ORGANIZA:

SGAN
sociedad gallega de nefrología

VIII CONGRESO
de la
SOCIEDAD GALLEGA DE NEFROLOGÍA

Enfermedad renal asociada a infección por virus SARS-COV2

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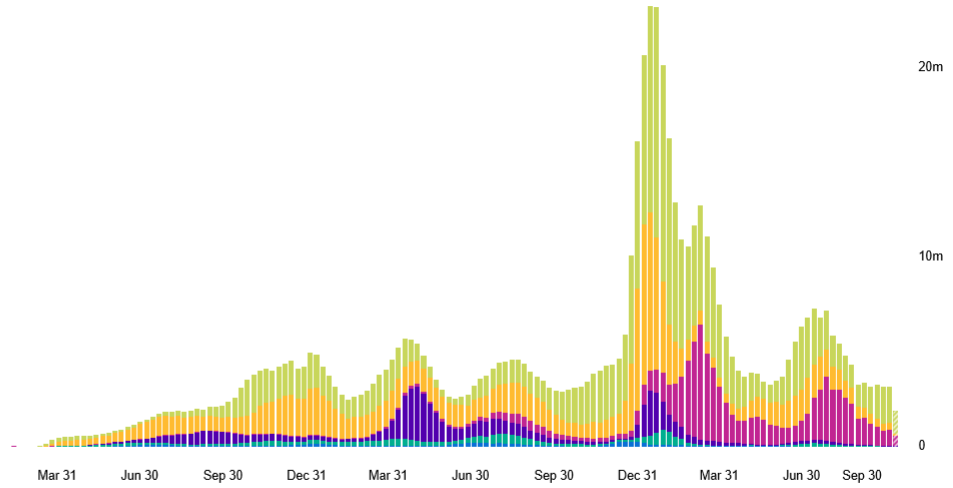
WHO coronavirus dashboard (21 Oct/2022)

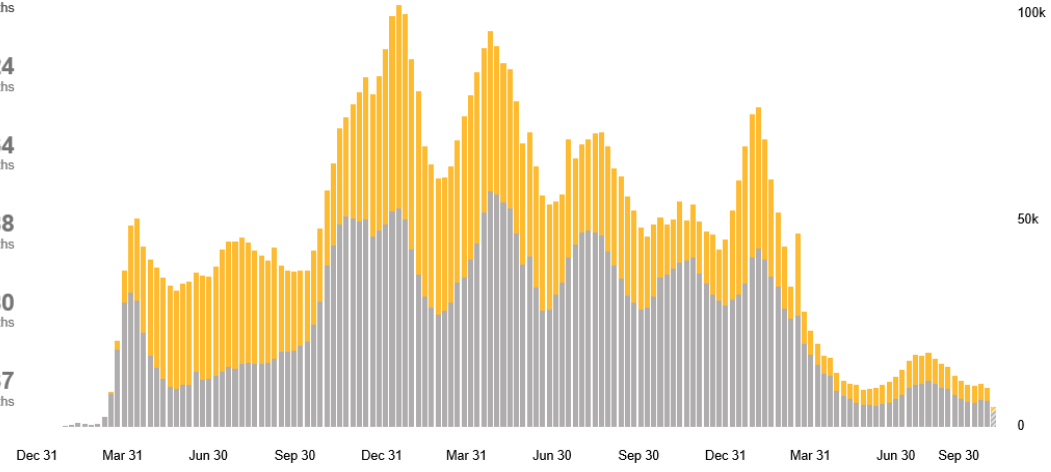
Europe	259.415.368 confirmed
Americas	179.348.492 confirmed
Western Pacific	92.254.621 confirmed
South-East Asia	60.396.653 confirmed
Eastern Mediterranean	23.132.136 confirmed
Africa	9.345.860 confirmed

Source: World Health Organization
Data may be incomplete for the current day or week.



Americas	2.848.030 deaths
Europe	2.109.324 deaths
South-East Asia	798.364 deaths
Eastern Mediterranean	348.588 deaths
Western Pacific	274.980 deaths
Africa	174.637 deaths

Source: World Health Organization
Data may be incomplete for the current day or week.



Overview

- Kidney injury caused by SARS-COV2
- New-onset and relapsing of autoinmune disorders after SARS-COV2
- Outcome after AKI in COVID-19 patients
- Therapies for COVID-19 in CKD patients
- Humoral response to SARS-COV2 vaccine in CKD patients

Potential Complications of COVID-19

Neurologic
- Cerebrovascular Disorders
- Corticospinal Damage
- Meningitis/Encephalitis
- Encephalopathy
- Cognitive + Motor Deficits

Systemic
- Acute Liver Failure
- Acute Kidney Injury
- Cytokine Storm
- Secondary Infection
- Septic Shock
- MIS-C

Vascular
- Vasculitis
- Endothelialitis

Cutaneous
- Erythema
- Chilblain-like lesions
- Urticaria-like lesions
- Vesicular lesions

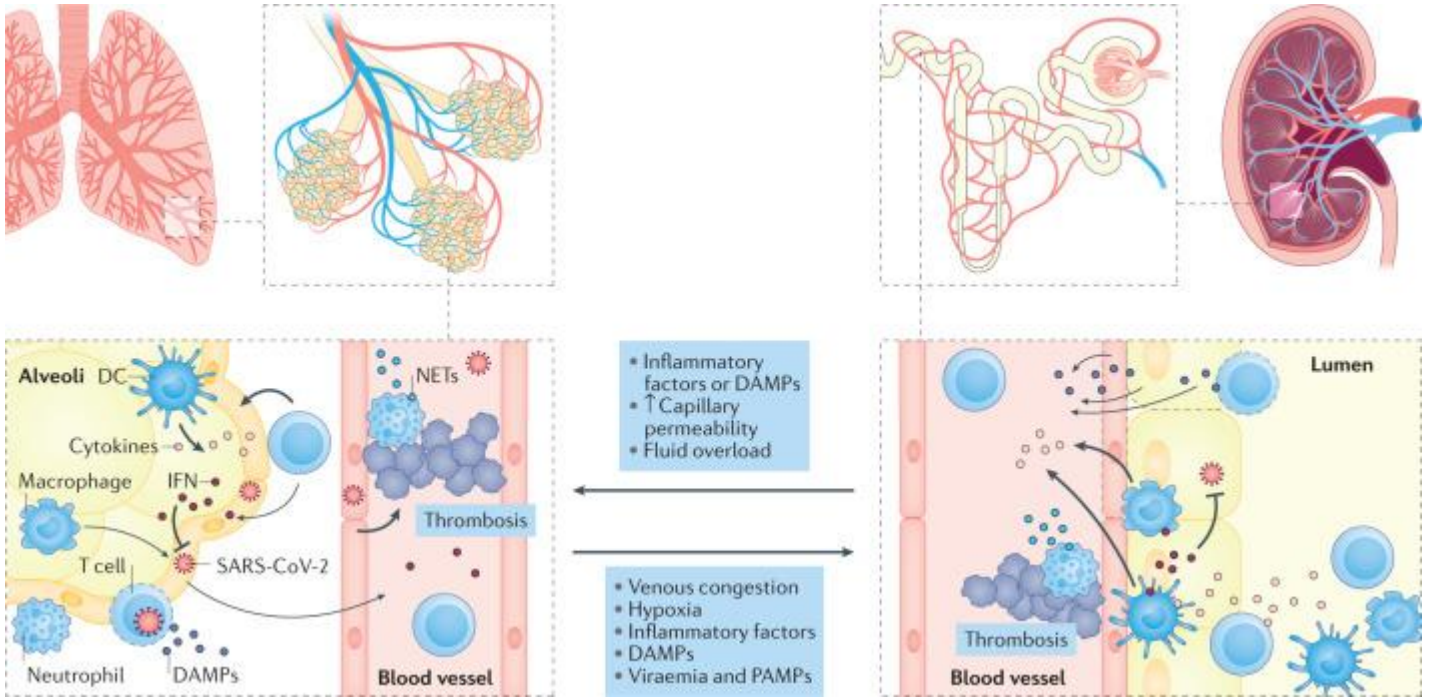
Cardiac
- MI (Types I & II)
- Heart Failure
- Viral Myocarditis
- Stress Cardiomyopathy
- Arrhythmia

Respiratory
- ARDS
- Pneumonia
- Dyspnoea

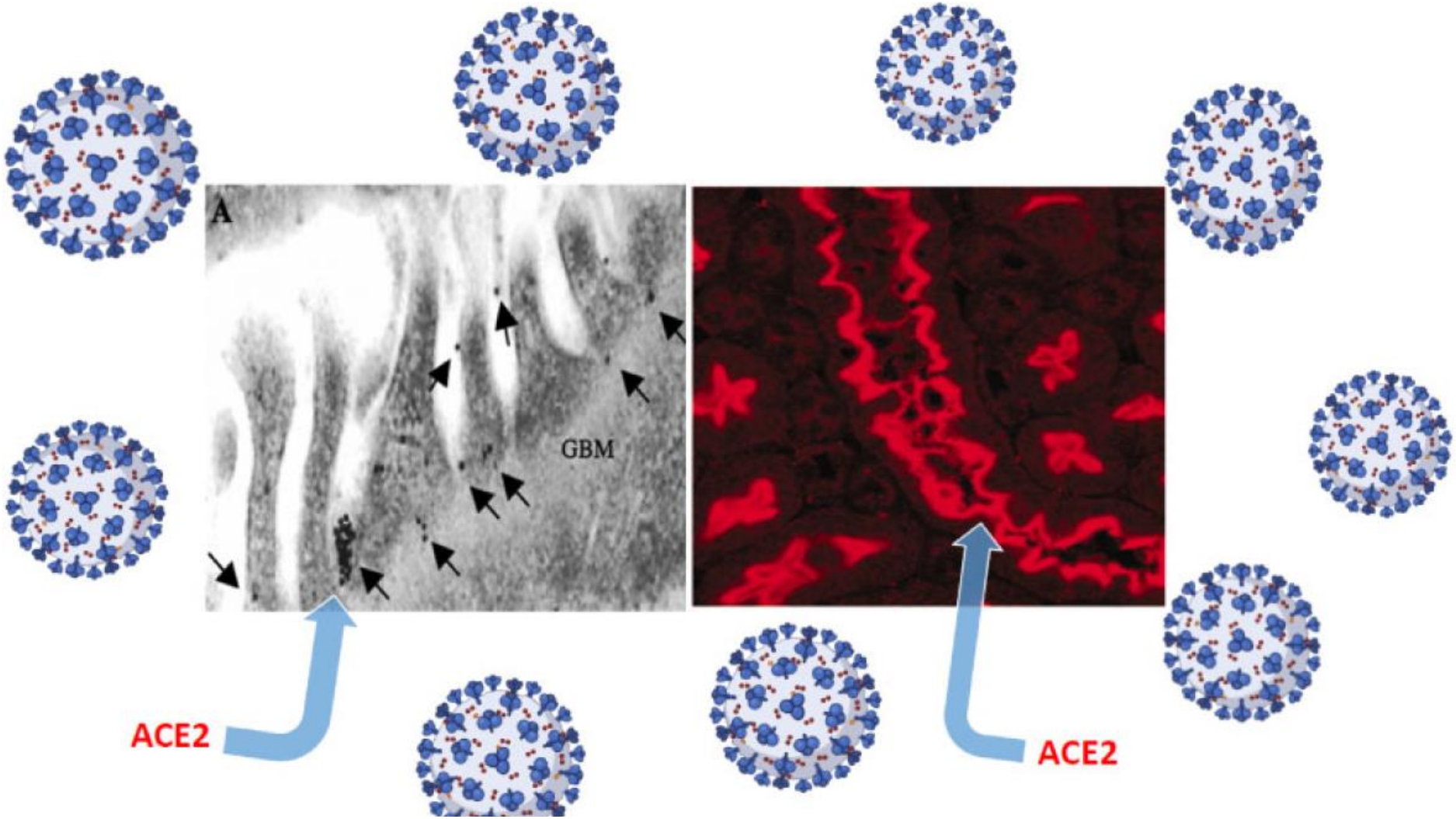
Hematologic
- Coagulopathy
  - PE
  - DVT
  - DIC
  - Organ Thromboemboli
  - Arterial emboli
- Thrombocytopenia

Mallah *et al. Ann Clin Microbiol Antimicrob* *(2021) 20:35*
https://doi.org/10.1186/s12941-021-00438-7

ARDS = Acute Respiratory Distress Syndrome **DVT** = Deep Vein Thrombosis, **DIC** = Disseminated Intravascular Coagulopathy, **MI** = Myocardial Infarction, **PE** = Pulmonary Embolism, **MIS-C** = Multi-inflammatory Syndrome in Children

