

# The NHS Long Covid Conference 2022

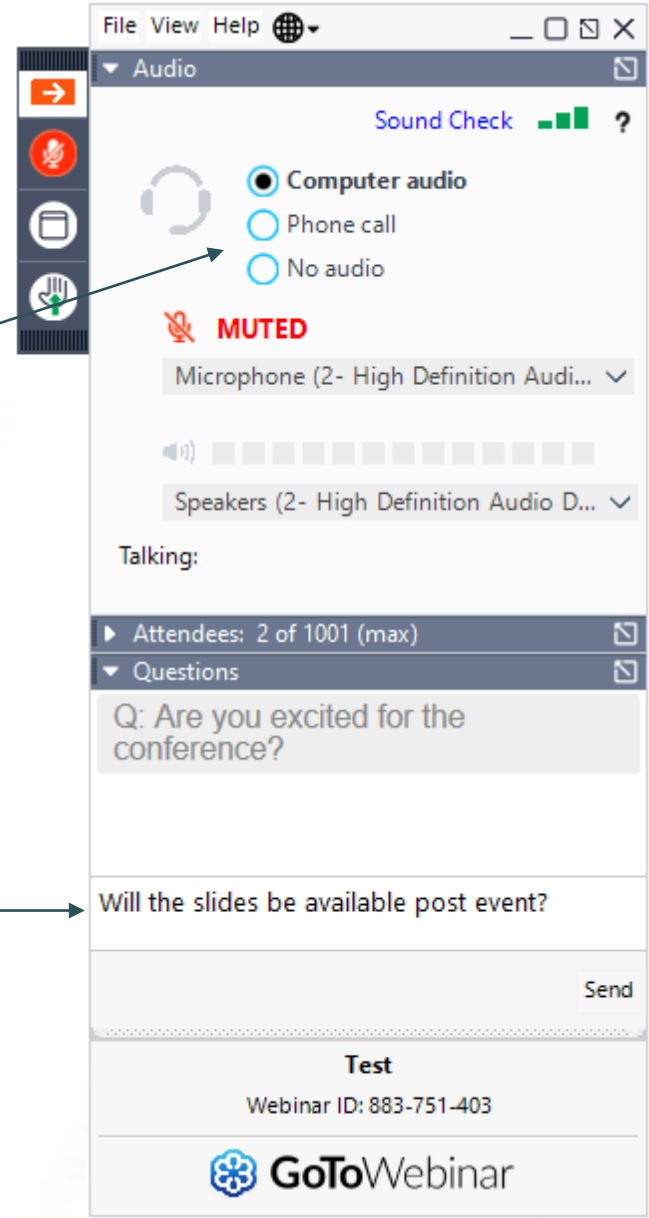
26<sup>th</sup> April 2022- 10:50am – 13:30pm – GoToWebinar

Webinar hosted by Convenzis Group Limited

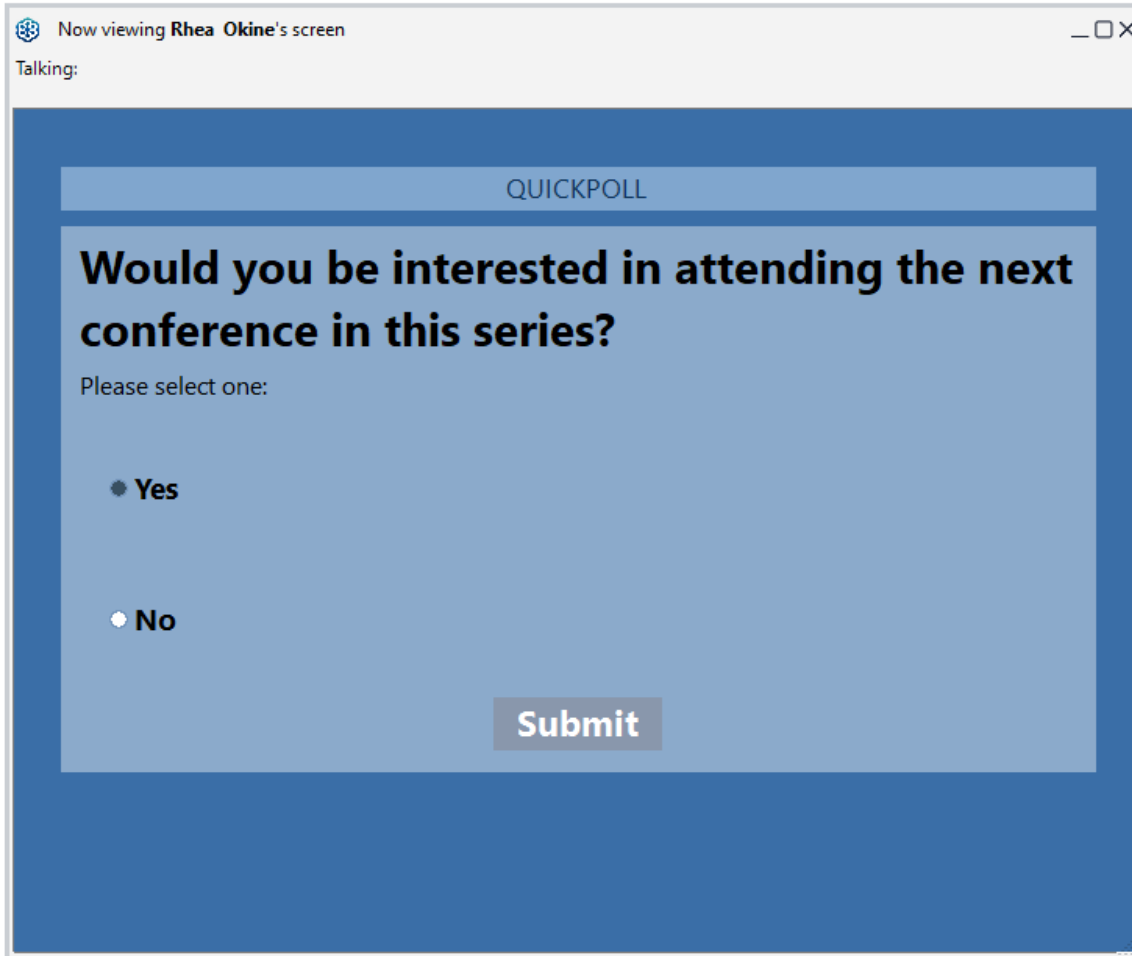


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# Polls



Now viewing Rhea Okine's screen

Talking:

QUICKPOLL

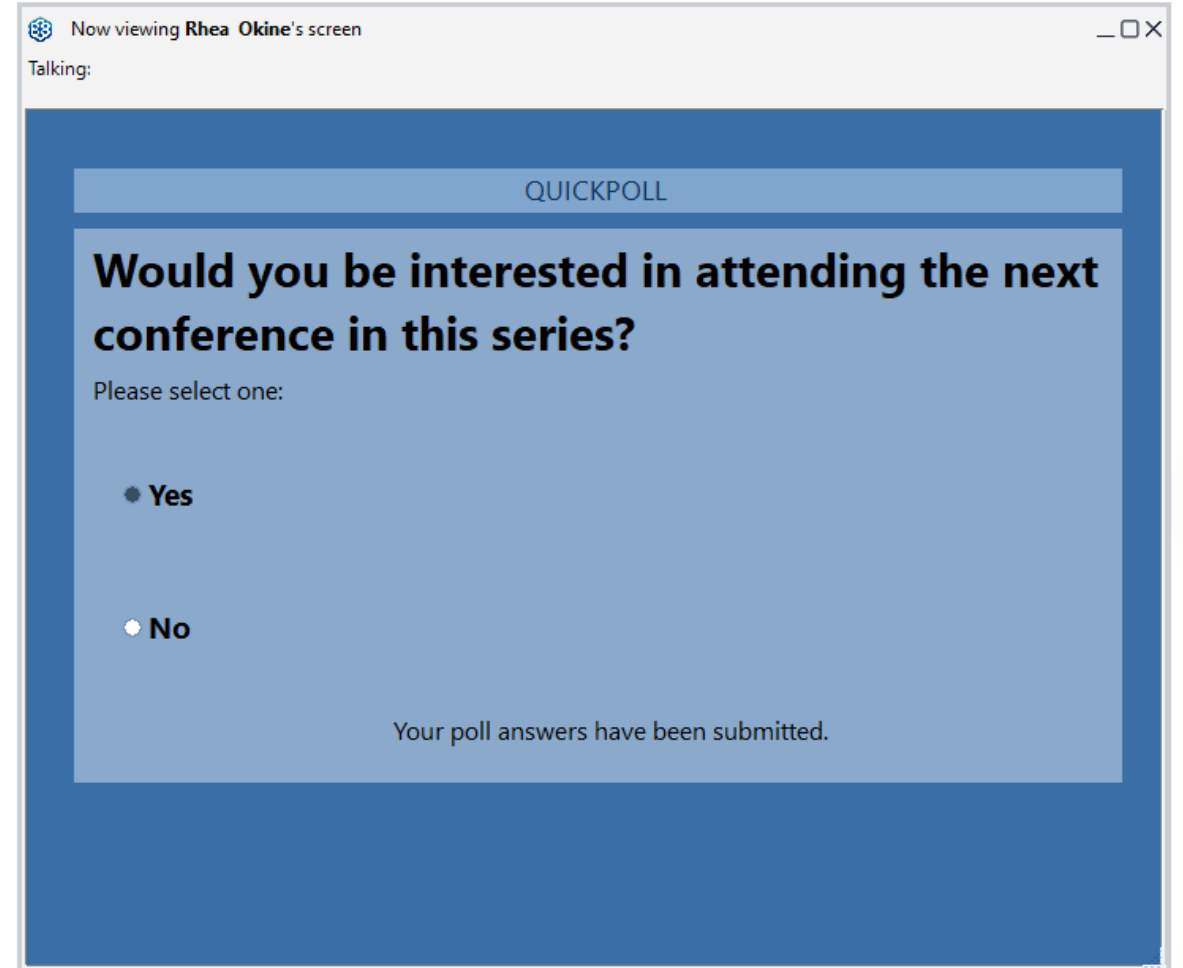
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Please select one:

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Click on **one** of the multiple choice options, then press 'Submit'



Now viewing Rhea Okine's screen

Talking:

QUICKPOLL

**Would you be interested in attending the next conference in this series?**

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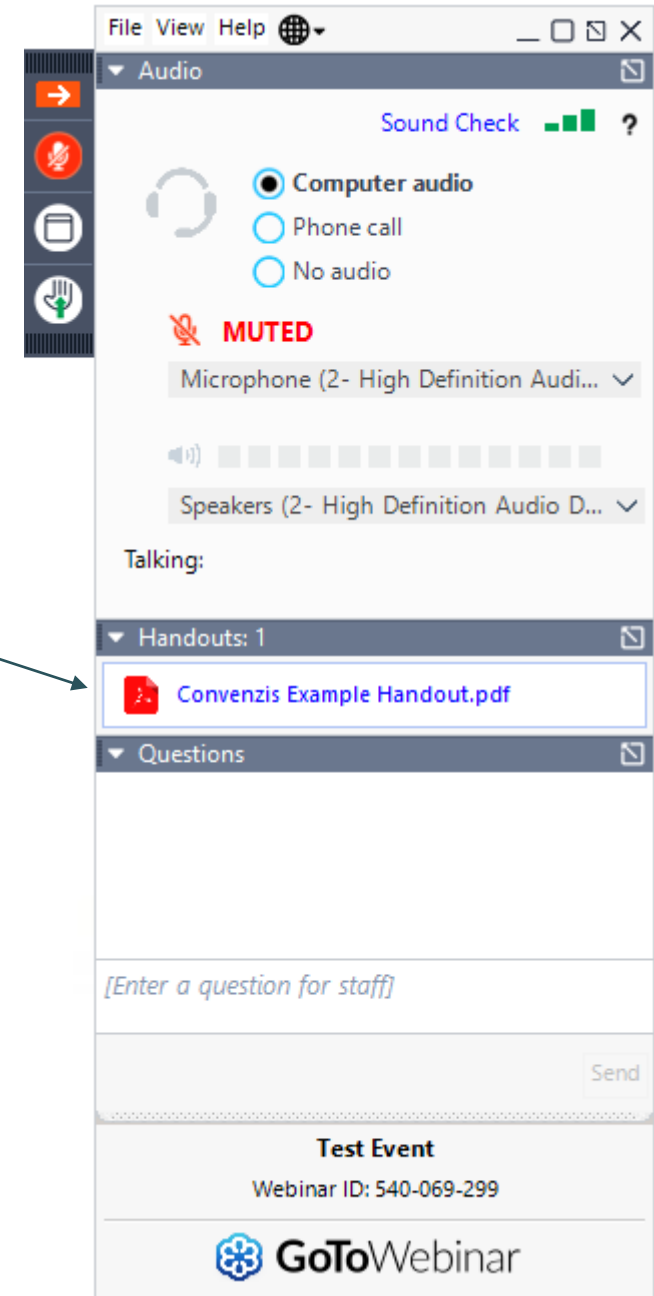
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Fiona Jenkins She/Her, Executive  
Director Therapies and Health  
Science at Cardiff and Vale University  
Health Board

# Long COVID Rehabilitation service, Cardiff and Vale University Health Board ( and the model in Wales)

March 2022

Dr. Fiona Jenkins MBE

Executive Director of Therapies and Healthcare Sciences

Cardiff and Vale University Health Board



# I will cover

- **Our approach**
- **The Impact of COVID**
- **The Cardiff and Vale Rehabilitation Programme**
- **Cardiff and Vale Rehabilitation Model and Meaningful Conversations Model**
- **Benefits Model 'Wheel'**
- **Long COVID Recovery – Service Definition**
- **Long COVID Rehabilitation Pathway**
- **Governance and Reporting Structure**
- **Understanding and reporting on Outcomes and Benefits**
- **Keeping Me Well website**
- **The 'Adferiad' (Recovery) Long COVID Service in Wales**
- **Questions**





# My Thanks to:

- Dr. Emma Cooke - Clinical Director for Allied Health Professionals C&V UHB
- Rachel Wallbank – C&V UHB AHP Lead for Long COVID
- Claire Madsen DoTHs Powys
- CEDAR team (evaluation)
- ICST ( Covid recovery app)
- Welsh Government; Ruth Crowder and our Health Minister Eluned Morgan, Baroness Morgan of Ely.



# Our Approach

- Integrated organisations- primary/secondary/mental health commission and provide
- Evolved the COVID recovery model in May 2020
- Inter-disciplinary therapy rehabilitation approach rather than re-enforcement of a siloed Multi-disciplinary therapy approach to assessment and intervention.
- Generalised specialist Long COVID Clinical Skills within all the therapists without the loss or dilution of specialist knowledge
- The team delivers psychologically informed rehabilitation in the context of interdisciplinary working, focused on addressing fatigue management, dysfunctional breathing, pacing etc. and of reducing pro-inflammatory behaviours and increasing anti-inflammatory behaviours.
- Psychologically informed approaches weaved through the scope of interventions are ACT, Compassion Focused Therapy, and being Trauma informed. These approaches/models helpful in creating meaning, and strengthening the sense of acceptance of 'where I am now' for the individual, together with behavioural change to support moving forwards



# Rehabilitation Programme

The Rehabilitation programme is made up of six component workstreams. The workstreams are interdependent and connected as our approach focuses on a blended way of working, change the way we offer services. Our workstreams contributes to CaV UHB Sustainability Action Plan and the Welsh Governments Equality and Diversity Policies.

## Keeping Me Well

The Keeping Me Well website is a CaV UHB website for therapies. The website provides useful information and resources that support the therapy services available in CaV, directs people to the right services, and supports people with self-care (e.g. teaches techniques to pace activity during recovery, techniques to improve fitness etc.)

## Long COVID Recovery

To support individuals to live well and recover from Long COVID. Through delivery of a set of group based interventions, the MDT team provides education and supportive self management strategies. The service provides 1-1 support and interventions from Clinical Psychology, Occupational Therapy, Physiotherapy, Speech and Language Therapy and Dietetics.

## Living Well

Living Well provides two sets of group based support to people with Musculoskeletal conditions (Hip or knee OA and low back pain). The ESCAPE programme, which provides exercise based support for 6 weeks (2 sessions per week), and the Foodwise programme which includes Dietetics Advice, with an active component, for 8 weeks (1 session per week).

## Recovery & Wellbeing College (Living Well Curriculum)

To provide free educational courses on a range of mental health, physical health, and wellbeing topics. The co-produced and co delivered programmes brings peers and professionals together, creating equity in value between lived and learnt experience. The college aims to bridge the gap between services by connecting physical and psychological recovery, creating a joint identity with co-production at the heart of what we do.

## Prepare Well (Orthopaedics)

The Prepare well (orthopaedic) service provides support to individuals that are on an orthopaedic pathway. Individuals are supported by the team, and those with lived experience, enabling them to develop their psychological and physical fitness ready for surgery and to recover well after. This is known to enhance experience, improve outcomes and create efficiency gains in service delivery.

## Prepare Well (Cancer)

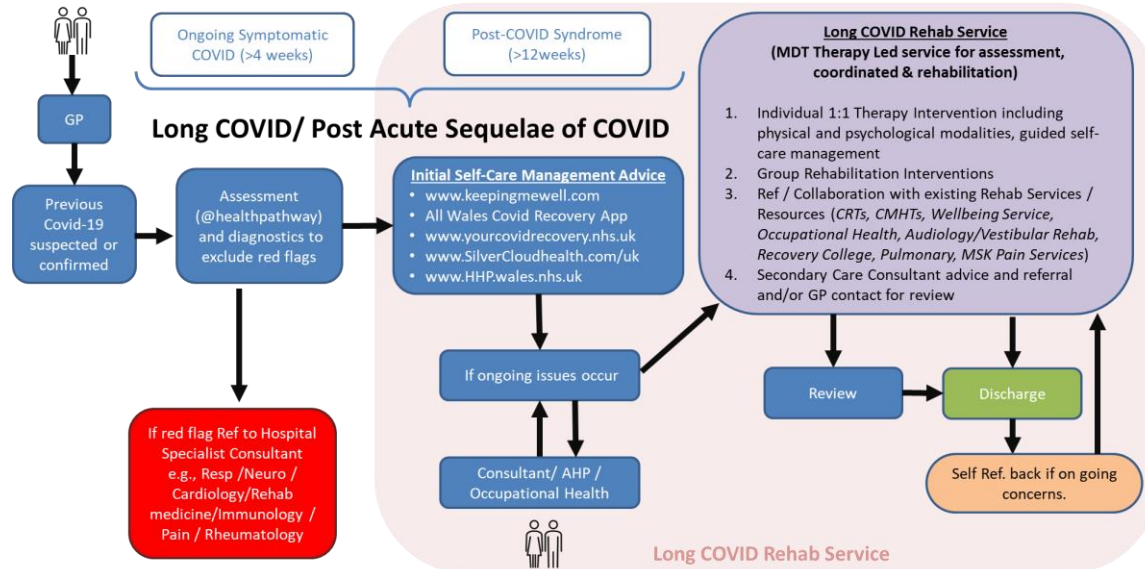
Prepare Well (Cancer) Service provides support to individuals in preparation for their cancer treatment. The support enables the individual to be as fit, strong and psychologically resilient as possible. Through nutrition, activity and exercise and wellbeing interventions, we endeavour to create better experiences and outcomes for people in preparation for treatment to help them to live well with and beyond cancer treatment.



# The unknown – understanding the impact of COVID

**The What:** COVID-19, caused by novel coronavirus SARS-CoV-2, has led to a pandemic that is increasing the burden of disease and disability across the UK. Our knowledge of the range of impairments and disabilities is still evolving; we do not know the long-term sequelae of the condition. In March 2020 it was assumed that it was a respiratory illness, however, it affects almost every organ in the body with emerging evidence that shows many of those survivors are likely to have significant on-going health problems, including breathing difficulties, enduring tiredness, reduced muscle function, impaired ability to perform vital everyday tasks and mental health problems such as Post Traumatic Stress Disorder, anxiety and depression. Two years on there is now increased awareness of the long-term legacy for individuals, not just those who have been admitted to hospital, but those who have self-treated at home and recovered from the acute infection but continue to have relapses and persistent symptoms.

## Long COVID Rehabilitation Pathway: Summary

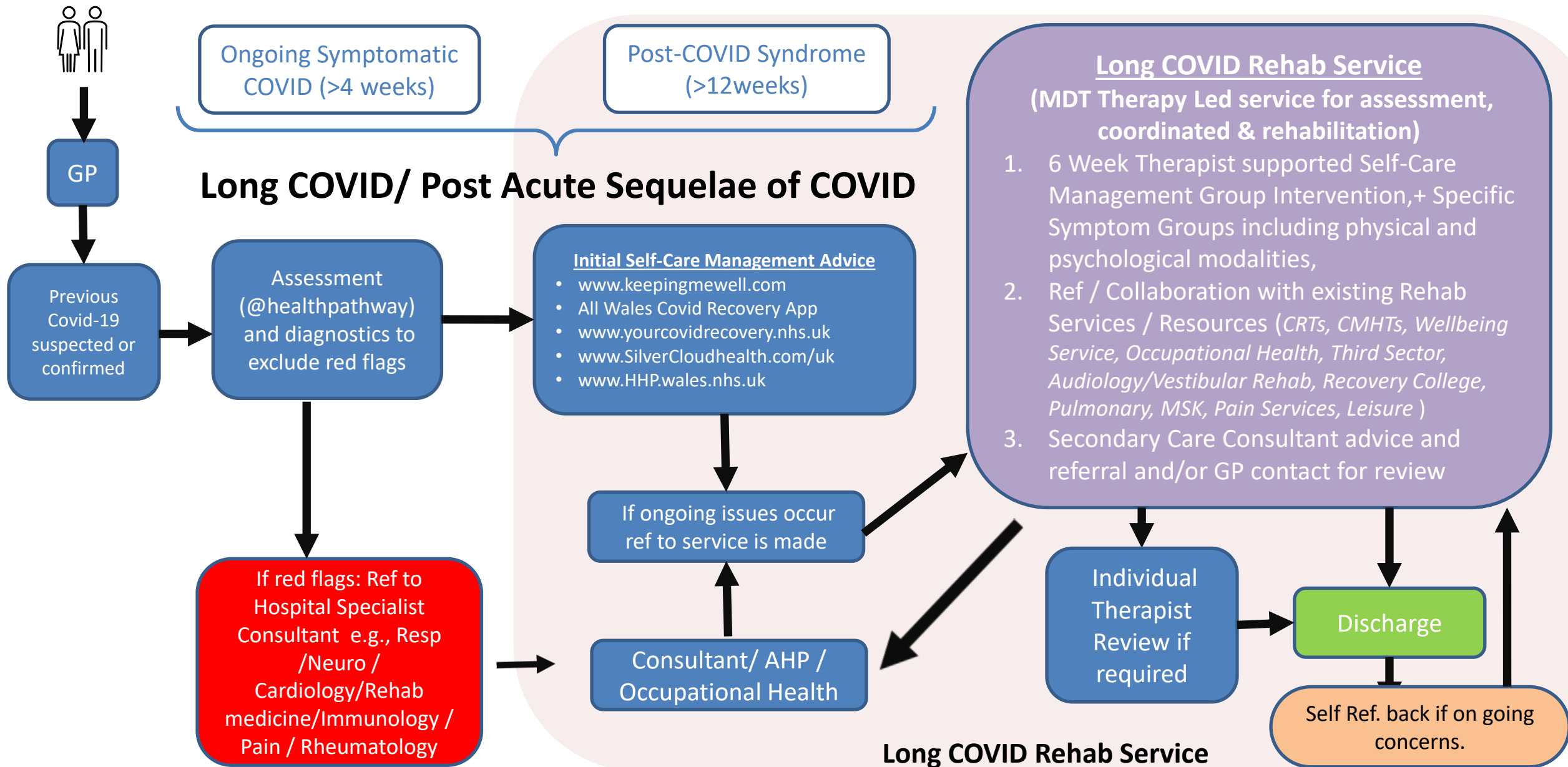


**The Why:** In Cardiff and Vale we are started to see increasing numbers of people with post COVID rehabilitation needs being referred to outpatient and community therapy services. Due to the nature of the condition, there was not one rehabilitation pathway that these individuals could access as they often require support from therapists / clinicians across several pathways. Individuals who were frail or had neurological involvement have access to coordinated multi-disciplinary community rehabilitation but other people, particularly those reporting chronic fatigue like symptoms could not access coordinated and individual centered rehabilitation. We knew from studies of people who had SARS in the 2003 epidemic that almost half the survivors went on to have chronic fatigue or other long-lasting symptoms. We were concerned that if people were unable to access timely and coordinated rehabilitation there was a risk of chronicity, high rates of anxiety and depression and people failing to recover fully from the virus which will inevitably increase the burden on existing stretch NHS services.

**Individual story:** "The last seven months has been a difficult period as it is the first time, thankfully, in my life that I have had a long illness. The future is still uncertain, but I do believe that the roller coaster ride I am on has enabled me to acknowledge the strength I have and hopefully will make me even stronger going forward. I must add that I have never been a fan of roller coasters and the last seven months has definitely confirmed that view"

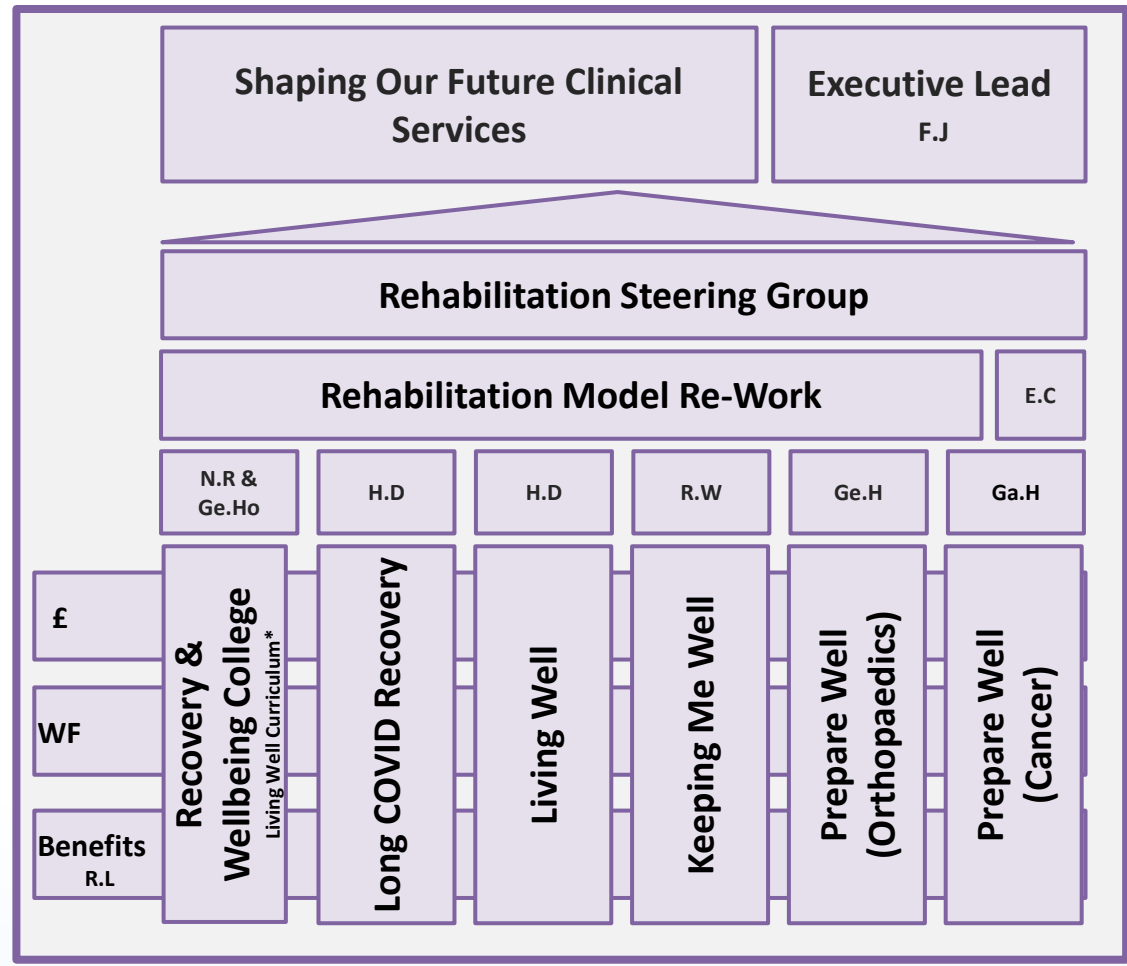
**The How:** General practitioners, secondary care consultants, and AHPs agreed that a 'non-medicalised', holistic, individualised approach was needed to support people to recover. Short term funding was agreed for 18 months to established an AHP led service to provide a single point of access for people reporting enduring symptoms of COVID. A long COVID Health pathway was developed. On the 6<sup>th</sup> January 2022, a discussion was had with the health system management board to ensure LHB wide visibility of the programme. There is also work being done to explore how to reach minority groups better. Through the Long COVID Community Conversation Sessions, we have been able to listen to patients and respond to their comments. Changes they have suggested will be implemented as we scale and mature the Long COVID Recovery service.

# Long COVID Rehabilitation Pathway: Primary/Secondary AHPs and medical staff



# Governance and Reporting Structure

We have established the Rehabilitation Programme to help coordinate and steer the changes within each of the component workstreams and to enable external SMEs and advisors to provide steer and guidance on key decision points. The programme as a whole is accountable for delivering the outcomes and benefits depicted on slide six.



# Cardiff and Vale Rehabilitation Model and Meaningful Conversations Model



Cardiff and Vale Rehabilitation Model of Care

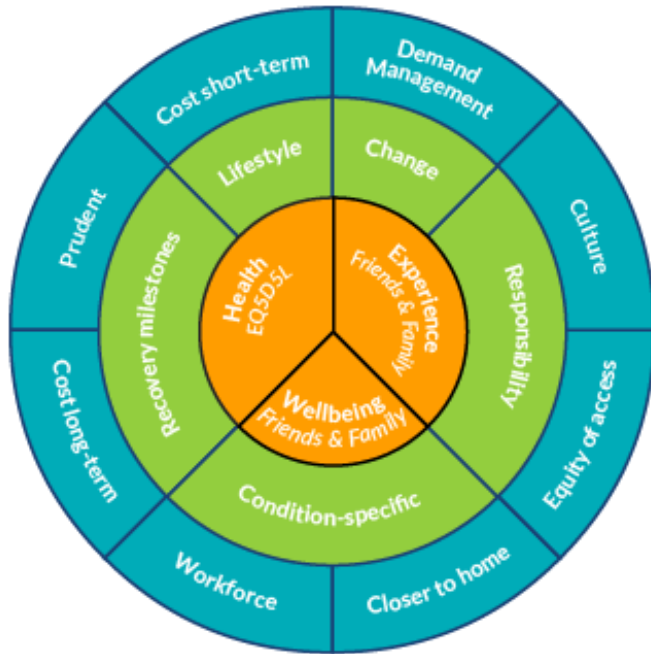


Meaningful Conversations Model

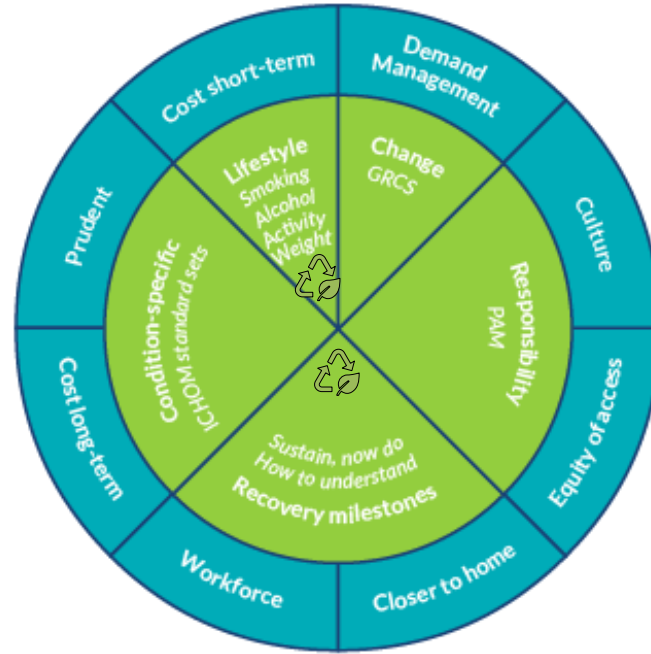


# Benefits Model 'Wheel'

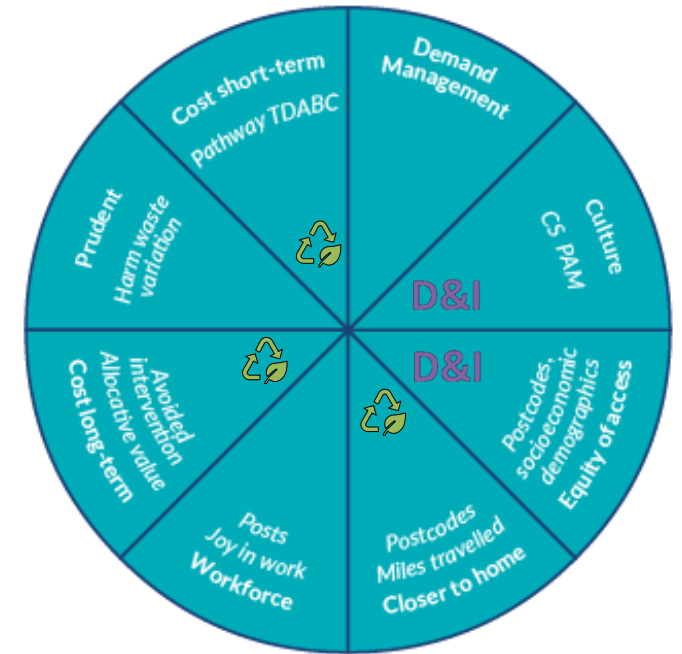
The 'wheel' was developed to represent the outcome measures we are using to present the benefits of the Rehabilitation Programme. Each work stream is able to 'pick and mix' between the different benefits which have been identified. The process of collecting these benefits has begun, however, at present there has not been sufficient data collected to present them.



