

COVID-19 Quo vadis 2021?

Therapie von COVID-19 in der hausärztlichen Praxis

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...it's like standing out at the falls, trying to fill a glass of water. It's overwhelming and it's impossible to keep up...

Paul E Sax

Fallvignette: 75-jähriger männlicher Patient in der Praxis

- Kopfschmerzen, Gliederschmerzen seit 3 Tagen, seit heute zusätzlich Anosmie und Gefühl von Fieber
- Vorerkrankungen:
 - Diabetes mellitus Typ 2, unter Metformin gut eingestellt
 - Arterielle Hypertonie behandelt mit Sartan
 - Dyslipidämie behandelt mit Statin
 - COPD behandelt mit Symbicort
 - Adipositas
- Temperatur 38.3°C, BD 123/72mmHg, P 96/min, SaO2 bei Raumluft 96%, AF 14/min
- Spastische Atemgeräusche über allen Lungenfeldern

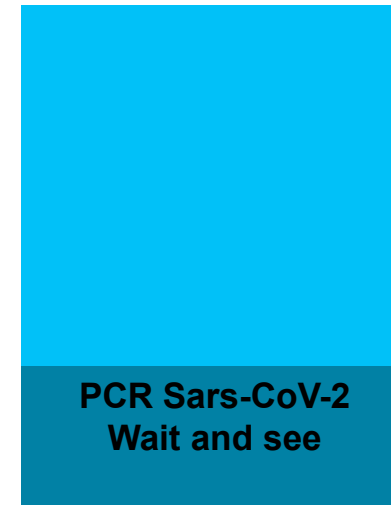
Nächster Schritt?



PCR Sars-CoV-2
Dexamethason 6mg
per os für 10 Tage



PCR Sars-CoV-2
Zuweisung USZ für
Beginn Remdesivir



PCR Sars-CoV-2
Wait and see

Die zwei Muskietiere

I. Dexamethason

II. Remdesivir

III. Convalescent plasma therapy (CPT)

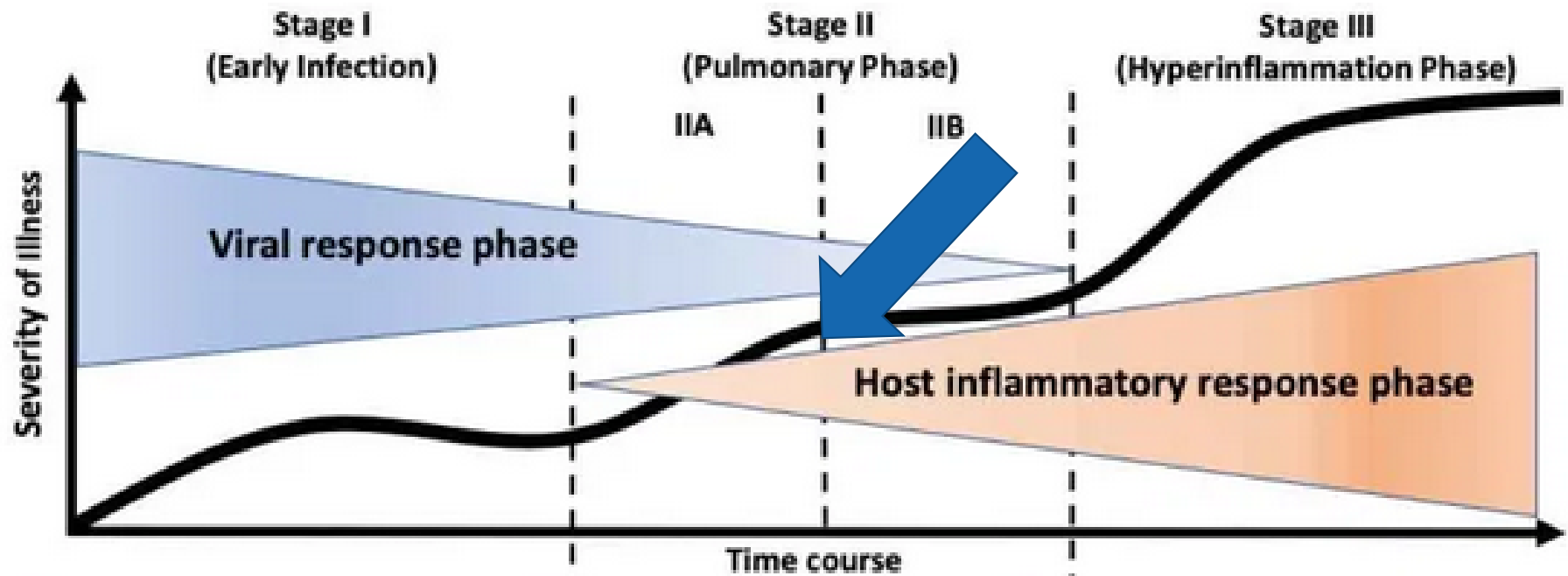
IV. Tocilizumab

V. L...

VI. Hydroxychloroquine



Keine wirksame Therapie für COVID-19 im ambulanten setting zugelassen (noch....)



	Stage I (Early Infection)	Stage II (Pulmonary Phase)	Stage III (Hyperinflammation Phase)
Clinical Symptoms	Mild constitutional symptoms Fever >99.6°F Dry Cough, diarrhea, headache	Shortness of Breath Hypoxia (PaO ₂ /FIO ₂ ≤ 300 mmHg)	ARDS SIRS/Shock Cardiac Failure
Clinical Signs	Lymphopenia, increased prothrombin time, increased D- Dimer and LDH (mild)	Abnormal chest imaging Transaminitis Low-normal procalcitonin	Elevated inflammatory markers (CRP, LDH, IL-6, D-dimer, ferritin) Troponin, NT-proBNP elevation

Fallvignette: 75-jähriger männlicher Patient in der Praxis

- Tag 8 nach Symptombeginn:
 - Dyspnoe bei Mobilisation
 - Leichter Druck auf der Brust
 - Persistierend Gefühl von Fieber
- Temperatur 38.6°C, BD 115/65mmHg, P 104/min, SaO₂ bei Raumluft 91%, AF 23/min
- Spastische Atemgeräusche über allen Lungenfeldern und abgeschwächtes Atemgeräusch über allen Lungenfeldern
- Röntgen-Thorax: angedeutete bilaterale Transparenzverminderungen

Nächster Schritt?

