

# Conséquences à long terme du COVID

## Blijvende gevolgen van COVID

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1<sup>er</sup> décembre 2022

# Déclaration de liens d'intérêt

- Liens d'intérêt :

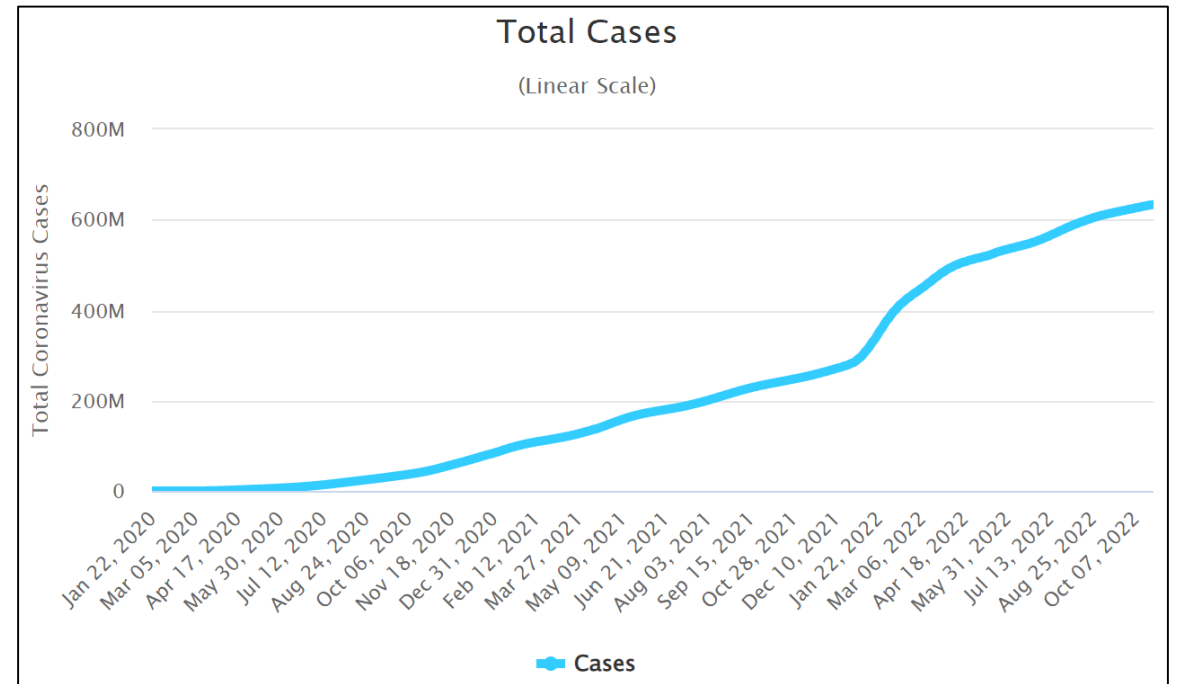
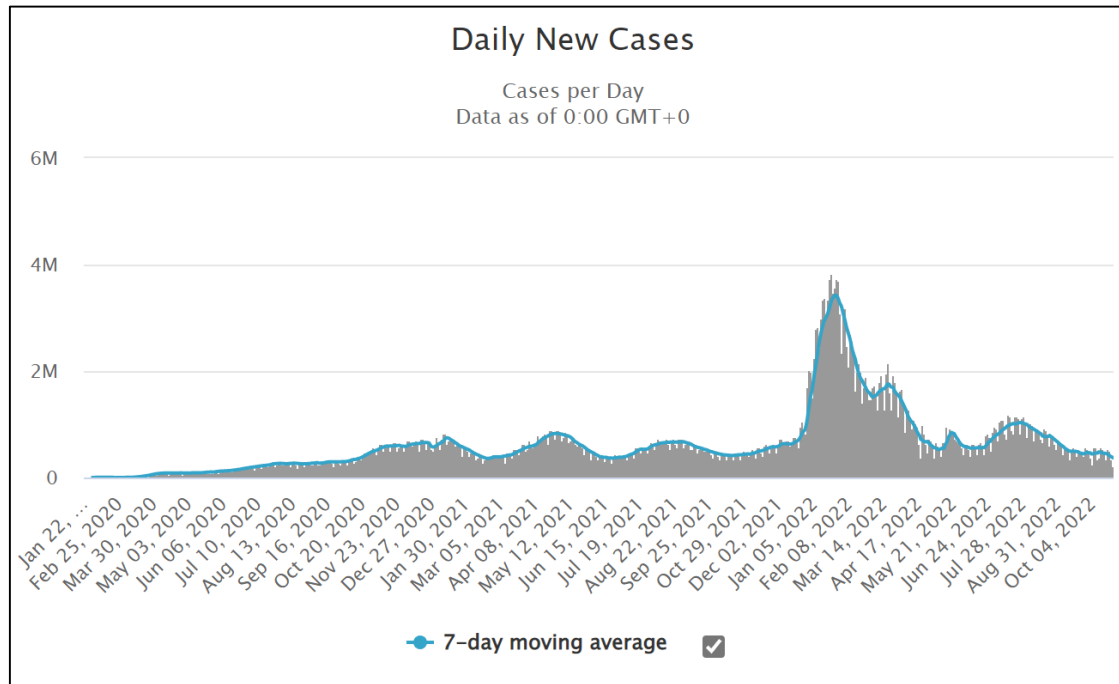
Honoraires de consultance et d'orateur: Boehringer Ingelheim, Roche, GlaxoSmithKline, AstraZeneca

Financement de recherches: Boehringer Ingelheim, Roche

Investigateur pour des essais cliniques: Roche, Galapagos, Respivant Sciences, Galecto Biotech, Pliant Therapeutics, Boehringer Ingelheim, BristolMyersSquibb

