POST-COVID SYNDROME AND NEUROCOVID RESEARCH PROTOCOL

Ludivine Witkowski

Neurologist, clinician researcher, Ass. Prof.

New Brunswick Internal Medicine Update - April 22nd, 2021

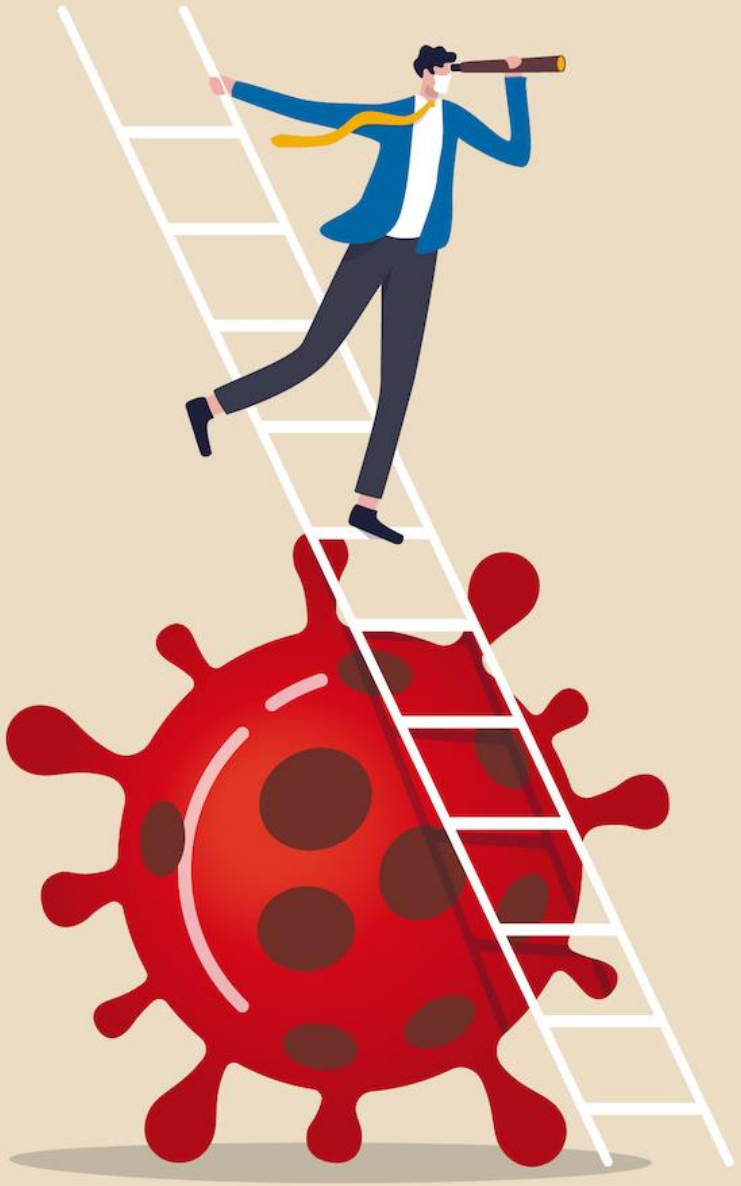
CONFLICTS OF INTEREST

- I have received a grant from the Centre de Formation Médicale du Nouveau-Brunswick for a research protocol about the long term cognitive deficits after Covid-19 infection.

PROGRAM

- 1. Definition
- 2. Incidence and risk factor
- 3. Symptoms
- 3. Hypothetic causes
- 5. Neurocovid-19 protocol
- 6. Take home messages

I. DEFINITION



TERMINOLOGY

- Also known as:
  - Post-acute sequelae of SARS-CoV-2 infection
  - Post-acute sequelae of COVID-19 (PASC)
  - Chronic COVID syndrome
  - Long-haul COVID

- Unprecise duration of symptoms is heterogeneous from 6 weeks to 6 months
- Usual duration is **12 weeks**