**Beginn Tavanic
Monitorisieren SaO2
und Zuweisung USZ
falls <90%**

**Beginn Tavanic
Zuweisung USZ für
Beginn Remdesivir**

**Zuweisung USZ für
Evaluation
Remdesivir und
Dexamethason**



Remdesivir

The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Final Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

Remdesivir



- Ursprünglich für Behandlung von Ebola entwickelt
- Langer Herstellungsprozess, hoch explosiv
- Nur intravenöse Verabreichungsform
- Vorerst befristete Zulassung für 2 Jahre durch Swissmedic
- Dosierung: 200mg als Ladedosis Tag 1, danach 100mg Tag 2-5
- Kosten: 2'207 CHF für 5 Tage Therapie

Remdesivir

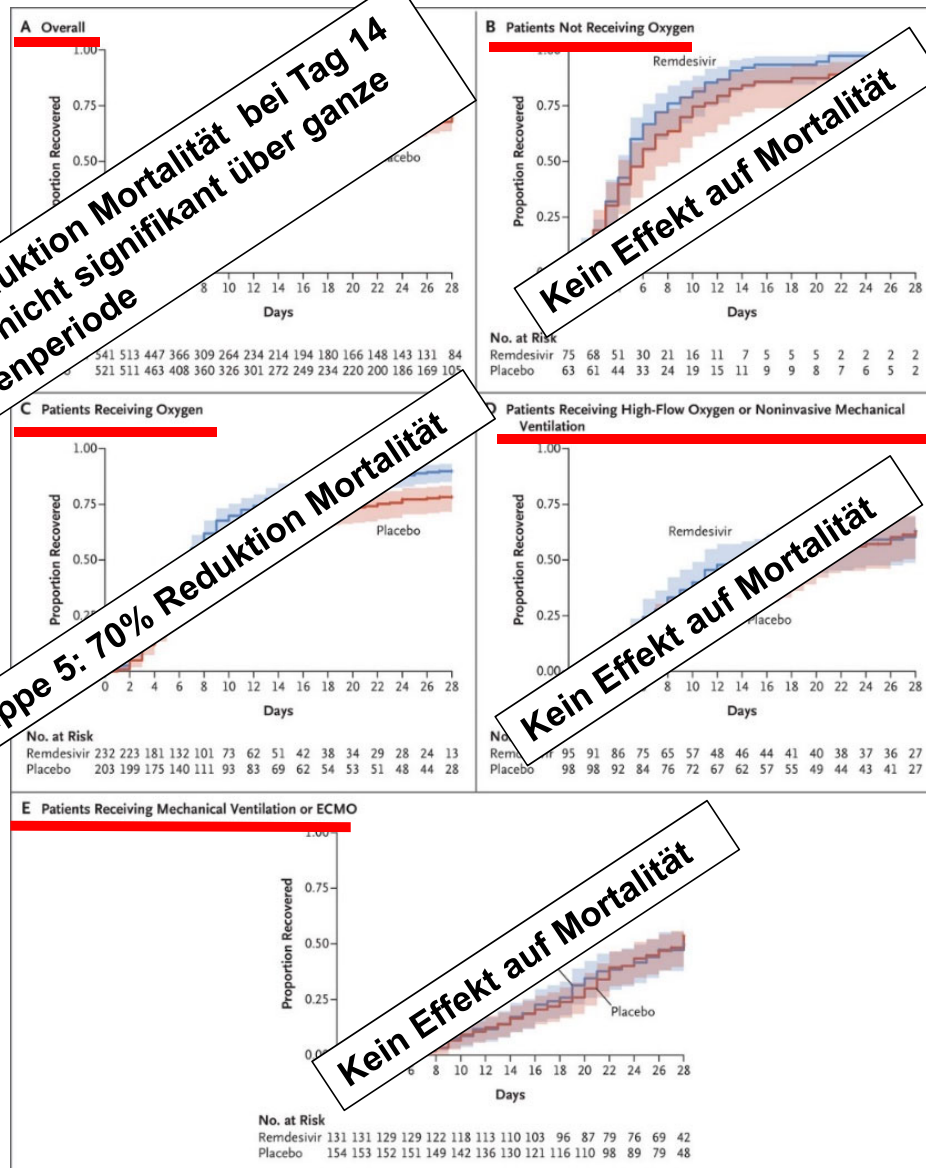


Table 2. Outcomes Overall and According to Score on the Ordinal Scale in the Intention-to-Treat Population.*

	Overall		Ordinal Score at Baseline							
	Remdesivir (N=541)	Placebo (N=521)	4		5		6		7	
			Remdesivir (N=75)	Placebo (N=63)	Remdesivir (N=232)	Placebo (N=203)	Remdesivir (N=95)	Placebo (N=154)	Remdesivir (N=154)	Placebo (N=154)
Recovery										
No. of recoveries	399	352	73	58	206	156	95	154	154	154
Median time to recovery (95% CI) — days	10 (9–11)	15 (13–18)	5 (4–6)	6 (4–7)	7 (6–8)	9 (8–10)	10 (9–11)	11 (10–12)	12 (11–13)	13 (12–14)
Rate ratio (95% CI) †	1.29 (1.12–1.49 [P<0.001])		1.29 (0.91–1.83)		1.29 (1.03–1.61)		1.29 (1.03–1.61)		1.29 (1.03–1.61)	
Mortality through day 14‡										
Hazard ratio for data through day 15 (95% CI)	0.55 (0.36–0.83)		0.42 (0.04–4.67)		0.42 (0.04–4.67)		0.42 (0.04–4.67)		0.76 (0.39–1.50)	
No. of deaths by day 15	35	61	1	1	17	17	17	14	21	21
Kaplan–Meier estimate of mortality by day 15 — % (95% CI)	6.7 (4.8–9.2)	11.9 (9.4–15.0)	1.3 (0.1–7.1)	1.6 (0.1–10.1)	7.3 (5.1–10.1)	8.4 (6.1–11.1)	17.9 (15.2–21.2)	17.3 (11.2–26.4)	10.9 (6.6–17.6)	13.8 (9.2–20.4)
Mortality over entire study period‡										
Hazard ratio (95% CI)	0.73 (0.54–0.98)		0.73 (0.54–0.98)		0.73 (0.54–0.98)		1.02 (0.54–1.91)		1.13 (0.67–1.89)	
No. of deaths by day 29	40	61	1	1	25	25	19	20	28	29
Kaplan–Meier estimate of mortality by day 29 — % (95% CI)	7.4 (5.5–9.7)	11.7 (9.2–14.5)	1.3 (0.1–7.1)	1.6 (0.1–10.1)	10.8 (8.0–14.1)	12.7 (8.8–18.3)	21.2 (14.0–31.2)	20.4 (13.7–29.8)	21.9 (15.7–30.1)	19.3 (13.8–26.5)
Ordinal score at day 15 (no. (%)§										
1	1	1	0	28 (44.4)	90 (38.8)	62 (30.5)	18 (18.9)	14 (14.3)	11 (8.4)	11 (7.1)
2	0	0	0 (0.0)	15 (23.8)	70 (30.2)	58 (28.6)	22 (23.2)	19 (19.4)	5 (3.8)	10 (6.5)
3	0	0	8 (10.7)	4 (6.3)	6 (2.6)	4 (2.0)	0	0	0	0
4	0	3 (6.3)	3 (4.0)	7 (11.1)	17 (7.3)	13 (6.4)	12 (12.6)	4 (4.1)	6 (4.6)	9 (5.8)
5	0	60 (11.5)	3 (4.0)	5 (7.9)	25 (10.8)	18 (8.9)	2 (2.1)	14 (14.3)	28 (21.4)	23 (14.9)
6	0	24 (4.6)	1 (1.3)	0	5 (2.2)	7 (3.4)	12 (12.6)	11 (11.2)	10 (7.6)	6 (3.9)
7	95 (17.6)	121 (23.2)	1 (1.3)	3 (4.8)	13 (5.6)	21 (10.3)	16 (16.8)	20 (20.4)	57 (43.5)	74 (48.1)
8	34 (6.3)	58 (11.1)	1 (1.3)	1 (1.6)	6 (2.6)	20 (9.9)	13 (13.7)	16 (16.3)	14 (10.7)	21 (13.6)
Odds ratio (95% CI)	1.5 (1.2–1.9)		1.5 (0.8–2.7)		1.6 (1.2–2.3)		1.4 (0.9–2.3)		1.2 (0.8–1.9)	

