

Post COVID Syndrom – aktueller Stand der Wissenschaft



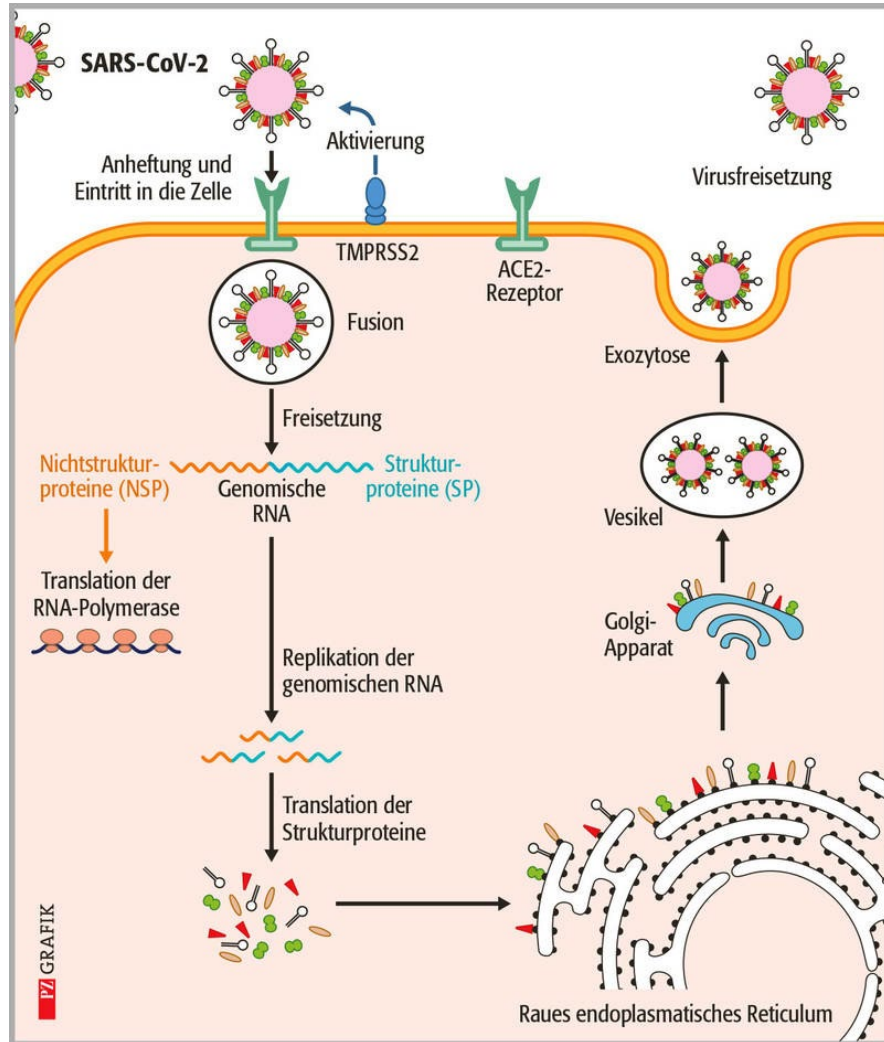


Long-Covid-Forscherin über Corona

6+ »Diese Krankheit kann Leben zerstören«

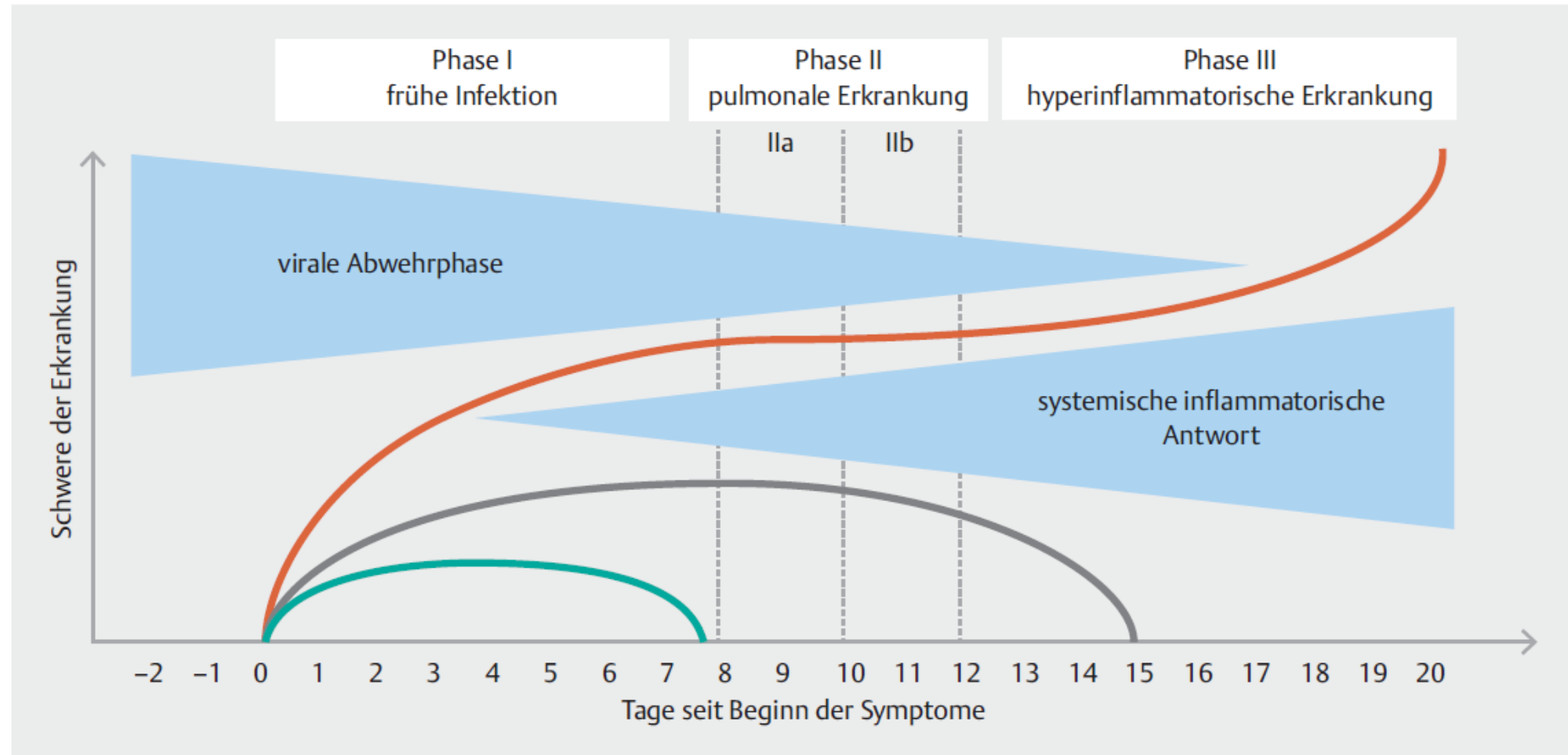
Yale-Professorin Akiko Iwasaki gehört zu den weltweit besten Immunologinnen: Hier verrät sie, wie sie gegen toxische Chefs kämpft, was Long-Covid-Erkrankten helfen könnte und warum sie bis heute Maske trägt.

COVID-19 – Spike Protein und ACE2 Receptor



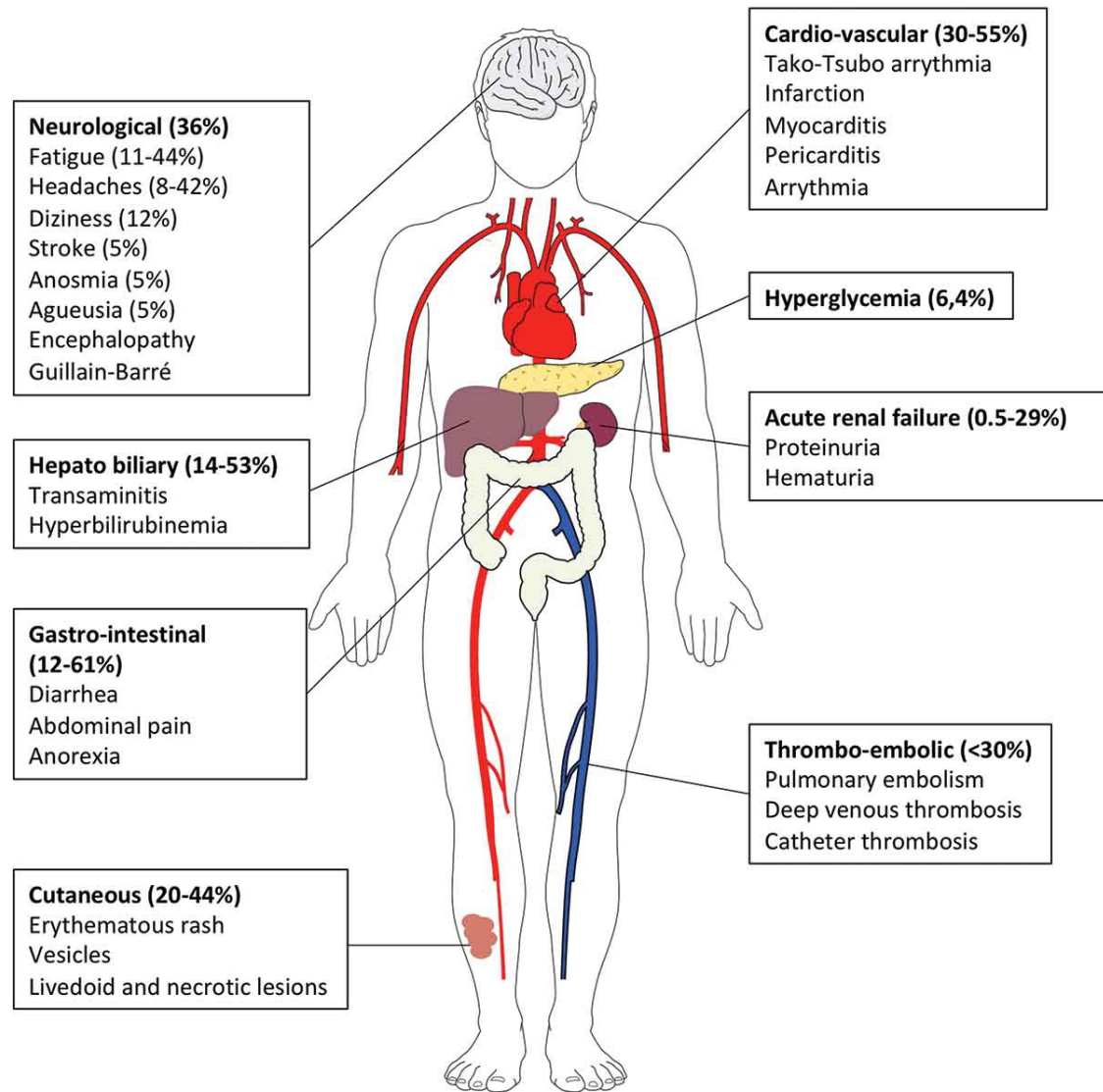
nasal	lung	ileum	heart	eye	liver
goblet/ basal/ ciliated	secretory/ basal/ multiciliated	epithelial enterocytes	myocyte	corneal epithelium	cholangiocytes
epithelial	proximal tubule	ductal epithelium	oligodendrocyte	epithelial	pericyte