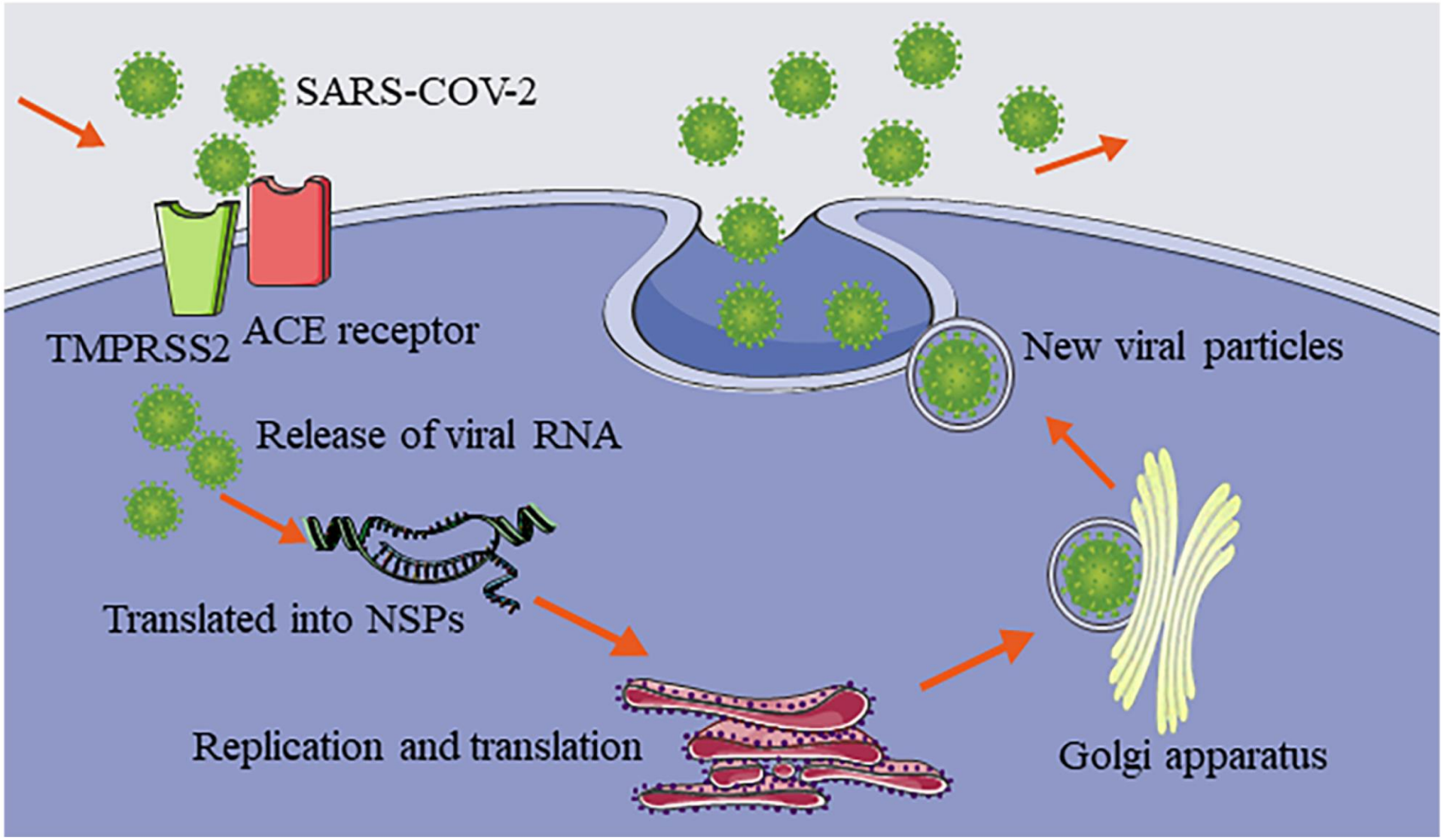


Legrand et al, Nature Review 2021



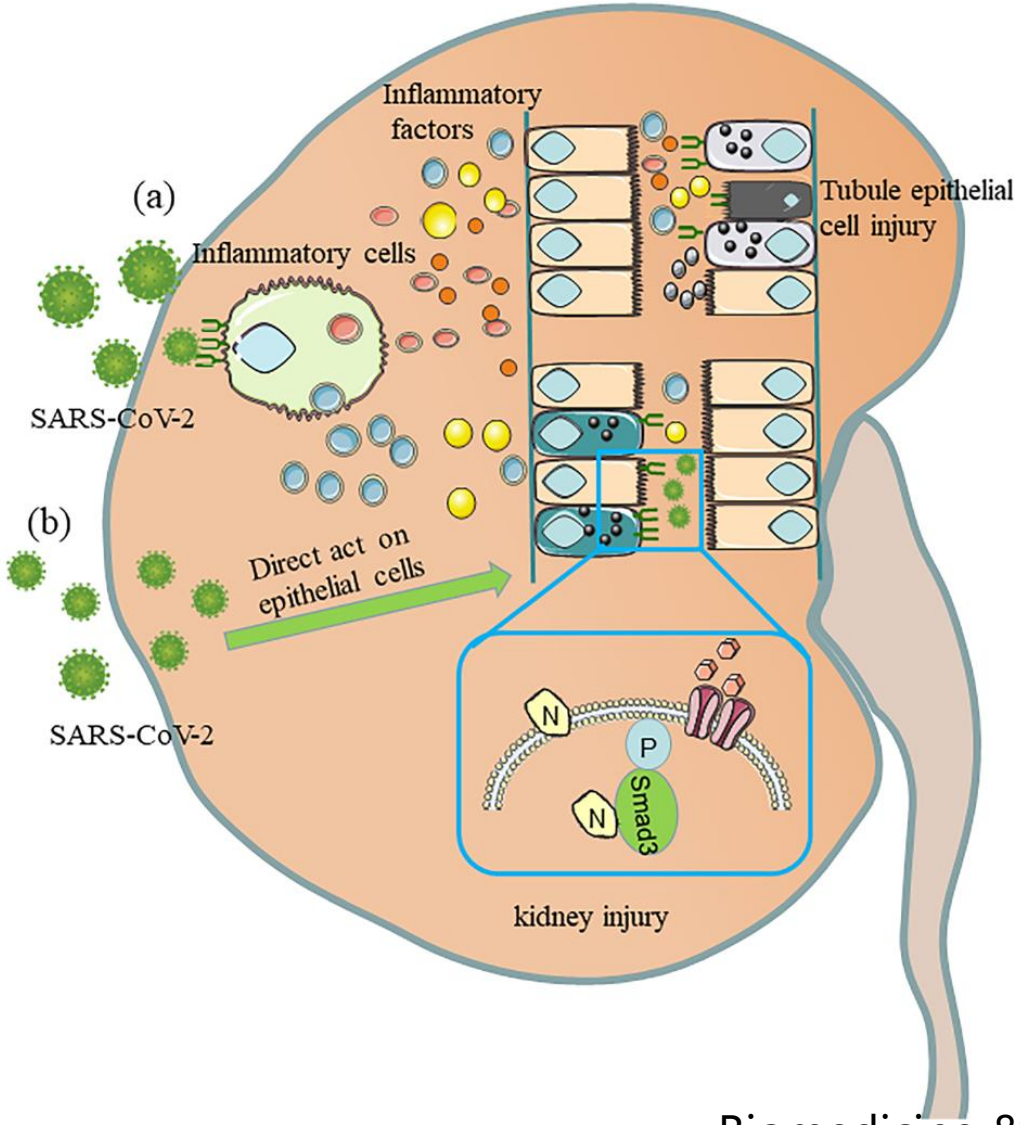
Clinical Kidney Journal, 2021, vol. 14, Suppl 1, i1–i5

Life cycle of SARS-CoV-2 in renal cells



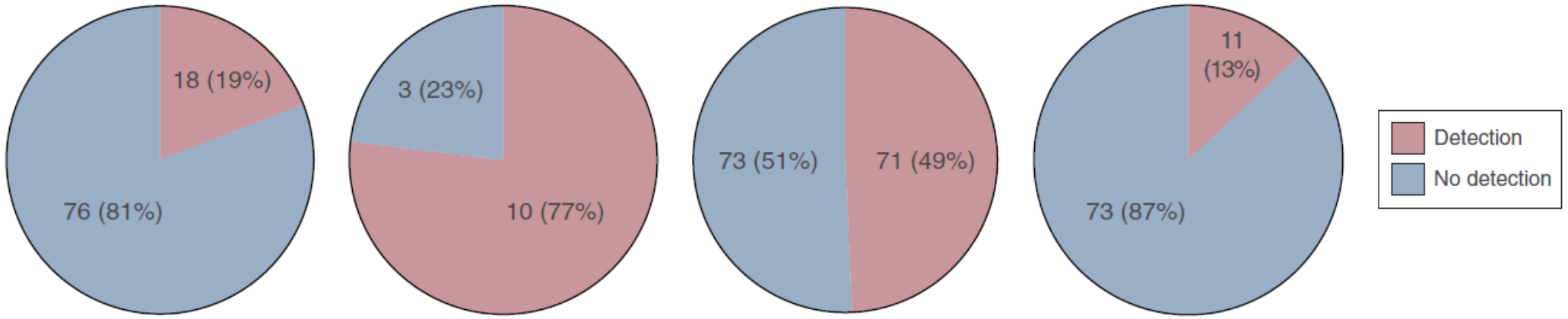
Biomedicine & Pharmacotherapy 156 (2022) 113807

Kidney injury caused by SARS-COV-2



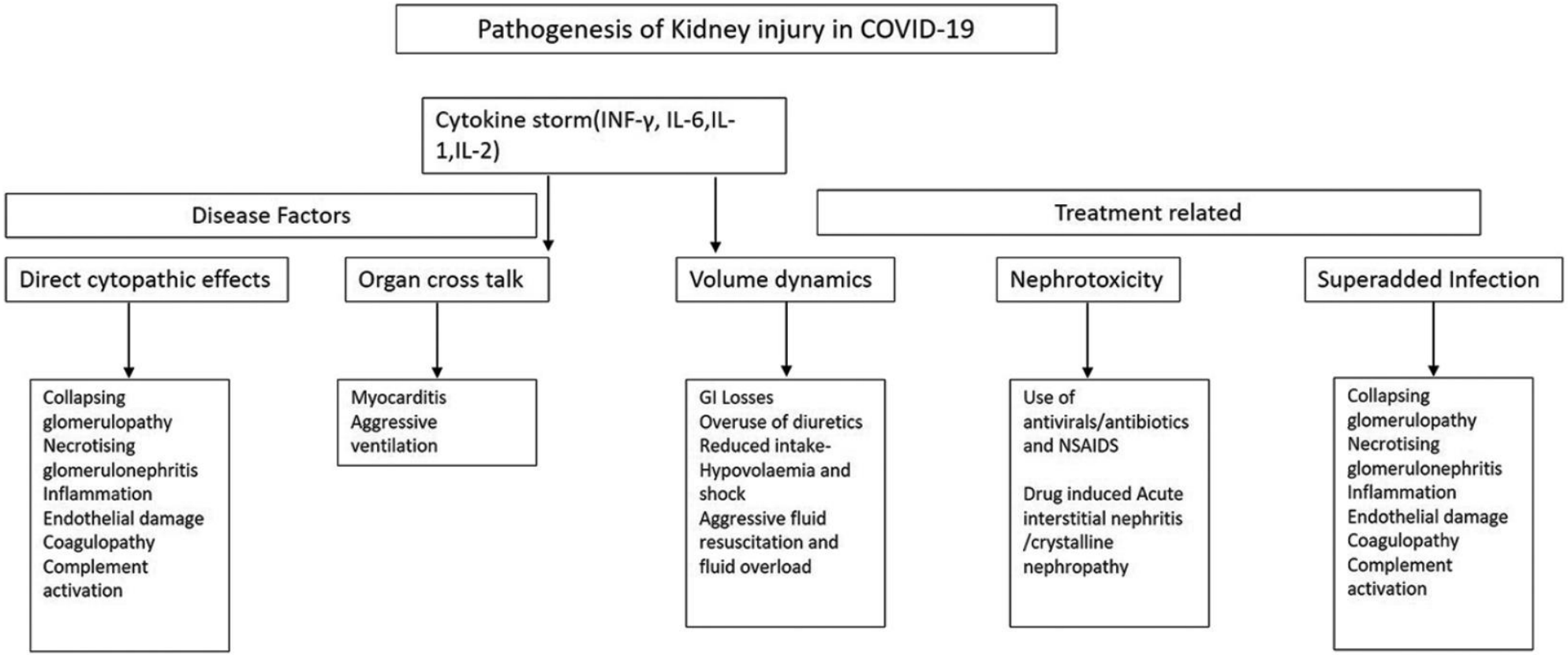
Biomedicine & Pharmacotherapy 156 (2022)

Summary of data against and in favor of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in kidneys from patients with coronavirus disease 2019 (COVID-19).



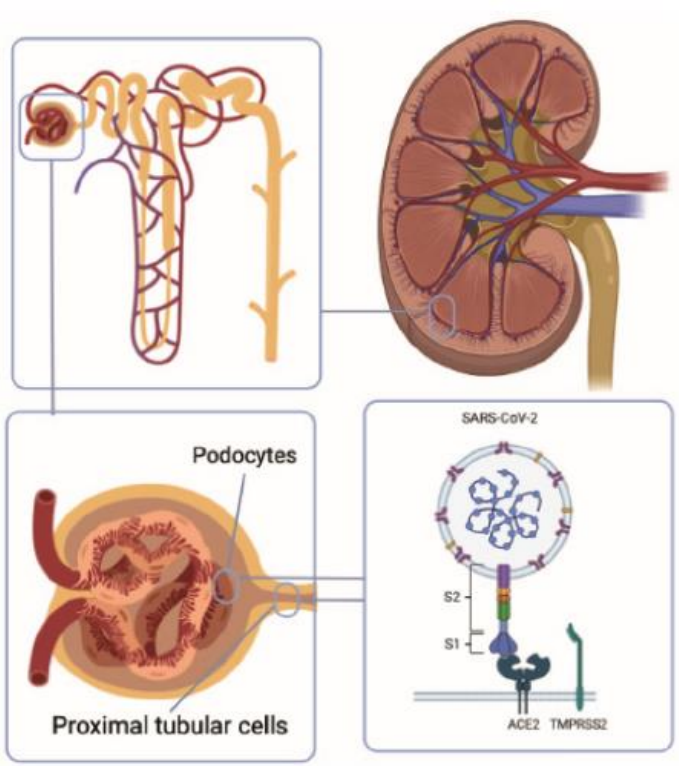
CJASN 16: 1755–1765, 2021. doi: https://doi.org/10.2215/CJN.04560421