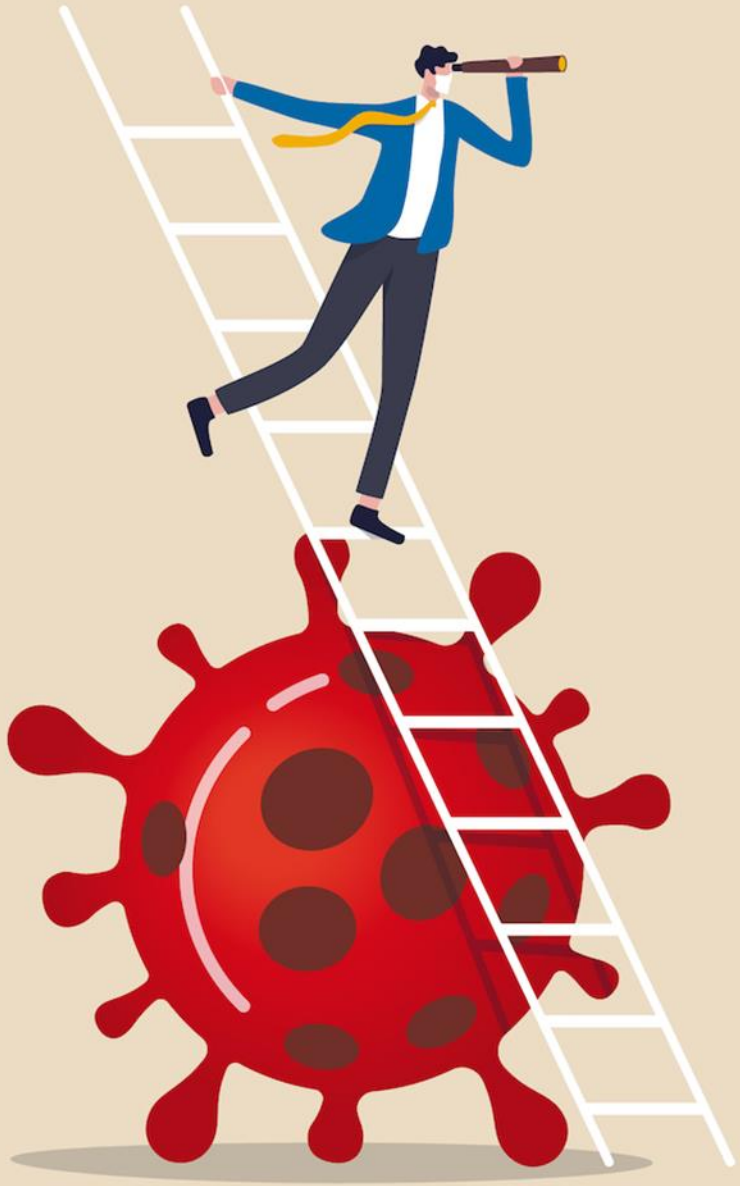
NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (NICE)

- **Acute COVID-19:** during the first **4 weeks**
- New or ongoing symptoms 4 weeks or more after, which is divided into:
  - **Ongoing symptomatic COVID-19** for effects from **4 to 12 weeks**
  - **Post-COVID-19 syndrome** for effects that persist **12 or more weeks** after onset

WIDE RANGE OF SYMPTOMS

- Including:
  - Fatigue
  - Headaches
  - Shortness of breath
  - Anosmia
  - Muscle weakness
  - Low fever
  - Cognitive dysfunction

INCIDENCE AND RISK FACTORS



INCIDENCE

- From 10 to 63 % depending of population and the duration definition
- Incidence declines over time
- **Among the general population:**
  - **20% and 33%** experienced symptoms lasting longer than a month.
  - **10%** experienced symptoms for longer than 12 weeks.

Office of National Statistics UK. Dec 2020.
Morbidity and Mortality Weekly Report, July 2020
The Guardian. Retrieved 28 December 2020.

- **Among the admitted population:**
  - Up to 80% of those who were admitted to the hospital experienced long-term problems including fatigue and shortness of breath.

ABC News. Oct 2020.

  - Bias because some could suffer from post-intensive care syndrome.
  - Among the 1733 patients followed six months after discharged, the most common symptoms were **fatigue or muscle weakness (63%), sleep difficulties (26%), and anxiety or depression (23%).**

The lancet. Jan 2021.