Measured by all workstreams (not incl. KMW)



Selectively measured (based on relevance)



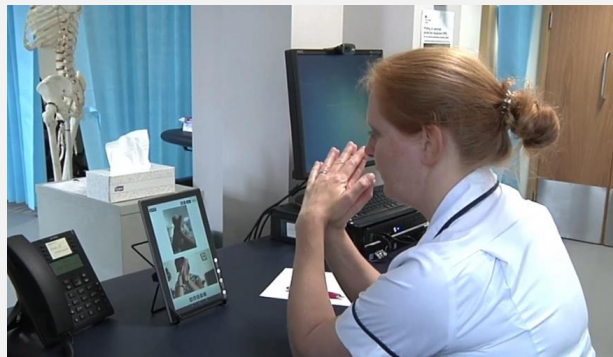
Captured from existing systems





# Long COVID Recovery – Service Definition

**Aim:** To support individuals to live well and recover from Long COVID. Through delivery of a set of group based interventions, the MDT team provides education and supportive self management strategies encompassing **fatigue management, breathing advice, cognition and psychological support, taste and smell retraining, pain management, bladder control, vocational advice and nutritional support**. In addition, the service provides 1-1 support and interventions from Clinical Psychology, Occupational Therapy, Physiotherapy, Speech and Language Therapy and Dietetics.



**Individual story:** "The last seven months has been a difficult period as it is the first time, thankfully, in my life that I have had a long illness. The future is still uncertain, but I do believe that the roller coaster ride I am on has enabled me to acknowledge the strength I have and hopefully will make me even stronger going forward. I must add that I have never been a fan of roller coasters and the last seven months has definitely confirmed that view"

**Individual story:** "The biggest things that have resonated with me are knowing that pacing is cognitive, sensory, emotional too and not just physical. 'Dropping the anchor' as Carys put it and not fighting anymore and saying my prescription is saying no at the moment. All these things are making a big difference- thank you" (Long Covid Recovery)

The interdisciplinary approach supporting evolvment of generalised specialist Long COVID Clinical Skills within all the therapists without the loss or dilution of specialist knowledge. Significant number of therapist came from a neurological background with an understanding and experience of a homogenous event/trigger with resulting heterogenous presentation of symptoms. The team delivers psychologically informed rehabilitation in the context of interdisciplinary working, focused on addressing fatigue management, dysfunctional breathing, pacing etc. and of reducing pro-inflammatory behaviours and increasing anti-inflammatory behaviours.

- Physio (0.7 WTE)
- OT (0.7 WTE)
- Admin (1 WTE)
- Service Lead (1 WTE)
- Dietician (0.7)
- Speech and Language therapist (0.7 WTE)
- Psychologist (0.7 WTE)
- Respiratory Physio (1 WTE)
- Psychology Assistant (1 WTE)
- Rehab Coach (1 WTE)

**The Service is currently able to support 100-120 referrals per month. We expect 1150 referrals in F/Y 2022/23.**



## How we have adapted our service

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1

Long COVID community sessions:

2

Flexibility in mode of delivery:

3

Seldom heard voices:

4

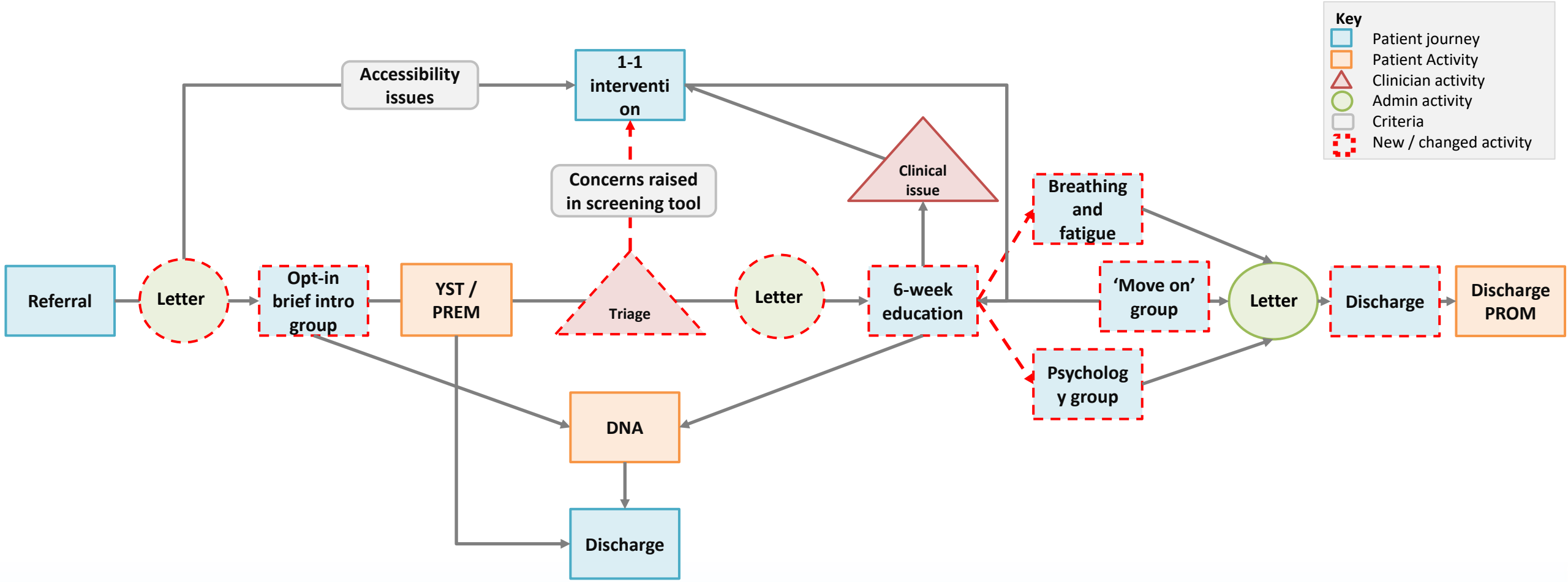
Other post infection/ acute illness syndromes:



# Updated pathway for LCR – April 2022

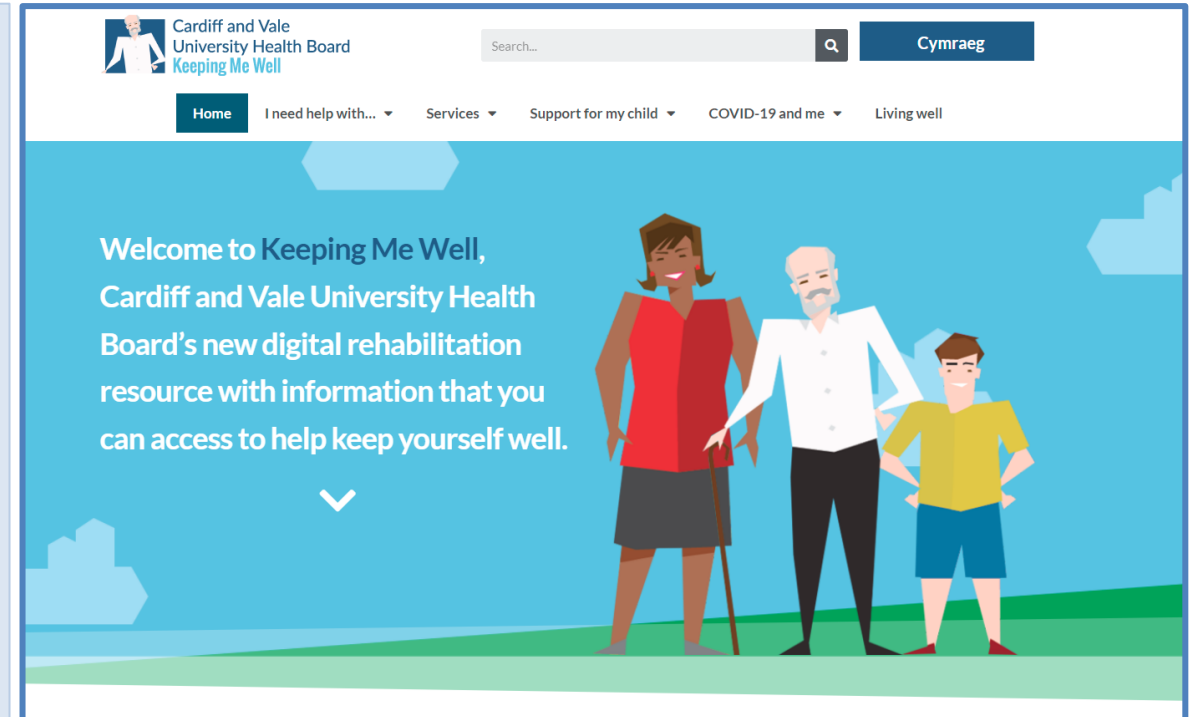
**Key**

- Patient journey
- Patient Activity
- Clinician activity
- Admin activity
- Criteria
- New / changed activity



# Keeping Me Well website

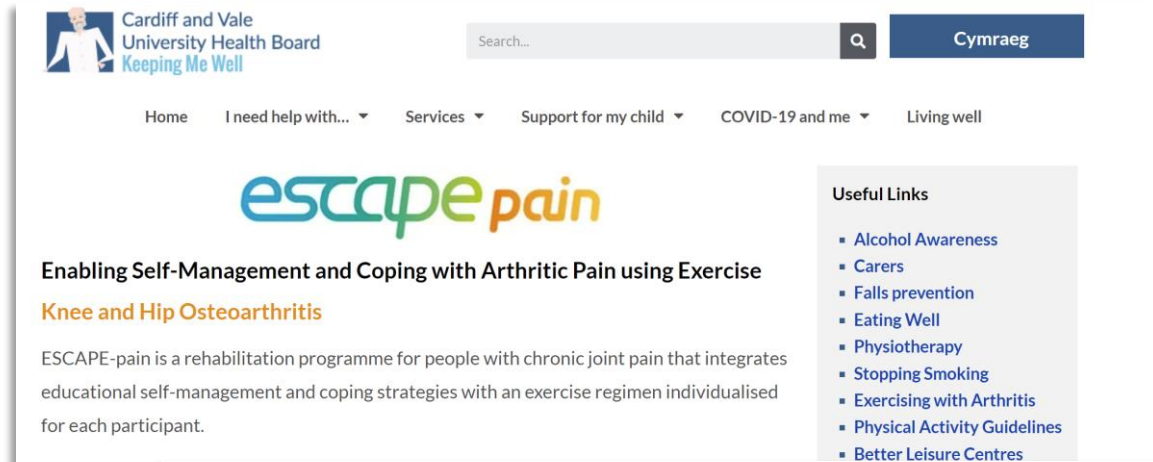
Keeping Me Well has been designed by Cardiff and Vale University Health Board's team of multi-disciplinary specialists to support you and your family to live well.



To view the website, follow this link - [Home - Keeping Me Well](#)



# Examples of our Keeping Me Well content



Cardiff and Vale University Health Board Keeping Me Well

Search... Cymraeg

Home I need help with... Services Support for my child COVID-19 and me Living well

## escape pain

### Enabling Self-Management and Coping with Arthritic Pain using Exercise

#### Knee and Hip Osteoarthritis

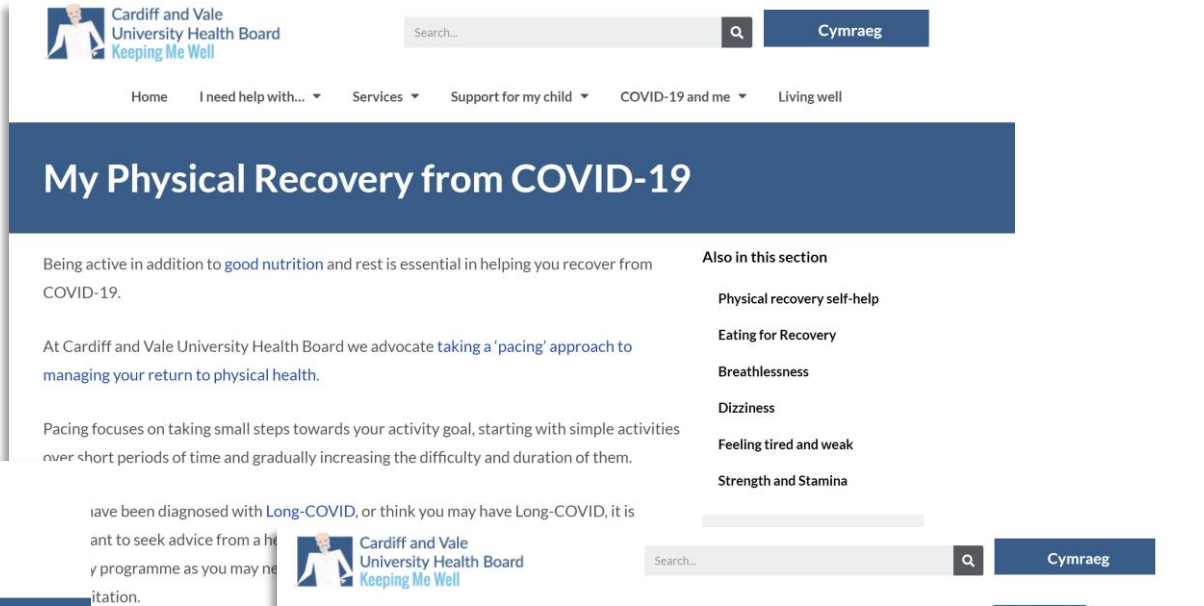
ESCAPE-pain is a rehabilitation programme for people with chronic joint pain that integrates educational self-management and coping strategies with an exercise regimen individualised for each participant.

It helps people themselves with how to cope with

The programme physical function

**Useful Links**

- Alcohol Awareness
- Carers
- Falls prevention
- Eating Well
- Physiotherapy
- Stopping Smoking
- Exercising with Arthritis
- Physical Activity Guidelines
- Better Leisure Centres



Cardiff and Vale University Health Board Keeping Me Well

Search... Cymraeg

Home I need help with... Services Support for my child COVID-19 and me Living well

## My Physical Recovery from COVID-19

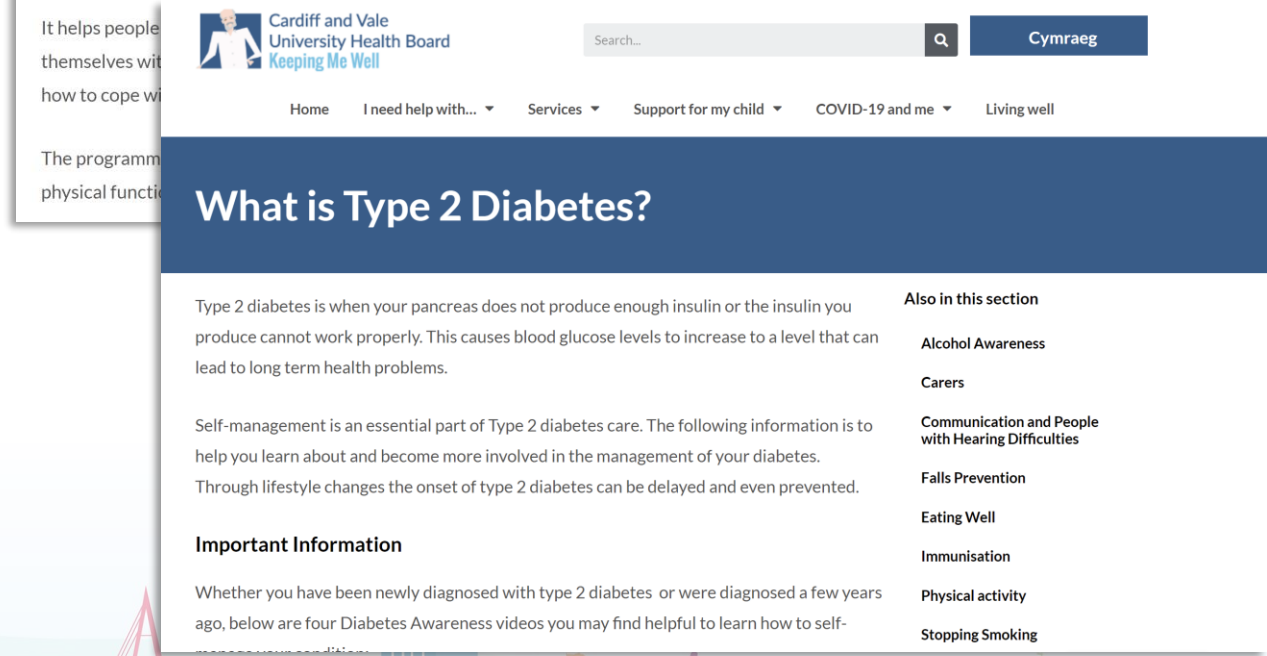
Being active in addition to good nutrition and rest is essential in helping you recover from COVID-19.

At Cardiff and Vale University Health Board we advocate taking a 'pacing' approach to managing your return to physical health.

Pacing focuses on taking small steps towards your activity goal, starting with simple activities over short periods of time and gradually increasing the difficulty and duration of them.

**Also in this section**

- Physical recovery self-help
- Eating for Recovery
- Breathlessness
- Dizziness
- Feeling tired and weak
- Strength and Stamina



Cardiff and Vale University Health Board Keeping Me Well

Search... Cymraeg

Home I need help with... Services Support for my child COVID-19 and me Living well

## What is Type 2 Diabetes?

Type 2 diabetes is when your pancreas does not produce enough insulin or the insulin you produce cannot work properly. This causes blood glucose levels to increase to a level that can lead to long term health problems.

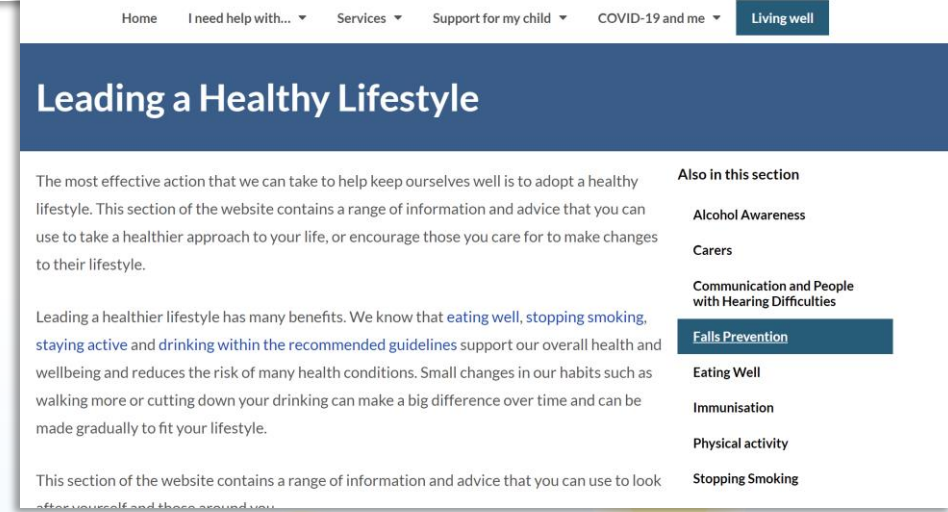
Self-management is an essential part of Type 2 diabetes care. The following information is to help you learn about and become more involved in the management of your diabetes. Through lifestyle changes the onset of type 2 diabetes can be delayed and even prevented.

### Important Information

Whether you have been newly diagnosed with type 2 diabetes or were diagnosed a few years ago, below are four Diabetes Awareness videos you may find helpful to learn how to self-manage your condition.

**Also in this section**

- Alcohol Awareness
- Carers
- Communication and People with Hearing Difficulties
- Falls Prevention
- Eating Well
- Immunisation
- Physical activity
- Stopping Smoking



Cardiff and Vale University Health Board Keeping Me Well

Search... Cymraeg

Home I need help with... Services Support for my child COVID-19 and me Living well

## Leading a Healthy Lifestyle

The most effective action that we can take to help keep ourselves well is to adopt a healthy lifestyle. This section of the website contains a range of information and advice that you can use to take a healthier approach to your life, or encourage those you care for to make changes to their lifestyle.

Leading a healthier lifestyle has many benefits. We know that eating well, stopping smoking, staying active and drinking within the recommended guidelines support our overall health and wellbeing and reduces the risk of many health conditions. Small changes in our habits such as walking more or cutting down your drinking can make a big difference over time and can be made gradually to fit your lifestyle.

This section of the website contains a range of information and advice that you can use to look after yourself and those around you.

**Also in this section**

- Alcohol Awareness
- Carers
- Communication and People with Hearing Difficulties
- Falls Prevention
- Eating Well
- Immunisation
- Physical activity
- Stopping Smoking



# NHS Wales COVID recovery App

- Developed by our Respiratory Health Improvement group commissioned ICST
- Includes input from clinicians across Wales
- Educational
- Self monitoring/motivating
- available free to download Google play or App store



- We thought an MDT approach would work, we now know it does
- We thought best to keep this provided in primary/community care, away from hospital based clinics, we know it works, and have access to specialist care when needed.. its not needed often, very few people needed secondary care intervention
- We want to morph this into services for people with post viral conditions more widely, e.g. ME/CFS and will progress this during 22-23
- The service has flexed and changed it's model to meet feedback from patients and the waiting list
- We continue to explore means to improve equity of access
- We assisted in developing in liaison with Welsh National Opera a national platform to support recovery which continues.
- Elephant in the room..... funding. This type of model we haven't resources previously, but we know there is demand, for both COVID but more widely a rehab approach for post viral recovery. Funding from Sept 21-March 22 initially , then full year 22-23. Need to develop plans for ongoing provision.









**Dr. Christina Ulm**

PhD Biochemistry / Biomedicine  
Director Scientific Sales Departement

# Causes and treatment options of long-term courses of COVID-19 - Study evidence i.v. vitamin C

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1. Pathophysiology of Long-COVID
2. Excursus: Study evidence on ascorbate infusions in COVID-19
3. Study evidence on i.v. vitamin C in Long COVID syndrome

Dr. Christina Ulm

PhD Biochemistry / Biomedicine

Director Scientific Sales Departement

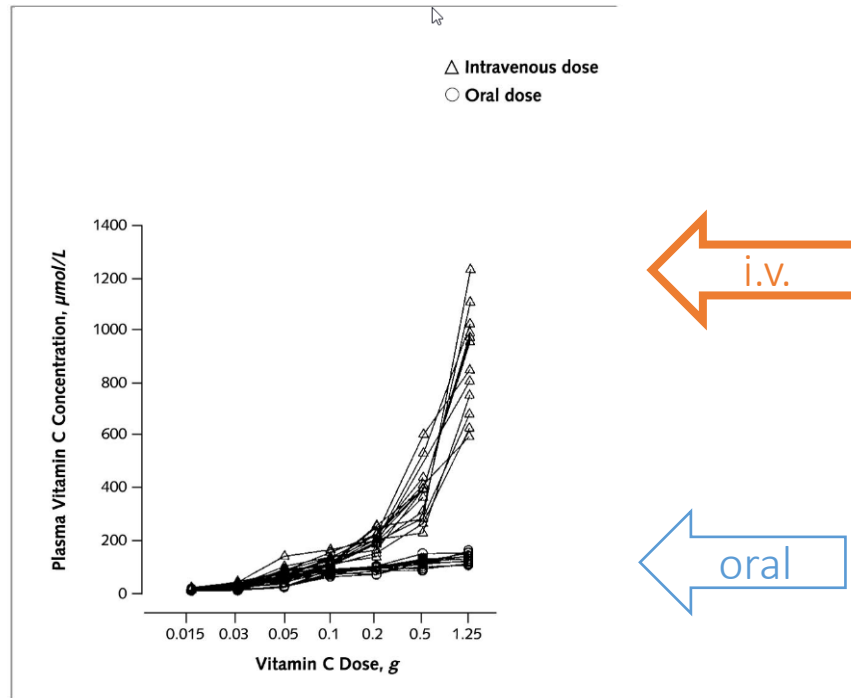


**Conflict of interest:** Expert advisor at Pascoe pharm. Präparate GmbH

# Pharmacokinetics: High plasma levels only possible i.v.

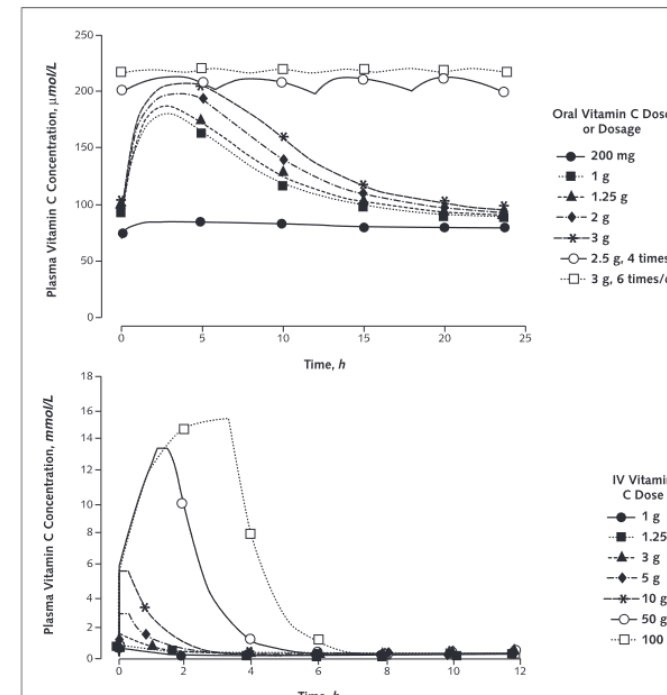
Padayatty, S.J.; Sun, H.; Wang, Y.; Riordan, H.D.; Hewitt, S.M.; Katz, A.; Wesley, R.A.; Levine, M. Vitamin C pharmacokinetics: implications for oral and intravenous use. *Ann Intern Med* 2004, 140, 533-537, doi:10.7326/0003-4819-140-7-200404060-00010.

Figure 1. Plasma vitamin C concentrations in healthy volunteers after intravenous or oral administration of vitamin C.



Plasma vitamin C concentrations are shown as a function of time after the 1.25-g oral or intravenous dose administered at steady state for that dose in 12 persons (3 men, 9 women). Inset: Peak plasma vitamin C concentrations as a function of dose after oral or intravenous administration of vitamin C. Seventeen persons (7 men, 10 women) received doses from 0.015 to 0.1 g, 16 persons (6 men, 10 women) received the 0.2-g dose, 14 persons (6 men, 8 women) received the 0.5-g dose, and 12 persons (3 men, 9 women) received the 1.25-g dose. Persons received each dose while at steady state for that dose.

Figure 2. Predicted plasma vitamin C concentrations in healthy persons after oral (top) or intravenous (IV) (bottom) administration of vitamin C.



oral:  
maximum 220µmol/L possible

i.v.:  
mmol/L possible;  
7.5 g i.v.: 2.38 mM

The 3-co  
µmol/L.

3-compartment pharmacokinetics model

Ongoing large RCTs use daily doses of 200 mg/kg bw

LOVIT: Lessening Organ dysfunction with VITamin C ([NCT03680274](#))

LOVIT-COVID: Lessening Organ Dysfunction With VITamin C - COVID-19 ([NCT04401150](#))

VICToRY: Vitamin C in Thermal injury ([NCT04138394](#))

REMAP-CAP: Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia



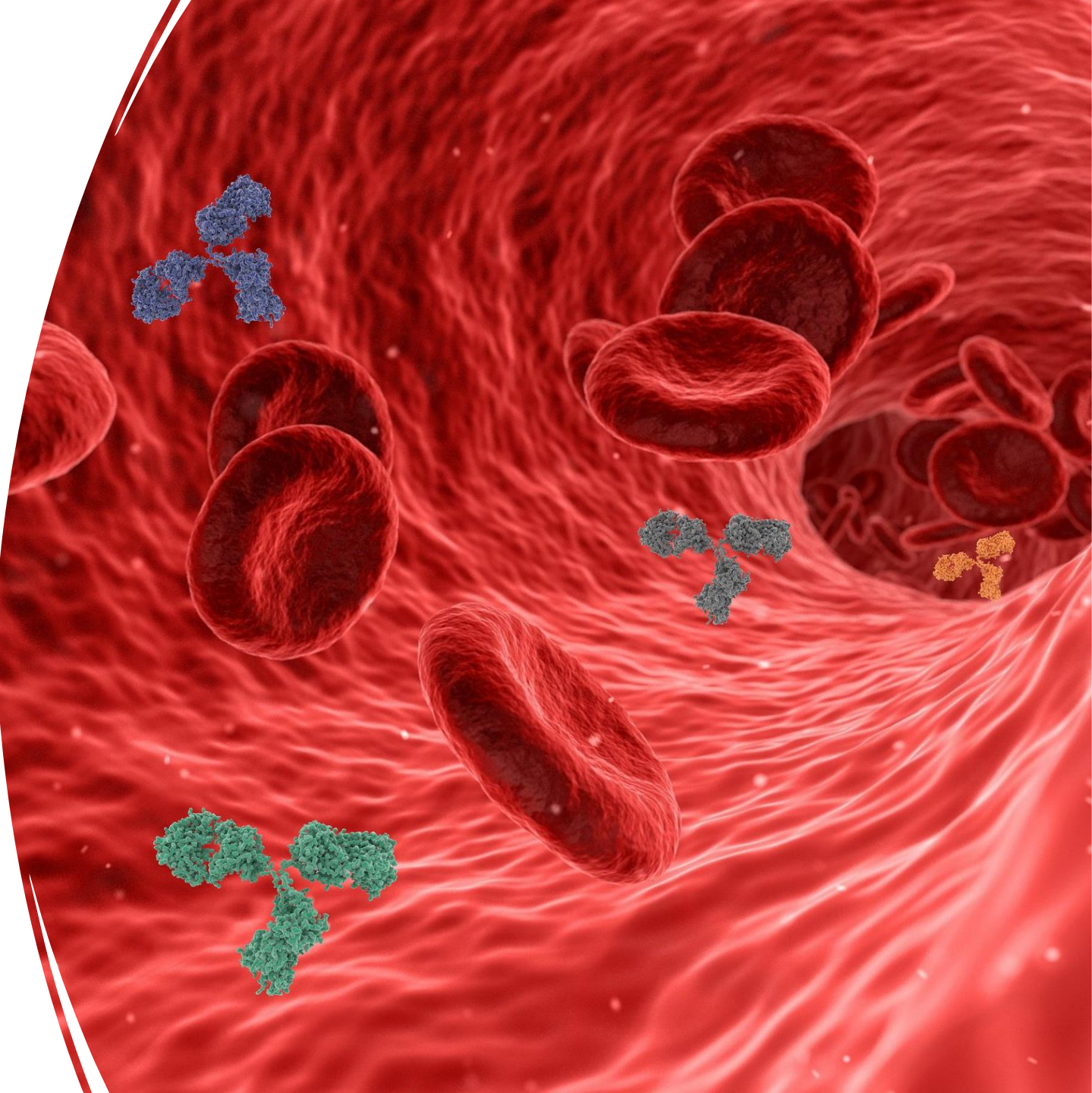
≅ 100 mg/kg bw (75 kg person)

Animals can increase their synthesis capacity to 200mg/kg bw

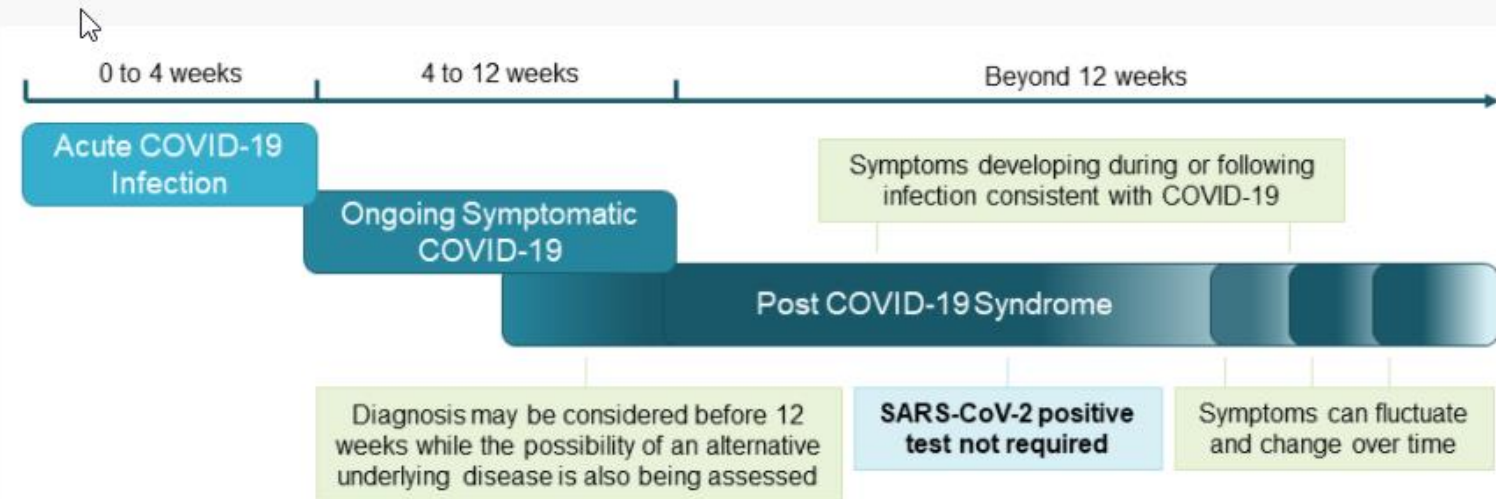
- Levine, M. (1986). "New concepts in the biology and biochemistry of ascorbic acid." *N Engl J Med* **314**(14): 892-902
- Hornig, D. (1975). "Distribution of ascorbic acid, metabolites and analogues in man and animals." *Ann N Y Acad Sci* **258**: 103-118.
- Linster, C. L. and E. Van Schaftingen (2007). "Vitamin C. Biosynthesis, recycling and degradation in mammals." *Febs J* **274**(1): 1-22.

