Nutri Link
Linking Science and Nutrition

Long Covid Practitioner Programme

WEBINAR ONE

Presented by Antony Haynes, Nutritional Therapist
BA(Hons), Dip ION, mCNHC, mBANT

Nutri Link
Linking Science and Nutrition

1. Monday 23rd September 12 noon
Introduction to Long Covid, review of symptoms, example case history. Review of Nutritional Therapy solutions.

2. Friday 27th September 12 noon
Functional Medicine model of Long Covid from Dr Leo Galland, including blood clotting, viral persistence, and mitochondrial disruption. Nutritional Therapy solutions.

3. Monday 30th September 12 noon
Exploration into Mast Cell Activation Syndrome (MCAS) and its involvement in Long Covid symptomology. Nutritional Therapy solutions.

4. Friday 4th October 12 noon
Viral persistence and viral reactivation as causes of Long Covid. Nutritional Therapy solutions. AND exploration of negative impact of spike protein on heme and all of its ramifications.

5. Monday 7th October 12 noon
Neurotransmitter imbalances as an explanation for multiple Long Covid symptoms. Nutritional Therapy solutions.

6. Monday 14th October 12 noon
Spike protein pathogenesis. Nutritional Therapy solutions. Review and summary and presentation of Model of Long Covid including lab tests and potential therapeutic interventions.

Nutri Link
Linking Science and Nutrition

1. **Monday 23rd September 12 noon**

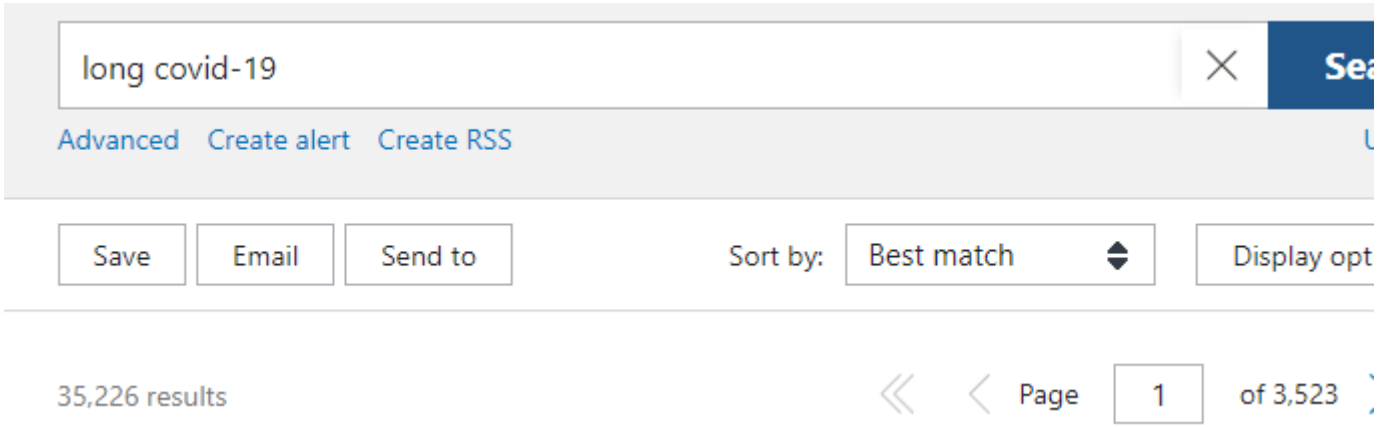
Introduction to Long Covid, review of symptoms, example case history.
Review of Nutritional Therapy solutions.

Research Papers on the Subject of Long Covid

“Long Covid”

“Long Covid Syndrome”

“Long Covid-19”



Definition of Long Covid

Although many clinical definitions have been provided, "long-COVID" can be defined as a condition occurring in patients with a history of SARS-CoV-2 infection, developing 3 months from the symptoms onset, persisting for at least 2 months, and not explained by alternative diagnoses.

Some formal definitions covered by the term long COVID

	Name	Definition
WHO[16]	Post-COVID condition	Usually, 3 months from the onset of COVID-19; symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis in individuals with a history of probable or confirmed SARS-CoV-2 infection
US Department of Health and Human Services[15]	Long COVID	Signs, symptoms, and conditions that continue or develop after initial COVID-19 infection and last more than 4 weeks
UK National Institute for Health and Clinical Excellence[17]	Ongoing symptomatic COVID-19	Symptoms that are unexplained by an alternative diagnosis and persist for 4–12 weeks after acute COVID-19
UK National Institute for Health and Clinical Excellence[17]	Post-COVID-19 syndrome	Symptoms that are unexplained by an alternative diagnosis and persist for more than 12 weeks after acute COVID-19

Greenhalgh, Trisha et al. Long COVID: a clinical update. The Lancet, Vol 404, Iss 10453, 707 – 724, Aug 2024. Full Paper

Long Covid Warning!

- March 2023
- Long COVID is a multisystemic illness encompassing ME/CFS, dysautonomia, impacts on multiple organ systems, and vascular and clotting abnormalities. It has already debilitated millions of individuals worldwide, and that number is continuing to grow.
- On the basis of more than 2 years of research on long COVID and decades of research on conditions such as ME/CFS, a significant proportion of individuals with long COVID may have lifelong disabilities if no action is taken.

Davis HE, McCorkell L, Vogel JM, Topol EJ. Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol. 2023 Mar;21(3):133-146. doi: 10.1038/s41579-022-00846-2. Epub 2023 Jan 13. Erratum in: Nat Rev Microbiol. 2023 Jun;21(6):408. Full Paper

Prevalence of Long-Covid

- Long COVID holds the potential to produce a second public health crisis on the heels of the pandemic itself. (Rando, 2021)
- According to recent global analyses, the cumulative prevalence of long-COVID seems to range between 9% and 63%, and is up to 6-fold higher than that of similar postviral infection conditions. (Lippi et al, 2023)
- At least **65 million** individuals worldwide are estimated to have long COVID, with cases increasing daily. (Davis et al, 2023)
- An estimated **1.9 million** people living in private households in the UK (2.9% of the population) were experiencing self-reported long COVID (ONS, March 2023)
- In the UK alone, Long COVID affects an estimated **1.8% of the population**. (Greenhalgh, 2024)

Rando HM, Bennett TD, Byrd JB, et al. Challenges in defining Long-Covid: Striking differences across literature, Electronic Health Records, and patient-reported information. medRxiv. March 2021. Full Paper

Lippi G, Sanchis-Gomar F, Henry BM. COVID-19 and its long-term sequelae: what do we know in 2023? Pol Arch Intern Med. 2023 Apr 19;133(4):16402. Full Paper

Davis HE, McCorkell L, Vogel JM, Topol EJ. Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol. 2023 Mar;21(3):133-146. Full Paper

Office of National Statistics

Greenhalgh, Trisha et al. Long COVID: a clinical update. The Lancet, Vol 404, Iss 10453, 707 – 724, Aug 2024. Full Paper

The Impact of Long COVID on the UK workforce

Nutri Link
Linking Science and Nutrition

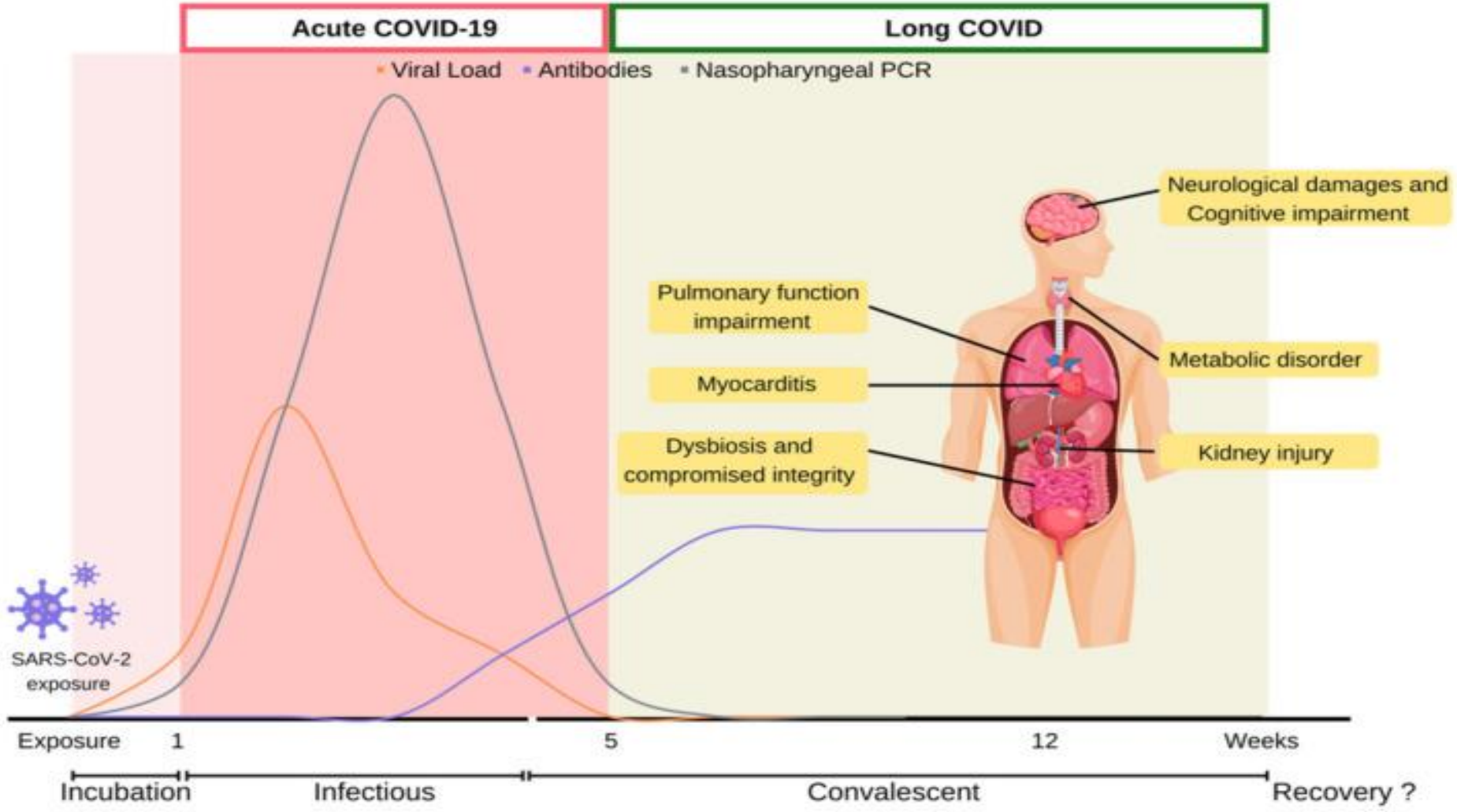
- COVID-19 is more likely to lead to Long COVID among persons of working age.
- Reuschke & Houston are the first to estimate the impact of Long Covid on employment in the UK.
- Using estimates of cumulative prevalence of Long COVID, activity-limiting Long COVID in the working-age population and of economic inactivity and job loss resulting from Long COVID, they provide evidence of the profound impact of Long COVID on national labour supply.
- Since the start of the pandemic, cumulatively **2.9 million people of working age** (7% of the total) in the UK have had, or still have, Long COVID.
- This figure will continue to rise due to very high infection rates in the Omicron wave.
- Since the beginning of the pandemic, economic inactivity due to long-term sickness has risen by 120,900 among the working-age population, fuelling the UK's current labour shortage.
- An estimated 80,000 people have left employment due to Long COVID. "We argue that governments need to tackle the twin challenges to public health and labour supply and provide employment protection and financial support for individuals and firms affected by Long COVID."