6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records

Lancet Psychiatry, april 2021 (UK)

Maxime Taquet, John R Geddes, Masud Husain, Sierra Luciano, Paul J Harrison

- **Primary cohort:** COVID-19 diagnosis and **2 control matched cohorts:** patients diagnosed with influenza and patients diagnosed with any respiratory tract infection
- **Outcomes:**
  - intracranial haemorrhage; ischaemic stroke; parkinsonism; Guillain-Barré syndrome; nerve, nerve root, and plexus disorders; myoneural junction and muscle disease; encephalitis; dementia; psychotic, mood, and anxiety disorders; substance use disorder; insomnia
- **Findings:**
  - **General population: incidence was 33%** (12% for a first diagnosis)
    - 0.56% intracranial haemorrhage, 2.10% ischaemic stroke, 0.11% parkinsonism, 0.67% dementia, 17% for anxiety disorder, and 1.40% for psychotic disorder.
  - **ICU patients: incidence was 46%** (25% for a first diagnosis)
    - 2.66% for intracranial haemorrhage, 7% for ischaemic stroke, 0.26% for parkinsonism, 1.74% for dementia, 19% for anxiety disorder, and 2.77% for psychotic disorder.

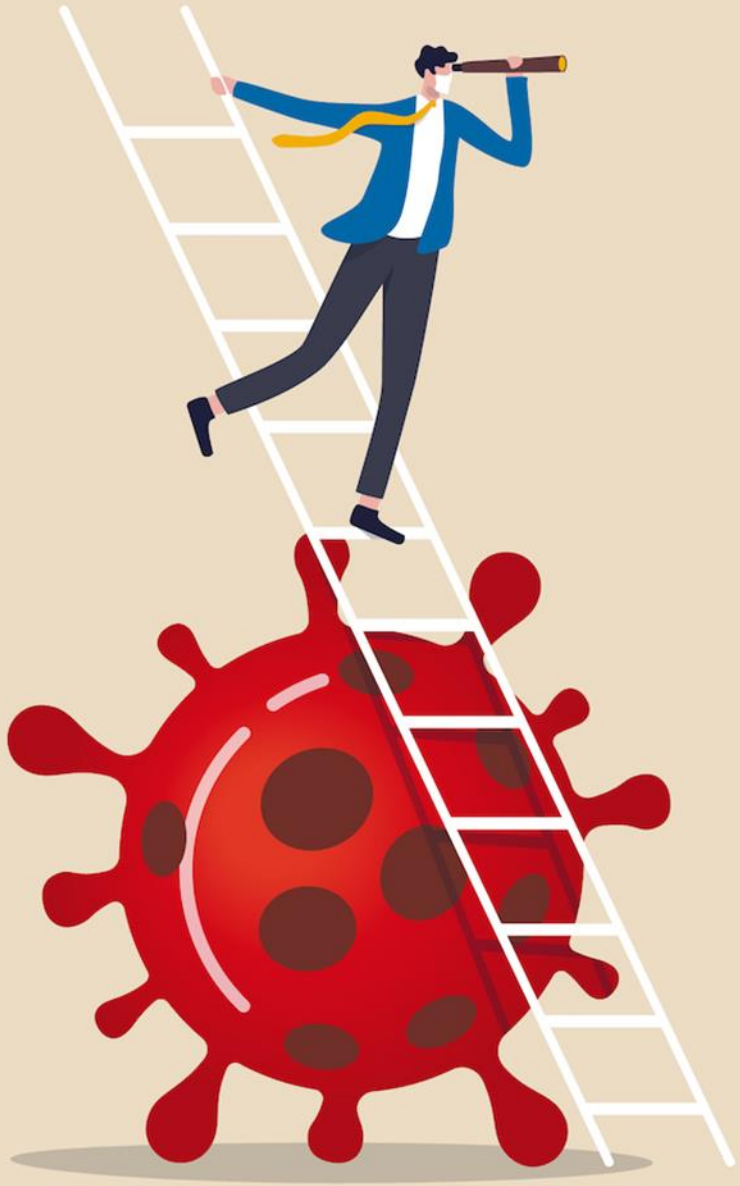
RISK FACTOR

- Risk factors for long COVID may include:
  - **Age** (particularly over 50)
  - **Excess weight**
  - **Asthma**
  - **Severe disease:**
    - Reporting more than five symptoms in the first week of COVID-19 infection
    - Hospitalization
    - ICU admission

