

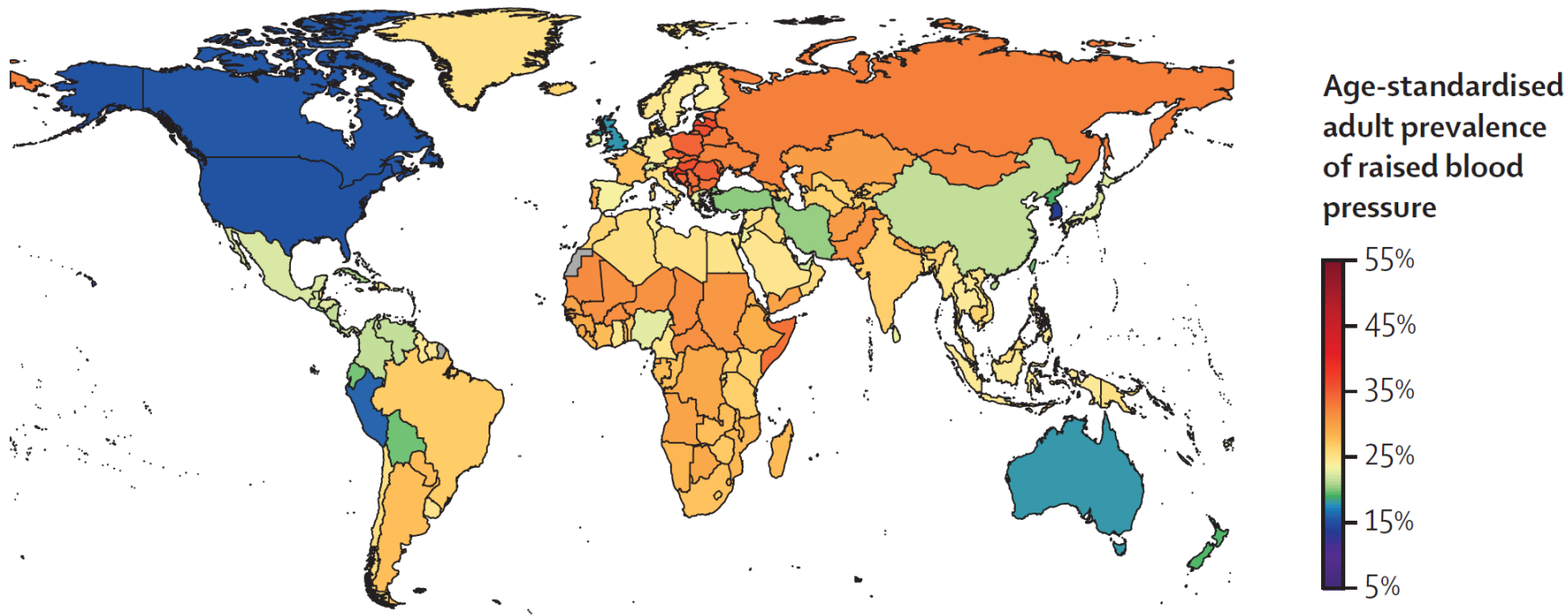
Hypertension and COVID 19

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Prevalence of HTN in men by countries