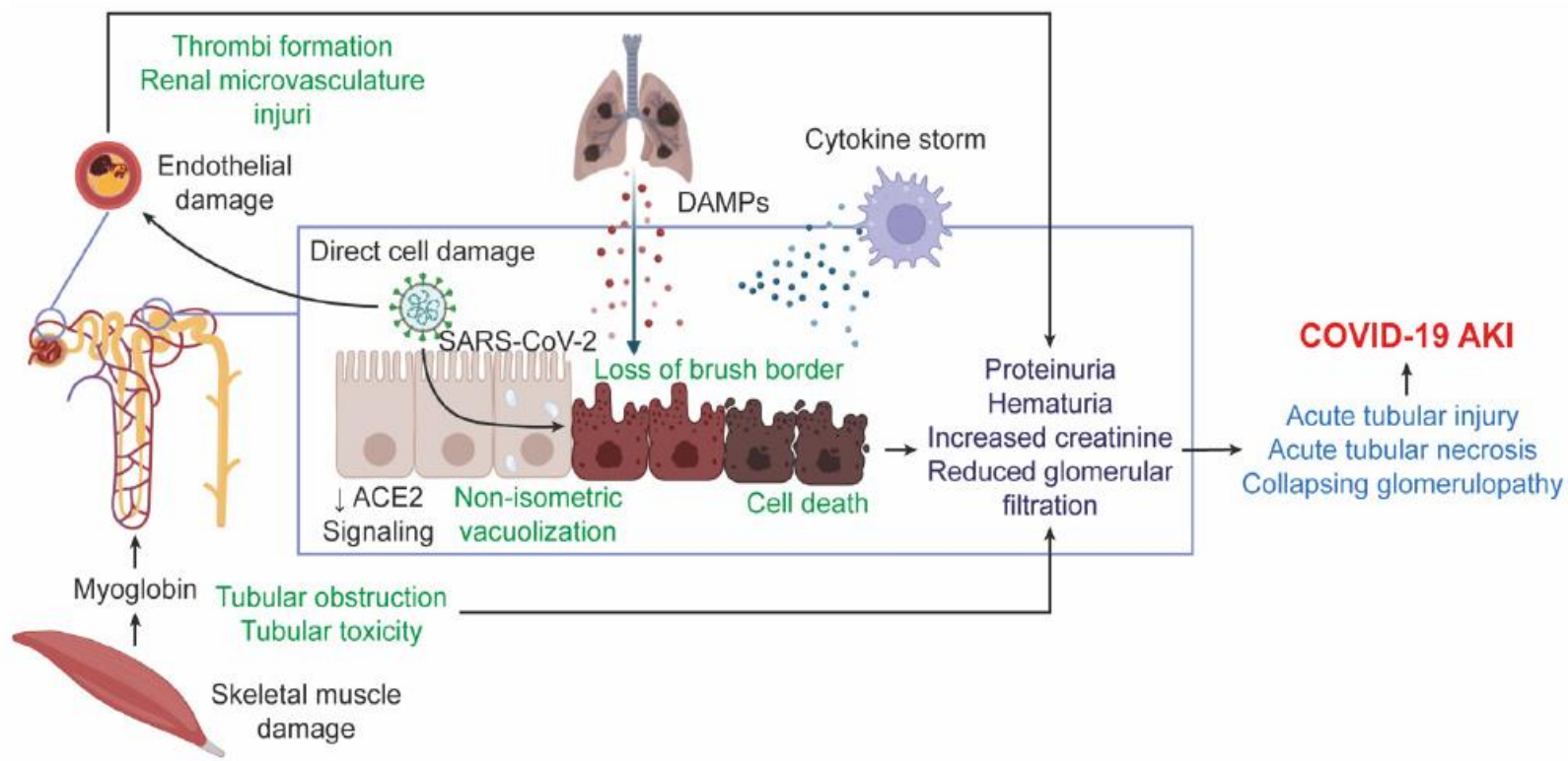
Pathogenic factors leading to renal injury in COVID-19



J Family Med Prim Care 2022;11:2302-10.

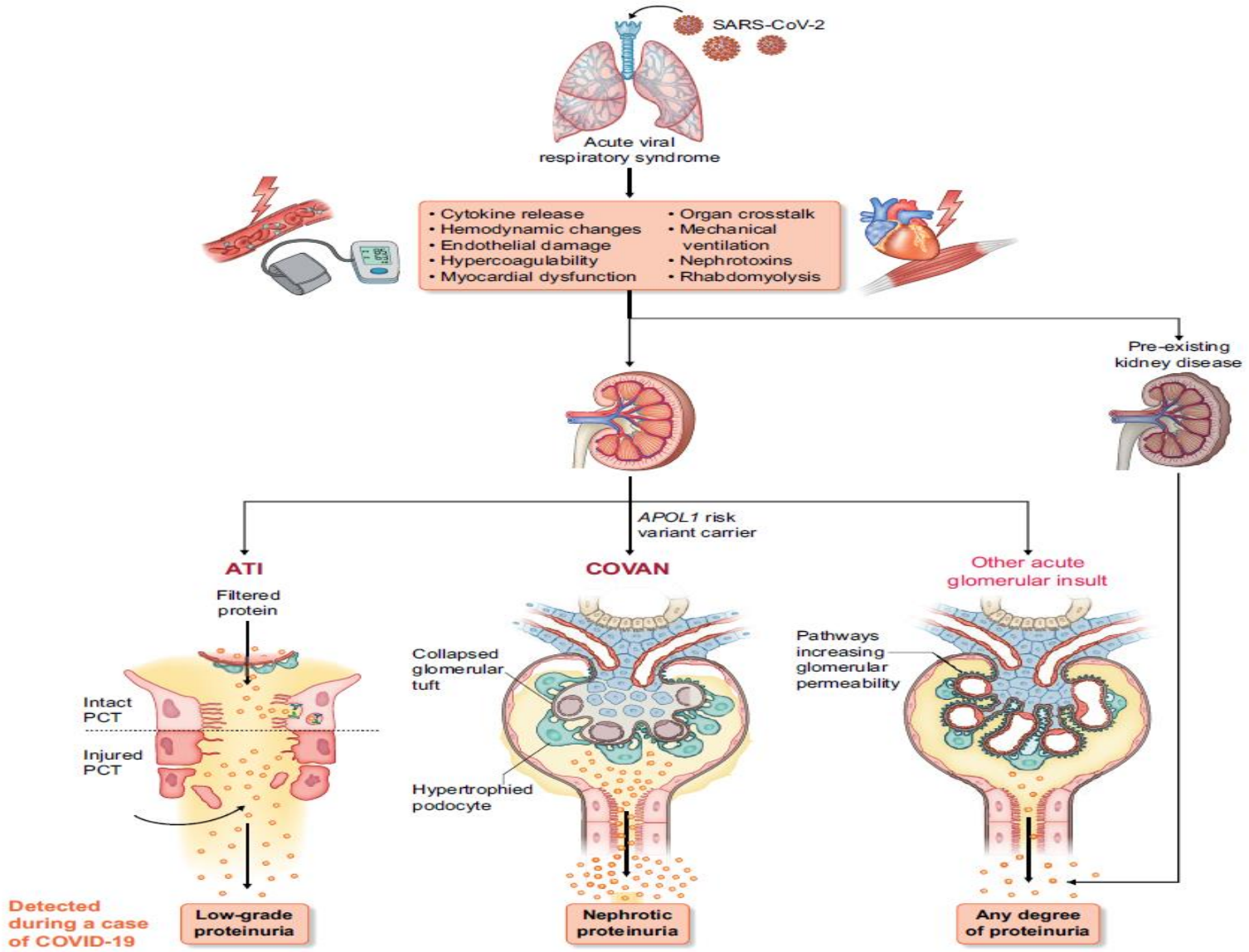
COVID-19 AKI





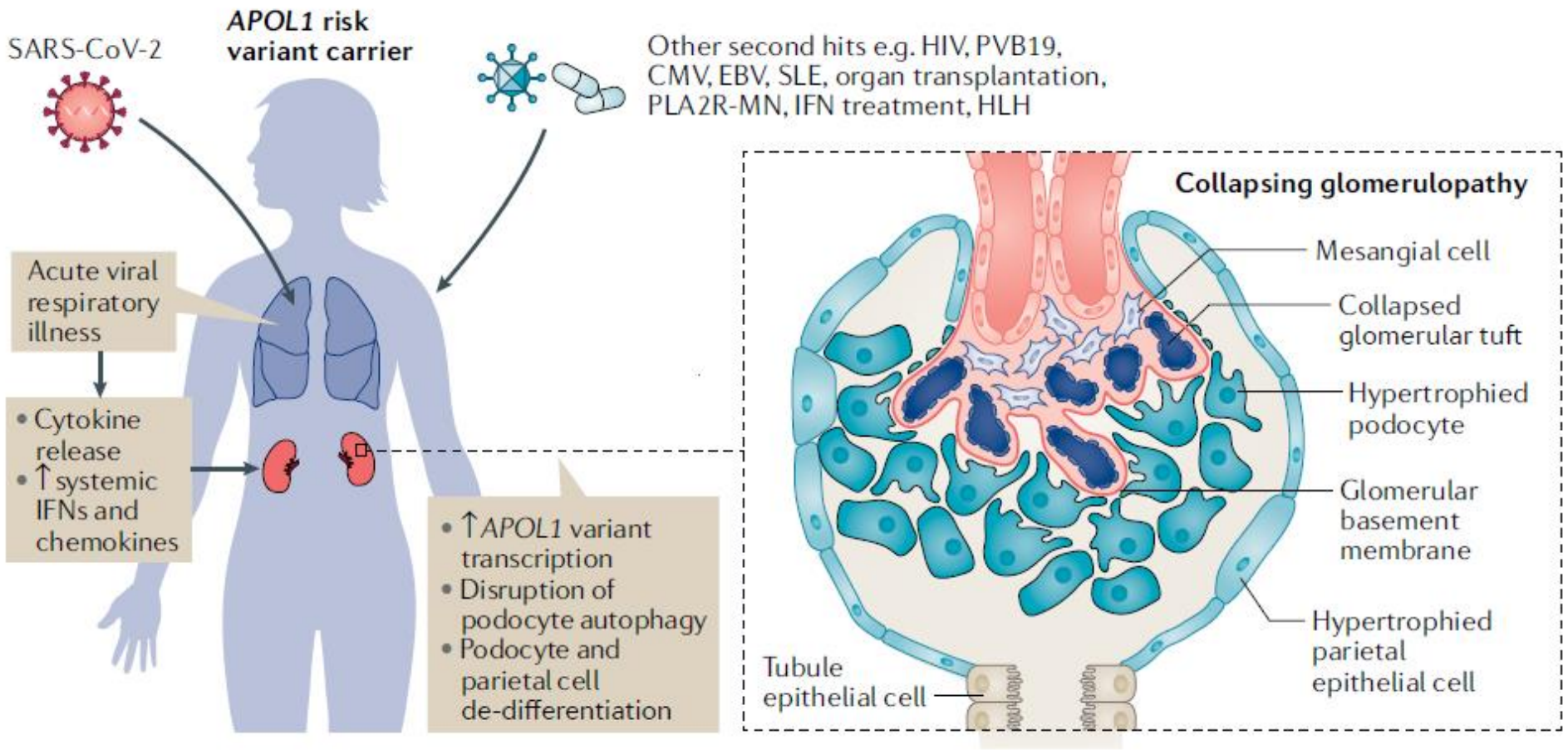
Diseases **2022**, *10*, 53. https://doi.org/10.3390/diseases10030053

