

# NEEDS AND FOLLOW-UP OF LONG-TERM COVID-19 PATIENTS

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# What is long COVID?

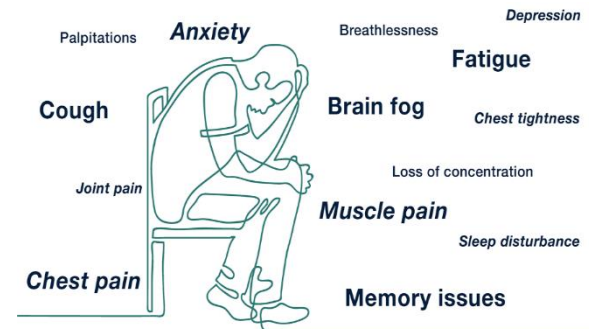
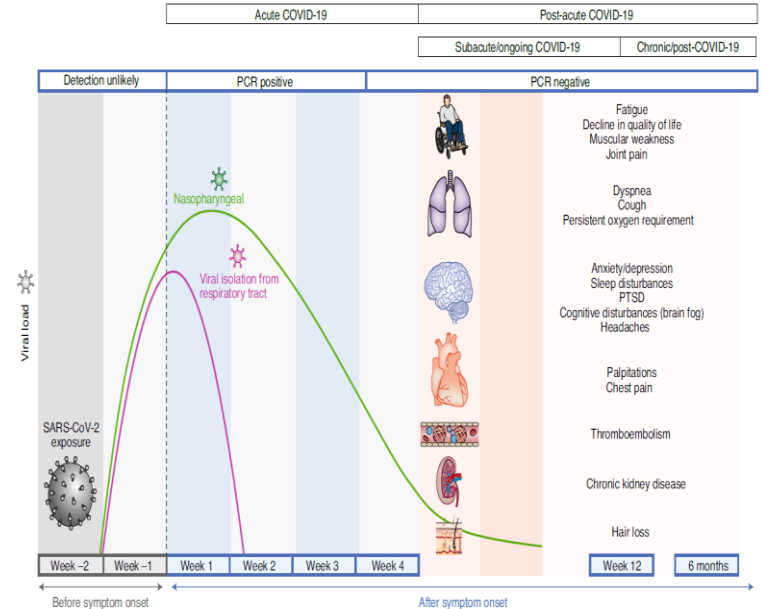
**ACUTE COVID-19**  
Recovery within 2 weeks



## LONG COVID

Signs and symptoms that develop during or after an infection consistent with COVID-19 and continue  $\geq 4$  weeks and are not explained by an alternative diagnosis:

- ❑ Ongoing symptomatic COVID-19: 4 to 12 weeks after infection)
- ❑ Post-COVID-19 syndrome:  $\geq$  than 12 weeks after infection



# KCE study: scope and approach

## I. DEFINITION, EPIDEMIOLOGY & PATHOPHYSIOLOGY LONG COVID

Pragmatic review (January 2021)



Systematic review – intermediate report  
(May and June 2021)



Systematic review – KCE report (October 2021)

## II. UNMET NEEDS

Patients with long COVID: survey – forum -  
interviews

Analysis current legislation & reimbursement rules

## III. KCE WEBPAGE

Intermediate report of literature review

Initiatives from abroad (NICE, HAS, ...)

Clinical studies about treatment (selection of high-quality studies)



# I. Systematic review: pathophysiology (May 2021)

- **Two types of publications**
  - Hypothesis underlying mechanisms
  - Patient data (e.g. medical imaging, blood sample analysis, autopsy)
- **Two categories:**
  - Organ injury at the early phase of infection;
  - Persisting and/or residual symptoms without evidence of readily measurable markers of organ injury.
- **Pathophysiological mechanisms:**
  - Virus-driven tissue damage
  - Dysregulated immune and inflammatory reactions in response to the infection, giving rise to multiple disorders (microcirculation disorders associated with coagulation and fibrosis pathway activation, auto-immune manifestations and metabolic disturbances)
- **But ... predominantly hypothesis based and many uncertainties remain**