**Patienten im Schnitt 5 Tage früher gesund
10 Tage versus 15 Tage
70 Prozent Reduktion Mortalität in Gruppe 5**

ORIGINAL ARTICLE

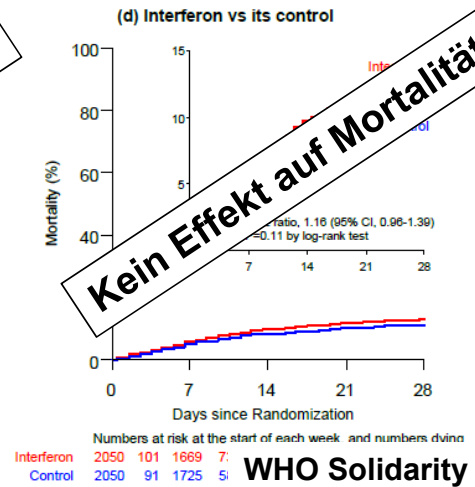
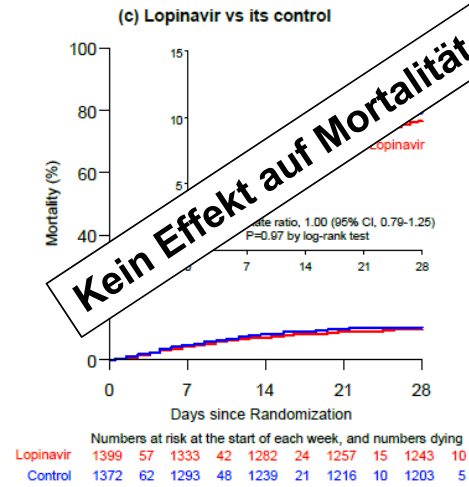
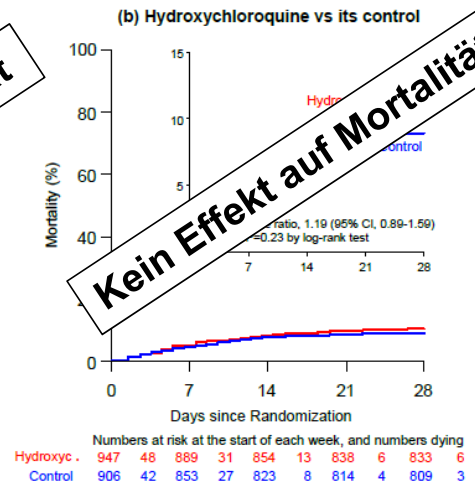
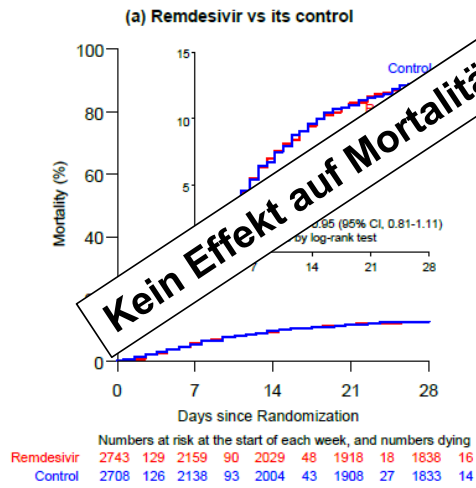
Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results

WHO Solidarity Trial Consortium*

CONCLUSIONS

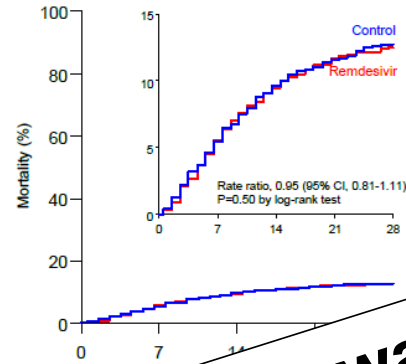
These remdesivir, hydroxychloroquine, lopinavir, and interferon regimens had little or no effect on hospitalized patients with Covid-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay. (Funded by the World Health Organization; ISRCTN Registry number, ISRCTN83971151; ClinicalTrials.gov number, NCT04315948.)