COVID-19 akute Erkrankung – klinischer Verlauf

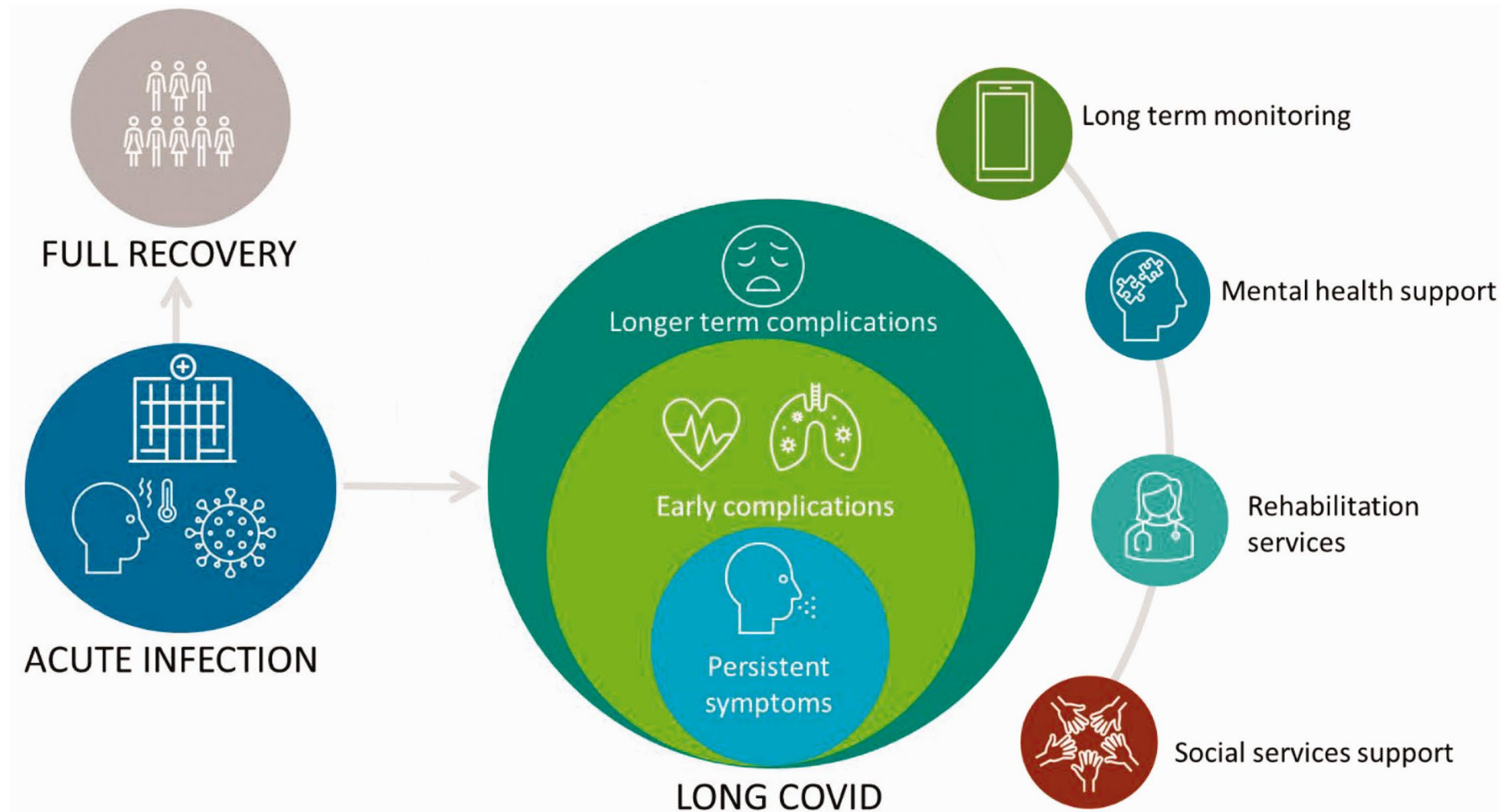


► **Abb. 1** Bedeutung der viralen Abwehr und der systemischen inflammatorischen Antwort für die Klinik von Patienten mit COVID-19. Klinische Verläufe von COVID-19 (leicht: grün; schwer: grau; kritisch: rot) werden im zeitlichen Verlauf dargestellt [14, 15].

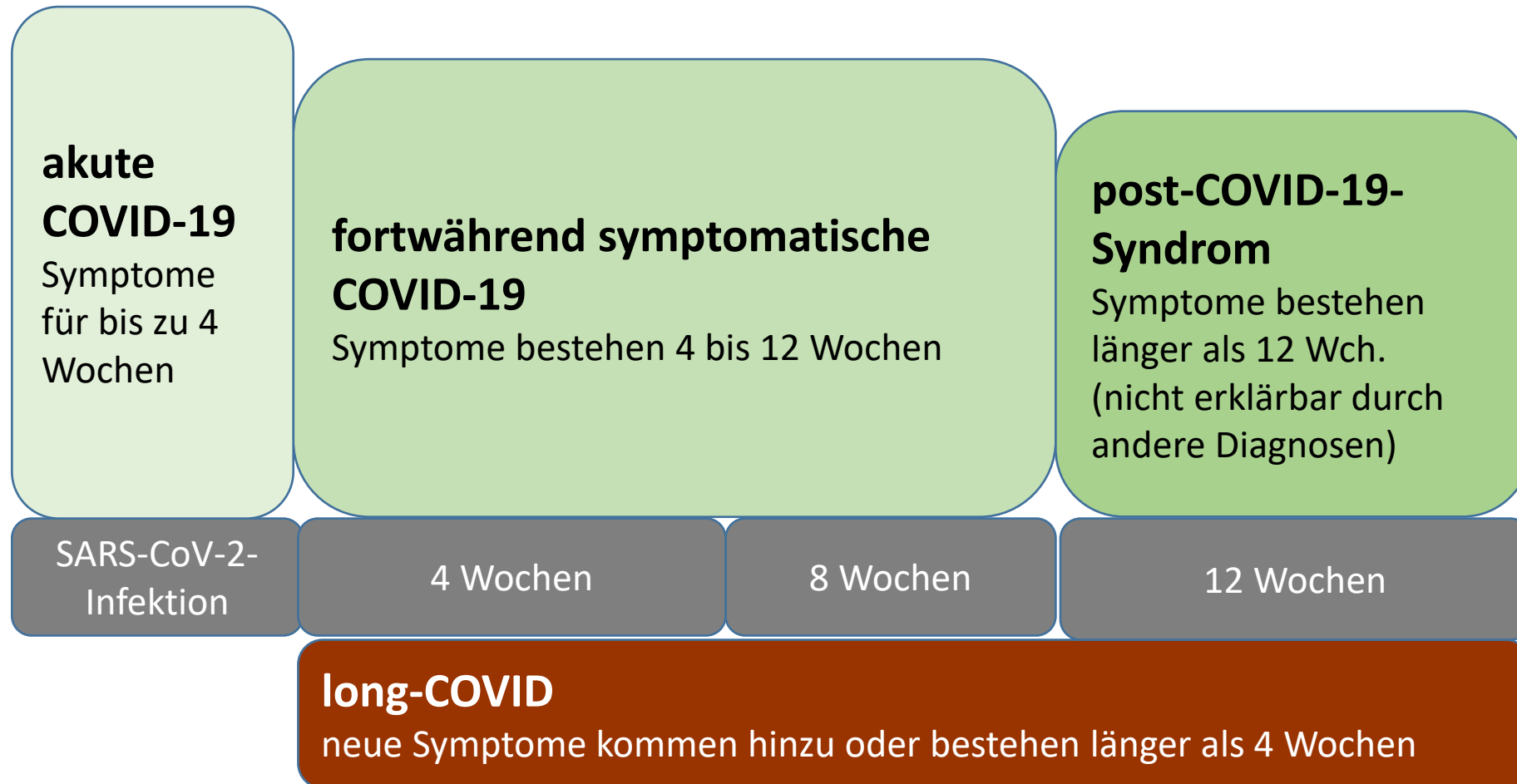
COVID-19 – Extrapulmonale Symptome



COVID-19 Klinische Verlaufsformen



COVID 19 Nomenklatur



COVID 19 Nomenklatur

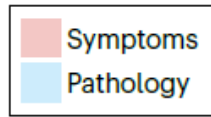
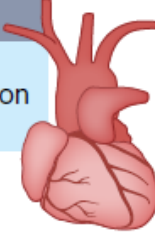
A clinical case definition of post COVID-19 condition by a Delphi consensus

6 October 2021

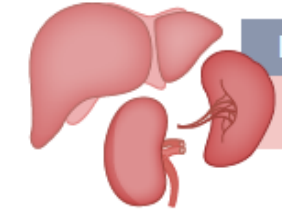


Post COVID-19 condition occurs in individuals with a **history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis.** Common symptoms include **fatigue, shortness of breath, cognitive dysfunction** but also others (see [Table 3](#) and [Annex 2](#)) which generally have an **impact on everyday functioning.** Symptoms may be **new onset**, following initial recovery from an acute COVID-19 episode, or **persist** from the initial illness. Symptoms may also **fluctuate or relapse** over time. A separate definition may be applicable for children.


Symptomspektrum post-COVID 19 Syndrom

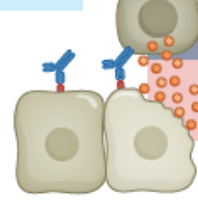
Heart	
<ul style="list-style-type: none"> • Chest pain • Palpitations 	<ul style="list-style-type: none"> • Cardiac impairment • Myocardial inflammation • POTS



Kidneys, spleen and liver	
<ul style="list-style-type: none"> • Organ injury 	




Lungs	
<ul style="list-style-type: none"> • Cough • Dyspnoea 	<ul style="list-style-type: none"> • Abnormal gas exchange



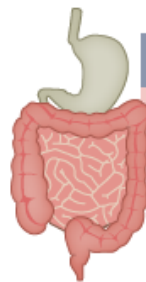
Immune system	
<ul style="list-style-type: none"> • Autoimmunity • MCAS 	



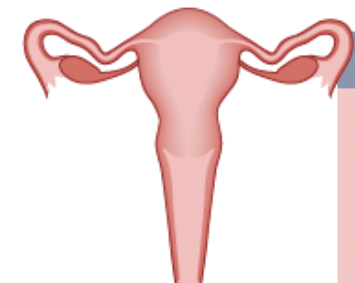
Pancreas	
<ul style="list-style-type: none"> • Diabetes • Pancreas injury 	



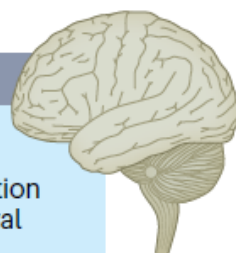
Blood vessels	
<ul style="list-style-type: none"> • Fatigue 	<ul style="list-style-type: none"> • Coagulopathy • Deep vein thrombosis • Endothelial dysfunction • Microangiopathy • Microclots • Pulmonary embolism • Stroke



Gastrointestinal tract	
<ul style="list-style-type: none"> • Abdominal pain • Nausea 	<ul style="list-style-type: none"> • Gut dysbiosis • Viral persistence and viral reservoir



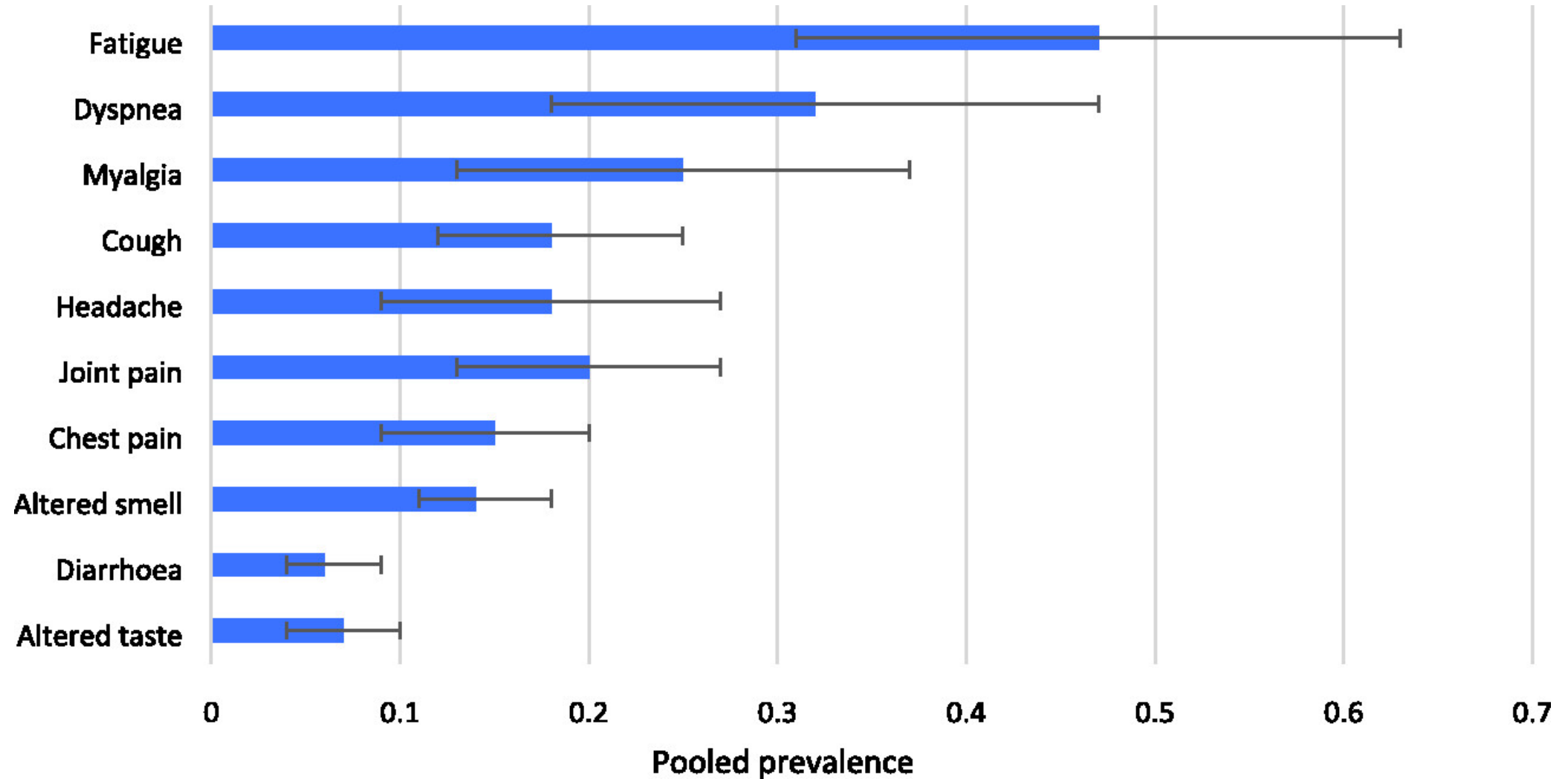
Reproductive system	
<ul style="list-style-type: none"> • Erectile dysfunction • Increased severity and number of premenstrual symptoms • Irregular menstruation 	<ul style="list-style-type: none"> • Reduced sperm count