# I. Systematic review: pathophysiology (May 2021)

## ■ Current findings from studies involving long COVID patients:

Systems	Mechanisms
Central nervous system	<ul style="list-style-type: none"><li>▪ Brain hypometabolism</li><li>▪ Brain inflammation</li></ul>
Smell/taste	<ul style="list-style-type: none"><li>▪ Neuroepithelial inflammation</li></ul>
Cardiovascular	<ul style="list-style-type: none"><li>▪ Macro and microvascular inflammation</li><li>▪ Endothelial dysfunction</li></ul>
Immune	<ul style="list-style-type: none"><li>▪ Multi-organ inflammation ([18F]FDG PET/CT , MRI)</li><li>▪ T-cell abnormalities</li></ul>
Respiratory	<ul style="list-style-type: none"><li>▪ Biomarkers of inflammation and fibrosis</li><li>▪ Persisting pulmonary inflammation</li></ul>
Gastro-intestinal	<ul style="list-style-type: none"><li>▪ Alterations of microbiota</li></ul>
Dermatological	<ul style="list-style-type: none"><li>▪ Vasculitis, leucocytes infiltration, microthrombi</li></ul>

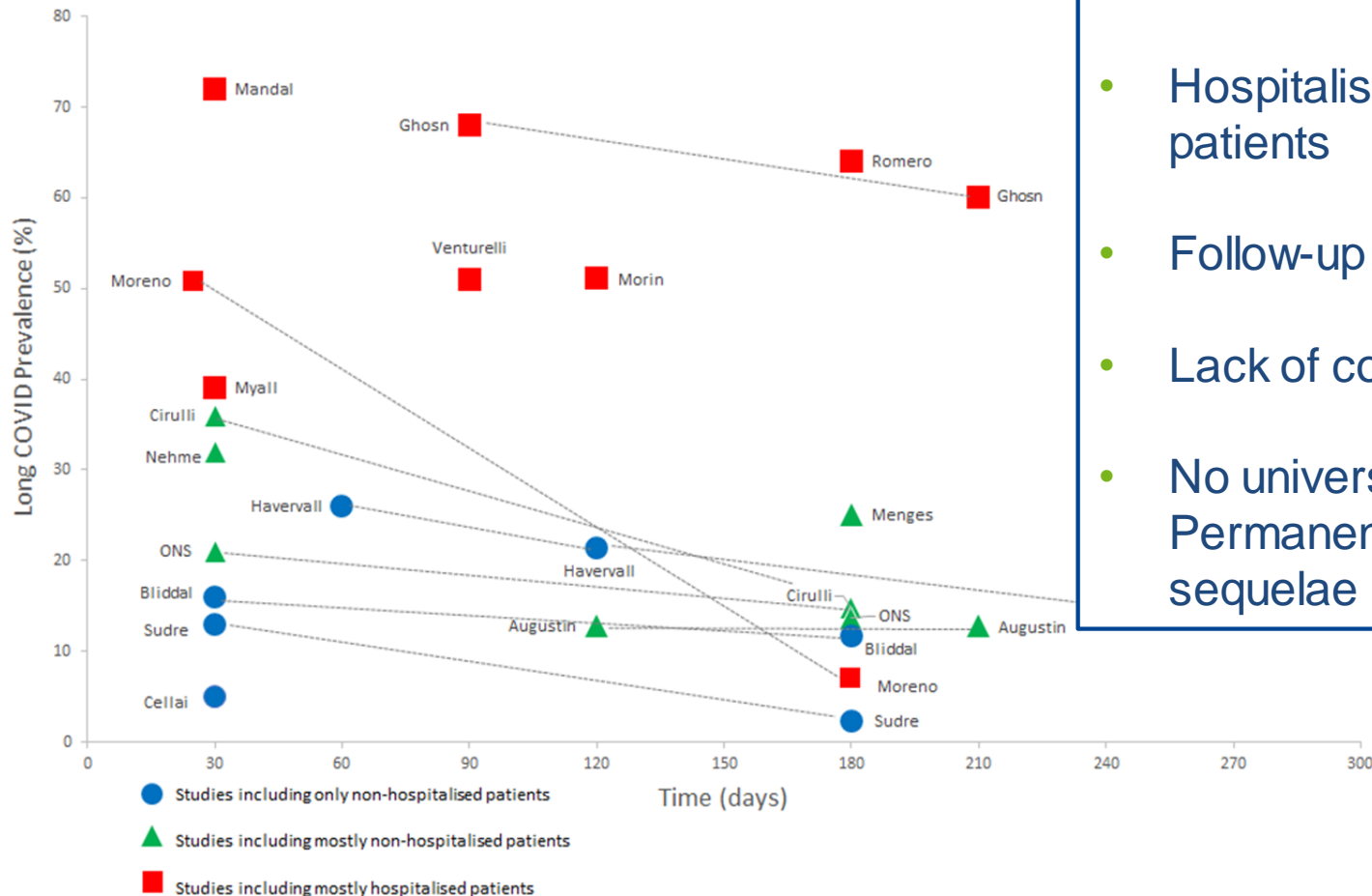
# I. Systematic review: pathophysiology (May 2021)