Reuschke D & Houston D. The impact of Long COVID on the UK workforce. Applied Economics Letters, 2023. Taylor & Francis. View Abstract

Disease Course of Covid-19 to Long Covid

Disease Course of Covid-19 to Long Covid

Nutri Link
Linking Science and Nutrition



Koc HC, Xiao J, Liu W, Li Y, Chen G. Long COVID and its Management. Int J Biol Sci. 2022 Jul 11;18(12):4768-4780. Full Paper

Nutri Link
Linking Science and Nutrition

Signs & Symptoms of Long Covid

Long Covid Signs & Symptoms

Nutri Link
Linking Science and Nutrition

- Long COVID is linked to more than 200 symptoms.
- Davis HE, Assaf GS, McCorkell L, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. EClinicalMedicine. 2021;38:101019. Full Paper

- With over 200 symptoms reported across 10 organ systems, it's indeed a complex and multifaceted condition.

- See following slides that list 100 of these symptoms.

Long Covid Signs & Symptoms

Nutri Link
Linking Science and Nutrition

Respiratory Symptoms:

- Persistent cough
- Shortness of breath
- Chest tightness
- Wheezing
- Coughing up mucus
- Feeling winded easily
- Difficulty breathing when lying flat
- Increased respiratory rate
- Decreased lung function
- Bronchitis-like symptoms

Cardiovascular Symptoms:

- Fatigue
- Weakness
- Dizziness
- Lightheadedness
- Fainting spells
- Rapid heartbeat
- Palpitations
- High blood pressure
- Low blood pressure
- Orthostatic intolerance

Long Covid Signs & Symptoms

Nutri Link
Linking Science and Nutrition

Neurological Symptoms:

- Headaches
- Brain fog
- Confusion
- Memory loss
- Concentration difficulties
- Mood changes (anxiety, depression)
- Irritability
- Insomnia / Sleep disturbances
- Restless leg syndrome
- Tremors
- Seizures (rare)

Musculoskeletal Symptoms:

- Muscle pain
- Joint pain
- Arthritis-like symptoms
- Fibromyalgia-like symptoms
- Tenderness to touch
- Swelling in hands and feet
- Carpal tunnel syndrome
- Plantar fasciitis

Long Covid Signs & Symptoms

Nutri Link
Linking Science and Nutrition

Gastrointestinal Symptoms:

- Diarrhoea
- Constipation
- Abdominal pain
- Bloating
- Gas
- Loss of appetite
- Weight gain/loss
- Nausea/vomiting
- Acid reflux
- Stomach cramps

Dermatological Symptoms:

- Skin rashes
- Hives
- Itching
- Dry skin
- Acne-like lesions
- Hair loss
- Nail problems (brittle, breaking)
- Cold sweats

Long Covid Signs & Symptoms

Nutri Link
Linking Science and Nutrition

Ophthalmologic Symptoms:

- Blurred vision
- Double vision
- Eye strain
- Red eyes
- Watery eyes
- Sensitivity to light
- Blind spots

Ear/Nose/Throat Symptoms:

- Hearing loss
- Ringing ears (tinnitus)
- Ear fullness
- Nasal congestion
- Sinus infections
- Throat soreness
- Hoarseness
- Voice changes

Long Covid Signs & Symptoms

Nutri Link
Linking Science and Nutrition

Psychiatric Symptoms:

- Anxiety disorders
- Depressive episodes
- Panic attacks
- PTSD-like symptoms
- Suicidal ideation
- Hallucinations (rare)
- Delusions (rare)

Endocrine/Hormonal Symptoms:

- Thyroid dysfunction
- Adrenal fatigue
- Hormonal imbalances
- Menstrual irregularities
- Erectile dysfunction
- Libido changes

Long Covid Signs & Symptoms

Nutri Link
Linking Science and Nutrition

Immune System Symptoms:

- Recurring infections
- Autoimmune reactions
- Allergic reactions
- Inflammation

Other Symptoms:

- Temperature regulation issues
- Sweating abnormalities
- Chills
- Flu-like symptoms
- General feeling unwell
- Lack of motivation
- Social withdrawal
- Cognitive impairment
- Emotional reactivity
- Dissociative symptoms

Long Covid Signs & Symptoms

Nutri Link
Linking Science and Nutrition

And there are another 100+ symptoms

that have been identified too

Long-Covid

- Characterising Long-Covid in an International Cohort: 7 months of symptoms and their impact.
- Hannah Davis, Gina Assaf, Lisa McCorkell, Hannah Wei, Ryan Low, Yochai Re'em, Signe Redfield, Jared Austin, Athena Akrami.
- **Body Politic Patient-Led Research Collaborative**

- Hannah Davis - https://tinyurl.com/49yfskvz - with graphics
- Johns Hopkins University - https://tinyurl.com/wdcar6py
- Research Gate - https://tinyurl.com/yce5rwpm
- MedRxiv - https://tinyurl.com/3jknm336

Characterising Long-Covid in an International Cohort: 7 months of symptoms and their impact

Nutri Link
Linking Science and Nutrition

- 3,762 respondents from 56 countries.
- 205 symptoms, 10 organ systems.
- Different timing of manifestation of symptoms.
- Symptom Clusters.
- No difference in those who had been tested positive for Covid-19 vs those who had not been tested.

Characterising Long-Covid in an International Cohort: 7 months of symptoms and their impact

Nutri Link
Linking Science and Nutrition

- Most common symptoms: fatigue, post exercise malaise, cognitive dysfunction.
- Virus finds its way into any and every organ and tissue, as post-mortem studies have shown.
- No difference in symptoms in different age groups. In fact, younger cohorts were affected more severely in these categories:
    - Attention
    - Thinking
    - Executive Function
    - Problem Solving
    - Slowed Thoughts
    - Confusion
    - Fast Thoughts

Characterising Long-Covid in an International Cohort: 7 months of symptoms and their impact

Nutri Link
Linking Science and Nutrition

Sensorimotor Symptoms

- **80.5%** had tingling, pins and needles, electric zaps, facial paralysis, facial pressure / numbness, & weakness experiences

Sleep

- **78.6%** had difficulty with sleep

Headaches

- **77%**, often acting as the precursor to post exertional malaise.

Emotions and Mood

- **88.3%**, with anxiety being the predominant symptom. (we will explore this in depth in Webinar 5)

Symptoms/Systems Affected

Nutri Link
Linking Science and Nutrition

- **Fatigue - 98.3%**
- **Post Exertional Malaise (PEM)** - **89%**
- **Cardiovascular symptoms - 86%,** with palpitations being most common
- **Pulmonary & Respiratory - 93%**, with shortness of breath being most common
- **Gastrointestinal - 85.5%**, with diarrhoea being the most common
- **Dermatological - 59.1%**

Characterising Long-Covid in an International Cohort: 7 months of symptoms and their impact

Nutri Link
Linking Science and Nutrition

- **Relapses** – **86%** suffered relapses for at least a few days, mostly brought on by exercise or stress.
- After 6 months, most patients had most symptoms. Some improvement was noticed.
- **73%** not able to work in same way as pre-Covid.
- **93%** were unable to work full time without risking their well-being or relapse.