Neurological system	
<ul style="list-style-type: none"> • Cognitive impairment • Fatigue • Disordered sleep • Memory loss • Tinnitus 	<ul style="list-style-type: none"> • Dysautonomia • ME/CFS • Neuroinflammation • Reduced cerebral blood flow • Small fibre neuropathy

65.000.000 Fälle weltweit
 10–30% Inzidenz in ambulanten Fällen
 50–70% Inzidenz in hospitalisierten Fällen

Häufigkeit von Post-COVID-Symptomen



Post COVID – Herausforderung Diagnostik

Organbezogene Störungen mit morphologischem Substrat bei PCS

Organ	Klinische Symptomatik	morphologische Manifestation und Befunde		patho-physiologische Mechanismen
		Bildgebung	Histologie, Immunhistologie, Molekularpathologie	
olfaktorisch/gustatorisches System siehe auch „ZNS und PNS“	Verlust oder Verminderung der Riech- u. Geschmackssinne (-Dysgeusie, Anosmie)	CT und MRT: diffus erhöhte Signalintensität des Riechkolbens, hyperintensive Foci oder Mikrob Blutungen, Verklumpung und Ausdünnung der Riechhäute (e46)	Leukozyten-Infiltration der Lamina propria mit apoptotischer Schädigung von Geschmacksknospen, Riechnervenfasern und zentralnervösem Riechzentrum Autopsie: fokale Atrophie des olfaktorischen Epithels (37)	ACE2-Rezeptoren im ZNS (olfaktorischer Bulbus, Amygdala, Hippocampus, Temporallappen, posteriorer cingulärer Cortex, Hirnstamm)
Lunge, obere Atemwege	Dyspnoe, persist. Husten, Exazerbation von Asthma (38)	CT: persistierende Veränderungen, z. B. Milchglas-trübung, interstitielle Verdickungen, periphere Retikulation, Fibrosierung, Bronchiektasien (e1)	unspezifische interstitielle Pneumonie (UIP), diffus alveoläre Fibrose und Vernarbung, organisierende Pneumonie (e47), Endothelitis, Mikrohämmorrhagien (e48), IHC-Nachweis von ACE2 ⁺ in der Lunge (spez. Typ-II-Pneumozyten und Alveolarmakrophagen) (e49)	persist. SARS-CoV-2-RNA im Lungengewebe (Virusreservoir) mit Überaktivierung der Alveolarepithelien (ACE2 ⁺) u. Reduktion der Alveolarmakrophagen, Entwicklung einer chron. vernarbenden Entzündung (e21); Nachweis von „profibrotic macrophage responses“ (e50, e51)
Herz/Myokard	atyp. Brustschmerz, thorakales Druckgefühl, Tachykardie, Palpitation (38, 39), Lungenstauung, Herzrhythmusstörungen, Perikardreiben	cMRI: COVID-19-assoziierte myokardiale Inflammation (e51)	endomyokardiale Biopsien: aktive lymphozytäre Inflammation (e51), Thromben in kleinen und größeren kardialen Gefäßen (39, e48), IHC-Nachweis von ACE2 ⁺ in den Myozyten (e49)	persist. virale Last induziert in ACE2 ⁺ -Myozyten und Myokardium Entzündung mit proinflammatorischen Zellen, infiltrierenden Monozyten, Neutrophilen und plasmazytoiden dendritischen Zellen (e21)
Gehirn (ZNS) und peripheres Nervensystem (PNS) siehe auch „olfaktorisch/gustatorisches System“	Müdigkeit, Fatigue, Nebel im Gehirn („brain fog“), Kopfschmerzen, Gedächtnis-/Konzentrationsstörungen, diverse psychiatrische Alterationen, Taubheitsgefühl, Tremor	18F-FDG-PET-basiertes Neuroimaging: hypometabolische ZNS-Regionen (olfaktorischer Gyrus, Temporallappen, inkl. Amygdala, Hippocampus, Hypothalamus, Hirnstamm, Kleinhirn) (e52)	virale Neuroinvasion, neuroimmunologische Reaktion im peripheren und zentralen Nervensystem mit gestörter Blut-Hirn-Schranke; autoptischer Nachweis von ACE2 in Zellen des Hirnstamms	Hypothese: neurotropes SARS-CoV-2 (infiziert neuronale Zellkulturen und Organanoide) befällt ACE2 ⁺ -Zellen (Neurone, Astrozyten) und Zellen des Hirnstamms (e53)

Risikofaktoren für das post COVID Syndrom

KASTEN

Risikofaktoren für ein Post-COVID-Syndrom (2, 24, 33–36, e41–e44)

- **biografische Faktoren**
 - kaukasische Bevölkerung
 - mittleres Lebensalter
 - weibliches Geschlecht
- **vorbestehende Erkrankungen**
 - Asthma bronchiale
 - schlechte psychische Gesundheit
 - Diabetes mellitus
 - Bluthochdruck
 - Fettleibigkeit
- **COVID-19-spezifisch**
 - multiple (> 5) akute Symptome
 - hohe akute Viruslast
 - niedrige baseline SARS-CoV-2-IgG
 - Durchfall
 - Impfstatus

(Aus [6]: Abdruck mit freundlicher Genehmigung der BÄK)

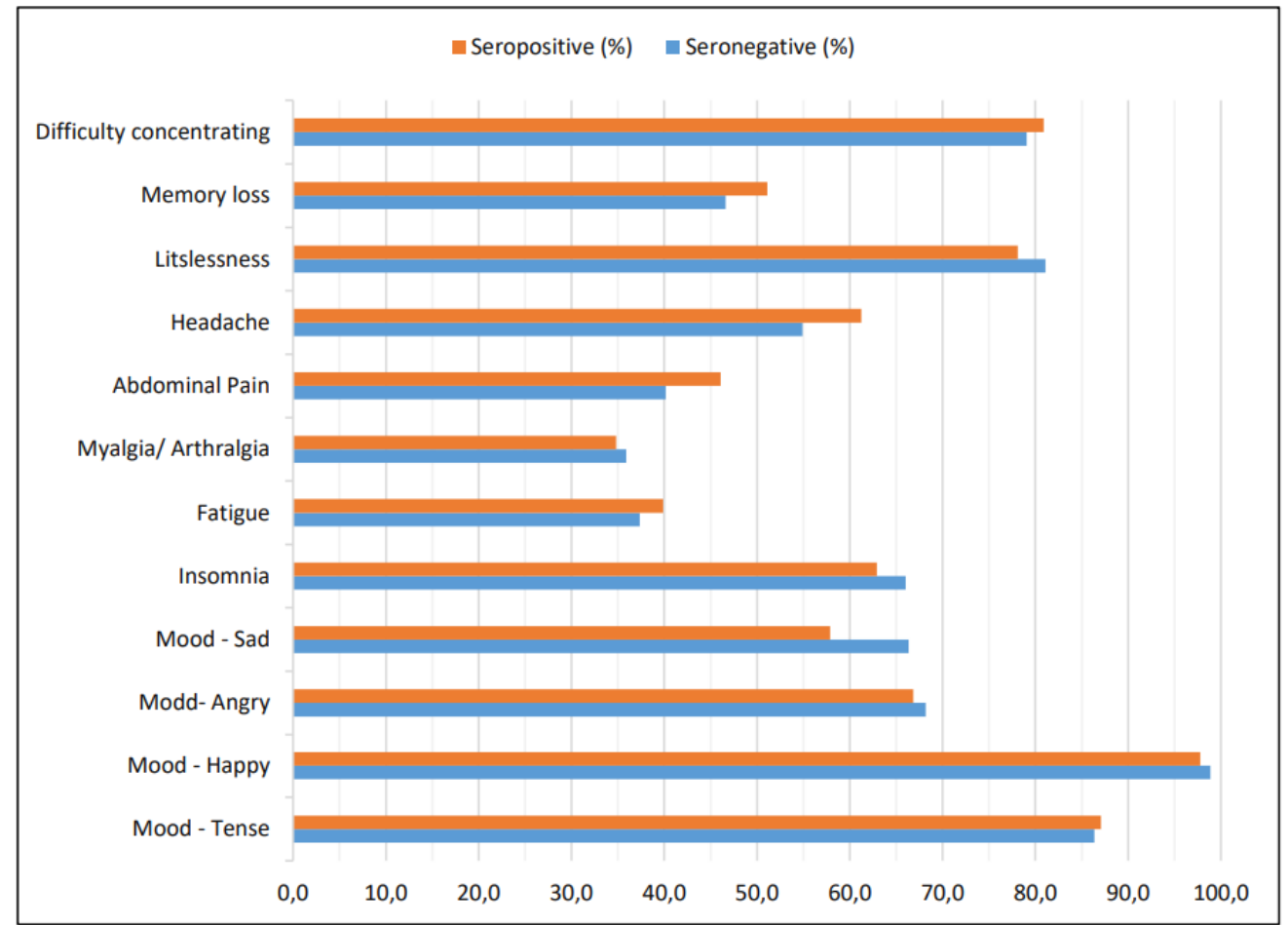
Long COVID Forschung – eine Herausforderung Hintergrundrauschen

- Initiale Vermischung mit Post-Intensive Care Syndrom
- Durch eine intensivmedizinische Behandlung verursacht, z.B.:
 - Muskelschwäche
 - 30% nach Beatmung
 - 50% nach Blutvergiftung
 - Kognitive Probleme, Nervenschäden
 - 30-80% nach längerem Aufenthalt

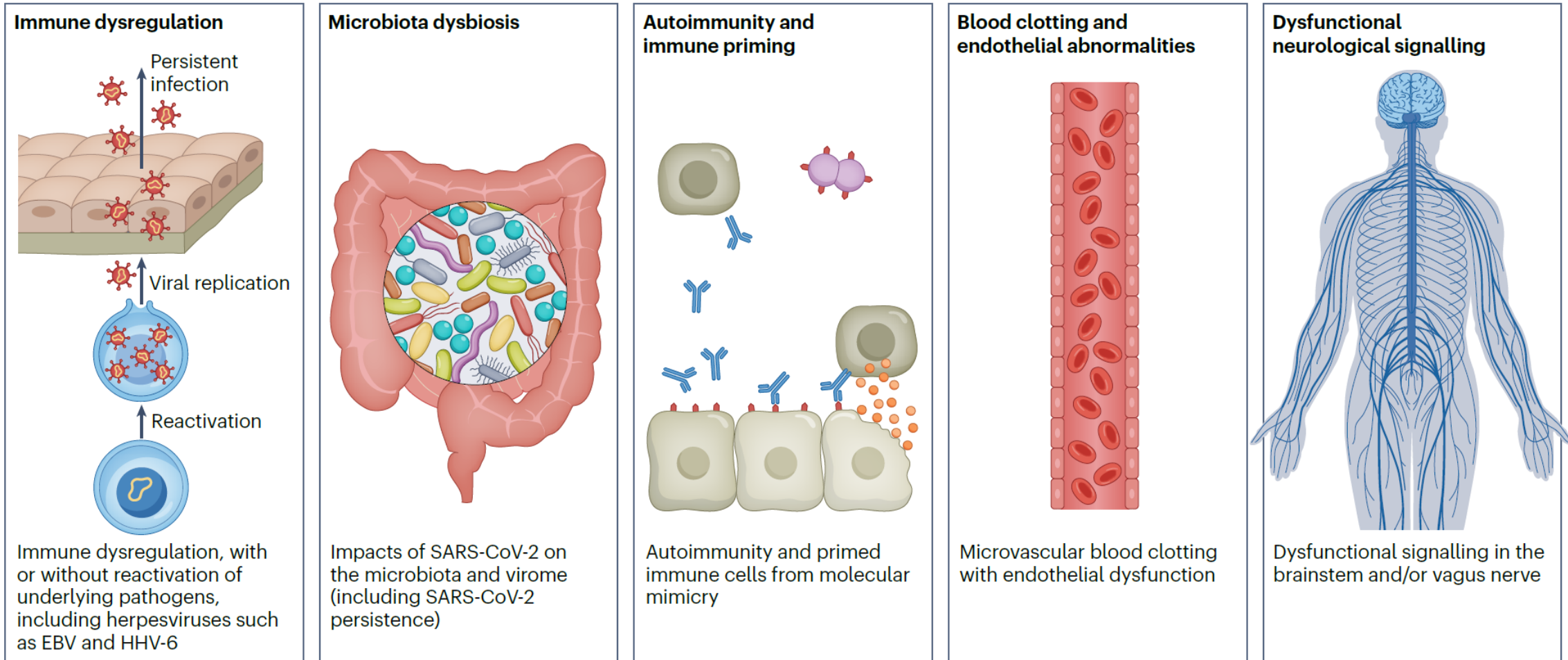


Long COVID Forschung – eine Herausforderung Hintergrundrauschen

- 1.560 Schülerinnen und Schüler (Klasse 8-12) in Sachsen
- 1.365 (88%) seronegativ, 188 (12%) seropositiv
- Keine signifikanten Unterschiede bzgl. Symptomen zwischen den Gruppen