## Limitations of studies:

- Small sample sizes
- Initial severity highly variable
- Variability of symptoms
- Timing of inclusion
- Healthy volunteers used as control group
- Difficulty to appraise specific mechanisms

## II. Systematic review: Epidemiology (June 2021)

### ESTIMATION OF PREVALENCE IS VARIABLE

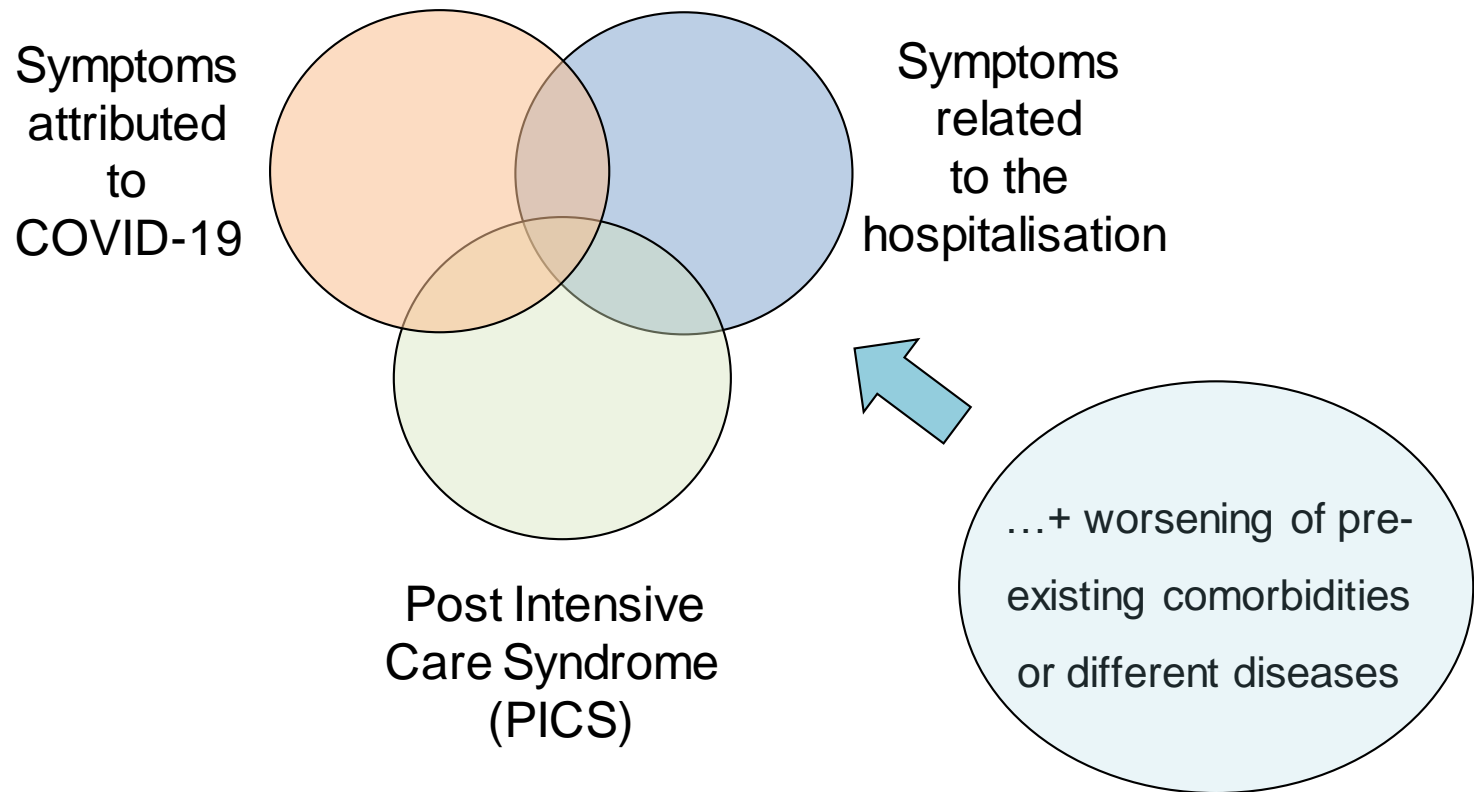


### STUDIES ARE HETEROGENEOUS

- Hospitalised and ambulatory patients
- Follow-up time variable
- Lack of control group
- No universal definition. Permanent organ damage as sequelae