Raised blood pressure, men 2015

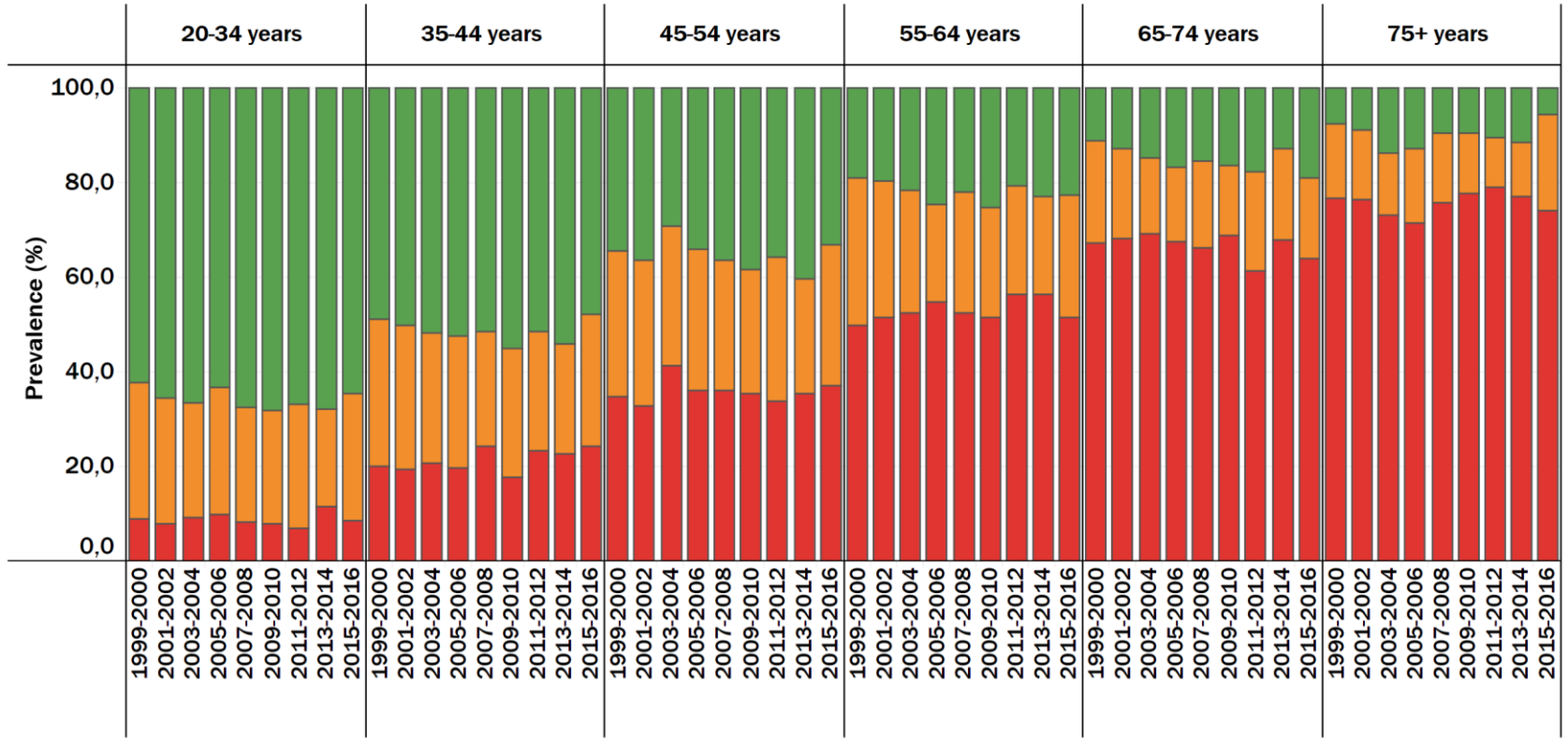


NCD Risk. Lancet 2017; 389: 37–55

ESTEBAN Study in France

- Population: 974 men (45%) and 1,197 women (55%) with two BP measures.
- **Prevalence of hypertension : 30.6%; men : 36.5% vs. women (25.2%); increase with age**
- Proportion of hypertension awareness: 50%.
- Proportion of treated with AHT medication among hypertensive adult: 47.3% [45.1-54.8].
- Proportion of pts with controlled BP among those treated: 55.0% (men: 44.9% women: 66.5%)

Prevalence of BP Status in US Adults by Age NHANES



*Categories of blood pressure status defined according to JNC 7 criteria

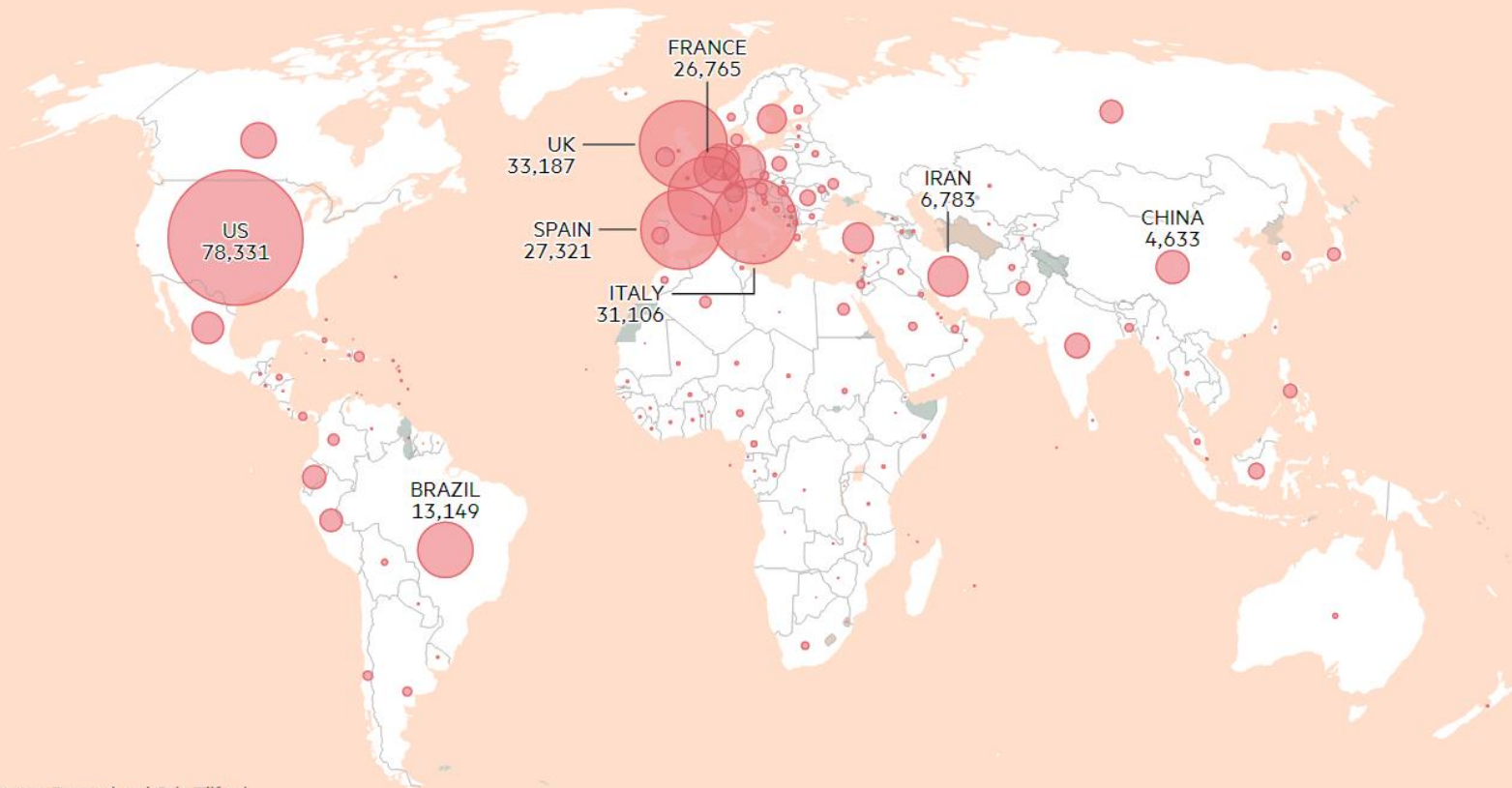
■ Normotension
 ■ Prehypertension
 ■ Hypertension

<https://healthmetrics.heart.org/prevalence-blood-pressure-status-us-adults-age-category->

