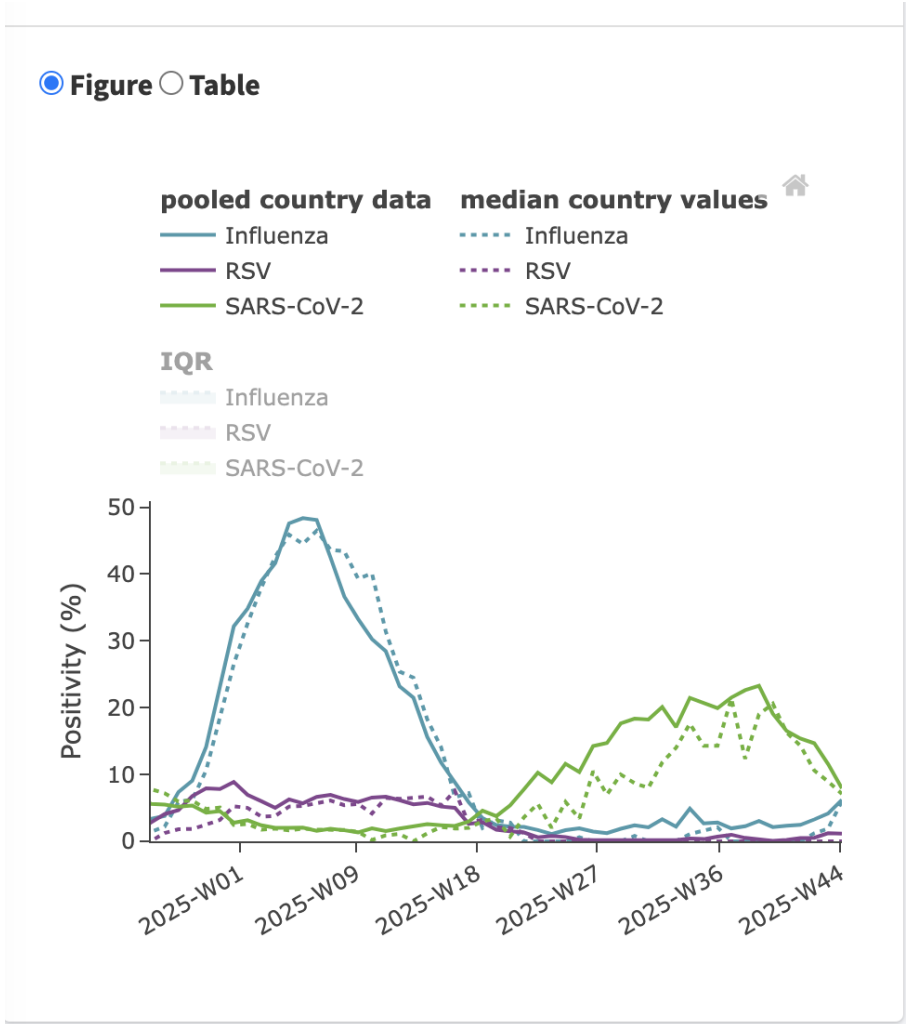
Zgodnje zdravljenje covida v postpandemičnem obdobju