- **Women** are less likely to develop severe acute COVID but more likely to develop long COVID than men

MedRxiv, December 2020.
Nature Medicine, Jan 2021

SYMPTOMS



NICE National Institute for Health and Care Excellence

Respiratory
Breathlessness
Cough

Cardiovascular
Chest tightness
Chest pain
Palpitations

Generalised
Fatigue
Fever
Pain

Neurological
Cognitive impairment (loss of concentration or memory issues)
Headache
Sleep disturbance
Peripheral neuropathy symptoms (pins and needles and numbness)
Dizziness
Delirium (in older populations)

Gastrointestinal
Abdominal pain
Nausea
Diarrhoea
Anorexia (in older populations)

Musculoskeletal
Joint pain
Muscle pain

Dermatological
Skin rashes

Psychiatric
Depression
Anxiety

Ear, nose and throat
Tinnitus
Earache
Sore throat
Dizziness
Loss of taste and/or smell

6-month consequences of COVID-19 in patients discharged from hospital: a cohort study

The Lancet, January 2021

Chaolin Huang*, Lixue Huang*, Yeming Wang*, Xia Li*, Lili Ren*, Xiaoying Gu*, Liang Kang*, Li Guo*, Min Liu*, Xing Zhou, Jianfeng Luo, Zhenghui Huang, Shengjin Tu, Yue Zhao, Li Chen, Decui Xu, Yanping Li, Caihong Li, Lu Peng, Yong Li, Wuxiang Xie, Dan Cui, Lianhan Shang, Guohui Fan, Jiuyang Xu, Geng Wang, Ying Wang, Jingchuan Zhong, Chen Wang, Jianwei Wang†, Dingyu Zhang†, Bin Cao†

- At 6 months after acute infection, COVID-19 survivors were mainly troubled with:
  - **fatigue or muscle weakness** (63%),
  - **sleep difficulties** (26%),
  - **anxiety or depression**(23%).

- Patients who were more severely ill during their hospital stay had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestations.

Received: 3 November 2020 | Revised: 13 November 2020 | Accepted: 16 November 2020