Pathogenesis of proteinuria in COVID-19



Clinical Kidney Journal, 2021, vol. 14, Suppl 1, i40–i47

Proposed pathogenesis of COVAN



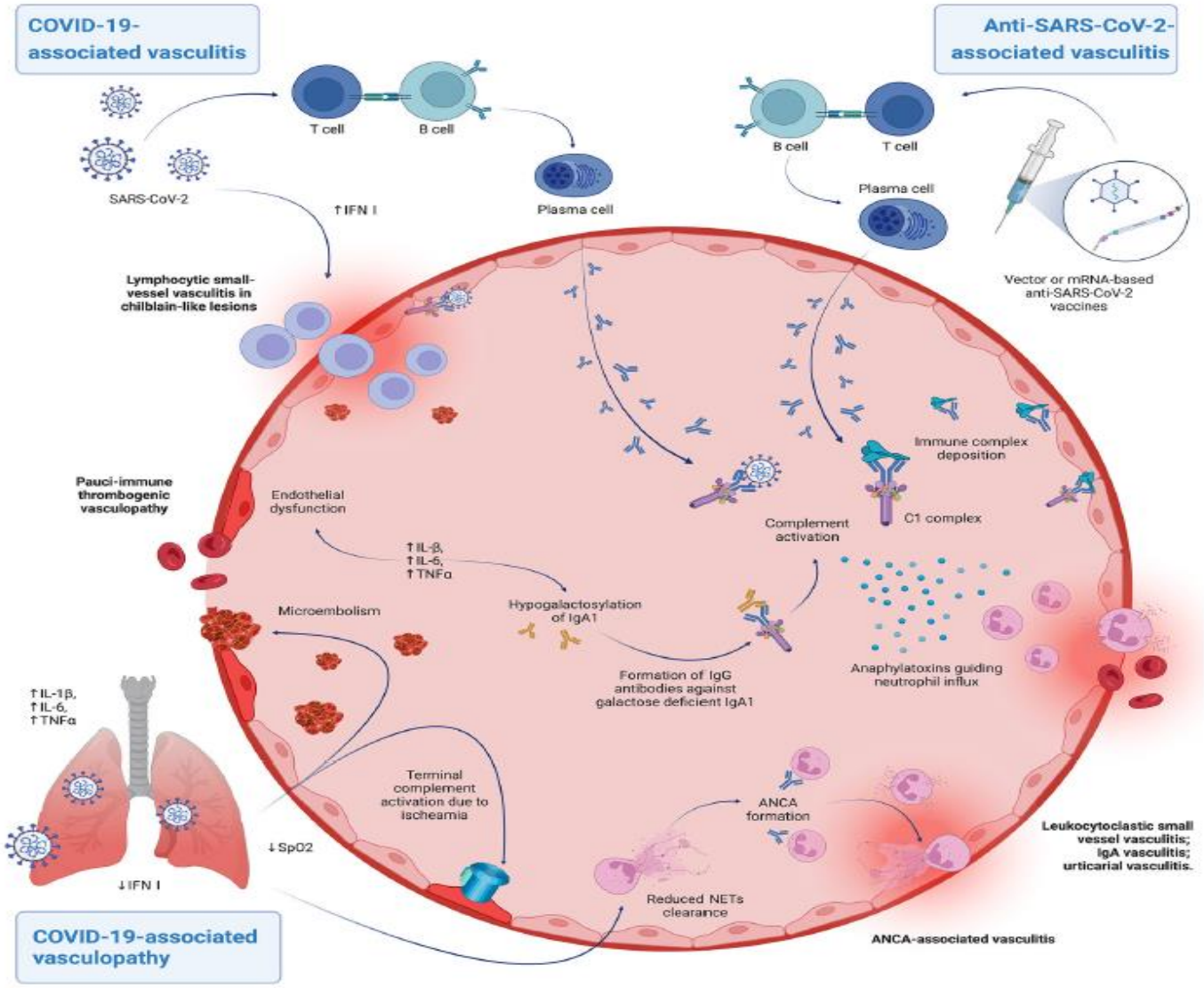
Nat Rev Nephrol 2020, 16:565-567

Coronavirus Disease 2019-Associated Thrombotic Microangiopathy

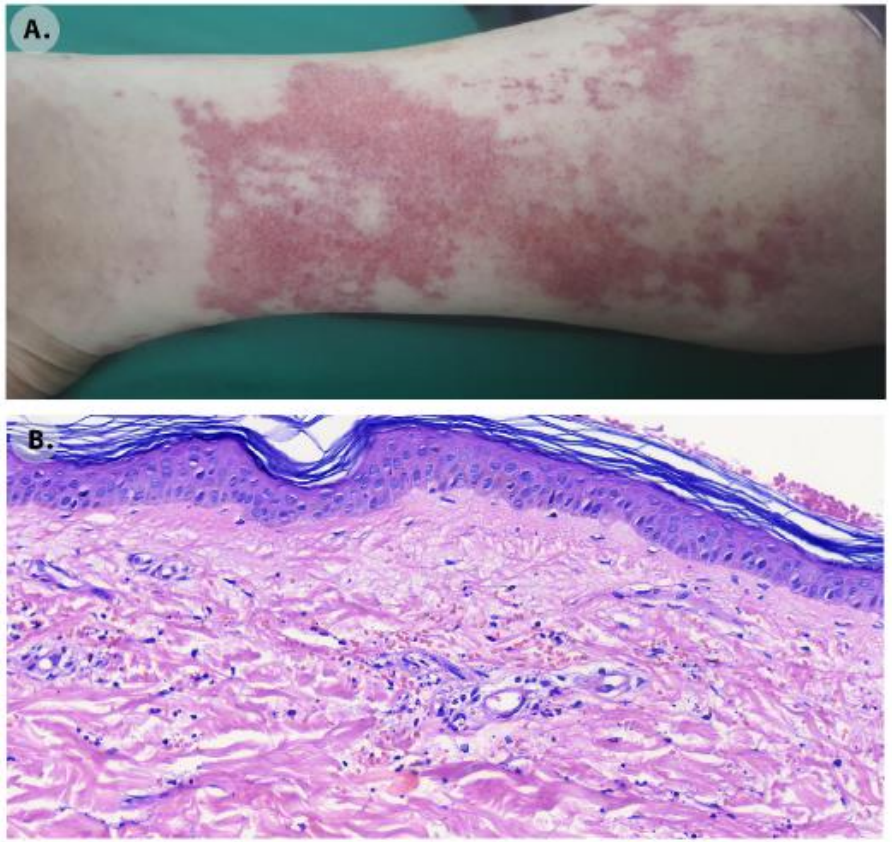
Patients with TTP	FFP	TPE + Steroid	TPE ± Steroid + Caplacizumab	TPE ± Steroid + Rituximab	TPE + Steroid + Rituximab + Caplacizumab
N = 18	2	5 + 1 *	3	5	2
Recovered	1	5	3	4	2
Died	1	1		1	
Patients with aHUS	TPE or FFP only	Steroid only	TPE + steroid only	Eculizumab or ravolizumab	No specific therapy or else
***N*= 28**	5	1	1	16 * 12 also TPE ± steroid	5
Recovery of renal function					
Complete	1			5	2
Partial/unknown magnitude	3	1	1	5	
ESRD	1			4	2
Died				2	1

Int. J. Mol. Sci. **2022**, *23*, 11307

Covid-19 associated vasculitis



Front Med (Lausanne). 2022 Aug 23;9:996288.



Journal of Autoimmunity 132 (2022) 102898

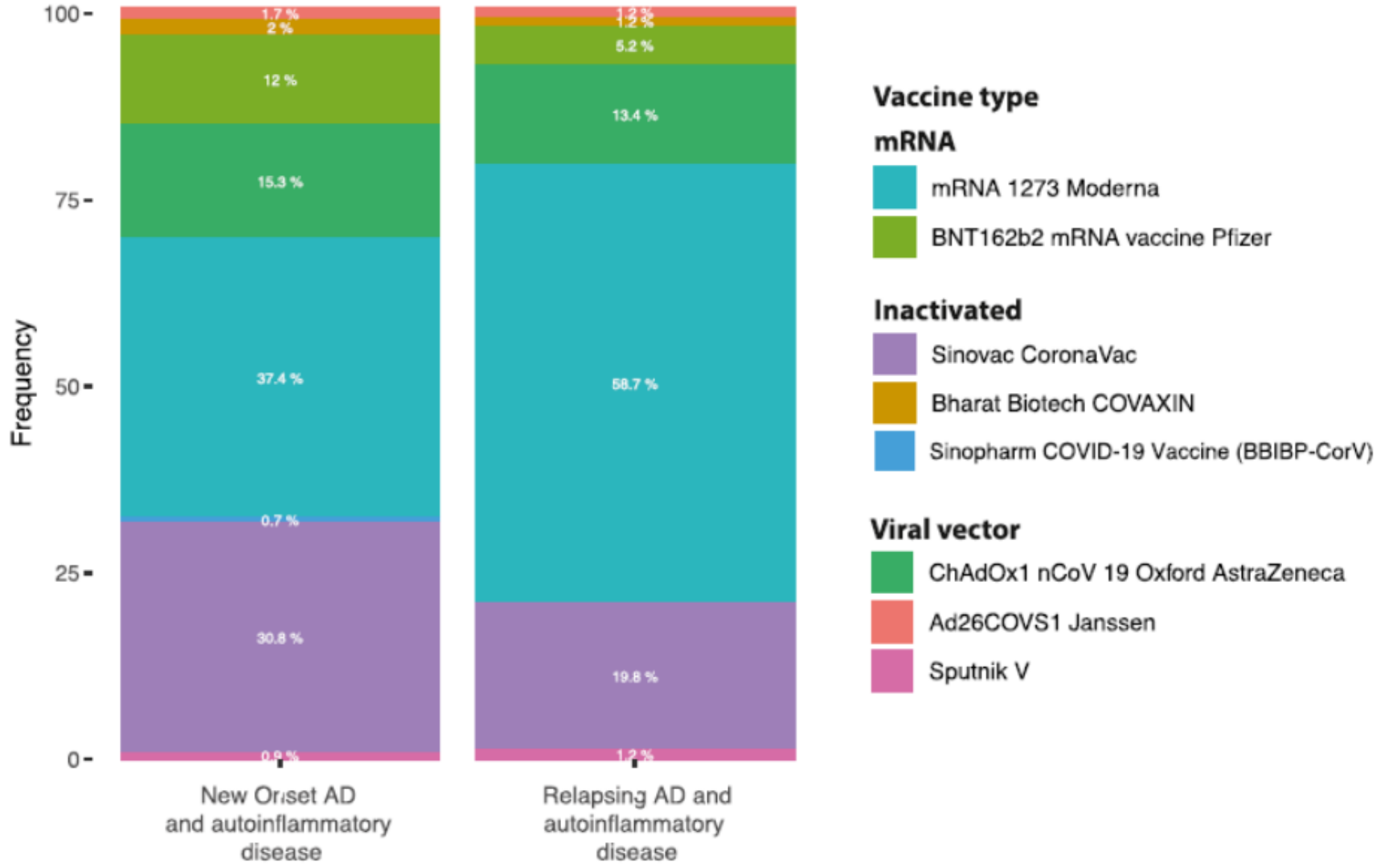
Distribution of reported cases by country according to new onset (red) and relapsing (blue) of the autoimmune/inflammatory disease.

Journal of Autoimmunity 132 (2022) 102898

Distribution of the main documented diseases after COVID-19 vaccination.

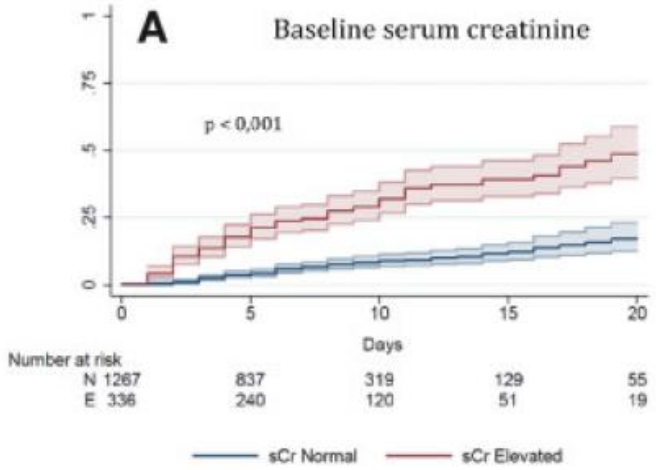
Journal of Autoimmunity 132 (2022) 102898

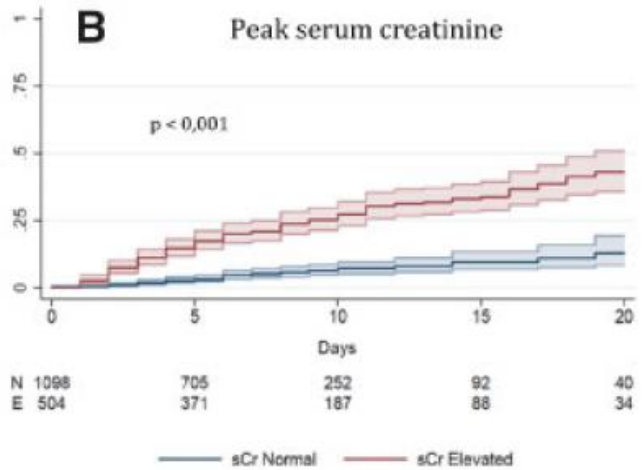
Autoimmune and autoinflammatory conditions after COVID-19 vaccine according to vaccine type

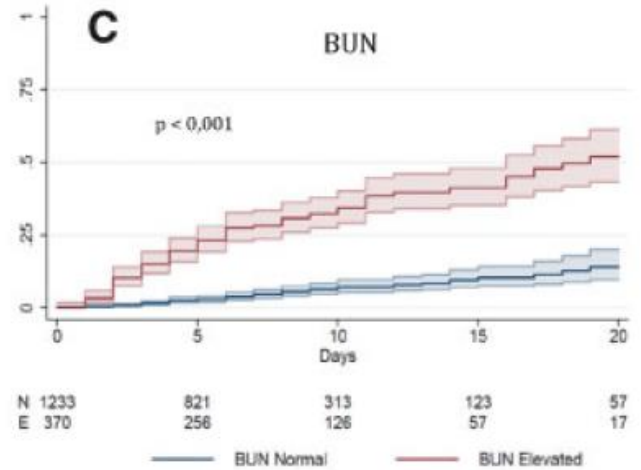


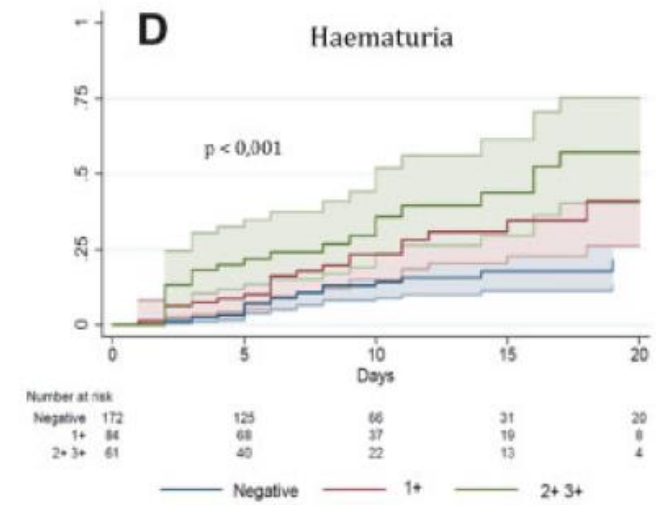
Journal of Autoimmunity 132 (2022) 102898

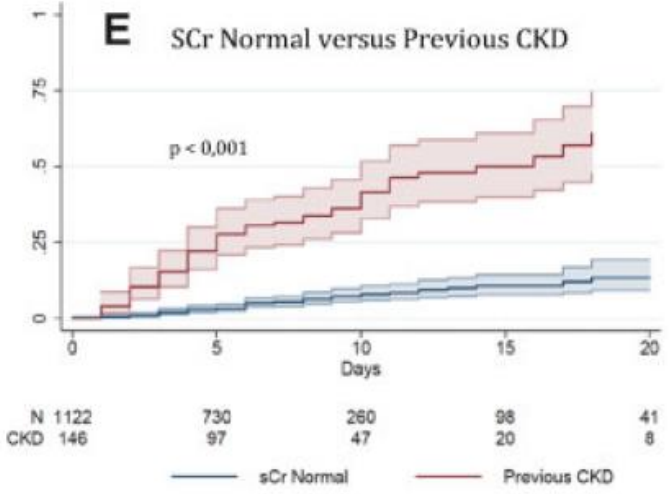
Renal disfunction and mortality in covid19 patients