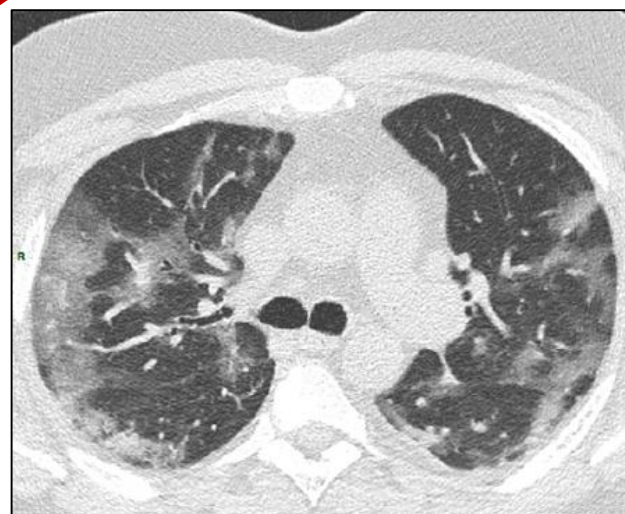
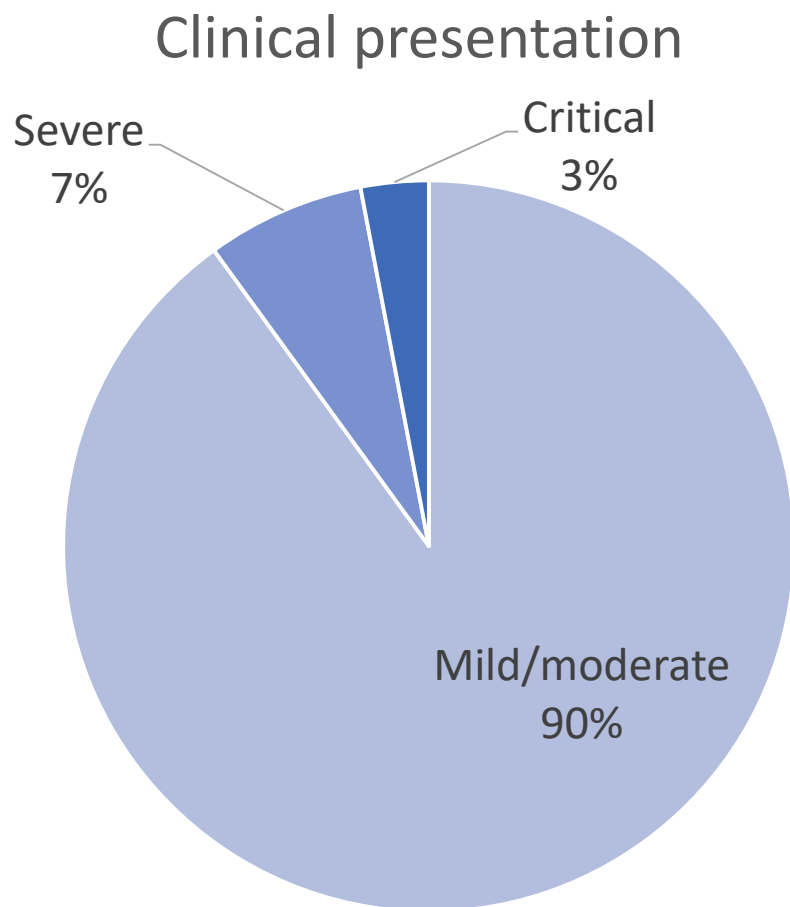
- Liens d'intérêt en relation avec la présentation : **aucun**