Gabriele Turel

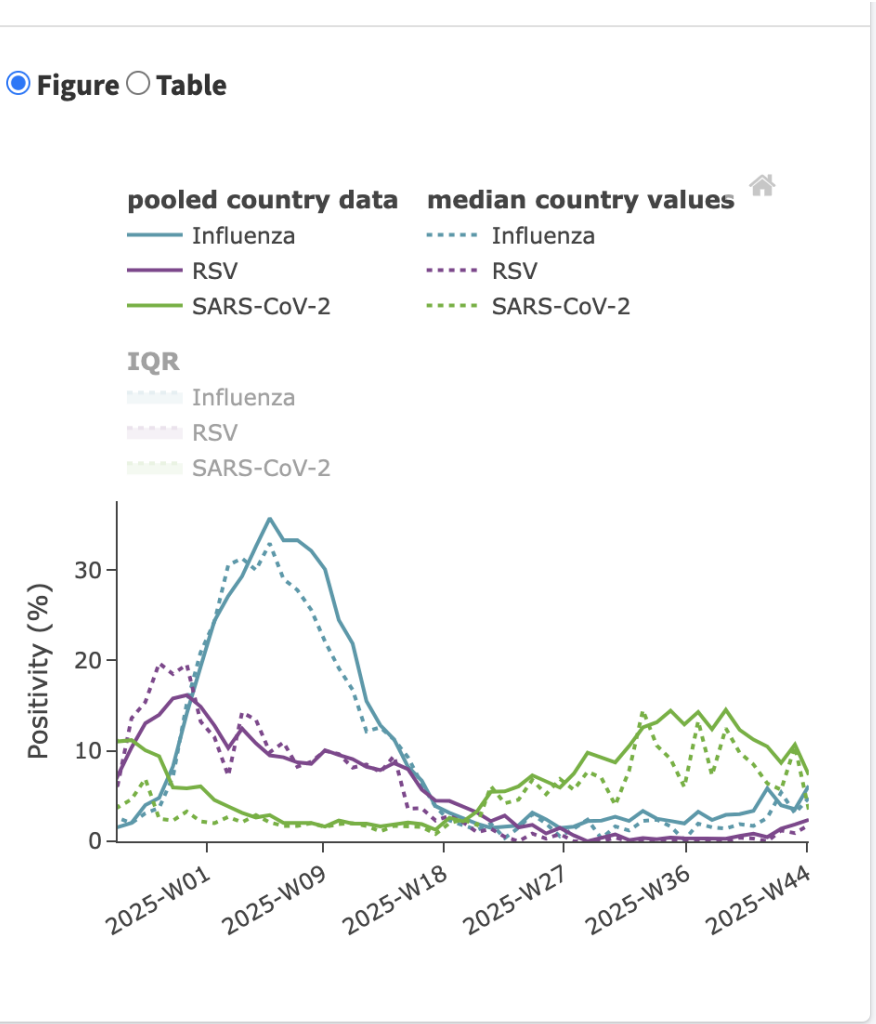
KIBVS 13.11.2025

Kje smo trenutno z ILI (Influenza like ilness)? – podatki ERVISS

Primarno zdravstvo

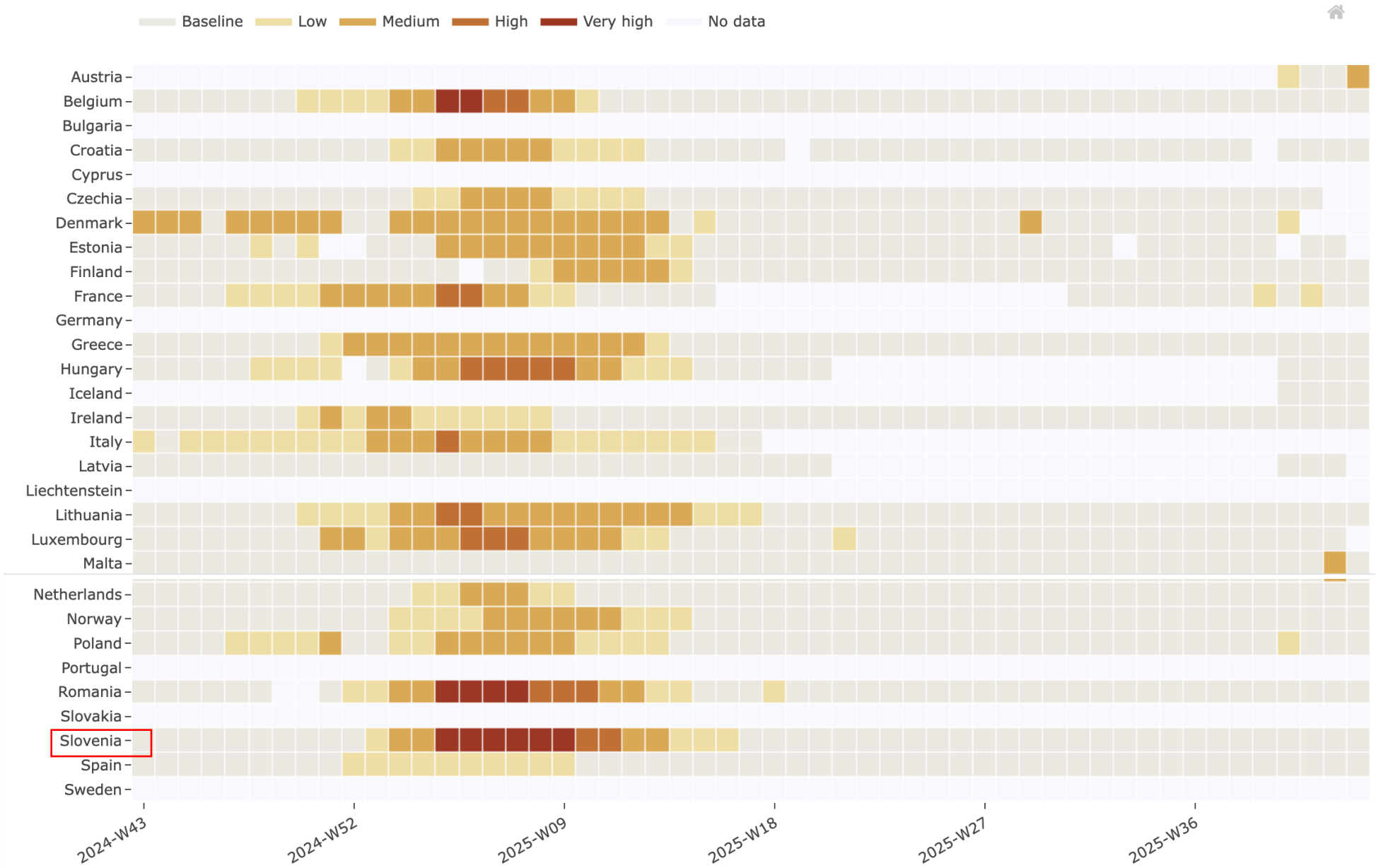


Bolnišnice

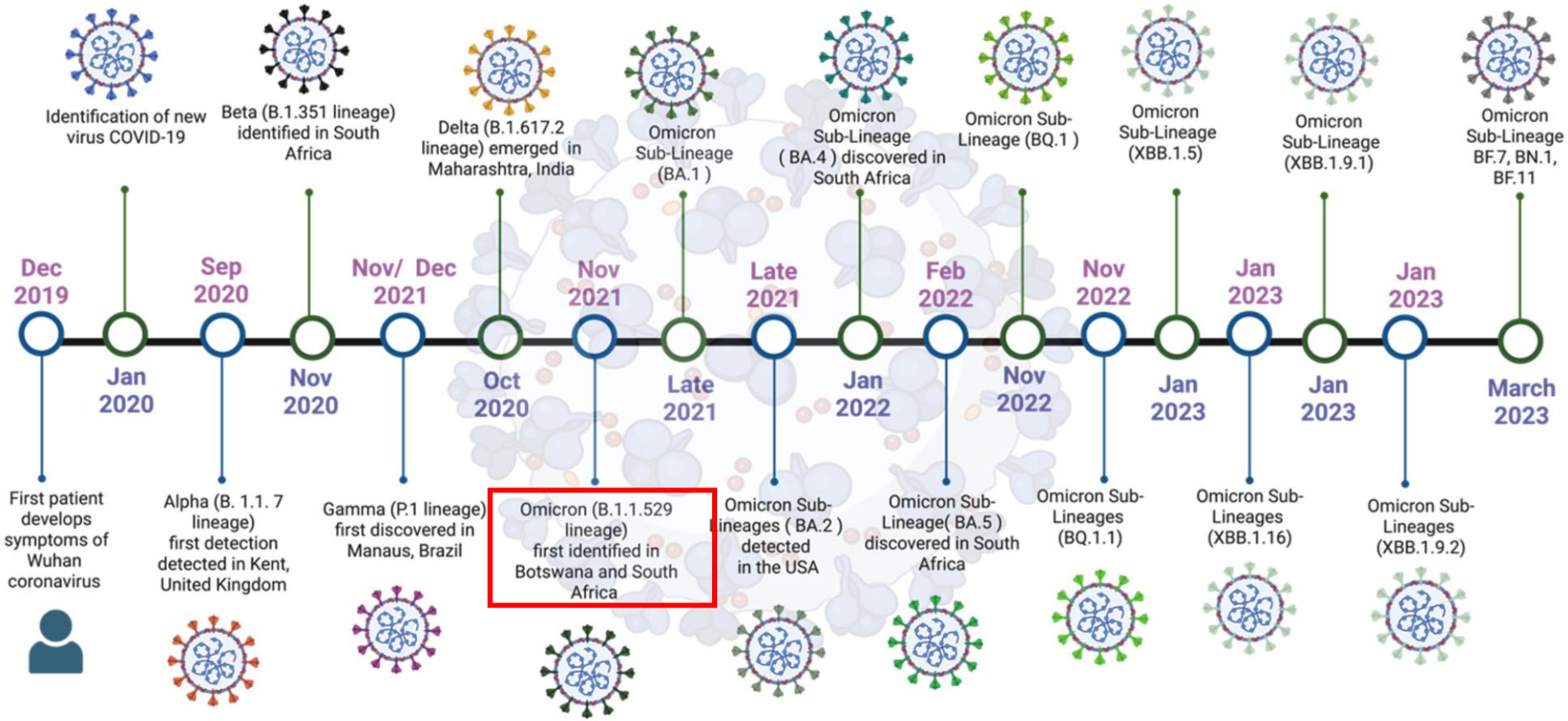


ECDC, 12.11.2025

Weekly intensity of influenza-like illness (ILI) activity by country

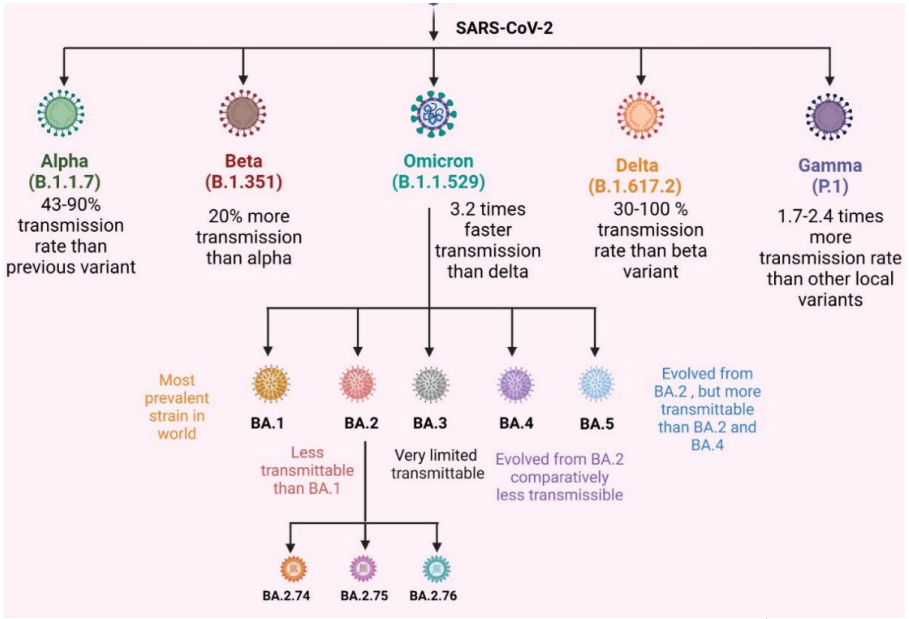


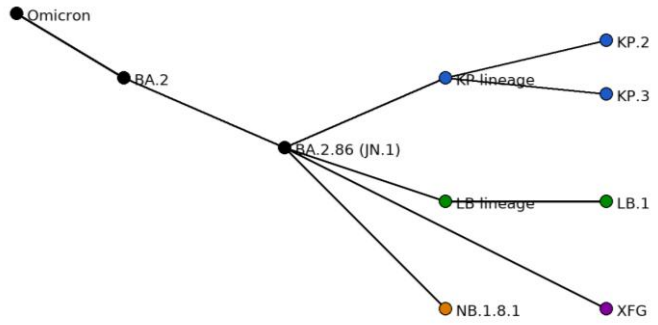
SARS-Coronavirus-2 and its variants
A Timeline

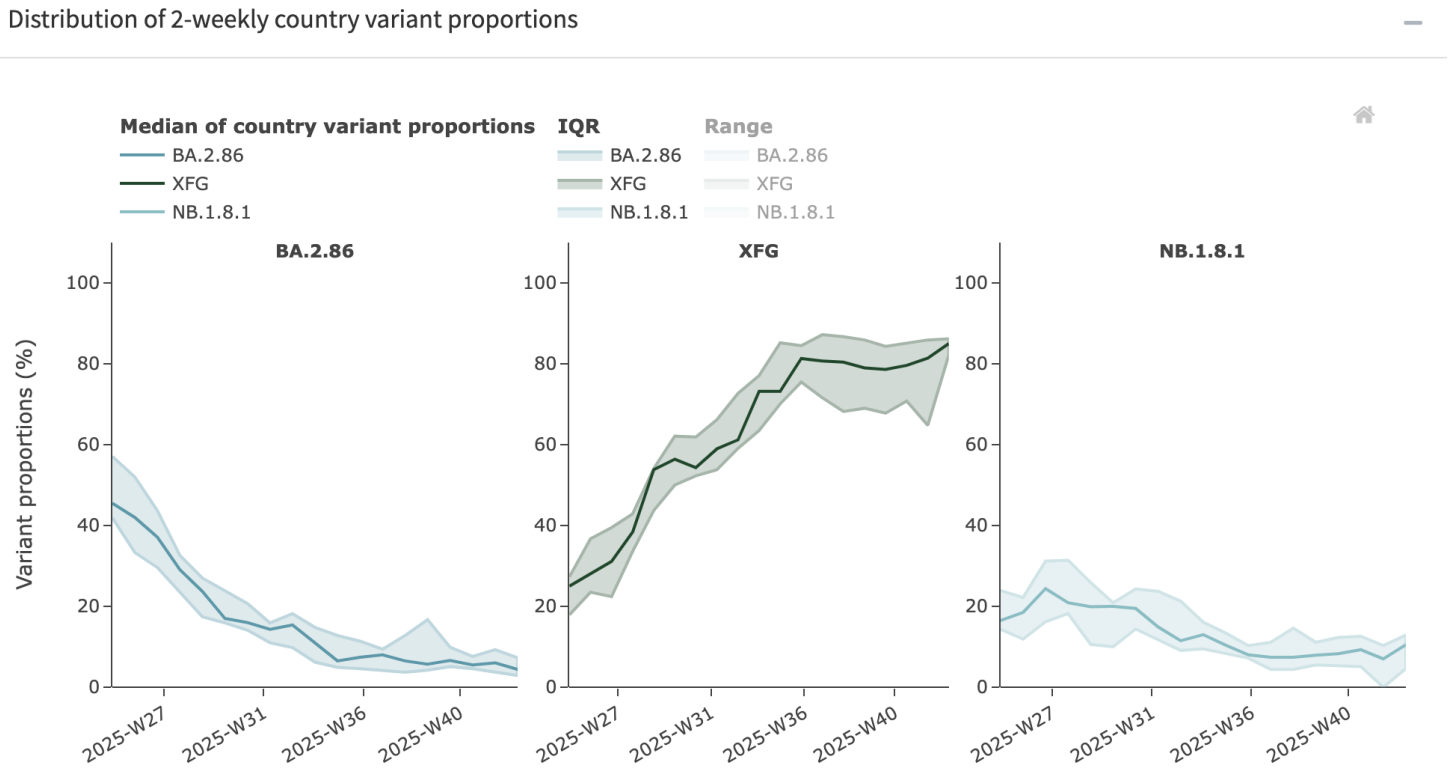


Prevladujoče podvariante c19

- ECDC, november 2025







Teža bolezni se zmanjšuje

- WHO je 5.5.2023 razglasila konec pandemije covid 2019
- Teganje je postalo obvadljivo za javno zdravje
- Bolnišnice niso več zavezane k poročanju o hospitalizacijah
- Covidna pljučnica je redkost
- Razlog?
  - Populacijska imunost
  - Nižja virulenca

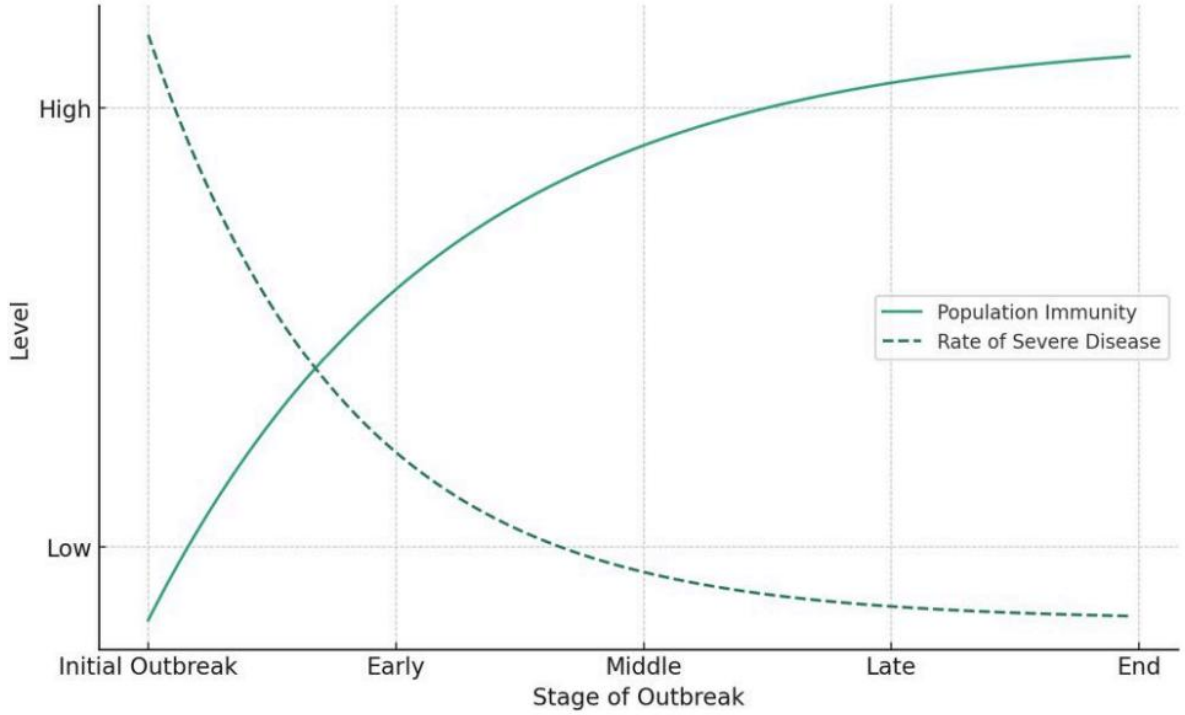
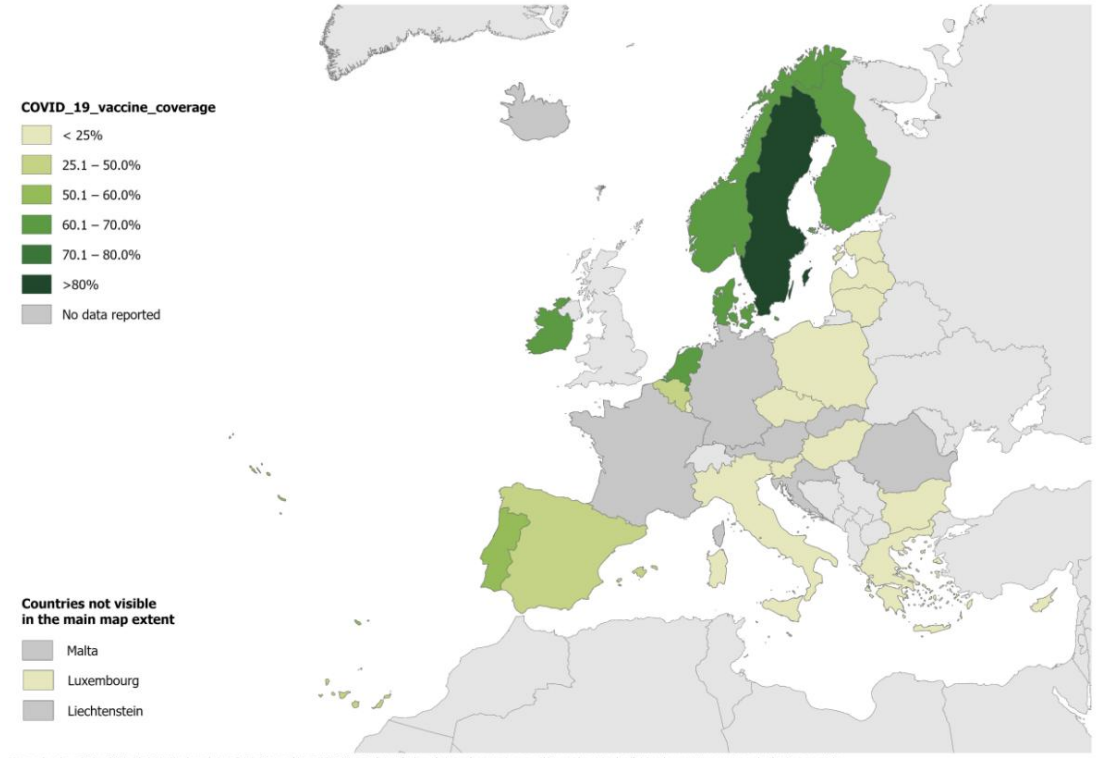


Figure 1. Population immunity versus rate of severe disease over stages of the outbreak.

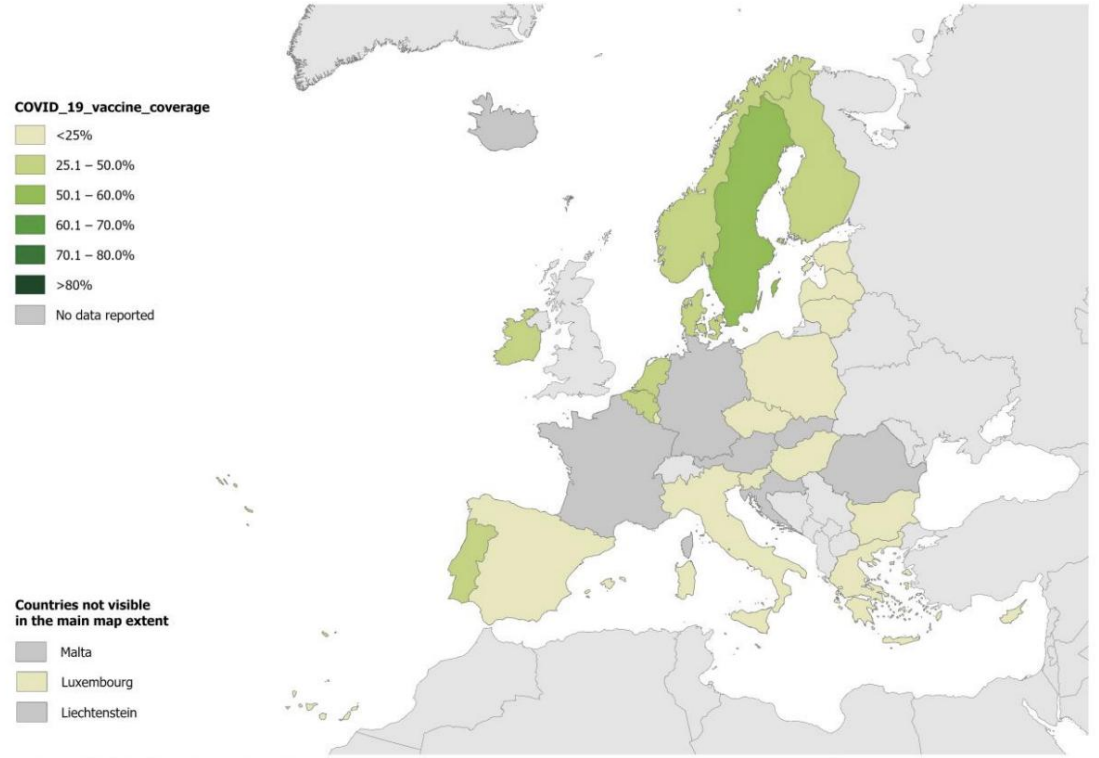
Precepljenost, ECDC

Figure 2. COVID-19 vaccine coverage among people aged 80 years and above, 21 EU/EEA countries, 1 August 2024 to 28 March 2025



Map produced on: 23 Apr 2025. Administrative boundaries: © EuroGeographics © UN–FAO © Turkstat.The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union.

