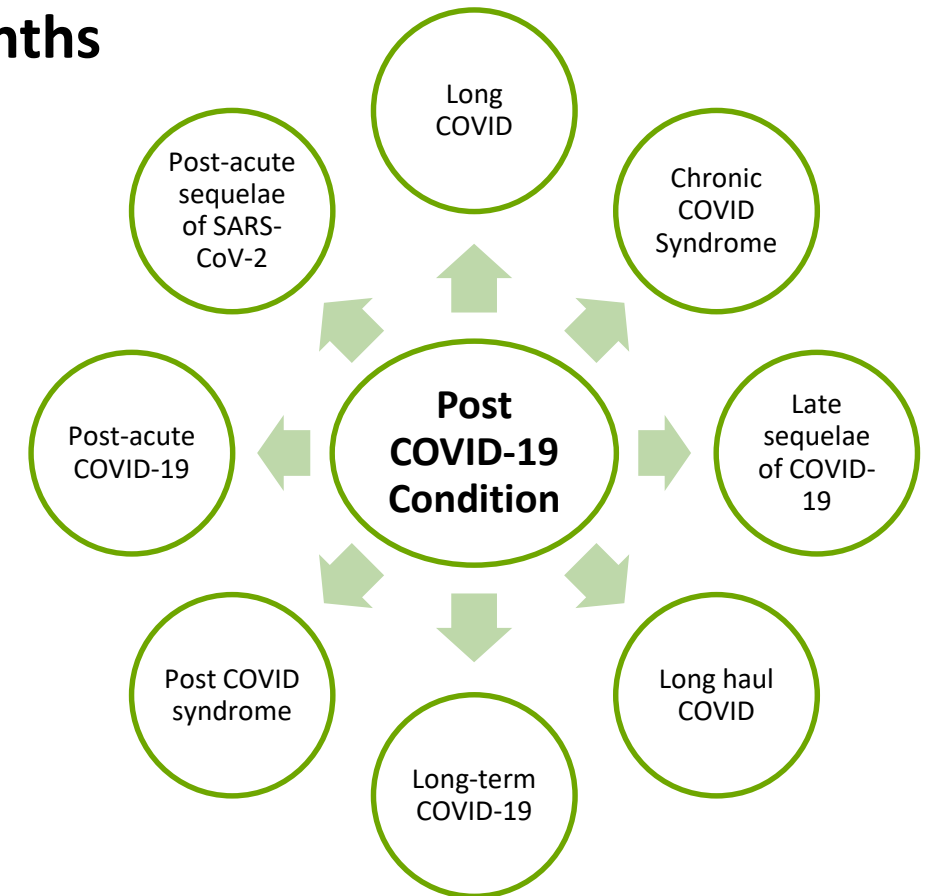
Defining Post COVID-19 Condition

Chronic effects of COVID-19 can last from weeks to months following acute infection