Potentielle Ursachen



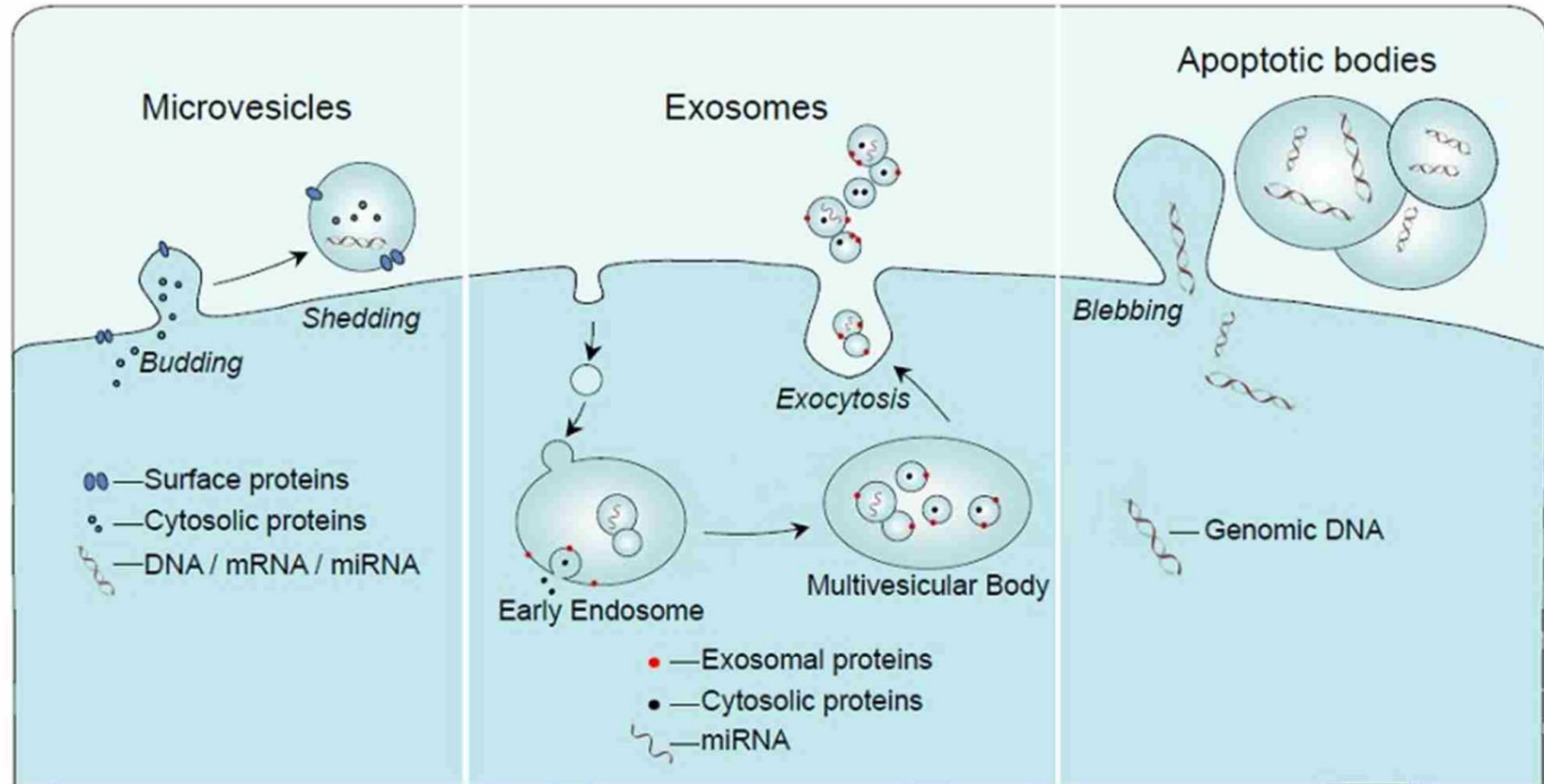
Potentielle Ursachen – Virale Persistenz

	RNA	Protein	PASC symptoms	Location
Tissue (biopsy)				
Goh et al. ³⁹	✓	S, N	✓	Appendix, skin and breast tissues 163 and 426 d after COVID-19
Zollner et al. ³⁸	✓	N	✓	Gut mucosa/epithelium tissue ~7 months after COVID-19
deMelo et al. ²⁷	✓	N	✓	Olfactory neuroepithelium tissue 110–196 d after COVID-19
Gaebler et al. ³³	✓	N	No	Intestinal tissue ~4 months after COVID-19
Cheung et al. ¹¹⁴	✓	S, N	NM	Colon, appendix, ileum, hemorrhoid, liver, gallbladder and lymph nodes 9–180 d after COVID-19
Hany et al. ²⁹	NM	N	NM	Gastric and gallbladder tissues 274–380 d after COVID-19
Miura et al. ³⁰	✓	N	No	Adenoid tonsil, adenoid tissue, nasal cytobrush and nasal wash from children with no documented COVID-19 or upper airway infection in the month before collection
Xu et al. ³⁷	✓	NM	No	Child adenoid and tonsil tissue up to 303 d after COVID-19
Peluso et al. ²⁴	✓	NM	✓	Colorectal lamina propria tissue 158–676 d after COVID-19
Yao et al. ²⁵	✓	S,N	✓	Fungiform papillae tongue tissue 6–63 weeks after COVID-19
Tissue (autopsy)				
Stein et al. ³¹	✓	N	NM	Dozens of human body and brain tissue types at least 31 d and up to 230 d after COVID-19
Roden et al. ³²	✓	NM	NM	Lung tissue up to 174 d after COVID-19
Rendiero et al. ²⁶	NM	S	NM	Lung tissue up to 359 d after COVID-19
Stool				
Natarajan et al. ¹¹⁵	✓	NM	✓	Stool up to 230 d after COVID-19
Yonker et al. ⁸⁴	✓	S, N	✓	RNA in stool of children with MIS-C 13–62 d after COVID-19, S and N protein in plasma
Jin et al. ¹¹⁶	✓	S	NM	Neonatal stool in infants born to mothers whose COVID-19 symptoms resolved more than 10 weeks before delivery
Blood				
Schultheiß et al. ⁴⁰	NM	S1	✓	Plasma at a median time of 8 months after COVID-19
Swank et al. ⁴¹	NM	S, S1, N	✓	Plasma up to 12 months after COVID-19
Peluso et al. ⁴⁴	NM	S1, N	✓	Plasma neuron-derived EVs 35–84 d after COVID-19
Peluso et al. ⁴²	NM	S1, S, N	✓	Plasma up to 16 months after COVID-19
Craddock et al. ⁴⁵	✓	S	✓	Spike linked to EVs in samples obtained at least 8–12 weeks (up to 1 year) after COVID-19
Tejerina et al. ¹¹⁷	✓	NM	✓	Plasma at a median time of 55 d after COVID-19 (also found in stool/urine at the same median time point)

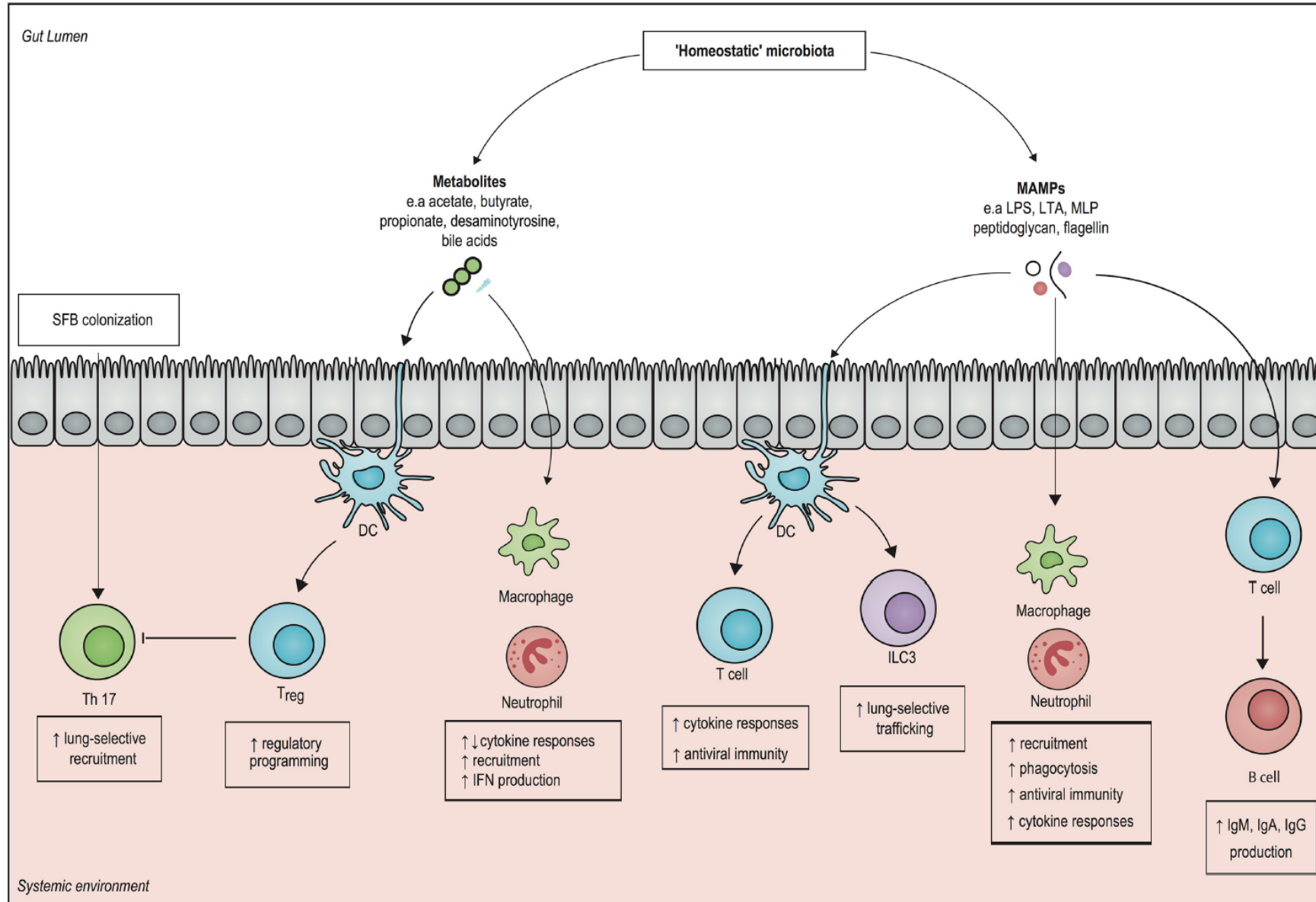
✓, identified; No, not present; NM, not measured; S and S1, spike protein.