Figure 1. COVID-19 vaccine coverage among people aged 60 years and above, 21 EU/EEA countries, 1 August 2024 to 28 March 2025



Map produced on: 7 May 2025. Administrative boundaries: © EuroGeographics © UN–FAO © Turkstat.The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union.

Letter to the editor...

Clinical Infectious Diseases

CORRESPONDENCE

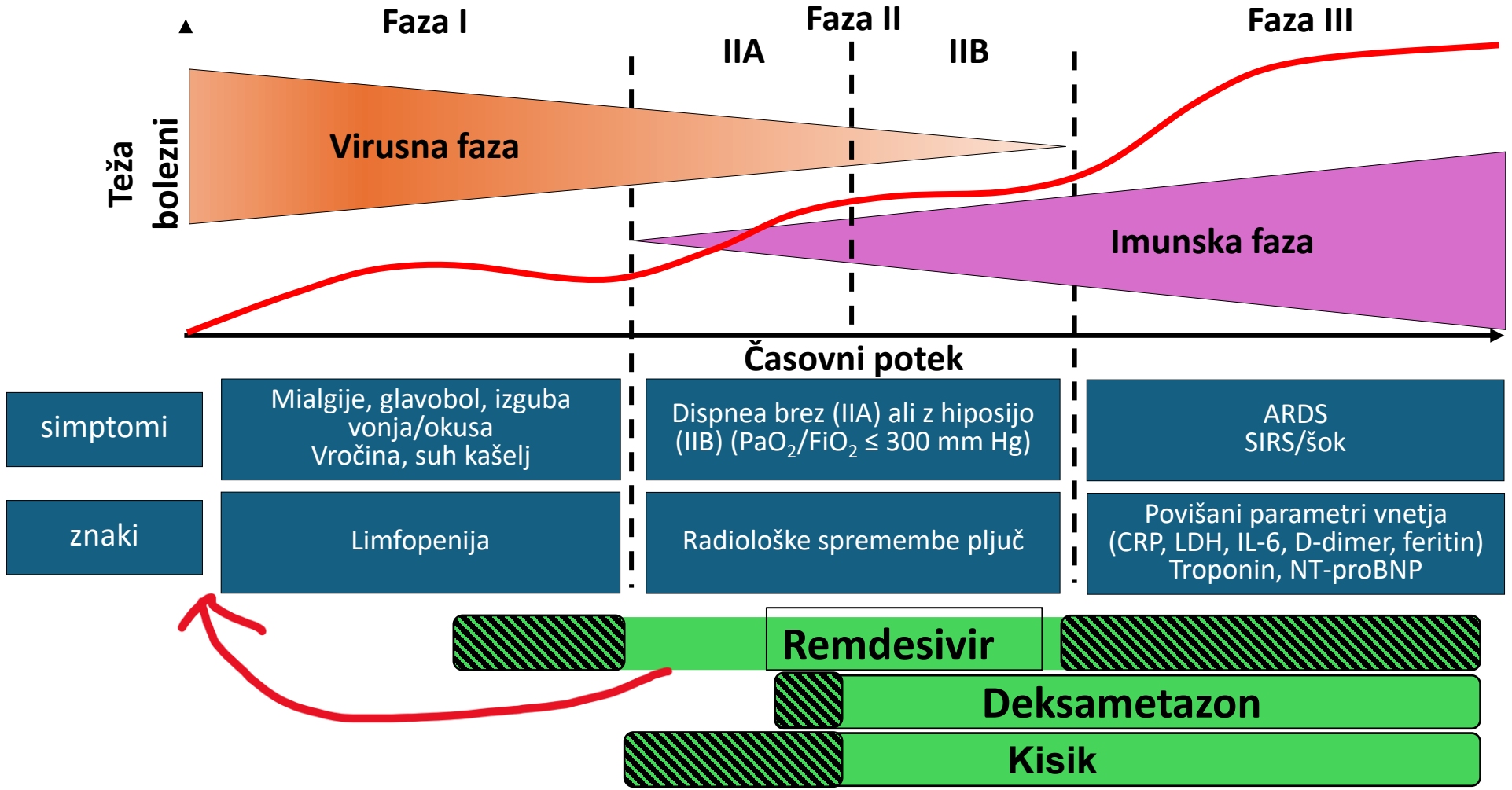
Recalibrating COVID-19 Booster Policy: Lessons From Hybrid Immunity and Global Equity Gaps

Nathkapach K. Rattanapitoon,[1] Nav La,[2] Chutharat Thanchonnang,[3] Schawanya K. Rattanapitoon[1]

- Imunost po cepljenju je krakotrajna – cca 6 mes
- Predlaga
  - Zelo tvegane skupine: 2x letno
  - Zmerno tvegane: 1x leto

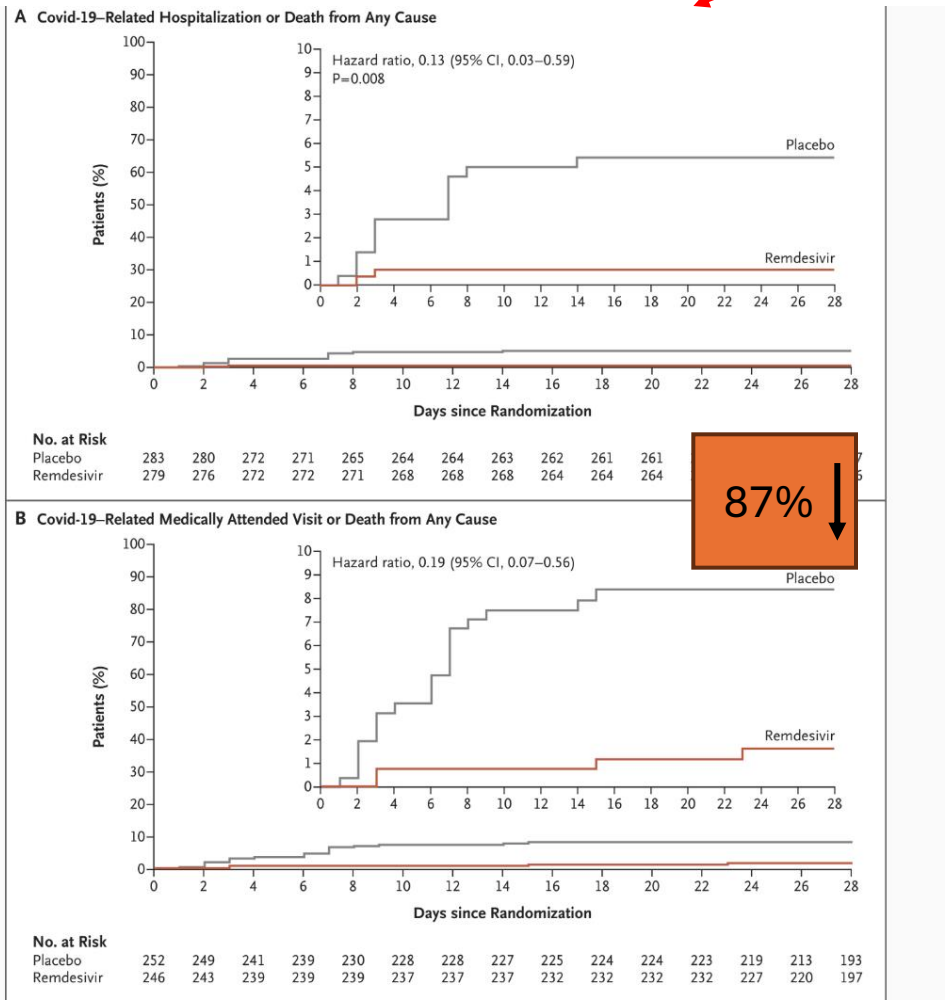
Tudi zdravljenje covida ima svoj razvoj

smernice se sklepajo “za nazaj”



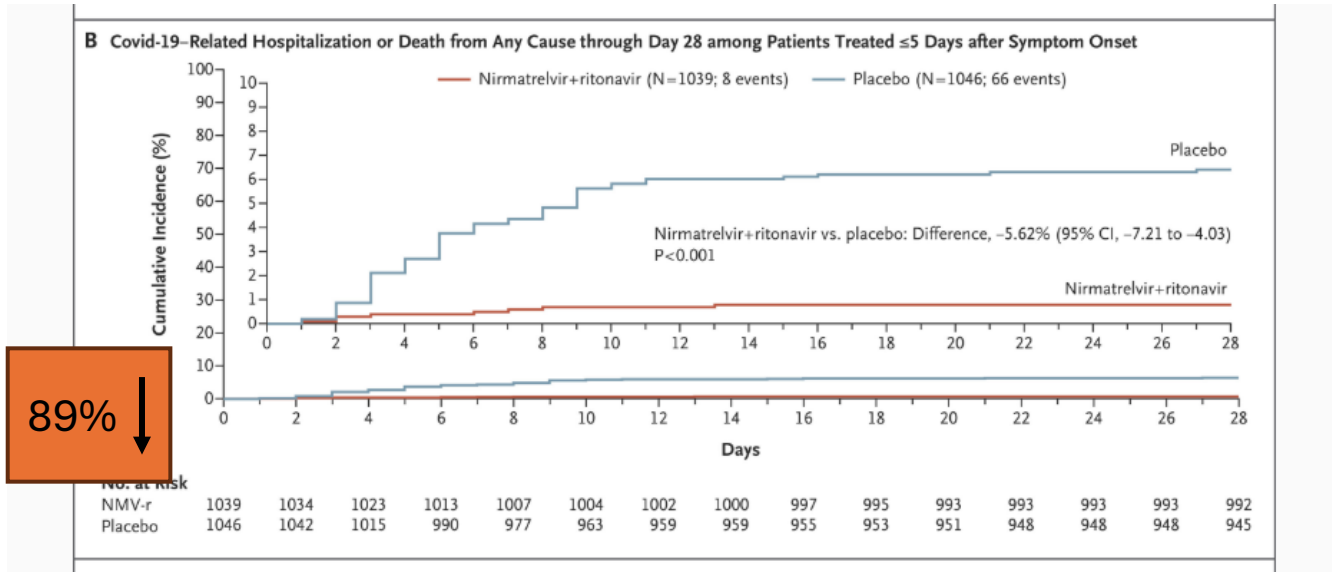
Siddiqi. J Heart Lung Transplant. 2020;39:405.

Remdesivir in Paxlovid



87%

From September 18, 2020, through April 8, 2021



89%

Between July 16 and December 9, 2021

Ali je fazi Omicrona še vedno tako?

Clinical Infectious Diseases

MAJOR ARTICLE

A Systematic Review and Meta-analysis of the Effectiveness of Remdesivir to Treat SARS-CoV-2 in Hospitalized Patients: Have the Guidelines Evolved With the Evidence?

Michele Bartoletti,[1,2] Essy Mozaffari,[3] Alpesh N. Amin,[4] Yohei Doi,[5,6] Paul Loubet,[7] Christina G. Rivera,[8] Michael Roshon,[9] Aaditya Rawal,[10] Emily Kaiser,[11] Maria Vutcovici Nicolae,[12] Shuai Fu,[12] Thomas F. Oppelt,[3] Mel Chiang,[3] Paul E. Sax,[13] and Andre C. Kalil[14]

- Sistematični pregled literature
- Zožili na 122 študij (21 RCT + 101 RW študij) – feb 2020 do apr 2022
- 25 174 pt. RCT + 1 279 859 pt. RW

Study	Design	N	Patients Not Requiring Oxygen, %	Treatment Duration, d	28/30-d Mortality	OR (95% CI)
ACTT-1, Beigel et al 2020	RCT	1051	13	10		0.71 (.50–1.02)
SIMPLE-Severe, Olender et al 2021	RCT	1767	14.1	5–10		0.70 (.50–1.00
Solidarity, Henao-Restrepo et al 2022	RCT	8275		10		0.92 (.82–1.04)
Wang 2020*	RCT	227	2	10		1.15 (.52–2.57)
Subsummary (RCT) (τ = 0; *P* = .053)						**0.90 (.81–1.02)**
Bechman et al 2022	Prospective cohort study	3949				0.63 (.51–.79)
Finn et al 2022	Prospective cohort study	2111				1.05 (.79–1.38)
Benfield et al 2021**	Retrospective study	2747				0.59 (.48–.72)
Caffrey et al 2023*	Retrospective study	16 416	16.8			0.58 (.50–.68)
Chokalingam et al 2022*	Retrospective study	49 712	64.2			0.93 (.89–.98)
De Vito et al 2022*	Retrospective study	1080				0.16 (.10–.25)
Diaz et al 2022*	Retrospective study	1138	36.9	5–10		0.56 (.37–.85)
Dobrowolska et al 2023 Delta period et al (May–Nov 2021)*	Retrospective study	1170		5–10		0.40 (.29–.56)
Dobrowolska et al 2023 Omicron period et al (Dec 2021–Apr 2022)*	Retrospective study	652		5–10		0.64 (.40–1.01)
Garibaldi et al 2022*	Retrospective study	1856	14.6	5		0.48 (.36–.64)
Leding et al 2023**	Retrospective study	3642	55.8			0.42 (.32–.55)
Marx et al 2022	Retrospective study	88	12.5			0.20 (.05–.75)
Mozaffari et al 2022*	Retrospective study	57 710	27.6			0.77 (.74–.81)
Mozaffari et al 2023 Delta period (May–Nov 2021)	Retrospective study	137 098	35			0.87 (.84–.89)
Mozaffari et al 2023 Omicron period (Dec 2021–Apr 2022)	Retrospective study	65 852	35			0.78 (.74–.81)
Mozaffari et al 2023 pre-Delta period (Dec 2020–Apr 2021)	Retrospective study	126 632	35			0.81 (.79–.84)
Subsummary (RWS) (τ = 0.387; *P* < .001)						**0.60 (.47–.76)**
Total summary (τ = 0.353; *P* = .001)						**0.69 (.55–.86)**

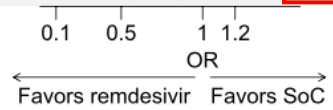
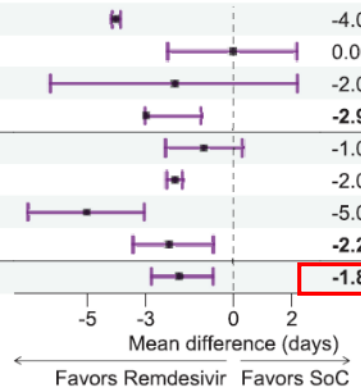


Figure 2. Forest plot for mortality at 28–30 days in hospitalized patients with coronavirus disease 2019, overall population [24–26, 28–34, 37–43]. *Corticosteroids were used in both remdesivir and no-remdesivir groups. **Corticosteroids were used in all patients receiving remdesivir. Note that the odds ratios (ORs) reported in the plot resulted from the meta-analysis based on the number of events reported in the original studies. The Solidarity trial assessed in-hospital mortality regardless of whether deaths occurred before or after day 28. Abbreviations: CI, confidence interval; RCT, randomized controlled trial; RWS, real-world study; SoC, standard of care.