Remdesivir: Solidarity WHO trial

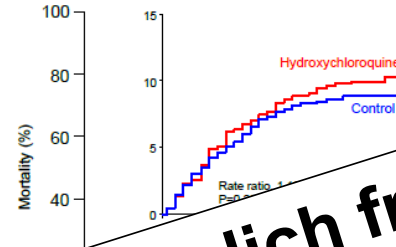


Remdesivir: Solidarity WHO Studie

(a) Remdesivir vs its control

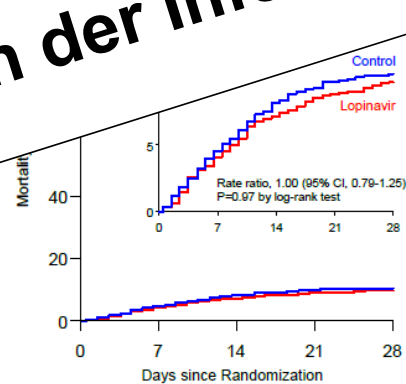


(b) Hydroxychloroquine vs its control

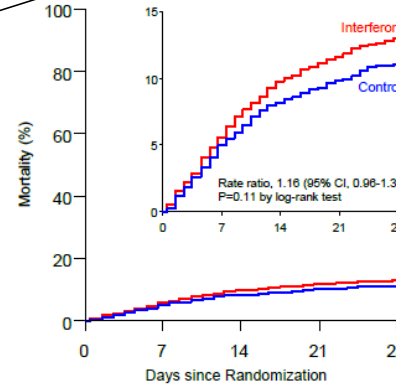


Remdesivir: wahrscheinlich früh in der Infektion zum Teil effektiv

(c) Lopinavir vs its control



(d) Interferon vs its control

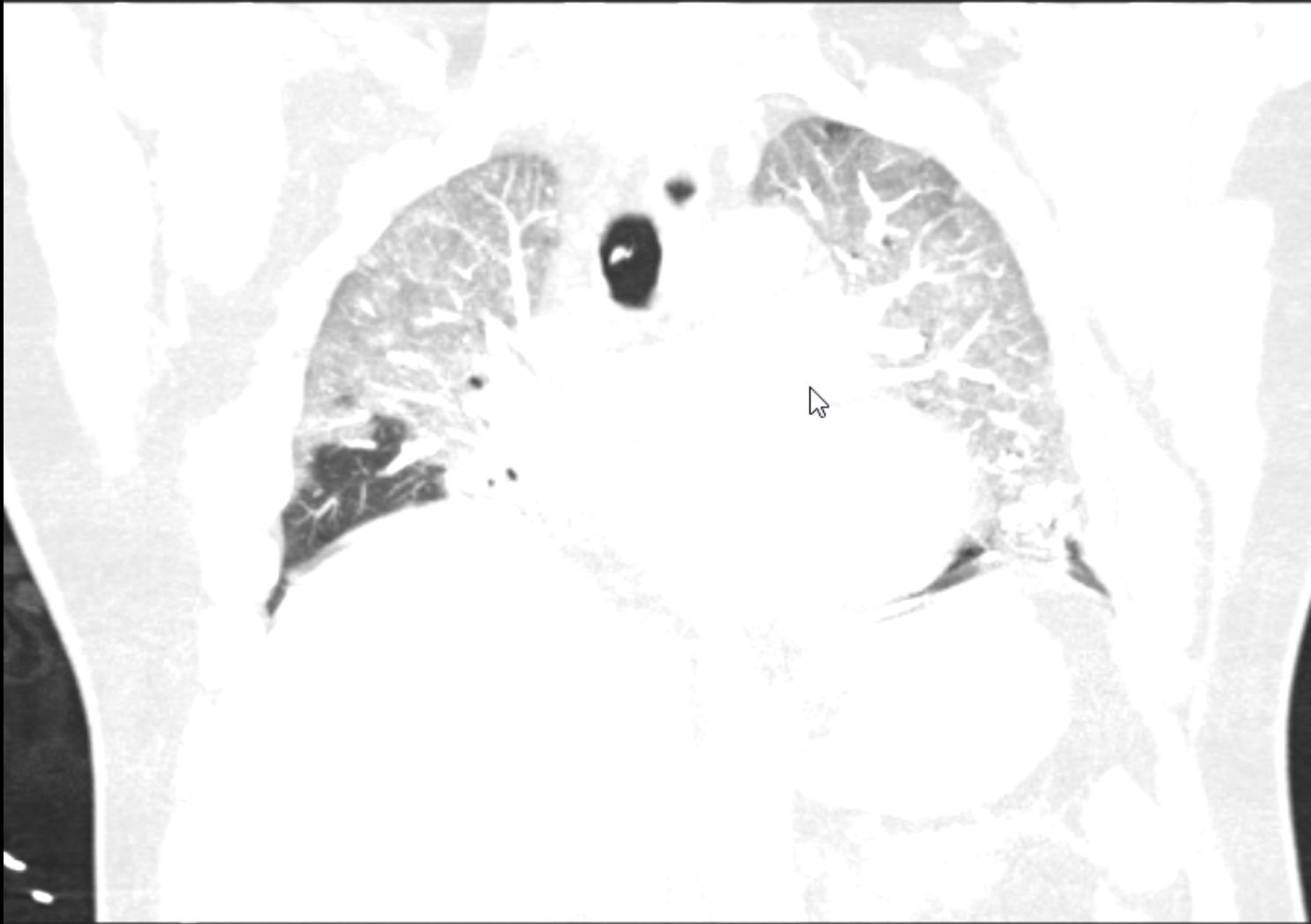


Numbers at risk at the start of each week, and numbers dying

Lopinavir	1399	57	1333	42	1282	24	1257	15	1243	10
Control	1372	62	1293	48	1239	21	1216	10	1203	5

Numbers at risk at the start of each week, and numbers dying

Interferon	2050	101	1669	73	1554	31	1483	24	1410	14
Control	2050	91	1725	58	1636	31	1563	21	1498	15