Most Common Long Covid Signs & Symptoms

Nutri Link
Linking Science and Nutrition

1. **Respiratory:** shortness of breath, congestion, persistent cough, etc.
2. **Neurological/psychiatric:** brain fog, malaise, tiredness, headaches, migraines, depression, inability to focus or concentrate, altered cognition, insomnia, vertigo, panic attacks, tinnitus, anosmia, phantom smells, etc.
3. **Musculoskeletal:** myalgias, fatigue, weakness, joint pains, inability to exercise, post-exertional malaise, inability to perform normal activities of daily life.
4. **Cardiovascular:** Palpitations, arrhythmias, Raynaud-like syndrome, hypotension, and tachycardia on exertion.
5. **Autonomic:** Postural tachycardia syndrome (POTs), abnormal sweating.
6. **Gastrointestinal disturbance:** anorexia, diarrhoea, bloating, vomiting, nausea, etc.
7. **Dermatologic:** itching, rashes, dermatographia.
8. **Mucus membranes:** running nose, sneezing, burning and itchy eyes.

Common Signs & Symptoms of Long-Covid

- Persistent fatigue - 69%
- Persistent breathlessness – 53%
- Persistent cough - 34%
- Depressed – 15%
- Deteriorating chest radiograph appearance at follow-up - 9%
- Persistently elevated d-dimer - 30.1%
- Persistently elevated CRP - 9.5%

Mandal S et al. 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. Thorax. 2020 Nov 10;thoraxjnl-2020-215818. Full Paper

13 Most Common Signs & Symptoms of Long-Covid

- Loss of smell or taste
- Fatigue
- Brain fog
- Dizziness
- Gastrointestinal symptoms
- Heart palpitations
- Changes in sexual desire or capacity
- Thirst
- Chronic cough
- Chest pain
- Abnormal movements
- Post-exertional malaise
- Feeling ill after even minor physical or mental effort

Nutri-Link Long Covid Symptom Tracker

Most Common Symptoms of Long Covid

Mild = 1, Moderate = 2, Severe = 3

SYMPTOM / SIGN	SCORE
Fatigue	
Brain Fog	
Poor Memory	
Anxiety / Poor Mood	
Shortness of breath	
Cough	
Altered sense of smell / taste	
Aches & pains (anywhere in the body)	
Muscle weakness	
Muscle / Joint pains	
Tingling and or numbness in arms, hands, legs, feet	
Palpitations	
Feeling Faint	
Cold hands, fingers, feet, toes	
Poor coordination	
Sleep disturbances	
Hearing loss	
Sensitivity to noise	
Gut symptoms	
Changes in menstrual cycle	
Have you passed blood clots during your periods more than usual?	
Worse PMT	
Swollen glands / lymph nodes	
Increased allergic reactivity	
Headaches	
TOTAL	

Nutri-Link Long Covid Symptom Tracker

Nutri Link
Linking Science and Nutrition

How & When to Use this Long Covid Questionnaire

- We've put together the most common 25 symptoms and signs of Long Covid, with 3 being for females only, into a simple scored questionnaire which can be used to track the progress of your clients.
- Ask each Long Covid client to complete the questionnaire before commencing any nutritional programme and then at regular intervals, be it every 2 to 4 weeks. Over time, the gap between filling out the questionnaires can be extended.
- The overall total indicates the degree of your client's improvement whilst following the programme you have recommended. This provides useful clinical information for you and confirmation back to the client.
- By comparing the individual scores you are in a position to see what specific effects your advice is having on your client's health and, in addition to verbal or other feedback, may help you to steer their therapeutic nutrition programme.
- You can consider creating a bar graph to reflect back the results over time to your clients.
- By using this Long Covid questionnaire with all of your clients with this syndrome, you will be able to accumulate useful data which you can share with prospective clients and others.

Nutri Link
Linking Science and Nutrition

Example Case History

Mr B.D.

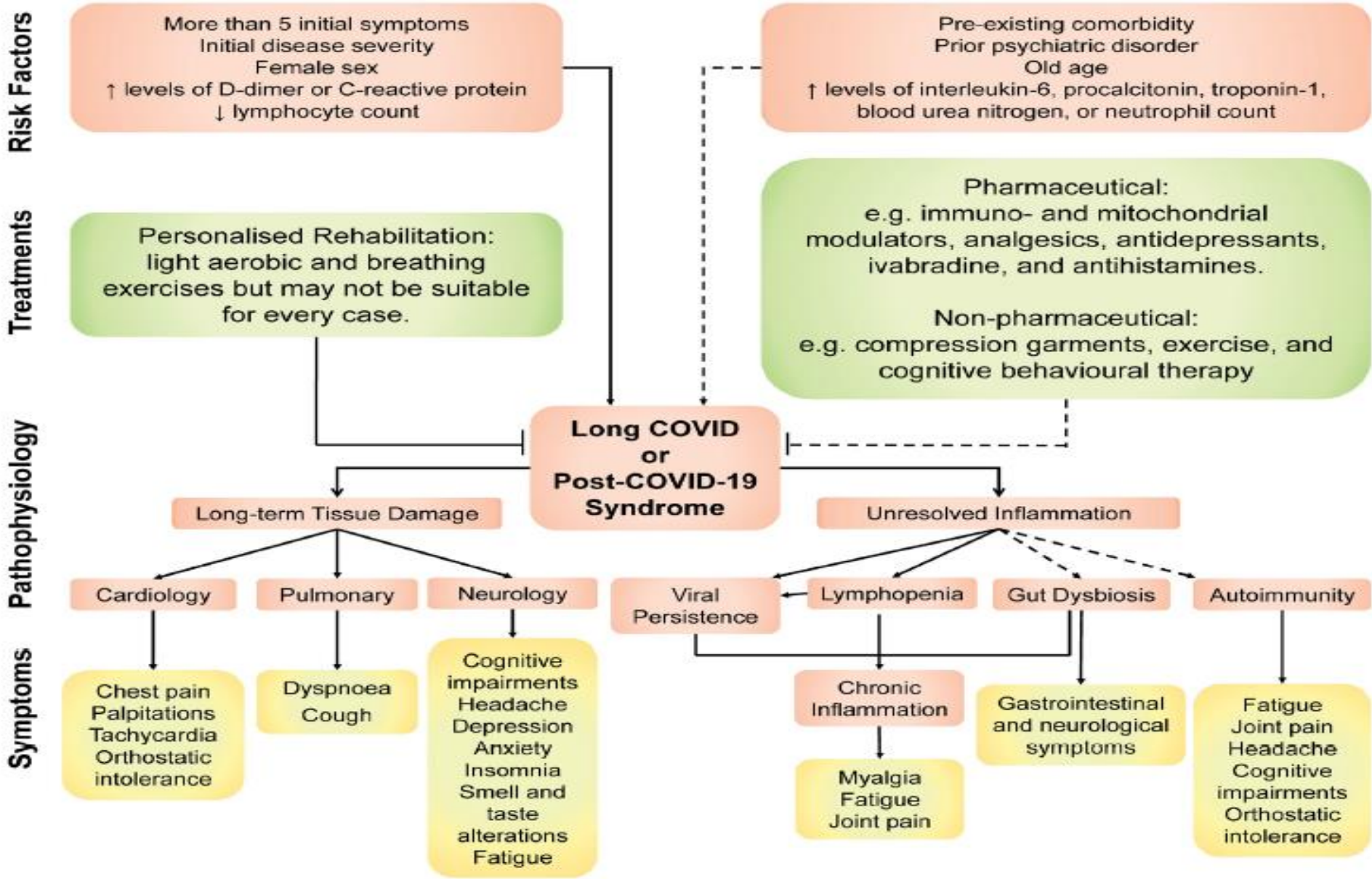
Summary Symptom Diagram

The diagram on the next slide taken from this review article in 2021 provides a useful summary that helps to explain why there is such a variety and large number of of symptoms.

Yong SJ. REVIEW ARTICLE. Long-Covid or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. INFECTIOUS DISEASES, 2021; VOL. 0, NO. 0, 1–18. Full Paper

An overview of the symptoms, putative pathophysiology, associated risk factors, and potential treatments involved in long COVID.

Note: Dashed lines represent areas where evidence is relatively lacking compared to non-dashed lines.



Any sign of a “cure”?

- “There are no proven treatments for Long COVID yet, and current management of the condition focuses on ways to relieve symptoms or provide rehabilitation.
- There is a dire need to develop and test biomarkers (e.g. blood tests) to diagnose and monitor Long COVID and to find therapies that address root causes of the disease.”

Greenhalgh, Trisha et al. Long COVID: a clinical update. The Lancet, Vol 404, Iss 10453, 707 – 724, Aug 2024. Full Paper

Evidence on Long COVID Diagnosis, Risk, Symptoms, and Functional Impact for Patients – June 2024 (i)

Nutri Link
Linking Science and Nutrition

- A formal COVID-19 diagnosis or positive test is not necessary to consider Long COVID diagnosis.
- Long COVID can cause more than 200 symptoms and affects each person differently. Long COVID is associated with a wide range of new or worsening health conditions impacting multiple organ systems. These can include cardiovascular, respiratory, mental health, gastrointestinal, nervous system, and metabolic symptoms. The report includes a full listing of all symptoms and conditions that have been associated with Long COVID.
- The risk of Long COVID increases with the severity of COVID-19 illness. The report estimates that people whose infection was sufficiently severe to necessitate hospitalization are 2 to 3 times more likely to experience Long COVID than are those who were not hospitalized, and among individuals who were hospitalized, those requiring life support in an intensive care unit may be twice as likely to experience Long COVID. However, people with mild disease can also develop Long COVID, and given the much higher number of people with mild versus severe disease, they make up the majority of people with Long COVID.