Mapping the coronavirus outbreak

As of 10:35am May 14 BST

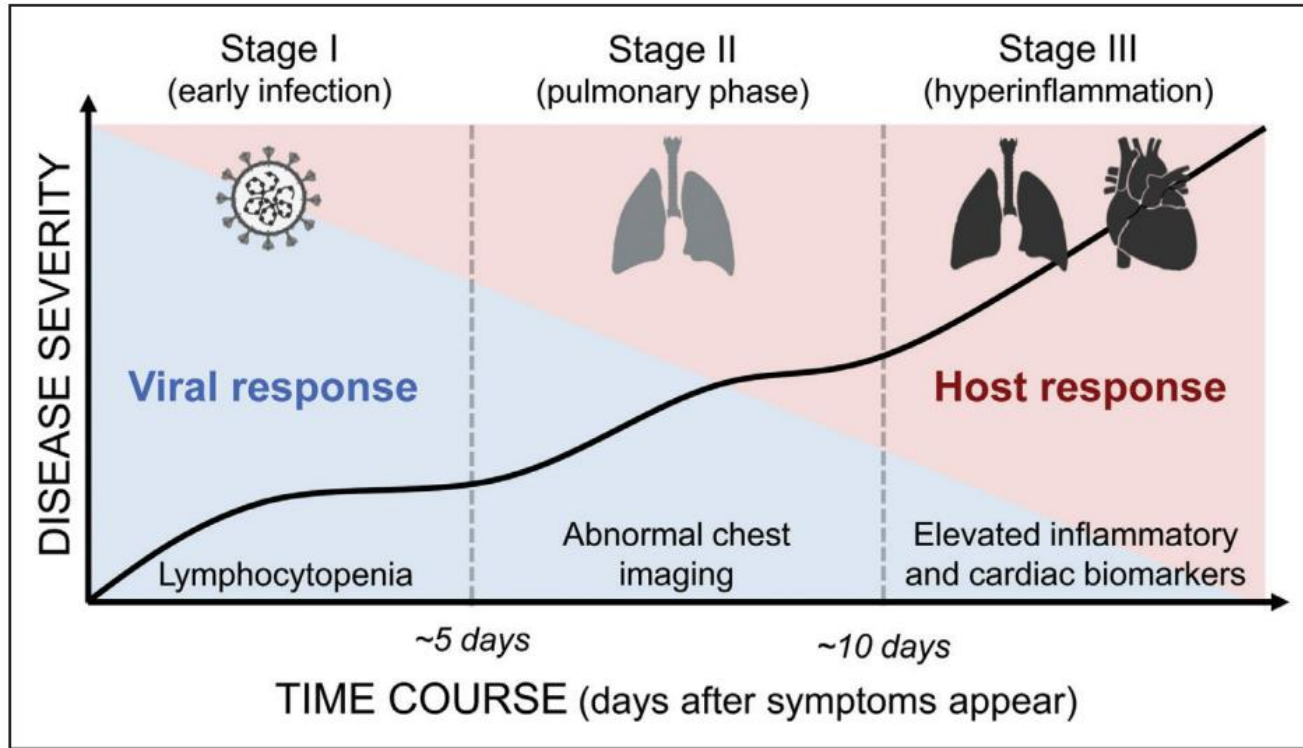
Confirmed cases **4,300,003** Deaths **290,702**



Graphic: Steven Bernard and Cale Tilford
Sources: ECDC; Covid Tracking Project; FT research

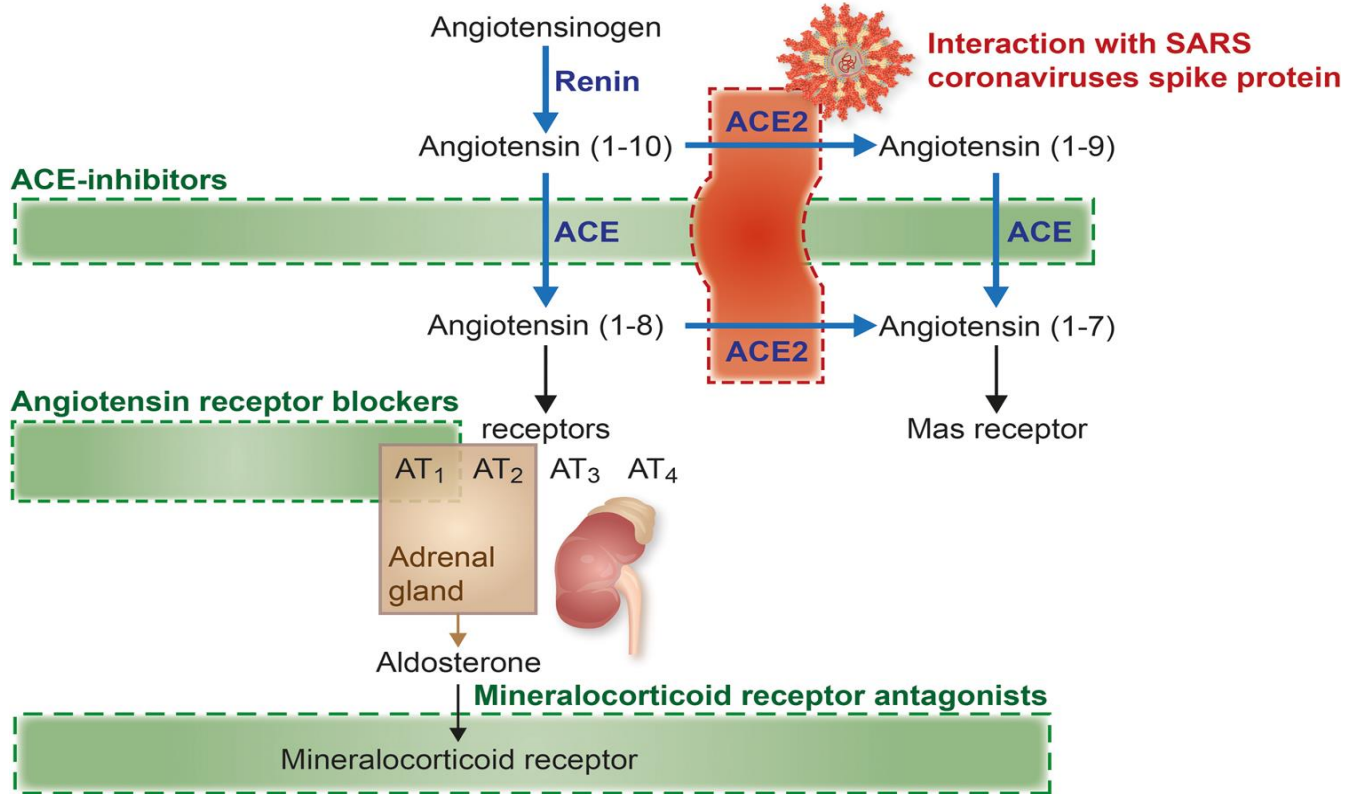
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Progression of the acute disease in COVID-19