Dexamethasone

ORIGINAL ARTICLE

Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

The RECOVERY Collaborative Group*

ABSTRACT

BACKGROUND

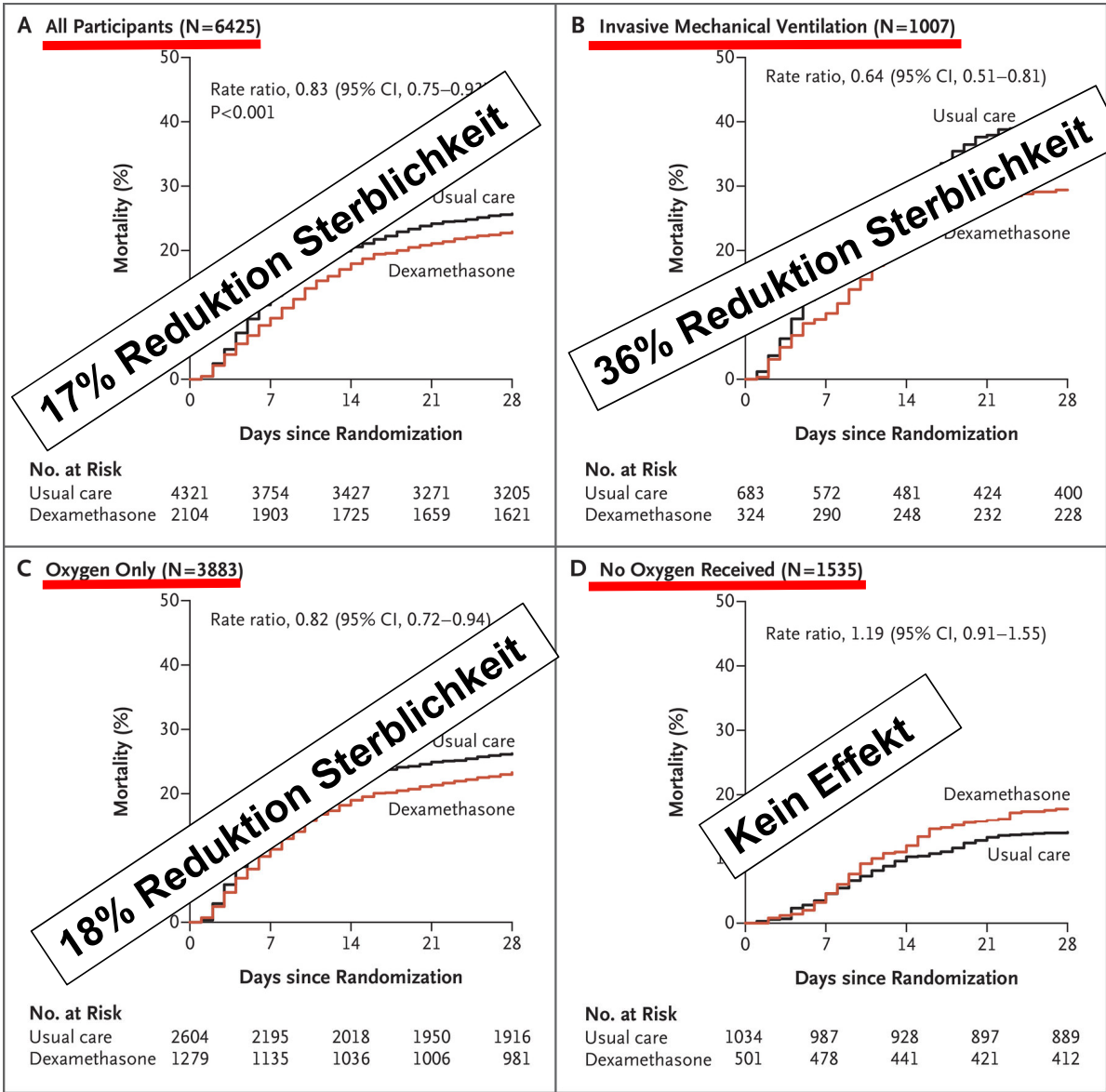
Coronavirus disease 2019 (Covid-19) is associated with diffuse lung damage. Glucocorticoids may modulate inflammation-mediated lung injury and thereby reduce progression to respiratory failure and death.

The members of the writing committee (Peter Horby, F.R.C.P., Wei Shen Lim, F.R.C.P., Jonathan R. Emberson, Ph.D., Marion Mafham, M.D., Jennifer L. Bell,

Dexamethason



- Dosierung: 6mg per os oder intravenös für 7-10 Tage
- Kosten der Therapie: ca. 20 CHF
- Weltweit verfügbar