Evidence on Long COVID Diagnosis, Risk, Symptoms, and Functional Impact for Patients – June 2024 (ii)

Nutri Link
Linking Science and Nutrition

- **“There is no curative treatment for Long COVID.”**

- Management of the condition is based on current knowledge about treating its symptoms and health effects. As with other complex chronic health conditions, medical treatment for Long COVID is focused on managing symptoms and optimizing quality of life and function.
- Recovery from Long COVID varies among individuals, and the data on recovery trajectories are rapidly evolving. While there is evidence that many people with Long COVID symptoms have improved by 12 months, data beyond that time frame is limited but suggestive that recovery might plateau or progress at a slower rate.
- Socioeconomic status, geographic location, health literacy, and race and ethnicity all affect access to health care — and have contributed to disparities in access to COVID-19 testing, vaccination, and therapeutics, including treatments for acute infection and specialized rehabilitation clinics for Long COVID.

New Report Reviews Evidence on Long COVID Diagnosis, Risk, Symptoms, and Functional Impact for Patients
News Release | June 5, 2024

Evidence on Long COVID Diagnosis, Risk, Symptoms, and Functional Impact for Patients – June 2024 (iii)

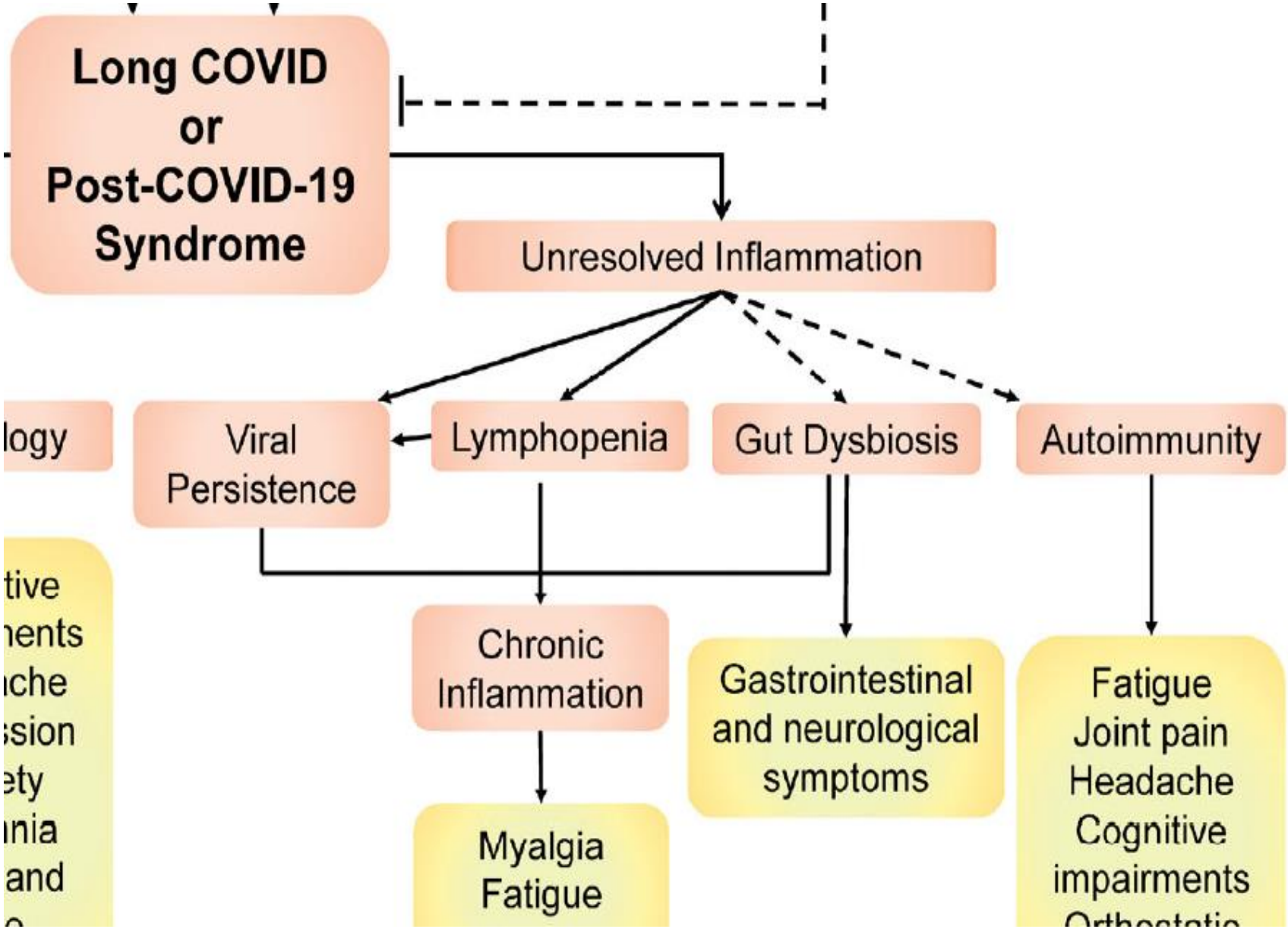
Nutri Link
Linking Science and Nutrition

- Complex, infection-associated chronic conditions are not new, and Long COVID shares many features with conditions like myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and fibromyalgia.

- Although the majority of children, including adolescents, recover fully from COVID-19, some develop Long COVID and experience persistent or intermittent symptoms that can reduce their quality of life. This can result in increased school absences and decreased participation and performance in school, sports, and other social activities. The trajectory for recovery in children and adolescents is better than in adults. More research is needed to understand Long COVID in children, as information from adult studies may not be directly applicable.

- Really?
  - Is there no treatment for Long COVID?
    - Only “management”?
      - What do you think and what is your experience?

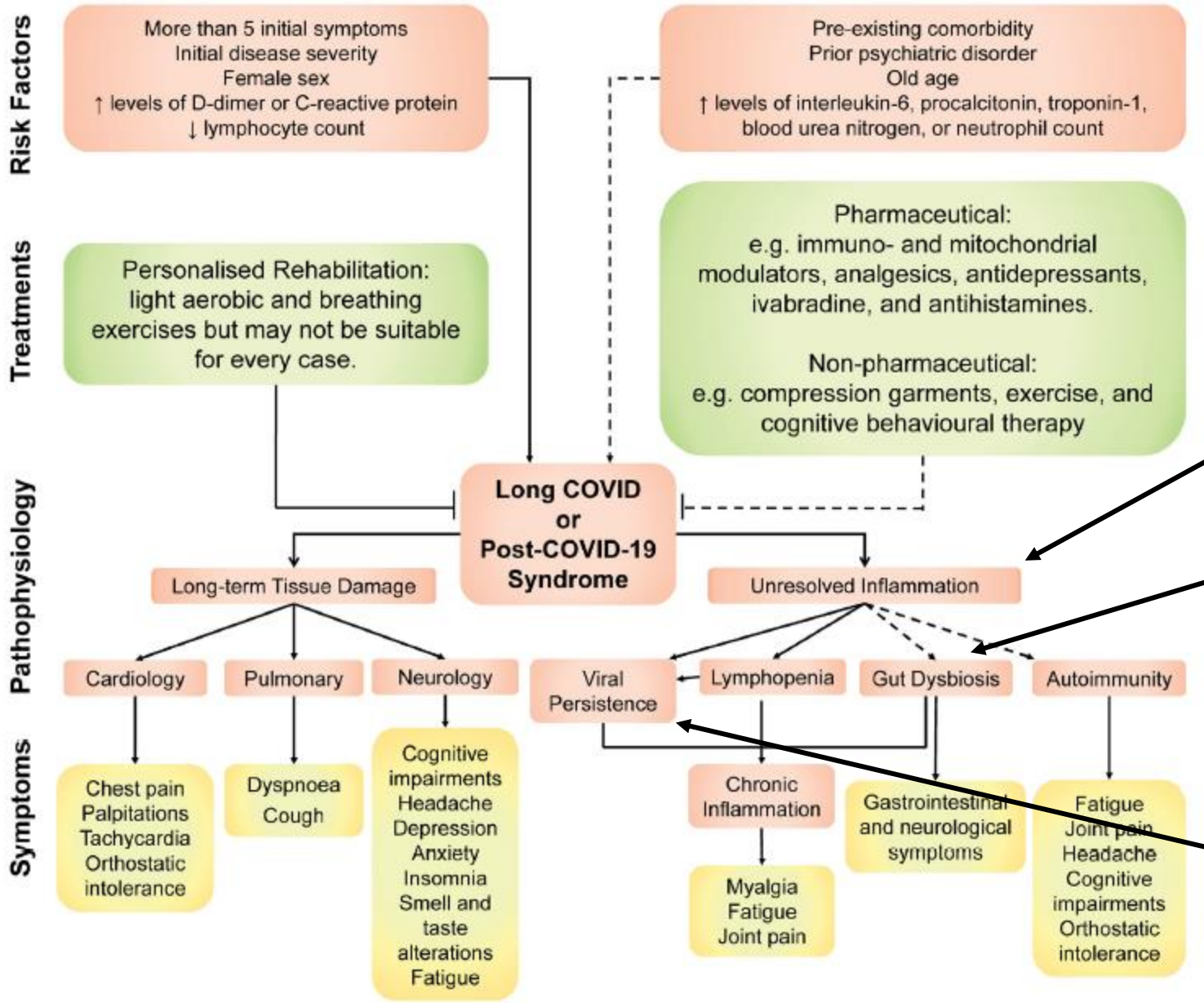
        - Let’s have a look at research evidence to the contrary!