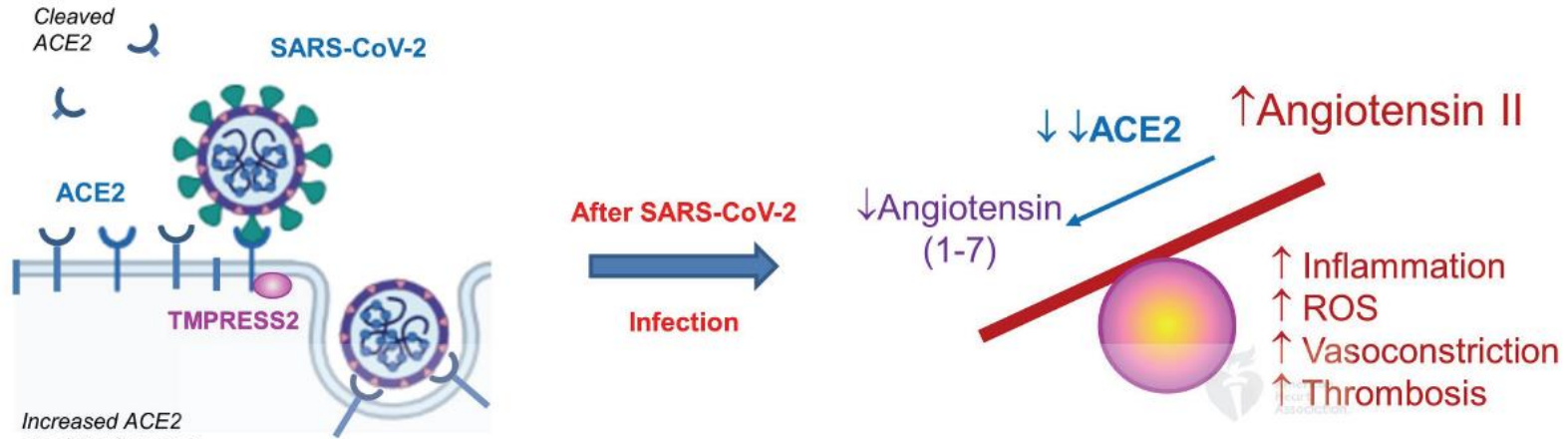


Pathophysiology of COVID 19
the key role of ACE2

Summary of the RAAS pathway



SARS-CoV-2 uses the ACE2 internalization receptor facilitated by TMPRSS2 protease



Increased ACE2 shedding/turnover in uninfected patients with hypertension, HF & diabetes

ACE2 internalized and down regulated with viral entry

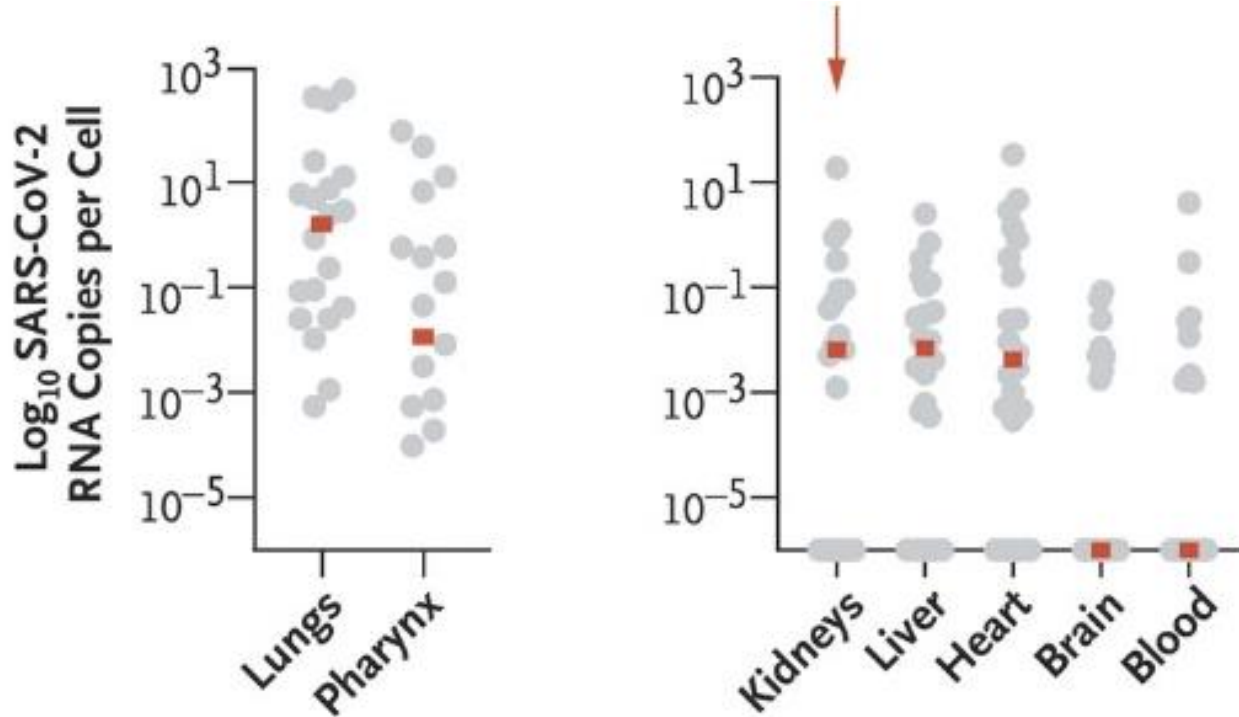
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Circulation