JAMA | **Original Investigation** | **CARING FOR THE CRITICALLY ILL PATIENT**

Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19

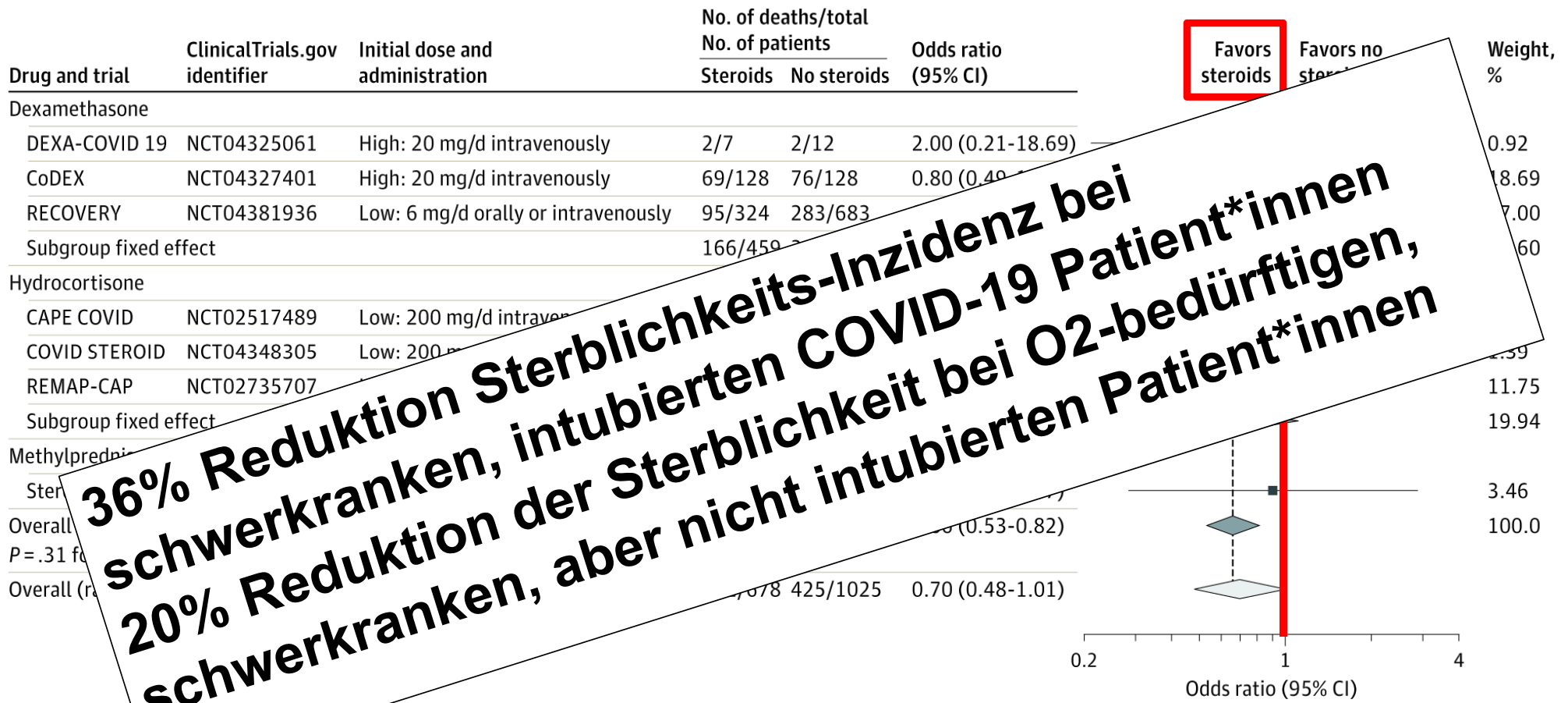
A Meta-analysis

The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group

IMPORTANCE Effective therapies for patients with coronavirus disease 2019 (COVID-19) are needed, and clinical trial data have demonstrated that low-dose dexamethasone reduced mortality in hospitalized patients with COVID-19 who required respiratory support.

OBJECTIVE To estimate the association between administration of corticosteroids compared with usual care or placebo and 28-day all-cause mortality.

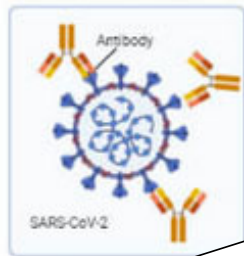
-  [Editorial page 1292](#)
-  [Related articles pages 1298, 1307, and 1317](#)
-  [Supplemental content](#)



Rekonvaleszentes Plasma

Use of Convalescent Plasma to Treat COVID-19 Patients

1 Antibodies that bind the SARS-CoV-2 (COVID-19) virus help patient recover

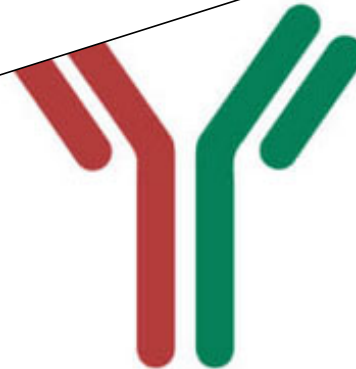
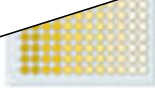


2 Recovered patient donates plasma rich with anti-SARS-CoV-2 antibodies



3 COVID-19 recieves donor plasma with antibodies

3 Plasma is tested for antibody strength and number



Möglicherweise Effekt bei früher Gabe bei Patienten auf Normalstation mit Sauerstoffbedarf Schnellere Negativierung der Sars-CoV-2 Viruslast

Fallvignette: 75-jähriger männlicher Patient zurück in der Praxis nach 2 Wochen Spital und 4 Wochen Reha

- Hospitalisation für 14 Tage auf Normalstation
 - Subsegmentale Lungenembolien
 - Therapeutisch niedermolekulares Heparin, aktuell für 3 Monate NOAK
 - Gabe von Remdesivir für 5 Tage
 - Gabe von Dexamethason für 10 Tage
- Aktuelle Beschwerden:
 - Ausgeprägte Müdigkeit mit Leistungsintoleranz
 - Vermehrtes Schwitzen
 - Anstrengungsdyspnoe
 - Mentale Verlangsamung, depressive Verstimmung, Angstattacken

Post COVID

thebmj Visual summary

"Long covid" in primary care

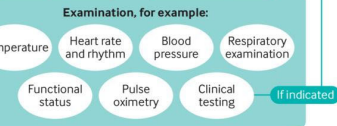
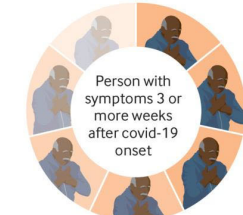
Assessment and initial management of patients with continuing symptoms

Post-acute covid-19 appears to be a multi-system disease, sometimes occurring after a relatively mild acute illness. Clinical management requires a whole-patient perspective. This graphic summarises the assessment and initial management of patients with delayed recovery from an episode of covid-19 that was managed in the community or in a standard hospital ward.

An uncertain picture
The long term course of covid-19 is unknown. This graphic presents an approach based on evidence available at the time of publication. However, caution is advised, as patients may present atypically, and new treatments are likely to emerge

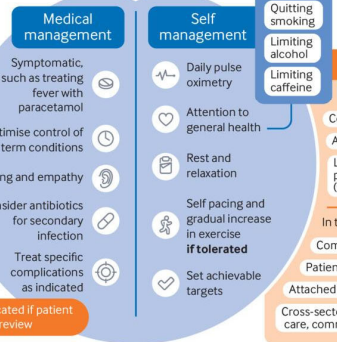
Managing comorbidities
Many patients have comorbidities including diabetes, hypertension, kidney disease or ischaemic heart disease. These need to be managed in conjunction with covid-19 treatment. Refer to condition specific guidance, available in the associated article by Greenhalgh and colleagues

Safety netting and referral
The patient should seek medical advice if concerned, for example:
Worsening breathlessness
PaO₂ < 96% Unexplained chest pain
New confusion Focal weakness
Specialist referral may be indicated, based on clinical findings, for example:
Respiratory if suspected pulmonary embolism, severe pneumonia
Cardiology if suspected myocardial infarction, pericarditis, myocarditis or new heart failure
Neurology if suspected neurovascular or acute neurological event
Pulmonary rehabilitation may be indicated if patient has persistent breathlessness following review



Investigations
Clinical testing is not always needed, but can help to pinpoint causes of continuing symptoms, and to exclude conditions like pulmonary embolism or myocarditis. Examples are provided below:
Blood tests
Full blood count, Electrolytes, Liver and renal function, Troponin, C reactive protein, Creatine kinase, D-dimer, Brain natriuretic peptides, Ferritin – to assess inflammatory and prothrombotic states
Other investigations
Chest x ray, Urine tests, 12 lead electrocardiogram

Social, financial, and cultural support
Prolonged covid-19 may limit the ability to engage in work and family activities. Patients may have experienced family bereavements as well as job losses and consequent financial stress and food poverty. See the associated article by Greenhalgh and colleagues for a list of external resources to help with these problems