- Unresolved Inflammation
- Viral Persistence
- Lymphopaenia
- Gut Dysbiosis
- Autoimmunity

Yong SJ. REVIEW ARTICLE. Long-Covid or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. INFECTIOUS DISEASES, 2021; VOL. 0, NO. 0, 1–18. Full Paper

An overview of the symptoms, putative pathophysiology, associated risk factors, and potential treatments involved in long COVID. Note: Dashed lines represent areas where evidence is relatively lacking compared to non-dashed lines.



Nutritional Therapy: Turmeric, Green Tea Extract, Boswellia, Lipoic Acid, NAC, CoQ10, Niacin, Zinc, Vit D, Vit C.

Probiotics, anti-microbials, gut lining support, digestive enzymes

Humic Acid, Olive Leaf Extract, Zn, Cu, NAC, Monolauric Acid

Yong SJ. REVIEW ARTICLE. Long-Covid or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. INFECTIOUS DISEASES, 2021; VOL. 0, NO. 0, 1–18. Full Paper

A Closer Look at Niacin

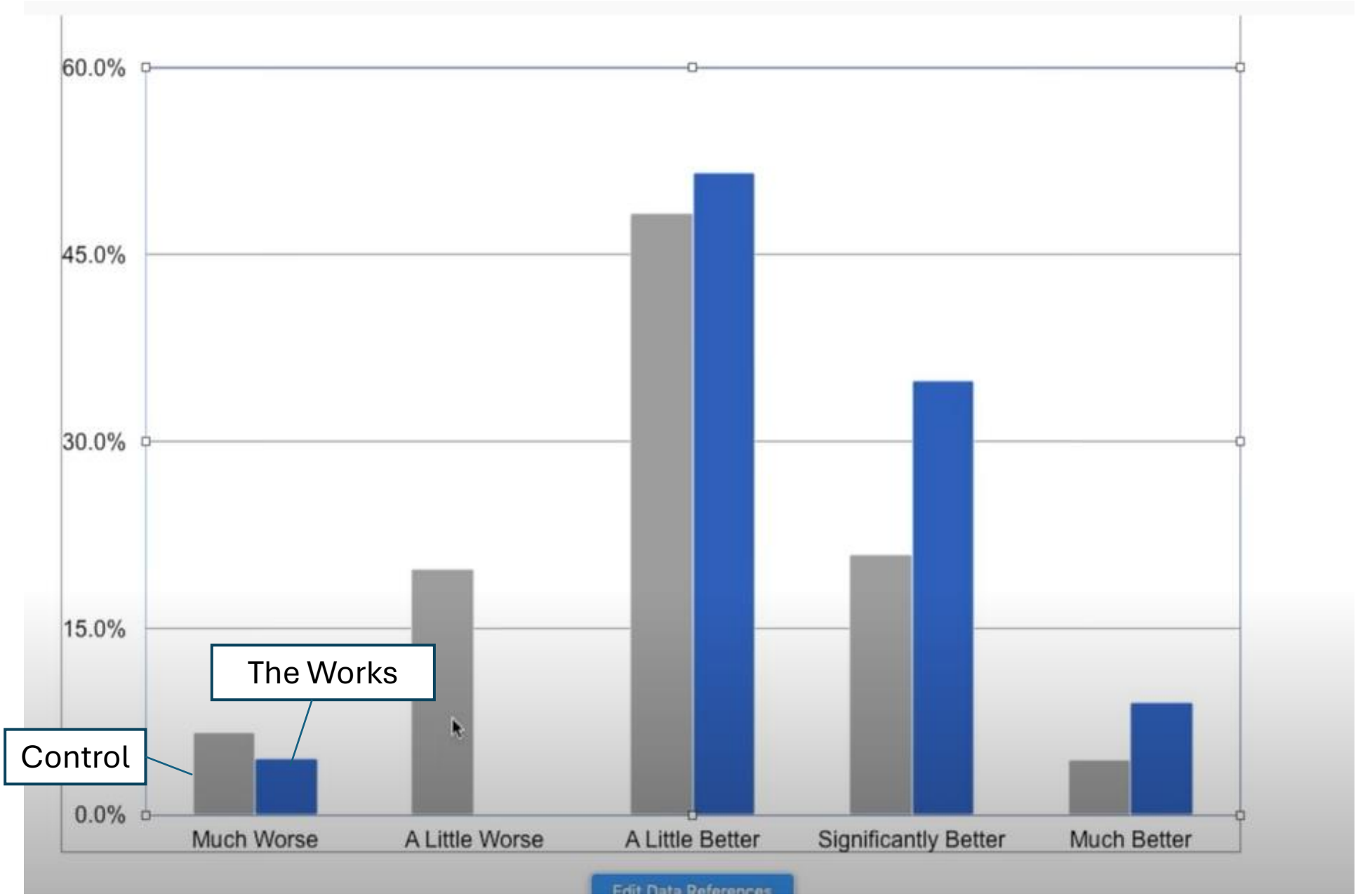
Importance of Niacin

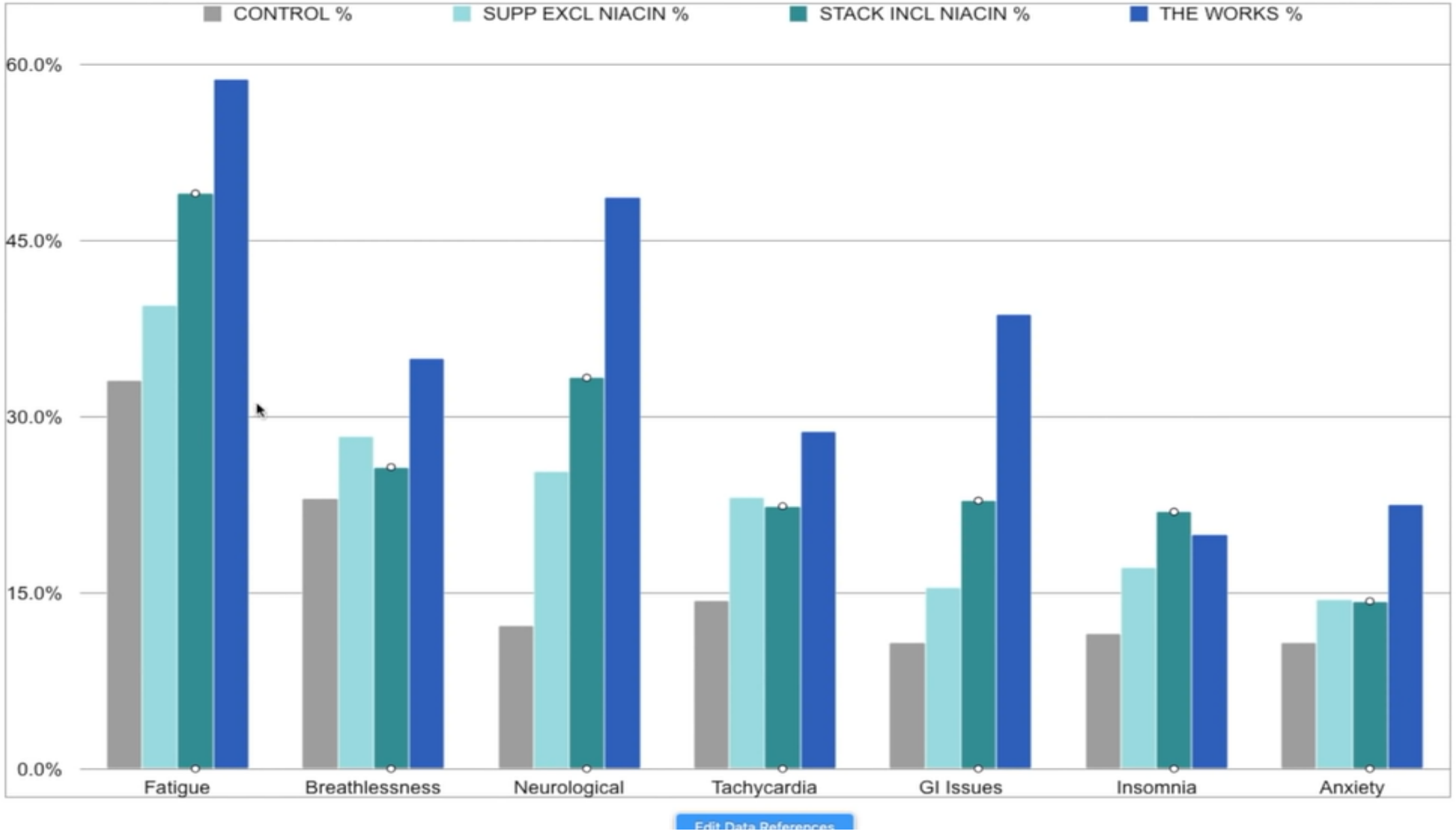
- In a small study with up to 402 participants with 139 controls.