Distribution of ACE2 and TMPRSS2 in organs, and symptoms of COVID-19

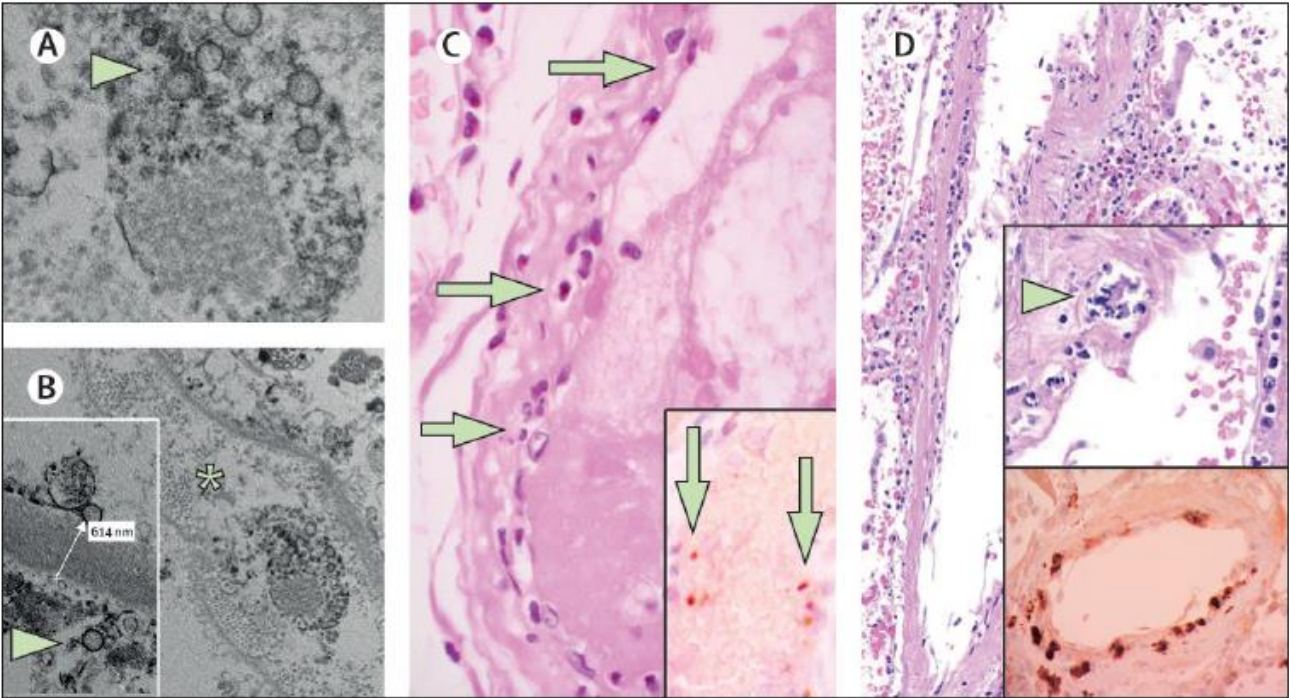
ACE2/TMPRSS2 Distribution	Symptoms/Lab Findings
Lymphocytes/Dendritic Cells	Fever (>99%), fatigue (70%), myalgia, lymphopenia
Lung (type 2 pneumocytes, bronchial epithelium)	Dyspnea (31%), dry cough (60%), respiratory failure
GI Smooth Muscle	Nausea (30%), Diarrhea
Myocardium	Myocarditis, heart failure, arrhythmias
Vasculature (smooth muscle)	Vasculitis, thrombosis, microangiopathy
Neurons	Anosmia, hypogeusia, encephalopathy, seizures, myopathy
Liver	Abnormal liver function
Kidney	Renal dysfunction

Multiorgan SARS-CoV-2 Tropism



Organotropism of SARS-CoV 2 may influence the course of Covid-19 disease and, possibly, aggravates preexisting conditions

Endothelial cell infection and endotheliitis in COVID-19



Presence of SARS-CoV-2 elements within endothelial cells and an accumulation of inflammatory cells, with evidence of endothelial and inflammatory cell death

Pathophysiology - Take Home Messages

- SARS-CoV-2 binds to the host receptor **ACE2** to mediate entry into cells;
- ACE2, which is expressed in the lungs, heart and vessels, is a key member of the RAS important in the pathophysiology of CVD;
- ACE2 in its full-length form is a membrane-bound enzyme, whereas its shorter (soluble) form circulates in blood at very low levels.
- CVD associated with COVID-19, likely involves **dysregulation of the RAS/ACE2** system due to SARS-CoV-2 and **due to comorbidities, such as hypertension;**

Is there an association between hypertension and the risk of COVID 19 and its severity?

Comorbidities of patients: systematic review of Chinese studies

Study	Diabetes n (%)		Hypertension (%)	
	Critical/Mortal	Non-critical	Critical/Mortal	Non-critical
Guan WJ	67 (26.9%)	63 (6.1%)	24 (35.8%)	141 (13.7%)
Huang C	13 (7.7%)	7 (25.0%)	2 (15.4%)	4 (14.3%)
Mo P	85 (14.1%)	3 (4.3%)	22 (25.9%)	15 (21.4%)
Peng YD	16 (25.0%)	19 (19.8%)	10 (62.5%)	82 (85.4%)
Shi Y	49 (14.3%)	22 (5.0%)	26 (53.1%)	73 (16.7%)
Wang D	36 (22.2%)	6 (5.9%)	21 (58.3%)	22 (21.6%)
Wang Z	14 (42.9%)	1 (1.8%)	5 (35.7%)	4 (7.3%)
Wu C	84 (19.0%)	6 (5.1%)	23 (27.4%)	16 (13.7%)
Yang X	32 (21.9%)	2 (10.0%)	—	—
Yuan ML	10 (60.0%)	0	5 (50.0%)	0
Zhou F	54 (31.5%)	19 (12.9%)	26 (48.1%)	32 (21.8%)