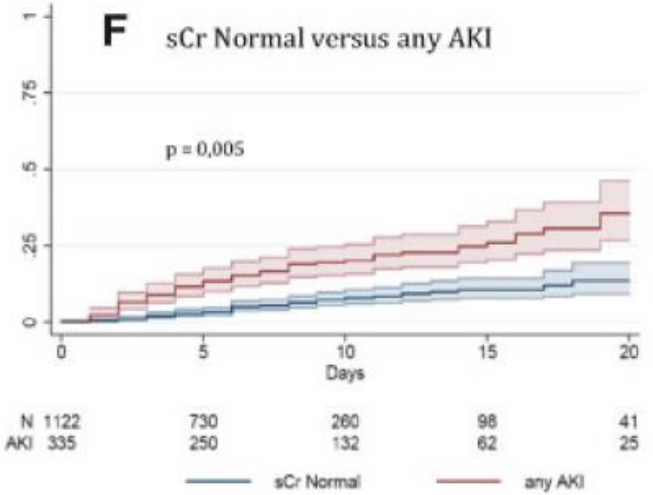






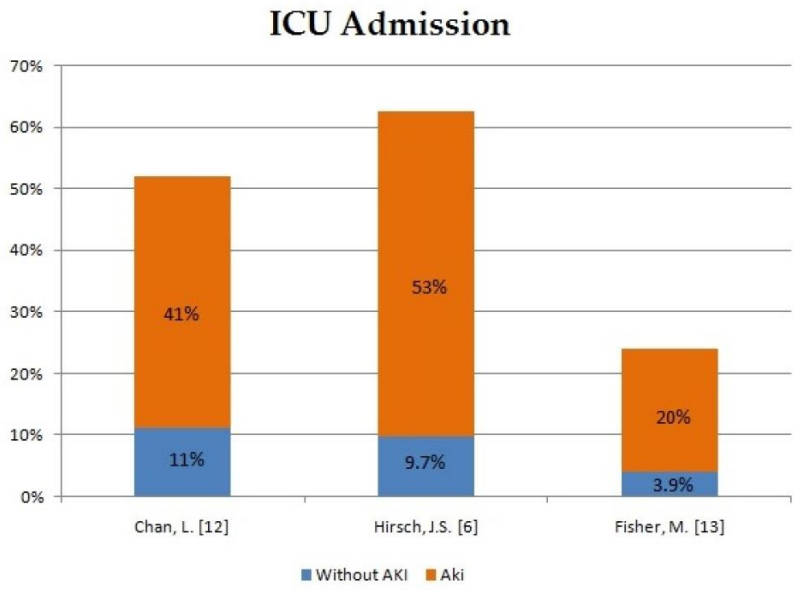


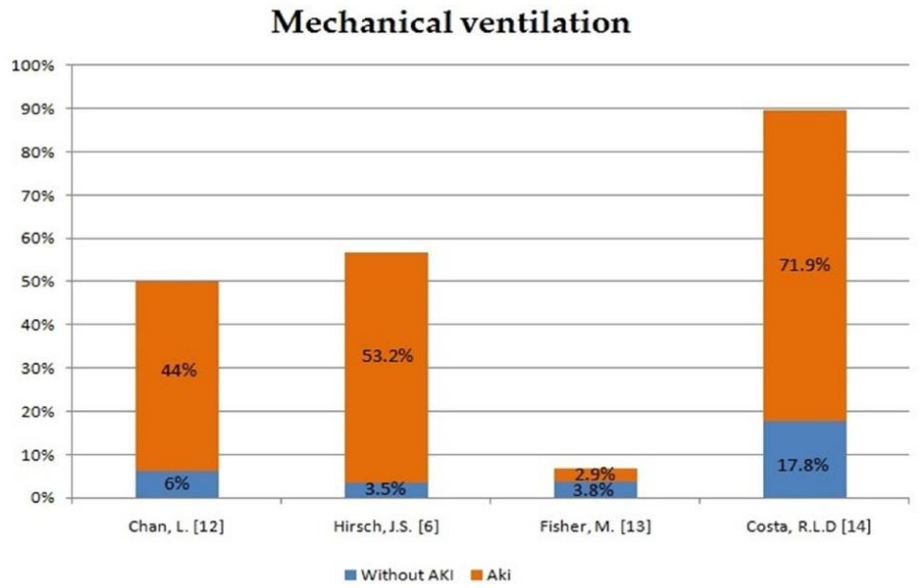


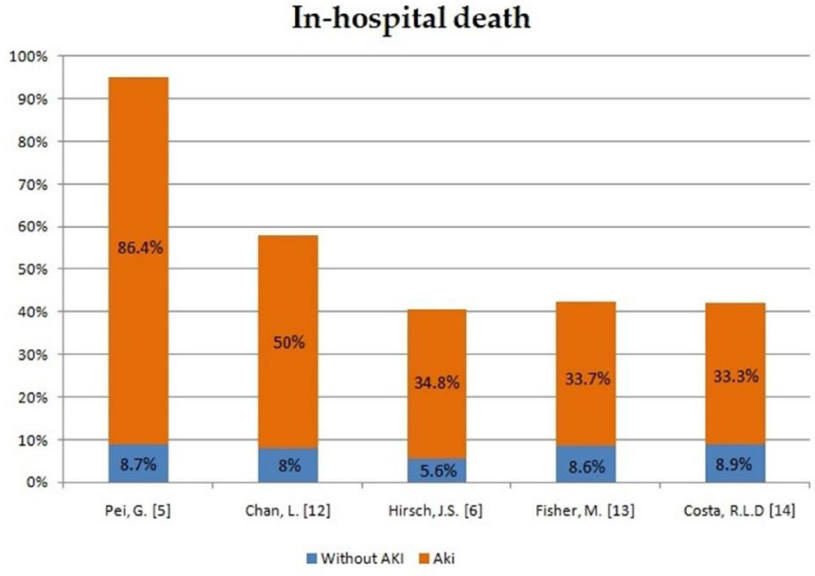


Nephrol Dial Transplant (2020) 35: 1353–1361
doi: 10.1093/ndt/gfaa189

Impact of AKI Development on Hospitalization and Mortality Rate





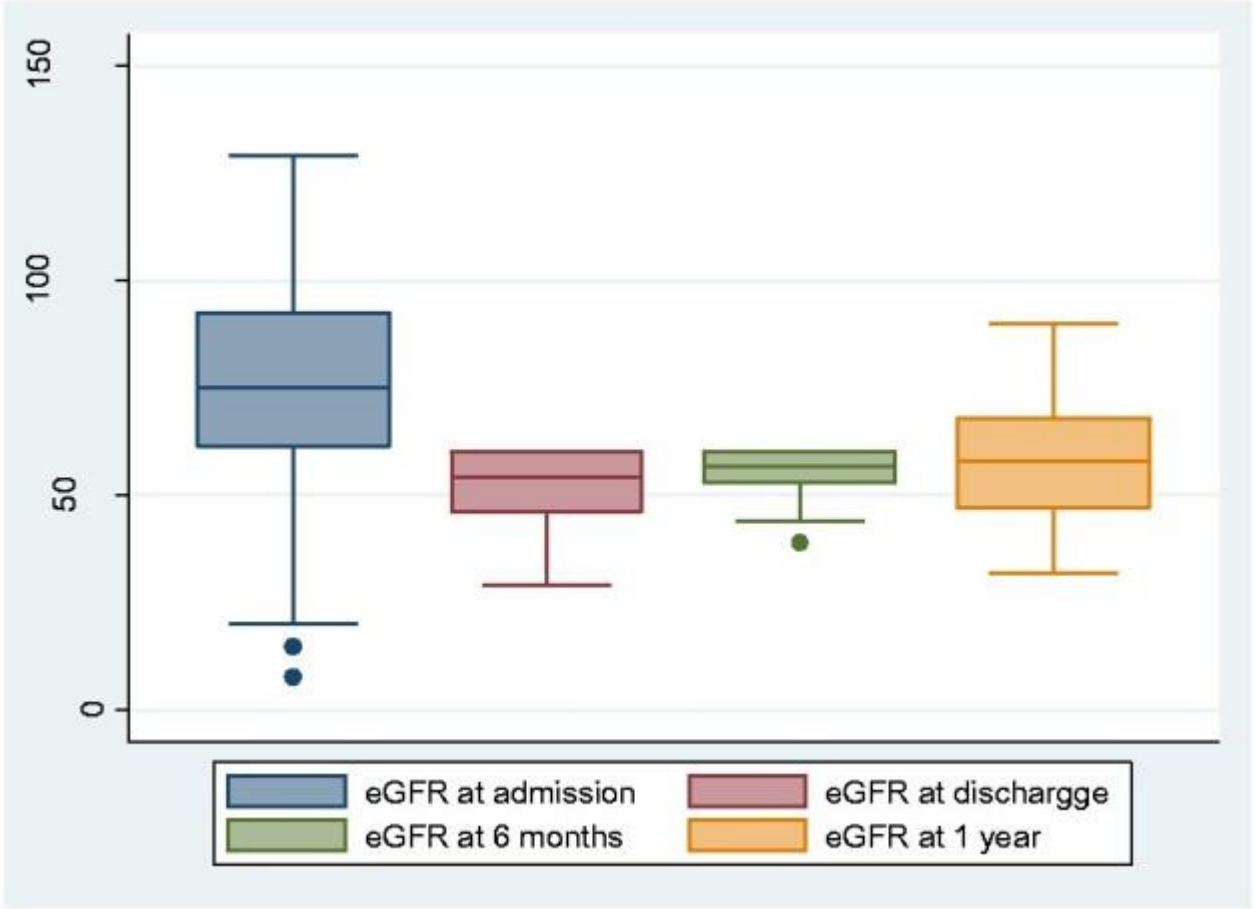


Hirsch et al, Kidney Int. 2020, 98, 209–218
Chan et al, J. Am. Soc. Nephrol. 2021, 32, 151–160
Fisher et al, J. Am. Soc. Nephrol. 2020, 31, 2145–2157
Costa et al, Braz. J. Nephrol. 2021
Pei et al, J. Am. Soc. Nephrol. 2020, 31, 1157–1165

Renal long-term outcome of critically ill COVID-19 patients with acute kidney failure and continuous renal replacement therapy

Clinical and demographic characteristics	Values
Sex (male/female), *n*/*n*	42/11
Age (years), median (IQR)	63 (31–78)
Baseline serum creatinine (mg/dL), mean ± SD	1.23 ± 0.93
Baseline eGFR (mL/min/1.73 m^2), mean ± SD	73.1 ± 26.7
Diabetes, *n* (%)	12 (23)
Hypertension, *n* (%)	40 (75)
Obesity, *n* (%)	20 (38)
CRRT prescription, %	CVVHD: 85 CVVH: 15
Time on CRRT (days), median (IQR)	18 (1–176)
Mortality, *n* (%)	39 (73.5)

CVVHD, continuous venovenous haemodialysis; CVVH, continuous veno-venous haemofiltration; IQR, interquartile range; SD, standard deviation.



Clinical Kidney Journal, 2021, vol. 14, no. 10, 2449–2450

Short and Long-term Recovery after Moderate/Severe Acute Kidney Injury in patients with and without COVID-19

Kidney360

Methods

Single Center Retrospective
March 2020 - July 2020
n = 3,299

Respiratory disease
COVID positive
n= 1,338
COVID negative
n= 1,961

Acute Kidney Injury
KDIGO Stages 2&3

Outcomes

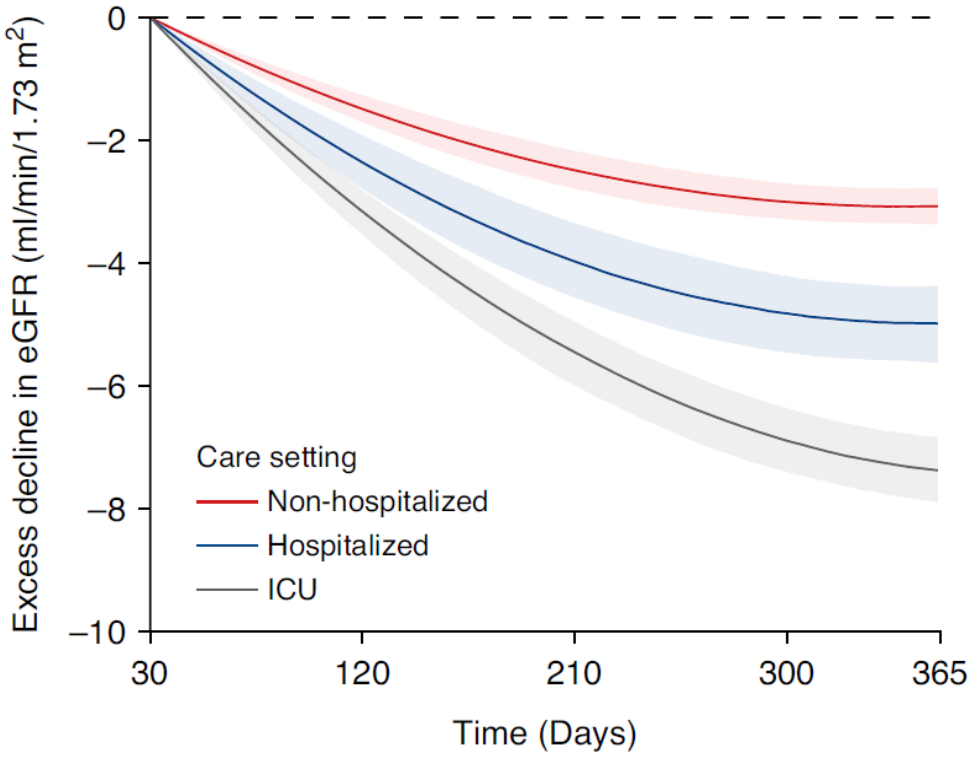
	Partial Recovery	Complete Recovery	Mortality	
n = 172 COVID-19 negative	74.4%	44.2%	11.6%	AKI-2/3 survivors n= 52
				23.5% Post-AKI CKD
n = 255 COVID-19 positive	50.6%	24.7%	23.9%	25.7% Follow-up 12 Mo