Klinično izboljšanje

Supplemental Figure S3. Forest plot for time to clinical improvement in hospitalized COVID-19 patients, overall population

Study	Design	N	%Not requiring oxygen	Treatment duration (days)	MD (95% CI)
ACTT-1, Beigel 2020	RCT	1062	13%	10	-4.00 (-4.15 to -3.85)
DisCoVeRy, Ader 2021*	RCT	832		5-10	0.00 (-2.23 to 2.18)
Wang 2020*	RCT	236	2%	10	-2.00 (-6.27 to 2.19)
Sub-summary (RCT) (tau=0, p<0.001)					**-2.98 (-3.01 to -1.09)**
Wong 2022a	Retrospective database study	1544	73.8%	5-10	-1.00 (-2.30 to 0.32)
Garibaldi 2022*	Retrospective study	36656	14.6%	5	-2.00 (-2.27 to -1.73)
Viray 2023	Retrospective study	318			-5.00 (-7.02 to -3.04)
Sub-summary (RWS) (tau=0.171, p=0.002)					**-2.20 (-3.43 to -0.67)**
Total summary (tau=0.158, p=0.001)					**-1.84 (-2.81 to -0.69)**



* Corticosteroids were used in both remdesivir and no remdesivir groups.
MD, mean difference; RCT, randomized controlled trial; RWS, real world study; SoC, standard of care.
Note: The MDs reported in the plot resulted from the meta-analysis based on the number of events reported in the original studies.

Ozdravitev

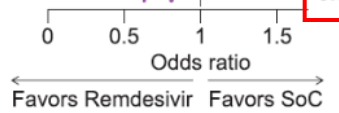
- 3 študije (1RCT, 2RW)

Metaanaliza: ni vpliva na čas do ozdravitve (srednja razlika: −0.31 [95% CI, −3.37 to 3.94])

Ponovna hospitalizacija

Supplemental Figure S4. Forest plot for risk of rehospitalization in hospitalized COVID-19 patients, overall population

Study	Design	N	%Not requiring oxygen	Treatment duration (days)	OR (95% CI)
ACTT-1, Beigel 2020	RCT	1062	13%	10	1.66 (0.88 to 3.11)
Finn 2022	Prospective cohort study	2111			0.68 (0.50 to 0.92)
Caffrey 2023*	Retrospective study	16416	16.8%		0.66 (0.59 to 0.73)
Mozaffari 2023 Delta period (May21-Nov21)	Retrospective study	127393	41%		0.63 (0.61 to 0.66)
Mozaffari 2023 Omicron period (Dec21-Apr22)	Retrospective study	81300	41%		0.87 (0.83 to 0.91)
Mozaffari 2023 Pre-delta period (Dec20-Apr21)	Retrospective study	231908	41%		0.66 (0.64 to 0.68)
Sub-summary (RWS) (tau=0.11, p<0.001)					**0.70 (0.63 to 0.78)**
Total summary (tau=0.11, p<0.001)					**0.72 (0.64 to 0.81)**



* Corticosteroids were used in both remdesivir and no remdesivir groups.
OR, odds ratio; RCT, randomized controlled trial; RWS, real world study; SoC, standard of care.
Note: The ORs reported in the plot resulted from the meta-analysis based on the number of events reported in the original studies.

Clinical Infectious Diseases

MAJOR ARTICLE

Infectious Diseases Society of America

HIV Medicine Association

OXFORD

Real-World Effectiveness of Nirmatrelvir-Ritonavir in Preventing Coronavirus Disease 2019–Associated Hospitalization: A Population-Based Cohort Study in the Province of Québec, Canada

Jean-Luc Kaboré,[1,©] Benoît Laffont,[1] Mamadou Diop,[1] Melanie R. Tardif,[1] Alexis F. Turgeon,[2,3] Jeannot Dumaresq,[4,5] Me-Linh Luong,[6] Michel Cauchon,[7] Hugo Chapdelaine,[8,9] David Claveau,[10] Marc Brosseau,[11,12] Elie Haddad,[13] and Mike Benigeri[1]

- 16 601 : 242 337 = Paxlovid : kontrolna skupina
- 15. Mar – 15. Okt 2022
- Omicron (BA.2 in BA 4/5)

- 74% zmanjšanje verjetnosti za hospitalizacijo v skupini, ki je prejela zdravljenje
  - Neglede na cepilni status (cepljeni še bolje)
  - Niso imeli podatka o prebolevnosti

CID, okt 2025

Table 4. Risk of Hospitalizations Among Outpatients With High Risk of Progression to Severe Coronavirus Disease 2019 Who Received Nirmatrelvir-Ritonavir Prescription, Compared With Controls

Primary Vaccination Status	Group	Before Propensity Score Matching			After Propensity Score Matching					
		Population, No.	Hospitalizations		Population	Hospitalizations		Adjusted Poisson Regression With Robust Error Variance[a]		
			No.	%	No.	No.	%	RR	95% CI	*P* Value
All (incomplete and complete primary vaccination)	Control	242 337	8293	3.4	14 756	1293	8.8	**1**	…	…
	Treated	16 601	356	2.1	14 756	325	2.2	**0.26**	**.23–.29**	**<.001**
Incomplete primary vaccination[b]	Control	18 123	1054	5.8	1300	166	12.8	**1**	…	…
	Treated	1548	31	2.0	1300	21	1.6	**0.13**	**.08–.20**	**<.001**
Complete primary vaccination (all)[c]	Control	224 214	7239	3.2	13 310	1060	8.0	**1**	…	…
	Treated	15 053	325	2.2	13 310	290	2.2	**0.28**	**.25–.32**	**<.001**
Last vaccine dose ≤6 mo prior	Control	139 544	4987	3.6	10 202	806	7.9	**1**	…	…
	Treated	11 538	249	2.2	10 202	228	2.2	**0.29**	**.25–.33**	**<.001**
Last vaccine dose >6 mo prior	Control	84 670	2252	2.7	2846	245	8.6	**1**	…	…
	Treated	3515	76	2.2	2846	57	2.0	**0.24**	**.18–.31**	**<.001**
Age <70 y (all)	Control	183 690	2037	1.1	6879	214	3.1	**1**	…	…
	Treated	8335	93	1.1	6879	78	1.1	**0.36**	**.28–.47**	**<.001**
Age <70 y (last dose ≤6 mo prior)	Control	105 265	1136	1.1	4766	135	2.8	**1**	…	…
	Treated	5927	67	1.1	4766	54	1.1	**0.40**	**.29–.55**	**<.001**
Age <70 y (last dose >6 mo)	Control	78 425	901	1.2	1933	54	2.8	**1**	…	…
	Treated	2408	26	1.1	1933	20	1.0	**0.37**	**.22–.61**	**<.001**
Age ≥70 y (all)	Control	40 524	5202	12.8	6176	841	13.6	**1**	…	…
	Treated	6718	232	3.5	6176	197	3.2	**0.23**	**.20–.27**	**<.001**
Age ≥70 y (last dose ≤6 mo prior)	Control	34 279	3851	11.2	5252	641	12.2	**1**	…	…
	Treated	5611	182	3.2	5252	167	3.2	**0.26**	**.22–.31**	**<.001**
Age ≥70 y (last dose >6 mo prior)	Control	6245	1351	21.6	835	181	21.7	**1**	…	…
	Treated	1107	50	4.5	835	27	3.2	**0.15**	**.10–.22**	**<.001**
Severely immunocompromised (all)	Control	2012	452	22.5	1096	224	20.4	**1**	…	…
	Treated	1388	70	5.0	1096	61	5.6	**0.28**	**.21–.36**	**<.001**
Severely immunocompromised (last dose ≤6 mo prior)	Control	1502	334	22.2	769	145	18.9	**1**	…	…
	Treated	1057	51	4.8	769	41	5.3	**0.29**	**.21–.40**	**<.001**
Severely immunocompromised (last dose >6 mo prior)	Control	510	118	23.1	304	58	19.1	**1**	…	…
	Treated	331	19	5.7	304	19	6.3	**0.32**	**.20–.52**	**<.001**

Abbreviations: CI, confidence interval; RR, relative risk.

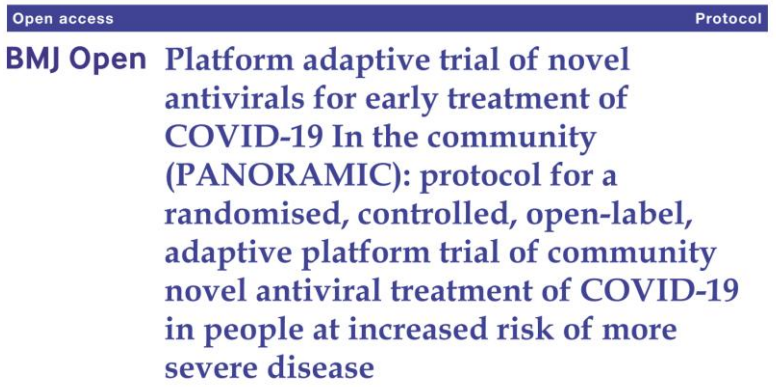
[a]Confounding variables used to create propensity score were included in the final regression model and comprised age, sex, region of residence, number of vaccine dose, time since last vaccine dose, coronavirus disease 2019 (COVID-19) wave, number of health conditions, respiratory and cardiovascular condition, immunosuppression condition, cancer conditions.

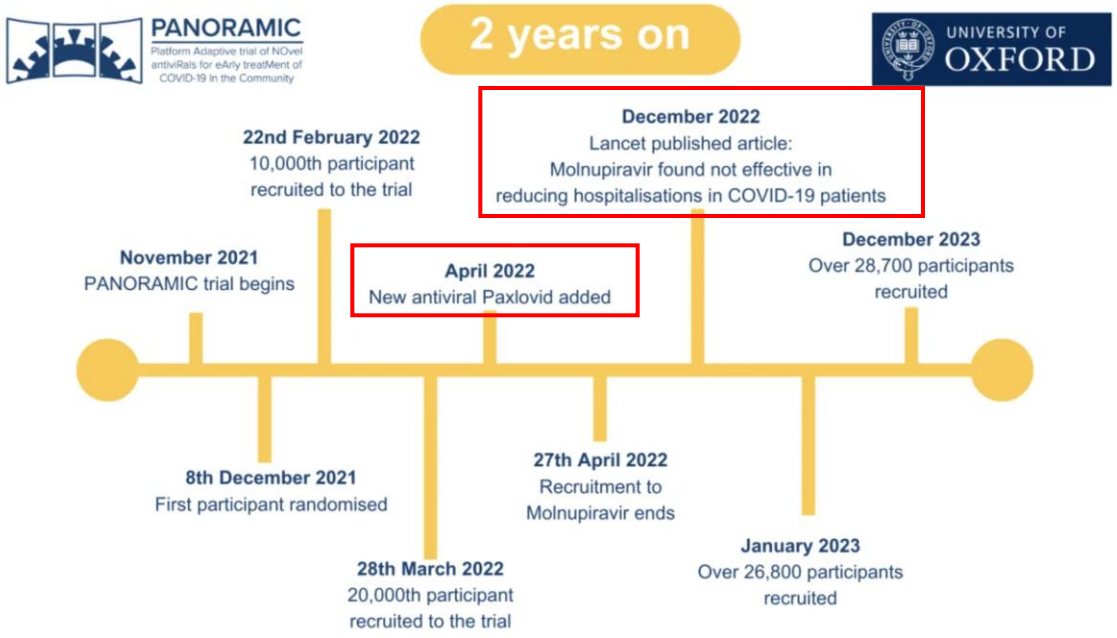
[b]The population with an incomplete primary vaccination course included participants who received no vaccine or only 1 dose of COVID-19 vaccine.

[c]The population with a complete primary vaccination course included participants who received ≥2 doses of vaccine.

Največja svetovna covid19 kohorta

- Zgodnje zdravljenje C19
- Remdesivirja ne preučujejo
- Podatkov za Paxlovid še ni
- **Molnupiravir**
  - Ne zmanjša tveganja za hospitalizacijo ali smrt med cepljenimi z visokim tveganjem
  - Okrevajo 4 dni hitreje
  - Nekoliko manj obremenjujejo zdravstveno službo
  - Zmanjša količino virusa v brisih





Clinical Infectious Diseases

EDITORIAL COMMENTARY

Is Paxlovid Still Worth It?