Characteristics of 5700 Patients Hospitalized With COVID-19 in NYC

	No. (%)
Demographic information	
Total No.	5700
Age, median (IQR) [range], y	63 (52-75) [0-107]
Sex	
Female	2263 (39.7)
Male	3437 (60.3)
Race ^a	
No.	5441
African American	1230 (22.6)

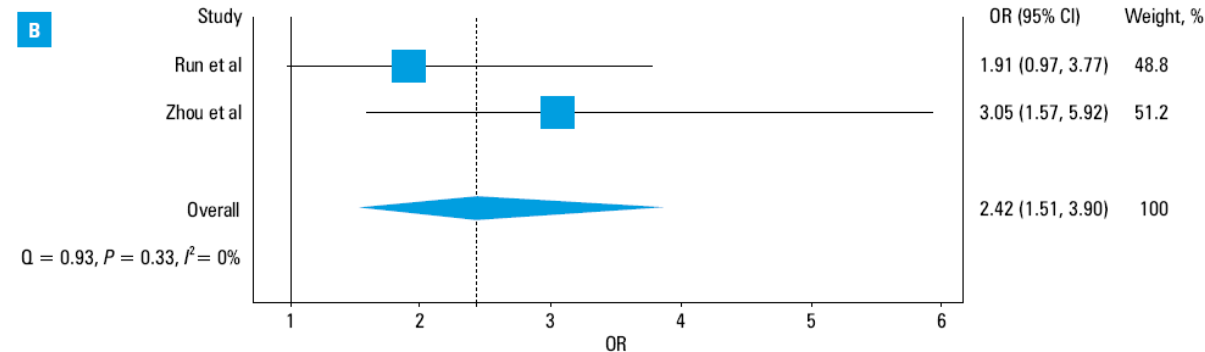
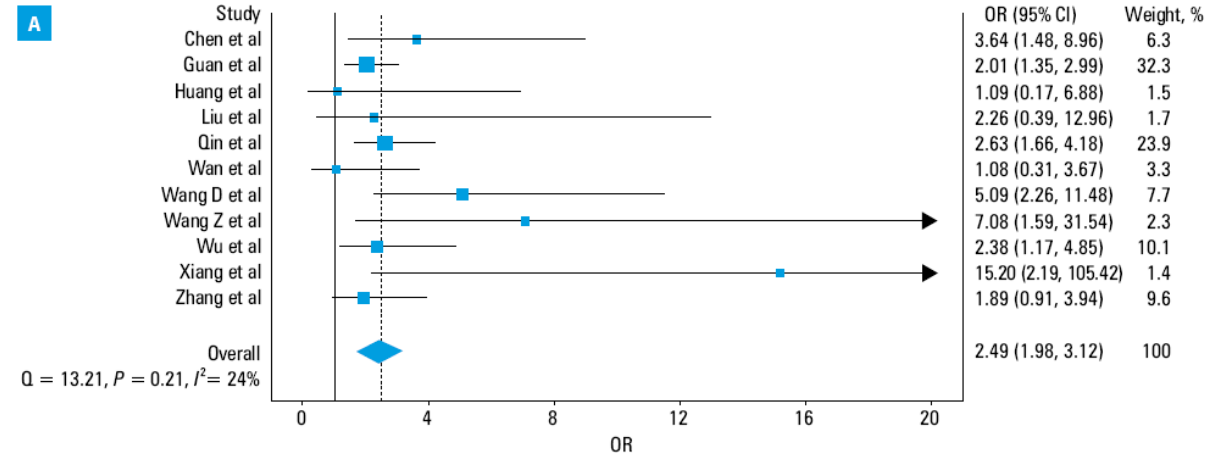
Comorbidities	
Total No.	5700
Cancer	320 (6)
Cardiovascular disease	
Hypertension	3026 (56.6)
Coronary artery disease	595 (11.1)
Congestive heart failure	371 (6.9)
Chronic respiratory disease	
Asthma	479 (9)
Chronic obstructive pulmonary disease	287 (5.4)
Metabolic disease	
Obesity (BMI ≥ 30)	1737 (41.7)
No.	4170
Morbid obesity (BMI ≥ 35)	791 (19.0)
No.	4170
Diabetes ^e	1808 (33.8)
Never smoker	3009 (84.4)
No.	3567

Death rate of patients with COVID-19 infection (WHO Data)

PRE-EXISTING CONDITION		DEATH RATE
Cardiovascular disease		10.5%
Diabetes		7.3%
Chronic respiratory disease		6.3%
Hypertension		6.0%
Cancer		5.6%
<i>no pre-existing conditions</i>		0.9%

SEX	DEATH RATE confirmed cases	DEATH RATE all cases
Male	4.7%	2.8%
Female	2.8%	1.7%

Associations between hypertension and the severity of COVID 2019 (A) and mortality (B)



Mortality rate by age group for patients admitted to ICU in northern Italy with COVID-19 disease

Age; years	< 50	51–60	61–70	> 70
With hypertension	31%	48%	77%	78%
Without hypertension	12%	30%	57%	79%

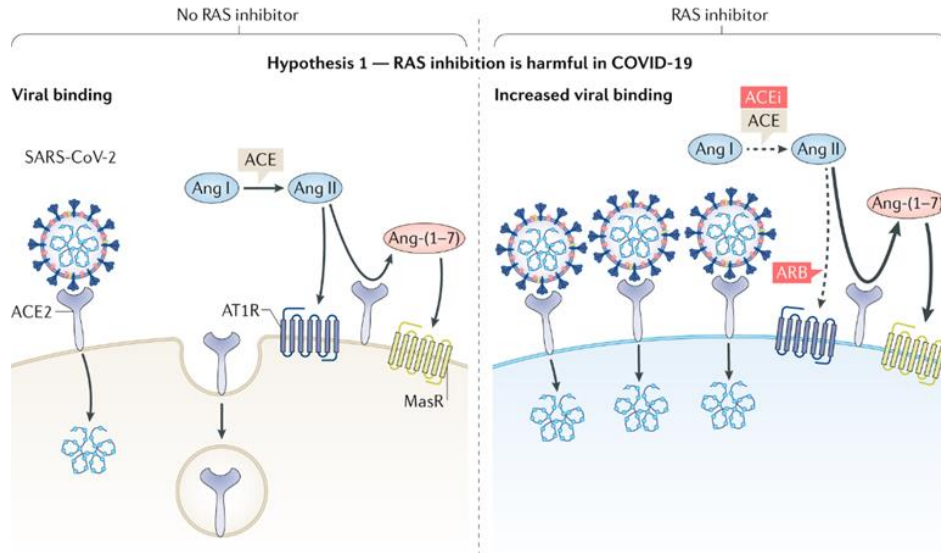
Key messages

1. The association between hypertension and risk of severe complications or death from COVID-19 infection is **confounded** by the lack of adjustment for **age**.
2. There is currently **no evidence to suggest that hypertension per se is an independent risk factor** for severe complications or death from COVID-19;