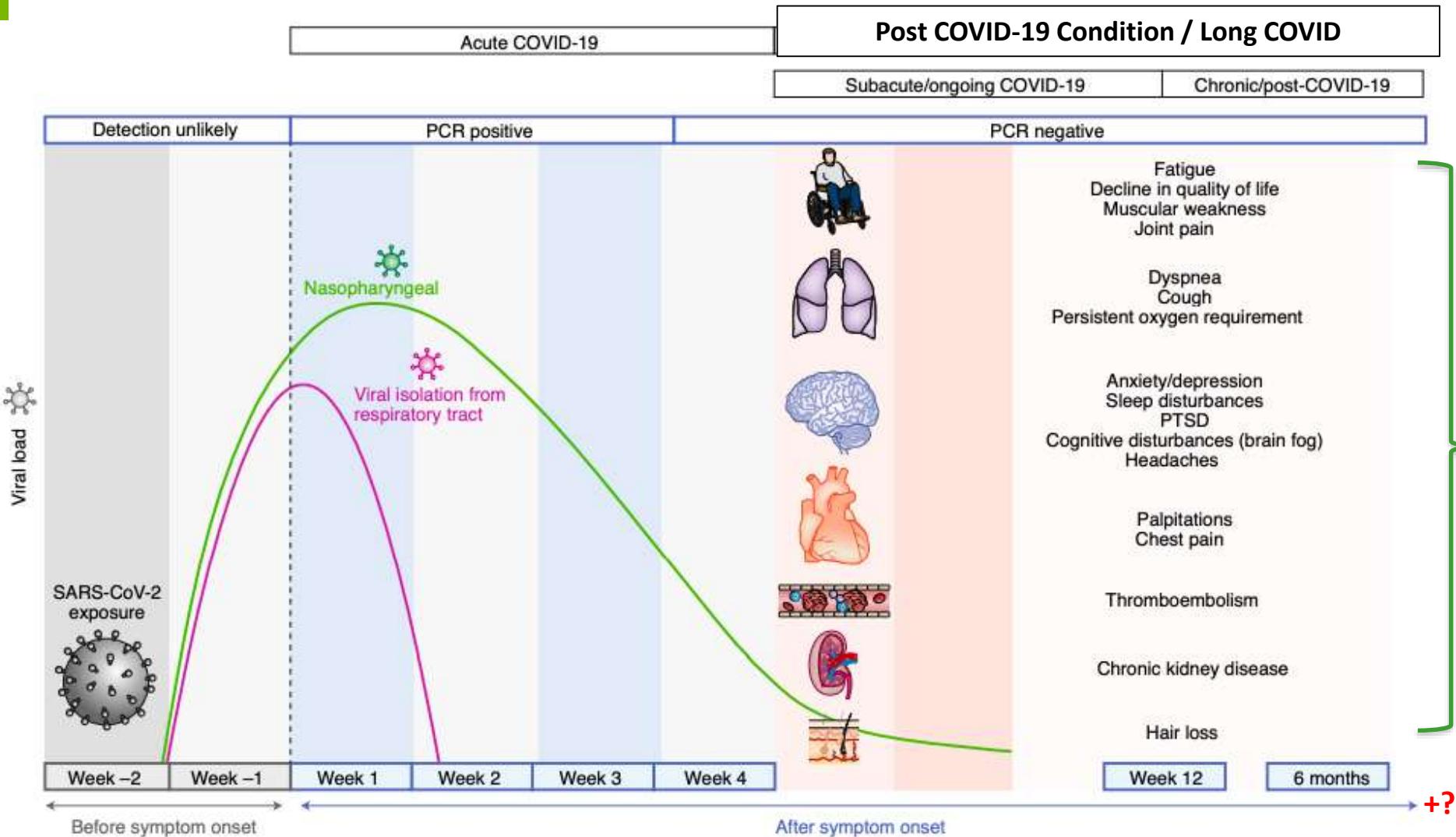
- Originally termed **Long COVID** by patient groups
- Associated with **the persistence of a range of heterogenous symptoms impacting different organ systems post-acute infection**

**Updated terminology proposed by the WHO:
Post COVID-19 Condition**

- Does not attribute causality or refer to duration



COVID-19 Timeline



Common symptoms across multiple organ systems

- ACE2 receptor is expressed by different organs (binds to SARS-CoV-2)

Unclear for how long symptoms will continue to manifest

Adapted from: Nalbandian, A et al. *Nat Med.* 2021 Mar 22.