DOI: 10.1111/apa.15673

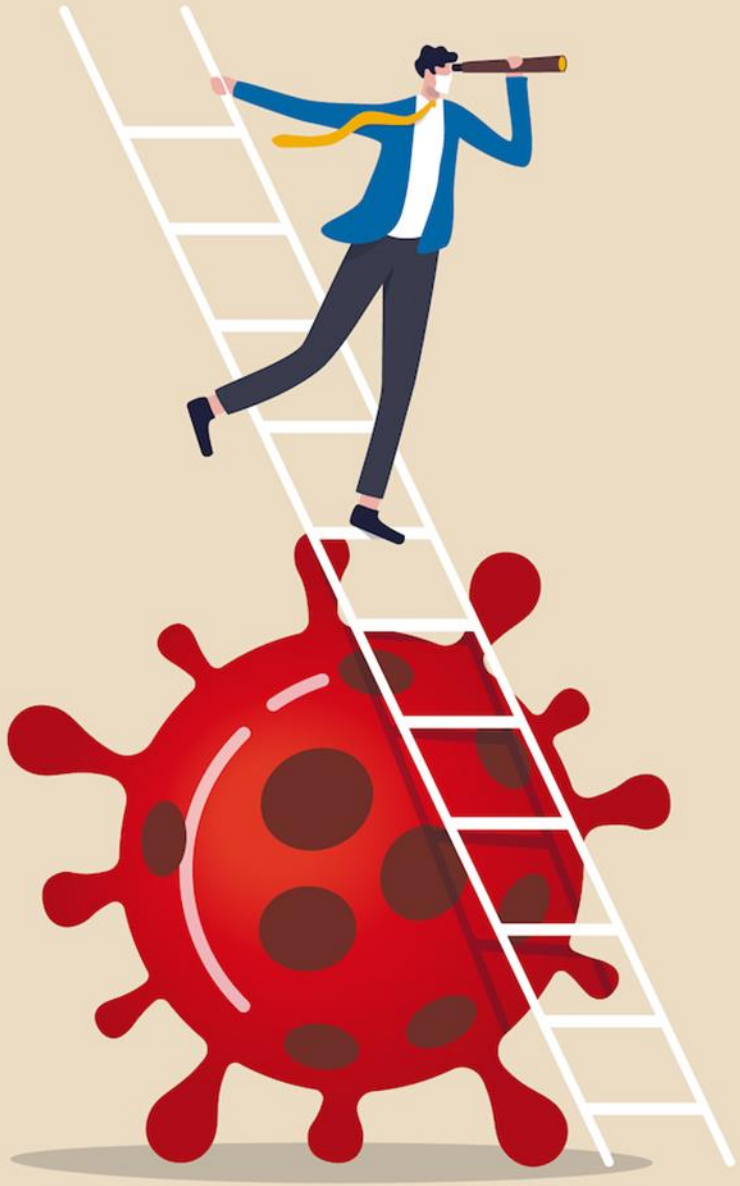
REGULAR ARTICLE

ACTA PÆDIATRICA
NURTURING THE CHILD
WILEY

Case report and systematic review suggest that children may experience similar long-term effects to adults after clinical COVID-19

- 5 children with potential long COVID (range 9–15 yo) and four were girls.
- They had symptoms for 6–8 months after their clinical diagnoses of COVID-19. None were hospitalized at diagnosis, but one was later admitted for peri-myocarditis.