# L'étendue du problème – De omvang van het probleem

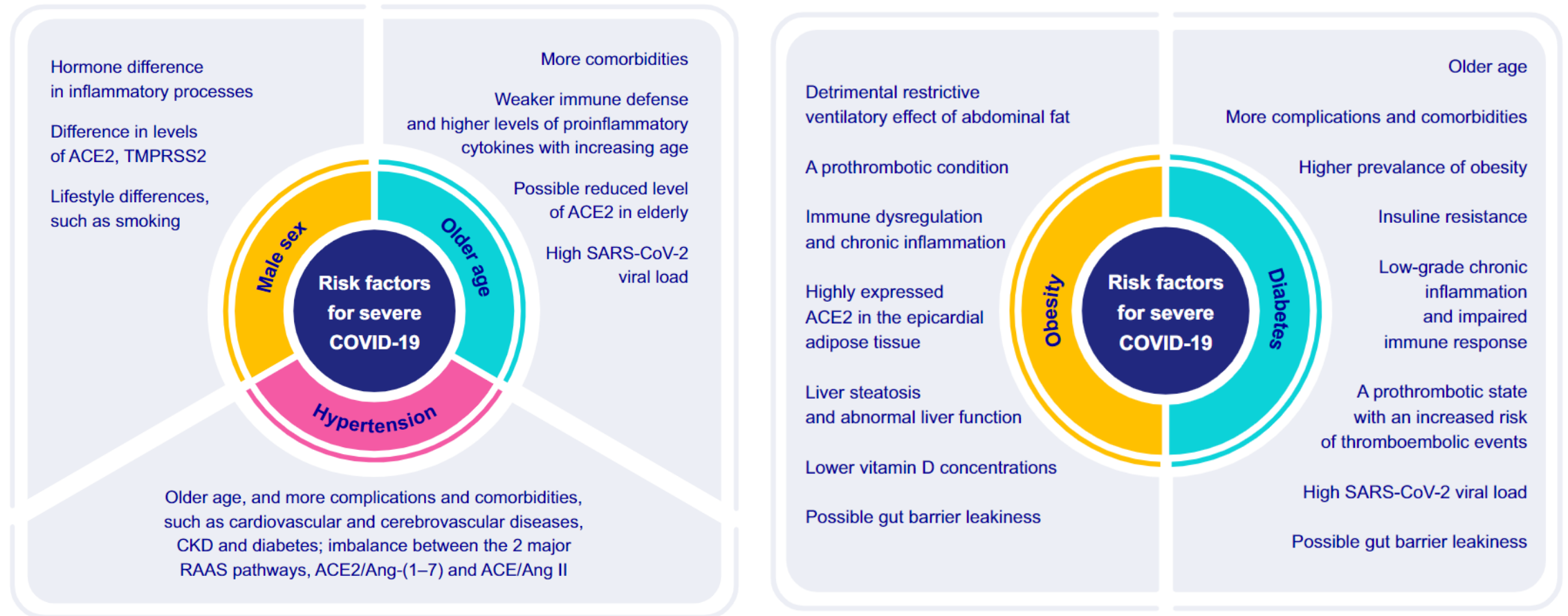


<https://www.worldometers.info/coronavirus/>

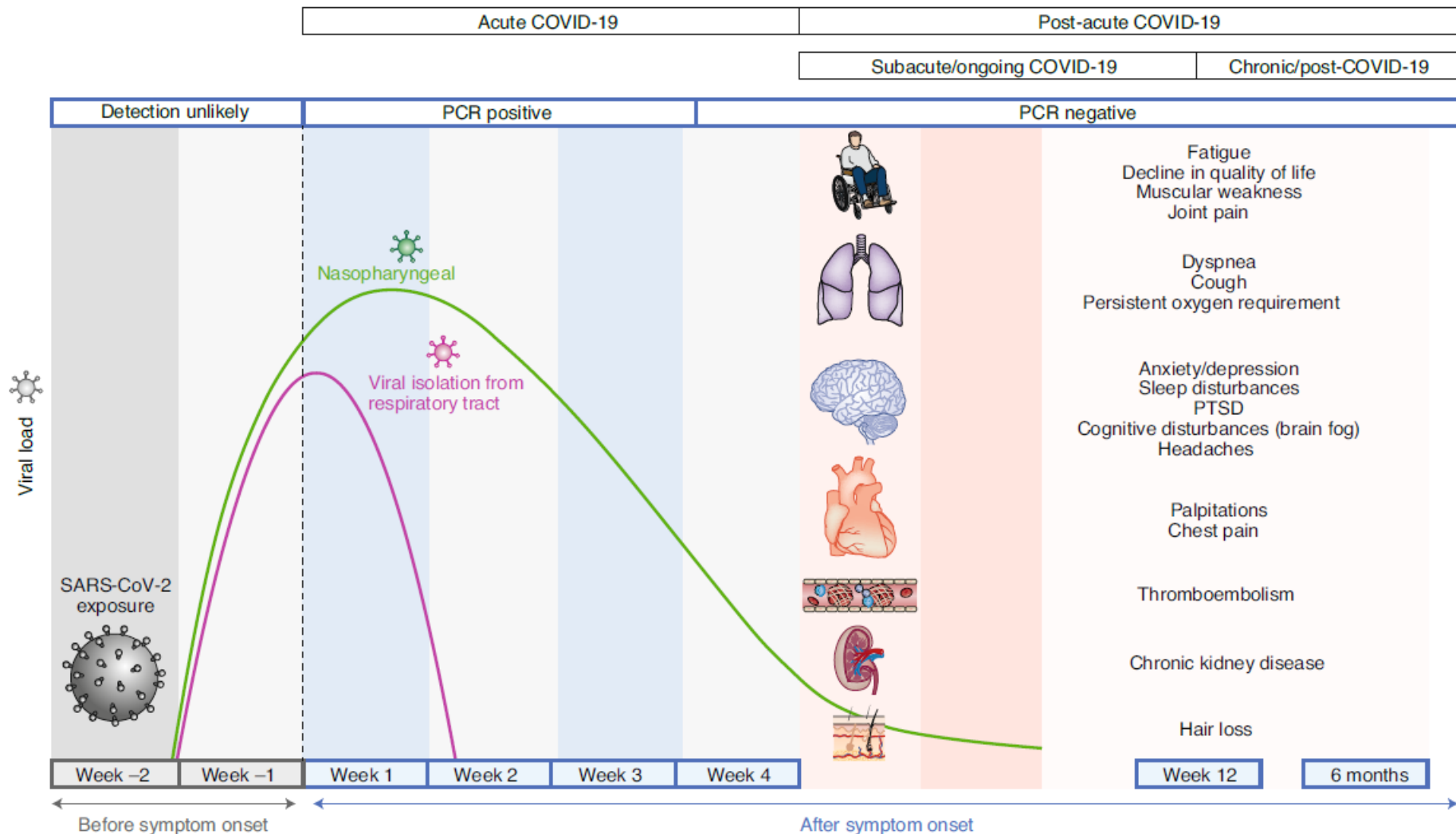
# L'étendue du problème – De omvang van het probleem



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# Syndrome chronique post-COVID: définition (OMS)

## Chronisch post-COVID-syndroom: definitie (WHO)

Post COVID-19  
CoV-2 infection  
least 2 months  
include fatigue  
an impact on  
an acute  
relapse of

JAMA Internal Medicine | [Original Investigation](#)

### Association of Self-reported COVID-19 Infection and SARS-CoV-2 Serology Test Results With Persistent Physical Symptoms Among French Adults During the COVID-19 Pandemic