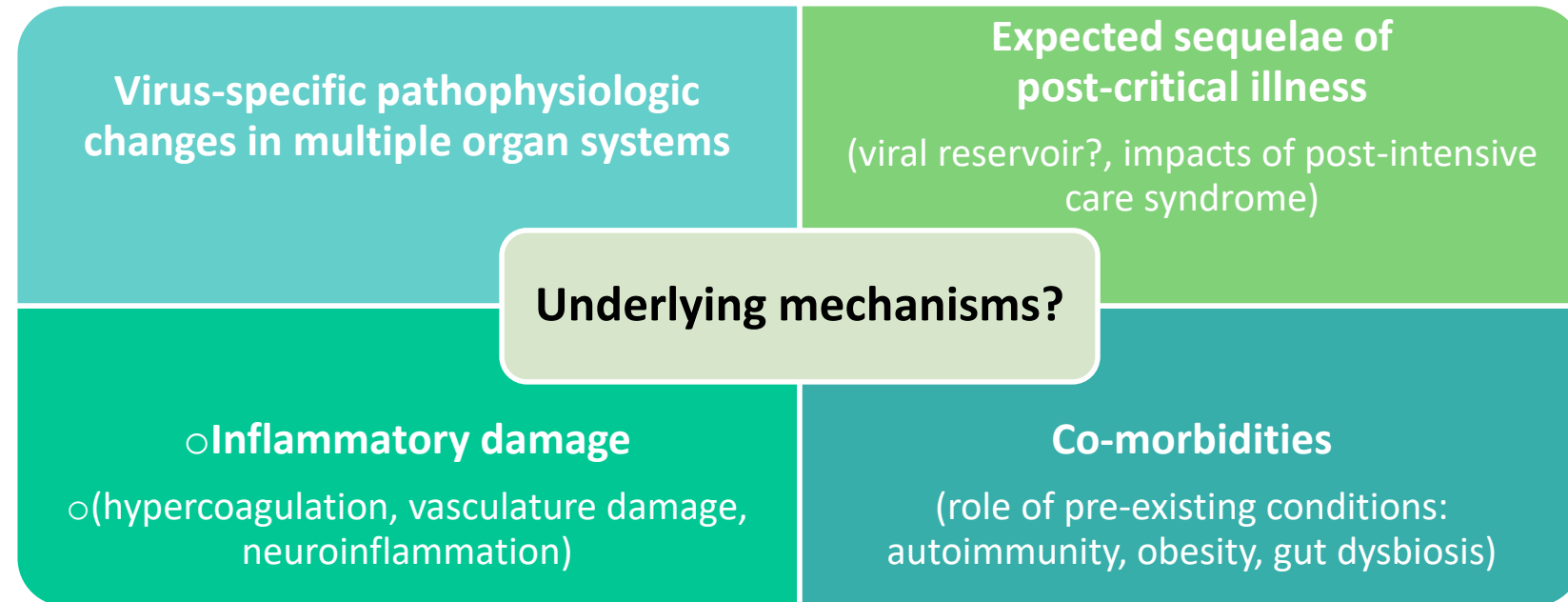
Current Knowledge & Existing Gaps



Pathophysiology

Underlying pathophysiology = unknown

- Several factors may be contributing to the post COVID-19 condition^{1,2,3,4,5}



Major gap: No clear biological mechanism to explain disease onset

→ Urgent need to understand the underlying biological mechanisms

1. Sudre CH, et al. *Nat Med*. 2021 Mar 10.
2. Taquet M, et al. *Lancet Psychiatry*. 2021 May.
3. Donati Zeppa S, et al. *Front Cell Infect Microbiol*. 2020 Nov 26.
4. Song WJ, et al. *Lancet Respir Med*. 2021 May.
5. Silva Andrade B, et al. *Viruses*. 2021 Apr 18

Diagnosis

Limited number of clinical studies report ~2%-80% of patients have symptoms for >12 weeks^{1,2,3,4}

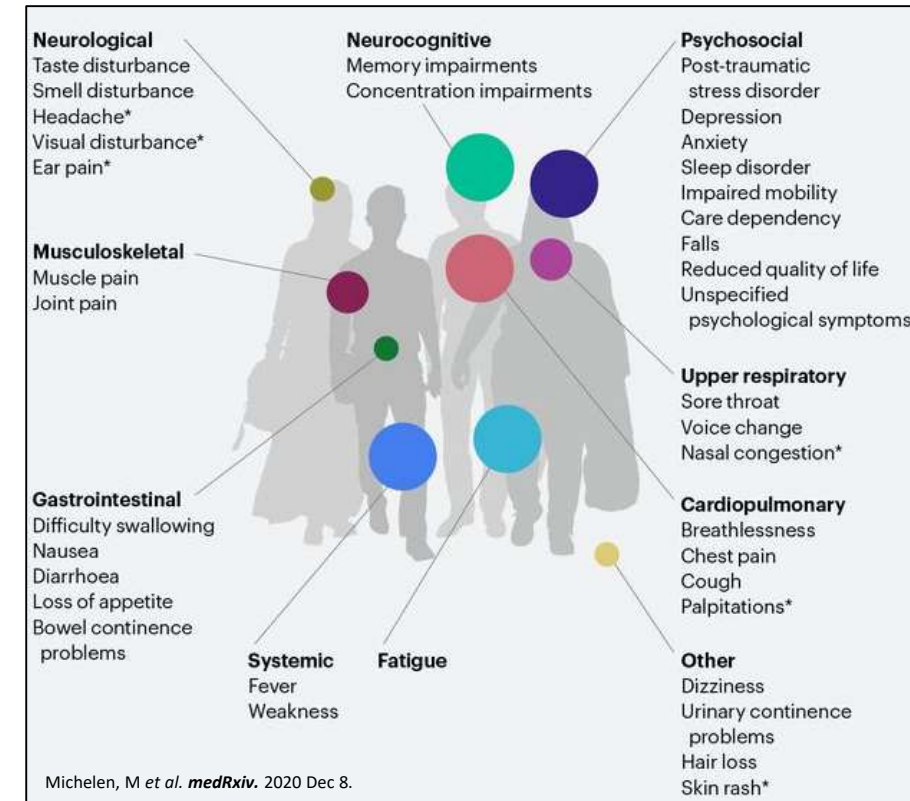
- No standardized diagnostic criteria: unclear how to manage patients without PCR+ or antibody+ test results for SARS-CoV-2 and those who were not initially diagnosed