**Is there a benefit or a risk in using RAS blockers
in the context of the COVID 19 pandemic?**

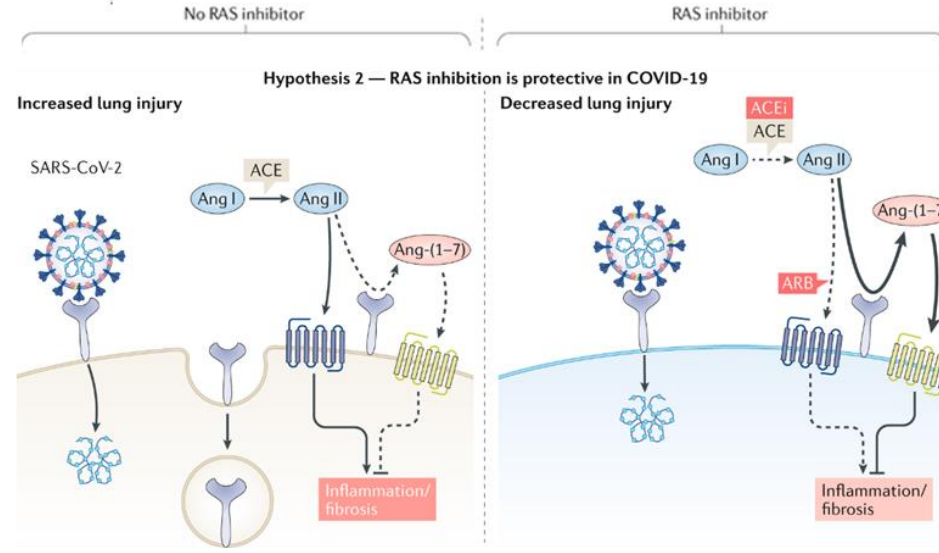
RAS inhibition: harmful or protective?

Harmful



Increase in viral binding?

Protective



Decreased lung injury?

OR for Covid-19 Associated with Use of RAS Blockers: in a population-based case–control study (Lombardy)

Variable	Odds Ratio for Covid-19 (95% CI) [†]	
	Unadjusted	Adjusted
Drugs [‡]		
Antihypertensive drugs overall	1.53 (1.43–1.63)	
ACE inhibitors	1.16 (1.08–1.24)	0.96 (0.87–1.07)
ARBs	1.20 (1.12–1.29)	0.95 (0.86–1.05)
Calcium-channel blockers	1.28 (1.18–1.38)	1.03 (0.95–1.12)
Beta-blockers	1.42 (1.33–1.51)	0.99 (0.91–1.08)
Diuretics as a whole	1.69 (1.57–1.83)	
Thiazide or thiazide-like diuretics	1.09 (1.01–1.17)	1.03 (0.86–1.23)
Loop diuretics	2.01 (1.83–2.20)	1.46 (1.23–1.73)
Mineralocorticoid-receptor antagonists	1.59 (1.37–1.85)	0.90 (0.75–1.07)

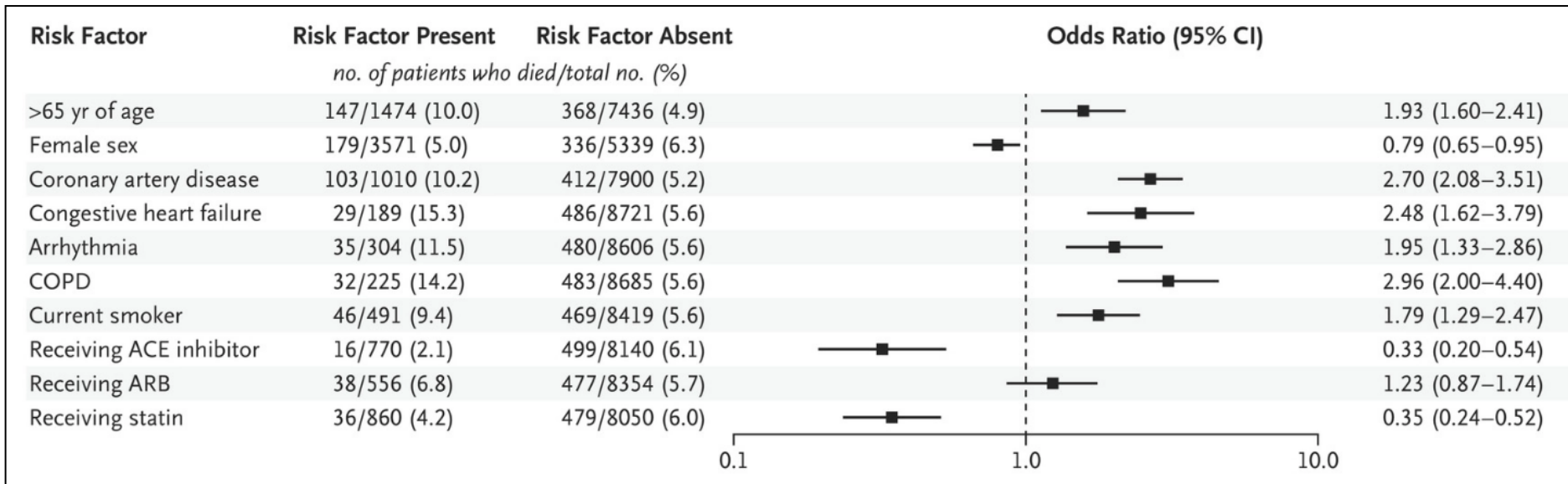
Adjusted for baseline covariates

Adjusted Odds Ratios for Covid-19 Associated with Use of RAAS Blockers and Other Antihypertensive Drugs.