# 1. Pathophysiology of Long-COVID

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## S1-Leitlinie Post-COVID/Long-COVID



Definitions based on NICE, SIGN & RCGP publication, "COVID-19 guideline scope: management of the long-term effects of COVID-19"



Figure 1 | Working definitions of Post-COVID-19 Syndrome based on guideline scope published by the National Institute for Health and Clinical Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), and the Royal College of General Practitioners (RCGP) on 30th October 2020.[6]

### Post-COVID cascade

- acute COVID-19
  - symptoms persist for up to 4 weeks
- persistent symptomatic COVID-19
  - symptoms persist for 4 to 12 weeks
- Post COVID-19 syndrome
  - symptoms persist for more than 12 weeks and cannot be explained by other diagnoses

## Cause for Long COVID

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- WHO:  
*“Long-COVID is triggered by an interaction of different disease mechanisms of the acute disease”*

World Health Organization. Expanding our understanding of post COVID-19 condition: report of a WHO webinar, 9 February 2021. 2021.

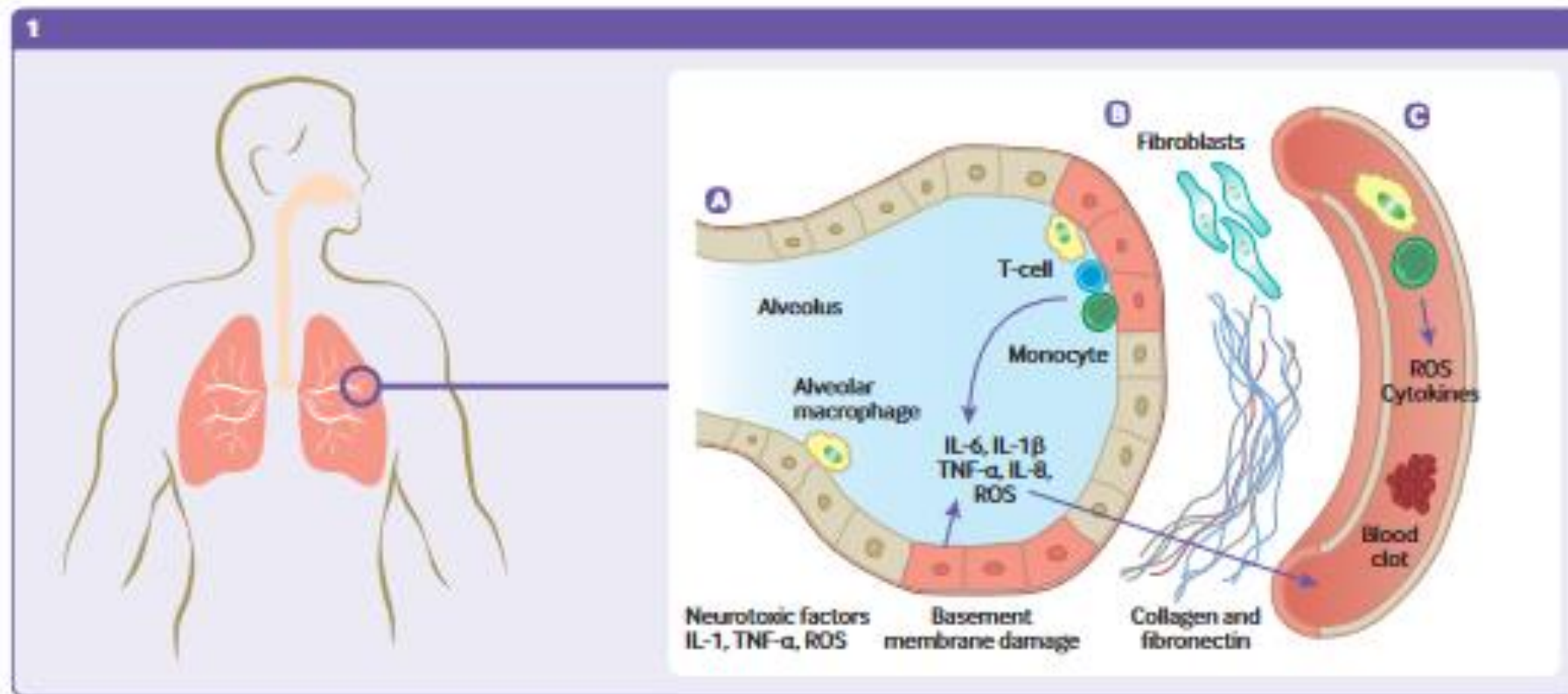
- Hyperinflammation
- vascular and nerve damage
- Immundysregulation:
  - Autoimmunity
  - Virus persistence, long-term infection

Koczulla, A.R.; Ankermann, T.; Behrends, U.; Berlit, P.; Böing, S.; al., e. S1-Leitlinie Post-COVID/Long-COVID. AWMF-online: 2021.



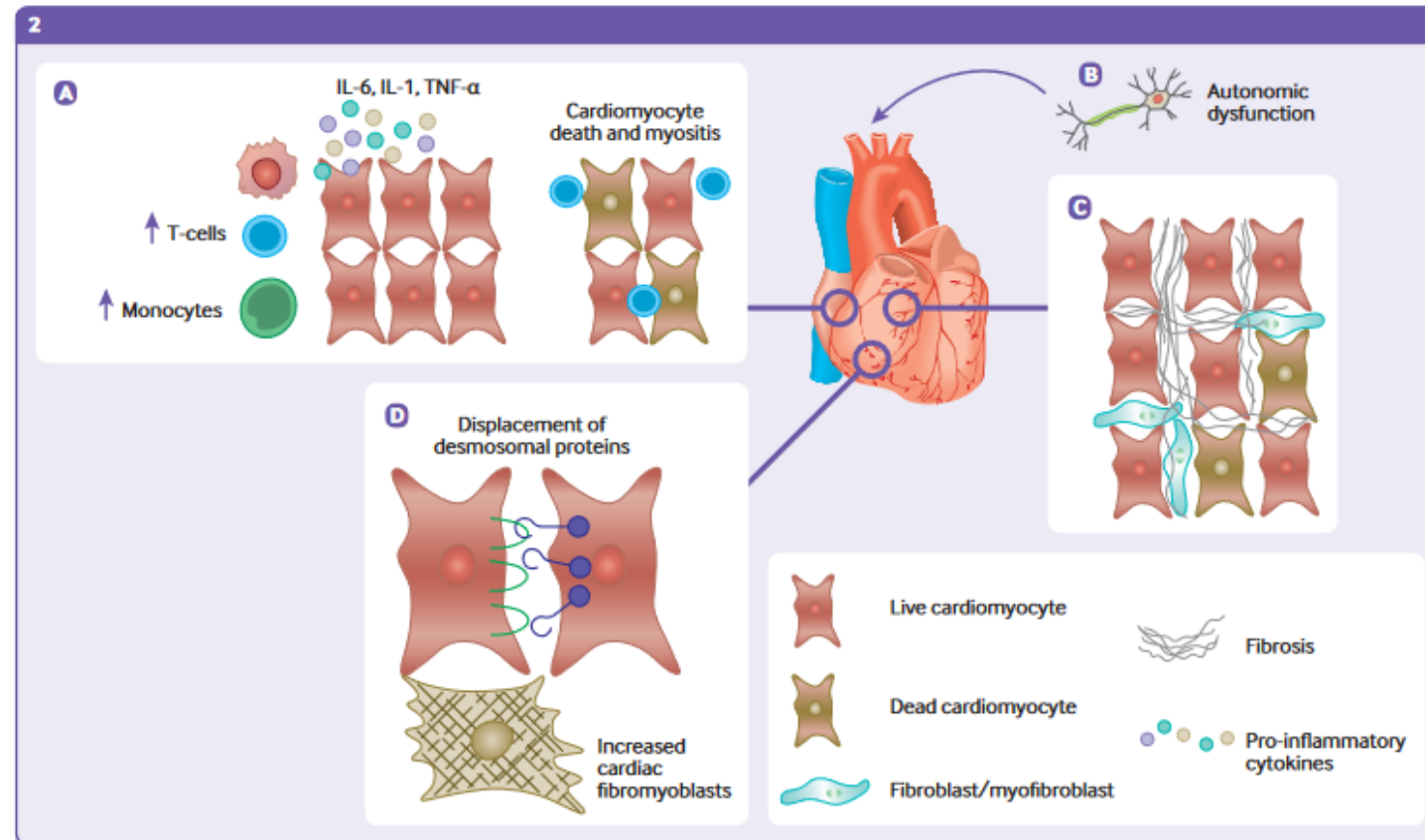
## Long-term effects in the lungs

Crook, H., et al., *Long covid-mechanisms, risk factors, and management*. BMJ, 2021. **374**: p. n1648.



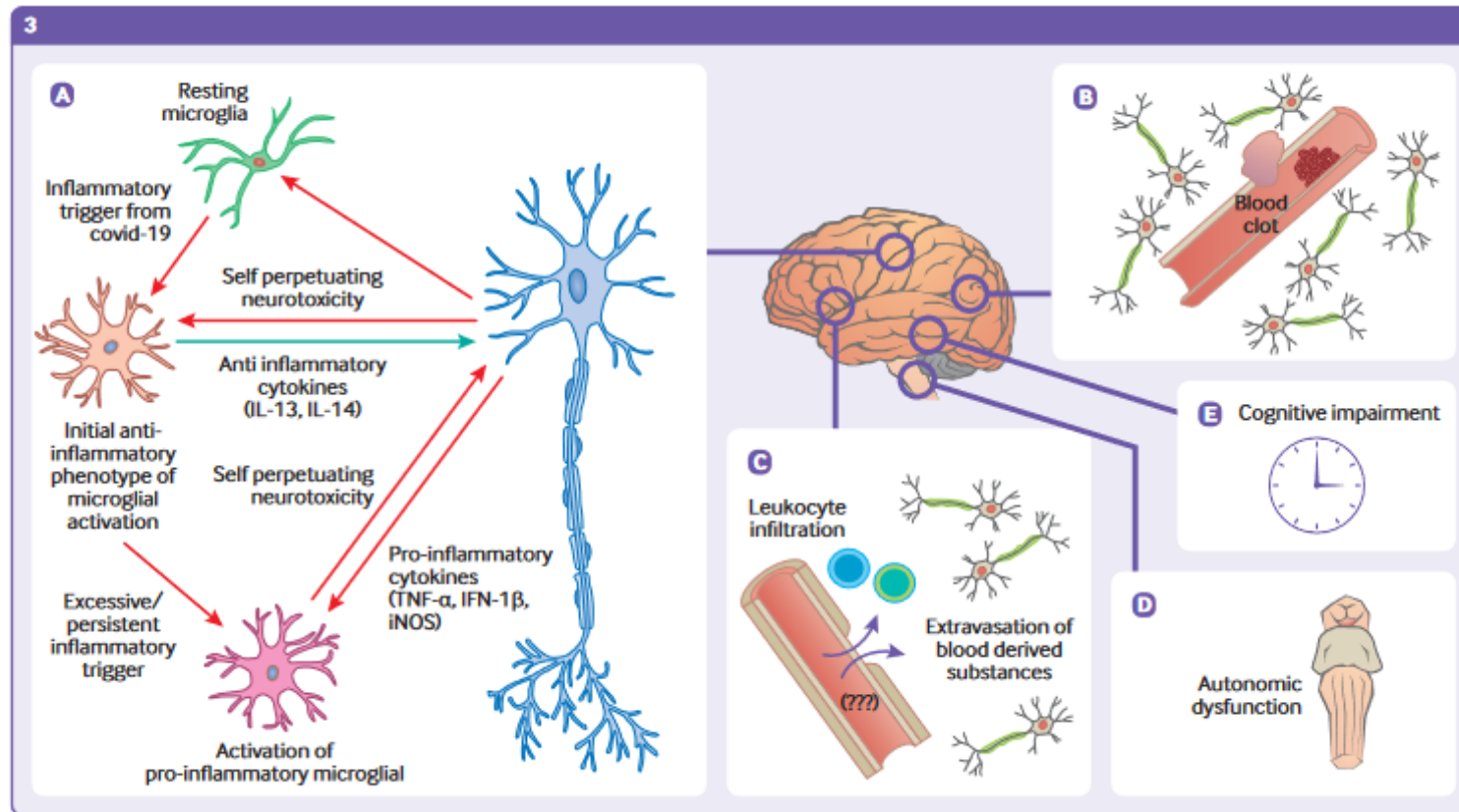
# Long-term effects on the heart

Crook, H., et al., *Long covid-mechanisms, risk factors, and management*. BMJ, 2021. **374**: p. n1648.



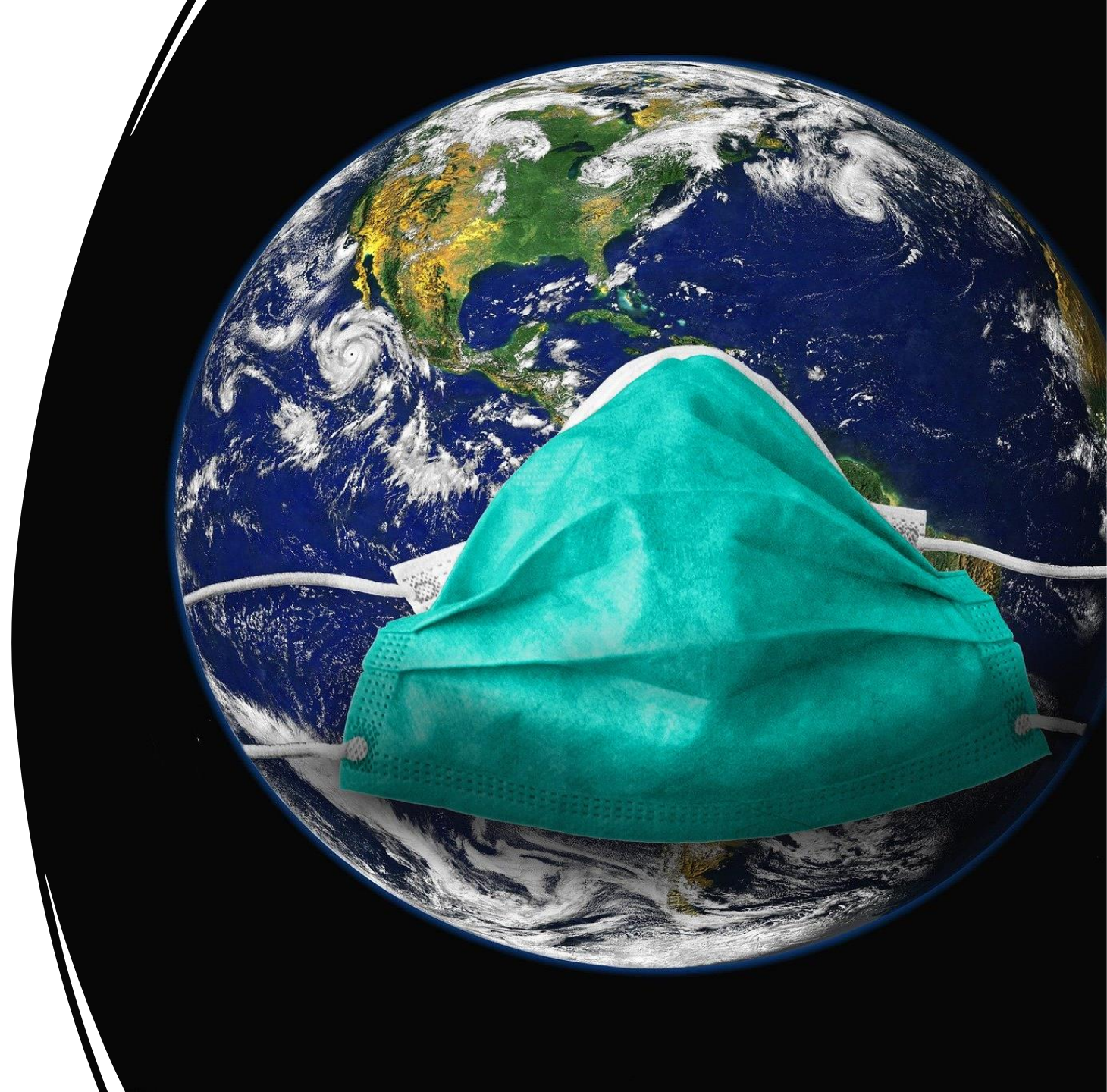
# Long-term effects in the CNS

Crook, H., et al., *Long covid-mechanisms, risk factors, and management*. BMJ, 2021. **374**: p. n1648.



## 2. Excursus: Study evidence on ascorbate infusions in COVID-19

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## What leads to severe courses in COVID-19?

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- **Excessive inflammation**
  - Tissue and vascular damage
- **Thromboses/microembolisms**
  - Organ damage
- **Immunosuppression**
  - Lymphopenia, T-cell suppression

Schonrich G, Raftery MJ, Samstag Y. Devilishly radical NETwork in COVID-19: Oxidative stress, neutrophil extracellular traps (NETs), and T cell suppression. *Adv Biol Regul* 2020;77:100741.

- a major cause of the causes of severe courses is oxidative stress
- 70 - 80 % of COVID patients have a vitamin C deficiency

Holford, P.; Carr, A.C.; Zawari, M.; Vizcaychipi, M.P. Vitamin C Intervention for Critical COVID-19: A Pragmatic Review of the Current Level of Evidence. *Life* 2021, 11, 1166. 2021, 11, 1166

## Oxidative stress is the linchpin of the infection process

Recommendation of the Charité authors:

Use vitamin C at an early stage to reduce the risk of severe courses!

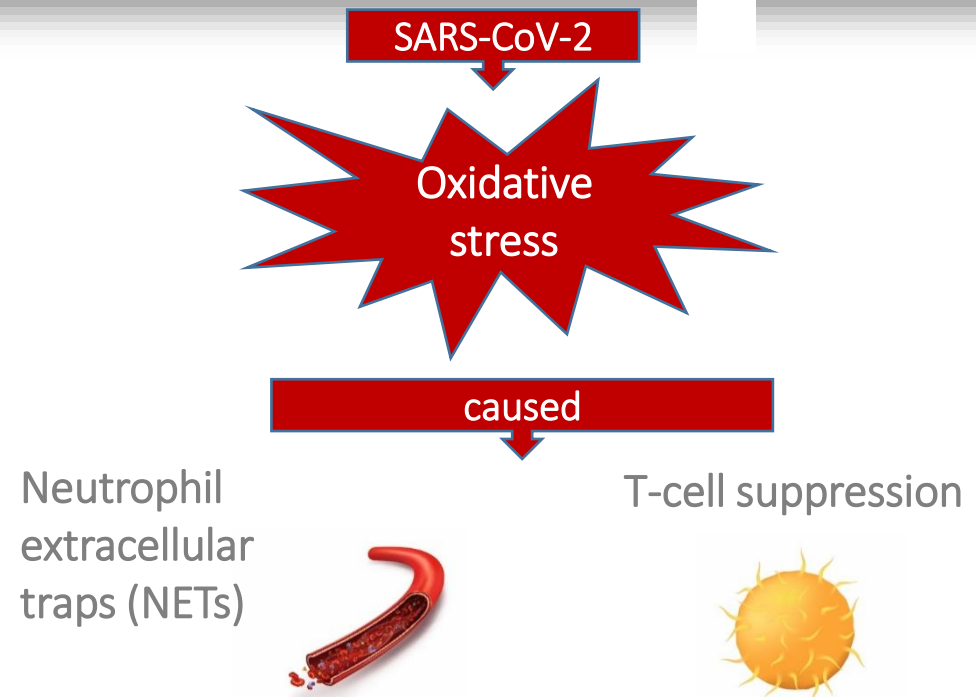


Devilishly radical NETwork in COVID-19: Oxidative stress, neutrophil extracellular traps (NETs), and T cell suppression

Günther Schönrich<sup>a, \*\*</sup>, Martin J. Raftery<sup>a</sup>, Yvonne Samstag<sup>b, \*</sup>

<sup>a</sup> Institute of Virology, Charité – Universitätsmedizin Berlin, Freie Universität Berlin, Humboldt-Universität zu Berlin, Berlin Institute of Health, Berlin, Germany

<sup>b</sup> Section Molecular Immunology, Institute of Immunology, Heidelberg University Hospital, Heidelberg, Germany



## Vitamin C important immunomodulator

### Immunomodulating:

- antimicrobial
- antibacterial
- antiviral
- antiparasitic
- antifungal
- antioxidant
- anti-inflammatory

Review Paper

### Immunomodulatory and Antimicrobial Effects of Vitamin C

Soraya Mousavi, Stefan Bereswill and Markus M. Heimesaat\*

*Institute of Microbiology, Infectious Diseases and Immunology, Gastrointestinal Microbiology Research Group, Charité - University Medicine Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany*

Received: 19 Jul 2019; accepted: 24 Jul 2019



*nutrients*



Review

### Vitamin C and Immune Function

Anitra C. Carr <sup>1,\*</sup> and Silvia Maggini <sup>2</sup>

... appropriate response against pathogens without unduly damaging the host.

Mousavi, S., S. Bereswill and M. M. Heimesaat (2019). "Immunomodulatory and Antimicrobial Effects of Vitamin C." *Eur J Microbiol Immunol (Bp)* **9**(3): 73-79.

Carr, A.C.; Maggini, S. Vitamin C and Immune Function. *Nutrients* **2017**, *9*, doi:10.3390/nu9111211.

## Vitamin C enhances the antiviral function of lung cells

Teafatiller, T.; Agrawal, S.; De Robles, G.; Rahmatpanah, F.; Subramanian, V.S.; Agrawal, A. Vitamin C Enhances Antiviral Functions of Lung Epithelial Cells. *Biomolecules* **2021**, *11*, doi:10.3390/biom11081148.



Article

### Vitamin C Enhances Antiviral Functions of Lung Epithelial Cells

Trevor Teafatiller <sup>1</sup>, Sudhanshu Agrawal <sup>2</sup>, Gabriela De Robles <sup>3</sup>, Farah Rahmatpanah <sup>3</sup>, Veedamali S. Subramanian <sup>1,\*</sup> and Anshu Agrawal <sup>2,\*</sup>

*"Vitamin C not only enhances antiviral activity at multiple levels, but also prevents lung fibrosis and damage"*




## Vitamin C: pragmatic, well-tolerated, supportive intervention for COVID-19

Holford, P.; Carr, A.C.; Zawari, M.; Vizcaychipi, M.P. Vitamin C Intervention for Critical COVID-19: A Pragmatic Review of the Current Level of Evidence. *Life* 2021, 11, 1166. 2021, 11, 1166, doi:<https://doi.org/10.3390/life11111166>.



Review

### Vitamin C Intervention for Critical COVID-19: A Pragmatic Review of the Current Level of Evidence

Patrick Holford <sup>1,\*</sup>, Anitra C. Carr <sup>2</sup> , Masuma Zawari <sup>2</sup> and Marcela P. Vizcaychipi <sup>3,4</sup>

<sup>1</sup> Founder of Institute for Optimum Nutrition, Ambassador House, Richmond TW9 1SQ, UK

<sup>2</sup> Nutrition in Medicine Research Group, Department of Pathology & Biomedical Science, University of Otago, Christchurch 8140, New Zealand; anitra.carr@otago.ac.nz (A.C.C.); masuma.zawari@otago.ac.nz (M.Z.)

<sup>3</sup> Faculty of Medicine, Imperial College, London SW7 2AZ, UK; m.vizcaychipi@imperial.ac.uk

<sup>4</sup> Intensive Care Medicine, Chelsea & Westminster Hospital, London SW10 9NH, UK

\* Correspondence: pat@patrickholford.com; Tel.: +44-(0)-7944-689108

### Vitamin C:

- essential for innate and acquired immune functions
- antioxidant
- anti-inflammatory
- antithrombotic
- immunomodulatory

→ 3 RCT and 6 retrospective cohort studies on vitamin C i.v. in COVID-19

### 3 RCT: Supportive vitamin C shows benefit

- Oxygen supply ↑
- Inflammatory marker ↓
- mortality among the seriously ill ↓
- faster recovery
- shorter hospital stays

Table 2. Randomised controlled trials investigating the effect of intravenous vitamin C (IVC) in patients with COVID-19.

Population Mean Age Location	Intervention Duration	Findings (IVC vs. Control)	Reference
54 patients with COVID-19-pneumonia and multiple organ injury Age = 67 ± 13 years Wuhan, Hubei, China	IVC <sup>1</sup> 24 g/day (n = 27) or placebo (n= 29) for 7 days	Higher PaO <sub>2</sub> /FiO <sub>2</sub> <sup>2</sup> (229 vs. 151 mmHg, <i>p</i> = 0.01) Lower Interleukin-6 (19 vs. 158 pg/mL, <i>p</i> = 0.04) Lower ICU <sup>3</sup> and hospital mortality in patients with SOFA <sup>4</sup> scores ≥3 (4 vs. 10 days, <i>p</i> = 0.03) No difference in ventilation-free days (26.5 vs. 10.5 days, <i>p</i> = 0.56)	[28]
150 patients with severe COVID-19 Age = 52–53 years Karachi, Pakistan	IVC 50 mg/kg/day + standard therapy or standard therapy (75 per group)	Patients became symptom-free earlier (7.1 ± 1.8 vs. 9.6 ± 2.1 days, <i>p</i> < 0.0001) Patients spent fewer days in the hospital (8.1 ± 1.8 vs. 10.7 ± 2.2 days, <i>p</i> < 0.0001) No difference in need for mechanical ventilation (16% vs. 20%, <i>p</i> = 0.4) No difference in mortality (9.3% vs. 14.6%, <i>p</i> = 0.3)	[30]
60 patients with COVID-19 Age = 57–61 years Tehran, Iran	IVC 6 g/day + standard therapy or standard therapy (30 per group) for 5 days	Lower body temperature on 3rd day of hospitalisation ( <i>p</i> = 0.001) Improvement in oxygen saturation on 3rd day of hospitalisation ( <i>p</i> = 0.014) No differences in length of ICU stay or mortality	[31]

<sup>1</sup> IVC: intravenous vitamin C, <sup>2</sup> PaO<sub>2</sub>/FiO<sub>2</sub>: ratio of partial pressure of oxygen to fraction of inspired oxygen, <sup>3</sup> ICU: intensive care unit, <sup>4</sup> SOFA: sequential organ failure assessment.

## Potential benefit of high-dose intravenous vitamin C for coronavirus disease 2019 pneumonia

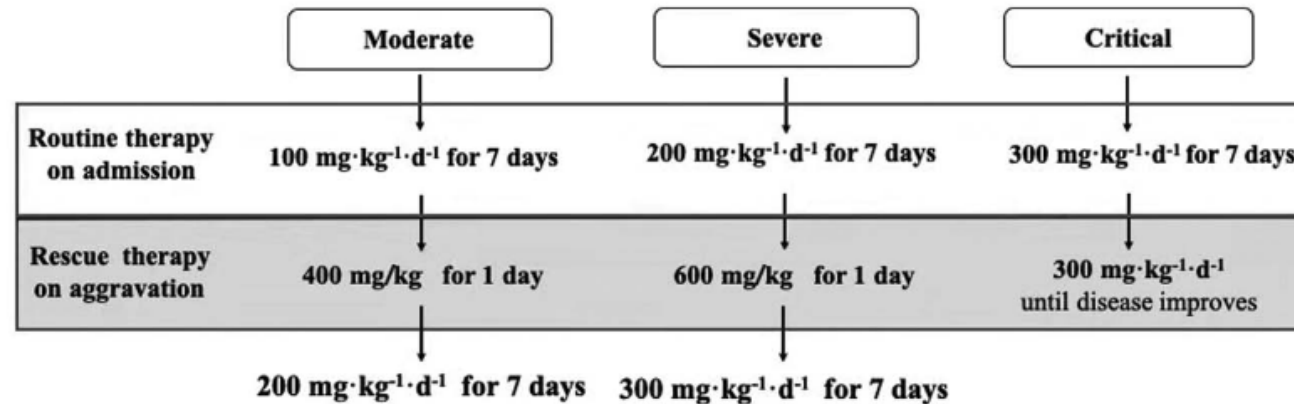
Bing Zhao<sup>1</sup>, Mengjiao Li<sup>1</sup>, Yun Ling<sup>2</sup>, Yibing Peng<sup>3</sup>, Jun Huang<sup>4</sup>, Hongping Qu<sup>5</sup>, Yuan Gao<sup>6</sup>, Yingchuan Li<sup>7</sup>, Bijie Hu<sup>8</sup>, Shuihua Lu<sup>9</sup>, Hongzhou Lu<sup>2</sup>, Wenhong Zhang<sup>10</sup>, Enqiang Mao<sup>1</sup>

<sup>1</sup>Department of Emergency, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China

Zhao, B.; Li, M.; Ling, Y.; Peng, Y.; Huang, J.; Qu, H.; Gao, Y.; Li, Y.; Hu, B.; Lu, S., et al. Potential benefit of high-dose intravenous vitamin C for coronavirus disease 2019 pneumonia. *Chin Med J (Engl)* **2022**, *135*, 23-25, doi:10.1097/CM9.0000000000001746.

Chinese Medical Journal 2022;135(1)

www.cmj.org



**Figure 1:** Flowchart of HDIVC protocol. Aggravation means disease severity transfers to the next level within 24 to 48 hours. HDIVC: High-dose intravenous vitamin C.