Heterogenous symptoms which fluctuate in intensity & frequency and are **similar to chronic fatigue syndrome and other post-viral conditions** (e.g. Epstein-Barr)¹ making diagnosis more challenging

Major gap: No standardized clinical definition

→ Urgent need for a working diagnosis to facilitate access to care

The WHO has developed a **Global Clinical Platform & Case Report Forms (CRF)** to facilitate harmonized assessment & data collection



1. Lopez-Leon S, et al. *Res Sq*. 2021 Mar 1.
2. Nalbandian A, et al. *Nat Med*. 2021 Mar 22.
3. Sudre CH, et al. *Nat Med*. 2021 Mar 10.
4. Chevinsky JR, et al. *Clin Infect Dis*. 2021 Apr 28.

Clinical Management & Rehabilitation

Current approach = symptom management rather than multidisciplinary care

- Involves consultations with multiple specialists and puts emphasis on self-management

Major gap: No standardized clinical management strategy

- Urgent need for coordinated, multidisciplinary, multispecialty approaches for assessment & care
- Need to identify effective therapeutics & drugs
 - **Role for vaccines** in managing symptoms?
Preprint: 23.2% of highly symptomatic patients (n=44) had **an increase in symptomatic resolution** following vaccination with an mRNA vaccine¹
- Need heterogeneity in care for diverse patient groups

Canada has some dedicated clinics (need more!)

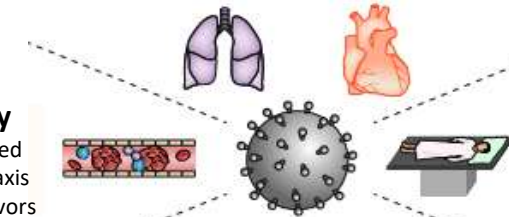


Types of multidisciplinary care needed

Pulmonary/cardiovascular

Symptom assessment (virtual or in-person) & follow-up at 4-6 and 12-weeks post-discharge

Consider 6MWT, PFT, chest X-ray, PE work-up, echocardiogram & HRCT of the chest as indicated



Hematology

Consider extended thromboprophylaxis for high-risk survivors

Neuropsychiatry

Screening for anxiety, PTSD, sleep disturbances and cognitive impairment



Renal

Early follow-up with nephrologists after discharge

Primary Care

Consideration of early rehabilitation
Patient education
Consider enrollment in research studies
Active engagement with patient advocacy groups

Modified from: Nalbandian, A *et al. Nat Med.* 2021 Mar 22.

Prevention

Hard to predict who will develop post-COVID-19 complications

- Development & severity **do not always correlate** with the extent and nature of **acute infection**

Limited studies suggest **more likely to develop in those who:**

- Were hospitalized during acute infection; have pre-existing respiratory disease; are older; are female; have other co-morbidities; have higher BMI^{1,2,3}

Major gap: No preventative strategies or prognostic markers

- Need to identify specific biomarkers or genetic host factors that can act as predictors
- Need studies to determine if treatment during acute phase is preventative
- Need studies to determine risk in specific groups
 - Hospitalized vs. non-hospitalized, severe vs. mild, symptomatic vs. asymptomatic, Indigenous people, women, racialized people, **children**, elderly, low socio-economic communities, LMICs