## II. Systematic review: Epidemiology (June 2021)

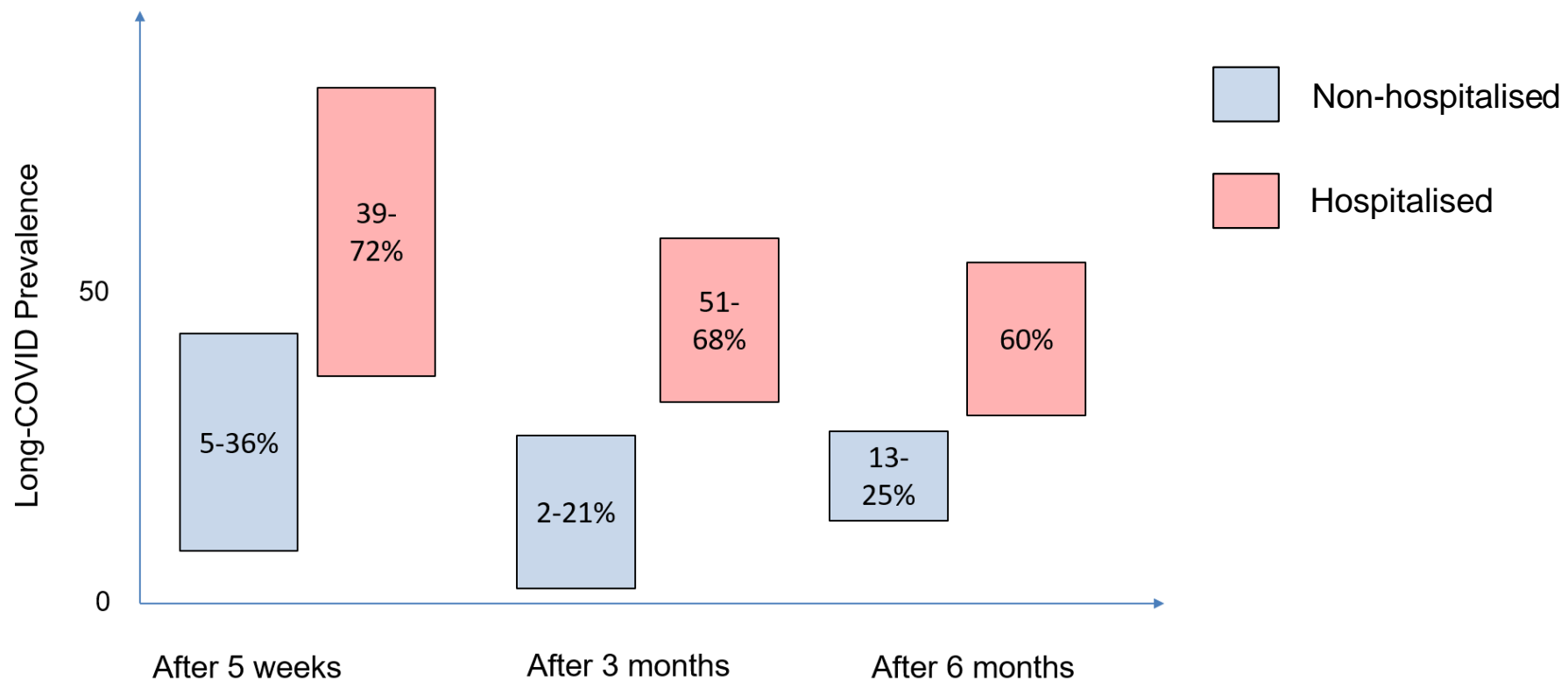
- Possible overlap of different issues:





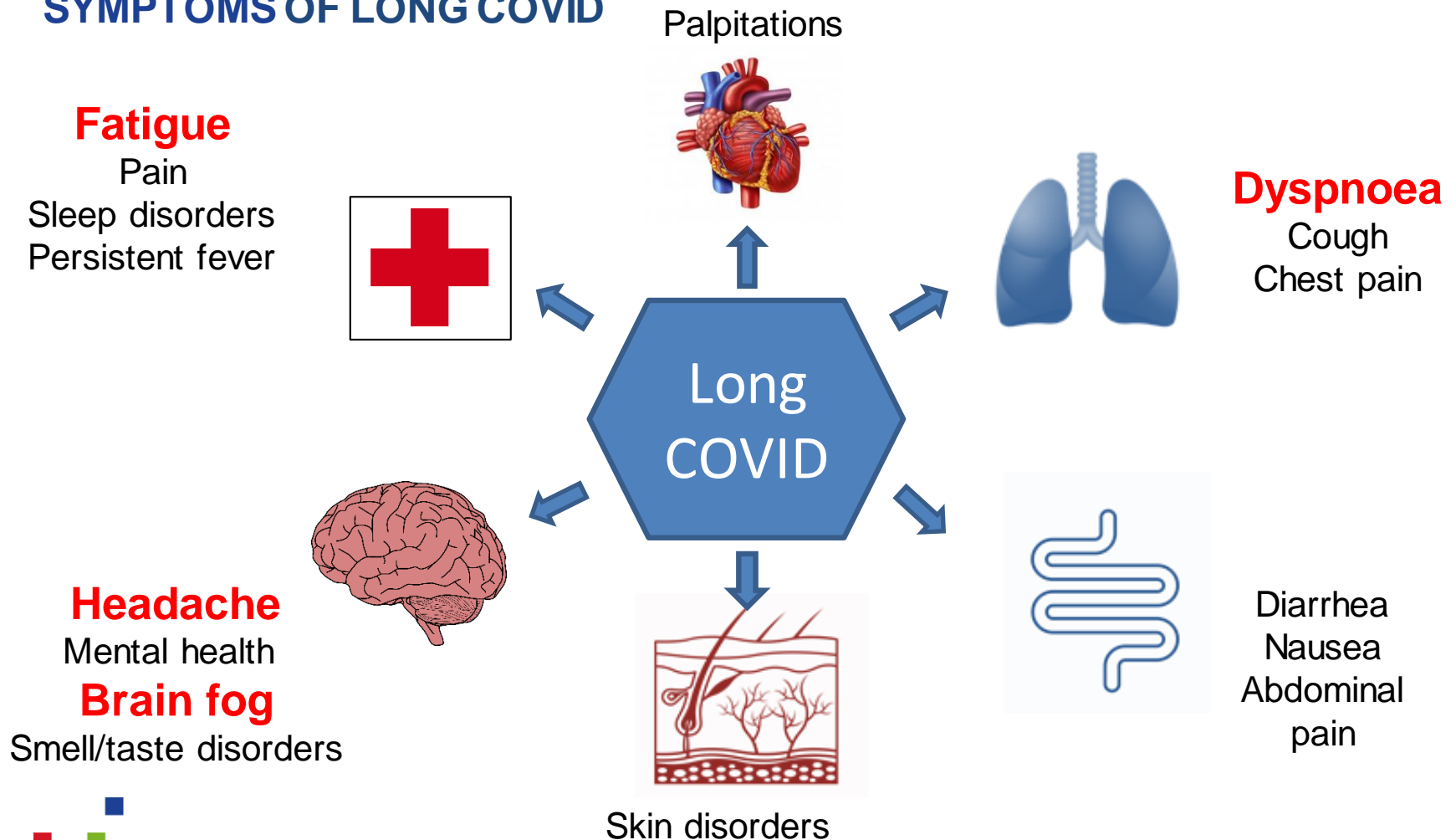
## II. Systematic review: Epidemiology (June 2021)

At 6 month follow-up, at least 10% of patients still present one or several symptoms



## II. Systematic review: Epidemiology (June 2021)

### SYMPTOMS OF LONG COVID



## II. Systematic review: Epidemiology (June 2021)

### RISK FACTORS OF LONG COVID

- Up to now, no reliable evidence for long COVID risk factors



## II. Systematic review: Epidemiology (June 2021)

### LIMITATIONS OF CURRENT EVIDENCE

- ❑ Lack of consistent definition of long COVID
- ❑ Heterogeneity of targeted population
- ❑ Study design variability (time of inclusion, follow-up, sample size)
- ❑ Risk of bias
- ❑ Underestimation (asymptomatic, non-tested)

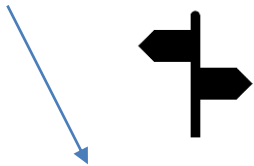


# III. CONCLUSION

Acute COVID-19



RECOVERY



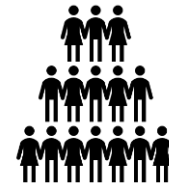
Persistent  
organ  
damage

Triggering of  
unknown  
mechanism



Long-COVID

± 10%



Comorbidities

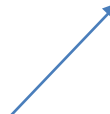


**SYMPTOMS  
(New or Persisting)**



Daily-life

PICS  
(ICU)



Hospitalisation  
consequences



# Contribution KCE study



## INSIGHT IN:

- Magnitude of the problem
- The condition & mechanisms
- Priority of patient needs

## ONLY A FIRST STEP

- More time and research will be needed afterwards to underpin the insights in the condition & treatment scientifically



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**KCE Trials Long COVID call**



# THANK YOU FOR YOUR ATTENTION