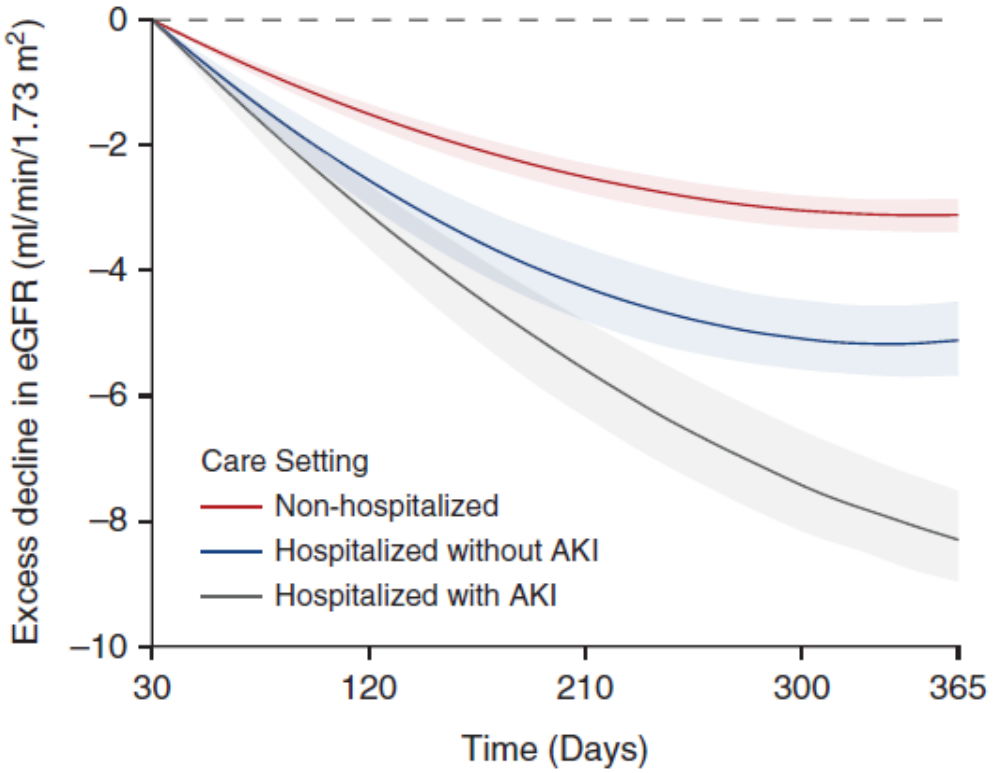
Multivariable analysis: Non-recovery was significantly associated with ICU admission, ARDS and mortality in patients with COVID-19
Machine Learning (XGBoost): Strongest predictors of recovery were initial Arterial paO2 & CO2, SCr, K, Lymphocyte count & CPK

Conclusions: Recovery from COVID-19-associated moderate/severe AKI, can be predicted using admission data and is associated with severity of respiratory disease and in-hospital death. The risk of CKD might be similar between COVID-19 positive and negative patients.

Siao Sun, Raji R. Annadi, Imran Chaudhri, *et al.* ***Short and Long-term Recovery after Moderate/Severe Acute Kidney Injury in patients with and without COVID-19.*** *Kidney360*. DOI: 10.34067/KID.0005342021.
Visual Abstract by **Verner Venegas**

Kidney Outcomes in Long COVID

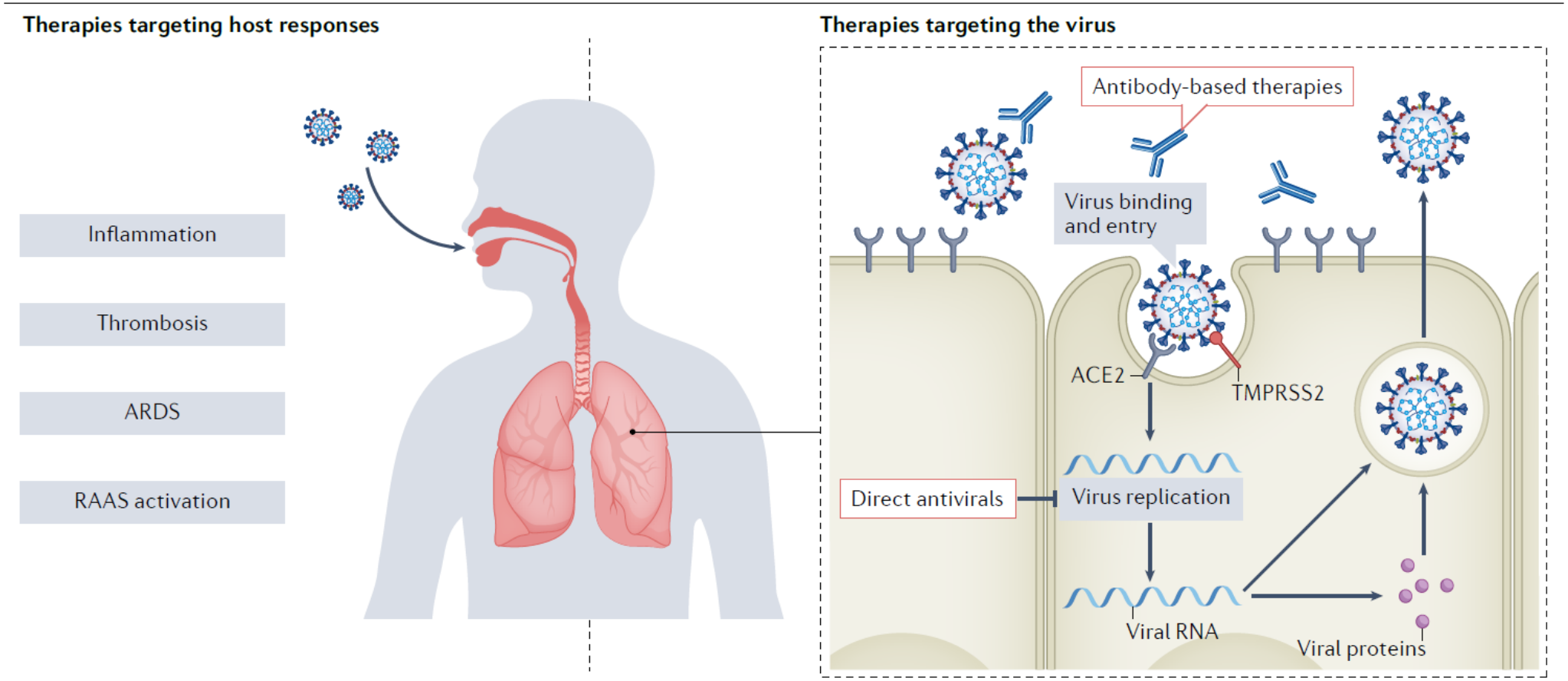




1726683 veteranos
89216 infectados por covid

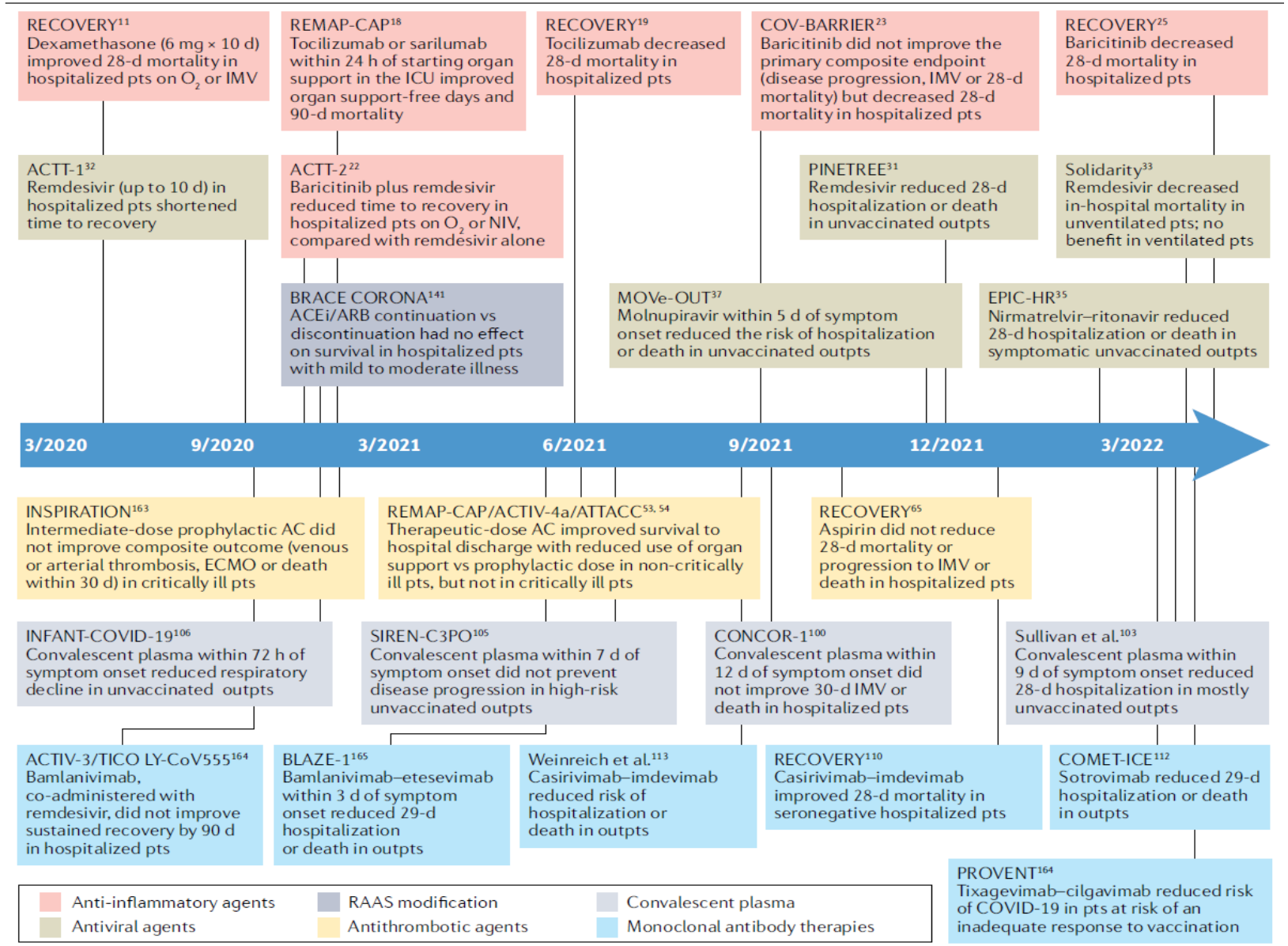
JASN **32**: 2851–2862, 2021

Classes of therapies for COVID-19



Murakami et al, Nature Review Nephrology 2022

Timeline of publication of pivotal phase III randomized clinical trials of COVID-19 therapies.



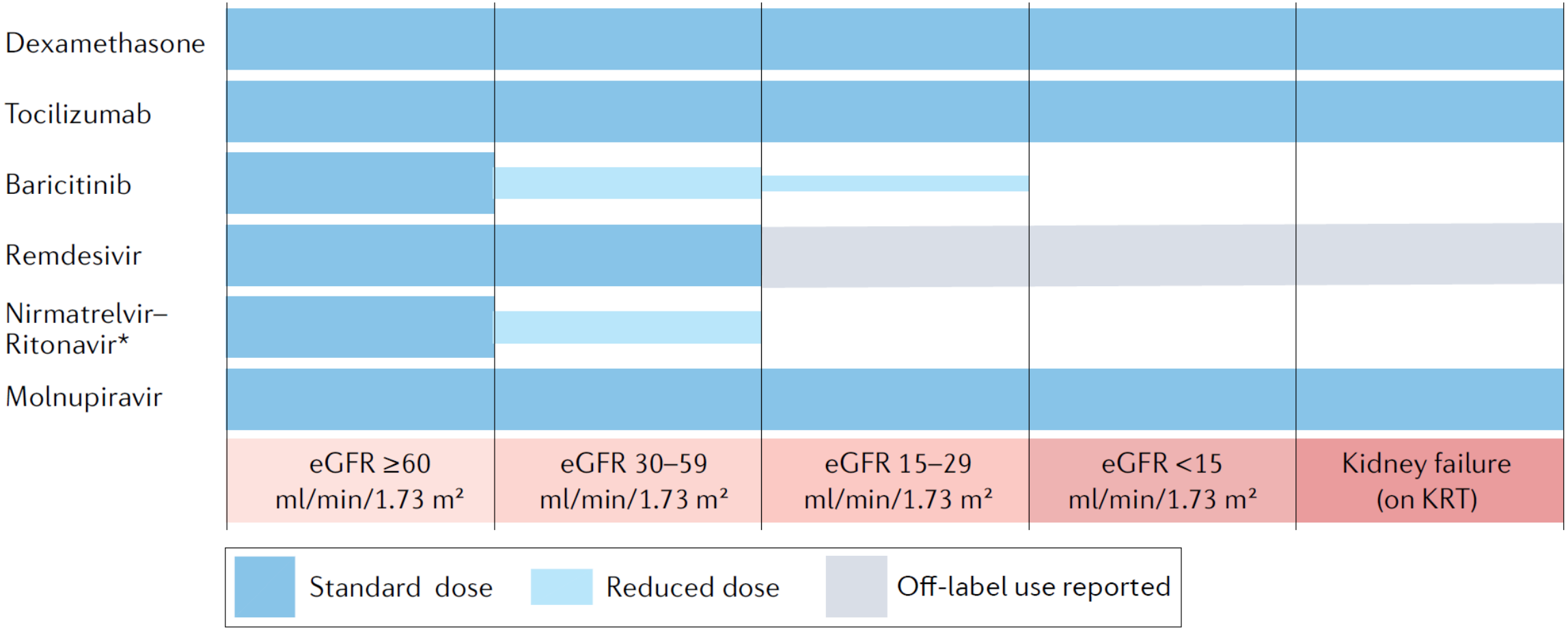
Murakami et al,
Nature Review Nephrology 2022