Access this article online

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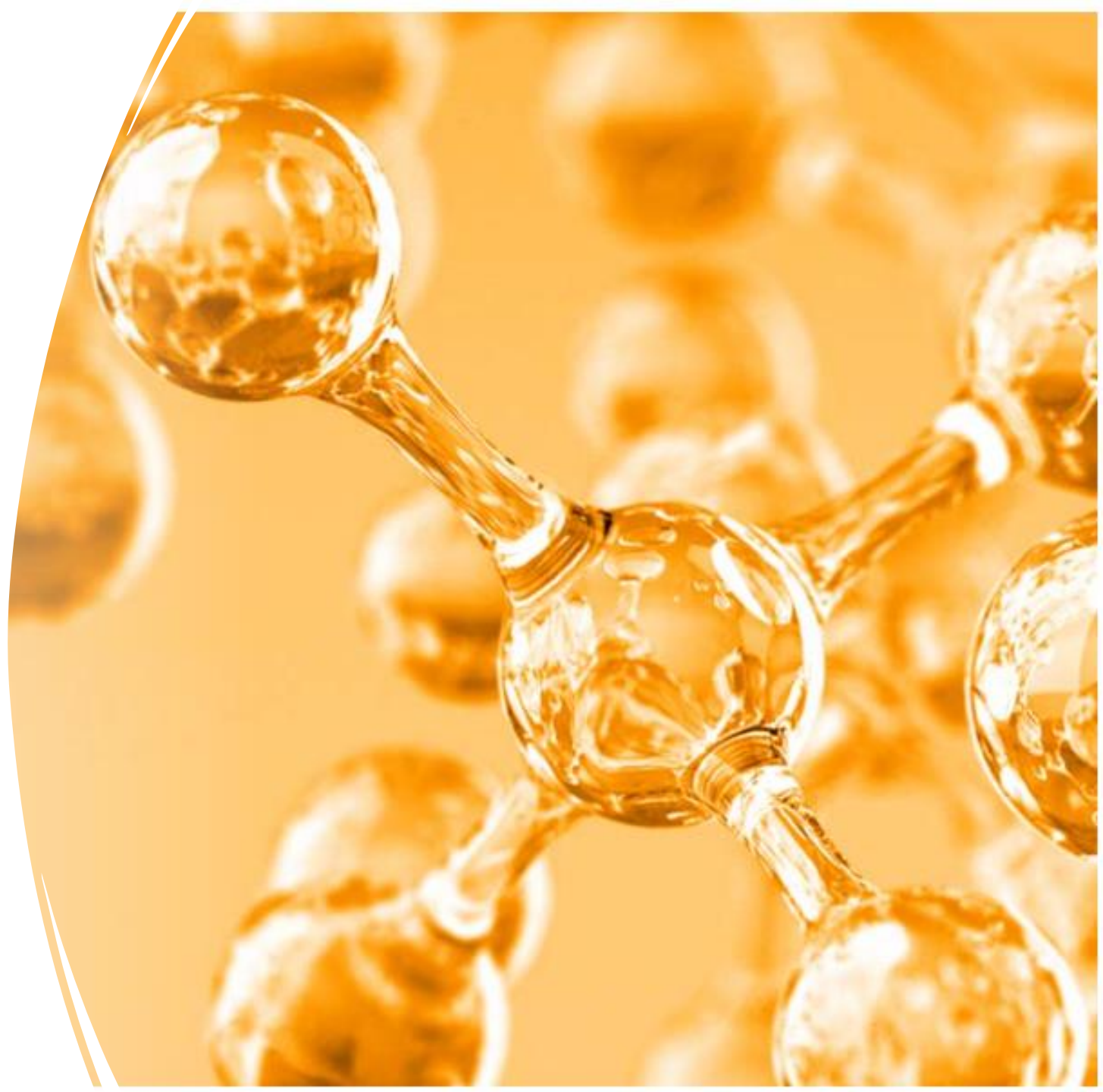


Website:  
www.cmj.org

DOI:  
10.1097/CM9.0000000000001746

### 3. Study evidence on i.v. vitamin C in Long-covid- Syndrome

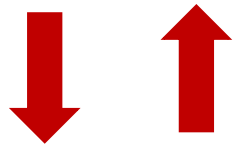
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# Long covid—mechanisms, risk factors, and management

Harry Crook,<sup>1</sup> Sanara Raza,<sup>1</sup> Joseph Nowell,<sup>1</sup> Megan Young,<sup>1</sup> Paul Edison<sup>1,2</sup>

Excessive inflammation +  
oxidative stress (ROS)



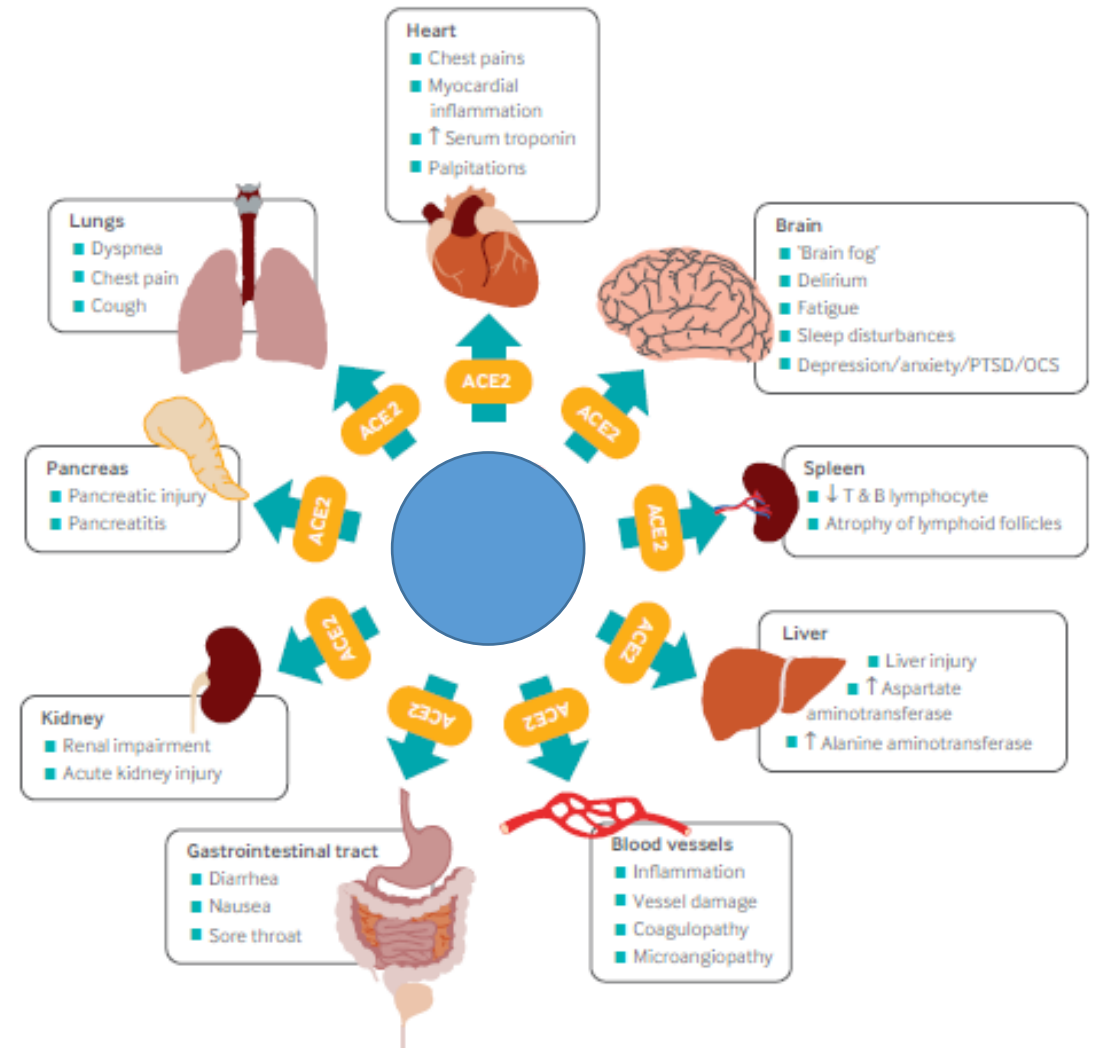
Fibrosis (organ dysfunction)

Thrombosis (hypoxia)

Autonomic nervous system dysfunction

Autoimmunity

BMJ: first publisher



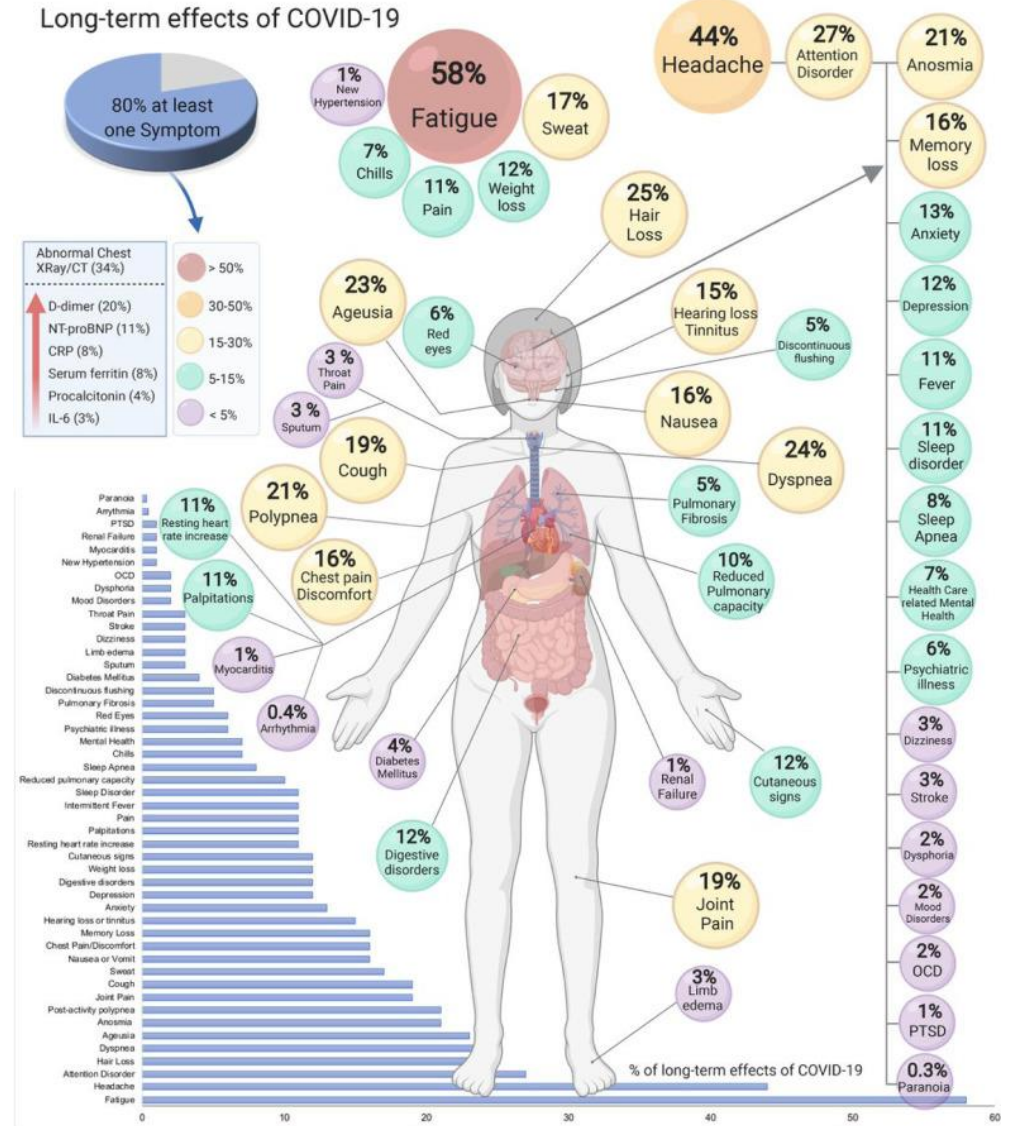
**Fig 1 | Multi-organ complications of covid-19 and long covid.** The SARS-CoV-2 virus gains entry into the cells of multiple organs via the ACE2 receptor. Once these cells have been invaded, the virus can cause a multitude of damage ultimately leading to numerous persistent symptoms, some of which are outlined here

# Meta-analysis on Long-COVID

- Fatigue
- Headache (inflammasome)
- cognitive problems
- Shortness of breath

... ..unfocused, tired, breathless!

Laboratory →  
inflammation, vascular, cardiac disorders



# Long COVID like CFS?

- 1/2021 New ICD-10 code number for Long COVID:
  - U09.9 Post-COVID-19 condition
  - Previously, post-viral fatigue syndrome was recorded under G93.3. chronic fatigue syndrome

Myalgic encephalomyelitis/chronic fatigue syndrome  
-> neuroimmunological disease

**464e** Gijs Bleijenberg, Jos W. M. van der Meer  
**Chronisches Fatigue-Syndrom**  
Für die deutsche Ausgabe Patricia Grabowski und Carmen Scheibenbogen

**DEFINITION**  
Das chronische Fatigue-Syndrom (CFS) ist eine Erkrankung unbekannter Ursache mit persistierender Fatigue und stark eingeschränkter Leistungsfähigkeit im Alltag. Neben der ausgeprägten Fatigue leiden die meisten Patienten unter Schmerzen, kognitiven Störungen und Schlafstörungen oder nicht erholsamem Schlaf. Das Kardinalsymptom von CFS ist die Zunahme der Beschwerden (> 24 Stunden) nach einer nicht im Verhältnis dazu stehenden körperlichen oder geistigen Anstrengung, im Englischen als postexertionelle Malaise bezeichnet. Weitere mögliche Symptome neben Kopfschmerzen, Halsschmerzen, druckschmerzhaften Lymphknoten, Muskelschmerzen und Gelenkschmerzen sind subfebrile Temperaturen, ein grippiges Gefühl, Zunahme von Allergien und Nahrungsmittelunverträglichkeiten, Reizdarmbeschwerden, Schlafstörungen und Reizempfindlichkeit. Die U.S. Centers for Disease Control and Prevention haben diagnostische Kriterien für das chronische Fatigue-Syndrom entwickelt. (Tab. 464e-1). Die sog. „Kanadischen Kriterien“, die 2003 veröffentlicht wurden und international inzwischen am häufigsten verwendet werden, sind umfangreicher und schließen auch weitere CFS-typische Symptome ein (Carruthers et al. 2011).

**ÄTIOLOGIE**  
Es gibt zahlreiche Hypothesen zur Ätiologie des chronischen Fatigue-Syndroms; eine definitive Ursache wurde aber bislang nicht gefunden. Die Unterscheidung zwischen prädisponierenden, auslösenden (präzipitierenden) und die Erkrankung unterhaltenden (perpetuierenden) Faktoren liefert ein Gerüst, das beim Verständnis dieser komplexen Krankheit hilft (Tab. 464e-2).

**PRÄDISPONIERENDE FAKTOREN**  
Meist beginnt CFS mit einem Infekt, der oft in eine Phase von Stress oder hoher körperlicher Aktivität fällt. Zwillingsstudien lassen eine familiäre Prädisposition vermuten, unterschiedliche Gen-Polymorphismen wurden beschrieben, ohne dass es bislang ein eindeutiges genetisches Risikoprofil gibt.

**AUSLÖSENDE FAKTOREN**  
Die meisten Patienten berichten von einer Infektion als Auslöser ihrer Erkrankung. Gut dokumentiert ist CFS infolge einer späten Epstein-Barr-Virus (EBV)-Erstinfektion (infektiöse Mononukleose), Enterovirus-, Dengueinfektion, Q-Fieber und Lyme-Krankheit, jedoch beginnt CFS bei vielen Patienten mit einem uncharakteristischen viralen Atemwegsinfekt. Bei einem kleinen Teil der Patienten (ca. 10 %) findet sich im Blut auch eine erhöhte Epstein-Barr-Viruslast als Hinweis auf eine mögliche Reaktivierung. Auch der Nachweis von IgM-Anti-

**EPIDEMIOLOGIE**  
Das chronische Fatigue-Syndrom tritt weltweit auf und hat bei Erwachsenen eine Prävalenz von 0,2–0,4 %, Frauen erkranken etwa

CFS usually starts with an infection, which often falls during a period of stress or high physical activity.

# Oxidative stress in CFS and PTSD

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Sykes, D.L., et al., *Post-COVID-19 Symptom Burden: What is Long-COVID and How Should We Manage It?* Lung, **2021**. **199**(2): p. 113-119 / Lee JS, Kim HG, Lee DS, Son CG. Oxidative Stress is a Convincing Contributor to Idiopathic Chronic Fatigue. Sci Rep **2018**;8:12890. / Morris G, Stubbs B, Kohler CA, *et al.* The putative role of oxidative stress and inflammation in the pathophysiology of sleep dysfunction across neuropsychiatric disorders: Focus on chronic fatigue syndrome, bipolar disorder and multiple sclerosis. Sleep Med Rev **2018**;41:255-65. / Kim TD, Lee S, Yoon S. Inflammation in Post-Traumatic Stress Disorder (PTSD): A Review of Potential Correlates of PTSD with a Neurological Perspective. Antioxidants (Basel) **2020**;9. / Alzoubi KH, Shatnawi AF, Al-Qudah MA, Alfaqih MA. Vitamin C attenuates memory loss induced by post-traumatic stress like behavior in a rat model. Behav Brain Res **2020**;379:112350

Oxidative stress causes neuronal damage in the hippocampus, amygdala and frontal cortex, which are responsible for regulating stress, emotions, anxiety and memory processing.

## Experimental:

Vitamin C mitigates memory loss due to oxidative stress in the hippocampus triggered by PTSD



## Cause of fatigue

Crook, H., et al., *Long covid-mechanisms, risk factors, and management*. BMJ, 2021. **374**: p. n1648.

fatigue is ongoing (NCT04841759). Vitamin C supplementation may prove useful in treating fatigue in patients with long covid, with a systematic review concluding that high dose intravenous vitamin C could be a beneficial treatment option.<sup>211</sup> LOVIT-COVID (NCT04401150) is an ongoing clinical trial aimed at assessing the effects of high dose intravenous vitamin C on hospitalized patients with covid-19.

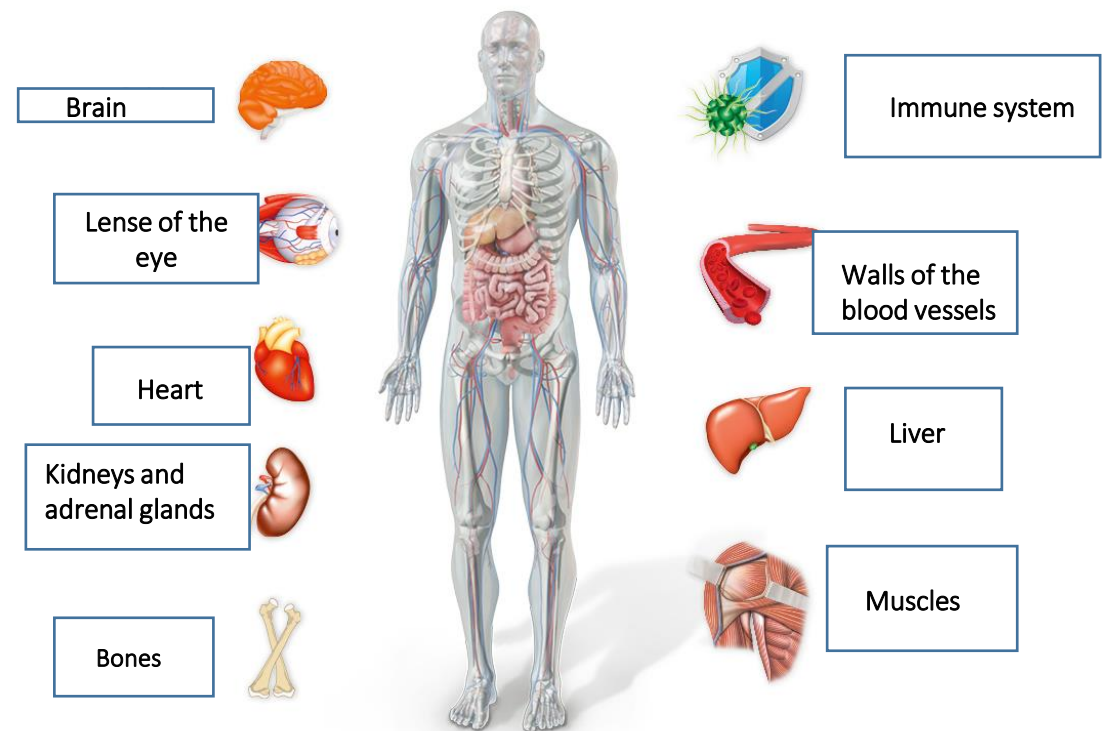
# Vitamin C status in Long-COVID ?

## Vitamin C deficiency symptoms:

- Fatigue
- weakness in performance
- Irritability / depressive mood / impairment of mental well-being
- Pain
- Susceptibility to infections and slower recovery after illnesses

## Vitamin C:

- effective antioxidant
- Cofactor in >150 metabolic processes



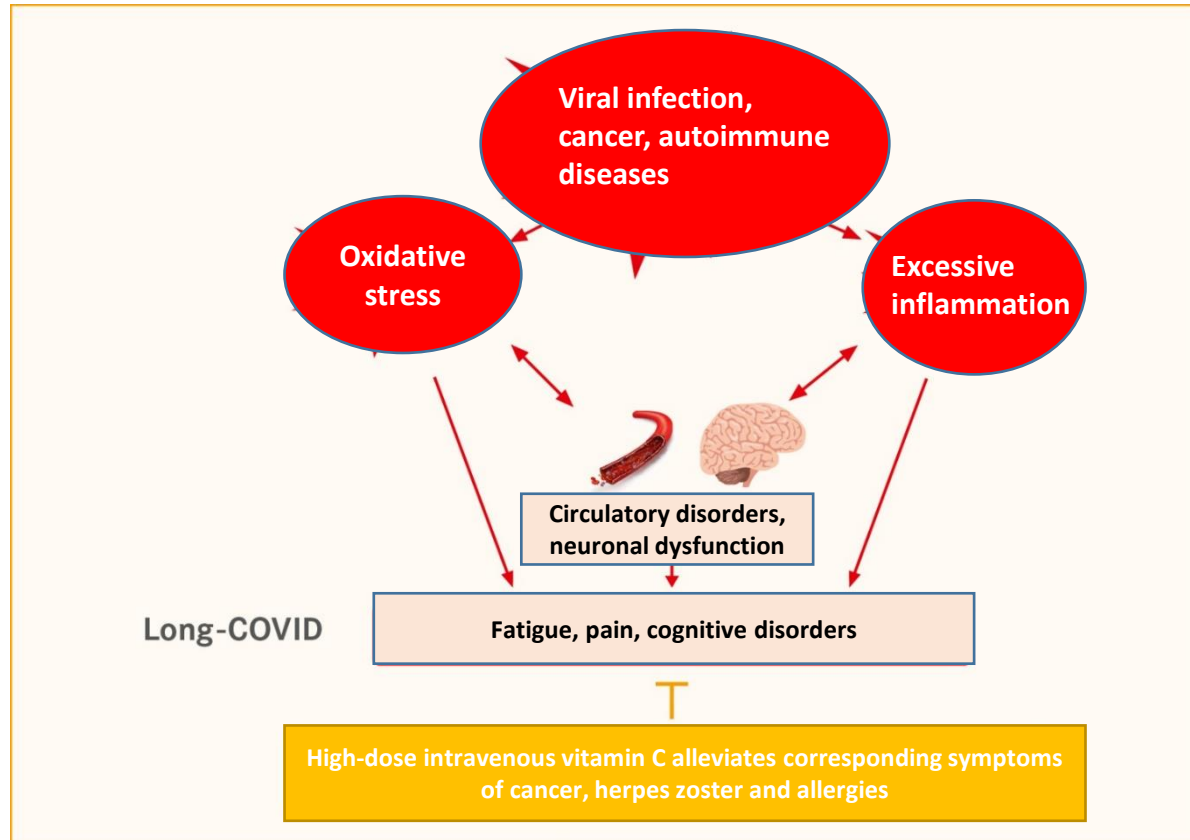
Review

## Feasibility of Vitamin C in the Treatment of Post Viral Fatigue with Focus on Long COVID, Based on a Systematic Review of IV Vitamin C on Fatigue

Claudia Vollbracht <sup>1,2,\*</sup> and Karin Kraft <sup>2</sup>

<sup>1</sup> Medical Science Department, Pascoe Pharmazeutische Präparate GmbH, 35383 Giessen, Germany  
<sup>2</sup> Department of Internal Medicine, University Medicine Rostock, 18057 Rostock, Germany;  
karin.kraft@med.uni-rostock.de  
\* Correspondence: claudia.vollbracht@pascoe.de

Vollbracht, C. and K. Kraft, *Feasibility of Vitamin C in the Treatment of Post Viral Fatigue with Focus on Long COVID, Based on a Systematic Review of IV Vitamin C on Fatigue*. *Nutrients*, 2021. **13**(4).

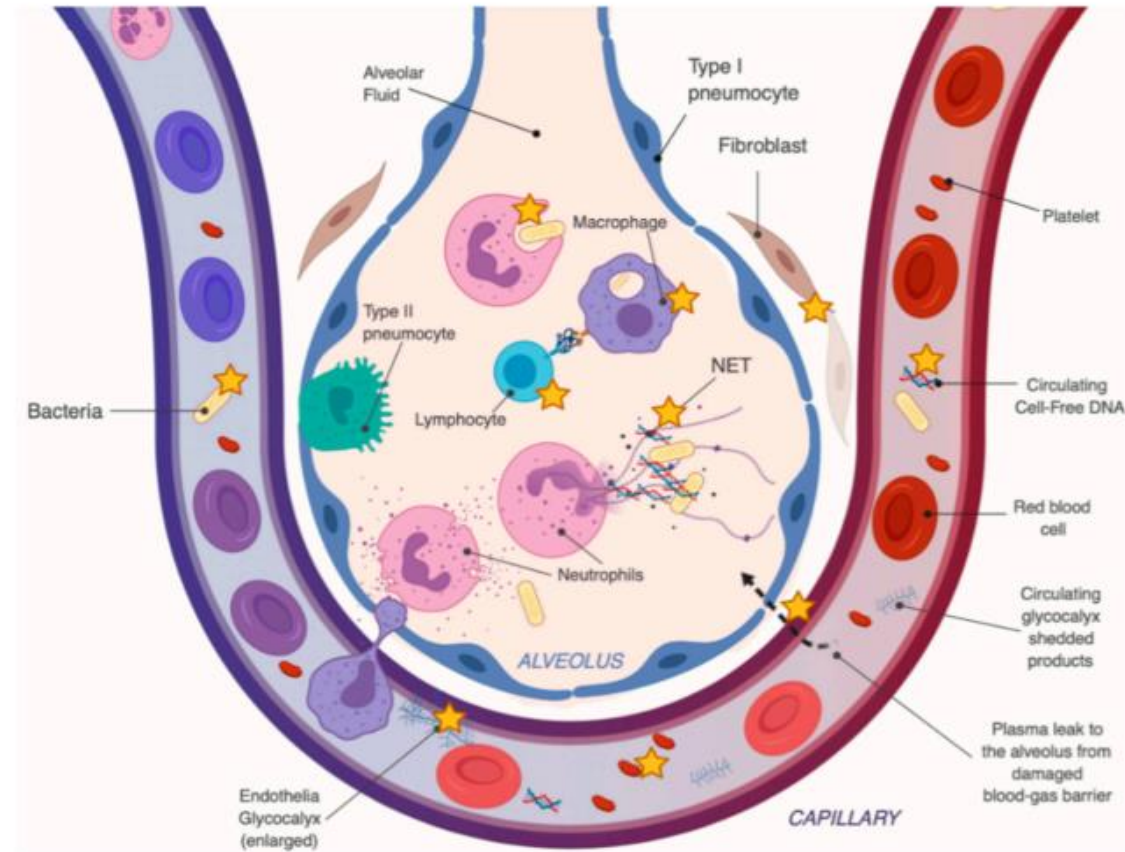


## Vitamin C:

- Antioxidant
- Anti-inflammatory
- Co-factor among others: Serotonin, dopamine, noradrenaline, endorphins ...

# Vitamin C: The immune modulator

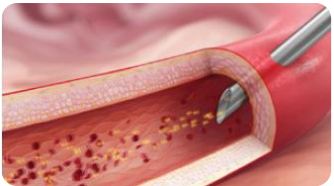
Kashiouris, M.G., et al., *The Emerging Role of Vitamin C as a Treatment for Sepsis*. *Nutrients*, 2020. **12**(2).



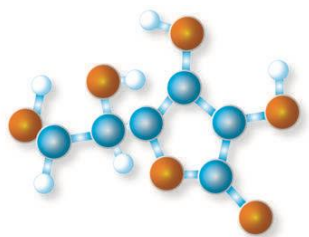
**Figure 4.** Pleiotropic effects of high-dose intravenous vitamin C (HDIVC) in sepsis-induced acute respiratory distress syndrome (ARDS). The orange star [★] points to possible therapeutic targets of HDIVC. The figure illustrates a human alveolus with the capillary membrane, and the blood-gas barrier during sepsis.

## 3 Key messages

Vitamin C deficiency is a pathogenic condition and weakens the immune system



Only infusions produce high active levels in the blood and compensate for a vitamin C deficiency



Vitamin C activates many anti-viral immune processes and at the same time protects the lungs, vessels and nerves from oxidative stress/excessive inflammation.