Potentielle Ursachen – Virale Persistenz

Rolle extrazellulärer Vesikel

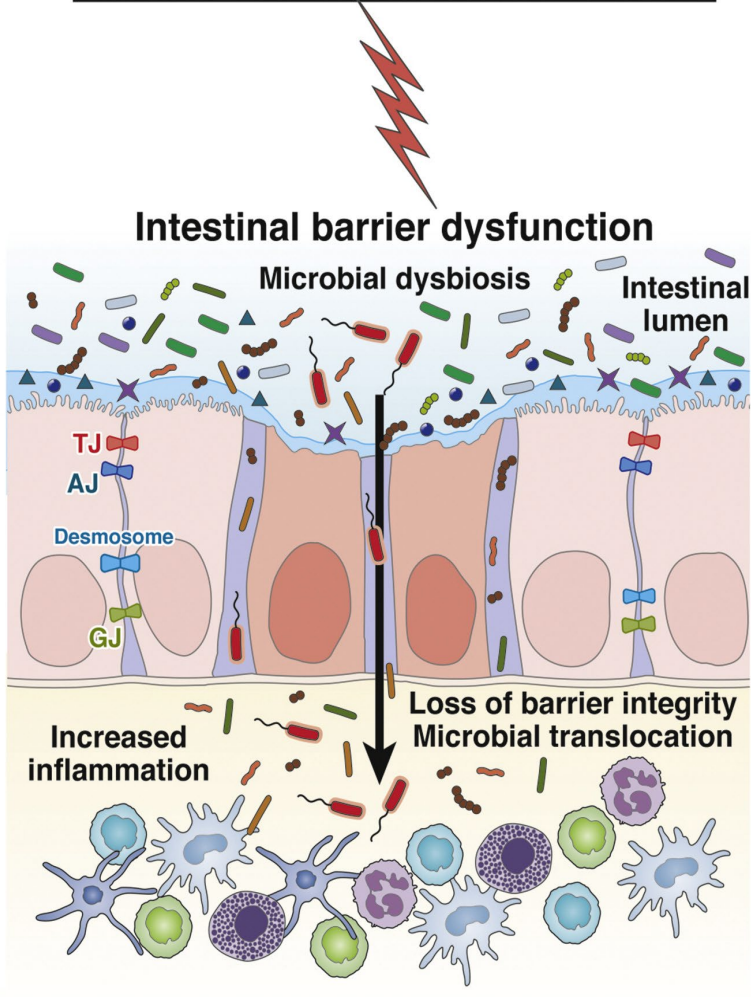


Darm-Immunchse

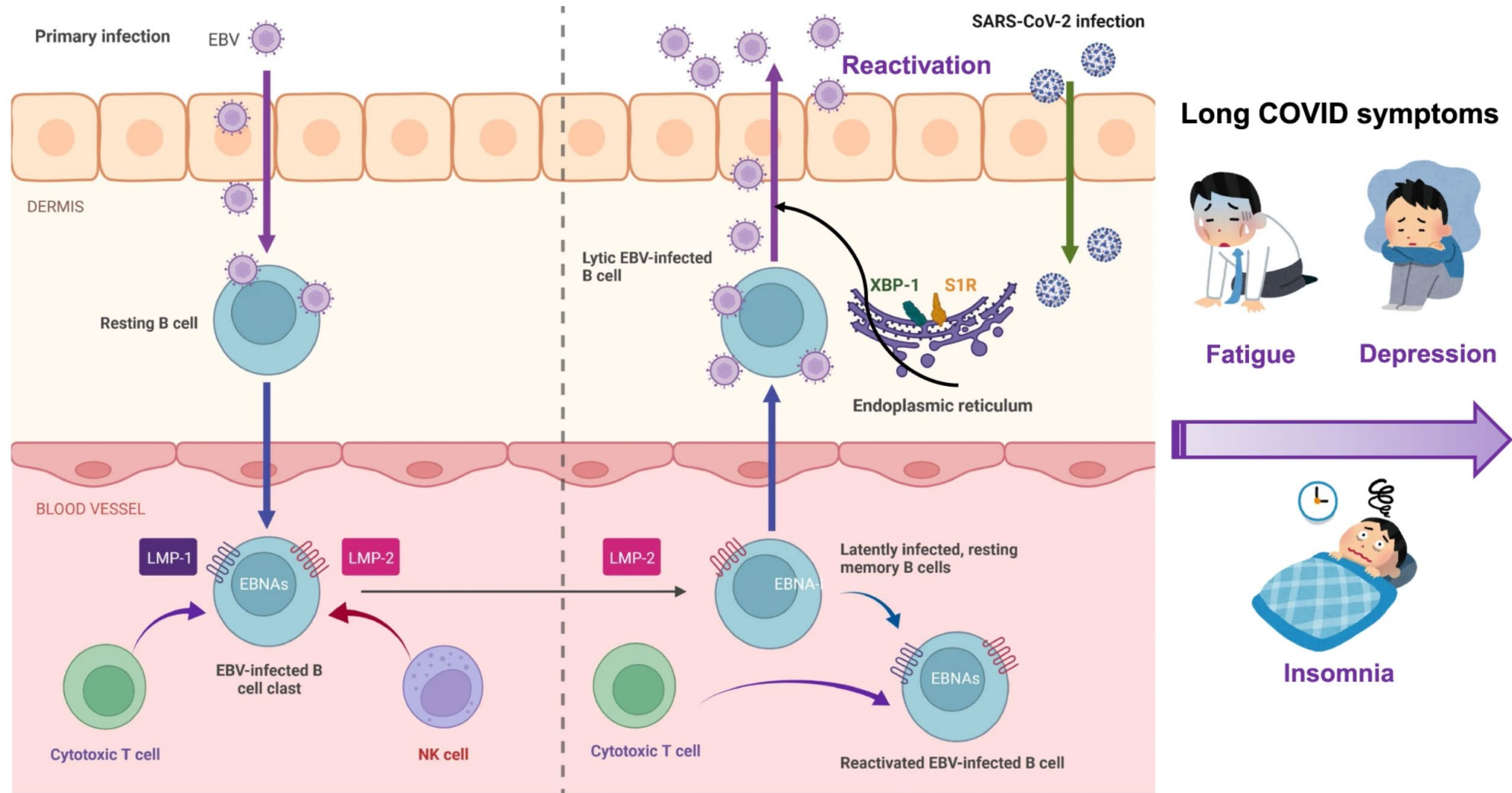


Intestinale Barrierestörung → Inflammation

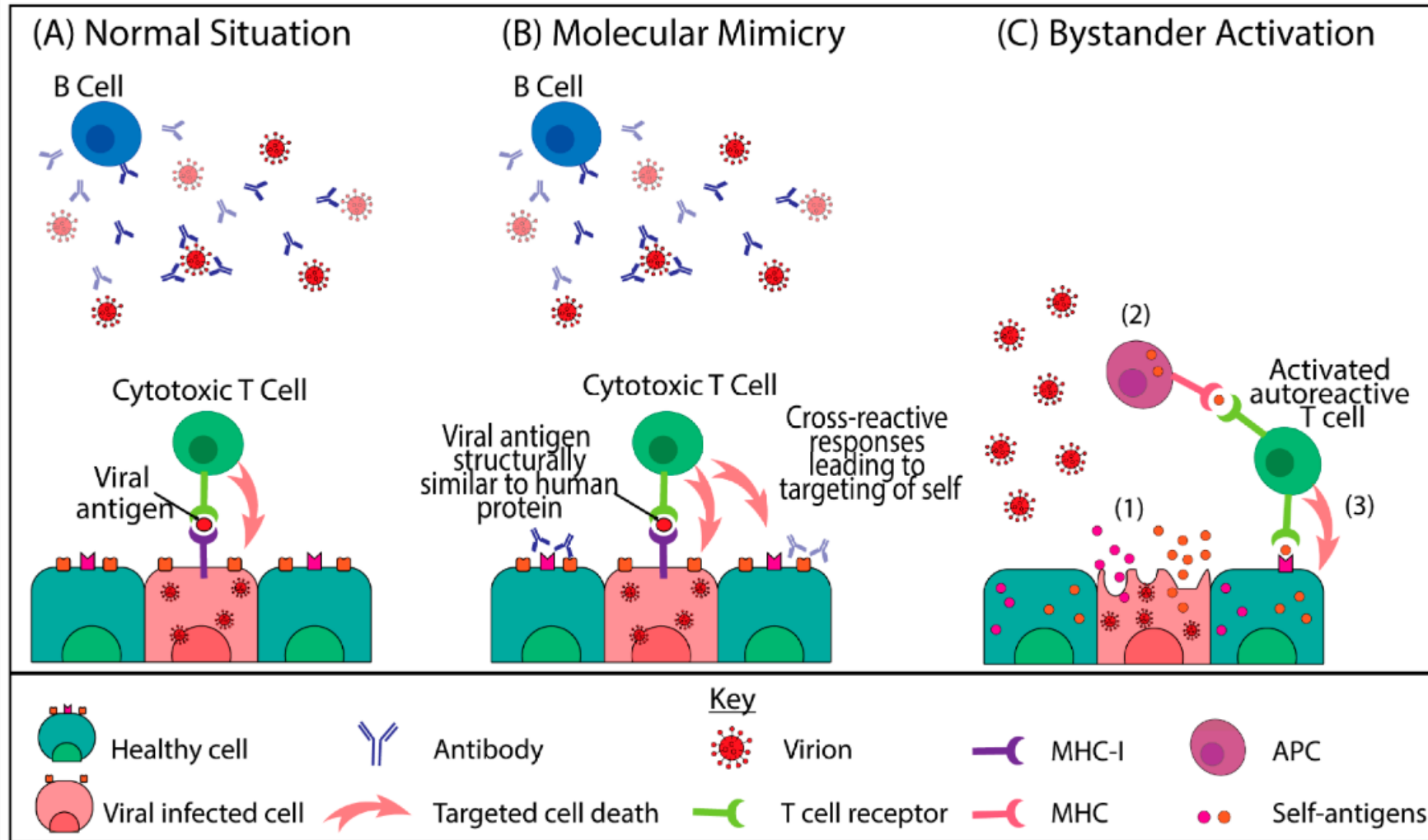
IBD, IBS, cancer, celiac disease, diabetes, food allergies, stress, alcohol, high fat, stress, smoking, NSAID, pathogens, etc.