Authorized or approved therapeutics for COVID-19

Drug	Setting	Patient population	Dosing regimen	Dose adjustment for kidney dysfunction	Date of FDA EUA or approval	Date of EMA authorization
Anti-inflammatory agents						
Tocilizumab	Inpatient	Patients receiving corticosteroids and on supplemental oxygen, a ventilator or ECMO	8 mg/kg i.v. once (max dose: 800 mg)	None	EUA, 24 June 2021[a]	6 December 2021
Baricitinib	Inpatient	Patients on supplemental oxygen, IMV or ECMO	4 mg once daily	eGFR ≥ 60: 4 mg daily; eGFR 30–59: 2 mg daily; eGFR 15–29: 1 mg daily; eGFR < 15: NR	EUA, 19 November 2020; FDA approved, 10 May 2022	Under review
Antiviral agents						
Remdesivir	Inpatient and outpatient	Symptoms (mild to moderate) for < 7 days	200 mg i.v. on day 1, then 100 mg i.v. daily from day 2 (3 days for non-hospitalized, 5 days or until discharge for hospitalized)	eGFR < 30: NR	EUA, 1 May 2020; FDA approved, 22 October 2020	3 July 2020
Nirmatrelvir–ritonavir (Paxlovid)	Outpatient	Symptoms (mild to moderate) for < 5 days	300 mg/100 mg oral twice daily for 5 days	eGFR 30–59: 150/100 mg twice daily for 5 days; eGFR < 30: NR	EUA, 22 December 2021	28 January 2022
Molnupiravir	Outpatient	Symptoms (mild to moderate) for < 5 days	800 mg orally twice daily for 5 days	None	EUA, 23 December 2021	Under review
Antibody-based therapies						
Convalescent plasma	Inpatient and outpatient	Hospitalized patients receiving supplemental oxygen, noninvasive ventilation or IMV, or ECMO	~200 ml IV	None	EUA, 23 August 2020	ND
Bamlanivimab/etesevimab[a]	Outpatient	Symptoms (mild to moderate)	700 mg/1400 mg i.v. once	None	EUA, 9 February 2021	Withdrawn from review 29 October 2021
Casirivimab/imdevimab[a]	Outpatient	Symptoms (mild to moderate) for < 10 days	600 mg/600 mg s.c. once	None	EUA, 21 November 2020	12 November 2021
Sotrovimab[b]	Outpatient	Symptoms (mild to moderate) for < 7 days	500 mg i.v. once	None	EUA, 26 May 2021	17 December 2021
Bebtelovimab	Outpatient	Symptoms (mild to moderate) for < 7 days and at a high risk of severe illness	175 mg i.v. once	None	EUA, 11 February 2022	ND
Tixagevimab/cilgavimab (Evusheld)	Outpatient	Pre-exposure prophylaxis and with moderate to severe immune compromise due to a medical condition or immunosuppressive medication	300 mg/300 mg i.m. once	None	EUA, 8 December 2021	25 March 2022

Murakami et al,
Nature Review Nephrology 2022

Anti-inflammatory and antiviral agents for COVID-19 including dose adjustment for kidney function impairment



Murakami et al, Nature Review Nephrology 2022

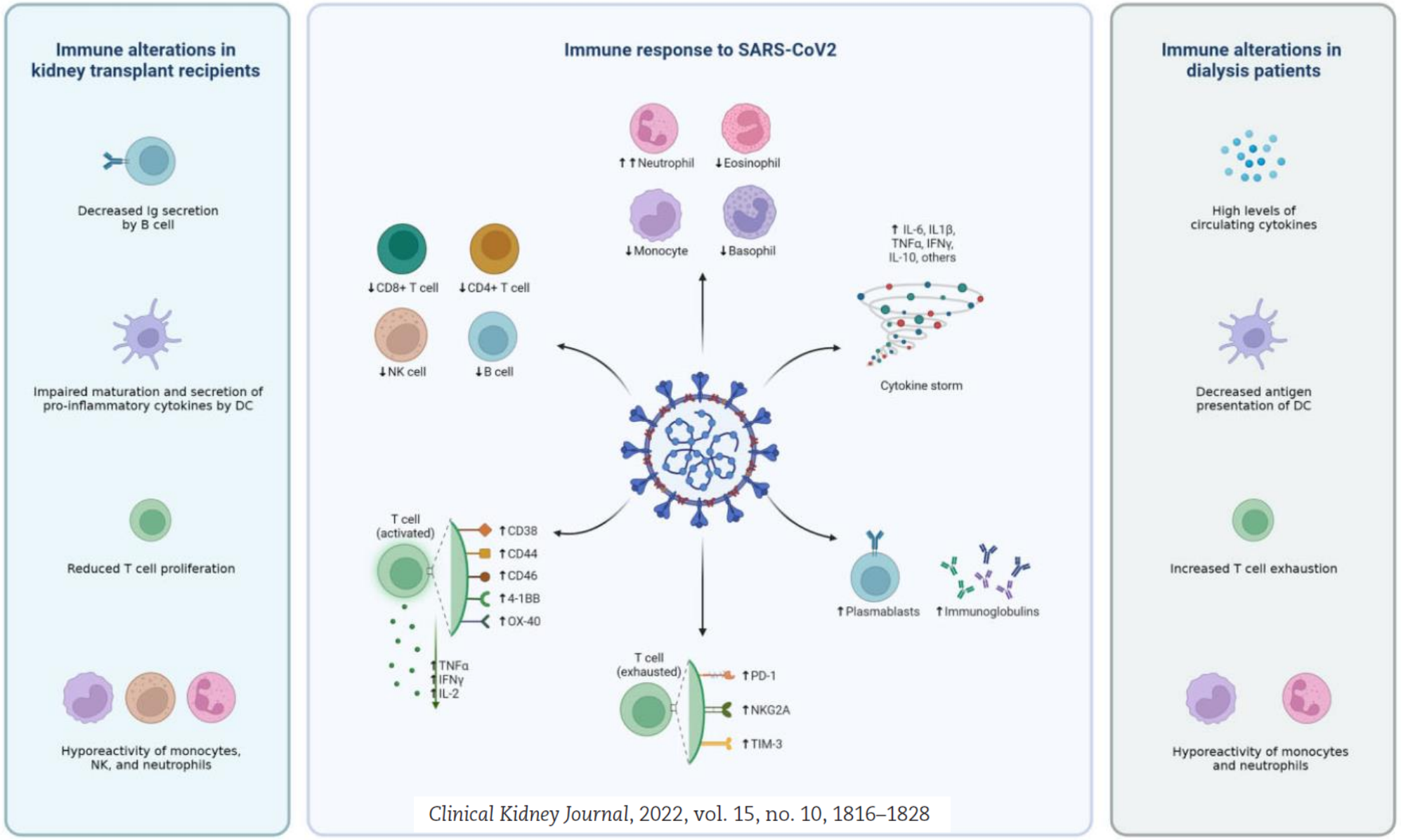
Major COVID-19 RCTs that assesed AKI outcomes

Trial name	No. of patients	Treatment arms	Patient population	Definition of AKI	AKI outcome
Anti-inflammatory therapies					
RECOVERY (dexamethasone)[11]	6,425	Dexamethasone versus usual care	Hospitalized adults	Receipt of KRT	RR 0.61 (95% CI 0.48–0.76)
RECOVERY (tocilizumab)[19]	4,116	Tocilizumab versus usual care	Hospitalized adults	Receipt of KRT	RR 0.72 (95% CI 0.58–0.90)
RECOVERY (baricitinib)[25]	8,156	Baricitinib versus usual care	Hospitalized adults	Receipt of KRT	RR 0.78 (95% CI 0.59–1.03)
ACTT-2 (ref.[22])	1,033	Baricitinib+RDV versus placebo+RDV	Hospitalized adults	AKI or kidney failure[a]	Baricitinib+RDV: 5/507 (1.0%) Placebo+RDV: 16/509 (3.1%)
Antiviral therapies					
ACTT-1 (ref.[32])	1,048	RDV versus placebo	Hospitalized adults	GFR decreased, AKI or failure[a]	RDV: 14/532 (2.6%) Placebo: 17/516 (3.3%)
Antithrombotic therapies					
INSPIRATION[163]	562	Intermediate- versus standard-dose anticoagulation	Critically ill adults	Receipt of KRT	OR 1.49; (95% CI 0.58–3.86)
RECOVERY (Aspirin)[65]	14,892	Aspirin versus usual care	Hospitalized adults	Receipt of KRT	RR 0.99 (95% CI 0.84–1.17)
Anti-SARS-CoV-2 (neutralizing) antibody therapies					
CONCOR-1 (ref.[100])	938	Convalescent plasma versus standard of care	Hospitalized adults	Receipt of KRT	RR 0.83 (95% CI 0.31–2.27)
RECOVERY (casirivimab/imdevimab)[110]	9,785	Casirivimab/imdevimab versus usual care	Hospitalized adults	Receipt of KRT	RR 1.04 (95% CI 0.86–1.28)
Therapies targeting the RAAS					
BRACE-CORONA[141]	659	Discontinuing versus continuing ACEi/ARB	Hospitalized adults	Receipt of KRT	RR 2.0 (95% CI 0.80–5.37)

ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin II receptor blocker; GFR, glomerular filtration rate; KRT, kidney replacement therapy; RAAS, renin–angiotensin–aldosterone system; RCT, randomized controlled trial; RDV, remdesivir; RR, relative risk. [a]Definitions not available.

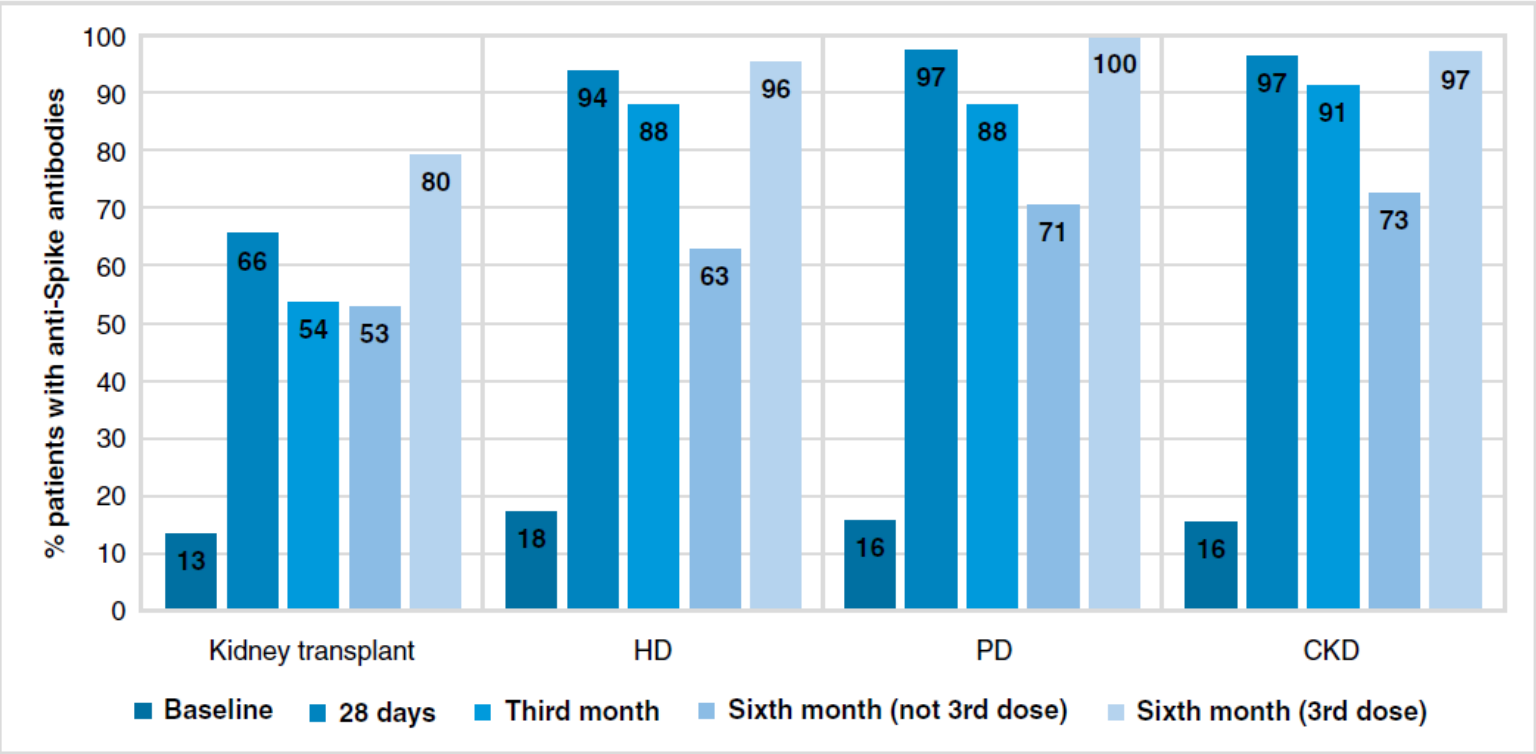
Murakami et al, Nature Review Nephrology 2022