- All 5 children had **fatigue, dyspnea, heart palpitations or chest pain**
- 4 had **headaches, difficulties concentrating, muscle weakness, dizziness and sore throats.**
- The systematic review identified 179 publications and none contained any information on long COVID in children.

HYPOTHETICAL CAUSES



CONFOUNDING

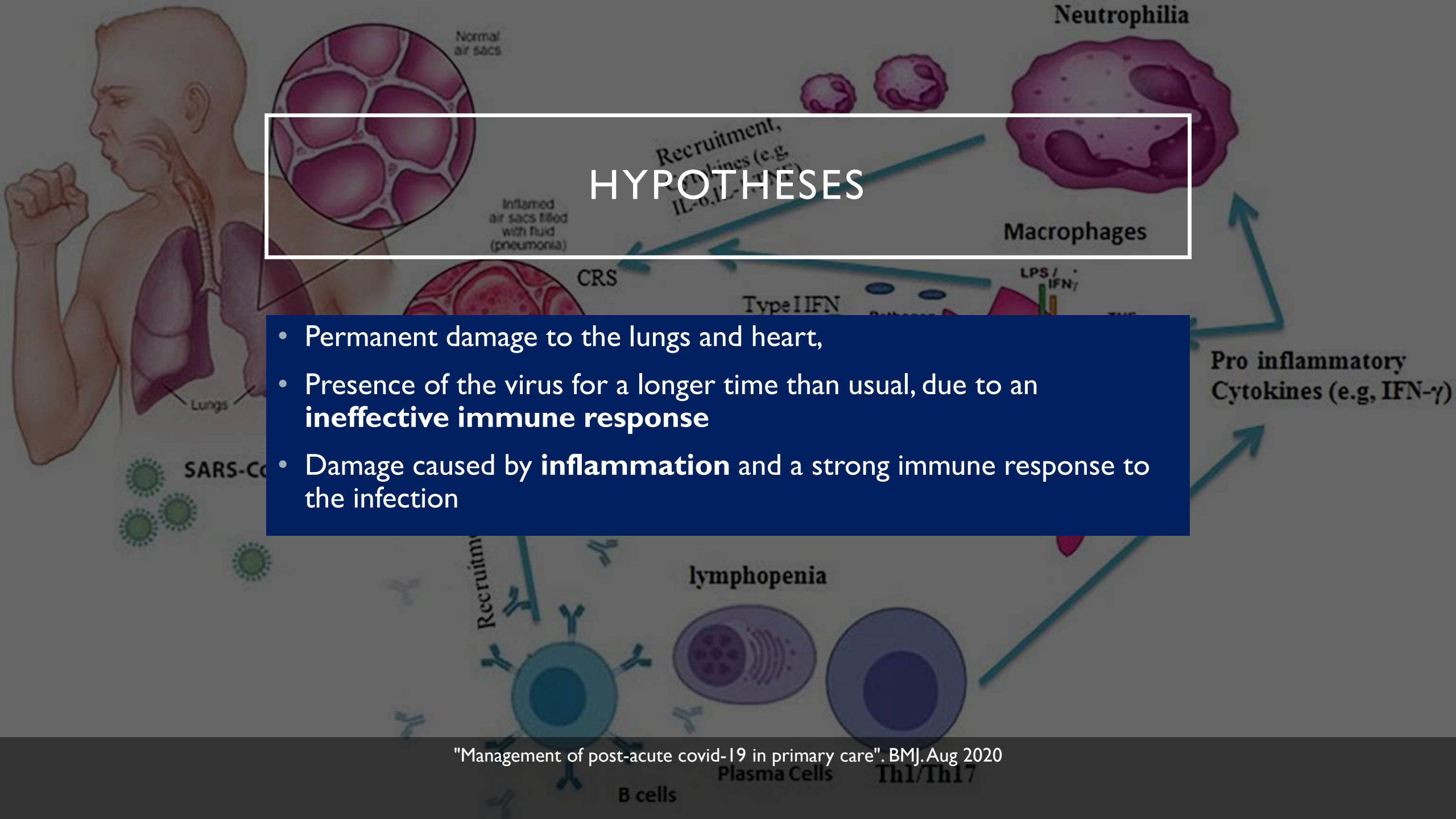
- It is unknown why most people recover fully within two to three weeks while others develop post-Covid syndrome.