Jeremy Samuel Faust[1] **and Gideon Meyerowitz-Katz**[2]

[1]Brigham and Women's Hospital Department of Emergency Medicine, Mass General Brigham Division of Health Services Research, Harvard Medical School, Boston, Massachusetts, USA; and [2]School of Health and Society, University of Wollongong, New South Wales, Australia

Table 1. Costs to prevent a COVID-19 hospitalization under different scenarios.

Study[a]	ARR, % (Rate Untreated or Placebo–Rate Paxlovid)	NNT	Cost in US$ (Initial Price) to Prevent 1 Hospitalization[b]	Cost in US$ (Current Price) to Prevent 1 Hospitalization[c]	Net Cost in US$ (Initial Price, Initial Hospitalization Cost)[d]	Net Cost in US$ (Current Price and Current Mean Hospitalization Cost)[e]
All ages						
EPIC-HR	5.5 (6.3–0.8)	18	9636	25 273	−12 116	12 201
Arbel et al	0.5 (1.0–0.5)	200	106 000	278 000	84 248	264 928
Aggarwal et al	0.6 (1.4–0.9)	167	88 333	231 667	66 581	218 595
Age ≥65 y						
EPIC-HR	13.8 (14.6–0.8)	7	3841	10 072	−17 911	−3000
Arbel et al	1.3 (1.8–0.4)	77	40 769	106 923	19 017	93 851
Aggarwal et al	2.0 (3.3–1.3)	50	26 500	69 500	4748	56 428
Age <65 y						
EPIC-HR	4.3 (5.1–0.8)	23	12 326	32 326	−9426	19 254
Arbel et al	No benefit	∞	∞	∞	∞	∞
Aggarwal et al	0.3 (1.0–0.7)	333	176 667	463 333	154 915	450 261

	Study Dates	Era	Immune Status			
EPIC-HR: 18–64 y	16 Jul–9 Dec 2021	Delta	Unvaccinated, no prior infection	…	…	…
Arbel et al: 40–64 y	9 Jan–31 Mar 2022	Early Omicron	>90% previous immunity in treatment group	…	…	…
Aggarwal et al: 18–64 y	26 Mar–25 Aug 2022	Omicron subvariant	Most ≥3 doses	…	…	…

Pri osebah > 65 let se je stopnja slabih izidov pri nezdravljenih z visokim tveganjem zmanjšala iz 14.6% (EPIC-HR) na 1,3-3-3% (opazovalne študije) in
NNTT se je znatno povečal

Slovenska priporočila za zgodnje zdravljenje covida

(prof. Lejko, strokovni kolegij 2022)

Tabela 1. Pridružene bolezni, ki predstavljajo tveganje za težek potek covida-19.*

*Starost še vedno predstavlja najpomembnejši dejavnik tveganja.

Starost ≥ 65 let
Prekomerna telesna teža ITM
Kronična ledvična bolezen
Rakave bolezni
Sladkorna bolezen
Kardiovaskularna bolezen
Arterijska hipertenzija
Kronična obstruktivna pljučna bolezen, zmerna do huda astma ali druge kronične respiratorne bolezni
Kajenje
Trenutno prejema imunosupresivno zdravljenje**
Okvara imunskega sistema **
Anemija srpastih celic
Medicinska tehnološka odvisnost, na primer traheotomija, gastrostomija ali predihavanje s pozitivnim tlakom (ki ni povezano s COVID-19).

**glej Tabelo 2

Omejitev predpisovanja, Paxlovid

Zadeva: Obvestilo o strokovnem mnenju Komisije za razvrščanje zdravil na listo v postopku razvrstitev novega zdravila Paxlovid (nirmatrelvir in ritonavir) na pozitivno listo zdravil

Zdravilo Paxlovid se predvidoma 1.12.2024 razvrsti na pozitivno listo P* z naslednjo omejitvijo predpisovanja:
Za zdravljenje koronavirusne bolezni 2019 (COVID-19) pri odraslih, ki ne potrebujejo dodatnega kisika; le pri naslednjih skupinah oseb z visokim tveganjem za napredovanje bolezni v hudo obliko:
1.1. Huda imunska oslabelost zaradi enega ali več pogojev:
- transplantacija po presaditvi čvrstih organov,
- zdravljenje malignih hematoloških bolezni,
- transplantacija krvotvornih matičnih celic,
- zdravljenje z zdravili, ki delujejo proti limfocitom B (npr. rituksimab)
- hude primarne imunske pomanjkljivosti;

1.2. zmerna imunska oslabelost zaradi enega ali več pogojev:
- zdravljenje malignih bolezni vključno s tumorji čvrstih organov,
- zdravljenje z imunosupresivnimi zdravili,
- HIV okužba z <200 CD4/$mm^{3,}$
- zmerne primarne imunske pomanjkljivosti,
- sladkorna bolezen,
- srčno popuščanje z NYHA ≥ 3,
- bolezni s hudo okvaro pljučne funkcije,
- ledvični bolniki z oGF ≥ 30 ml/min/1,73 m^2, ki imajo pridruženo katerokoli zgoraj navedeno stanje; pri bolnikih z oGF < 30 ml/min/1,73 m^2 je uporaba zdravila kontraindicirana.

Ta omejitev bo zamenjala protokol Klinike za infekcijske bolezni in vročinska stanja, ki je sedaj objavljen v Centralni bazi zdravil.

Slovenska priporočila za zgodnje zdravljenje covida

Tabela 1. Pridružene bolezni, ki predstavljajo tveganje za težek potek covida-19.*
*Starost še vedno predstavlja najpomembnejši dejavnik tveganja.

Starost ≥ 65 let
Prekomerna telesna teža ITM
Kronična ledvična bolezen oGF <30 + NYHA>3 ali SB ali kr.plj.b
Rakave bolezni
Sladkorna bolezen
Kardiovaskularna bolezen Srčno popuščanje NYHA 3 ali >
Arterijska hipertenzija
Kronična obstruktivna pljučna bolezen, zmerna do huda astma ali druge kronične respiratorne bolezni
Kajenje bolezni s hudo okvaro pljučne funkcije
Trenutno prejema imunosupresivno zdravljenje**
Okvara imunskega sistema **
Anemija srpastih celic
Medicinska tehnološka odvisnost, na primer traheotomija, gastrostomija ali predihavanje s pozitivnim tlakom (ki ni povezano s COVID-19).

**glej Tabelo 2

Priporočila za zgodnje zdravljenje C19

Nadnacionalna

- WHO (avg 2025)
- IDSA/CDC (okt 2025)
- ESCMID (2022)

Nacionalna

- NICE (maj 2025)
- Kanadska (apr 2025)
- Švicarska (avg 2025)
- Nemška (feb 2025)

Therapeutics and COVID-19

Living guideline
August 2025

World Health Organization

Population

This recommendation applies only to people with these characteristics:

Patients with confirmed covid-19

Disease severity

Non-severe	Severe	Critical
Absence of signs of severe or critical disease	Oxygen saturation <90% on room air	Requires life sustaining treatment
	Signs of pneumonia	Acute respiratory distress syndrome
	Signs of severe respiratory distress	Sepsis
		Septic shock

Infographic co-produced by the BMJ and MAGIC; designer Will Stahl-Timmins (see BMJ Rapid Recommendations).

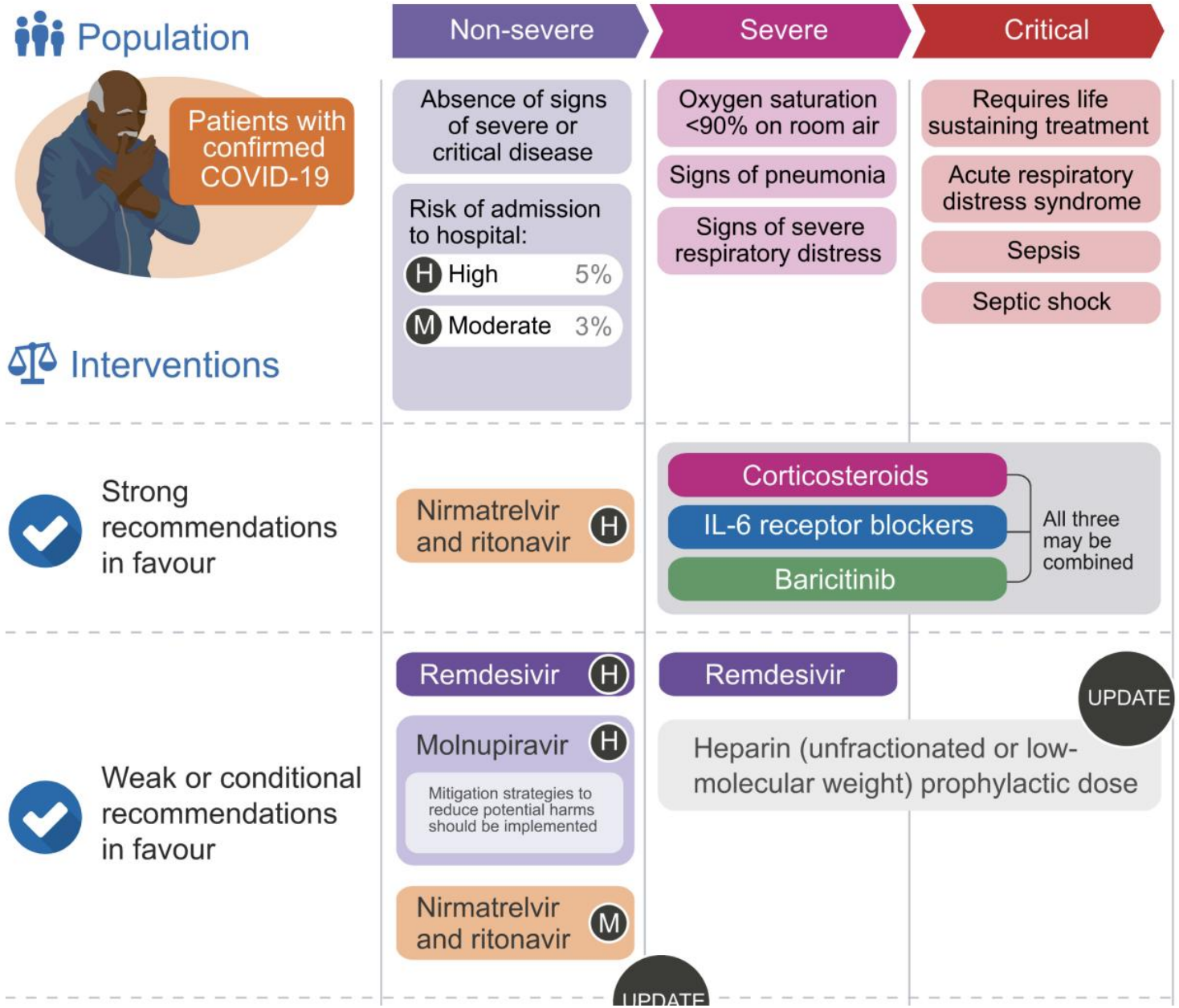
WHO – dejavniki tveganja za težek potek

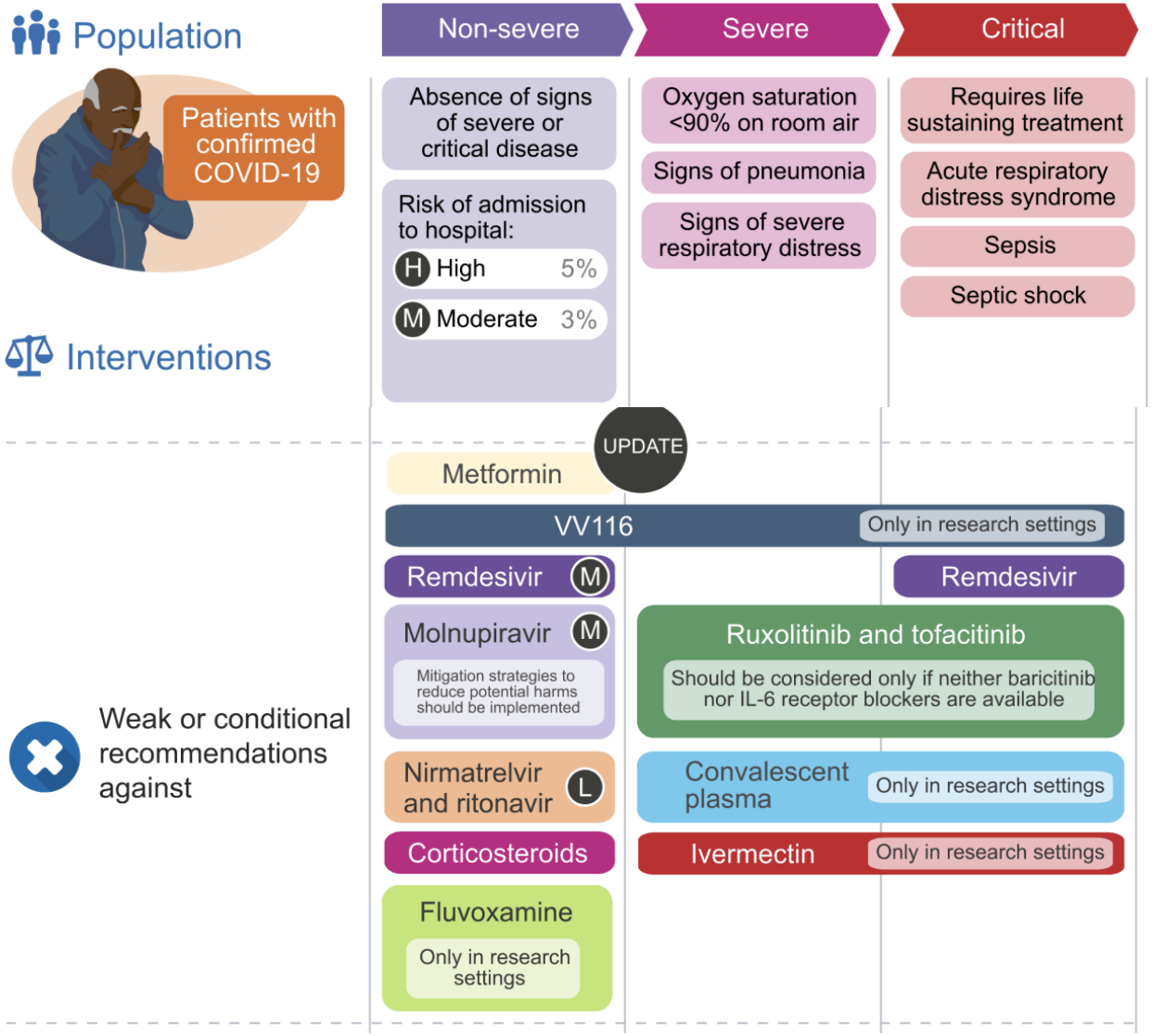
- **Patients at high risk (6%) of hospitalization** includes those with diagnosed immunodeficiency syndromes, those who have undergone solid organ transplant and are receiving immunosuppressants, and those with autoimmune illness receiving immunosuppressants.
- **Patients at moderate risk (3%) of hospitalization** are those over 65 years, those with obesity, diabetes and/or chronic cardiopulmonary disease, chronic kidney or liver disease, active cancer, those with disabilities, and those with comorbidities of chronic disease.
- **Patients at low risk (0.5%) of hospitalization** includes those who are neither moderate nor high risk. Most patients are low risk.