Joane Matta, PhD; Emmanuel Wiernik, PhD; Olivier Robineau, MD, PhD; Fabrice Carrat, MD, PhD; Mathilde Touvier, PhD; Gianluca Severi, PhD; Xavier de Lamballerie, MD, PhD; Hélène Blanché, PhD; Jean-François Deleuze, PhD; Clément Gouraud, MD, MSc; Nicolas Hoertel, MD, PhD; Brigitte Ranque, MD, PhD; Marcel Goldberg, MD, PhD; Marie Zins, MD, PhD; Cédric Lemogne, MD, PhD; for the Santé, Pratiques, Relations et Inégalités Sociales en Population Générale Pendant la Crise COVID-19-Sérologie (SAPRIS-SERO) Study Group

SARS-CoV-2  
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OPEN

# Symptoms and risk factors for long COVID in non-hospitalized adults

Anuradhaa Subramanian<sup>1</sup>, Krishnarajah Nirantharakumar <sup>1,2,3</sup>✉, Sarah Hughes <sup>1,4,5,6,7</sup>, Puja Myles<sup>8</sup>, Tim Williams<sup>8</sup>, Krishna M. Gokhale<sup>1</sup>, Tom Taverner<sup>1</sup>, Joht Singh Chandan <sup>1</sup>, Kirsty Brown <sup>1,9</sup>, Nikita Simms-Williams<sup>1</sup>, Anoop D. Shah<sup>10</sup>, Megha Singh<sup>1</sup>, Farah Kidy<sup>1,11</sup>, Kelvin Okoth<sup>1</sup>, Richard Hotham<sup>1</sup>, Nasir Bashir <sup>12</sup>, Neil Cockburn<sup>1</sup>, Siang Ing Lee<sup>1</sup>, Grace M. Turner<sup>1,4,13</sup>, Georgios V. Gkoutos <sup>2,3,14,15,16</sup>, Olalekan Lee Aiyegbusi <sup>1,4,5,6,7,15</sup>, Christel McMullan<sup>1,4,7,13,17</sup>, Alastair K. Denniston <sup>2,3,4,6,15,16</sup>, Elizabeth Sapey<sup>16,18,19</sup>, Janet M. Lord<sup>13,15,18,20</sup>, David C. Wraith <sup>15,21</sup>, Edward Leggett<sup>8</sup>, Clare Iles<sup>8</sup>, Tom Marshall<sup>1</sup>, Malcolm J. Price<sup>1,15</sup>, Steven Marwaha<sup>22,23</sup>, Elin Haf Davies<sup>24</sup>, Louise J. Jackson <sup>1</sup>, Karen L. Matthews<sup>25</sup>, Jenny Camaradou<sup>25</sup>, Melanie Calvert <sup>1,2,3,4,5,6,7,13,15,19</sup> and Shamil Haroon <sup>1</sup>

UK-based retrospective cohort

- 486149 cases
- 1944580 matched controls



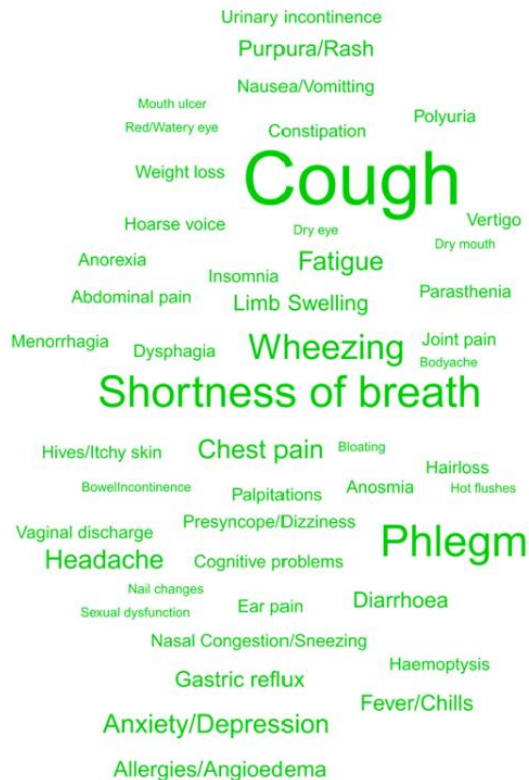
80%

Class 1



5.8%

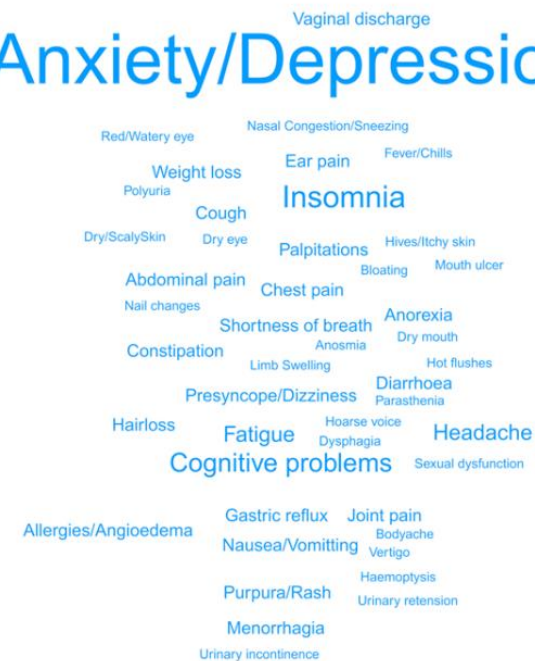
Class 2



14.2%

Class 3

Anxiety/Depression



## Signs and symptoms



Fever  
Fatigue  
'Brain fog'  
Headache  
Neuropathy  
Sleep problems  
Loss of smell/taste  
Memory disturbances