# Sneak preview



## **Oxidative stress and hyper-inflammation as major drivers of severe COVID-19 and Long COVID: Implications for the benefit of high-dose intravenous vitamin C**

**Claudia Vollbracht<sup>1</sup> and Karin Kraft<sup>2</sup> \***

<sup>1</sup>Medical Science Department, Pascoe Pharmazeutische Präparate GmbH, 35383 Giessen, Germany

<sup>2</sup>University Medicine Rostock, 18057 Rostock Germany

**\* Correspondence:**

Karin Kraft

Karin.Kraft@med.uni-rostock.de

**Keywords:** ascorbic acid<sup>1</sup>, covid 19<sup>2</sup>, long/post covid<sup>3</sup>, fatigue<sup>4</sup>, oxidative stress<sup>5</sup>, hyperinflammation<sup>6</sup>, autoimmunity<sup>7</sup>, cognitive dysfunctions<sup>8</sup>

# Thank you for your attention

---

Dr. Christina Ulm  
PhD Biochemistry / Biomedicine  
Director Scientific Sales Departement



See what everyone sees and think  
what no one has thought yet.  
(Albert Szent-Györgyi)

## Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion

See full Summary of Product Characteristics (SmPC) before prescribing; available at <https://www.medicines.org.uk/>

**Active ingredient:** 1 vial with 50 ml concentrate for solution for injection/infusion contains 7.5 g ascorbic acid. **Indication:** treatment of clinical vitamin C deficiency states not amenable to dietary supply or oral replacement therapy. Indicated in adults. **Dosage Adults:** The usual dose is 0.5 to 1.0 g ascorbic acid (corresponding to 3.3 – 6.7 ml concentrate). Severe trauma or surgery can require higher daily dosages of at least 3 g ascorbic acid to restore normal plasma levels. Depending on the disease situation, up to 7.5 g ascorbic acid (50 ml concentrate) per day may be used for infusion. **Children** younger than 12 years of age must not receive more than 5-7 mg ascorbic acid/kg body weight per day. High doses of Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion are contraindicated in children under 12 years. No data are available on the use of Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion in adolescents. **Instructions for use/handling:** The preservative-free concentrate for solution for injection/infusion is for **single** use only. It has to be used immediately after opening. Any unused solution must be discarded. Prior to use, Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion must be diluted with isotonic NaCl solution. A dilution ratio of one part of Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion plus 2 parts of isotonic saline solution. After dilution, slow intravenous injection or infusion must be performed by a physician. The duration of use depends on the course of the illness and the results of laboratory tests. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients, oxalate urolithiasis, hyperoxaluria, iron storage disorder/iron overload (e. g. thalassemia, hemochromatosis, sideroblastic anemia, erythrocyte concentrate transfusions), renal insufficiency (KDIGO GFR stages G4 and 5 ( $< 30\text{ml/min/1.73m}^2$ ), glucose-6-phosphate dehydrogenase deficiency/defect, children under 12 years of age: high doses of vitamin C. **Warnings/precautions for use:** Renal insufficiency (KDIGO GFR stage G3 (30 to  $< 60\text{ml/min/1.73 m}^2$ ). Patients with impaired kidney function have a higher risk of oxalate precipitation in urine due to vitamin C supplementation. Therefore, a strict monitoring of renal function (e.g. GFR, albumin) should be done. Patients with a predisposition for the formation of renal calculi are at risk for the development of calcium oxalate stones when using high-dose vitamin C. It is recommended not to exceed a daily vitamin C intake of 100-200 mg in patients with a history of recurrent kidney stone formation. Each injection vial of Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion contains 42.3 mmol (972 mg) sodium. This has to be taken into consideration by patients on a controlled sodium diet. Adequate fluid intake has to be assured (approximately 1.5 – 2 l per day). It is also recommended to avoid additional oxalate-rich foods during therapy with ascorbic acid. In isolated cases, patients with a history of difficulty breathing (such as obstructive or restrictive bronchial and lung disease) may experience acute dyspnea when treated with high-dosed ( $\geq 7.5\text{ g}$ ) of Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion. Lower initial doses are therefore recommended in these patients. After the administration of gram doses, the ascorbic acid level in the urine may rise as much that the performance of tests for certain clinical-chemical parameters (glucose, uric acid, creatinine, inorganic phosphate) may be affected and the tests may yield false results. Testing for occult blood in the feces may also yield false-negative results. **Note to be considered in the treatment of diabetic patients:** Parenterally administered ascorbic acid interferes with the blood glucose determination assay. **Pregnancy and breastfeeding:** Daily doses of 100 to 500 mg ascorbic acid should not be exceeded in pregnant women and nursing mothers. Due to its high vitamin C content, Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion is not suited for the use in pregnancy and lactation. **Adverse reactions (very rare,  $< 1/10,000$ ):** Respiratory hypersensitivity reactions (e.g. dyspnoea/respiratory distress), cutaneous hypersensitivity reactions (e.g. exanthema, urticaria, pruritus), transient circulation problems (e.g. dizziness, nausea, cephalgia, impaired vision), reactions such as chills and elevated temperature were observed in patients with acute infections, large doses may cause gastrointestinal disorders (e. g. nausea, vomiting, diarrhoea) or result in hyperoxaluria and renal oxalate calculi may form if the urine becomes acidic and doses of 600 mg or more daily have a diuretic action. **Legal category:** Prescription only medicine. **Cost:** £31 per 50ml vial





Rowan Burnstein, Cambridgeshire  
and Peterborough Long Covid  
Service, Clinical Lead at Cambridge  
University Hospitals NHS Foundation  
Trust

& Louise Goswell, Service lead at  
Cambridgeshire and Peterborough  
NHS Foundation Trust

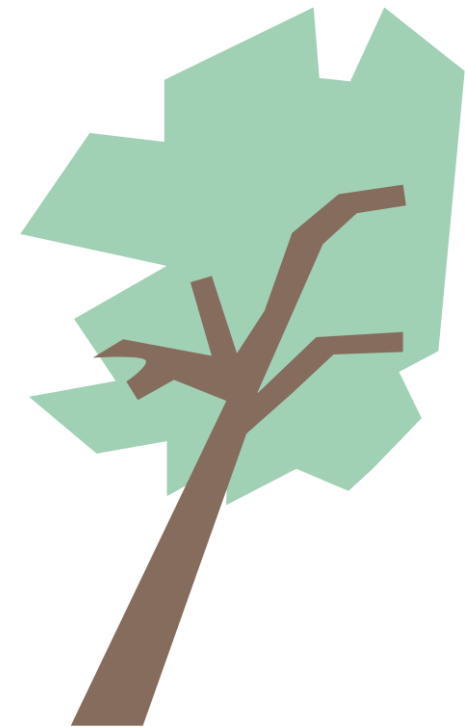
# A Novel, ICS-based, Patient-centred, Multidisciplinary Service

Rowan Burnstein – Clinical Lead  
Louise Goswell – Service Manager



# Objectives

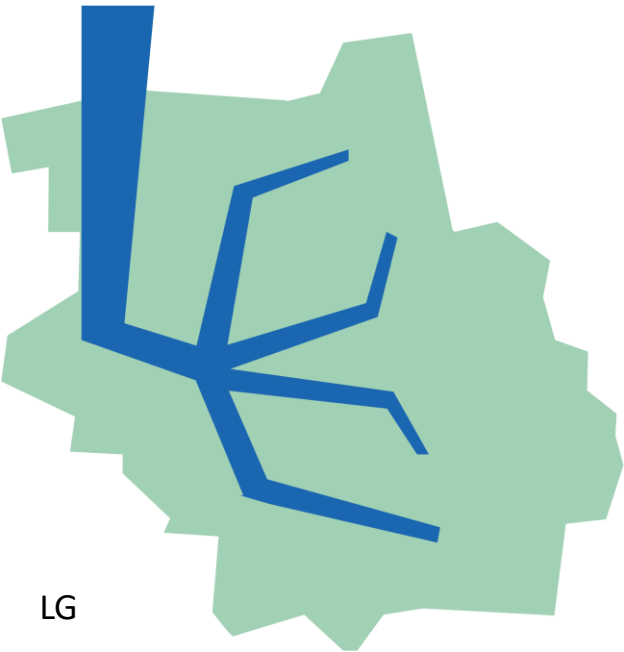
- What is Integration?
- Post Covid19 Syndrome – an opportunity
- The interface
- Challenges
- The C&P Model
- How do we achieve it
- Practical Strategies
- Examples



# What do we mean by 'Integration'

**'Integrated care** is about giving people the support they need, joined up across local councils, the NHS, and other partners. It removes traditional divisions between hospitals and family doctors, between physical and mental health, and between NHS and council services'

NHS England, 2022



# Post Covid19 Syndrome – An opportunity to do things differently



# Post Covid19 Syndrome – The Challenge of the Disease

- New
- We do not understand why people get it
- We don't have a cure
- We do not know the long term impact for the individual patient
- For a subgroup of patients it is chronic
- Multitude of symptoms that do not necessarily align to traditional disease presentations or management
- Care predominantly within primary and community services but needs secondary care input
- Not built into service specs. etc
- The “systems” such as they are for managing chronic diseases are already overburdened

# The Challenges of Integration: Secondary Care perspective v Community Perspective

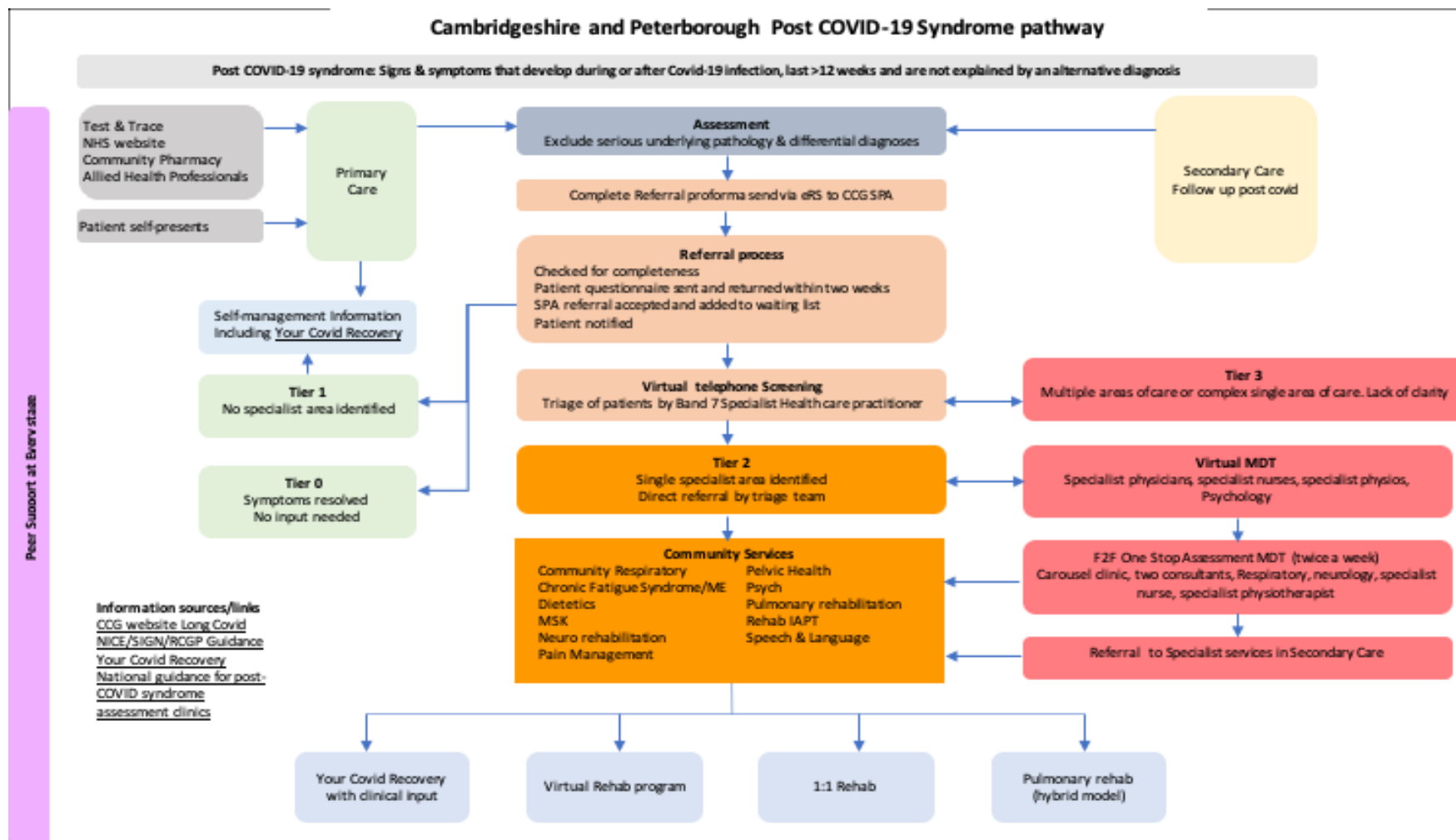
- Knowing your **stakeholders**
- Knowing your **topic area** – a challenge with a new syndrome!
- Understanding of **roles**
- **Trust**
- **Time**
- **Beliefs**/pre-conceived ideas
- Individual system **pressures**
- **IT systems**
- **Finance**







# The Cambridgeshire & Peterborough Model - Assessment



**REFERRALS FROM ASSESSMENT SERVICE**  
Incl. Offer of Peer to Peer Support

Peer Support Worker offered throughout pathway

**'YOUR COVID RECOVERY' (Tier 1)**  
Including Clinical In-put

**Discharge back to GP**

**Other Health, Social Care and Whole System Referral Options**

- Richmond Fellowship
- Access to Work
- Long Covid Coordination Hub
- Etc

**VIRTUAL REHABILITATION PROGRAMME (Tier 2)**  
8 weeks

- Fatigue (x 2)
- Anxiety & Depression
- Brain Fog
- Breathlessness
- Pain Physiology
- Exercise & Rehabilitation
- Vocational Rehab & Resources

**Clinical 1:1 FU Phone Call**

**Post Programme Evaluation**  
3 months

**1:1 REHABILITATION (Tier 3)**  
Home Visits & Virtual

**OT Focus**

- Vocational Rehab
- Fatigue & Brain Fog
- Lifestyle Redesign

**PT Focus**

- Dysfunctional Breathing
- Exercise tolerance

**DC SOS for 6 months**

**Onward referral to specialist services**

- ENT
- SALT
- BIS
- CFS/ME
- IAPT
- Dietetics
- Etc

**Pulmonary Rehab Service – hybrid offer**  
Including access to the Virtual Rehabilitation Programme resources

# The Interface for Primary Care

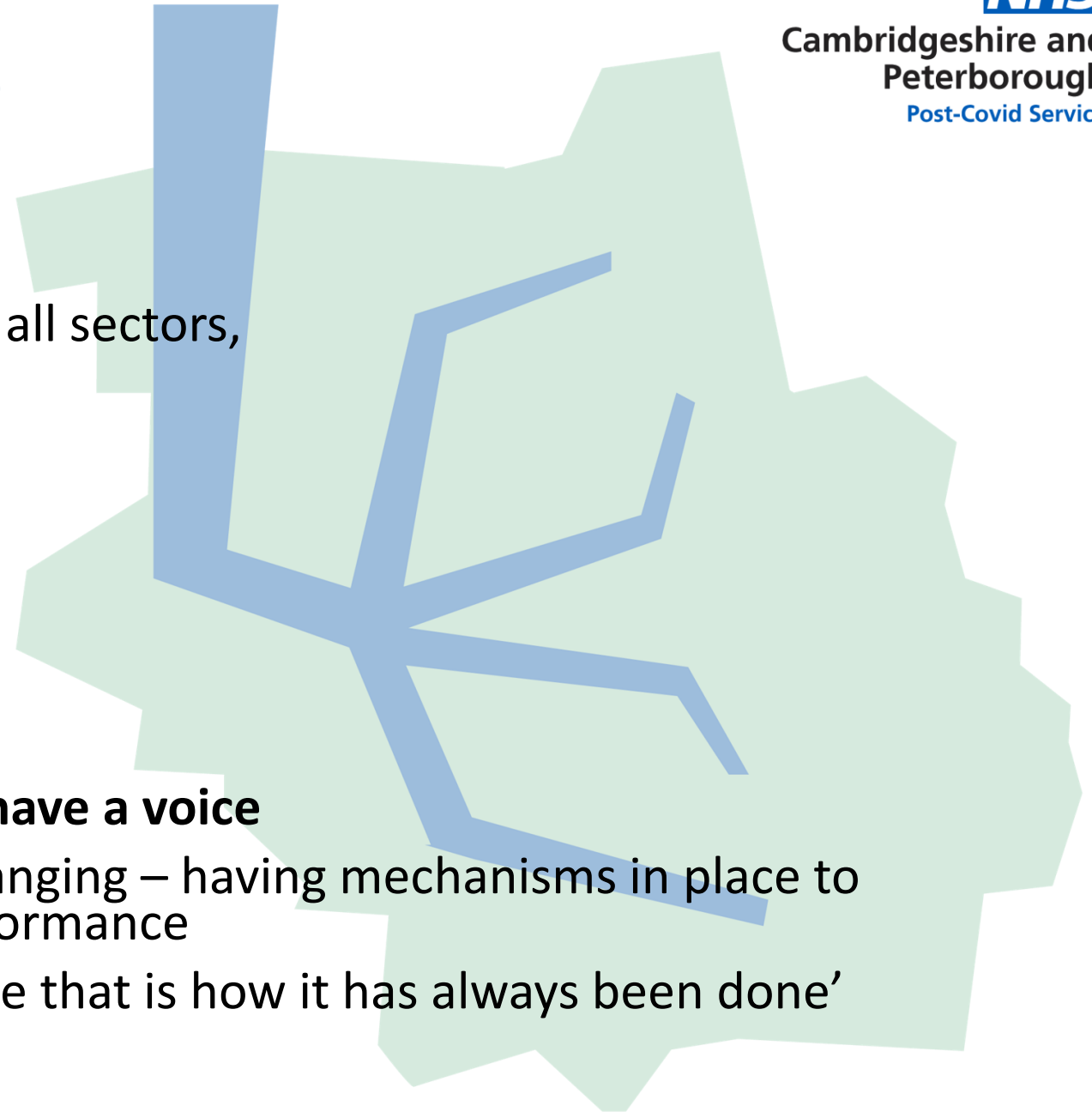
- We have created a **‘one stop’ service** – for both *assessment and management* – including assessment that spans primary, community and secondary care
- Responding to the complexity of this syndrome – i.e. multiple symptoms, clusters, variability – requiring a multi and inter-disciplinary approach to managing these patients
- Mutual understanding and trust between primary care and us as the provider
- Primary Care need to be confident that they do not have to make multiple referrals to upstream or downstream services
- The majority of the rehab element is “inhouse” – ensuring seamless care that is fluid for patients

# The Interface with Secondary Care

- Targeted
- Important to “de-medicalise” symptoms
- Equally important to exclude conditions that need ongoing secondary care input/follow up
- Potential to result in a lot of investigations with “no” diagnostic value (although negative results may also be beneficial).
- Managing patient expectations/understanding of the role of secondary care is pivotal

# How do we achieve it?

- Leadership
- Core team, meeting regularly crossing all sectors,
- Shared vision
- Challenge barriers
- Stakeholders – do not forget patients!
- Collaboration
- Shared Learning
- **Respect**
- **Listen – every member of staff must have a voice**
- Continuously adapting, improving, changing – having mechanisms in place to enable assessment and review of performance
- Do not be bound by barriers – ‘because that is how it has always been done’



# Practical Strategies

- Primary Care – engage on all levels – CCG, PCN and Surgery level
- Ask for feedback, from all sectors and especially patients
- Inform and communicate feedback is being implemented
- Ensure everyone feels valued
- Acknowledge skill
- Learn from others – benchmark, network, reach out
- Embrace “new practices”
- Blatant “self promotion”

# Integrated Resources

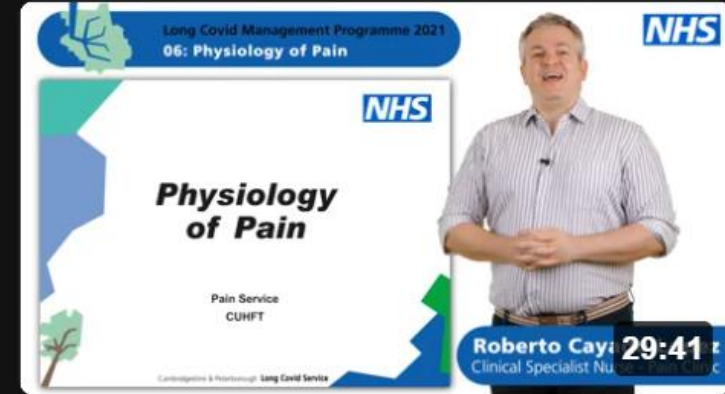
- Resources for patients have been recorded in order to support patients through self management
- Currently being re-recorded in order for them to be used by other Post-Covid services across the country



Search videos, people, and more



Rache 36:17



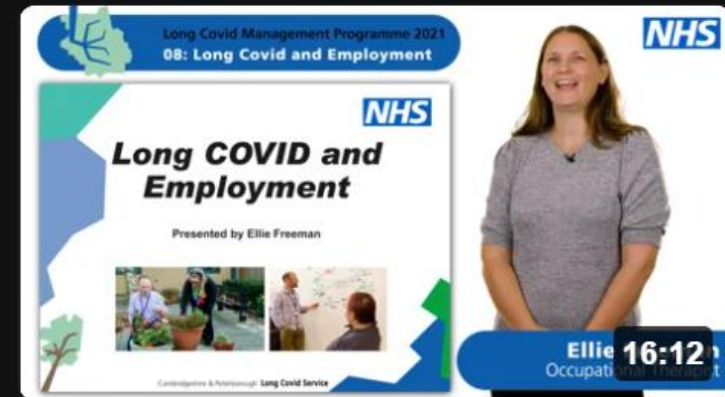
06 Physiology of Pain [e02]  
October 13, 2021



04 Management of Difficult  
October



08 Long Covid and Employment [e02]



07 Return to work  
October



07 Return to work  
October

# Patients are key in helping integration across the system

**NHS**  
Cambridgeshire and Peterborough  
Post-Covid Service

## Did you have Covid-19 more than three months ago?

Are you still experiencing fatigue, breathlessness, brain fog, pain, anxiety, low mood or other symptoms?

**If so, we can help.**

Talk to your GP and ask for a referral to the Long Covid Service – a team of specialists who can support your recovery.

**Patient Postcards**

**NHS**  
Cambridgeshire and Peterborough  
Post-Covid Service

## Did you have Covid-19 more than three months ago

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Post-Covid Service  
Redshank House  
Hinchingsbrooke Business Park  
Kingfisher Way  
Huntingdon  
PE29 6FN

**Posters**



# Take home messages

1. Patient centred
2. Core, focused multisector, multidisciplinary team
3. Think outside the box
4. Believe there is a way to make most things happen

# Thank you for listening!





Dr Katrina Delargy, Founder and CEO  
at TIYGA Health

# The use of data to improve understanding of *long* covid

Katrina Delargy  
TIYGA HEALTH



# Time Is Your Greatest Asset (TIYGA)

“For clinicians, being able to and choosing to spend *time* on understanding what truly matters to patients when making decisions together is an achievement that makes the work of clinicians meaningful and rewarding. Yet many clinicians have insufficient *time* to engage in shared decision making.”

April 19, 2019

**Shared Decision Making and the Importance of Time**

[Arwen H. Pieterse, PhD<sup>1</sup>](#); [Anne M. Stiggelbout, PhD<sup>1</sup>](#); [Victor M. Montori, MD, MSc<sup>2</sup>](#)

Author Affiliations

*JAMA*. 2019;322(1):25-26. doi:10.1001/jama.2019.3785



# Long covid patients need...

- ▶ Recognition
- ▶ Research
- ▶ Rehabilitation

WHO's director general, Tedros Ghebreyesus, February 2021 – talking about “long covid”

[bmj.com/content/372/bmj.n405](https://www.bmj.com/content/372/bmj.n405)

- ▶ There is **no standard test** for long Covid; it is a diagnosis of exclusion meaning that healthcare professionals will test for and **eliminate other possible causes of illness** before diagnosing long Covid. This is reflected in the World Health Organisation's (WHO) definition of 'Post Covid-19 condition' which prescribes that the **symptoms 'cannot be explained by an alternative diagnosis'**.

<https://researchbriefings.files.parliament.uk/documents/CDP-2022-0063/CDP-2022-0063.pdf>  
House of Commons Library, March 2022





# NICE priorities for research on Long-Covid

ng188, March 2022

1. What are effective clinical interventions?
2. Does management effectiveness vary according to population group (e.g. sex, age, ethnicity, socioeconomic stats, pre-existing disability etc)
3. Are there clusters of symptoms that predict response to intervention?
4. Does early exercise rehabilitation improve Long-Covid syndrome?
5. What is the true prevalence and incidence of long covid, and how does this vary by vaccination status?
6. Do symptoms of Long-Covid vary between populations – e.g. is the manifestation different in adolescents or older adults compared to working age adults?
7. What is the clinical course of Long-Covid?
8. Development and validation of screening tools for Long-Covid at the population level.

<https://www.nice.org.uk/guidance/ng188/resources/covid19-rapid-guideline-managing-the-longterm-effects-of-covid19-pdf-51035515742>



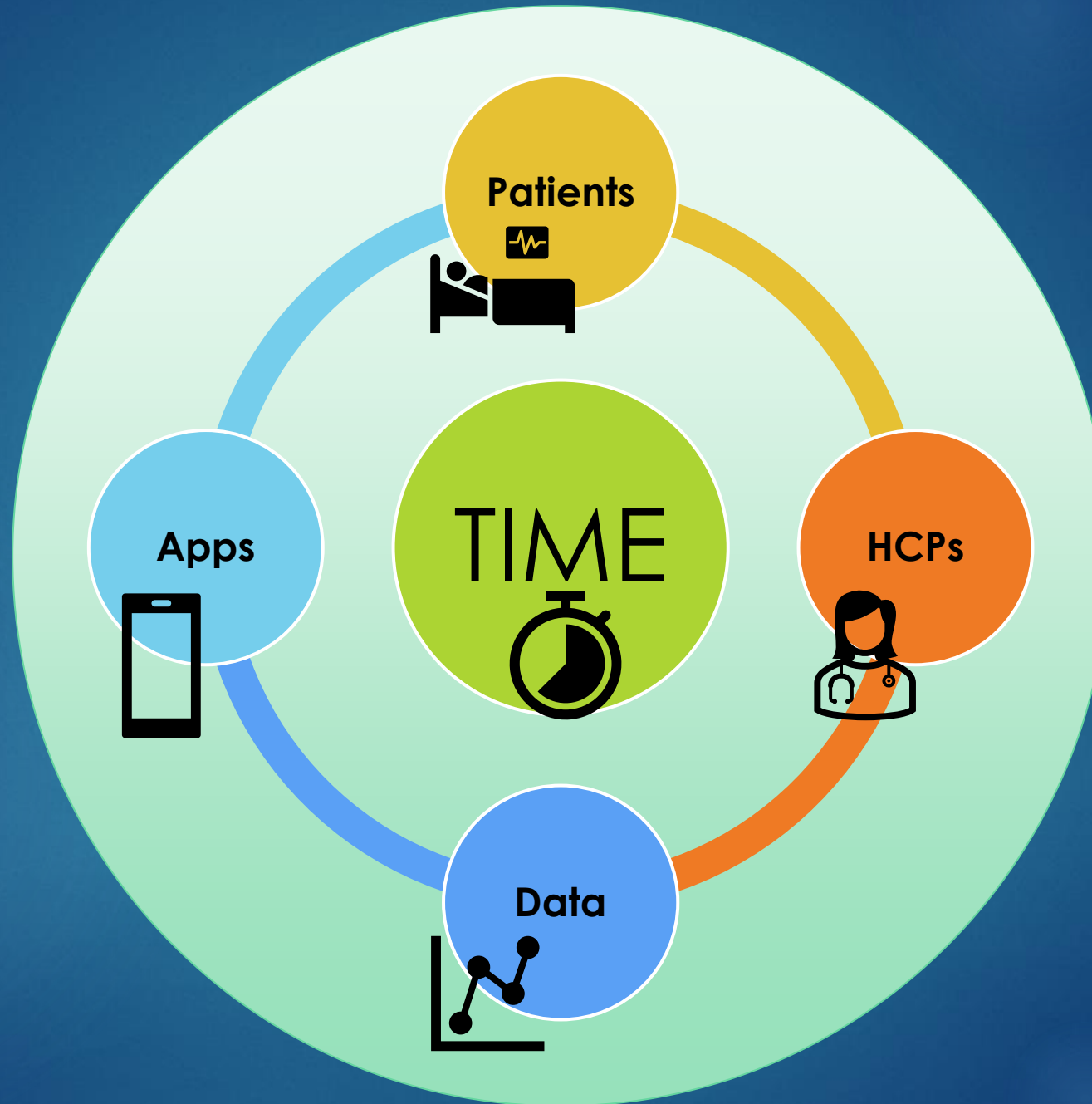
The average person **uses 9 mobile apps per day** and **30 apps per month**.

The average smartphone user spends **3 hours and 10 minutes each day** using their device.

About **2 hours and 51 minutes of this time is spent on apps** (apps account for roughly 90% of smartphone usage).

Research shows that there are **80+ apps installed on the average smartphone**. But with that said, people aren't using all of those apps.

**49% of people open an app 11+ times each day.**



**Digital health apps balloon to more than 350,000 available on the market.**

More than **90,000** digital health apps were released last year – an average of **250 per day** – according to the IQVIA Institute for Human Data Science's **2021** trends report. Apps that focus on managing **specific diseases or health conditions now make up 47% of apps, compared with 28% in 2015**. Mental health, diabetes and cardiovascular disease-related apps make up almost half of condition-specific apps.

<https://www.mobihealthnews.com/news/digital-health-apps-balloon-more-350000-available-market-according-iqvia-report>





*"I've switched from being the nurse to the patient, my eyes have been opened. If I ever return to practice I will do so through a different set of eyes"*

<https://www.tiyga.health/post/guest-blog-living-with-long-covid-the-invisible-illness-by-saskia-mulder>



"As a proportion of the UK population, prevalence of self-reported long COVID was greatest in people **aged 35 to 49 years, females**, people living in more deprived areas, those **working in teaching and education, social care or healthcare**, and those with another activity-limiting health condition or disability."

<https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19/latestinsights> 4 March 2022



# Pandemic and pingdemic.....

## Use of mobile?

While the **pandemic has brought increased reliance on the internet and online services**, the digital divide continues to prevent the benefits of internet connectivity being available to all. A small percentage of the population do not have internet access – with older people and those in lower socio-economic groups less likely to be connected – but other barriers also exist, in the **lack of skills and confidence** that some internet users have, and in the availability of suitable devices to access internet services. **The smartphone appears to be the ‘base layer’ of connectivity, with more users in lower socio-economic groups relying on this device for internet access without a computer. Fortytwo per cent of internet users in the DE socio-economic group only use devices other than a computer to go online**, raising questions about how restricted some groups may be in activities like filling in online forms.

Fig 1.14 Do you go online using any of these devices? Answers here for smartphone.

Group	16-24	25-44	35-44	45-54	55-64	65+	AB	C1	C2	DE
%	87	91	93	92	85	59	85	89	88	79

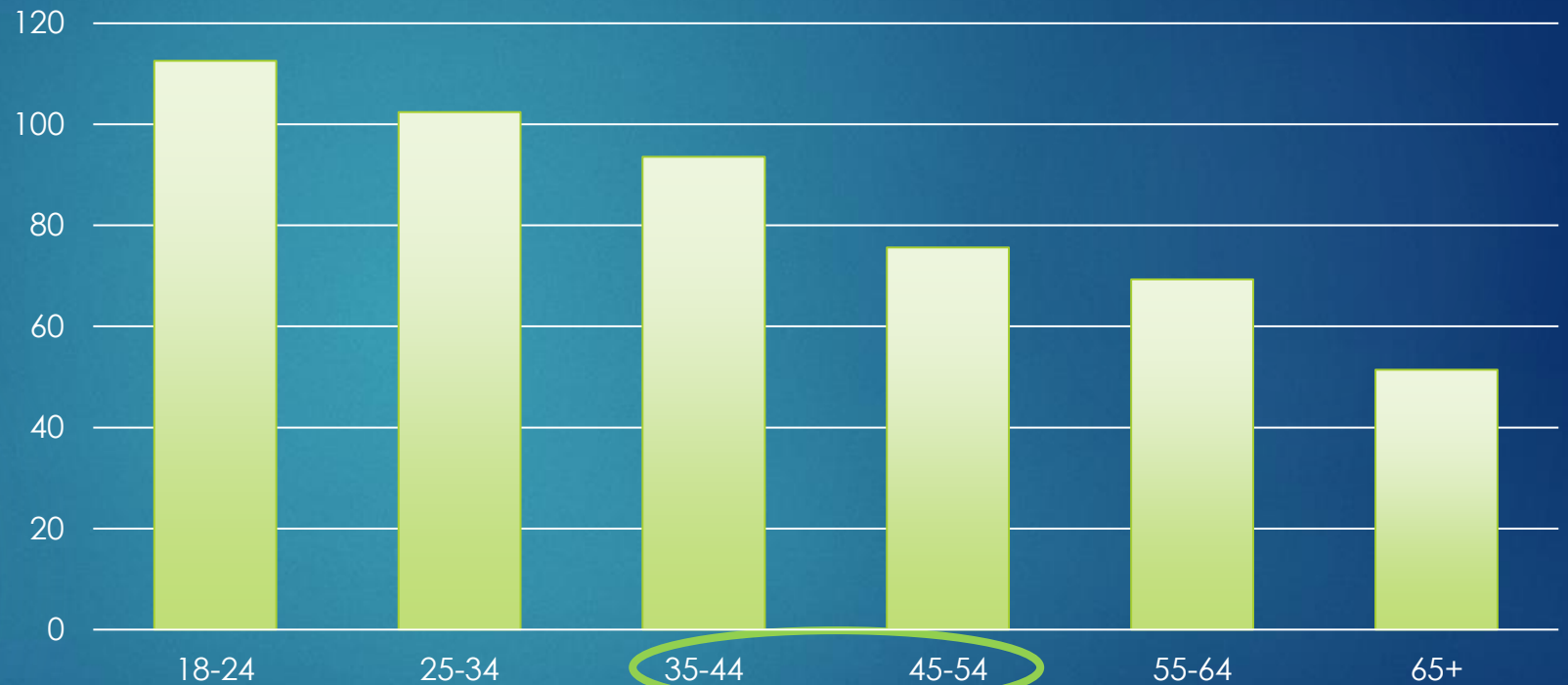
Source:

Ofcom Adults'  
Media Literacy  
Tracker 2020



As expected, **younger adults spend more time on apps** than older adults. There's steady decrease in the usage for older demographics, ending with those **65+ years olds, who spend 51.4 hours a month on apps, or about 1 hour, 43 minutes a day.**

Average monthly hours per user – using apps



“Patients over 50 don't use apps”

True or false?

**Long covid patients are mostly age 35-49**  
**ONS, March 2022**



# Why are health apps less widely used?



## Most Popular Google Play Store App Categories

You can measure the success of an app category based on penetration. According to Statista, these are the app categories with the highest penetration rate among Android users.

- 1.Tools — 99.81%
- 2.Communication — 99.93%
- 3.Business — 99.33%
- 4.Video Players & Edit— 96.63%
- 5.Travel & Local — 95.7%
- 6.Social — 95.02%
- 7.Productivity — 91.67%
- 8.Music & Audio — 88.38%
- 9.Entertainment — 83.85%
- 10.News & Magazines — 81.11%
- 11.Photography — 75.77%
- 12.Books & Reference — 70.74%
- 13.Lifestyle — 65.67%
- 14.Personalization — 61.62%
- 15.Games (Casual) — 58.86%
- 16.Games (Puzzle) — 56.5%
- 17.Games (Arcade) — 55.08%
- 18.Shopping — 35.79%
- 19.Games (Action) — 34.19%
- 20.Weather — 32.46%



**Health and fitness popularity on the App Store is 3.41%.**

*(Source: Business of Apps)*

**Most people have become more conscious of their health during the pandemic.** However, **health and wellness apps** on Apple Store are at the bottom of the barrel when it comes to popularity, with **about 3%**. According to health app usage statistics, things aren't any different in the Play Store either because the sector has **around 4%**.