Defining a threshold for an important reduction in risk of hospitalization for patients with non-severe COVID-19

No evidence was identified to inform the guideline development group (GDG) regarding what patients with non-severe covid-19 perceive as an important reduction in risk of hospitalization. The GDG initially inferred an absolute reduction of 6% as being the threshold for a patient-important effect. For the fourteenth iteration, the GDG defined 1.5% as a new threshold for an important reduction in risk of hospitalization in patients with non-severe COVID-19. The GDG acknowledged the residual uncertainties regarding anticipated baseline risks in the three defined risk groups - with the living prognosis review unable to provide evidence to inform these judgments - as well as the defined threshold for an important reduction in hospitalization.

The GDG acknowledged that inherent uncertainties remain regarding baseline risks defined for individuals with non-severe COVID-19 at low, moderate and high risk of hospitalization; these baseline risks have natural implications on the absolute risk reduction that is considered patient-important. Reliable risk prognostication models for hospitalization and other patient-important outcomes for patients with non-severe illness remain limited. Similarly, regional data and event rates from the control arms of included trials may both help inform baseline risk estimates, but carry their own respective limitations (i.e. access to reliable data for the former, and issues with generalizability for the latter).


Population
Non-severe
Severe
Critical
Patients with confirmed COVID-19
Absence of signs of severe or critical disease
Risk of admission to hospital:
H High 5%
M Moderate 3%
Oxygen saturation <90% on room air
Signs of pneumonia
Signs of severe respiratory distress
Requires life sustaining treatment
Acute respiratory distress syndrome
Sepsis
Septic shock
Interventions
Strong recommendations in favour
Nirmatrelvir and ritonavir H
Corticosteroids
IL-6 receptor blockers
Baricitinib
All three may be combined
Weak or conditional recommendations in favour
Remdesivir H
Remdesivir
UPDATE
Molnupiravir H
Mitigation strategies to reduce potential harms should be implemented
Heparin (unfractionated or low-molecular weight) prophylactic dose
Nirmatrelvir and ritonavir M
UPDATE


Population
Non-severe
Severe
Critical
Patients with confirmed COVID-19
Absence of signs of severe or critical disease
Risk of admission to hospital:
H High 5%
M Moderate 3%
Oxygen saturation <90% on room air
Signs of pneumonia
Signs of severe respiratory distress
Requires life sustaining treatment
Acute respiratory distress syndrome
Sepsis
Septic shock
Interventions
UPDATE
Metformin
VV116
Only in research settings
Remdesivir M
Remdesivir
Molnupiravir M
Mitigation strategies to reduce potential harms should be implemented
Ruxolitinib and tofacitinib
Should be considered only if neither baricitinib nor IL-6 receptor blockers are available
Nirmatrelvir and ritonavir L
Convalescent plasma
Only in research settings
Corticosteroids
Ivermectin
Only in research settings
Fluvoxamine
Only in research settings
Weak or conditional recommendations against

IDSA, 14/10/2025 - dejavniki tveganja za težek potek

Example of increased but not high-risk factors for progression

Example health condition	Example therapeutics[1]
• Age 65-74 years • ASCVD • Asthma • Cardiomyopathy • Cerebral Vascular Disease • Chronic liver diseases • Chronic lung diseases • Cirrhosis • Dementia • Diabetes Mellitus • Disabilities including Down Syndrome • End stage renal disease • Heart failure • HIV with CD4 > 200 • Inflammatory bowel disease • Mental health conditions • Obesity • Parkinson's Disease • Physical inactivity • Pregnancy (current or recent) • Smoking history • Solid tumor (> 12 months prior) • Tuberculosis	• Anti-IL-6 • Anti-IL-12 and 23 • Corticosteroids 10-20 mg for ≥4 weeks

Note: [1] Example therapeutics that are less likely to predispose to substantial immunosuppression

Example of high-risk factors for progression

Example health condition	Example therapeutics[2]
• Age ≥ 75 years • Fewer than 1% peripheral B-cells assessed in past 6 months • Congenital agamma-globulinemia • Hematopoietic stem cell transplant (HSCT) <2 years or active graft versus host disease • Hematological malignancy on therapy • HIV infection with CD4 <200 • Other severe primary immunodeficiency • Solid organ transplant • Solid tumor on treatment	• B-cell depleting agents in past 12 months (e.g., rituximab, ofatumumab, ocrelizumab, others) • CAR-T therapy in past 12 months • Abatacept • Tyrosine kinase inhibitor (e.g., ibrutinib, acalabrutinib, others) • High-dose corticosteroids (≥20 mg prednisone or equivalent for ≥4 weeks) • Anthracycline derivates

Note: [2] Example therapeutics that predispose to substantial immunosuppression

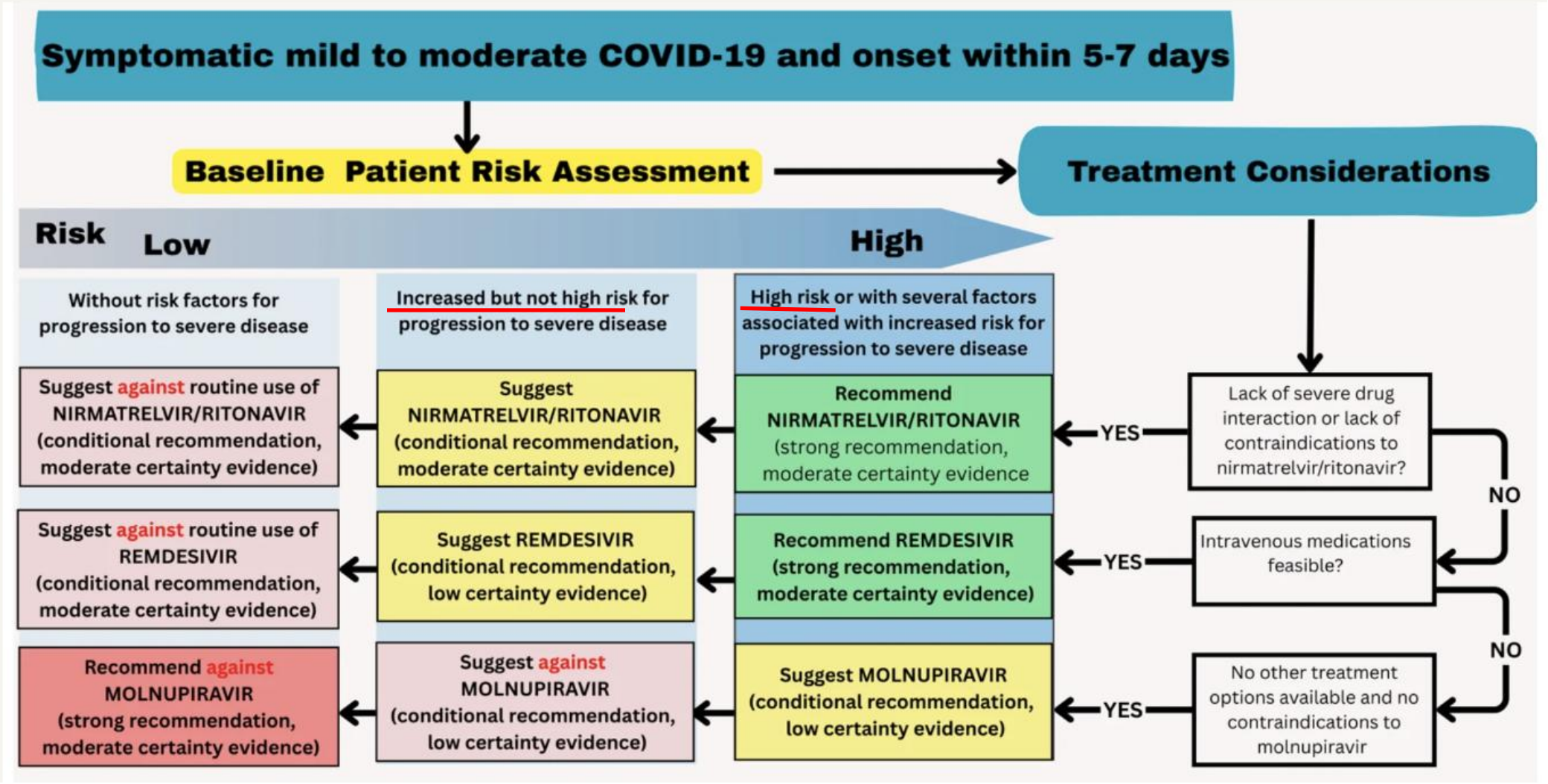
Oral nirmatrelvir/ritonavir *(Paxlovid)*
- eGFR ≥ 60 mL/min: 300 mg (2 x 150 mg tablets), plus ritonavir 100 mg (1 tablet) every 12 hours x 5 days
- eGFR ≥ 30 to < 60 mL/min: 150 mg (1 tablet) plus ritonavir 100 mg (1 tablet) every 12 hours for 5 days
- eGFR < 30 mL/min or HD: 300 mg (2 x 150 mg tablets), plus ritonavir 100 mg (1 tablet) daily x 1 day, then 150 mg (1 tablet) plus ritonavir 100 mg (1 tablet) daily for 4 days
- Within 5 days of symptom onset

Intravenous remdesivir *(Veklury)*
- Day 1: 200 mg i.v. once
- Day 2 and 3: 100 mg i.v. daily
- No renal or hepatic adjustments
- Within 7 days of symptom onset

Oral molnupiravir *(Lagevrio)*
- 800 mg (4 x 200 mg capsules) every 12 hours for 5 days
- No renal or hepatic adjustments
- Avoid pregnancy
- Within 5 days of symptom onset

IDSA, 14/10/2025

Figure. Approaches to Treatment of Mild to Moderate COVID-19



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Guidelines

ESCMID COVID-19 living guidelines: drug treatment and clinical management

Michele Bartoletti [1, 2, *], Ozlem Azap [3], Aleksandra Barac [4, 5], Linda Bussini [1], Onder Ergonul [6], Robert Krause [7], José Ramón Paño-Pardo [8, 9], Nicholas R. Power [10], Marcella Sibani [11], Balint Gergely Szabo [12, 13], Sotirios Tsiodras [14], Paul E. Verweij [15], Ines Zollner-Schwetz [7], Jesús Rodríguez-Baño [16]

ESCMID, 2022

3. Are some people more at risk of COVID-19 than others?

Age accounts for most of the increase in risk of severe COVID-19. People 60 years of age and older, as well as those with underlying health conditions, are more at risk of developing severe symptoms. The health conditions that increase the risk of severe disease include:

- hypertension
- diabetes
- cardiovascular disease
- chronic respiratory disease
- pregnancy
- immune suppression.

Male patients in these groups appear to be at a slightly higher risk than female patients. Unvaccinated people are at higher risk for severe disease and death compared with vaccinated people, as the vaccine gives effective protection against severe disease and death.