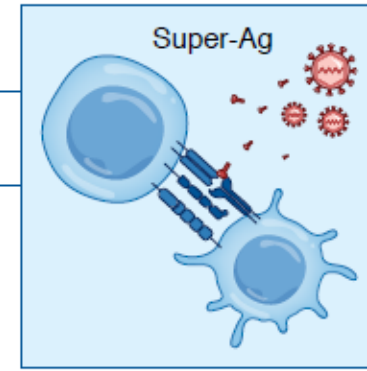
Chest pain  
Heart palpitations  
Shortness of breath



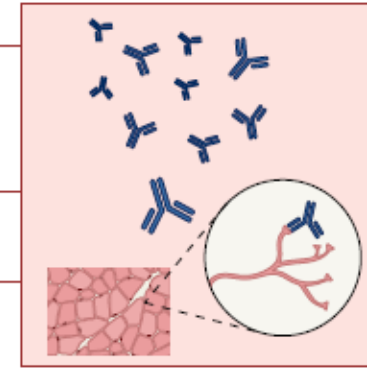
Dysmotility  
Loss of appetite  
Difficulty in swallowing

## Potential mechanisms

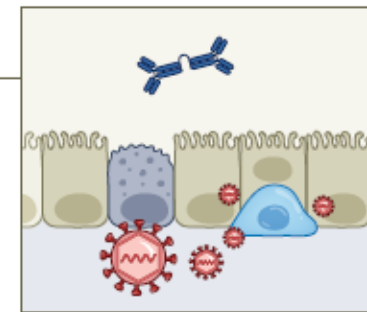
### Immune dysregulation



### Autoimmunity



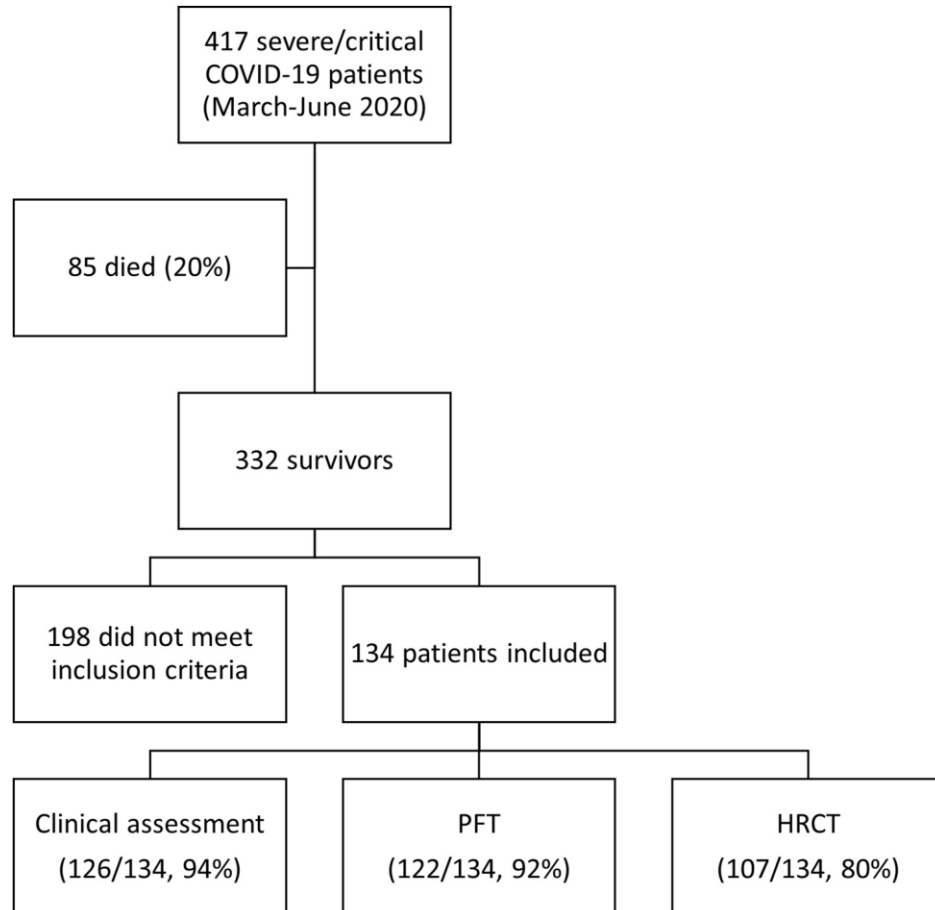
### Viral persistence



Autonomic dysregulation

# Séquelles respiratoires – 3 mois

## Respiratoire gevolgen – 3 maanden



### ***A 3 mois de l'infection***

- ✓ 25% dyspnée
- ✓ 35% fatigue
- ✓ 3% oxygène à l'effort

#### Pulmonary function tests results at three-month follow-up.

N = 122

FEV1/FVC ratio (% , median, IQR)	96 (83–106)
FVC (% predicted values, median, IQR)	88 (78–98)
N patients with impaired FVC (Z-score $\leq -2$ ) (N, %)	24 (19)
FEV1 (% predicted values, median, IQR)	91 (81–102)
N patients with impaired FEV1 (Z-score $\leq -2$ ) (N, %)	19 (15)
N patients with impaired FEF25-75 (Z score $\leq -2$ ) (N, %)	5 (3.73)
DLCO (% predicted values, median, IQR)	74 (61–89)
N patients with impaired DLCO (Z-score $\leq -2$ ) (N, %)	58 (46)