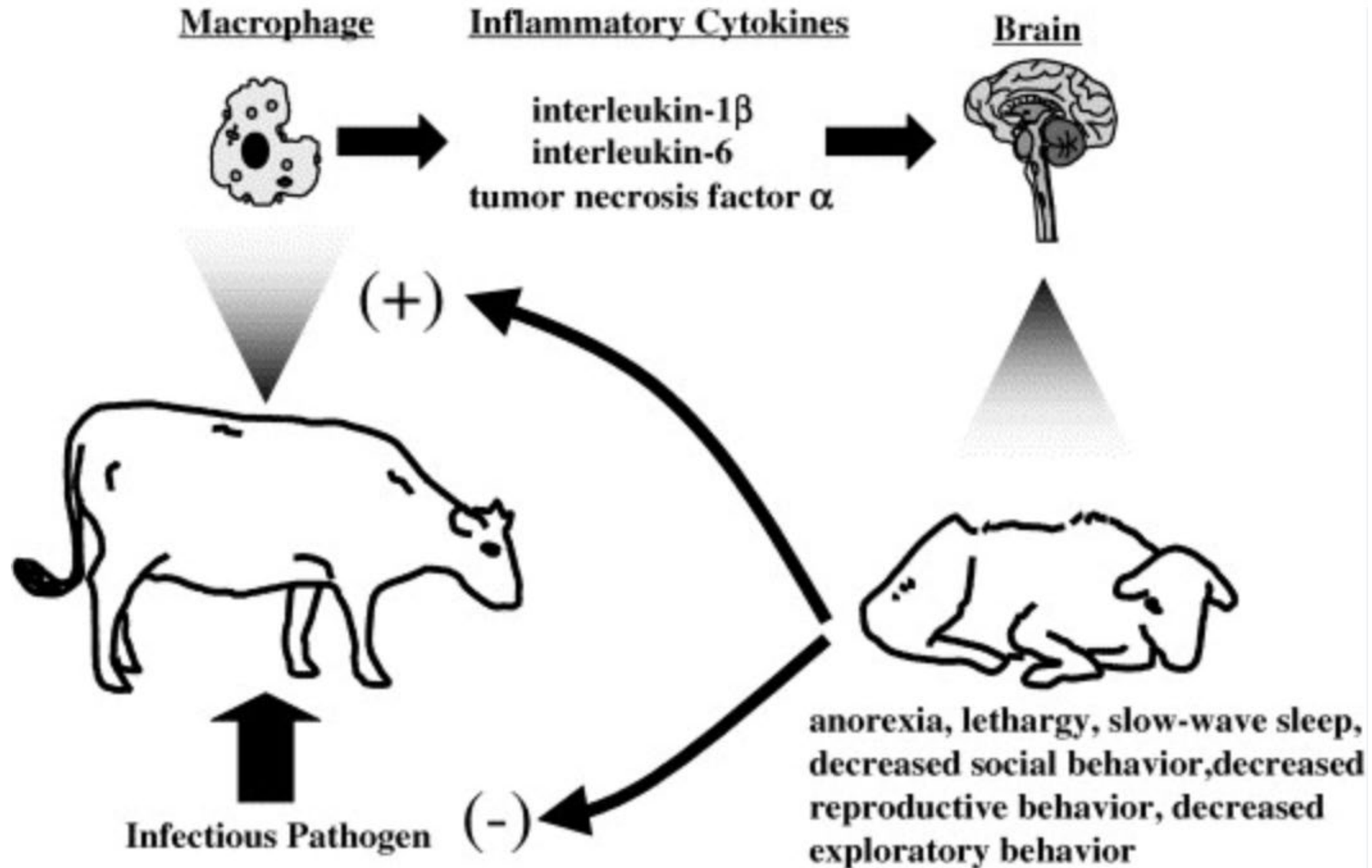
EBV Reaktivierung → Inflammation



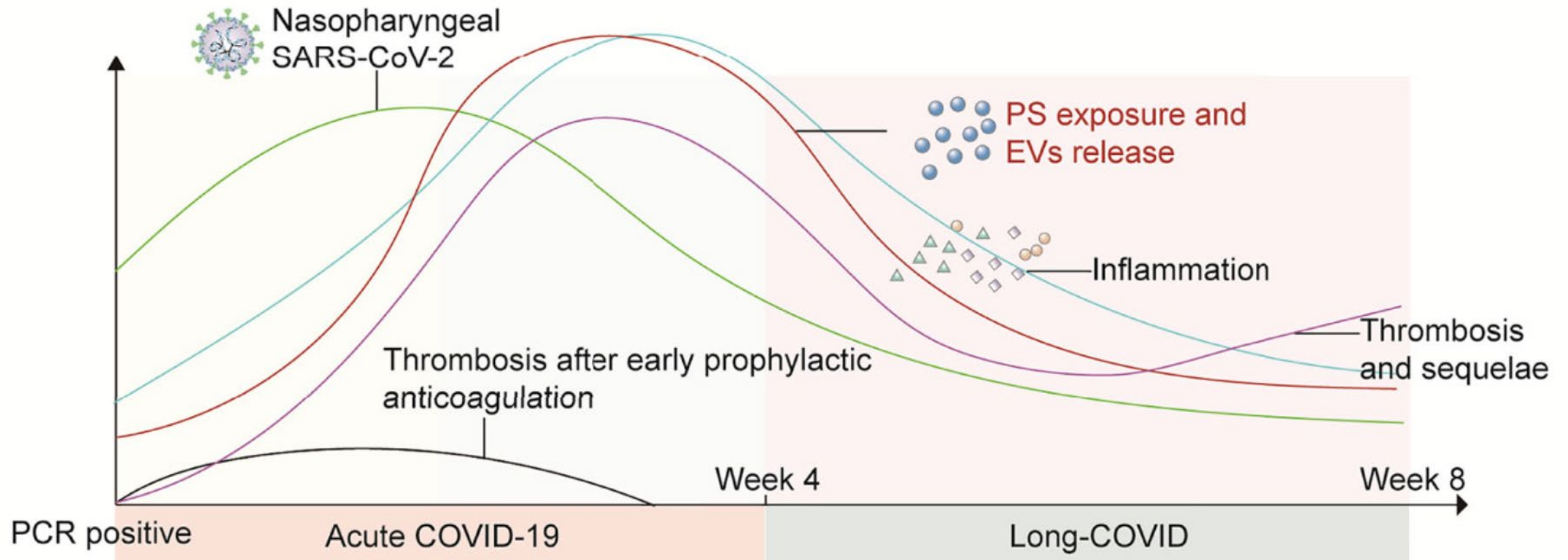
Molekulares Mimikry → Inflammation



Inflammation → Vagus → Krankheitsverhalten



Inflammation → Thrombosen → Inflammation



Inflammation → Thrombosen → Inflammation

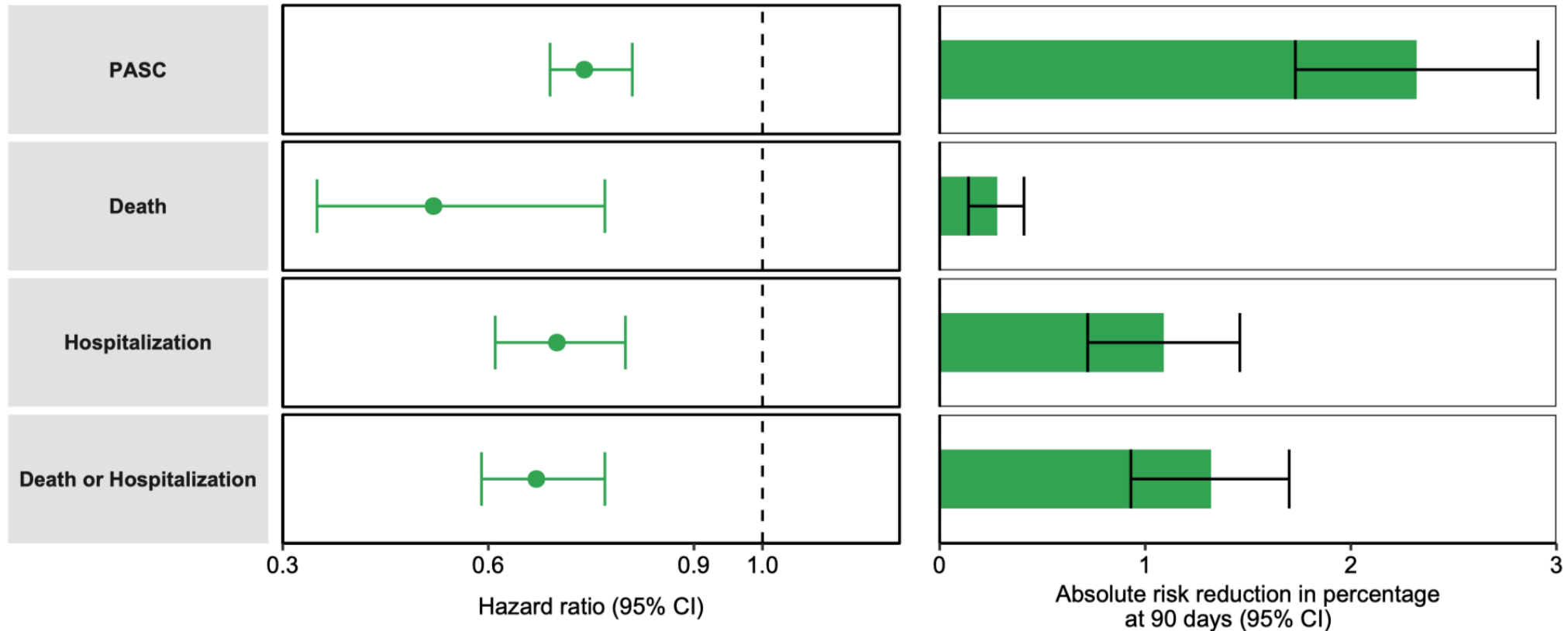
References	Population	Purpose	Results	Conclusions
(Giannis et al., 2020)	N=4906	Postdischarge thromboembolic outcomes and mortality	VTE was diagnosed in 76 patients (1.55%) postdischarge and included 44 DVTs (0.90%), 42 PEs (0.85%), 2 splanchnic vein thrombosis (0.04%), and 3 other vein thromboses (0.06%).	Postdischarge VTE, ATE, and ACM occurred frequently after COVID-19 hospitalization. Postdischarge anticoagulation reduced risk by 46%.
(Patell et al., 2020)	N=163	Postdischarge thrombosis and hemorrhage	The cumulative incidence of thrombosis (including arterial and venous events) at day 30 following discharge was 2.5%; the cumulative incidence of venous thromboembolism alone at day 30 postdischarge was 0.6%.	The rates of thrombosis and hemorrhage appear to be similar following hospital discharge for COVID-19.
(Pasini et al., 2021)	N=75	Serum metabolic profile in pasc syndrome: clinical implication	All patients had very high serum concentrations of ferritin and D-Dimer. 73% had elevations in erythrocyte sedimentation rate and CRP. 27% had elevations in LDH.	The persistence of altered D-Dimer levels raises the possibility of long-term risks of thromboembolic disease.
(Pretorius et al., 2021)	N=49	Investigate whether the persistent symptoms of long-COVID are due to the presence of persistent circulating plasma microclots that are resistant to fibrinolysis.	The plasma samples from long COVID/PASC still contain large anomalous (amyloid) deposits (microclots).	Clotting pathologies in both acute COVID-19 infection and in long COVID/PASC might benefit from following a regime of continued anticlotting therapy to support the fibrinolytic system function.
(von Meijenfeldt et al., 2021)	N=52	Studied the hemostatic status of patients with a resolved COVID-19 infection.	One patient developed a deep vein thrombus with small pulmonary embolisms in the 4 months after hospital discharge. PAI-1 levels were higher in patients compared with controls, both on admission and at 4-month follow-up.	COVID-19 patients have sustained prothrombotic changes as evidenced by enhanced thrombin-generating capacity and decreased plasma fibrinolytic potential at 4 months after hospital discharge.

Zwischen 1,6 und 2,5% Thrombosen bei Entlassung






Protektive Maßnahmen – frühe Therapie




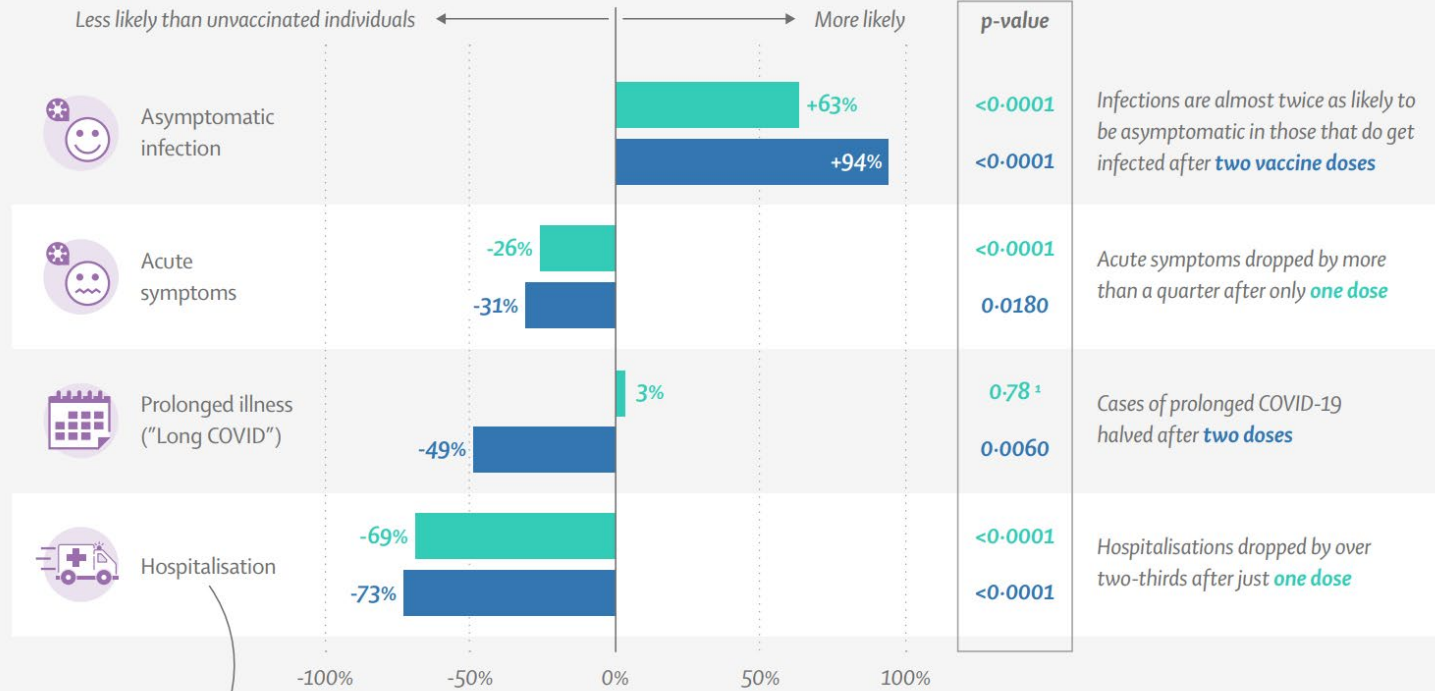
Nirmatrelvir/Ritonavir in der Frühphase reduziert Wahrscheinlichkeit von post COVID

Preventive Maßnahmen - Impfung

Likelihood of events due to SARS-CoV-2 infection, compared with unvaccinated individuals

 After one vaccine dose

 After two doses



27%

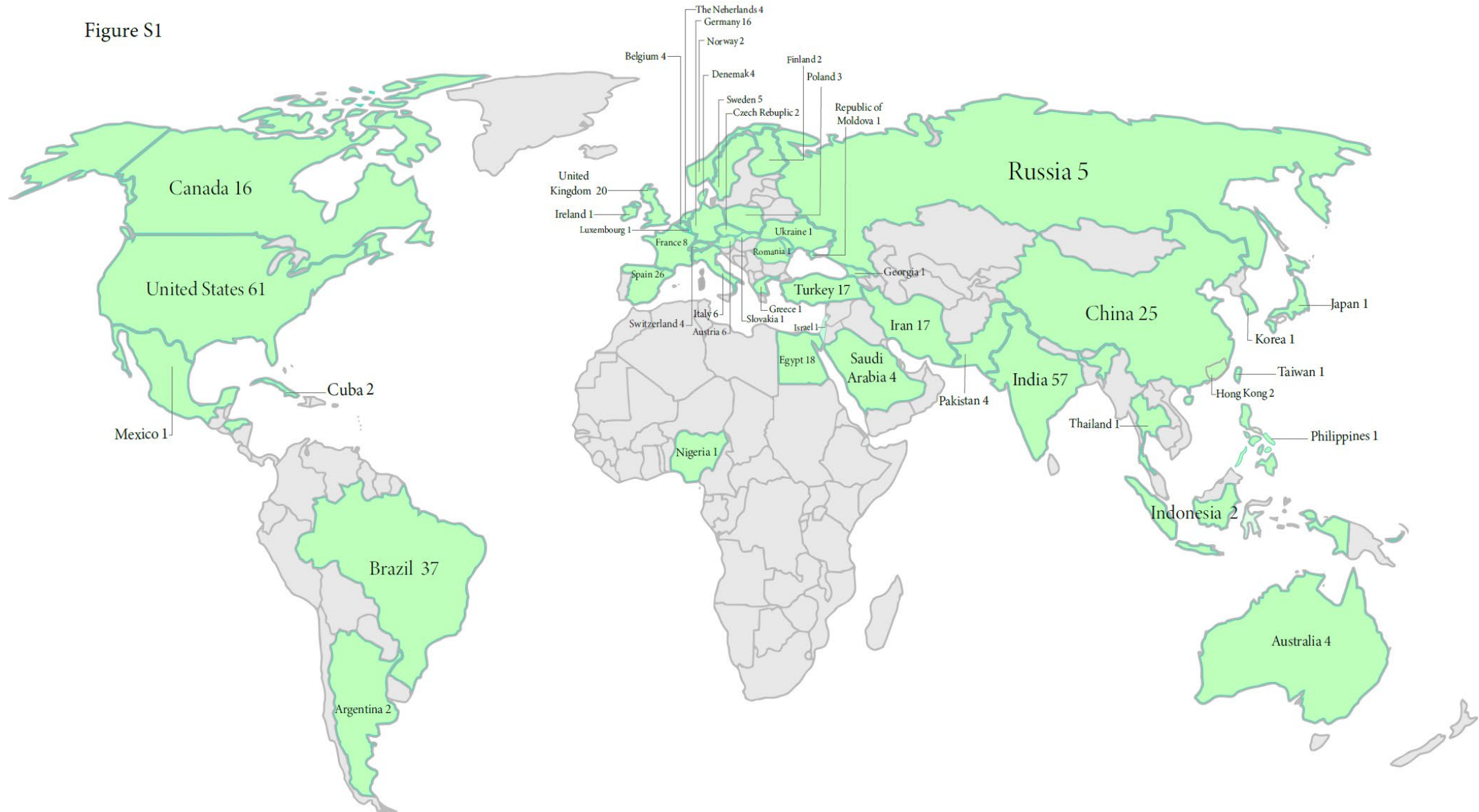
The mortality rate of patients hospitalised >21 days post-vaccination. This remains at levels similar to those observed in the "first wave" of the pandemic in the UK (March-April 2020)²