ECDC, junij 2023

Clinical Microbiology and Infection 31 (2025) 1655–1666

Contents lists available at ScienceDirect

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journal homepage: www.clinicalmicrobiologyandinfection.com

Position paper

Management of COVID-19 in immunocompromised patients: an European Society of Clinical Microbiology and Infectious Diseases consensus document

Michele Bartoletti [1,2], Ozlem Azap [3], Aleksandra Barac [4,5], Manel Ben Selma [6], Onder Ergonul [7], Effrossyni Gkrania-Klotsas [8], Paolo Antonio Grossi [9,10], Robert Krause [11,12], Blin Nagavci [13,14], José Ramón Paño-Pardo [15,16,17], Ligia Camera Pierrotti [18], Nicholas Power [19], Jesús Rodríguez-Baño [16,20,21], Marcella Sibani [22], Monica A. Slavin [23,24], Balint Gergely Szabo [25,26], Beatrice Tazza [27], Nicole Ngai Yung Tsang [28], Sotirios Tsiodras [29], Ines Zollner-Schwetz [11,12], Roy F. Chemaly [30,*], on behalf of the ESCMID Study Group for Infections in Compromised Hosts and the ESCMID Study Group for Respiratory Viruses

ESCMID kriteriji za IK

1. Primarne imunske motnje
2. Rak
   - Aktivna bolezen
   - St/p zdravljenju raka <1 leto
   - Izključeni pac. z lokaliziranim kožnim rakom ali zgodnje oblike raka (npr. pljučni rak stadij I)
3. HIV: CD4<200 celic/mm^3 ali <14%
4. Tx čvrstih organov < 1 leto
5. HRCT ali CAR-T < 1 leto
6. Terapija s sistemskimi KS, prednison (oz.ekvivalent) > ali = 20 mg/d >14 dni ali skupno >600 mg
7. Prejemniki bioloških imunomodulatornih zdravil
8. Prejemnikih antirevmatikov, ki vplivajo na celično imunost in drugih imunosupresivov

Priporočila za zdravljenje

Table 1
Summary of questions and statements

Question	Setting/condition	Statement
(1) How should immunocompromised patients with mild/moderate or severe COVID-19 be treated at the first occurrence of infection?	Mild disease	Initial standard treatment with either nirmatrelvir/ritonavir, remdesivir, or monoclonal antibodies (when available and active against circulating variants) Consider prolonged and/or combination therapy in selected highly immunosuppressed patients
	Moderate/severe disease	Consider combination and prolonged therapy
(2) Should a second course (or multiple courses) of treatment be administered in case of persistent or relapsed COVID-19?	Mild and persistent or relapsed COVID-19	Consider a second course of monotherapy with an oral antiviral agent such as nirmatrelvir/ritonavir, or intravenous remdesivir in case of major concerns for drug −drug interactions
	Mild and persistent or relapsed COVID-19 in high-risk patients	Consider prolonged monotherapy (7−14 d) or escalation to a combination regimen in case of clinical progression to severe infection
	Moderate/severe	Consider combination therapy and potentially prolonging therapy in case of non-resolving symptoms
(3) In case of combination therapy, which regimens should be favoured?	Initial treatment	Consider nirmatrelvir/ritonavir + remdesivir
	Salvage treatment	Consider adding to the standard regimen either monoclonal antibodies (when available and active against circulating variants) and/or intravenous immunoglobulins

NICE National Institute for Health and Care Excellence

NICE guidance

Nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19

Technology appraisal guidance
Published: 29 March 2023
Last updated: 1 May 2025

www.nice.org.uk/guidance/ta878

Risk factors for progression to severe COVID-19 in adults defined by the independent advisory group commissioned by the Department of Health and Social Care (June 2023)

Down's syndrome and other genetic disorders

All individuals with Down's syndrome or other chromosomal disorders known to affect immune competence

Solid cancer

- Metastatic or locally advanced inoperable cancer
- Lung cancer (at any stage)
- People receiving any chemotherapy (including antibody-drug conjugates), PI3K inhibitors or radiotherapy within 12 months
- People who have had cancer resected within 3 months and who received no adjuvant chemotherapy or radiotherapy
- People who have had cancer resected within 3 to 12 months and receiving no adjuvant chemotherapy or radiotherapy are expected to be at less risk (and thus less priority) but still at increased risk compared with the non-cancer populations

Haematological diseases and recipients of haematological stem cell transplant (HSCT)

- Allogeneic HSCT recipients in the last 12 months or active graft versus host disease (GVHD) regardless of time from transplant (including HSCT for non-malignant diseases)
- Autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases)
- Individuals with haematological malignancies who have received CAR-T cell therapy in the last 24 months, or until the lymphocyte count is within the normal range
- Individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months, or radiotherapy in the last 12 months
- All people who do not fit the criteria above, and are diagnosed with:
  - myeloma (excluding monoclonal gammopathy of undetermined significance [MGUS])
  - AL amyloidosis
  - chronic B-cell lymphoproliferative disorders (chronic lymphocytic leukaemia, follicular lymphoma)
  - myelodysplastic syndrome (MDS)
  - chronic myelomonocytic leukaemia (CMML)
  - myelofibrosis
  - any mature T-cell malignancy
- All people with sickle cell disease
- People with thalassaemia or rare inherited anaemia with any of the following:
  - severe cardiac iron overload (T2 * less than 10 ms)
  - severe to moderate iron overload (T2 * greater than or equal to 10 ms) plus an additional comorbidity of concern (for example, diabetes, chronic liver disease or severe hepatic iron load on MRI)
- Individuals with non-malignant haematological disorders (for example, aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (for example, anti-CD20, anti-thymocyte globulin [ATG] and alemtuzumab) within the last 12 months

Renal disease

- Renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who have:

- received B-cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], ATG)
- an additional substantial risk factor that would in isolation make them eligible for monoclonals or oral antivirals

- Non-transplant renal patients who have received a comparable level of immunosuppression
- People with chronic kidney disease (CKD) stage 4 or 5 (an estimated glomerular filtration rate [eGFR] less than 30 ml per min per 1.73 m^2) without immunosuppression

Liver diseases

- People with cirrhosis Child-Pugh (CP) class A, B and C, whether receiving immune suppressive therapy or not. Those with decompensated liver disease (CP B and C) are at greatest risk
- People with a liver transplant
- People with liver disease on immune suppressive therapy (including people with and without cirrhosis)

Solid organ transplant recipients

Solid organ transplant recipients not in any of the above categories.

Immune-mediated inflammatory disorders (diseases in which autoimmune or autoinflammation-based pathways are implicated in disease, for example, inflammatory arthritis, connective tissue diseases, inflammatory skin diseases, inflammatory gastrointestinal disease)

- People who have received a B-cell depleting therapy (anti-CD20 drug, for example, rituximab, ocrelizumab, ofatumumab, obinutuzumab) in the last 12 months
- People who have been treated with cyclophosphamide (IV or oral) in the 6 months prior to positive PCR or relevant COVID test
- People who are on corticosteroids (equivalent to 10 mg or more per day of prednisolone) for at least the 28 days prior to positive PCR or relevant COVID test
- People who are on biologics or small molecule JAK inhibitors
- People who are on current treatment with mycophenolate mofetil, oral tacrolimus, azathioprine, mercaptopurine, or similar agents (for major organ involvement such as kidney, gastro-intestinal tract, liver, lung, brain), methotrexate (for interstitial lung disease or asthma only) and/or ciclosporin. No minimum dose threshold is suggested
- People who are on current treatment (or within the last 6 months) with S1P modulators (fingolimod, ponesimod or siponimod), or alemtuzumab or cladribine within the last 12 months
- People who exhibit at least one of: (a) uncontrolled or clinically active disease (that is, required recent increase in dose or initiation of new immunosuppressive drug or IM steroid injection or course of oral steroids within the 3 months prior to positive PCR or relevant COVID test); and/or (b) other high risk comorbidities (for example, body mass index [BMI] greater than 30, diabetes mellitus, hypertension, major organ involvement such as significant kidney, liver, nervous system or lung inflammation or significantly impaired renal, liver, nervous system and/or lung function)

Respiratory

- Asthma in people on oral corticosteroids (defined above). Any asthma patient taking immunosuppressants for their asthma including but not exclusively methotrexate, ciclosporin. Frequent exacerbations requiring 4 or more courses of prednisolone per year, usually 40 mg per day for 5 days or more
- COPD on long term home non-invasive ventilation (NIV). Patients on long term oxygen therapy. People with moderate or severe disease (FEV1 less than or equal to 50% predicted) who have required 4 or more courses of prednisolone 30 mg for 5 days or greater in last 12 months

- Interstitial lung disease (ILD) – all patients with idiopathic pulmonary fibrosis
- Sub-types of ILD, for example, connective tissue disease related, sarcoidosis, hypersensitivity pneumonitis, NSIP (non-specific interstitial pneumonia) who have received a B-cell depleting therapy in last 12 months, or IV or oral cyclophosphamide in the 6 months prior to testing positive for COVID-19. Any ILD patient on current treatment with corticosteroids, mycophenolate mofetil, azathioprine, tacrolimus, cyclosporin or methotrexate. No minimum dose criteria
- Any people with any type of ILD who may not be on treatment due to intolerance but has severe disease with an FVC predicted less than 60%
- NIV and tracheostomy ventilated – all patients requiring this type of support regardless of the underlying disorder (which might include COPD, obesity hypoventilation syndrome, scoliosis, bronchiectasis, neurodisability and genetic muscular diseases [refer to neurology section]).
- Lung cancer patients, refer to 'Solid cancer' section above
- Lung transplant patients (refer to solid organ transplant section)
- Pulmonary hypertension (PH): groups 1 and 4 from PH classification

Immune deficiencies

- Common variable immunodeficiency (CVID)
- Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig)
- Hyper-IgM syndromes
- Good's syndrome (thymoma plus B-cell deficiency)
- Severe combined immunodeficiency (SCID)
- Autoimmune polyglandular syndromes or autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
- Primary immunodeficiency associated with impaired type 1 interferon signalling
- X-linked agammaglobulinaemia (and other primary agammaglobulinaemias)
- Any person with secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy

HIV/AIDS

- People with high levels of immune suppression, have uncontrolled or untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis
- People on treatment for HIV with CD4 less than 350 cells per mm^3 and stable on HIV treatment or CD4 greater than 350 cells per mm^3 and additional risk factors (for example, age, diabetes, obesity, cardiovascular, liver or renal disease, homeless, alcoholic dependency)

Neurological disorders

- Conditions associated with neuromuscular respiratory failure requiring chronic ventilatory support:
  - motor neurone disease
  - Duchenne muscular dystrophy
- Conditions that require use of specific immunotherapies:
  - multiple sclerosis (MS)
  - myasthenia gravis (MG)
  - other immune-mediated disorders
- Dementia, neurodegenerative and neuroimmune disorders when associated with severe frailty (for example, levels 7 or 8 on Clinical Frailty Scale, as part of a personalised care plan):
  - Alzheimer's disease, vascular disease, Lewy body disease, or frontotemporal atrophy
  - Parkinson's disease

- Huntington's disease
- progressive supranuclear palsy and multiple system atrophy
- motor neurone disease
- multiple sclerosis and other immune-mediated neurological disorders

Table 3: Treatment of patients with NON-hospitalised adults and children aged over 12 years and older with COVID-19, who are symptomatic.

Treatment	Paxlovid (nirmatrelvir plus ritonavir) First Line	Sotrovimab Second line	Molnupiravir Third line
Eligibility criteria for treatment	• The patient does not need supplemental oxygen for COVID-19 (may require oxygen for other conditions) **AND** • Confirmed by PCR or POCT **AND** Symptomatic with COVID-19 and not improving **AND** **The patient meets one of the following criteria:** • At an increased risk of progression to severe COVID-19, as defined in here **OR** **OR** **AND** **AND** • ≥12yrs and ≥40kg and post pubescent[4] **AND** • Treatment is commenced within 5 days of symptom onset **AND**	• The patient does not need supplemental oxygen for COVID-19 (may require oxygen for other conditions) **AND** • Confirmed by PCR or POCT **AND** • Symptomatic with COVID-19 and showing no signs of clinical recovery **AND** • Is at an increased risk of progression to severe COVID-19, as defined in here **AND** • > 12 years of age and at least 40kg **AND** • Treatment with Paxlovid is contraindicated or not clinically suitable. **AND** • Treatment is delivered within 5 days of symptom onset **AND** • There are no drug contra-indications e.g., hypersensitivity to any active substances or excipients	• The patient does not need supplemental oxygen for COVID-19 (may require oxygen for other conditions) **AND** • Confirmed by PCR OR POCT **AND** • Is at an increased risk of progression to severe COVID-19, as defined in here **AND** • Treatment is commenced within 5 days of symptom onset **AND** • >18 years of age and not pregnant **AND** • Treatment with Paxlovid or Sotrovimab is contraindicated or not clinically suitable **AND** • There are no drug contra-indications e.g., hypersensitivity to any active substances or excipients

Table 2: Treatment of inpatients who have COVID-19 without requiring supplemental oxygen for COVID-19

Therapy should be selected in order of recommendations e.g. if first line not suitable, review if the second line option is suitable etc.

Treatment	Paxlovid (nirmatrelvir plus ritonavir) First Line	Sotrovimab Second line	Remdesivir Third line
Eligibility criteria for treatment	• The patient does not need supplemental oxygen for COVID-19 (may need oxygen for other conditions.) **AND** • Confirmed by PCR or POCT. **AND** • Symptomatic with COVID-19 **AND** **Are any of the following:** • At an increased risk of progression to severe COVID-19, as defined here **OR** **AND** • ≥12 years of age and ≥40kg [4] **AND** • Treatment is commenced within 5 days of symptom onset	• The patient does not need supplemental oxygen for COVID-19 (may need oxygen for other conditions.) **AND** • Confirmed by PCR or POCT **AND** • Symptomatic with COVID-19 and showing no signs of clinical recovery **AND** • At an increased risk of progression to severe COVID-19, as defined here **AND** • ≥ 12 years of age and at least 40kg **AND** • Treatment with Paxlovid is contraindicated or not possible. **AND** • Treatment is delivered within 5 days of symptom onset **AND** • Patient does not have a new supplemental oxygen requirement specifically for the management of COVID-19 **AND** • There are no drug contra-indications e.g., hypersensitivity to any active substances or excipients.	• Confirmed by PCR or POCT **AND** • The patient does not need supplemental oxygen for COVID-19, however (may need oxygen for other conditions). **AND** • The patient is ≥18 years old **OR** • The patient is 4 weeks to 17 years old and weighs at least 40kg **AND** • The patient has a high risk of serious illness as defined here (link) **AND** • Is within 7 days of symptom onset *(discuss immunocompromised patients with specialist* team)* **AND** • ALT < 5 x ULN and NO history of chronic liver disease **AND** • There are no drug contra-indications e.g., hypersensitivity to any active substances or excipients **AND** • Treatment with Paxlovid and sotrovimab is contraindicated or not possible

Kanada

BC COVID THERAPEUTICS COMMITTEE (CTC)

Clinical Practice Guide for the Use of Therapeutics in Mild-Moderate COVID-19

April 2025 Update: More precise definitions of high-risk patients who benefit from treatment, update on the Provincial Rapid Antigen Program, consolidation of practical information from the Step-by-Step Assessment (now archived) into one document.

RECOMMENDATIONS

Who is Recommended to Receive Antiviral Treatment for Mild-Moderate COVID-19?