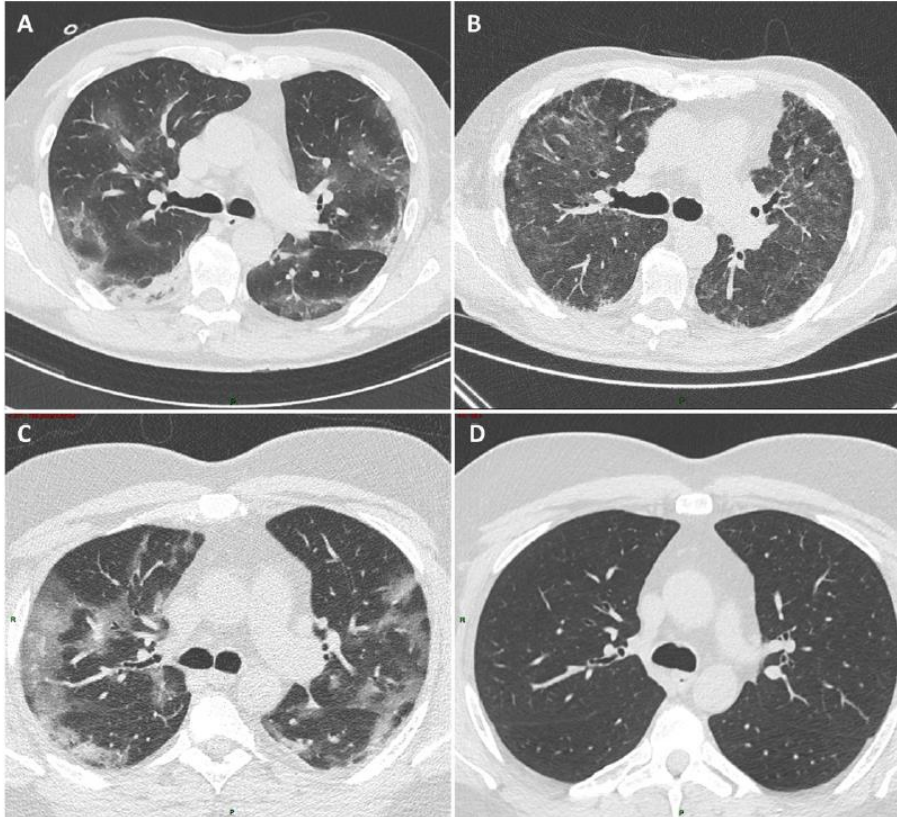
FEV1: forced expired volume in 1 s; FVC: forced vital capacity; DLCO: lung diffusion capacity; FEF25-75: forced expiratory flow at 25–75% of forced vital capacity.

# Séquelles respiratoires – 3 mois

## Respiratoire gevolgen – 3 maanden

Baseline

3-month follow-up



Residual fibrosis and GGO

Recovery

- 20% séquelles >5%
- 17% ont des signes de fibrose

### ***Facteurs de risque pour séquelles***

- ✓ Durée de séjour en USI
- ✓ Durée de ventilation mécanique

### ***Facteurs associés à la dyspnée/fatigue***

- ✓ Aucun statistiquement significatif!

# Séquelles respiratoires – 3 mois

## Respiratoire gevolgen – 3 maanden

	HRCT extent<5%	HRCT extent≥5%
Dyspnea	27%	10%
No dyspnea	56%	7%

N=100

66% of consistency  
34% of discrepancy

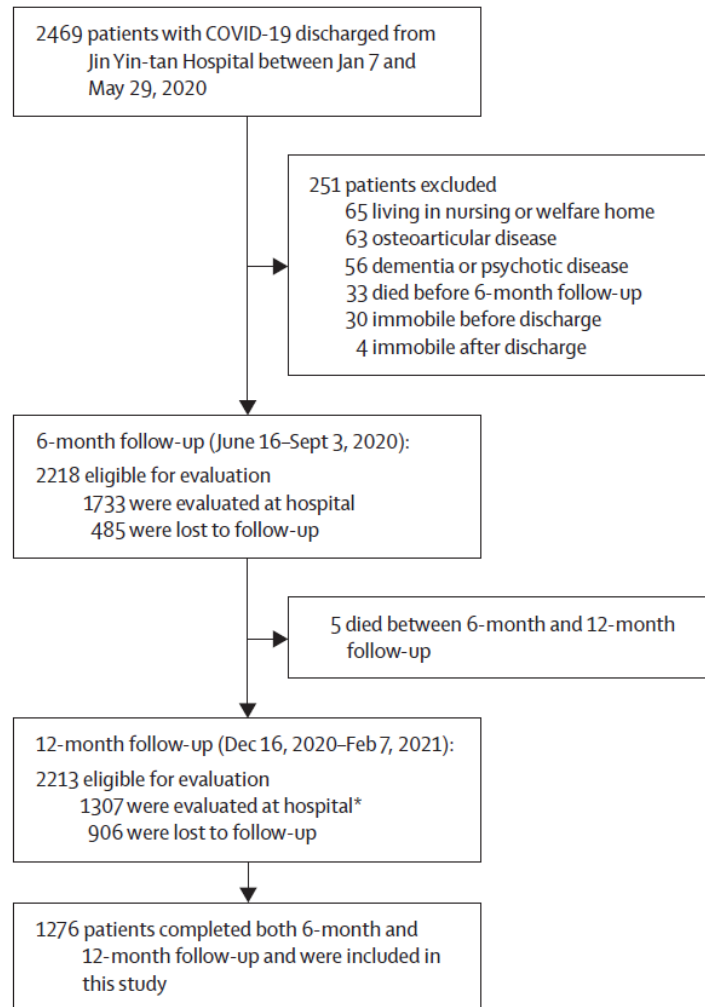
	DLCO>60%	DLCO≤60%
Dyspnea	29%	11%
No dyspnea	43%	17%