- **Confounding factors:**
  - Post-intensive care syndrome,
  - Post-viral fatigue,
  - Reinfection (e.g., with another strain of the virus),
  - Physical deconditioning due to a lack of exercise while ill,
  - Post-traumatic stress.

National Institute for Health Research. October 2020
BMJ, aug 2020

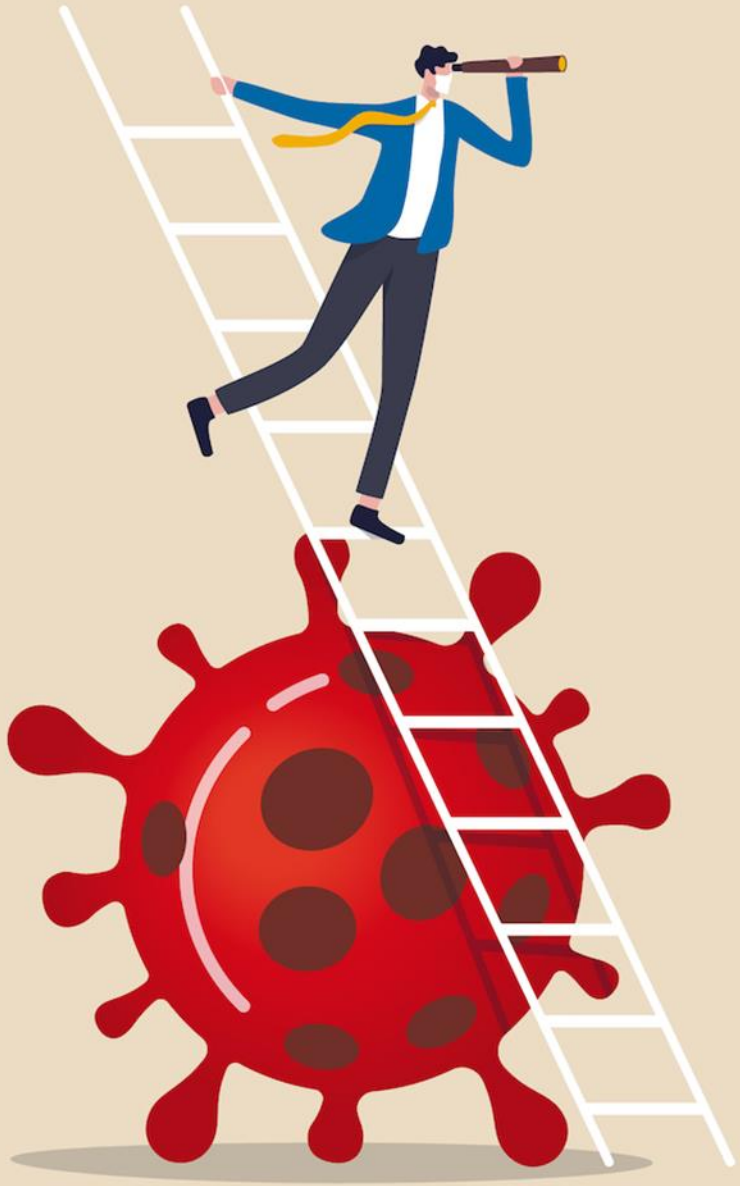
HYPOTHESES

- Permanent damage to the lungs and heart,
- Presence of the virus for a longer time than usual, due to an **ineffective immune response**
- Damage caused by **inflammation** and a strong immune response to the infection



"Management of post-acute covid-19 in primary care". BMJ. Aug 2020

NEUROCOVID-19 RESEARCH PROTOCOL



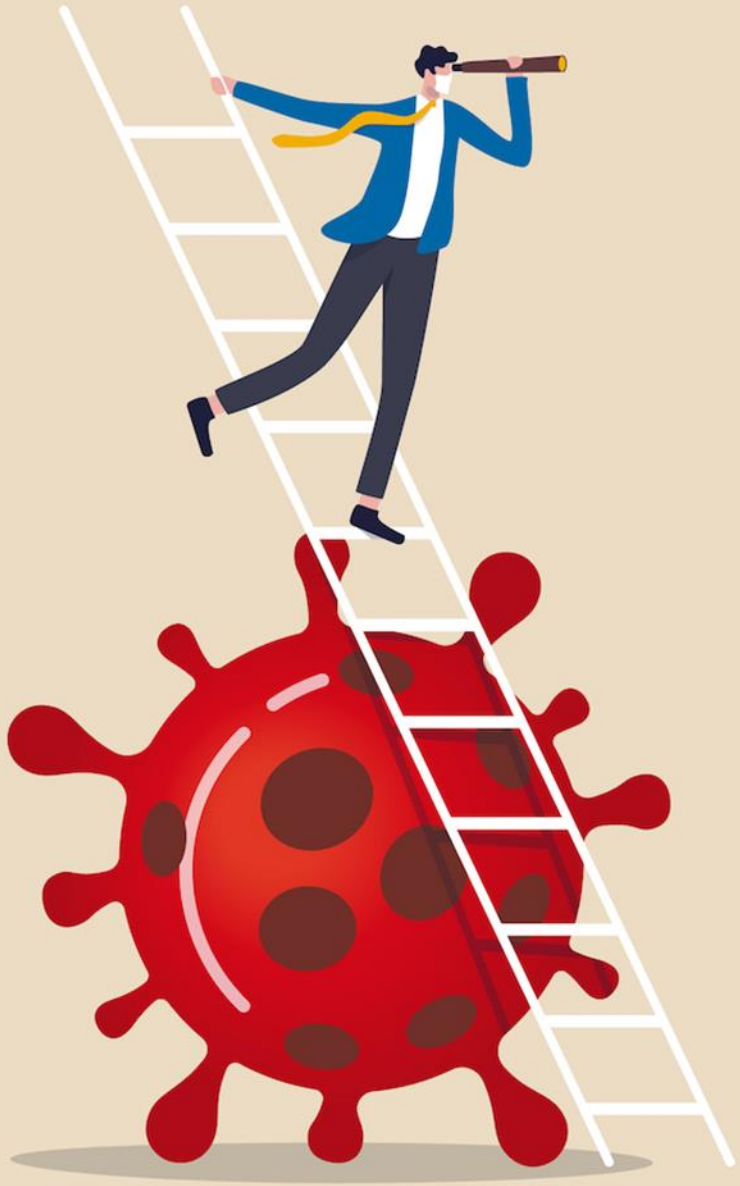
NEUROCOVID-19 RESEARCH PROTOCOL

- PI: L. Chamard-Witkowski and J. Jbilou, Co-PI: M-C. Losier, G. Girouard, E. Libert, Z. Beroual