- Low histamine diet
- Supplements incl niacin
- Anti-histamine drugs

- Niacin in particular resulted in most reported improvements.
- It works because it restores your body's supply of NADH

The Works:
Low histamine diet
Supplements
Anti-histamines




CONTROL %
SUPP EXCL NIACIN %
STACK INCL NIACIN %
THE WORKS %
60.0%
45.0%
30.0%
15.0%
0.0%
Fatigue
Breathlessness
Neurological
Tachycardia
GI Issues
Insomnia
Anxiety
Edit Data References

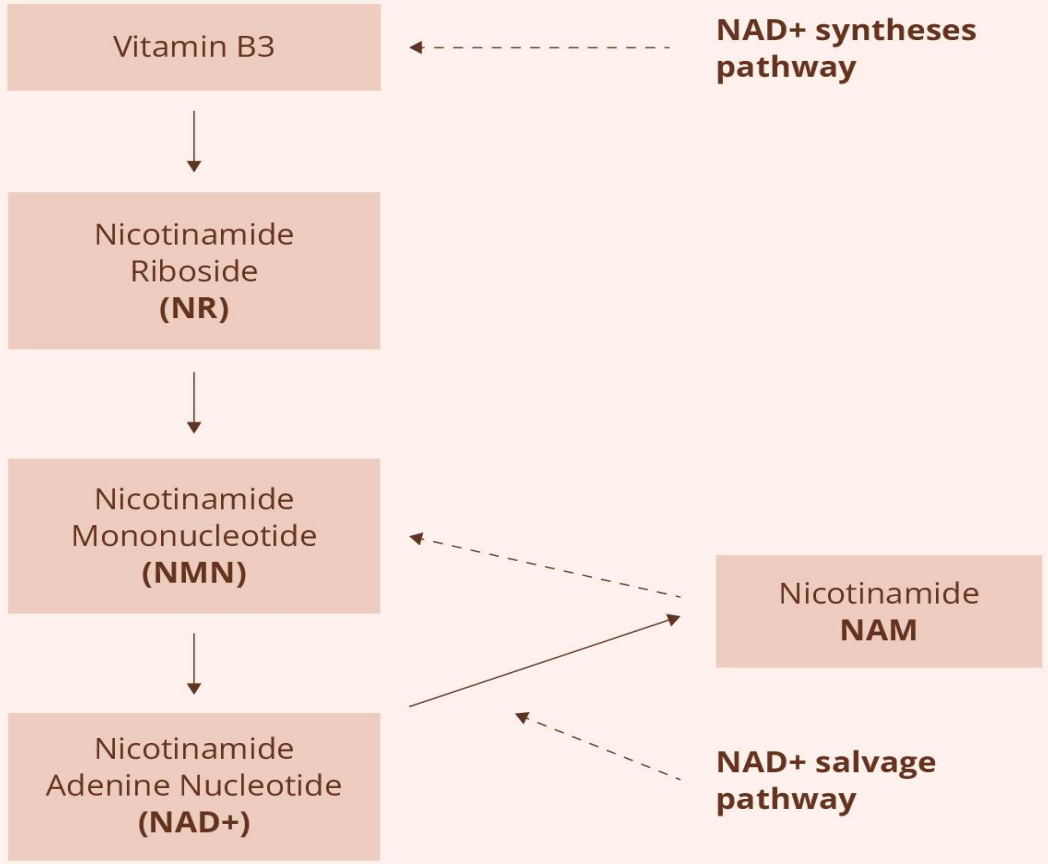
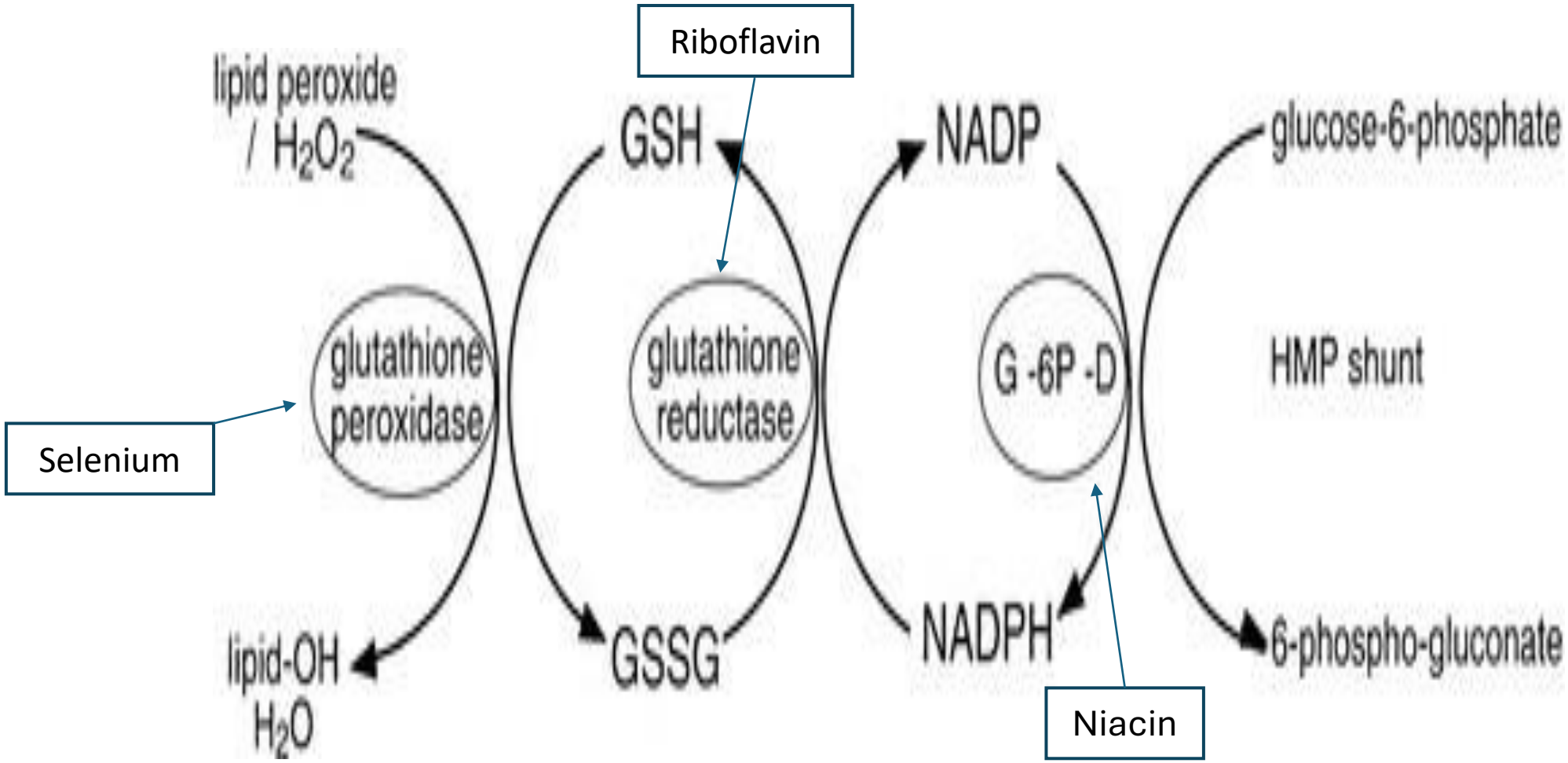