<https://techjury.net/blog/app-usage-statistics/#gref>

<https://buildfire.com/app-statistics/>

Need



Curious

Recommended

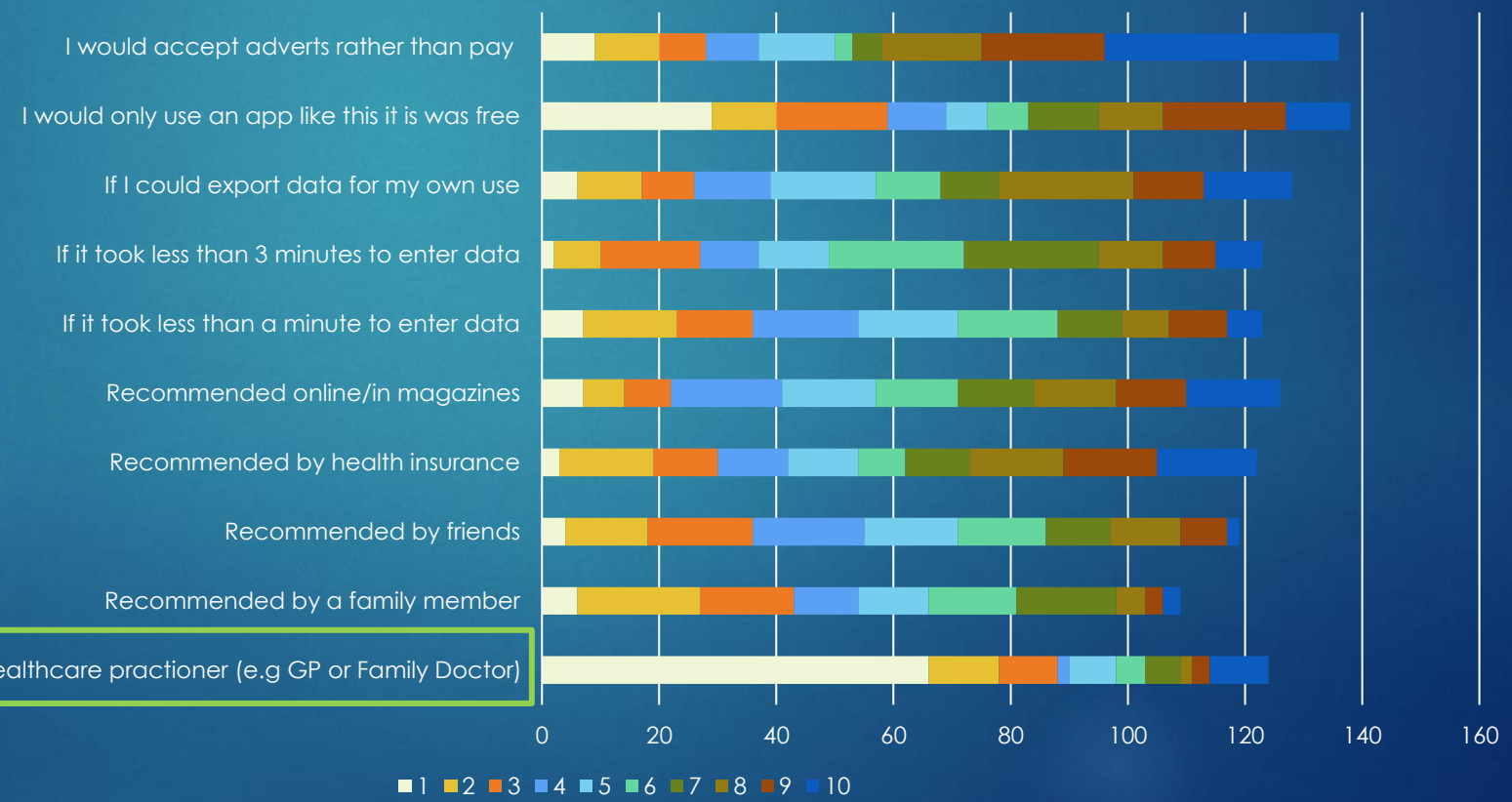
Enjoy/Fun

# Are healthcare providers recommending apps to their patients?

What would determine if you used an app for managing your health condition(s)? 1=most important 10=least important 147 answered, 5 skipped

**70% scored 1, 2 or 3/10**  
**High importance for app being recommended by a HCP**

Recommended by a Healthcare practitioner (e.g GP or Family Doctor)





# Many types of app are available

- ❖ **A**rrangements – scheduling, booking, ordering, paying
- ❖ **B**rochure – promotional, introductory
- ❖ **C**ommunication – messaging, networking, explaining
- ❖ **D**ata – enter, send, receive, display, analyse, track
- ❖ **E**ducation – how to do, how it works, what it means
- ❖ **F**un – games, puzzles, music, films
- ❖ **G**reetings – welcome, introduction, timings
- ❖ **H**elp – what to do if/when
- ❖ **I**nformation – explanation, process, description, statistics, rules, times etc
- ❖ **A**nd more.....





**Just use this app on your  
(phone or) tablet every  
day.....**

**The message  
sounds similar,  
but will the  
compliance be  
the same?**

**Will the  
intended  
benefit occur?**



**Just take one of these  
tablets every day....**

# UK population, Covid-19 and app use for symptom tracking

By mid-2019, pre-covid:

- working age population (those aged 16 to 64 years) - **41.7 million**
- 65 years and over - **12.4 million**
- 70 years and over - **9.0 million**
- 85 years and over - **1.6 million**

<https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/bulletins/annualmidyearpopulationestimates/mid2019estimates>

During the pandemic:

More than **4.7 million users** in the ZOE Covid app study



Research Paper : Volume 38, The Lancet,  
101019, August 01 2021, Hannah Davis et al.

Characterising long COVID in an  
international cohort : 7 months of  
symptoms and their impact

New Scientist, 26 Feb 2022

*“Just because a condition is  
unexplained, it doesn’t mean it is  
unexplainable.”*

*“The research momentum that has  
built up around long covid offers  
hope to the millions of people who  
have it but also to the millions with  
other functional disorders.”*

What role can **simple data capture apps** play in data capture from long covid patients?

- For patients with fatigue, brain fog who may have **recall difficulties and limited cognitive and physical energy**
- To record **sequence, severity and frequency** of a wide range of symptoms – list not covered by standards
- To record **self-management** choices used and response to them
- To discover **who is getting better** or not and **transfer learning** to those who are struggling if at all possible
- How should the data be **analysed, visualised, reported etc for different audiences and roles?**
- **How long** will patients **continue recording data?**
- What **insights** could be obtained from such data?

# App : for patients with fatigue and brain fog

This is very helpful to track your own symptoms on a daily basis as I was previously writing symptoms down each day - as they range so much from one extreme to the other.

Brilliant idea & very worthwhile. It is good for monitoring/tracking symptoms. Will be key for giving to doctors to aid treatment plans. All the data points captured on the pilot study are spot on.

Have you any feedback on the TIYGA app?

How can it help long covid patients? What data do you think should be captured from people in your situation?

It's beyond helpful to know that we're getting some help here in NI! I think making a link between all the varying symptoms would be so incredible - why are healthy people not able to breathe if their lungs are ok? What is the root cause?

App great way of keeping track of each day

The App helps because - It validates our experience It allows us to see/note what we are suffering from on a daily basis It gives us confidence that someone cares enough to research into the symptoms of Long Covid

Think it's been brilliant as it will log all covid patients as I've myself have different symptoms to others who suffer from long covid.





## LONG COVID – OUR CONCLUSIONS SO FAR

Symptoms for 11 organ systems vary

- (i) Between individuals
- (ii) Over time

“I would say for me the aching joints, burning legs and low energy are there daily..... the breathlessness comes and goes along with chest pain if I overdo it.....if I pace my day – my breathlessness is less impacted”

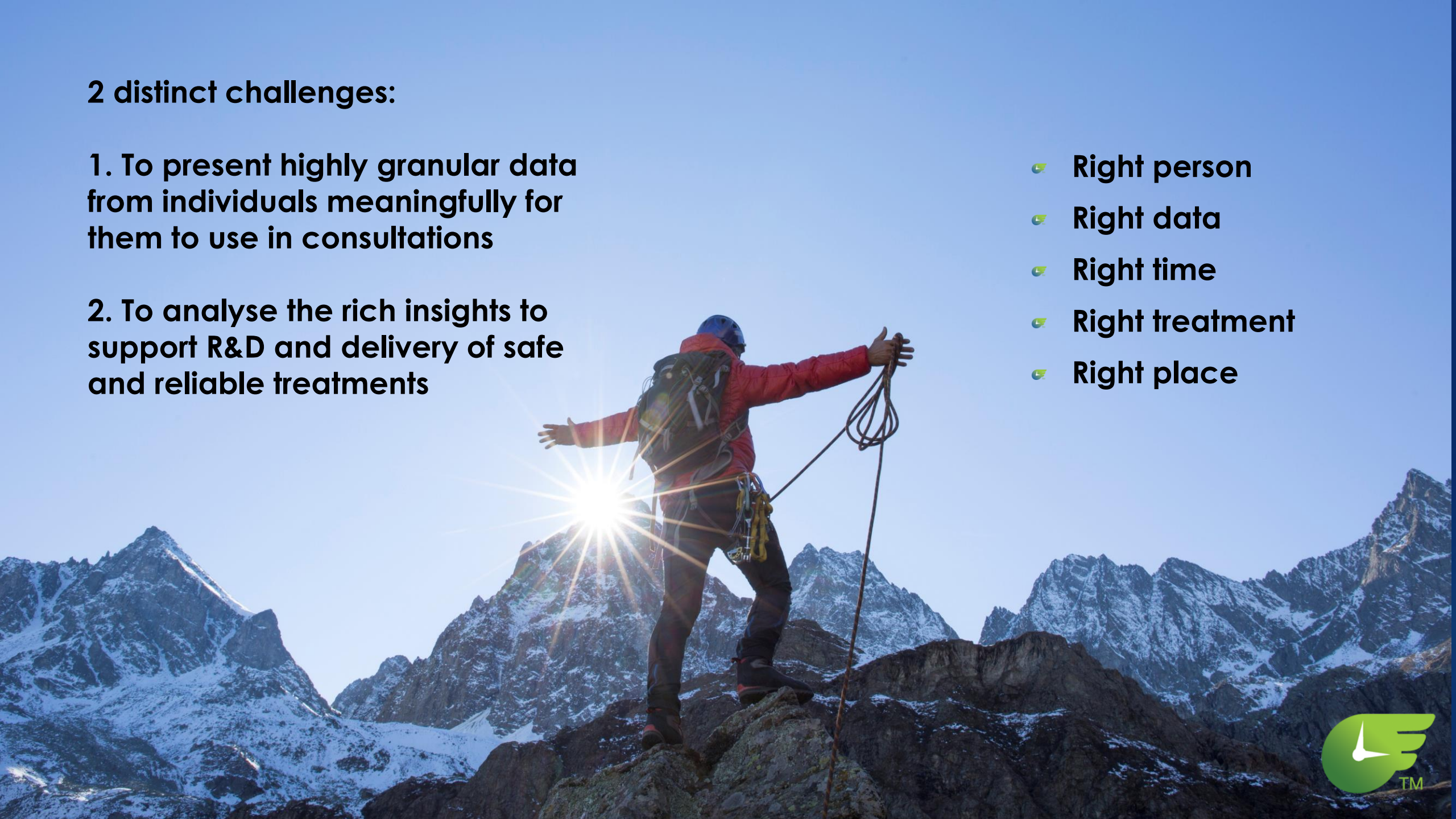


## 2 distinct challenges:

1. To present highly granular data from individuals meaningfully for them to use in consultations

2. To analyse the rich insights to support R&D and delivery of safe and reliable treatments

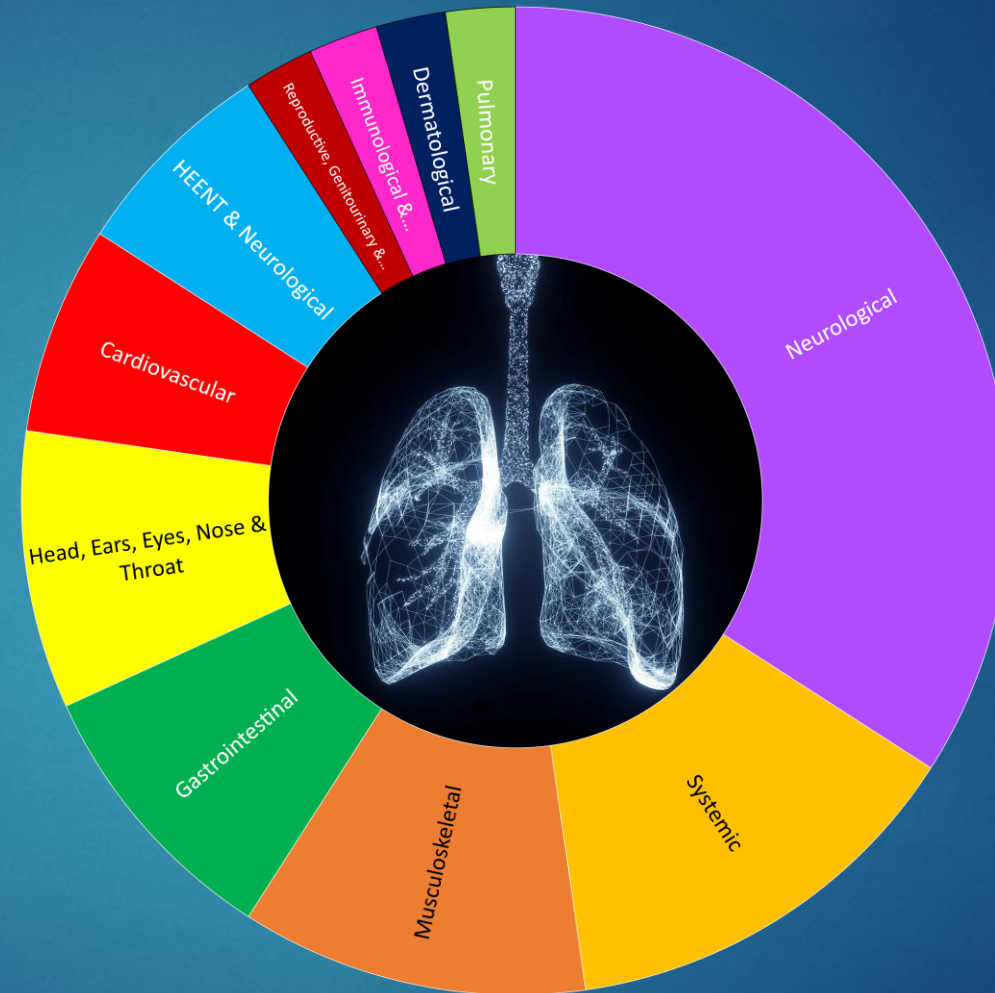
- Right person
- Right data
- Right time
- Right treatment
- Right place



Taxonomy based on:

Research Paper : Volume 38, The Lancet, 101019, August 01 2021, Hannah Davis et al.

Characterising long COVID in an international cohort : 7 months of symptoms and their impact



Long covid patients

Reporting data since May 2021

Reporting on approx. 50 symptoms

Data entered ~daily on 0-10 scales

Example from 1 patient – many organ systems affected

Data supplied by



# Making the most of precious time

Recent research showed that the UK offers some of the **shortest GP consultations amongst economically-advanced nations at 9.2 minutes** – with another study finding that the average GP consultation involved discussion of two and a half health problems.

<https://www.rcgp.org.uk/about-us/news/2019/may/15-minute-minimum-consultations-continuity-of-care.aspx#:~:text=Recent%20research%20showed%20that%20the,and%20a%20half%20health%20problems.>



# Background about 2 Patients

## Patient 1

- ▶ Female, age 35-44
- ▶ Pre-covid was Deputy Ward Sister (full time)
- ▶ Also worked as Complementary Therapist
- ▶ Fit and healthy pre-covid
- ▶ First symptoms of Covid-19 March 19<sup>th</sup> 2020
  - ▶ Sore throat, tickly cough, tightness in chest and fatigue (no PCR tests then)

## Patient 2

- ▶ Male, age 35-44
- ▶ Pre-covid was Operations Manager for a distribution company
- ▶ No underlying health problems; rarely sick
- ▶ First symptoms of Covid-19 in January 2021
  - ▶ developed a cold and cough initially and a PCR test confirmed diagnosis, wasn't feverish but had breathing problems

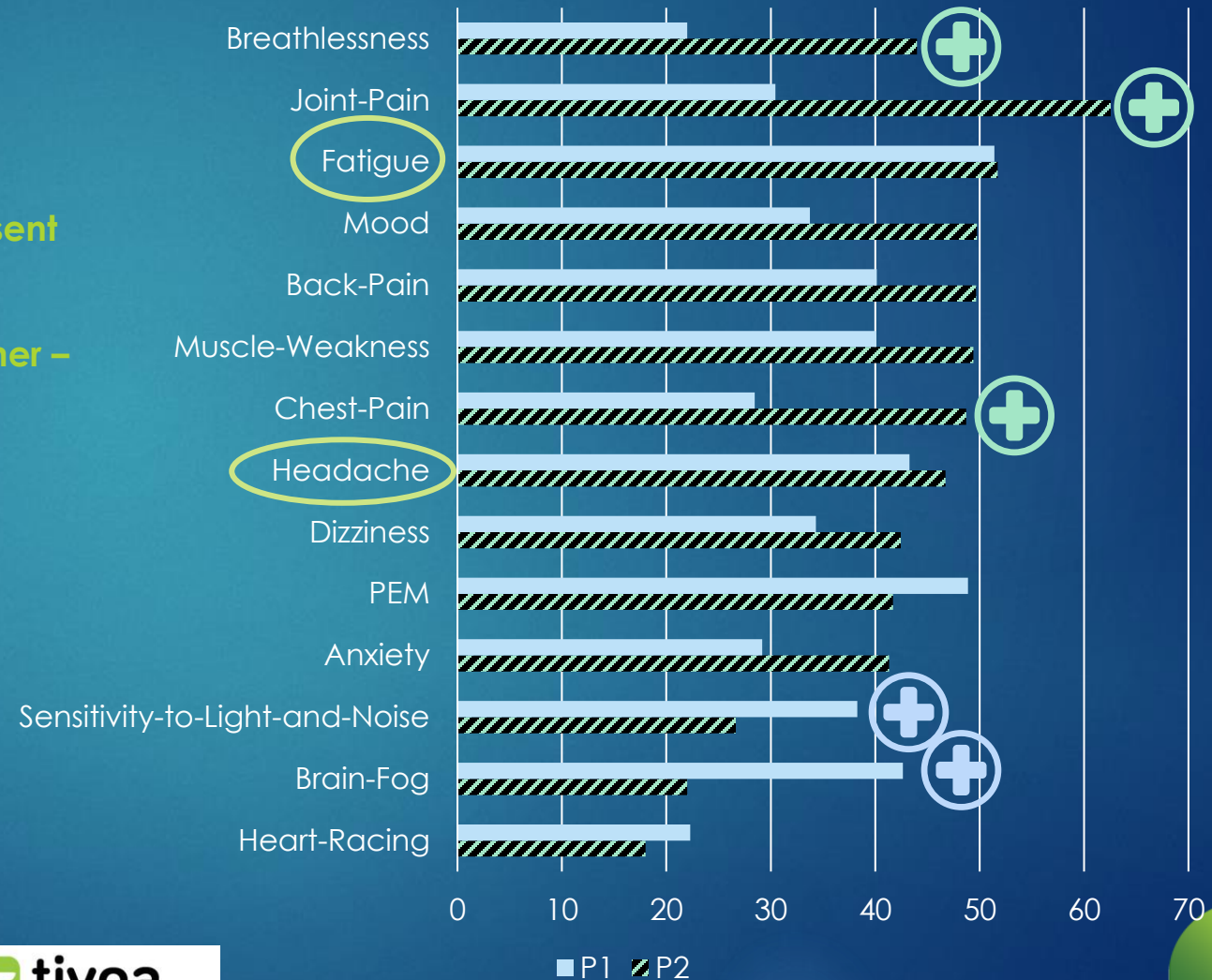


# Comparing both patients

The same common and enduring symptoms are present

Some symptoms are much stronger for one or the other – both had different initial covid (Variant) symptoms – different mechanisms at work?

Common and enduring symptoms in 2 app users (cumulative monthly average scores)

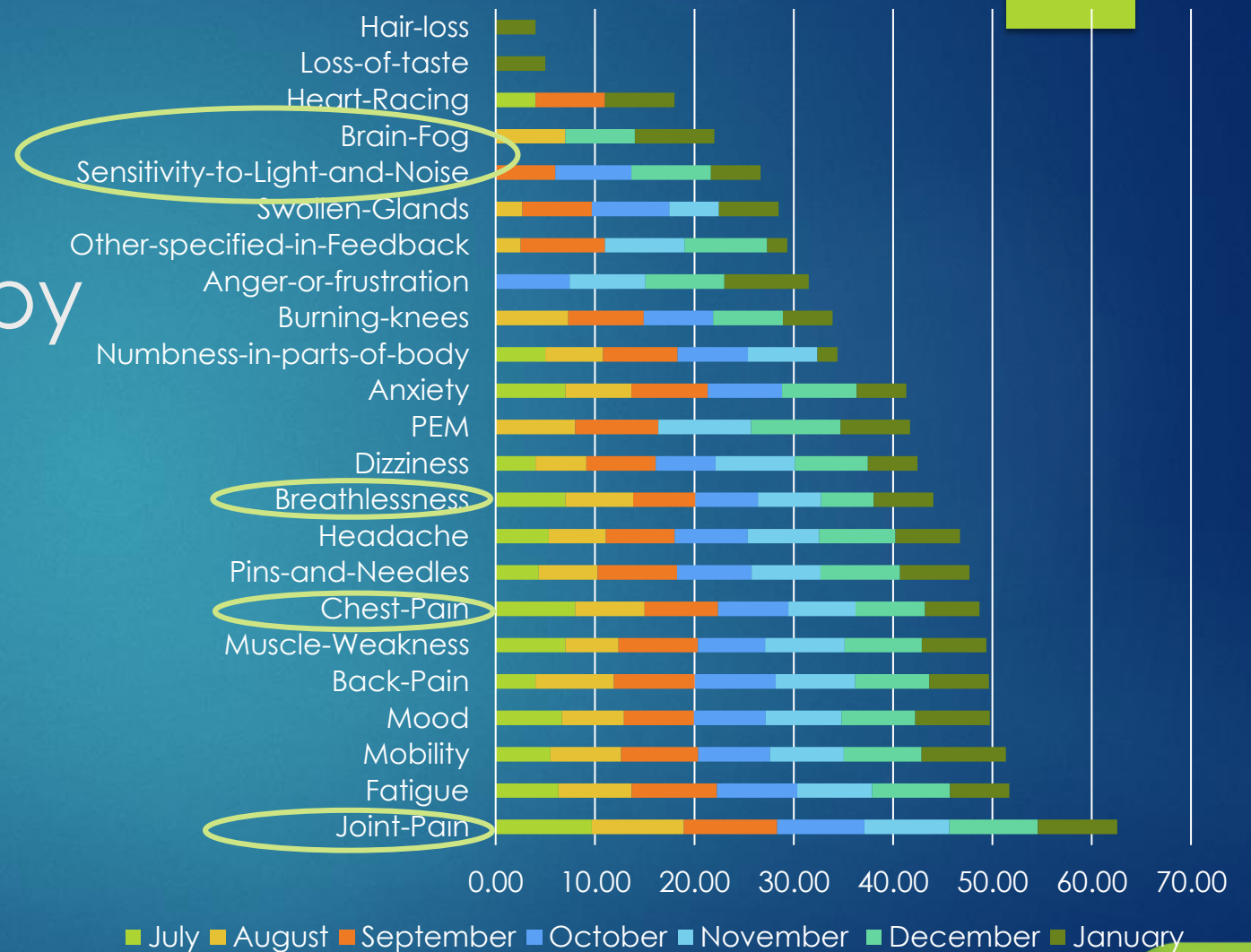




# Symptom scores by month (Patient 2)

23 symptoms reported (0-10)  
 154 day+ symptom tracking  
 Free text notes  
 Self-management records  
 Started reporting 29/7/21  
 Paused due to health, restarted

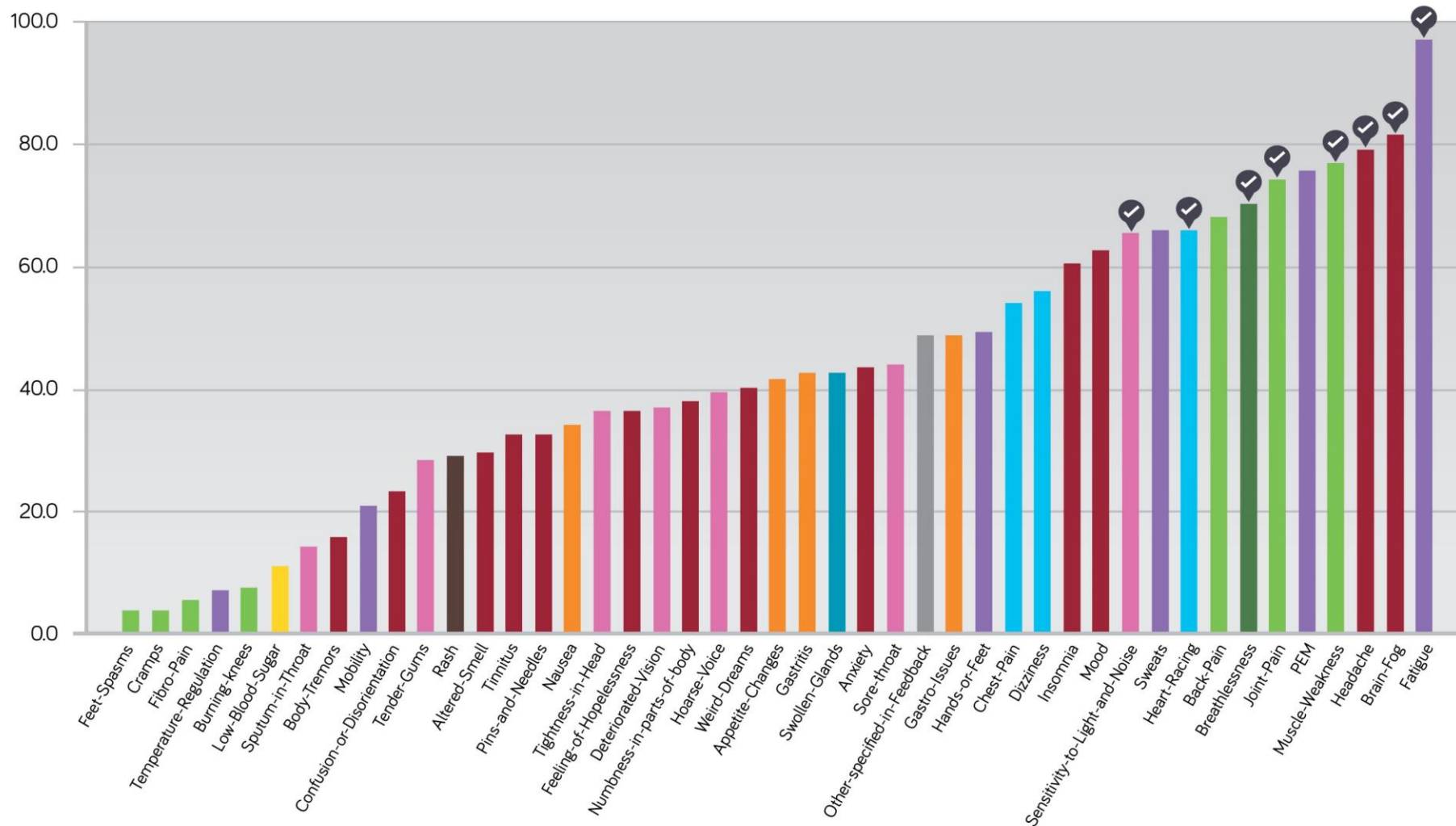
Monthly averages  
 (note: July and January have very few data)



Symptoms were mapped onto the organ systems using the taxonomy of Davis et al

- Not rated, ticked:
- Floaters in eyes
  - Frequently passing urine
  - Menstrual cycle
  - More sputum
  - Pulsating foot
  - Stress
  - Swollen ankles

## Ranking of Mean Symptom Scores by Long Covid Patients over up to 130 days



Data supplied by



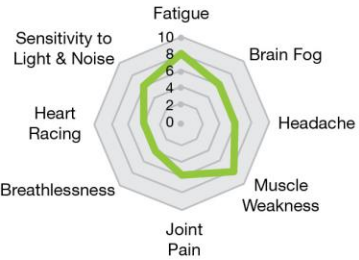
NB - Our attribution to body systems is based on...

- Reported by all
- Neuropsychiatric
- Gastrointestinal
- Musculoskeletal
- Pulmonary
- Pulmonary
- Cardiovascular
- Systemic
- HEENT (Head, Ears, Eyes, Nose, Throat)
- Reproductive, Genitourinary and Endocrine
- Dermatological
- Immunology/Autoimmune

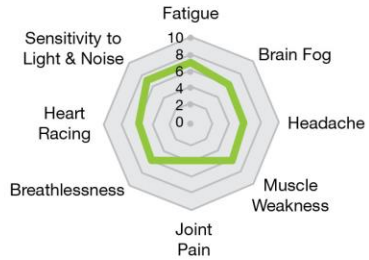


# Covid Patients Symptoms

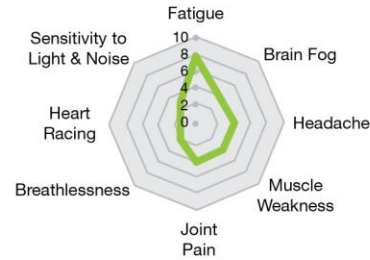
Person 1



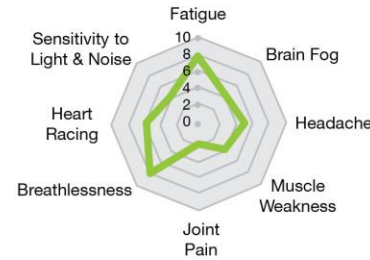
Person 2



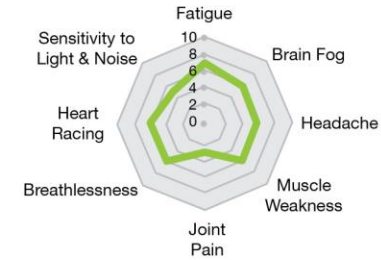
Person 3



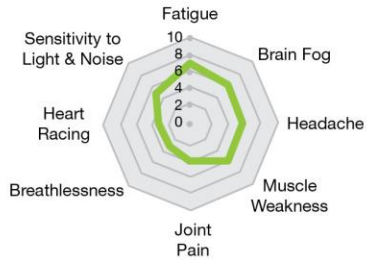
Person 4



Person 5



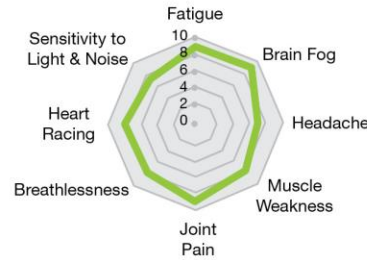
Person 6



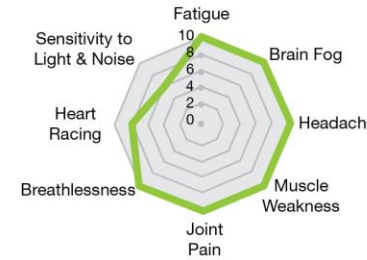
Person 7



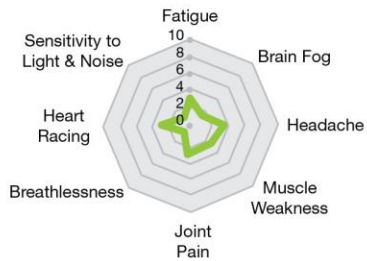
Person 8



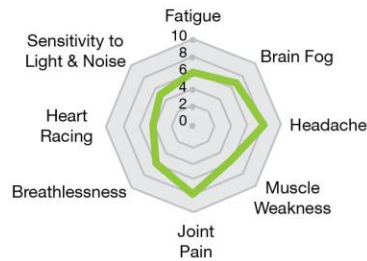
Person 9



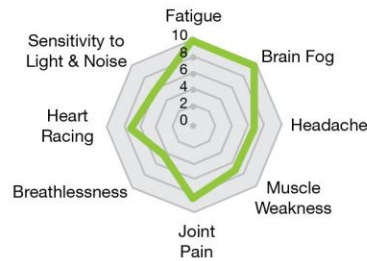
Person 10



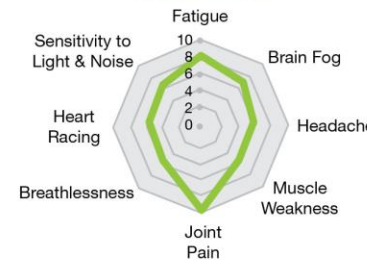
Person 11



Person 12



Person 13



1. Fatigue
2. Brain Fog
3. Headache
4. Muscle Weakness
5. Joint Pain
6. Breathlessness
7. Heart Racing
8. Sensitivity to Light and Noise