Read more:

Post-vaccination SARS-CoV-2 infection: risk factors and illness profile in a prospective, observational community-based case-control study

Therapiestudien alle Kategorien

Figure S1



N=388

Therapiestudien alle Kategorien - Ansätze

Rehabilitation (168)

- Exercise (51)
- General rehabilitation including telerehabilitation (46)
- Respiratory muscle training (17)
- Cognitive rehabilitation (7)
- Virtual reality rehabilitation (7)
- Breathing and chest mobilization exercises (6)
- Olfactory training (6)
- Yoga rehabilitation (6)
- Heart rate variability biofeedback (2)
- Vocal-based respiratory training (2)
- Activity tracker and a bespoke mobile phone application
- Akili Interactive digital treatment 'AKL-T01'
- Benson's relaxation technique
- BREATHE program for long COVID
- Counterweight-Plus/DIRECT diet weight management program
- Long COVID optimal health program
- Lymphatic drainage massage
- Manual therapy (hand operated technique and breathing exercises)
- Neurofeedback therapy
- NexJ Connected Wellness
- Online singing, breathing and wellbeing program (ENO Breathe)
- PowerBreathe® and Therosold PEP® tools
- Proprioceptive training
- Rehabilitation robot (Luna by EGZOTech ©)
- REMM-HIIT
- Slow-paced breathing
- Sniffin' sticks Duftquartett
- Whole body vibration training

Psychotherapy (12)

- Cognitive behavioral therapy (3)
- Adhera® Digital Health Intervention
- Amygdala and insula retraining program
- HUS internet therapy for bodily stress syndromes
- LISTEN intervention
- Mind body syndrome therapy
- Mindful self-compassion training
- PACS coping and recovery intervention
- Telemedicine mindfulness-based protocol
- Wearable brain sensing wellness device (Muse™-S)

Education (4)

- Cognitive psychoeducation
- Education and strategies intervention
- Medical psychoeducational talks
- Pain and self-management education

Pharmacotherapy (77)

- Clochicine (5)
- Nintedanib (4)
- Pirfenidone (4)
- Ivermectin (2)
- Methylprednisolone (2)
- Mometasone (2)
- Montelukast (2)
- Prednisolone (2)
- Treamid (bisamide derivative of dicarboxylic acid) (2)
- Anhydrous enol-oxaloacetate
- Apixaban
- Atorvastatin
- AXA1125
- Bioarginina C
- Budesonide
- Caffeine
- Cerebrolysin
- Donepezil
- Echinochrome A
- Erythropoietin
- Famotidine
- Fampridine (sustained release)
- Fibrotac
- Gabapentin
- Immulina™ (spirulina)
- ImmunoSEB + ProbioSEB CSC3 (probiotic complex)
- Intranasal Insulin
- Ibudilast
- Ivabradine
- Lactoferrin
- Leronlimab

Pharmacotherapy Cont.

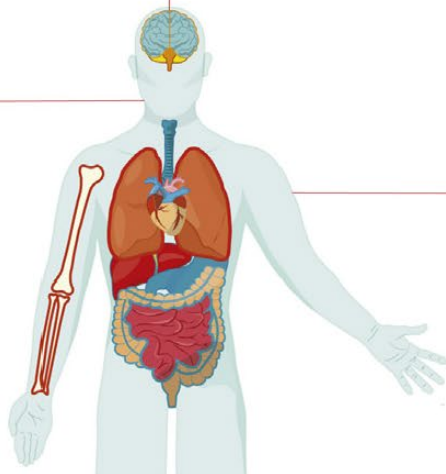
- Loratadine
- LYT-100 (deupirfenidone)
- Metoprolol succinate
- Mycophenolate mofetil
- MYMD1® (Isomyosmine)
- Naltrexone
- Niagen (vitamin B3)
- Omni-Biotic® Pro-Vi 5
- Pentoxifylline
- Pimozide
- Prednisone
- Prospekta
- Remdesivir
- Rivaroxaban
- Rosuvastatin
- RSLV-132
- Ruconest
- S-1226 (8%)
- Sacubitril / Valsartan
- Somatropin
- Sulodexide
- Taxifolin Aqua
- Temelimumab (formerly GNBAC1)
- Theophylline
- TNX-102
- Vitamin D3
- Vortioxetine
- Xltran Plus™ or Xltran™
- Zofin™ (formerly Organiceil Flow)

Complementary and Alternative Medicine (64)

- TCM (25)
- Ayurveda (24)
- Homeopathic medications (4)
- ADAPT-232 (Chisan®)
- Coenzyme Q10
- Cracie bojungikki-tang extract
- Curcumin/boswellia serrata/ascorbic acid mixture
- Gyeongbang gyeongok-go
- Hanpoong Soonsimhwan
- IMMUNODAAT™ botanical ingredient
- Nutraceuticals
- Omega-3 (Eicosapentaenoic acid + docosahexaenoic acid)
- Targeted wellness formula C™
- 5-aminolevulinic acid phosphate

Others (43)

- Transcranial current direct stimulation (9)
- Photobiomodulation (4)
- Transcutaneous auricular vagus nerve stimulation (4)
- Electrical stimulation (2)
- Hyperbaric oxygen (2)
- Allogeneic culture-expanded adipose-derived mesenchymal stem cells
- Allogenic marrow stromal cells
- Bone marrow mesenchymal stem cell derived extracellular vesicles
- CIMAvax-EGF®
- Cold knee casts
- Cranial electrotherapy stimulation
- High tone power therapy
- Hope Biosciences adipose-derived mesenchymal stem cells – allogeneic (HB-adMSCs)
- Human immunoglobulin G
- Hydrogen-oxygen generator with nebulizer
- Inogen One® G4 (portable oxygen concentrator)
- Intraoperative use of PEEP - Fixed and individualized
- Lactobacillus plantarum 299v in fermented oat drink
- Microannula harvest adipose derived tissue stromal vascular fraction (tSVF)
- MON002 (autologous monocytes)
- Personalized multidisciplinary day-hospital intervention
- Plasma exchange
- Platelet rich plasma
- Pulsed ultrasound
- Resistive capacitive monopolar radio frequency at 448 kHz (INDIBA®)
- Stellate ganglion block
- Whole-body cryotherapy



Symbols next to each intervention represent the targeted system:

- Pulmonary system: 🫁
- Cardiovascular system: ❤️
- Non-system specific: 🧑
- Mental health: 🧠

- Musculoskeletal system: 🦴
- Nervous system: 🧠
- Gastrointestinal system: 🍌

Therapiestudien alle Kategorien - Vergleichbarkeit

The top 20 primary outcome measures in terms of frequency (*N*)

Rank	Primary outcome measures	N
1	6-minute walk test	58
2	Pulmonary function testing	43
3	Changes in symptoms of PACS	24
4	36-Item Short-Form Survey	23
5	Cardiopulmonary exercise test/peak oxygen consumption (VO _{2 max})	20
6	European Quality of Life 5 Dimensions 5 Level Version	19
7	Visual Analogue Scale	17
8	Fatigue Severity Scale	16
9	Post-COVID-19 Functional Status Scale	12
10	Sniffin' Sticks Test	12
11	Modified Medical Research Council Dyspnea Scale	10
12	Chalder Fatigue Scale (CFQ-11)	9
13	Fibrosis in high-resolution computed tomography of the lung	9
14	Incidence of treatment-emergent adverse effects	9
15	Inspiratory muscle strength or maximal inspiratory pressure	9
16	Borg Dyspnea Scale	8
17	Changes in blood oxygenation	8
18	Fatigue Assessment Scale	8
19	Handgrip strength dynamometer	8
20	Routine blood test	7
20	SGRQ	7

PACS, post-acute COVID-19 syndrome; SGRQ, St. George's Respiratory Questionnaire.

Therapiestudien – Randomisierte Kontrollierte Studien

Trial	Interventions under comparison	PC/subtype	Country	Current state	No. of subjects	NCT
Immunomodulatory						
Phase 2 RCT	IgG vs. methylprednisolone vs. saline	PC neurological	USA	Recruiting	45	NCT05350774
Phase 3 RCT (open)	Atorvastatin vs. standard care	LC neurocognitive	Australia	Recruiting	400	NCT04904536
Phase 2 RCT	Plasma Exchange Therapy vs. sham	PC	Spain	not yet recruiting	50	NCT05445674
Phase 2 RCT	Immunoabsorption vs. sham	PC ME/CFS (CCC) and autoantibodies	Germany	Not yet recruiting	66	NCT05710770
Phase 3 RCT	Montelukast vs. placebo	LC respiratory	Spain	Recruiting	284	NCT04695704
Phase 2 RCT	Ampligen vs. saline	PC ME/CFS (CDC)		Not yet recruiting	80	NCT05592418
Phase 3 RCT	Prednisolone (low dose) vs. placebo Vitamin B1/6/12 vs. placebo	PC	Germany	Recruiting	340	NCT05638633
Phase 2 RCT	Efgartigimod vs. placebo	PC POTS	USA	Recruiting	42	NCT05633407
Phase 2/3 RCT adaptive	Ibudilast vs. Pentoxifylline vs. placebo	PC	Canada	Not yet recruiting	1,000	NCT05513560
Phase 2 RCT	Baricitinib vs. placebo	PC cognitive	USA	Not yet recruiting	30	NCT05858515
Phase 2 RCT	BC007 aptamer vs. placebo	LC fatigue	Germany/ Europe	Not yet recruiting	114	EudraCT2022-003452-14
Phase 4 RCT	Loratidine vs. placebo	LC	India	Not yet recruiting	64	CTRI/2022/07/043679



Therapiestudien – Randomisierte Kontrollierte Studien

TABLE 1 Randomized controlled trials in PCS registered in clinical trial platforms*.

Trial	Interventions under comparison	PC/subtype	Country	Current state	No. of subjects	NCT
Vascular						
Phase 2 RCT	Hyperbaric oxygen therapy vs. sham	PC or LC	Sweden	Recruiting	80	NCT04842448
Phase 2 RCT	Vericiguat vs. placebo	PC ME/CFS (CCC or IOM) and endothelial dysfunction	Germany	Not yet recruiting	104	NCT05697640
Antiviral						
Phase 2 RCT	Paxlovid vs. Ritonavir vs. placebo	PC	USA	Recruiting	200	NCT05576662
Phase 2 RCT	Temelimab vs. placebo	PC neuropsychiatric	Switzerland	Recruiting	200	NCT05497089
Phase 3 RCT	Meplazumab (anti-CD147) vs. placebo	PC (at least one symptom)	China	Not yet recruiting	144	NCT05813587
Neuro-modulators						
Phase 4 RCT (open)	Dextroamphetamine vs. app	PC cognitive	USA	Recruiting	120	NCT05597722
Phase 2 RCT	Low-dose Naltrexone (LDN) vs. placebo	PC ME/CFS	Canada	Not yet recruiting	160	NCT05430152
Phase 2 RCT	Lithium vs. placebo	LC fatigue and/or brain fog	USA	Recruiting	50	NCT05618587
Phase 2 RCT	Vortioxetine vs. placebo	PC cognitive	Canada	Complete	200	NCT05047952
Phase 2 RCT	Fampridine vs. placebo	PC cognitive	Switzerland	Recruiting	44	NCT05274477
Phase 2 RCT	Ketamine vs. placebo	PC depressive	USA	Recruiting	12	NCT05690503

*ClinicalTrials.gov, <https://clinicaltrials.gov/>; EU Clinical Trials Register <https://www.clinicaltrialsregister.eu/>; International Clinical Trials Registry Platform (ICTRP), <https://www.who.int/clinical-trials-registry-platform> (date 22.5.2023); RCT, randomized controlled trial; PC: Post-COVID-19 Condition or Syndrome, LC: Long Covid; NCT: National Clinical Trials Number = ClinicalTrials.gov Identifier.



Impfung bei bestehendem post COVID

Bei bestehendem Post-COVID führte die COVID-19-Impfung zu einer Modifikation (Verbesserung und Verschlechterung) der Post-COVID-Symptome, die teilweise nur passager anhielt

(Arnold DT, et al., *Ann Intern Med.* 2021;174:1334–1336. doi: 10.7326/M21-1976.
Ayoubkhani D, et al. *BMJ.* 2022;377:e069676. doi: 10.1136/bmj-2021-069676.
Gaber TA-ZK et al., <https://www.bjimp.org/content/are-mrna-covid-19-8>.
Strain WD et al., 2022;10:652. doi: 10.3390/vaccines10050652.)