Immune responses to SARS-CoV-2 in dialysis patients and KTRs



Clinical Kidney Journal, 2022, vol. 15, no. 10, 1816–1828

Humoral Response to Third Dose of SARS-CoV-2 Vaccines in the CKD Spectrum



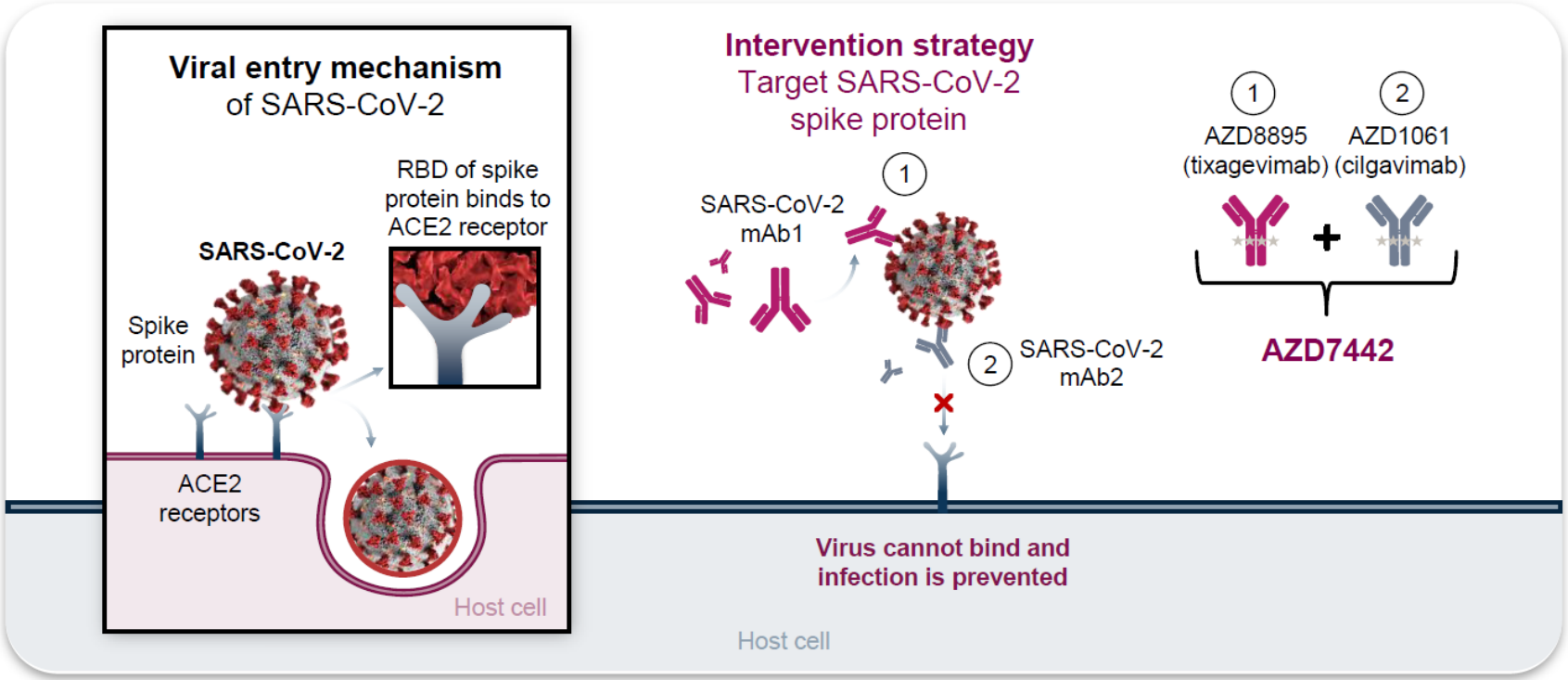
Sample size of each CKD group	Baseline (n=1126)	28 days (n=1736)	Third month (n=1371)	Sixth month (not 3rd dose) (n=331)	Sixth month (3rd dose) (n=624)
Kidney transplant	289	350	302	47	118
HD	622	155	894	217	451
PD	129	1091	75	34	20
CKD	86	140	100	33	35

Respuesta inmune y seguridad d
vacunación COVID-19 en paciente
ERC avanzada, en diálisis y
trasplantados renales
SENCOVAC

Quiroga et al ,cJASN 2022

Tixagevimab/Cilgavimab: preexposure prophylaxis

Background: AZD7442 binds to SARS-CoV-2 spike protein to prevent virus entry into host cells[1–4]



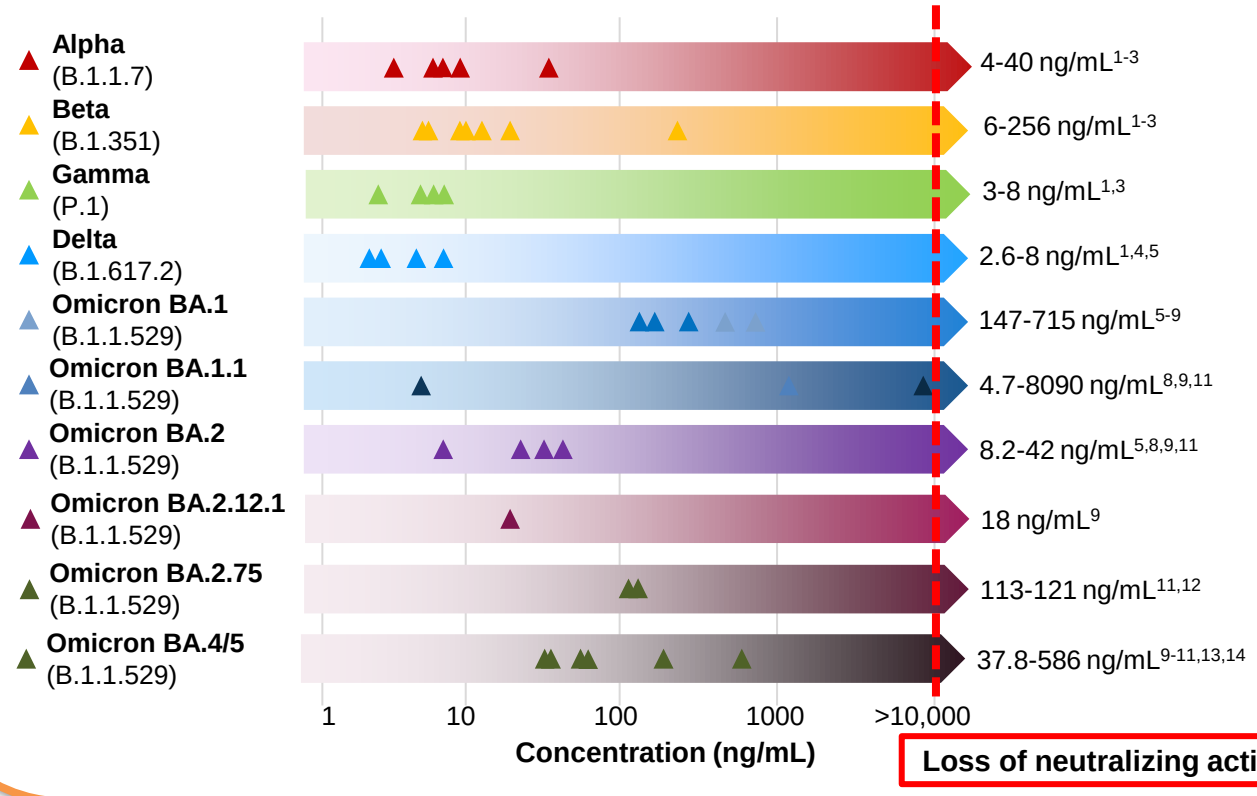
ACE2, angiotensin-converting enzyme 2; mAb, monoclonal antibody; RBD, receptor-binding domain; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

1. Cevik M et al. *BMJ*. 2020;371:m3862. 2. Taylor PC et al. *Nat Rev Immunol*. 2021;21:382–393. 3. Zost SJ et al. *Nature*. 2020;584:443–449. 4. Dong J et al. *Nat Microbiol*. doi:10.1038/s41564-021-00972-2.

Bernal AJ et al, NEJM, Dec 16, 2021

TIXA/CILGA Retains Neutralizing Activity Against SARS-CoV-2 VOCs, Including Omicron Sub-lineages[1-15]

TIXA/CILGA's IC_{50} (ng/mL) Against SARS-CoV-2 VOCs[a]



TIXA/CILGA demonstrated prophylaxis efficacy at median follow-up of 6.5 months (PROVENT: RRR, 83%)[15]

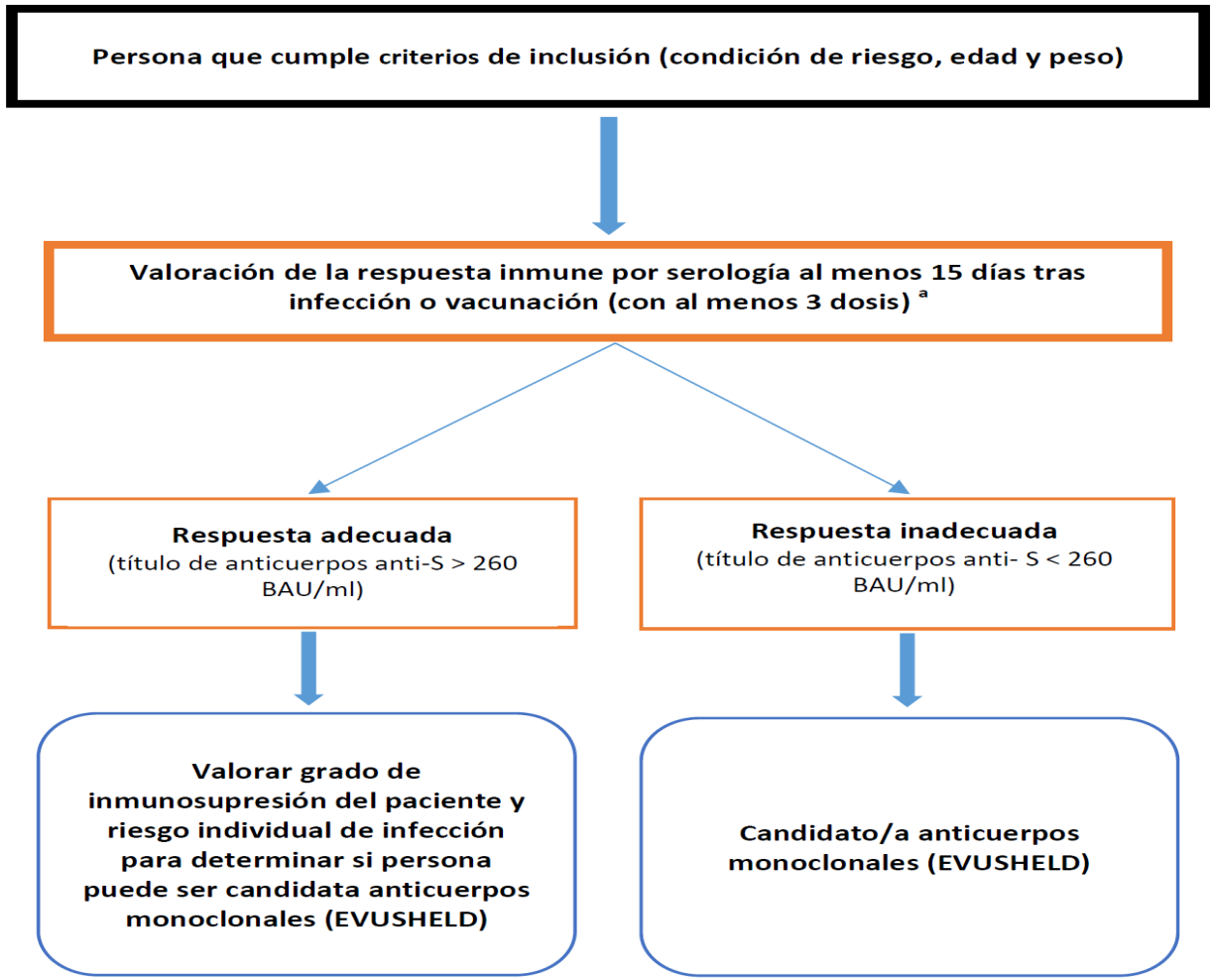
TIXA/CILGA maintains neutralization against all Omicron sub-lineages[5-14]

[a]IC_{50} is the concentration of an inhibitory substance or antagonist that reduces a given biological process or biological component by 50%[16]; Some of the information provided is based off preprint research papers that have not been peer reviewed. IC_{50} = half-maximal inhibitory concentration; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; TIXA/CILGA = tixagevimab/cilgavimab; VOCs = variants of concern.

1. National Center for Advancing Translational Sciences. Evusheld: tixagevimab (tixagevimab) and cilgavimab (cilgavimab) mAbs for SARS-CoV-2 antiviral resistance information (version 5). https://opendata.ncats.nih.gov/variant/datasets?id=107; 2. Dejnirattisai W et al. *Cell*. 2021;184:2939-2954.e9; 3. Chen RE et al. *Nat Med*. 2021;27:717-726; 4. Liu C et al. *Cell*. 2021;184:4220-4236.e13; 5. Bruel T et al. *Nat Med*. 2022;28:1297-1302; 6. Dejnirattisai W et al. *Cell*. 2022;185:467-484.e15; 7. VanBlargan LA et al. *Nat Med*. 2022;28:490-495; 8. Case JB et al. Preprint published online. *bioRxiv*. 2022; 9. Cao Y et al. Online ahead of print. *Nature*. 2022; 10. Tuekprakhon A et al. Preprint article and supplementary material published online. *bioRxiv*. 2022; 11. Yamasoba D et al. Preprint published online. *bioRxiv*. 2022; 12. Cao Y et al. Preprint published online. *bioRxiv*. 2022; 13. Touret F et al. *Sci Rep*. 2022;12:12609; 14. Takashita E et al. *N Engl J Med*. 2022;387:468-470; 15. European Medicines Agency. Summary of Product Characteristics for EVUSHELD. https://www.ema.europa.eu/en/documents/product-information/evusheld-epar-product-information_en.pdf; 16. Neubig RR et al. *Pharmacol Rev*. 2003;55:597-606.

Pacientes inmunodeprimidos /portadores de trasplante renal candidatos a recibir Evusheld

7. Flujograma para la selección de personas candidatas a recibir Evusheld (ver texto en apartados 4 y 5)



Gracias @NefroHGUGM

Nos basta una mano
para matar.
Necesitamos dos para
acariciar, para
aplaudir y todas las del
mundo para conseguir
la **PAZ**

—Gloria Fuertes—