May-Sept 2021

All patients reported these 8 symptoms every month, not necessarily every day

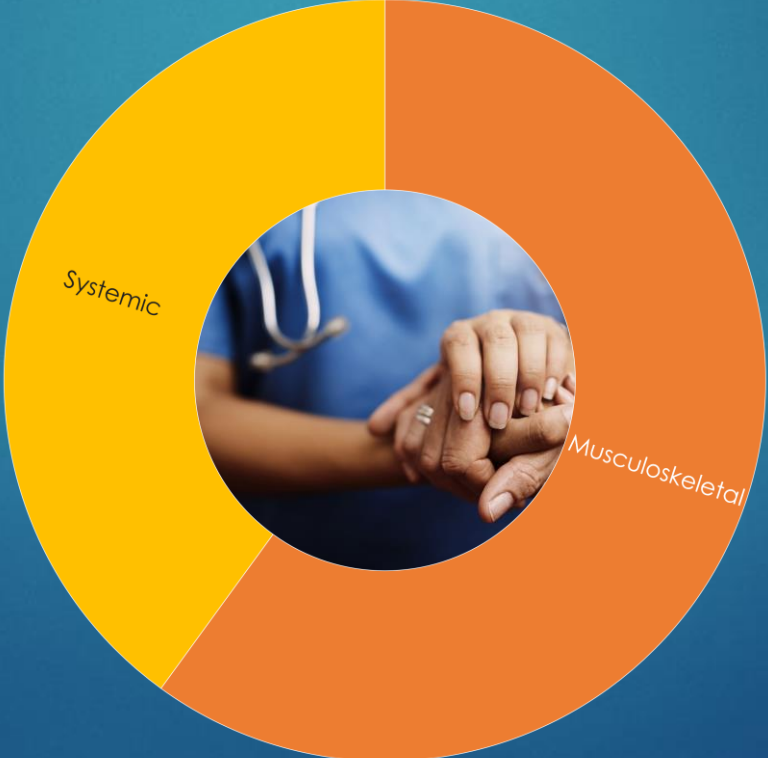


# Charts for the continuously recorded symptoms (not all) by organ system

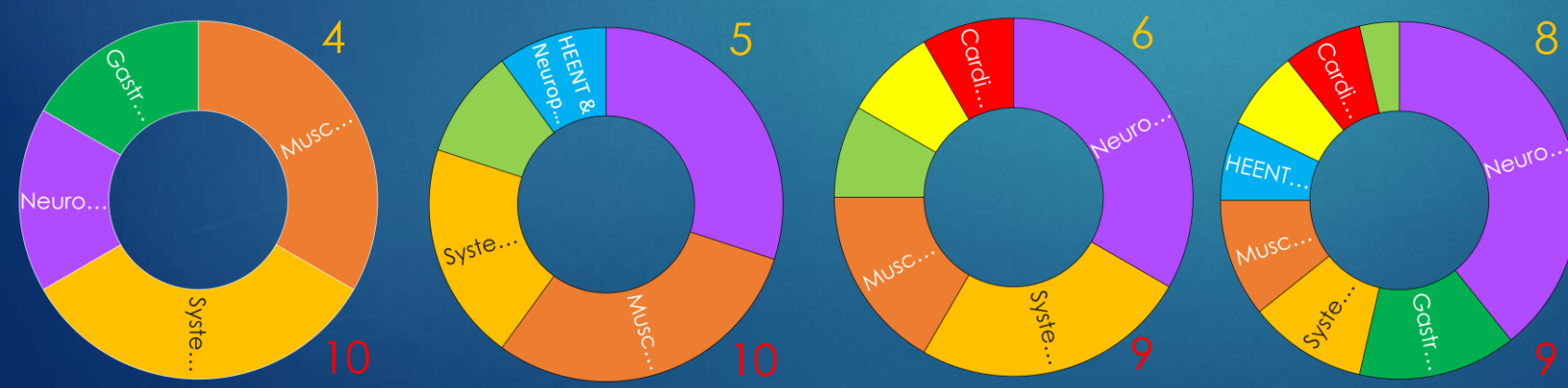
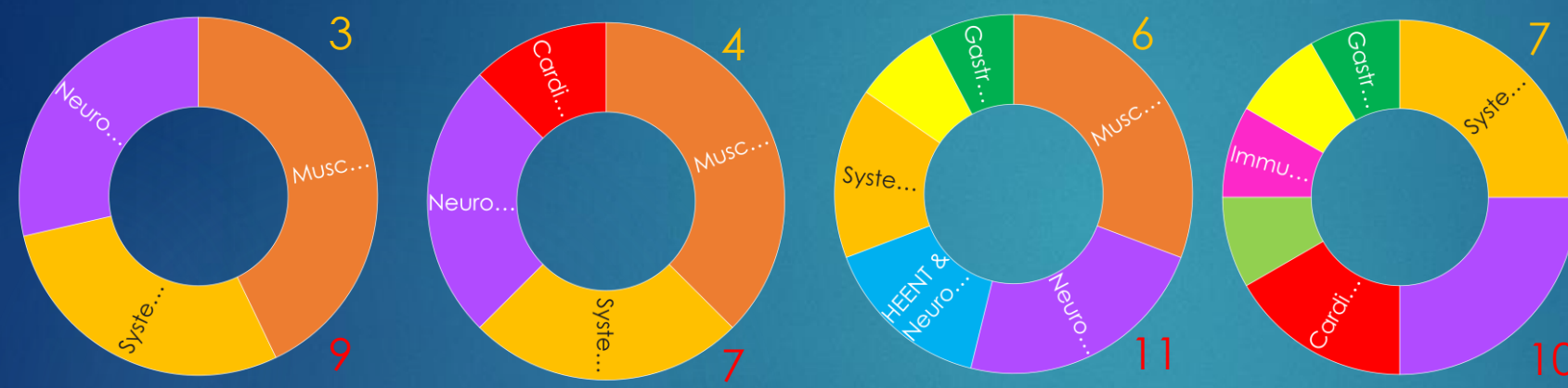
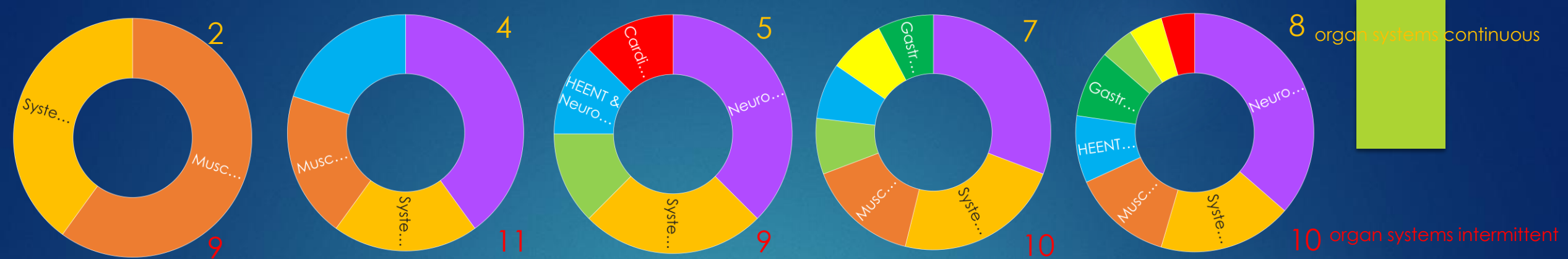
Everyone is different.

No two people's app data showed an identical pattern.

Data analysis March 2022



Symptoms were mapped onto the organ systems using the taxonomy of Davis et al



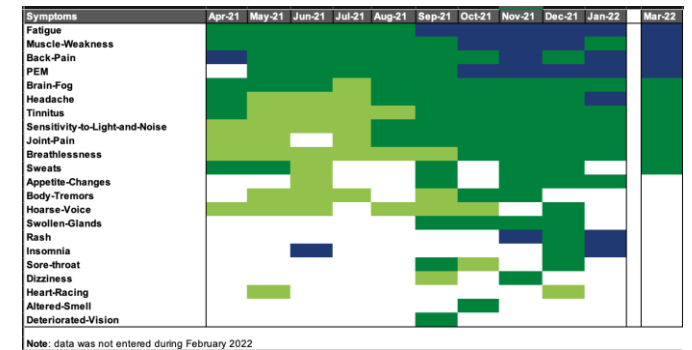
## Symptoms – per organ system affected

Organ system key	
Cardiovascular	Red
Dermatological	Dark Blue
Gastrointestinal	Green
Head, Ears, Eyes, Nose & Throat	Yellow
HEENT & Neurological	Cyan
Immunological & Autoimmune	Pink
Musculoskeletal	Orange
Neurological	Purple
Pulmonary	Light Green
Reproductive, Genitourinary & Endocrine	Dark Red
Systemic	Yellow-Orange

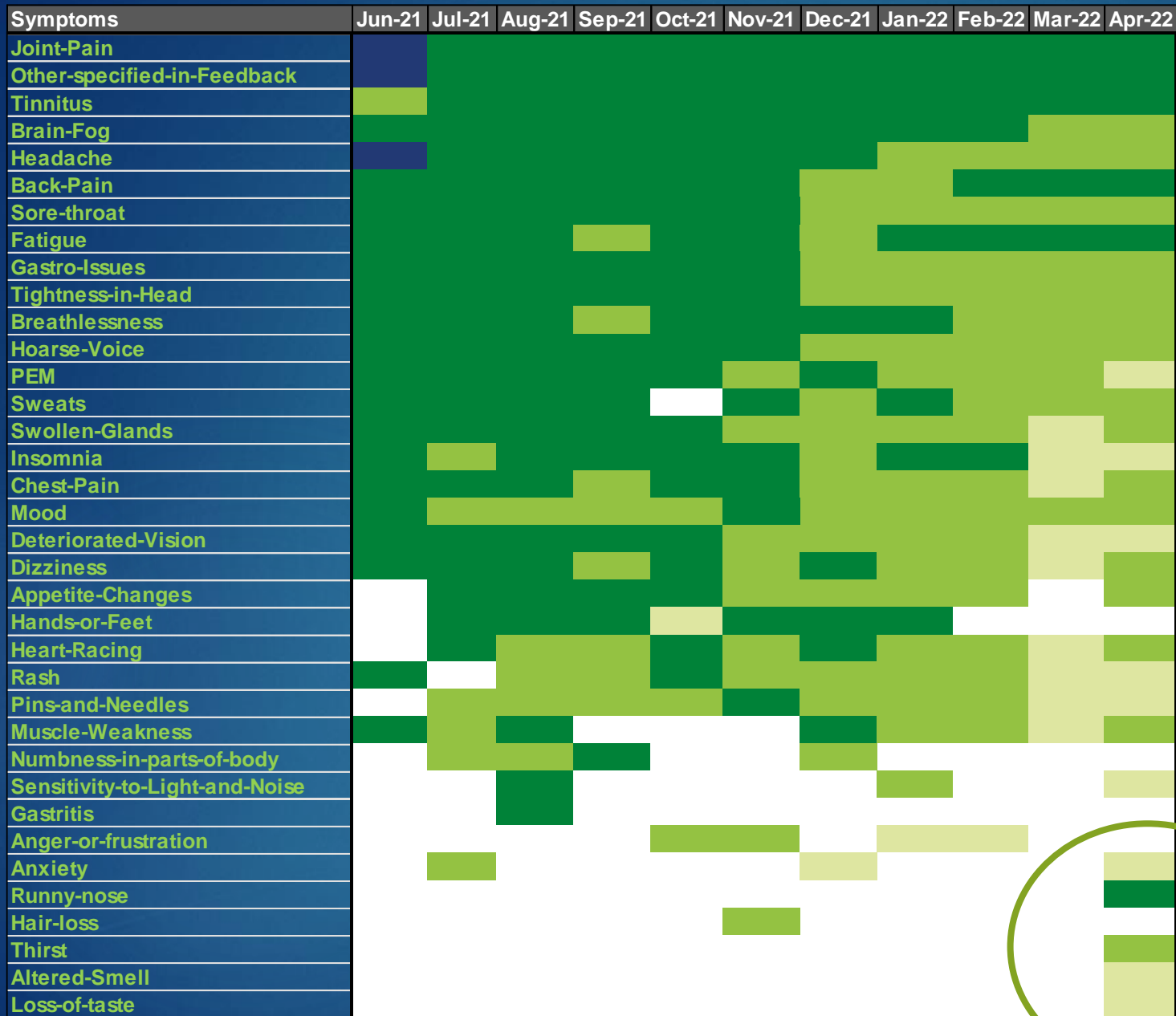
See quickly  
which patient is  
getting better  
and which  
patient is  
getting  
worse.....



Average symptom score	
0-0.20	
0.20-1.99	
2-4.99	
5-7.99	
8-10	



Note: data was not entered during February 2022

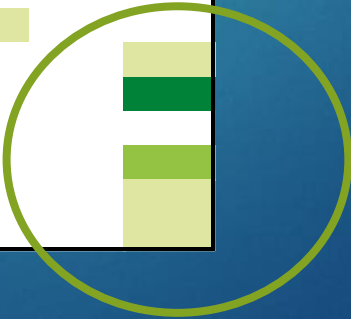


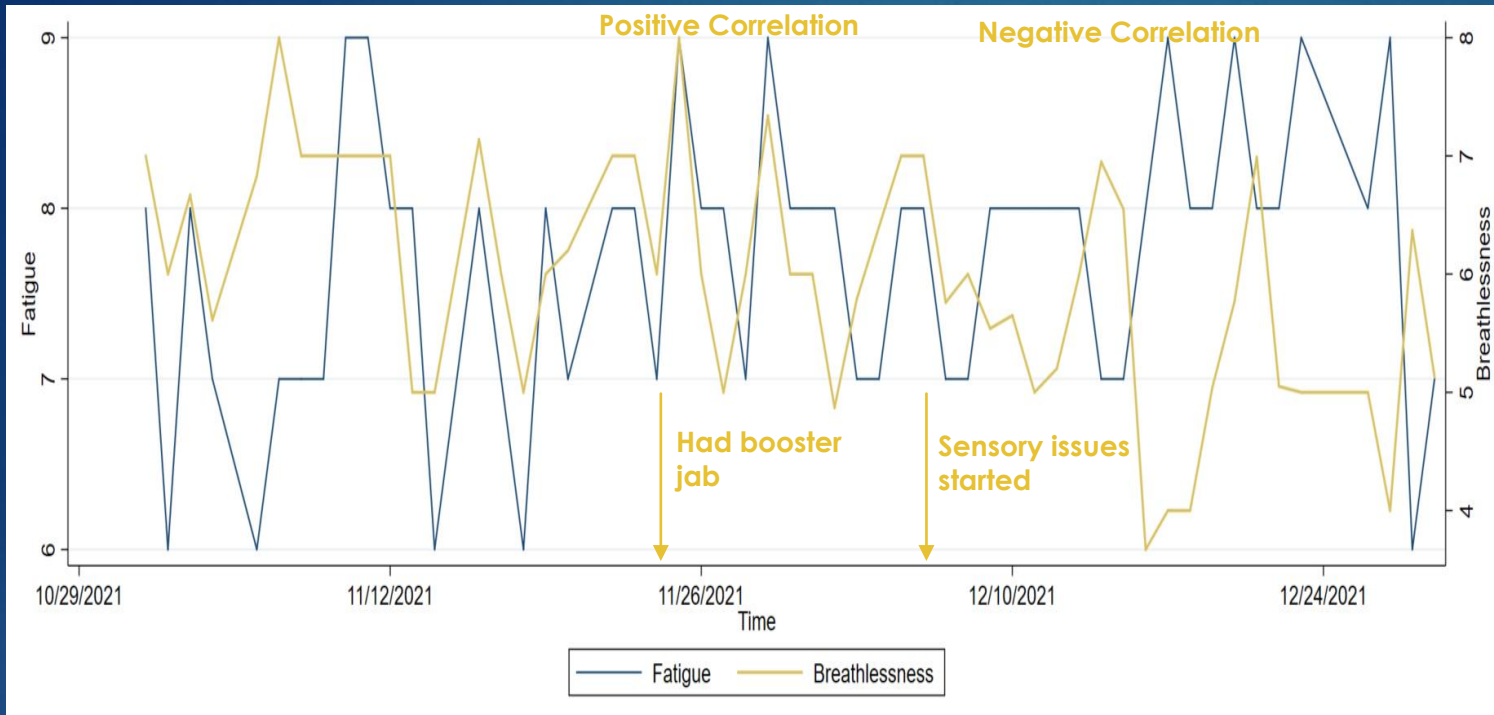
Highlight sets of symptoms characteristic of known diseases

Signal reason to use existing test methods to qualify or eliminate possible diagnosis

Or check for new covid variants or jabs

New symptoms added to list in April





Fatigue & Breathlessness correlation reversed – suddenly

Onset of sensory issues due to weather, activity, medication, injections?

“...keep getting these funny sensations ..” 6<sup>th</sup> December

“Almost electric sensations over body...” 5<sup>th</sup> December

“...keep getting electric sensations in the back of my legs...” 4<sup>th</sup> December



# What advice do you wish you were given after you first knew you your covid symptoms were lasting longer than expected?

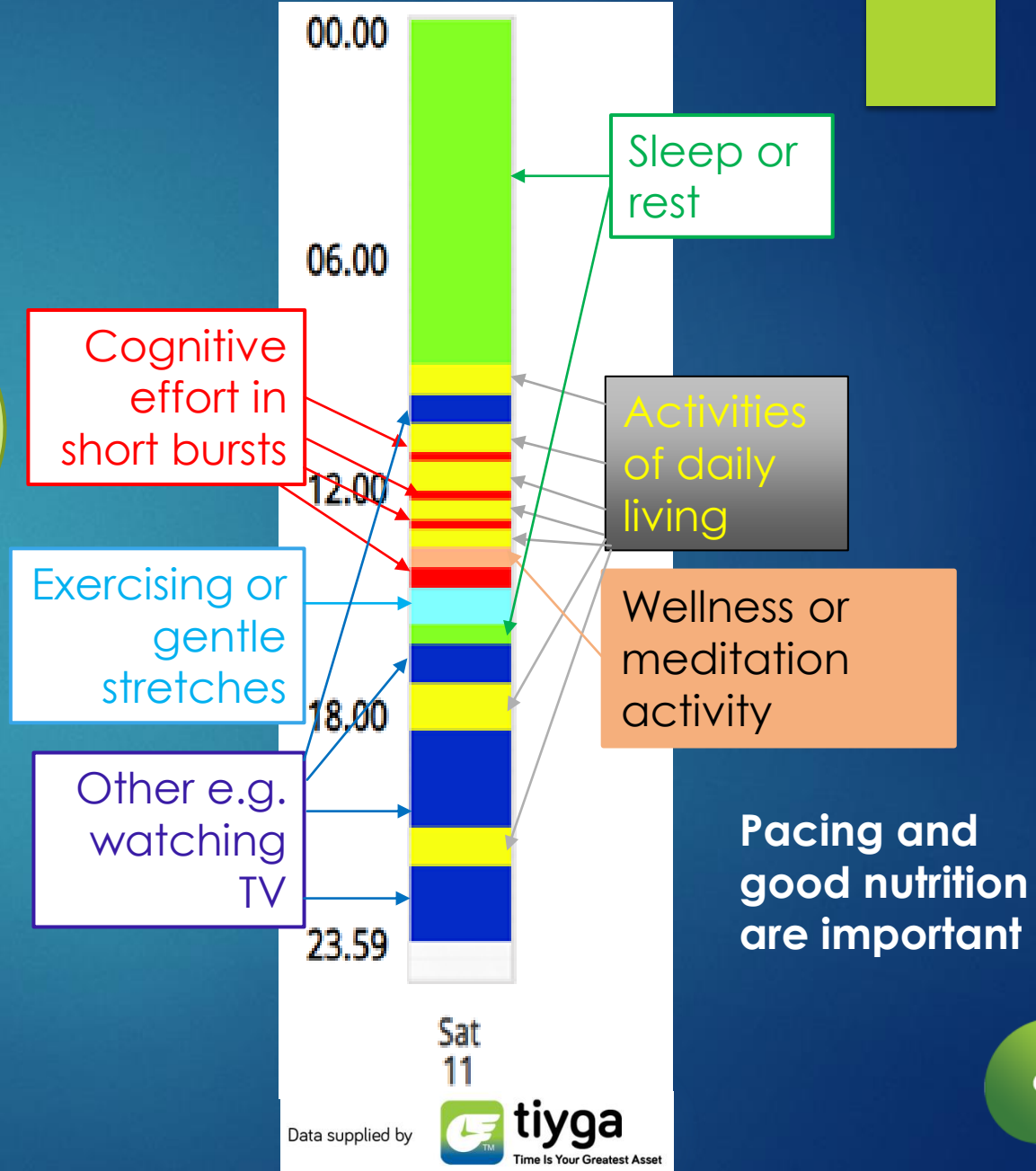
I wish I had rested more. I didn't think I had the option to really slow down, and as a result all last year was spent pushing my body to its limit.

Pacing is key even on a good day.. take time for yourself daily and don't over do it. recommend to get physio and strengthening exercises and get support from close friends or family.. sometimes it's very lonely so be in touch with a few people and maybe one or two groups with people who are going through the same as you..

That it is an up and down recovery rather than a linear upwards trajectory

That pushing through does not work for Covid. If I had rested and paced at the start maybe I wouldn't be where I am now

Not to exercise & push through the symptoms!! To rest right from the start & not put pressure on myself to return to normal too soon.



# 24x7 report when you are able to – communication with minimal recall bias

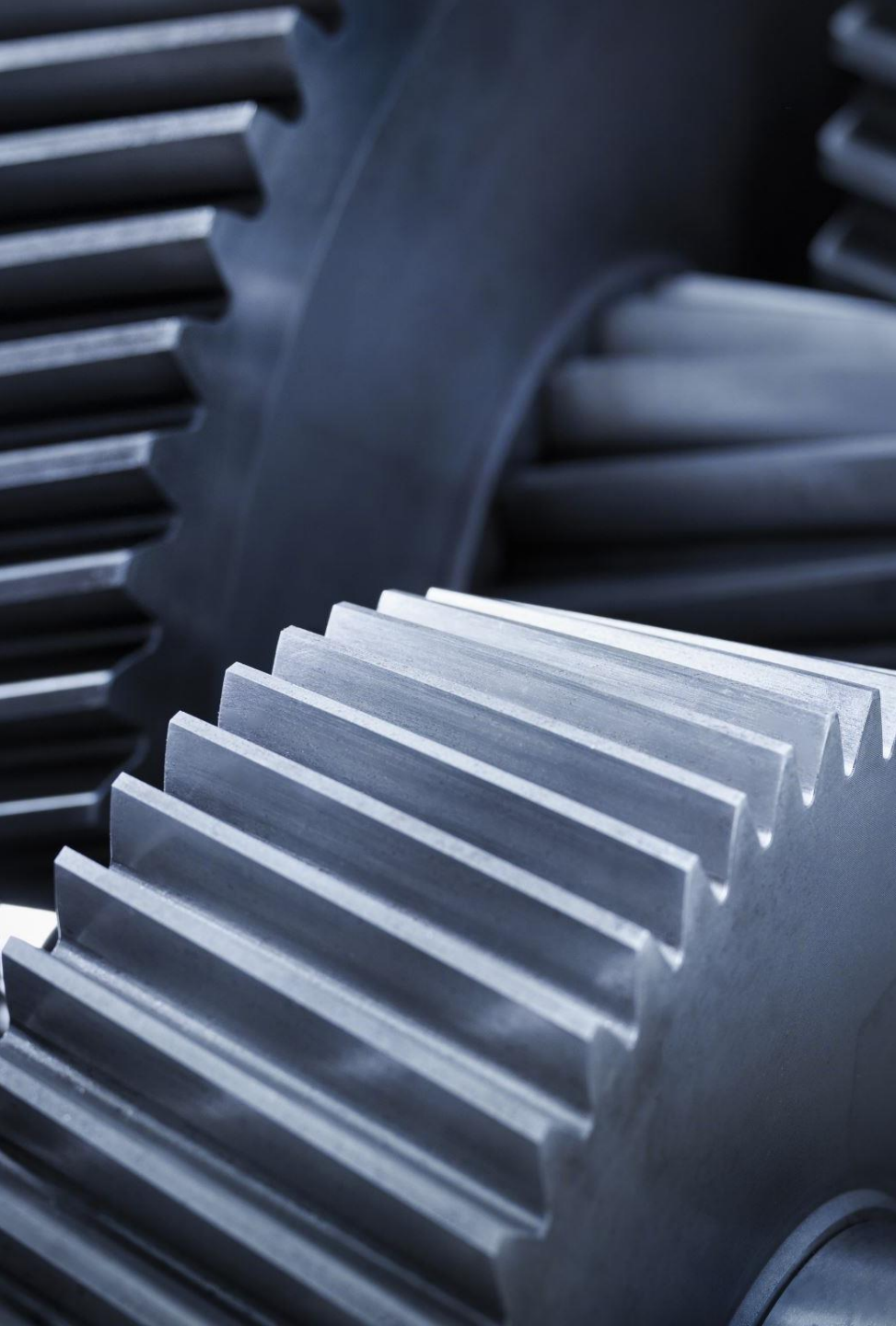
## ▶ Patient



## ▶ Healthcare Professional



Use when convenient and appropriate – when you have time to think, or when you need to have a record



# Data is the new oil, let's refine it

- ▶ Does long covid require a **precision medicine approach**?
- ▶ Does long covid **catalyse/accelerate** a range of (age-related) illnesses?
- ▶ Can app-data be used **to triage patients** for specific therapies?
- ▶ Would a **digital therapeutic** and online support programme of pacing activity and nutrition management help recovery?
- ▶ How do we get the **right data to the right person at the right time** to ensure the right treatment is given early enough?

.....or should we think of data as the new currency?





# tiyga

**TIYGA™ - Voice of the Patient**

# Thank you

KATRINA DELARGY, TIYGA HEALTH

[WWW.TIYGAHEALTH.CO.UK](http://WWW.TIYGAHEALTH.CO.UK)

@TIYGAHEALTH

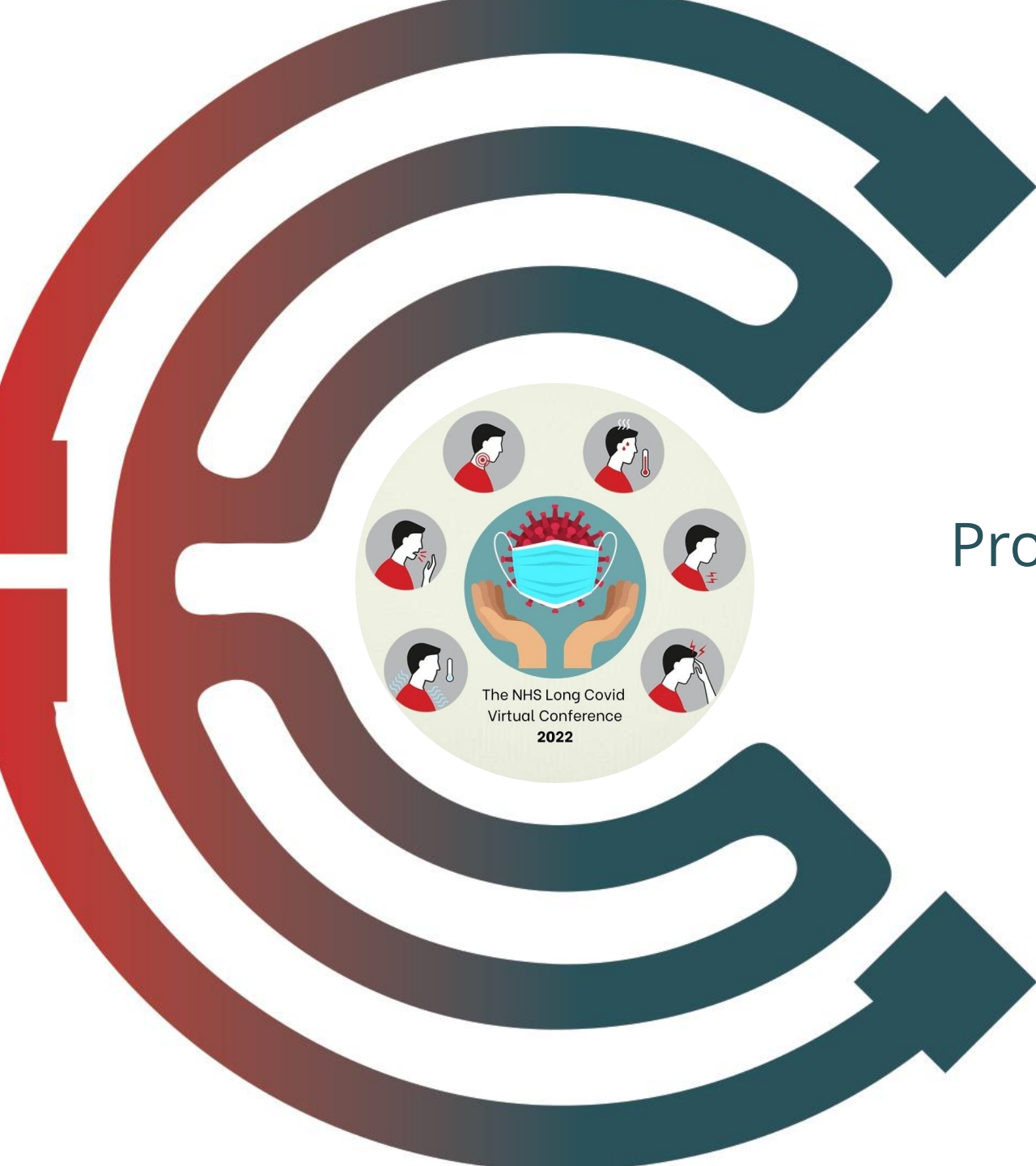
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Philip McMillan,  
Doncaster and Bassetlaw NHS Trust,  
Physician, Lead COVID-19  
autoimmune researcher, Dementia  
Authority



Daniel Altmann/ He,  
Professor of Immunology at Imperial  
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# The Immunology of Long Covid

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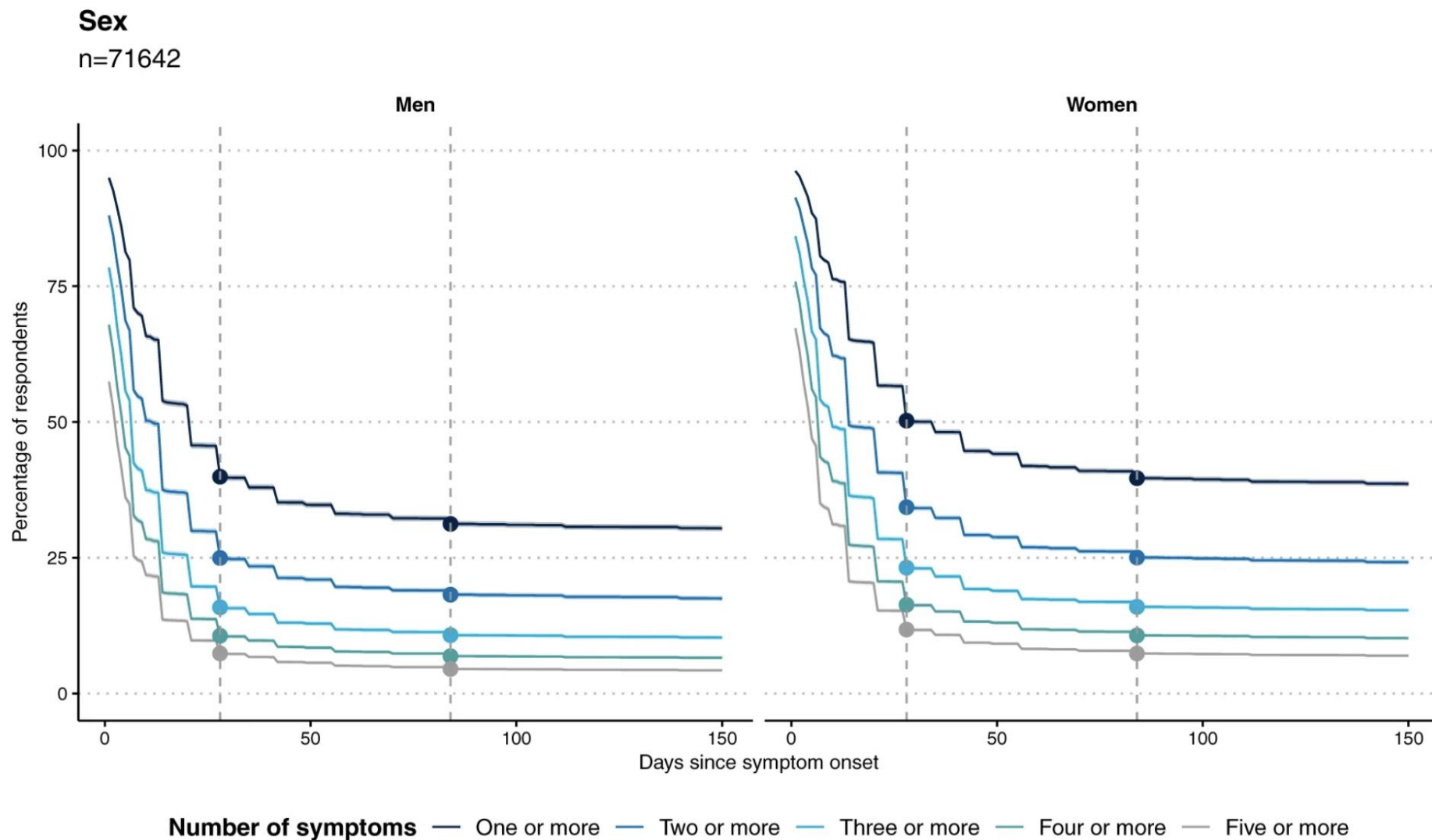
Imperial College  
London



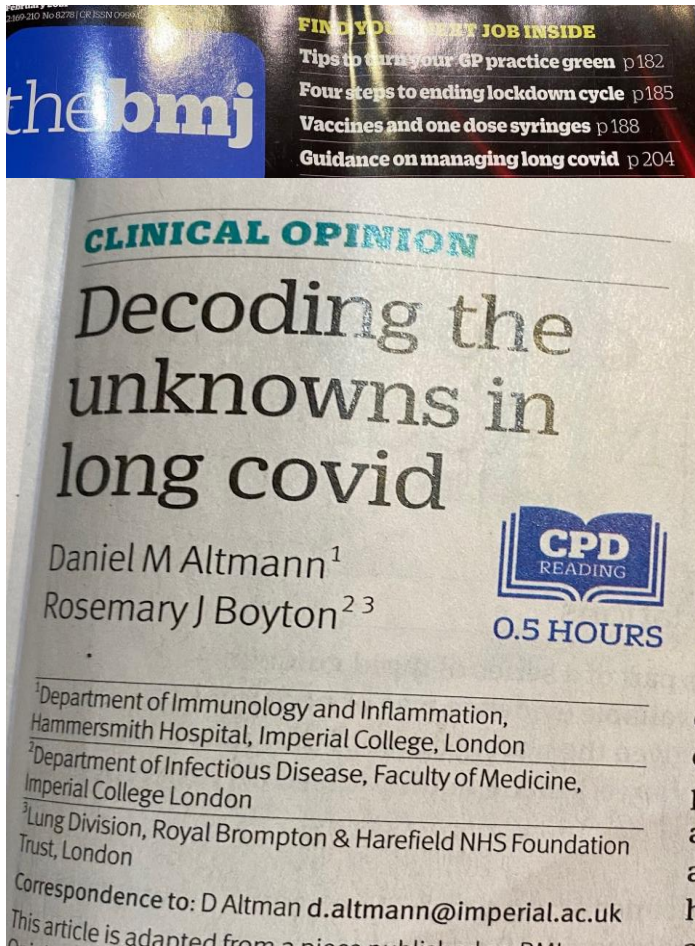


## Fig. 2: Persistence of symptoms over time.

From: [Persistent COVID-19 symptoms in a community study of 606,434 people in England](#)



Plots showing persistence of symptoms as a proportion of those who reported symptoms at any time, among  $n = 71,642$  respondents for whom we had 150 days' observation time. Women have higher rates of persistent symptoms; a slower decline in symptom prevalence is observed after 12 weeks in both sexes. The vertical dashed lines show 4 and 12 weeks post symptom onset, respectively.