- Research protocol in Dumont Hospital, granted by CFMNB
- **Demographic, health history, psychologic** and **cognitive** testing by phone 12 weeks or more after Covid-19 infection in NB
- 50 patients included for now
- Objective: describe **cognitive dysfunction** in post-Covid syndrome patients and find **risk factors**
- If your patient wants to attend:
  - Call **869 - 7211** and leave a message along with contact information

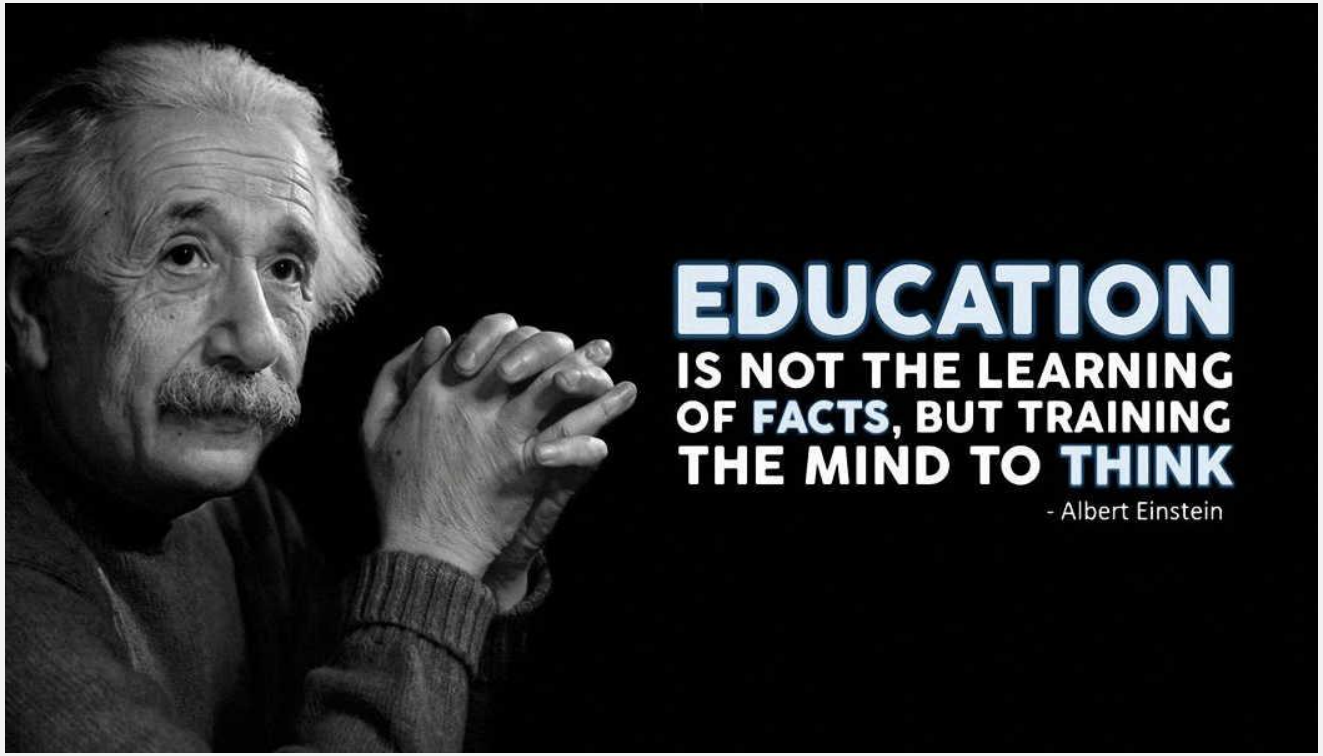
CENTRE DE FORMATION MÉDICALE
DU NOUVEAU-BRUNSWICK

TAKE-HOME MESSAGES



TAKE-HOME MESSAGES

- Post-Covid syndrome is **still unclear**
- Admitted: ongoing symptoms still present **12 weeks** after acute infection
- **Principal symptoms:**
  - Fatigue, shortness of breath, cognitive dysfunction, sleep disorders, intermittent fevers, gastrointestinal symptoms, anxiety and depression.
- **Neuropsychiatric third wave ?** Incidence of 33%...
- Risk factors:
  - **Age, excess weight, asthma, severe acute infection**



- Importance of **planning intervention** of long-term recovery for main target population
- Importance of **vaccination**