1. Puntmann VO et al. *JAMA Cardiol.* 2020 July 27.

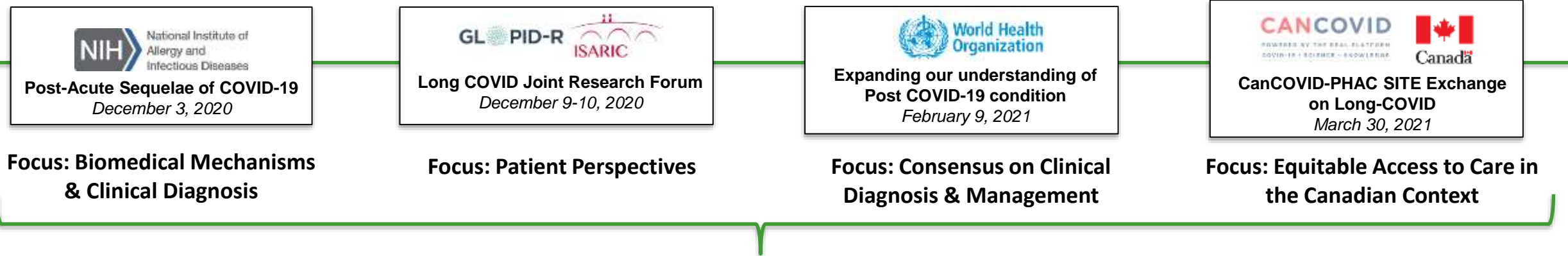
2. Nalbandian A, et al. *Nat Med.* 2021 Mar 22.

3. Goërtz YMJ et al. *ERJ Open Res.* 2020 Oct 26.

Research Priorities & Actions: Canada & Beyond



Knowledge Mobilization Activities



Common emerging themes:

Need: A globally **coordinated, multifaceted, multidisciplinary** research approach

Need: **Active patient engagement** → Patients have called for **recognition, rehabilitation & research**

- Numerous support groups have been created to **help articulate patient voices & facilitate patient engagement**
- Patients require a **holistic and equitable** approach in service provision (biomedical, mental, social & economic)



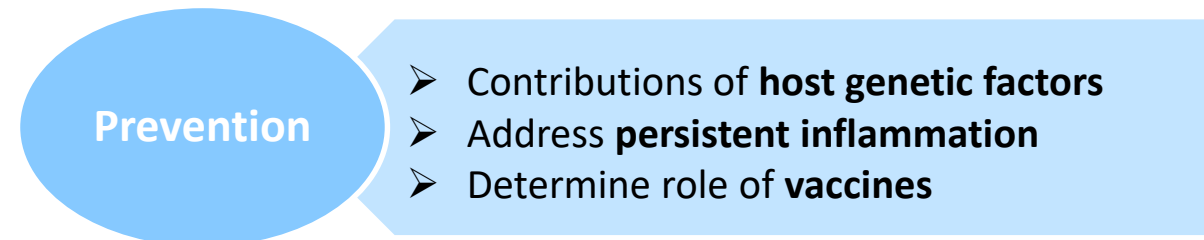
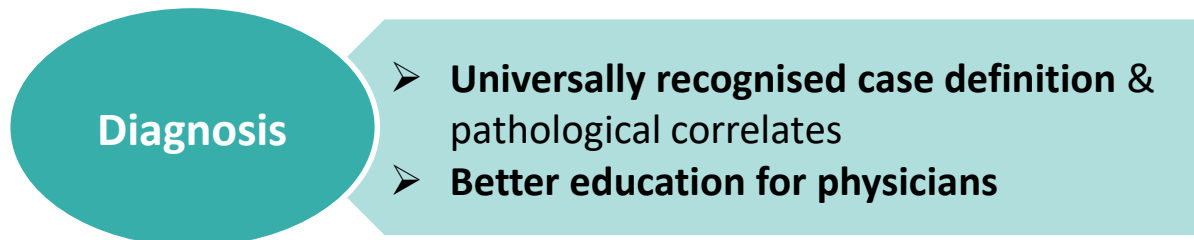
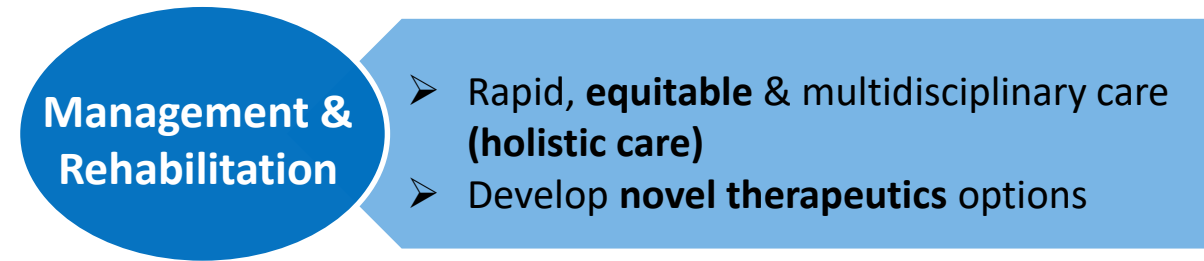
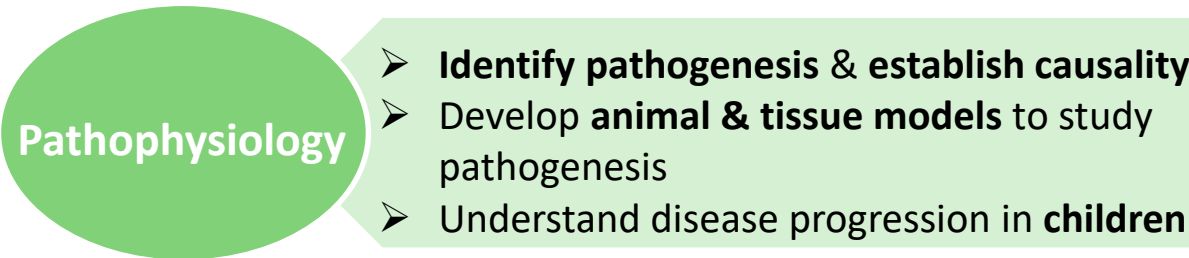
**June 10 2021 Post COVID-19 Condition CIHR Knowledge Mobilization Forum
(Bringing together researchers, patients and other key stakeholders)**