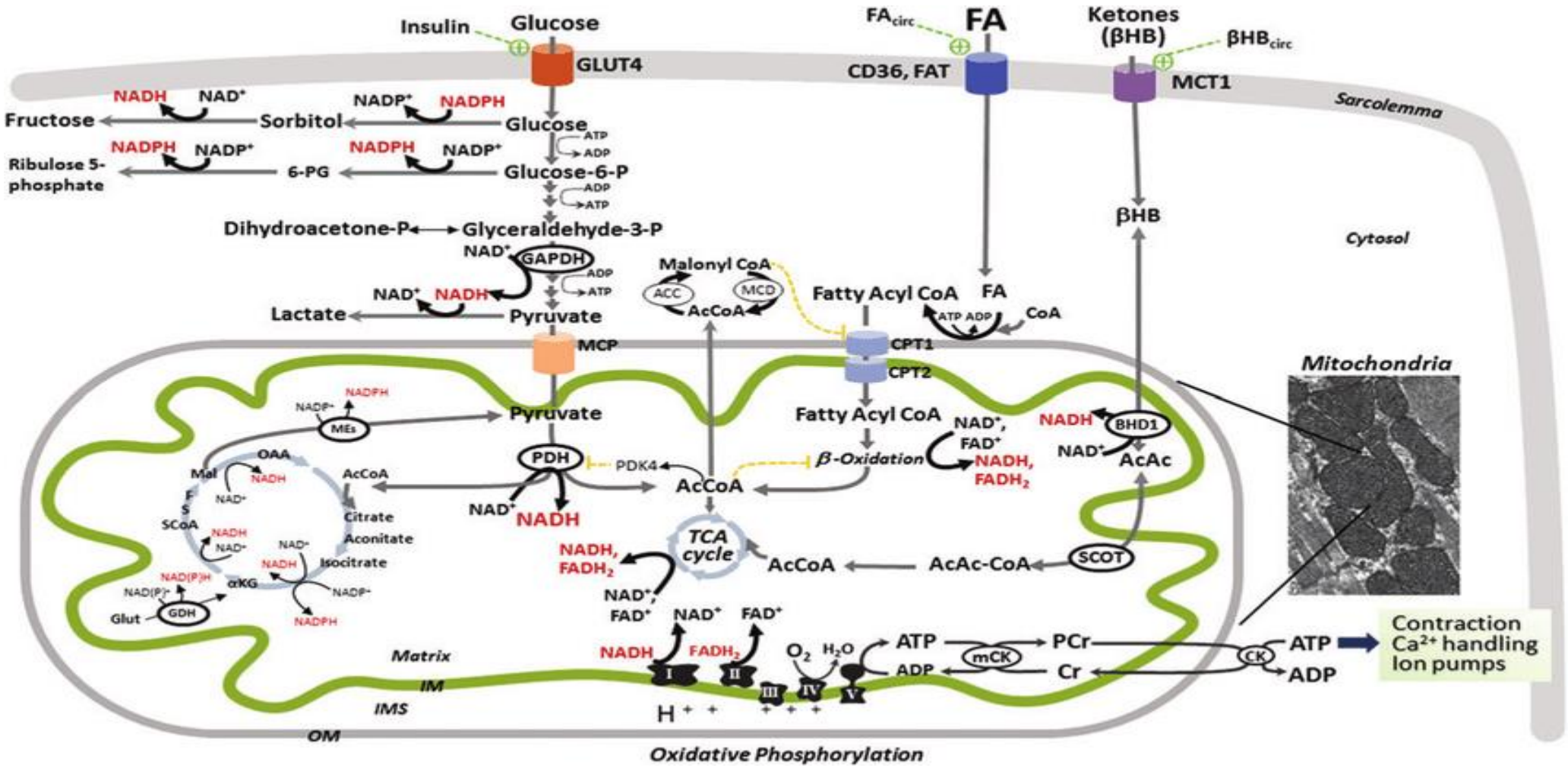
Figure 1.

Important steps in the synthesis of NAD+ from vitamin B3 and the salvage (recycling) pathway for NAD+. Precursor supplements NA and NMN amplify the synthesis pathway.

HMP shunt, NADPH & Glutathione



NAD's Role in Energy Production



Nutri Link
Linking Science and Nutrition

Vitamin D & Long Covid?

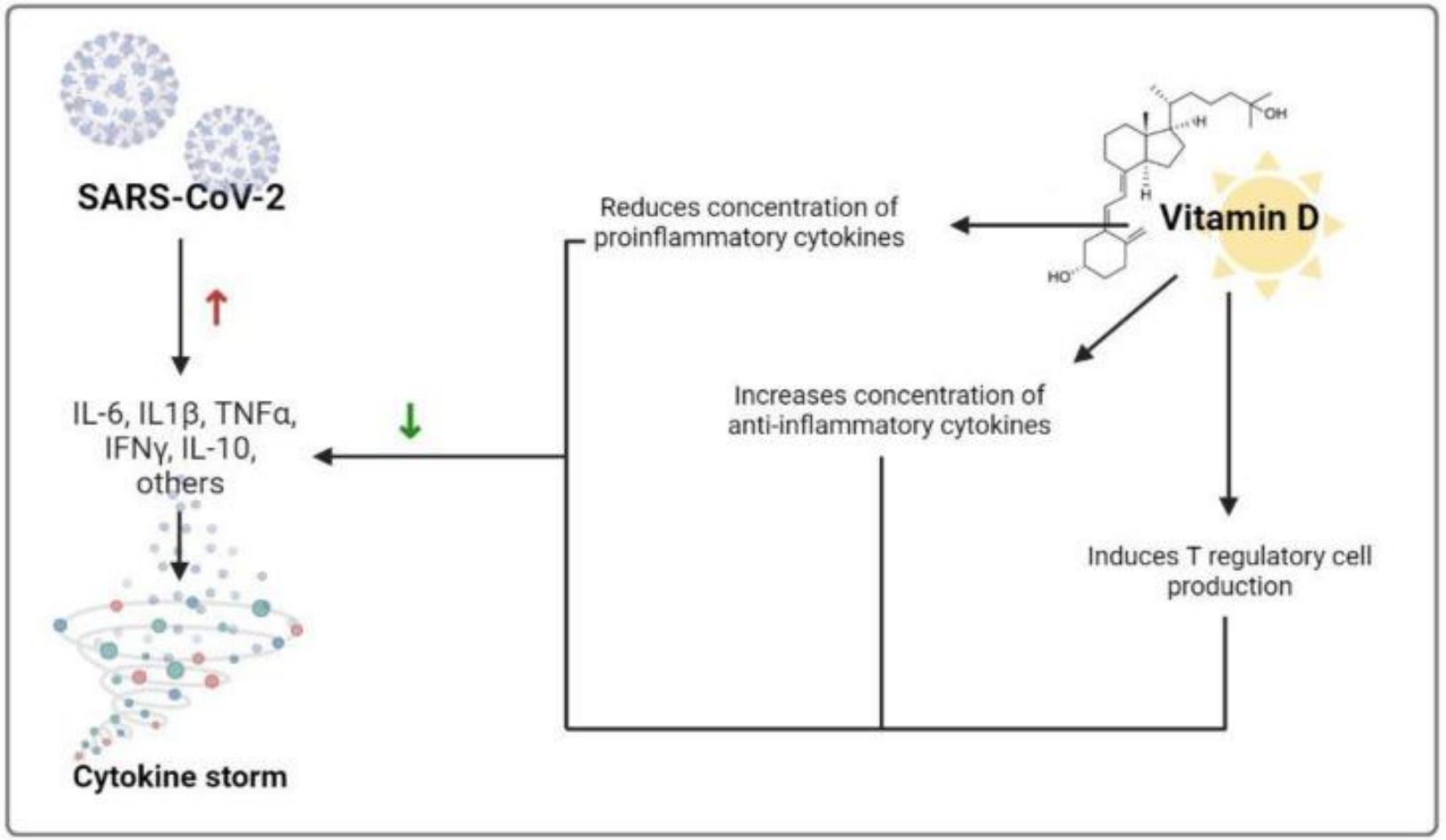
Vitamin D in Long Covid?

Nutri Link
Linking Science and Nutrition

- Vitamin D is an immunomodulatory hormone with proven efficacy against various upper respiratory tract infections. Vitamin D can inhibit hyperinflammatory reactions and accelerate the healing process in the affected areas, especially in lung tissue. Moreover, vitamin D deficiency has been associated with the severity and mortality of COVID-19 cases, with a high prevalence of hypovitaminosis D found in patients with COVID-19 and acute respiratory failure.
- Thus, there are promising reasons to promote research into the effects of vitamin D supplementation in COVID-19 patients. However, no studies to date have found that vitamin D affects post-COVID-19 symptoms or biomarkers. Based on this scenario, this review aims to provide an up-to-date overview of the potential role of vitamin D in long COVID-19 and of the current literature on this topic.

Barrea L, Verde L, Grant WB, Frias-Toral E, Sarno G, Vetrani C, Ceriani F, Garcia-Velasquez E, Contreras-Briceño J, Savastano S, Colao A, Muscogiuri G. Vitamin D: A Role Also in Long COVID-19? Nutrients. 2022 Apr 13;14(8):1625. Full Paper

Mechanisms by which vitamin D could decrease the risk of cytokine storm



Barrea L, Verde L, Grant WB, Frias-Toral E, Sarno G, Vetrani C, Ceriani F, Garcia-Velasquez E, Contreras-Briceño J, Savastano S, Colao A, Muscogiuri G. Vitamin D: A Role Also in Long COVID-19? Nutrients. 2022 Apr 13;14(8):1625. Full Paper

Vitamin D vs biomarkers of Long Covid

Nutri Link
Linking Science and Nutrition

Evidence that vitamin D reduces concentrations of biomarkers associated with long COVID.

Biomarker	Approach	Finding	Reference
D-dimer, a coagulation biomarker	High-dose vitamin D supplementation on COVID-19 patients	No effect	[78]
Procalcitonin	Supplementation with 5000 IU/d vs. 1000 IU/d for 36 and 33 COVID-19 patients	No effect	[77]
Neutrophils count	Supplementation with 5000 IU/d vs. 1000 IU/d for 36 and 33 COVID-19 patients	Significant increase	[77]

Barrea L, Verde L, Grant WB, Frias-Toral E, Sarno G, Vetrani C, Ceriani F, Garcia-Velasquez E, Contreras-Briceño J, Savastano S, Colao A, Muscogiuri G. Vitamin D: A Role Also in Long COVID-19? Nutrients. 2022 Apr 13;14(8):1625. Full Paper

Vitamin D in Long Covid?

Nutri Link
Linking Science and Nutrition

- One of the reasons why vitamin D supplementation may be ineffective in treating long COVID-19 is that the SARS-CoV-2 virus can downregulate vitamin D receptors.
- This has been observed for cytomegalovirus infection [Reider, 2016; Robak, 2020], hepatitis B virus [Gotlieb, 2018], and hepatitis C virus [Abdel-Mohsen, 2018].
- EBV has been found to block activation of gene expression through is EBNA-3-ptotein [Yenamandra, 2010].
- If downregulation is not complete, it might be that very high vitamin D doses would be able to have some effect, but not in the cells with VDRs downregulated.