- A story narrated in real-time, making it currently unknowable whether Long Covid will come to be seen as a condition most typically lasting months, years, or lifelong
- Many come from those who self-isolated unwell at home, did not access a PCR and so have no formal health record evidence of COVID-19
- An uncharted pathophysiology, demanding a better answer than 'post-viral syndrome' or the notion that people are 'bound to feel a bit rough coming out of hospital'
- Diagnostic tests are needed, not least to facilitate access to services
- **Moving forward the goals must move beyond the observational to the interventional**
- If 10-20% of the globe's COVID-19 infections lead to long Covid, we already face a legacy of 20-40 million long-term cases to manage globally. This has massive ramifications for the lives of the affected, for healthcare planning and provision and for employment law (see EU; USA)
- Unless we move rapidly towards resolving mechanism, how to offer rational therapeutics?

# Post-COVID-19 assessment in a specialist clinical service: a 12-month, single-centre, prospective study in 1325 individuals

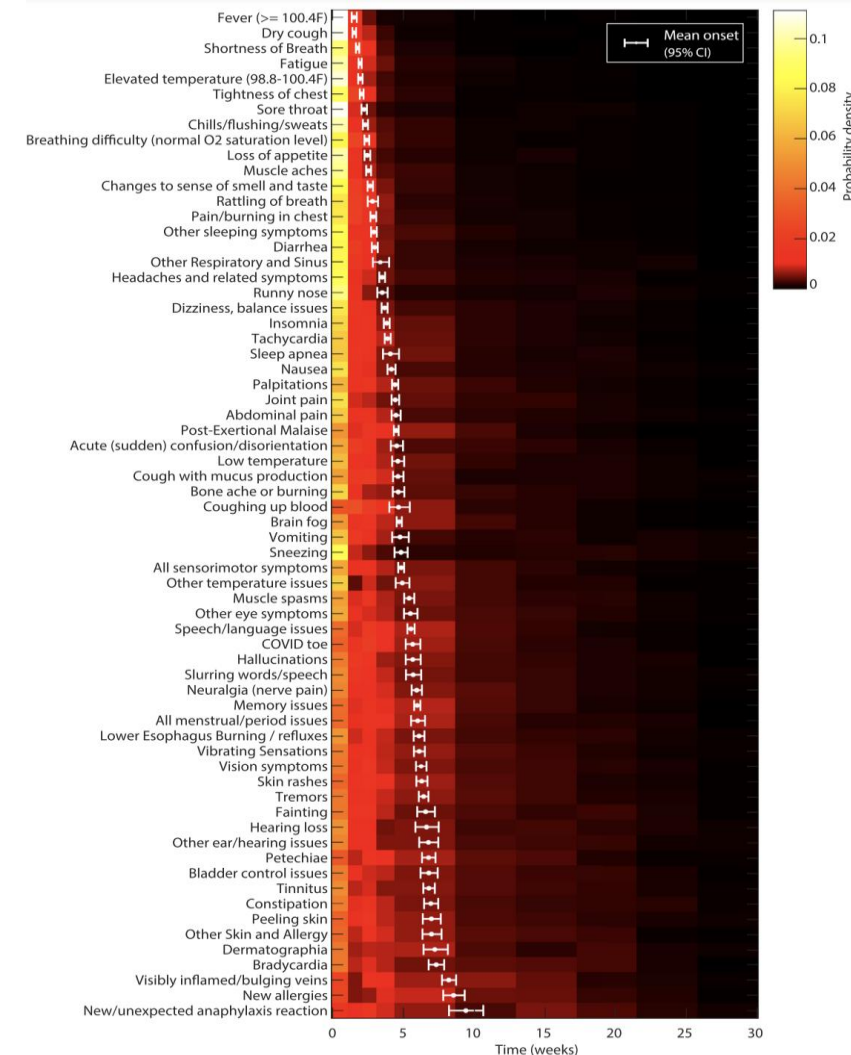
Melissa Heightman,<sup>1</sup> Jai Prashar,<sup>1,2</sup> Toby E Hillman,<sup>1</sup> Michael Marks,<sup>1,3</sup> Rebecca Livingston,<sup>1</sup> Heidi A Ridsdale,<sup>4</sup> Robert Bell ,<sup>1,2</sup> Michael Zandi,<sup>1</sup> Patricia McNamara,<sup>1</sup> Alisha Chauhan,<sup>1</sup> Emma Denny,<sup>1,2</sup> Ronan Astin,<sup>1</sup> Helen Purcell,<sup>1</sup> Emily Attree,<sup>5</sup> Lyth Hishmeh,<sup>6</sup> Gordon Prescott,<sup>7</sup> Rebecca Evans,<sup>1,2</sup> Puja Mehta,<sup>1,2</sup> Ewen Brennan,<sup>1</sup> Jeremy S Brown,<sup>1,2</sup> Joanna Porter,<sup>1,2</sup> Sarah Logan,<sup>1</sup> Emma Wall,<sup>1,2,8</sup> Hakim-Moulay Dehbi,<sup>2</sup> Stephen Cone,<sup>1</sup> Amitava Banerjee ,<sup>1,2,9</sup>

- Not a disease just of post-hospitalized, or more severe in post-hospitalized
- Non-hospitalized were more likely to require support for breathlessness and fatigue, BUT
- Post-hospitalized more likely to have pulmonary emboli, lung interstitial disease, other organ impairment
- Fewer than half were able to return to full-time work
- At 6-12 months after infection both groups still had high levels of functional impairment
- ‘as with other long-term conditions, care of patients experiencing Long Covid requires consistent integrated patient-centred approaches to investigation and management’.
- ‘At public health and policy level, the burden of post Covid morbidity demands focus on suppressing the infection in all age-groups’

Research paper

## Characterizing long COVID in an international cohort: 7 months of symptoms and their impact

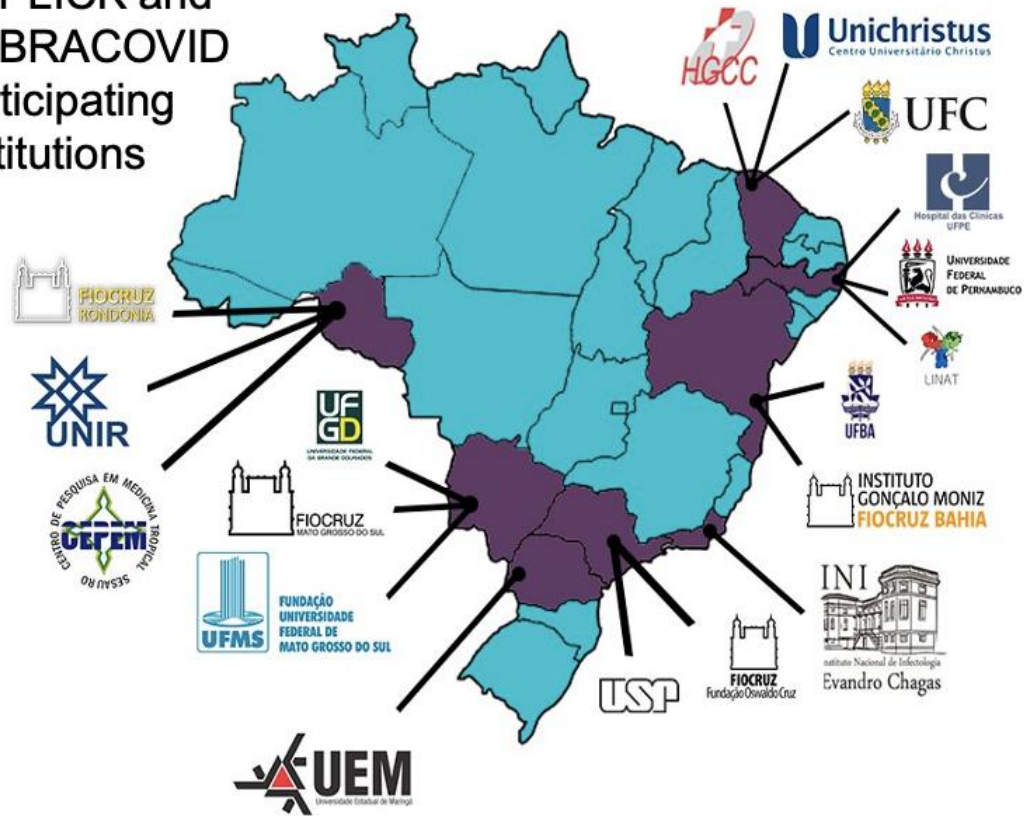
Hannah E. Davis<sup>a,1</sup>, Gina S. Assaf<sup>a,1</sup>, Lisa McCorkell<sup>a,1</sup>, Hannah Wei<sup>a,1</sup>, Ryan J. Low<sup>a,b,1</sup>, Yochai Re'em<sup>a,c,1</sup>, Signe Redfield<sup>a</sup>, Jared P. Austin<sup>a,d</sup>, Athena Akrami<sup>a,b,1,\*</sup>



## Some (non-mutually exclusive) working hypotheses for Long Covid investigations

- Residual damage to ACE2-positive infected tissue (though this might be expected to make Long Covid a condition correlated with severity of acute infection)?
- Ongoing immune stimulation from reservoirs (gut) of persistent infection (-meriting greater focus on anti-virals..?)
- Acute infection causes chronic perturbation of immune subsets (see glandular fever/EBV; CMV)
- Acute infection causes activation of an autoimmune response (including pro-thrombotic autoantibodies) (see Chikungunya virus)
- Endotheliitis

## REPLICK and REBRACOVID participating institutions




**REPLICK** – a collaborative consortium across Brazil to recruit patients with acute or chronic Chikungunya symptoms for comparative genomics, transcriptomics, metabolomics, immunomics, including autoantibody profiling



André Siqueira, médico infectologista do [@inifiocruz](https://www.instagram.com/inifiocruz), comenta o aumento de casos de chikungunya no Rio de Janeiro em 2019

Search...



## £19.6 million awarded to new research studies to help diagnose and treat long COVID

Published: 18/07/2021 Read Time: 11 minutes Print



People experiencing long COVID will benefit from a comprehensive package of new NIHR-funded research to help improve understanding of the condition, from diagnosis and treatment through to rehabilitation and recovery.

An extensive range of 15 projects from across the UK have been awarded a total of £19.6 million to examine causes of long COVID, trial drugs to tackle it, and investigate symptoms such as breathlessness and 'brain fog' that have become synonymous with the condition. Studies will also evaluate health services, such as long COVID clinics, and explore ways patients can monitor the condition to optimise their recovery and return to work.

Recent research shows that as many as [a third of people who report being infected with the coronavirus also report long COVID](#). The condition can present with a number of ongoing symptoms including fatigue, breathlessness and cognitive impairment known as 'brain fog'.

[NIHR's long COVID themed review](#), which considered over 300 papers and academic opinion pieces from across the world, indicated that long COVID could be up to four syndromes: post-ICU syndrome; long-term organ damage; post-viral syndrome, and, potentially, an entirely novel syndrome that could more specifically be identified as 'long COVID'.

Health and Social Care Secretary, Sajid Javid, said: "Long COVID can have serious and debilitating long-term effects for thousands of people across the UK, which can make daily life extremely challenging. This new research is absolutely essential to improve diagnosis and treatments and will be life-changing for those who are battling long-term symptoms of the virus."

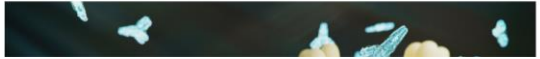
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**Major new funding opportunity for local government based public health research collaborations**



**Global COVID-19 surgery study scoops scientific world record**



## Immune analysis of long COVID to inform rational choices in diagnostic testing and therapeutics

## The WILCO Study – 'Working out the Immunology of Long Covid'

### Immunology Research into COVID-19 and Long Covid

Imperial College London IRAS ID:  
295732



We're trying to understand why some people make a full recovery after COVID-19 while others go on to develop long-term symptoms. To do this, we are looking for volunteers to help us do research into the immune response following infection.

We are looking for people in any of these groups:

- Never had COVID-19 but have received COVID-19 vaccine doses
- Had COVID-19 and made a full recovery within 4-weeks (and may have since received vaccine doses)
- Had COVID-19 and have since suffered from the long-term symptoms described as Long Covid. These may include fatigue, 'brain-fog', exhaustion on walking, breathlessness, chest pain.

**What the study involves** - we would email you a short questionnaire and ask you to return it to us for analysis. We will then invite people showing specific sets of symptoms to pay a visit to the hospital where we will take a small blood test, about the size of an egg-cup of blood. This will be taken to our lab for analysis of immunity to the virus and other features of immune function. We may invite you for a repeat test around 4-months later. We may also ask you to do a '6-minute walk test' and donate a stool sample.

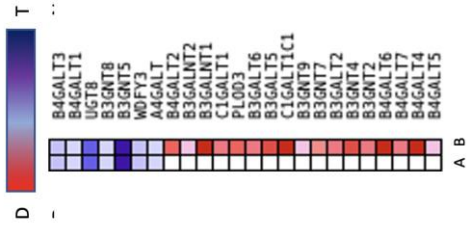
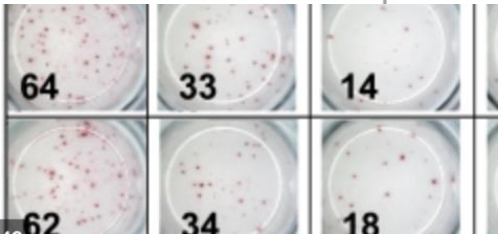
**If you might be interested in taking part please contact the investigator,  
Prof Danny Altmann: [altmannlongcovidstudy@imperial.ac.uk](mailto:altmannlongcovidstudy@imperial.ac.uk)**



A panel of investigations to define Long Covid diagnostic markers, conducted in relation to symptom spectrum and detailed history:

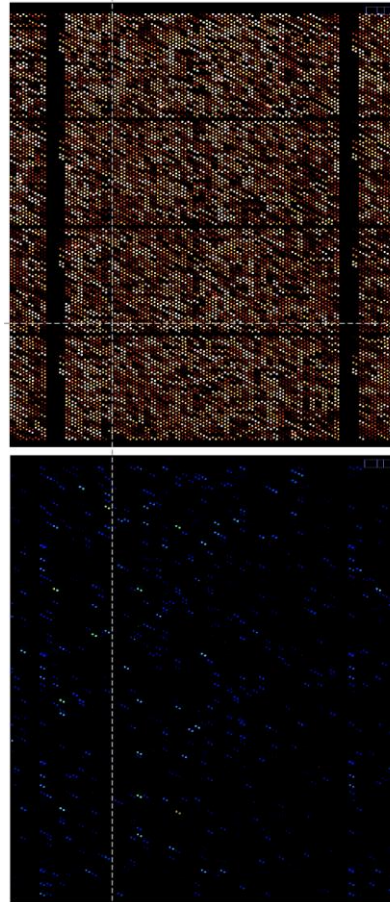


- Flow cytometry to look at immune subsets in PBMC
- Comprehensive autoantibody screening assessed by whole proteome arrays
- Autoimmune T cell responses assessed against self-antigen peptide panels
- Analysis of RNA expression to look for changes in immune programmes



# Decoding the autoantibody and autoimmune T cell correlates of SARS-CoV-2-Long Covid symptoms

- PHOSP-COVID
- Persistent symptoms in the COVIDsortium healthcare worker cohort
- COVERSCAN MRI cohort
- NIHR Long Covid cohorts
- REBRACOVID (Brazil) cohort post P.1 infection
- ISARIC4c
- Non-hospitalized community cases from support groups
- STIMULATE-ICP
- Paediatric Long Covid (EVALENA)



Principal component analysis (PCA) selection of most strongly implicated autoantigen signatures to develop accessible serological validation

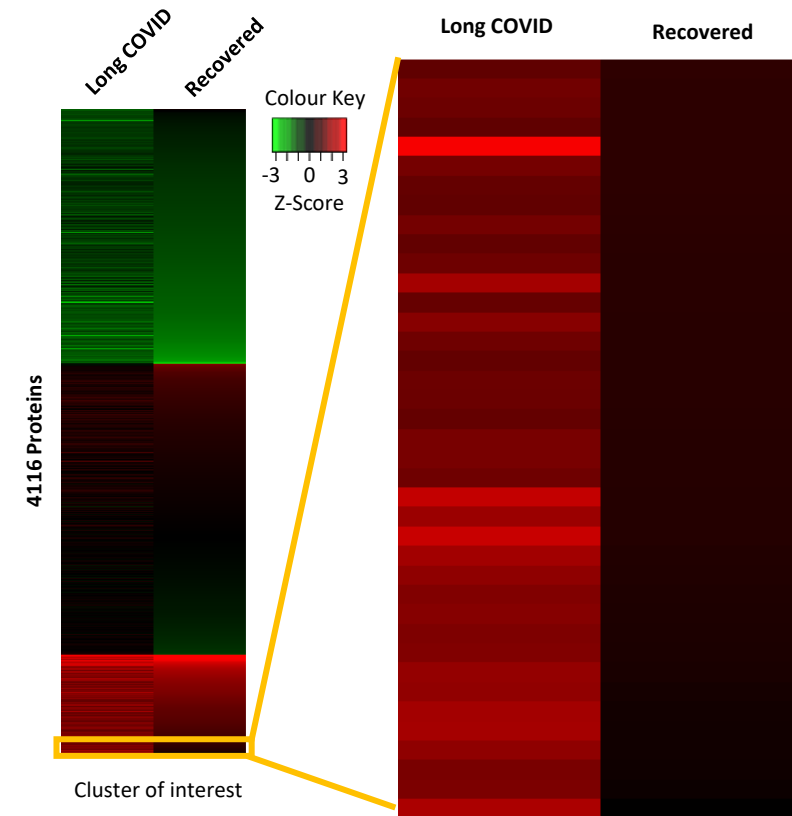
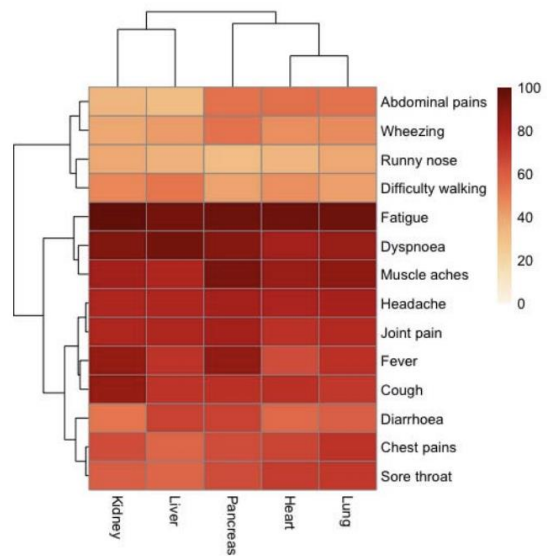
PCA selection of most strongly implicated autoantigens to probe for T cell autoreactivity (- generate recombinant autoantigens and peptide panels)



Simplified Long Covid biosignatures for diagnostic tests

# Collaboration with the Coverscan/Perspectum MRI cohort (Rajarshi Banerjee)

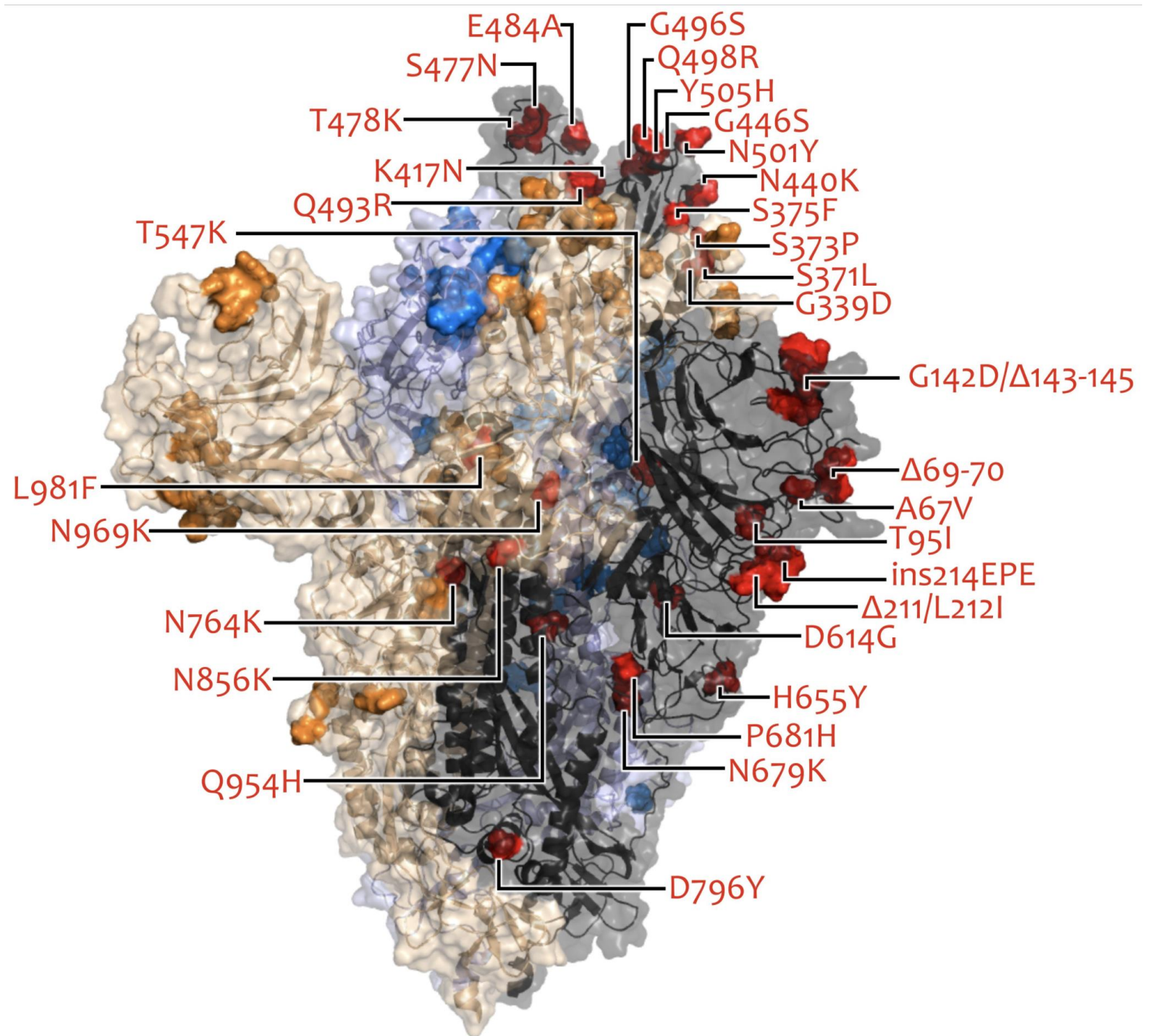
Figure 4: Clustering of reported symptoms and organ impairment for individuals with long-COVID (n=201).



**Heatmap of Z-score of autoantigens detected in serum from COVERSCAN patients with or without long COVID (selected for MRI lung changes)**

Proteins were clustered using k-mean clustering (k=3) of Euclidean distance. The yellow box depicts a cluster of autoantigens enriched in long COVID but not in recovered COVID-19

From:  
<https://www.cogconsortium.uk/cog-uk/sars-cov-2-variants>



## The Omicron/BA.2 wave and Long Covid

While it has been clear from the outset that risk of Long Covid is not correlated simply with the severity of acute infection, there was every reason to hope that with large-scale rollout of effective vaccines and a period of domination by a somewhat less severe SARS-CoV-2 mutant, there would be few additions to the sufferers joining Long Covid support groups.

Far from any subsidence in new Long Covid cases, the massive, ongoing caseloads of the Delta, Omicron and BA.2 waves has brought a large cohort of new sufferers. These waves having disproportionately impacted primary and secondary schools, many of the new sufferers are children.

“...thinking about SARS-CoV-2 and Long Covid – and our response to it – has had to shift and readjust, virtually on a monthly basis. This is now a highly infectious, upper-respiratory virus able to reinfect repeatedly (and thus, self-evidently, disqualified from the epithet of being a booster of natural herd immunity), leaving the healthy-vaccinated unwell and unable to work for several days each time, the old or vulnerable in danger of hospitalisation and death. If we renege on mitigations as each round of infection draws more of all ages into chronic disability, this may be the blunder that we rue for decades to come, even after the acute wave of 2020/21 lockdowns and deaths has become, for most, a distantly remembered nightmare”.

### Long Covid could create a generation affected by disability, expert warns

Prof Danny Altmann, immunologist at Imperial College London, says UK's approach fails to take the impact of infections seriously



A protester holds up a placard demanding research into long Covid during a demonstration in Parliament Square, London on 9 March. Photograph: Martin Pope/SOPA Images/Rex/Shutterstock

Long Covid could create a generation affected by disability, with people forced out of their homes and work, and some even driven to suicide, a leading expert has warned.

Nicola Davis Science correspondent  
@NicolaKSDavis  
Wed 23 Mar 2022 07:15 GMT



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Sat 16 Apr 2022 12:00 BST



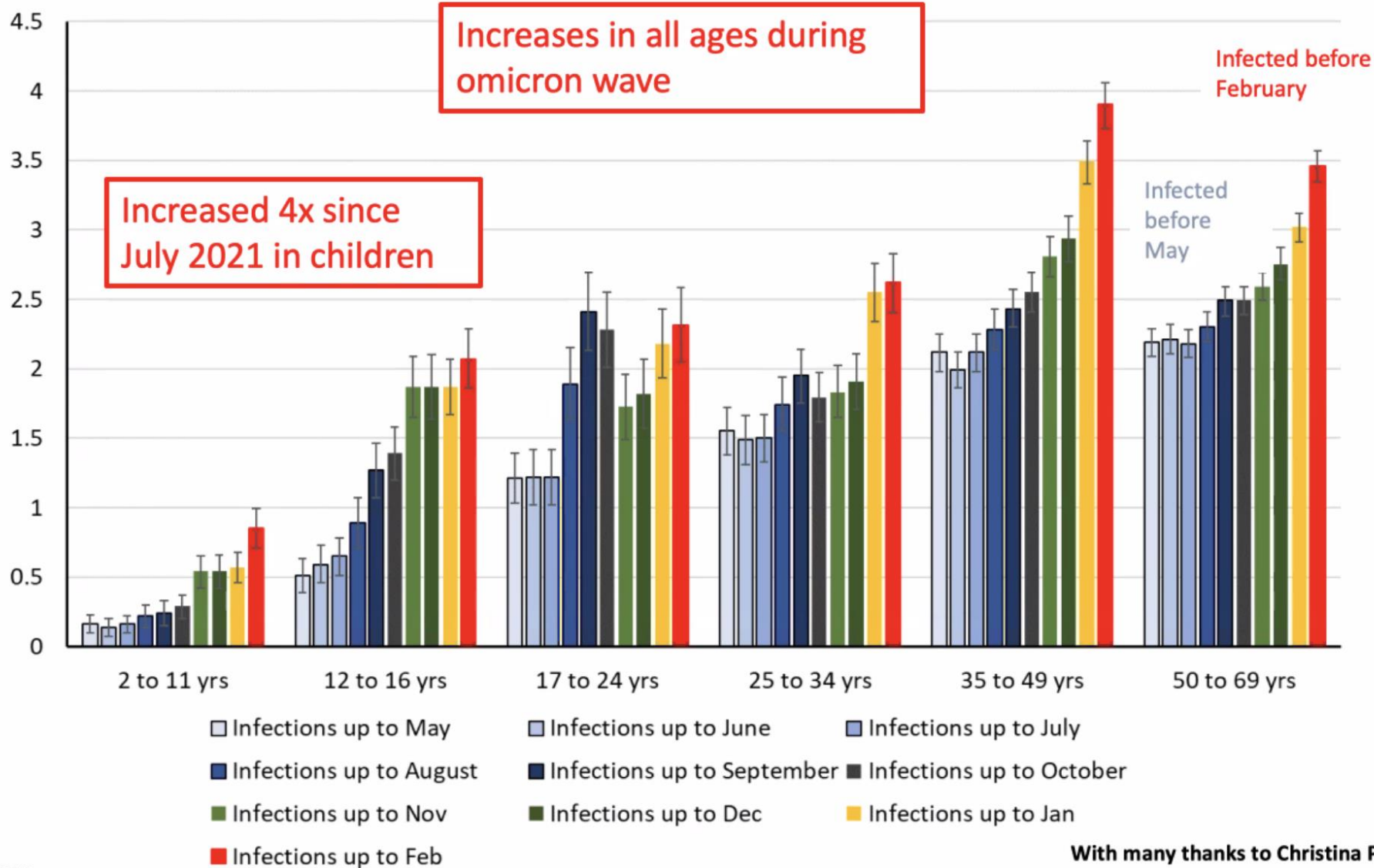
Vaccines are no match for long Covid.  
Treating it is science's next great challenge  
*Danny Altmann*

Failure to recognise the need for a response could be a blunder we rue for decades to come



# Percentage of population living with “Long Covid” (symptoms lasting at least 4 weeks) by age over time (ONS survey)

Percent of age group



With acknowledgement and thanks to Christina Pagel and Deepti Gurdusani

With many thanks to Christina Pagel for this chart



Colleagues in the ICL lab,  
the Barts Covidsortium  
HCW Consortium and in  
Brazil:

Roque Almeida  
Andre Siqueira  
Moacy Rego  
Giselle Duarte  
Rodrigo Stabeli  
Ian McDonald  
Sasha Bailey  
James Moon  
Aine McKnight  
Charlotte Manisty  
Mahdad Noursadeghi  
George Joy

Joseph Gibbons  
Corinna Pade  
Leo Swadling  
Ana Valdes  
Stuart Astbury  
Louisa James  
Hamish King  
Benny Chain  
Mala Maini  
Thomas Treibel  
Mel Jensen  
Amanda Semper  
Tim Brooks  
Kevin Mills  
Wendy Heywood  
Tom Baldwin

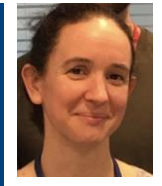




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