N=119

54% of consistency  
46% of discrepancy

# Séquelles respiratoires – 12 mois

## Respiratoire gevolgen – 12 maanden



➤ Au moins un symptôme: 49% (620/1272)

➤ Dyspnée  $\geq$  grade 1 mMRC: 30%

### ***Facteurs de risque pour diffusion basse***

✓ Age (OR 1.30, p=0.04)

✓ Sexe féminin (OR 1.43, p=0.002)

# Séquelles respiratoires – 12 mois

## Respiratoire gevolgen – 12 maanden

	Total (n=1276)			Scale 3: not requiring supplemental oxygen (n=318)			Scale 4: requiring supplemental oxygen (n=864)			Scale 5–6: requiring HFNC, NIV, or IMV (n=94)		
	6 month	12 month	p value	6 month	12 month	p value	6 month	12 month	p value	6 month	12 month	p value
Sequelae symptom												
Any one of the following symptoms	831/1227 (68%)	620/1272 (49%)	<0.0001	211/307 (69%)	151 (47%)	<0.0001	543/828 (66%)	420/860 (49%)	<0.0001	77/92 (84%)	49 (52%)	<0.0001
Fatigue or muscle weakness	636/1230 (52%)	255/1272 (20%)	<0.0001	158/307 (51%)	65 (20%)	<0.0001	410/831 (49%)	169/860 (20%)	<0.0001	68/92 (74%)	21 (22%)	<0.0001
mMRC score												
0	872/1185 (74%)	891/1271 (70%)	0.014	231/309 (75%)	238/317 (75%)	0.68	591/792 (75%)	596/860 (69%)	0.0015	50/84 (60%)	57 (61%)	0.83
≥1	313/1185 (26%)	380/1271 (30%)	..	78/309 (25%)	79/317 (25%)	..	201/792 (25%)	264/860 (31%)	..	34/84 (40%)	37 (39%)	..