Emerging Research Priorities

Several research priorities have emerged from these knowledge mobilization activities^{1,2,3,4}

- Need for a **patient-centred approach**, with **controlled, longitudinal** cohort studies with **diverse patient groups** to track long-term outcomes using **standardized & harmonized** data collection



1. Andrea M, et al. *Ann Intern Med.* 2021 Mar 20; 2. Norton A, et al. *Lancet Infect Dis.* 2021 May; 3. Carson G, et al. *BMC Med.* 2021 Mar 31; 4. Herridge et al. Pre-print. 2021.

CIHR-Funded Research

CIHR COVID-19 Rapid Research Funding Opportunity (May 2020)

- Over **10 projects** (~\$14M funding) **directly examining long-term implications** of SARS-CoV-2 infection
 - Other large funded networks / projects may also be able to examine long-term impacts

Cohort Studies

- Capture data & biologics to enable **population-level surveillance**
- **Up to 1 year** of follow-up (*CanCOV*)
- Patients with **suspected or confirmed COVID-19** (*Emergency Department Rapid Response Network*)
- Use of **AI technologies** to track outcomes (*CovidFree@home*)
- **Pregnancy cohorts** to understand impact on **mother & infant health** (*CHILD; COPE*)

Clinical Management & Rehabilitation

- Study the **functional recovery** & need for **targeted rehabilitative treatments**
- Large platform (*COREG*) to **collect outpatient case data for up to 9 months** (collaboration with WHO)

Long-term Impact on Organ Systems

- Imaging systems to determine impact on **lungs** & other organs (*MOIST*)
- Imaging systems to examine **neuroinflammation** & associated development of **mental illnesses**
- Measure impact on **cognitive function, brain structure, and brain function** in elderly (*CLSA*)

Predictive Markers

- Link **serological, genomic and patient characteristics** to long-term disease outcomes

Dedicated Canadian & Global Research Actions

CIHR

- **Emerging COVID-19 Research Gaps and Priorities Funding Opportunity (March 2021):** Specific research area focused on **identifying, defining & addressing** the post-COVID-19 condition to understand the **biological & psychological impacts** (*funding decisions expected in June 2021*)

NIHR & UKRI

- Previous calls: **~£25M to better understand long term effects of COVID-19 on physical & mental health**
- Current call: **~£20M focused on non-hospitalised adults & children with post-COVID-19 condition**
 - Therapies and Interventions; Management & Evaluation of Services; Diagnostics; Other topics

NIH

- **Post-Acute Sequelae of SARS-CoV-2 Infection Initiative (NIH PASC): \$1.15B/4 years**
- Focus: Understand the **biological basis** of PASC & **factors contributing to vulnerability**
 - Current call: SARS-CoV-2 Recovery Cohort Studies; Clinical Science, Data Resource & PASC Biorepository Cores

Thank you!



CIHR IRSC

Canadian Institutes of Health Research Instituts de recherche en santé du Canada