In einer Studie konnte eine Reduktion der Post-COVID-induzierten Hausarztbesuche berichtet werden

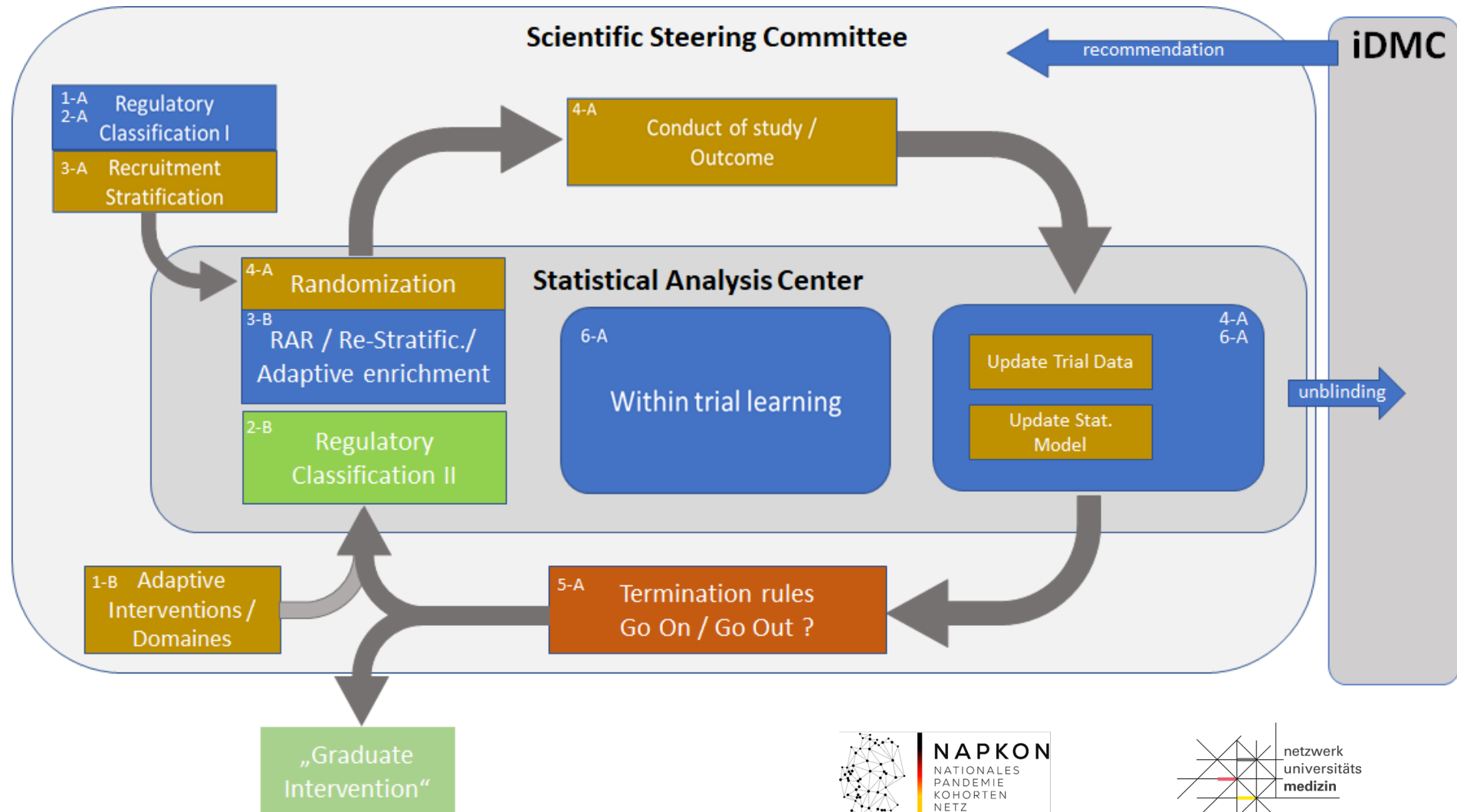
(Whittaker HR, et al. *BMJ.* 2021 doi: 10.1136/bmj-2021-065834)

Zwei Studien konnten keinen Einfluss der Impfung auf Post-COVID nachweisen

(Peghin M, et al. *Clin Microbiol Infect.* 2022 doi: 10.1016/j.cmi.2022.03.016.
Wisnivesky JP, et al (2022). <https://link.springer.com/10.1007/s11606-022-07465-w>.)

Ein therapeutischer Effekt kann aus der vorliegenden Evidenz nicht sicher abgeleitet werden.

Ausblick: RAPID – Randomized Assessments of Post COVID Syndrome Treatments

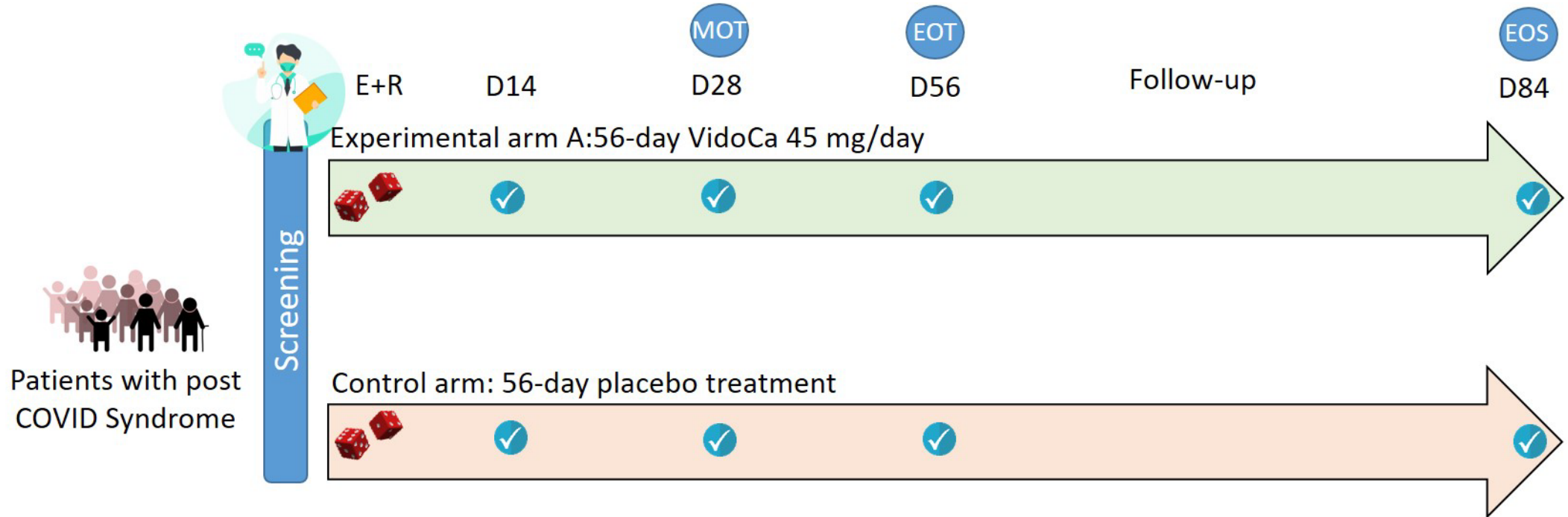


Vidofludimus Calcium (IMU-838)

Dihydroorotate Dehydrogenase (DHODH) Inhibitor → hemmt Synthese des Nucleotides Pyrimidin →

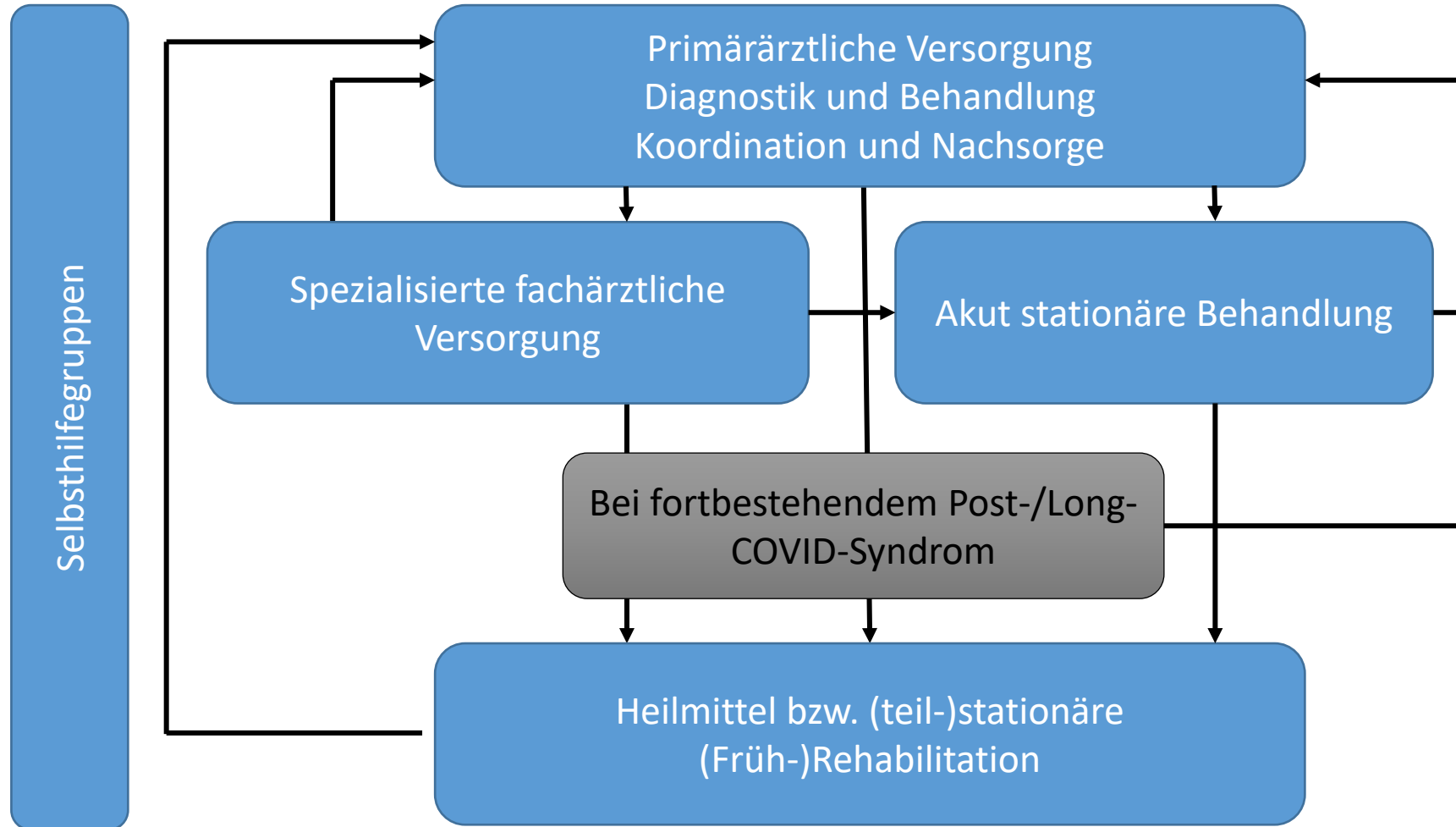
- a) Blockade der intrazellulären viralen Replikation → breite Wirksamkeit gegenüber verschiedenen Viren SARS-CoV-2, EBV, CMV und andere
- b) Hemmung der Lymphozytenaktivierung → Reduktion der Freisetzung von Zytokinen (Botenstoffe der Entzündung) → anti-entzündliche Aktivität

Studienablauf



E+R = Enrolment and randomization
EOT = end of treatment
EOS = end of study

Versorgungskonzept



Hilfreiche Informationen



START | AKTUELLES | ÄRZTE/FORSCHER*INNEN ▾ | WAS IST ME/CFS? ▾ | LONG COVID | POLITIK ▾ | PRESSE ▾ | FAQ ▾ | WIR ▾



Was ist Long COVID?

Long COVID umfasst Symptome, die nach einer akuten COVID-19-Erkrankung neu auftreten und Wochen oder Monate nach Erkrankungsbeginn anhalten.



Symptome



Häufigkeit



Long COVID &
ME/CFS



Pathophysiologie



Diagnostik



Therapie



Herausforderungen

Zusammenfassung

- Das post COVID Syndrom ist eine reale Erkrankung
- Höchst variabler Schweregrad und klinische Präsentation
- Entstehung von post COVID noch nicht vollständig geklärt, aber es gibt Fortschritte:
 - Viruspersistenz
 - Immunologisches Mimikry
 - Mikrobiomveränderungen
 - Thrombotische Aktivität
 - Vagusinflammation
- Patient:innen als wichtige Treiber der Beschreibung und Erforschung
- Betreuung von Patient:innen in post COVID Ambulanzen zeitintensiv und teuer
- Gleichzeitig hohe Nachfrage → fast alle Ambulanzen überfüllt
- Erste Therapiestudien weltweit initiiert



Vielen Dank für Ihre Aufmerksamkeit.

Nun zu Ihren Fragen,
die wir anonym behandeln.
Bitte schicken Sie diese an:

info@gesundheitsforum-ukf.de