Variable	Odds Ratio for Covid-19 (95% CI)*				
	ACE Inhibitors	ARBs	Calcium-Channel Blockers	Diuretics	Beta-Blockers
Severity of clinical manifestations†					
Mild to moderate	0.97 (0.88–1.07)	0.96 (0.87–1.07)	1.01 (0.92–1.10)	1.07 (0.97–1.19)	0.98 (0.89–1.07)
Critical or fatal	0.91 (0.69–1.21)	0.83 (0.63–1.10)	1.15 (0.91–1.44)	0.96 (0.74–1.26)	1.07 (0.84–1.37)
Sex‡					
Female	0.95 (0.81–1.12)	0.89 (0.76–1.05)	1.06 (0.92–1.23)	1.12 (0.94–1.34)	1.04 (0.91–1.20)
Male	0.98 (0.87–1.11)	0.98 (0.86–1.11)	1.00 (0.90–1.11)	1.02 (0.91–1.15)	0.97 (0.87–1.08)
Age at diagnosis§					
<60 Yr	0.94 (0.71–1.25)	0.89 (0.67–1.18)	1.13 (0.88–1.46)	0.99 (0.75–1.31)	1.00 (0.78–1.29)
≥60 Yr	0.97 (0.87–1.08)	0.95 (0.85–1.06)	1.01 (0.93–1.11)	1.07 (0.97–1.19)	0.99 (0.90–1.08)

Adjusted for baseline covariates

Independent Predictors of In-Hospital Death: observational database analysis from 169 hospitals in Asia, Europe, and North America



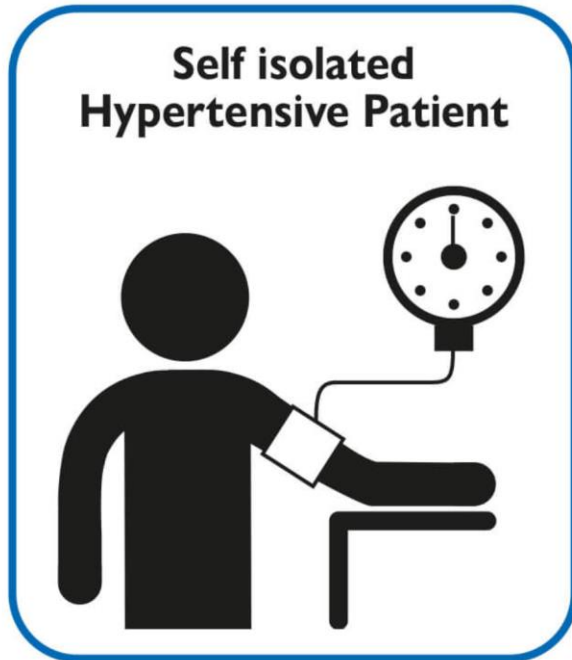
Subgroup analysis evaluating the association between ACEI and death in patients with hypertension

Variable	Odds Ratio	95% CI (Low)	95% CI (High)
Age (years)	1.023	1.011	1.034
Female sex	0.690	0.472	1.010
ACE inhibitor	0.266	0.156	0.453

Key messages

1. There is **no evidence that ACEI or ARB is associated with increased risk** of SARS-CoV-2 infection, of severe Covid-19 among those infected, or of in-hospital death.
2. Treatment of hypertension should **follow existing recommendations** in the ESC-ESH Guidelines.

Hypertension management in the COVID-19 context

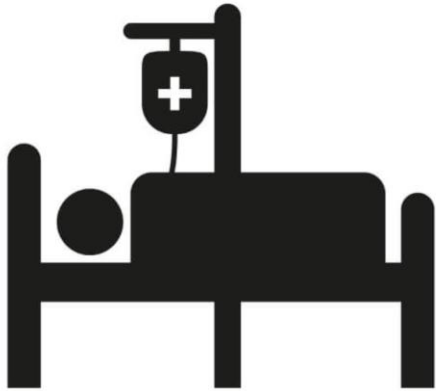


- Continue treatment with antihypertensive medication according to ESC-ESH guidelines 2018
- No need to adjust medication or stop ACE-inhibitors or ARBs because of COVID-19 pandemic

- Continue to monitor blood pressure at home if possible
- No need for routine clinical review at clinical during the COVID-19 pandemic
- Use video or phone consultation with patient if required

Hypertension management in the COVID-19 context

Hospitalized Hypertensive Patient with COVID-19 infection



- Unless hypotensive or there is acute kidney injury
- Continue treatment with antihypertensive medication according to ESC-ESH guidelines 2018
- No need to adjust medication or stop ACE-inhibitors or ARBs because of COVID-19 pandemic

- Monitor for arrhythmias which may be more common in hypertensive patients with cardiac disease
- Check plasma potassium as hypokalemia is common in hospitalized COVID-19 patients
- Parenteral antihypertensive medications will only rarely be necessary in ventilated patients

FICHE

Réponses rapides dans le cadre du COVID-19 - HTA - Suivi des patients

Document de travail - 7 mai 2020

- 1. Connaître les risques de développer une forme grave de COVID-19 chez les patients hypertendus,**
- 2. Encourager la poursuite des traitements antihypertenseurs et sensibiliser sur les risques qu'entraînerait une interruption de traitement,**
- 3. Encourager la poursuite d'un suivi médical, en privilégiant la téléconsultation,**
- 4. Rappeler l'importance de l'automesure et des règles hygiéno-diététiques dans la prise en charge de l'hypertension,**
- 5. Préciser la conduite à tenir en cas d'aggravation de l'hypertension, et de symptômes évoquant une infection COVID-19.**