Vitamin D in Long Covid? References

- Rieder F.J., Gröschel C., Kastner M.-T., Kosulin K., Laengle J., Zadnikar R., Marculescu R., Schneider M., Lion T., Bergmann M., et al. Human cytomegalovirus infection downregulates vitamin-D receptor in mammalian cells. J. Steroid Biochem. Mol. Biol. 2016;165:356–362. Full Paper
- Robak O., Kastner M.-T., Stecher C., Schneider M., Andreas M., Greinix H., Kallay E., Honsig C., Steininger C. Cytomegalovirus Infection Downregulates Vitamin D Receptor in Patients Undergoing Hematopoietic Stem Cell Transplantation. Transplantation. 2020;105:1595–1602. View Abstract
- Gotlieb N., Tachlytski I., Lapidot Y., Sultan M., Safran M., Ben-Ari Z. Hepatitis B virus downregulates vitamin D receptor levels in hepatoma cell lines, thereby preventing vitamin D-dependent inhibition of viral transcription and production. Mol. Med. 2018;24:53. Full Paper
- Abdel-Mohsen M.A., El-Braky A.A.-A., Ghazal A.A.E.-R., Shamseya M.M. Autophagy, apoptosis, vitamin D, and vitamin D receptor in hepatocellular carcinoma associated with hepatitis C virus. Medicine. 2018;97:e0172. Full Paper
- Yenamandra S.P., Hellman U., Kempkes B., Darekar S.D., Petermann S., Sculley T., Klein G., Kashuba E. Epstein-Barr virus encoded EBNA-3 binds to vitamin D receptor and blocks activation of its target genes. Cell Mol. Life Sci. 2010;67:4249–4256. Full Paper

Vitamin D in Long Covid?

Nutri Link
Linking Science and Nutrition

- Vitamin D is known to have pleotropic effects far beyond bone health and is associated with immune modulation and autoimmunity. “We hypothesize that vitamin D levels are associated with persistent symptoms following COVID-19.”
- Researchers investigated the relationship between vitamin D and fatigue and reduced exercise tolerance, assessed by the Chalder Fatigue Score, six-minute walk test and modified Borg scale.
- A total of 149 patients were recruited at a median of 79 days after COVID-19 illness.
- **No relationship between vitamin D** and the measures of ongoing ill-health assessed in the study was found following multivariable regression analysis. These results suggest that persistent fatigue and reduced exercise tolerance following COVID-19 are independent of vitamin D.

Townsend L, Dyer AH, McCluskey P, O'Brien K, Dowds J, Laird E, Bannan C, Bourke NM, Ní Cheallaigh C, Byrne DG, Kenny RA. Investigating the Relationship between Vitamin D and Persistent Symptoms Following SARS-CoV-2 Infection. Nutrients. 2021 Jul 15;13(7):2430. Full Paper

Nutritional Supplements for Long Covid?

Nutri Link
Linking Science and Nutrition

- Naturally-occurring food supplements, such as acetyl L-carnitine, hydroxytyrosol and vitamins B, C and D hold significant promise in the management of post-COVID syndrome.
- In this pilot observational study, researchers evaluated the effect of a food supplement containing hydroxytyrosol, acetyl L-carnitine and vitamins B, C and D in improving perceived fatigue in patients who recovered from COVID-19 but had post-COVID syndrome characterised by chronic fatigue.
- The results suggest that the food supplement could proceed to clinical trials of its efficacy in aiding the recovery of patients with long COVID.

Naureen Z, Dautaj A, Nodari S, Fioretti F, Dhuli K, Anpilogov K, Lorusso L, Paolacci S, Michelini S, Guda T, Kallazi M, Bertelli M. Proposal of a food supplement for the management of post-COVID syndrome. Eur Rev Med Pharmacol Sci. 2021 Dec;25(1 Suppl):67-73. View Abstract

Ginseng extracts for Long Covid?

Nutri Link
Linking Science and Nutrition

- A plant extract supplement from Panax ginseng and Eleutherococcus senticosus (Siberian ginseng) effectively relieved post-COVID fatigue and improved health status in 201 long COVID patients.

Rossato MS, Brilli E, Ferri N, Giordano G, Tarantino G. Observational study on the benefit of a nutritional supplement, supporting immune function and energy metabolism, on chronic fatigue associated with the SARS-CoV-2 post-infection progress. Clin Nutr ESPEN. 2021 Dec;46:510-518. Full Paper

CoQ10 for Long Covid?

Nutri Link
Linking Science and Nutrition

- Supplementation with Coenzyme Q10 (CoQ10) is found to reduce fatigue frequency and relieve oxidative stress among ME/CFS patients.
- There is a biologically plausible mechanism for expected improvement with MitoQ's superior bioavailability to cells and to mitochondria within them, and by how it can restore oxidative balance and therefore improve mitochondrial function.
- Currently, high-dose CoQ10 treatment is being investigated in a Phase II clinical trial in long COVID patients (NCT04960215).

Wood E, Hall KH, Tate W. Role of mitochondria, oxidative stress and the response to antioxidants in myalgic encephalomyelitis/chronic fatigue syndrome: A possible approach to SARS-CoV-2 'long-haulers'? Chronic Dis Transl Med. 2021;7:14–26. Full Paper

Natural Flavonoids for Long Covid?

Nutri Link
Linking Science and Nutrition

- Dietary supplements may also have beneficial effect in modulating systemic inflammation and immunity.
- Natural flavonoids such as luteolin and quercetin are promising immunomodulatory agents which have showed inhibitory effects on mast cells.

Hagenlocher Y, Lorentz A. Immunomodulation of mast cells by nutrients. Mol Immunol. 2015 Jan;63(1):25-31. View Abstract

Probiotics for Long Covid?

Nutri Link
Linking Science and Nutrition

- The influence of microbiota on immunity is well known, and long COVID leads to significant changes in gut flora. (Chen, 2021)
- Dietary pro-biotics and pre-biotics are being evaluated on their impacts on clinical symptoms, immune function and biomarkers in long COVID patients (NCT04813718).
- Liu et al's study (2022) provided observational evidence of compositional alterations of gut microbiome in patients with long-term complications of COVID-19. Further studies should investigate whether microbiota modulation can facilitate timely recovery from post-acute COVID-19 syndrome.

Chen C, Haupert SR, Zimmermann L, Shi X, Fritsche LG, Mukherjee B. Global Prevalence of Post-Acute Sequelae of COVID-19 (PASC) or Long COVID: A Meta-Analysis and Systematic Review. medRxiv. 2021. 2021. 11.15.21266377. Full Paper

Liu Q, Mak JWY, Su Q, Yeoh YK, Lui GC-Y, Ng SSS. et al. Gut microbiota dynamics in a prospective cohort of patients with post-acute COVID-19 syndrome. Gut. 2022;71:544. View Abstract

Gut Microbiota in Long Covid

Nutri Link
Linking Science and Nutrition

- “Dysbiosis has also been reported in long COVID patients, mainly in the gut, little is known about the possible involvement of the microbiota in the development of this disease.
- The relevance of long COVID has probably been underestimated, and the available data suggest that the microbiota could be playing a pivotal role on the pathogenesis of the disease.
- Different studies that analyse the persistency of gut dysbiosis in COVID-19 patients and/or subjects with long COVID suggest that SARS-CoV-2 infection induces long-lasting gut dysbiosis in COVID-19 patients who develop long COVID.
- However, the gut microbiota of COVID-19 patients who do not develop long COVID is restored at 6 months after the initial infection.
- New studies analysing the gut microbiota of COVID-19 patients in recovery at different timepoints will be necessary to characterise the dynamics of this recovery, and to study why such dynamics are different in the subjects who develop long COVID.”

Álvarez-Santacruz C, Tyrkalska SD, Candel S. The Microbiota in Long COVID. Int J Mol Sci. 2024 Jan 22;25(2):1330. Full Paper

Many interventions to consider

- As we probably already know, there are many different nutritional interventions to consider for Long Covid.
- We are going to explore the most relevant nutritional therapeutics in this webinar series.
- Here's what's next:

Friday 27th September 12 noon
Functional Medicine model of Long Covid from Dr Leo Galland, including blood clotting, viral persistence, and mitochondrial disruption. Nutritional Therapy solutions.

Nutri Link
Linking Science and Nutrition

1. Monday 23rd September 12 noon
Introduction to Long Covid, review of symptoms, example case history. Review of Nutritional Therapy solutions.

2. Friday 27th September 12 noon
Functional Medicine model of Long Covid from Dr Leo Galland, including blood clotting, viral persistence, and mitochondrial disruption. Nutritional Therapy solutions.

3. Monday 30th September 12 noon
Exploration into Mast Cell Activation Syndrome (MCAS) and its involvement in Long Covid symptomology. Nutritional Therapy solutions.

4. Friday 4th October 12 noon
Viral persistence and viral reactivation as causes of Long Covid. Nutritional Therapy solutions. AND exploration of negative impact of spike protein on heme and all of its ramifications.

5. Monday 7th October 12 noon
Neurotransmitter imbalances as an explanation for multiple Long Covid symptoms. Nutritional Therapy solutions.

6. Monday 14th October 12 noon
Spike protein pathogenesis. Nutritional Therapy solutions. Review and summary and presentation of Model of Long Covid including lab tests and potential therapeutic interventions.

Nutri Link
Linking Science and Nutrition

End of Webinar One