# Séquelles respiratoires – 24 mois

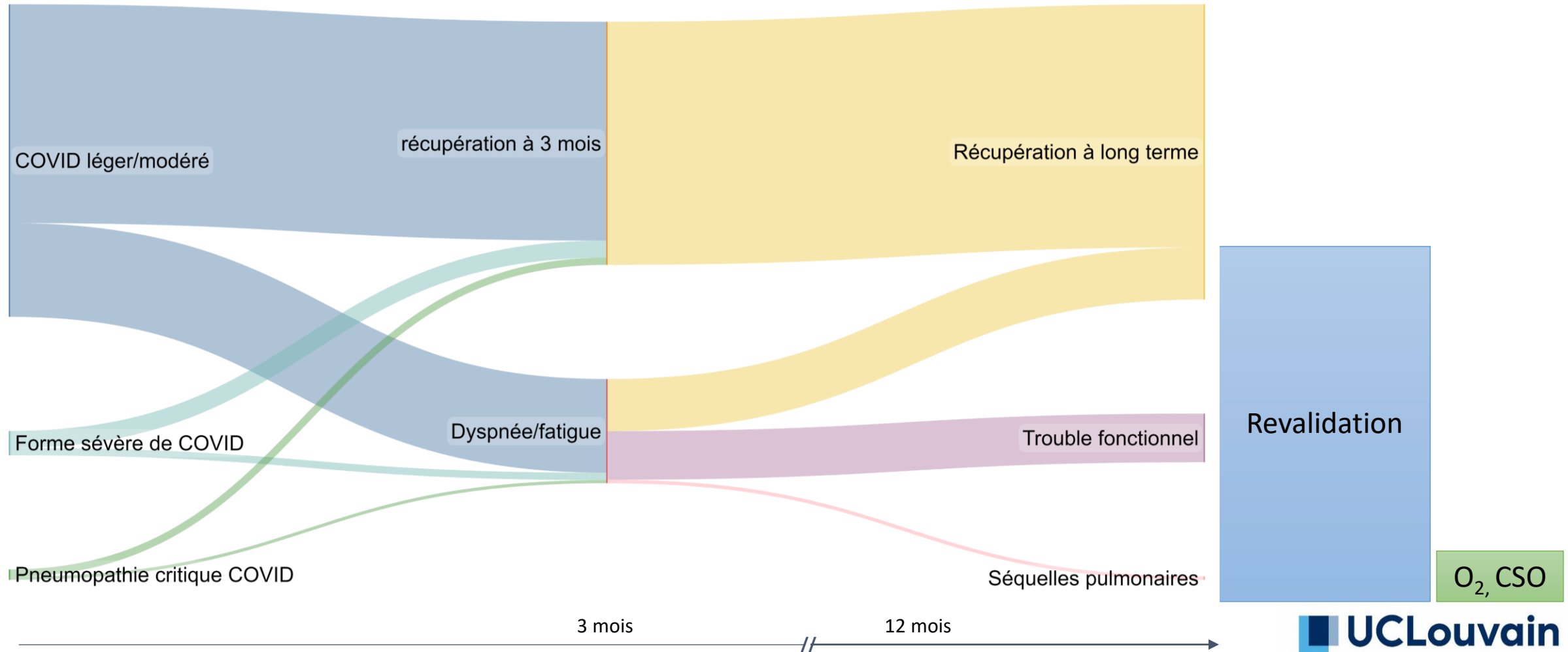
## Respiratoire gevolgen – 24 maanden

	Total (n=1192)			Scale 3 (n=295)			Scale 4 (n=806)			Scale 5-6 (n=91)		
	6 months	12 months	2 years	6 months	12 months	2 years	6 months	12 months	2 years	6 months	12 months	2 years
<b>Sequelae symptoms</b>												
Any of the following symptoms	777/1149 (68%)	583/1188 (49%)*	650/1190 (55%)†‡	194/286 (68%)	141 (48%)*	158/294 (54%)†	509/774 (66%)	395/802 (49%)*	440/805 (55%)†	74/89 (83%)	47 (52%)*	52 (57%)†
Fatigue or muscle weakness	593/1151 (52%)	240/1188 (20%)*	357/1190 (30%)†‡	143/286 (50%)	60 (20%)*	89/294 (30%)†‡	385/776 (50%)	161/802 (20%)*	235/805 (29%)†‡	65/89 (73%)	19 (21%)*	33 (36%)†
Sleep difficulties	313/1151 (27%)	206/1188 (17%)*	298/1190 (25%)‡	75/286 (26%)	47 (16%)*	70/294 (24%)‡	205/776 (26%)	146/802 (18%)*	203/805 (25%)‡	33/89 (37%)	13 (14%)*	25 (27%)
<b>mMRC dyspnoea score</b>												
0	816/1104 (74%)	834/1187 (70%)*	1023/1191 (86%)†‡	216/288 (75%)	222/294 (76%)	253 (86%)†‡	551/734 (75%)	556/802 (69%)	694/805 (86%)†‡	49/82 (60%)	56 (62%)	76 (84%)†‡
≥1	288/1104 (26%)	353/1187 (30%)*	168/1191 (14%)†‡	72/288 (25%)	72/294 (24%)	42 (14%)†‡	183/734 (25%)	246/802 (31%)	111/805 (14%)†‡	33/82 (40%)	35 (38%)	15 (16%)†‡
<b>Mental health</b>												
Anxiety symptom (GAD-7≥5)	NA	NA	98/1187 (8%)	NA	NA	26/294 (9%)	NA	NA	66/802 (8%)	NA	NA	6 (7%)
Depression symptom (PHQ-9≥5)	NA	NA	75/1190 (6%)	NA	NA	25 (8%)	NA	NA	45/804 (6%)	NA	NA	5 (5%)
PTSD symptom (PCL-C ≥38)	NA	NA	27/1189 (2%)	NA	NA	12 (4%)	NA	NA	14/803 (2%)	NA	NA	1 (1%)



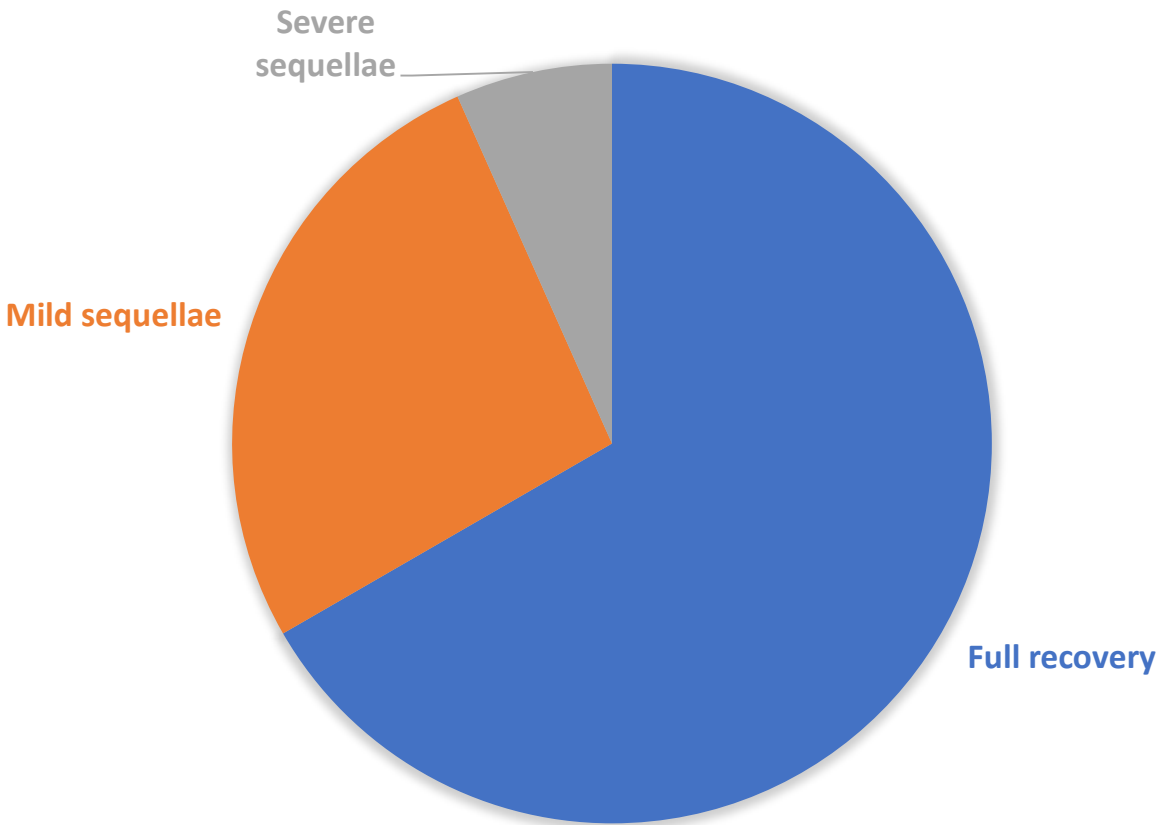
# Séquelles respiratoires post-COVID – synthèse

## Post-COVID respiratoire gevolgen – samenvatting



# Conclusion - conclusie

## POST-COVID



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Merci de votre attention!  
Dank u voor uw aandacht!



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European  
Reference  
Networks

**ERN-LUNG**  
RARE RESPIRATORY DISEASES



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