Mental health
In the consultation:
Continuity of care
Avoid inappropriate medicalisation
Longer appointments for patients with complex needs (face to face if needed)
In the community:
Community linkworker
Patient peer support groups
Attached mental health support service
Cross-sector partnerships with social care, community services, faith groups

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Post COVID

thebmj Visual summary

"Long covid" in primary care

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Other investigations

- Chest x ray
- Urine tests
- 12 lead electrocardiogram

Clinical assessment

04

Full history
From date of first symptom

Current symptoms
Nature and severity

Examination, for example:

- Temperature
- Heart rate and rhythm
- Blood pressure
- Respiratory examination
- Functional status
- Pulse oximetry
- Clinical testing (if indicated)

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Assessing comorbidities

Have you considered... including diabetes, kidney disease or disease. These are aged in covid-19. If to condition is, available in article by colleagues

Setting and referral

When should you seek medical help, for example:

- Unexplained chest pain
- Focal weakness

Referral findings, for example:

- Neurology if suspected neurological event
- Cardiology if suspected myocardial infarction, pericarditis, myocarditis or new heart failure
- Neurology if suspected neurovascular or acute neurological event

Pulmonary rehabilitation may be indicated if patient has persistent breathlessness following review

Medical management

- Symptomatic, such as treating fever with paracetamol
- Optimise control of long term conditions
- Listening and empathy
- Consider antibiotics for secondary infection
- Treat specific complications as indicated

Self management

- Daily pulse oximetry
- Attention to general health
- Rest and relaxation
- Self pacing and gradual increase in exercise if tolerated
- Set achievable targets

Diet

- Sleep
- Quitting smoking
- Limiting alcohol
- Limiting caffeine

Mental health

In the consultation:

- Continuity of care
- Avoid inappropriate medicalisation
- Longer appointments for patients with complex needs (face to face if needed)

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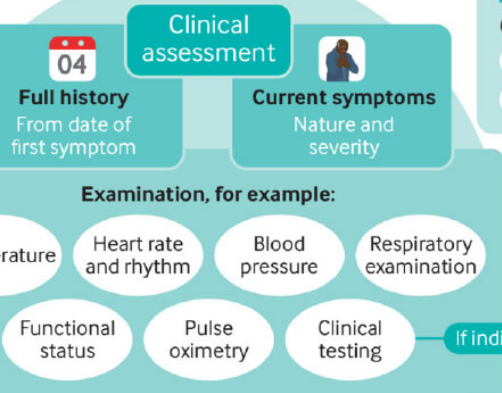
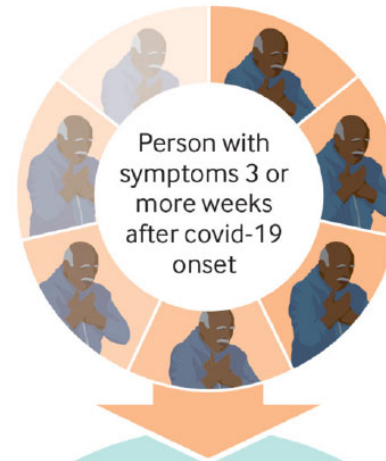
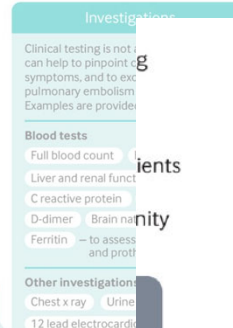
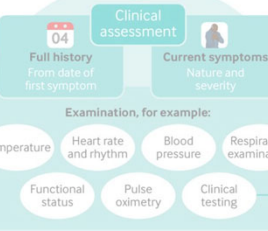
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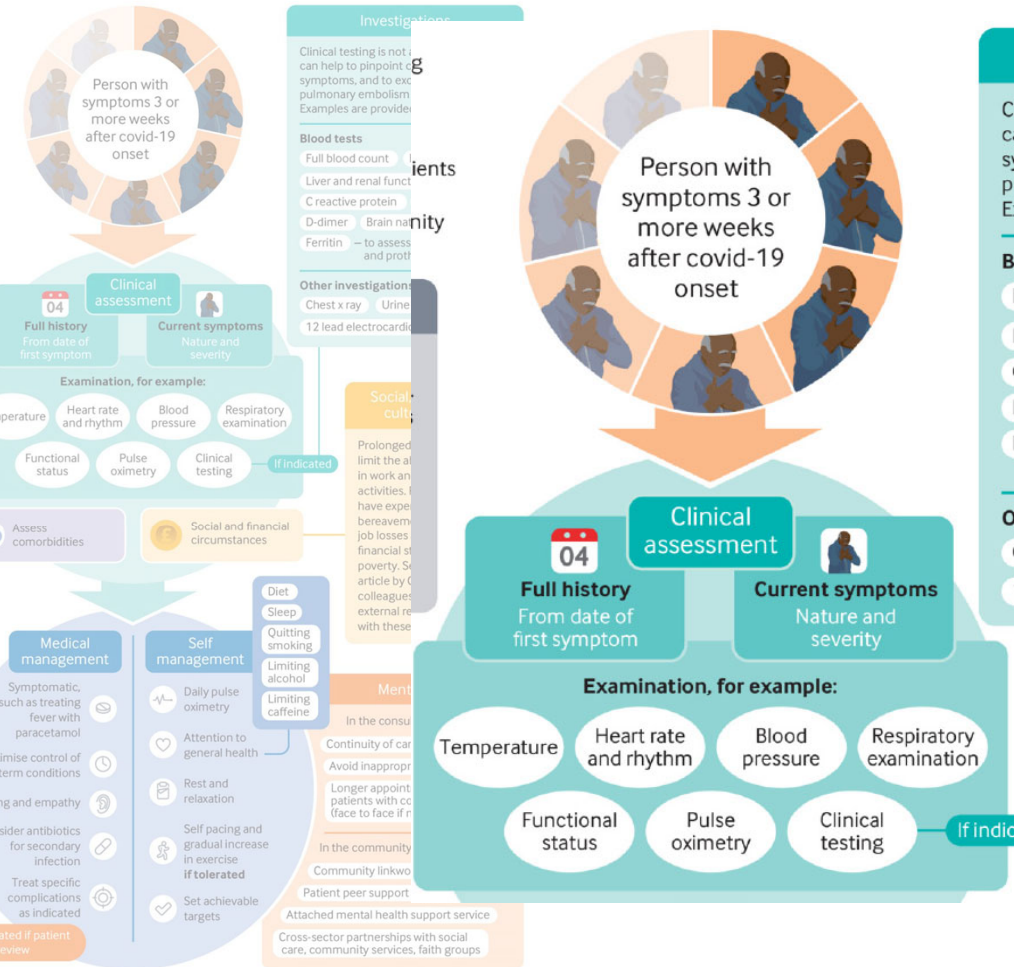
Post COVID

thebmj Visual summary

Post-acute covid-19 appears to be a multi-system disease, sometimes occurring after a relatively mild acute illness. Clinical management requires a whole-patient perspective. This graphic summarises the assessment and initial management of patients with delayed recovery from an episode of covid-19 that was managed in the community or in a standard hospital ward.