Patients who test **positive for SARS-CoV-2**, with **appreciable** symptoms and a non-reassuring presentation and trajectory, who are at an **increased risk for hospitalization** or progression to severe COVID-19, such as:

- Individuals with **moderate* to severe immunosuppression**, due to:
  - Solid organ transplant
  - Active treatment for a hematological malignancy
  - Allogeneic bone marrow or stem cell transplant in the last year
  - Autologous bone marrow or stem cell transplant in the last 6 months
  - Receipt of chimeric antigen receptor (CAR) T-cell therapy in the last 6 months
  - Receipt of anti-CD-20 or B-cell depleting agents in the last 2 years[1]
  - Receipt of moderately immunosuppressive agents[2]
  - Receipt of systemic treatment for cancer, including for solid tumors, in the last 6 months (3 months for hormonal therapy)
  - Moderate-severe primary immunodeficiency
  - Advanced or untreated HIV
- Individuals **≥60 years** who have **serious medical conditions**, who have been shown to significantly and consistently benefit from antivirals, such as those with:
  - End-stage renal disease (eGFR < 30ml/min or dialysis)
  - Diabetes treated with insulin

- Severe or end-stage lung conditions such as COPD, asthma, interstitial lung disease, cystic fibrosis, or neurological conditions requiring Bi-Pap or ventilation
- Severe intellectual or developmental disabilities
- Rare blood and genetic disorders such as sickle cell disease, thalassemia, urea cycle defects

* Individuals **younger than 60 years** with a moderately immunosuppressive condition such as prostate or breast cancer or an immunological condition treated with a single moderately immunosuppressive drug[2] have not been shown to routinely benefit from treatment with antivirals. Clinical judgement and consideration of other risk factors is strongly recommended.

1. **Severely immunosuppressive agents: Anti-CD-20 agents:** rituximab, ocrelizumab, ofatumumab, obinutuzumab, ibritumomab, tositumomab; **B-cell depleting agents**: epratuzumab, MEDI-551, belimumab, BR3-Fc, AMG-623, Atacicept, antiBR3, alemtuzamab
2. **Moderately immunosuppressive agents: Biologics**: abatacept, adalimumab, anakinra, benralizumab, brodalumab, canakinumab, certolizumab, dupilumab, etanercept, golimumab, guselkumab, infliximab, interferon products (alpha, beta, and pegylated forms), ixekizumab, mepolizumab, natalizumab, omalizumab, resilizumab, risankizumab, sarilumab, secukinumab, tildrakizumab, tocilizumab, ustekinumab, or vedolizumab**; Oral immune-suppressing drugs**: azathioprine, baricitinib, cyclophosphamide, cyclosporine, leflunomide, dimethyl fumerate, everolimus, fingolimod, mycophenolate, siponimod, sirolimus, tacrolimus, tofacitinib, upadacitinib, methotrexate, or teriflunomide; **Oral steroids on an ongoing basis**: dexamethasone, hydrocortisone, methylprednisolone, or prednisone at a dose of 20 mg/day of prednisone equivalent; **Immune-suppressing infusions/injections**: cladribine, cyclophosphamide, glatiramer, methotrexate

- "high risk" pacienti so imeli cca 3% tveganje za hospitalizacijo na začetku "Omicron vala", zdravljenje je tveganje znižalo za 1/2
  - NNT 67 (verjetno sedaj še večje)

Švica

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SARS-CoV-2 /COVID-19 - Antiviral and immunomodulatory treatment considerations for early therapy and advanced disease

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Introduction

Introduction

The clinical picture of COVID-19 has been constantly changing. The biphasic course initially seen in high-risk patients is currently seen very rarely. Main effort is to identify patients at high risk for optimal vaccination and early treatment aimed at preventing severe disease. The challenge is to define high-risk patients, as this risk has been mitigated by infection- and/or vaccine-induced immunity.

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Indication

- High-risk patients, according to the list below. Treatment can also be considered in older adults on a case by-case basis, depending on underlying comorbidities, immune and immunization status, or previous severe COVID-19 event. Early treatment can also be considered in patients hospitalized due to SARS-CoV-2-infections or with nosocomial SARS-CoV-2 infections, after evaluation of risk-benefit.
- Most experts limit the use of early therapy to the list of patients at high risk.

Patients at high risk for a severe course

- HIV-infection with CD4 cell count <200/µl
- Primary immunodeficiency
- Treatment with Anti-CD20- or Anti-CD19-antibodies (and other B-cell depleting agents) or Bruton-Tyrosin-Kinase- inhibitors
- High dose steroids (>20mg prednisone (or the equivalent dose)/d)
- Hematological malignancies (e.g. leukemia, lymphoma, GVHC, autologous and allogeneic HSCT, CAR-T cell therapies, multiple myeloma, myeloproliferative diseases, neutropenia <1000/µl for one week or more)
- Sickle cell disease
- Recipients of a solid organ
- Cancer with a current cytotoxic therapy

General considerations for treatment

- *Immunocompromised patients, whether hospitalized or not but without the need for oxygen, may be included in an academic clinical trial in Lausanne, Basel, Geneva, or Zurich (OPTICOV clinical trial.gov NCT05587894). Contact: **opticov@hug.ch**, contact 079 553 35 76*
- Treatment should be started early after start of symptoms (first 5 days). In immunocompromised patients with prolonged shedding and persistent symptoms, treatment can be introduced at any time after infection
- SARS-CoV-2 must be confirmed (by rapid antigen test or RT-PCR)
- For some medications, interactions must be checked before administration, or alternative first line drugs can be chosen

Nemčija

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S3-Leitlinie - Empfehlungen zur Therapie von Patienten mit COVID-19

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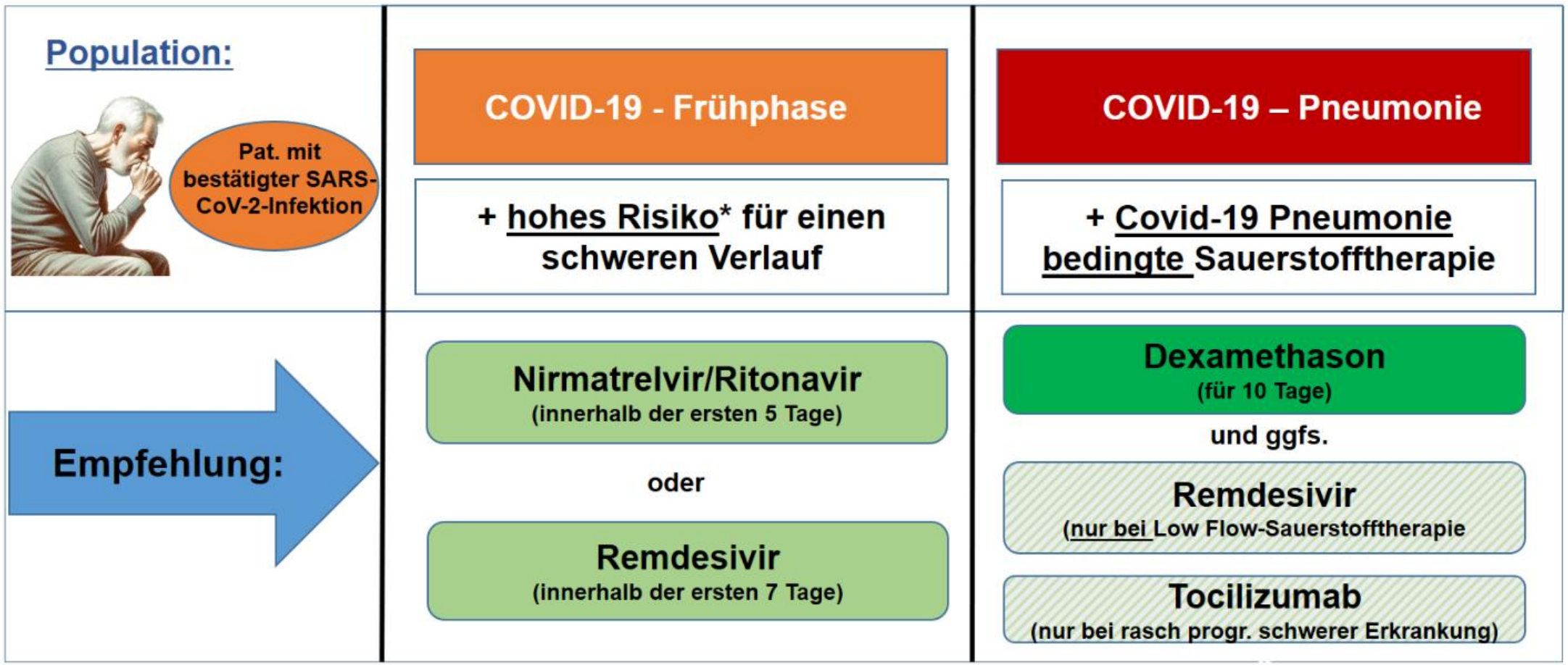
Deutsche Gesellschaft für Angiologie (DGA)
Deutsche Gesellschaft für Rheumatologie (DGRh)
Patientenvertretung (individueller Betroffener)

Skupine tveganja - Nemčija

- **Visokim tveganje za hospitalizacijo (pribl. 6 %)**
  - bolniki po presaditvi čvrstih organov
  - po zdravljenju s protitelesi, usmernjenimim priti anigenom na limfocitih B
  - Po CAR-T-celičnim zdravljenju,
  - močno imunosuprimirani (npr. med kemoterapijo, s hudimi imunski okvarami, ki prizadenejo antivirusno imunost, po avtologni ali alogenski presaditvi krvotvornih matičnih celic pred imunološko rekonstitucijo).
- **Skupine bolnikov z zmernim tveganjem (pribl. 3 %) za hospitalizacijo:**
  - bolniki starejši od 65 let in/ali z naslednjimi komorbidnostmi:
    debelost, sladkorna bolezen, bolezni srca in ožilja, kronične pljučne bolezni, kronične bolezni jeter ali ledvic, aktivne rakave bolezni, trisomija 21 ter bolniki z drugimi kroničnimi boleznimi, ki povzročajo komorbidnosti.
- **Skupine bolnikov z nizkim tveganjem (pribl. 0,5 %) za hospitalizacijo:**
  - sem sodijo tisti, ki nimajo niti zmernega niti visokega tveganja.
  - večina bolnikov spada v skupino z nizkim tveganjem.



“Odločitev **za ali proti protivirusnemu zdravljenju** naj bo v klinični praksi **posamezno prilagojena** glede na **individualni profil tveganja**, vključno z imunskim statusom in komorbidnostmi bolnika.”

3.3.2.1. Nirmatrelvir/Ritonavir

EMPFEHLUNG 1	**Evidenzbasierte Empfehlung, bestätigt 12/2024**	
Empfehlungsgrad: **B ⇑**	**Nirmatrelvir/Ritonavir sollte bei Personen mit einem hohen Risiko für einen schweren Verlauf* in der Frühtherapie (innerhalb der ersten 5 Tage) eingesetzt werden.** Hinweis: Aufgrund des potentiellen Wechselwirkungspotentials sollen relevante Interaktionen mit bestehender Medikation vor Therapiebeginn überprüft und bewertet werden. *hohes Risiko für einen schweren Verlauf = siehe 3.2	
Qualität der Evidenz: **Frühphase** 28-Tage-Sterblichkeit: niedrig ⊕⊕⊖⊖ Hospitalisierung/Tod bis Tag 28: niedrig ⊕⊕⊖⊖ Unerwünschte Ereignisse: moderat ⊕⊕⊕⊖	Literatur: Hammond J et al. N Engl J Med. 2022 Feb 16. doi: 10.1056/NEJMoa2118542 Reis S et al. Cochrane Database of Systematic Reviews 2023, Issue 11. Art. No.: CD015395. DOI: 10.1002/14651858.CD015395.pub3	
	Starker Konsens	

3.3.2.2. Remdesivir

EMPFEHLUNG 2	**Evidenzbasierte Empfehlung, bestätigt 12/2024**	
Empfehlungsgrad: **B ⇑**	**a) Remdesivir sollte bei Personen mit einem hohen Risiko für einen schweren Verlauf* als Frühtherapie (innerhalb von 7 Tagen) eingesetzt werden** *hohes Risiko für einen schweren Verlauf = siehe 3.2	
	Ergänzende Empfehlung (EK), bestätigt 12/2024	
Expertenkonsens (EK)	**b) Remdesivir kann bei Patienten mit COVID-19 Pneumonie und Low-Flow-Sauerstofftherapie eingesetzt werden**	
Qualität der Evidenz: **Frühphase** Hospitalisierung/Tod bis Tag 28: moderat ⊕⊕⊕⊖ **Fortgeschrittene Erkrankung (COVID-19-Pneumonie)** Expertenkonsens	Literatur: Grundeis F et al. Cochrane Database Syst Rev. 2023 Jan 25;1(1):CD014962. doi: 10.1002/14651858.CD014962.pub2. Amstutz A et al. Lancet Respir Med. 2023 May;11(5):453-464. doi: 10.1016/S2213-2600(22)00528-8. Lee TC et al. Clin Microbiol Infect. 2022 Sep;28(9):1203-1210. doi: 10.1016/j.cmi.2022.04.018.	
	Starker Konsens	

Predlog slovenskih priporočil (Paxlovid + Remdesivir)

Tabela 1. Pridružene bolezni, ki predstavljajo tveganje za težek potek covida-19.*
*Starost še vedno predstavlja najpomembnejši dejavnik tveganja.

Starost ≥ 65 let Leta?? > 75
Prekomerna telesna teža ITM
Kronična ledvična bolezen oGF <30 + NYHA 3 ali > ali SB ali kr.plj.b
Rakave bolezni
Sladkorna bolezen z okvarami tarčnih organov? trajanje?..
Kardiovaskularna bolezen srčno popuščanje NYHA 3 ali >
Arterijska hipertenzija
Kronična obstruktivna pljučna bolezen, zmerna do huda astma ali druge kronične respiratorne bolezni
Kajenje bolezni s hudo okvaro pljučne funkcije
Trenutno prejema imunosupresivno zdravljenje**
Okvara imunskega sistema **
Anemija srpastih celic
Medicinska tehnološka odvisnost, na primer traheotomija, gastrostomija ali predihavanje s pozitivnim tlakom (ki ni povezano s COVID-19).

**glej Tabelo 2

+ napredovala nevrološka okvara
+ napredovala okvara jetrne funkcije
+ indiv. presoja/posvet z infektologom