"Long covid" in primary care

Assessment and initial management of patients with continuing symptoms



Safety netting and referral

The patient should seek medical advice if concerned, for example:

- Worsening breathlessness
- PaO₂ < 96%
- Unexplained chest pain
- New confusion
- Focal weakness

Specialist referral may be indicated, based on clinical findings, for example:

- Respiratory** if suspected pulmonary embolism, severe pneumonia
- Cardiology** if suspected myocardial infarction, pericarditis, myocarditis or new heart failure
- Neurology** if suspected neurovascular or acute neurological event

Pulmonary rehabilitation may be indicated if patient has persistent breathlessness following review

Medical management

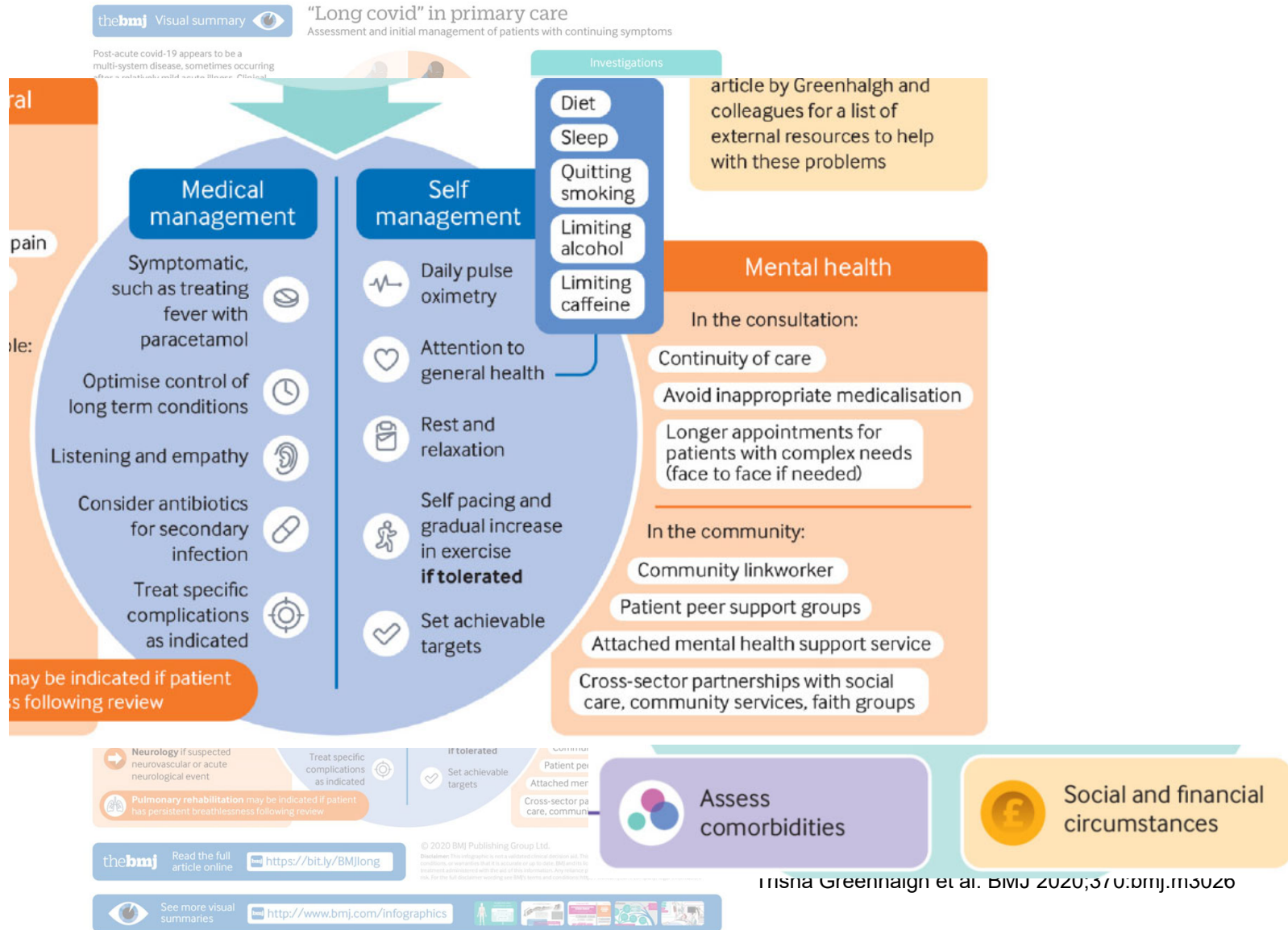
- Symptomatic, such as treating fever with paracetamol
- Optimise control of long term conditions
- Listening and empathy
- Consider antibiotics for secondary infection
- Treat specific complications as indicated

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Post COVID



Konklusion

- Aktuell keine spezifische Therapie für COVID-19 Infektion im ambulanten Rahmen zugelassen oder empfohlen
- Eine bakterielle Super-Infektion bei COVID-19 ist selten und Antibiotika meistens nicht indiziert
- Die Indikation zur Hospitalisation basiert auf klinischen Kriterien:
 - Progrediente Dyspnoe
 - SaO₂ bei Raumluft <92% bzw. Sauerstoffbedarf
- Thrombo-embolische Ereignisse sind häufig und sollten niederschwellig gesucht werden
- Aktuell 2 Therapeutika *standard of care* bei hospitalisierten Patienten mit Sauerstoffbedarf:
 - Remdesivir für 5 Tage im frühen Stadium der Behandlung
 - Dexamethason 6mg per os für 7-10 Tage inkl. intubierte Patienten
- Post-akutes COVID-19 Syndrom in ca. 10-30%
 - Hohe Rate an Spontanheilung
 - Angepasstes, graduelles sportliches Training
 - Symptom-basierte Abklärungen (z.B. EKG Ausschluss Perimyokarditis, CT Thorax Ausschluss LE)