

# Tossicodipendenza e Covid-19

29/04/2021 al 20/05/2021 organizzato da

ISTITUTO SUPERIORE DI SANITÀ

Dipartimento Malattie Infettive

**SARS-CoV-2 e COVID-19: manifestazioni cliniche della malattia, modalità di trasmissione, procedure assistenziali a rischio, indagini diagnostiche e trattamenti terapeutici.**



SOCIETÀ ITALIANA MULTIDISCIPLINARE PER LA PREVENZIONE DELLE INFEZIONI NELLE ORGANIZZAZIONI SANITARIE

Angelo Pan



Ospedale  
di Cremona

Sistema Socio Sanitario



Regione  
Lombardia  
ASST Cremona

Divisione di Malattie Infettive

# Conflitti di interesse

## Relazioni a congressi

- Pfizer
- Inhixa

## Partecipazione a congressi:

- Janssen
- ViiV



富嶽三十六景 神奈川沖浪裏

丁未年四月

神奈川沖浪裏



**National Library of Medicine**  
*National Center for Biotechnology Information*



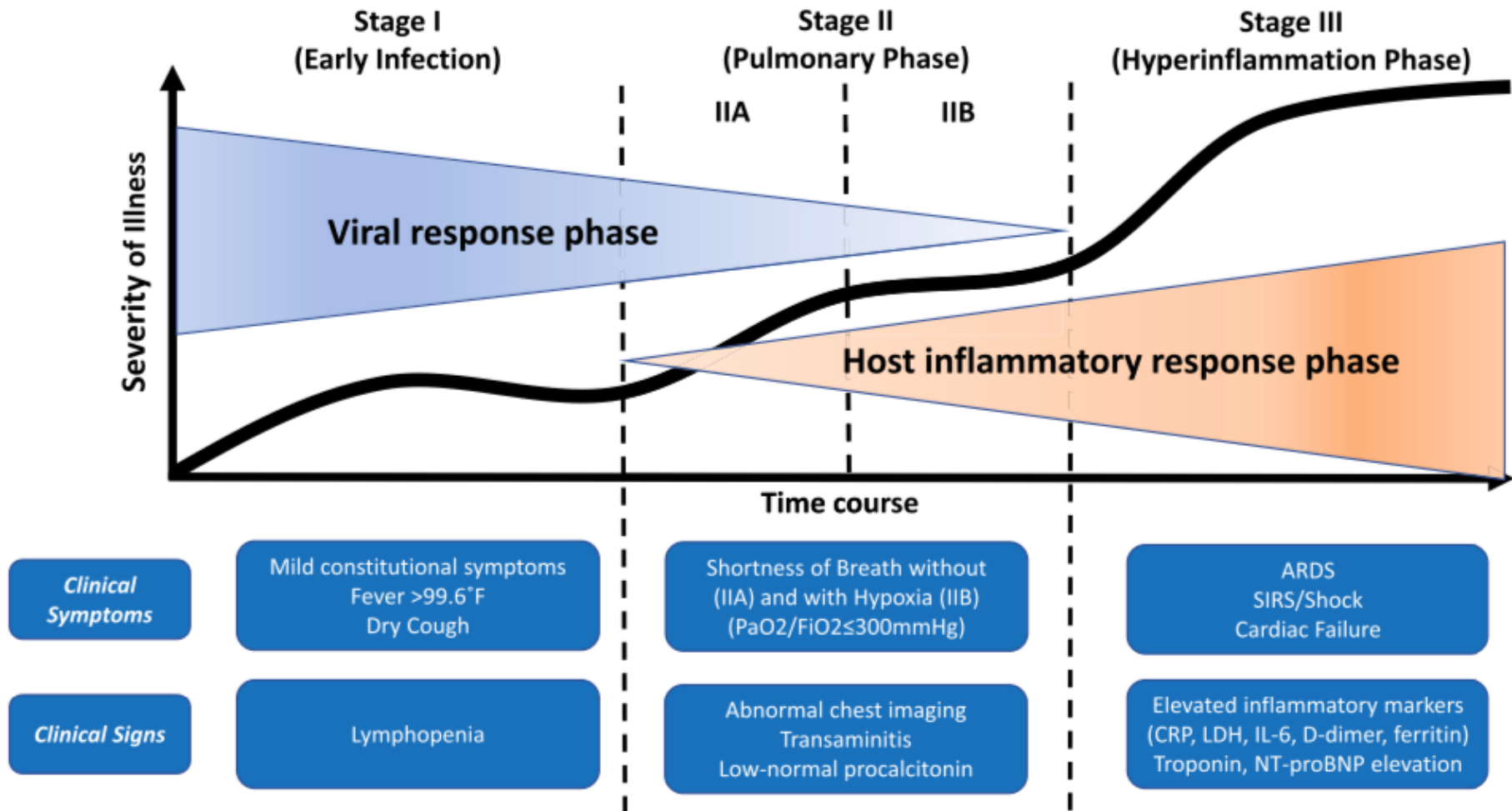
- **HIV, dal 1981: 379.104**
- **Covid-19, dal 2020: 126.144**

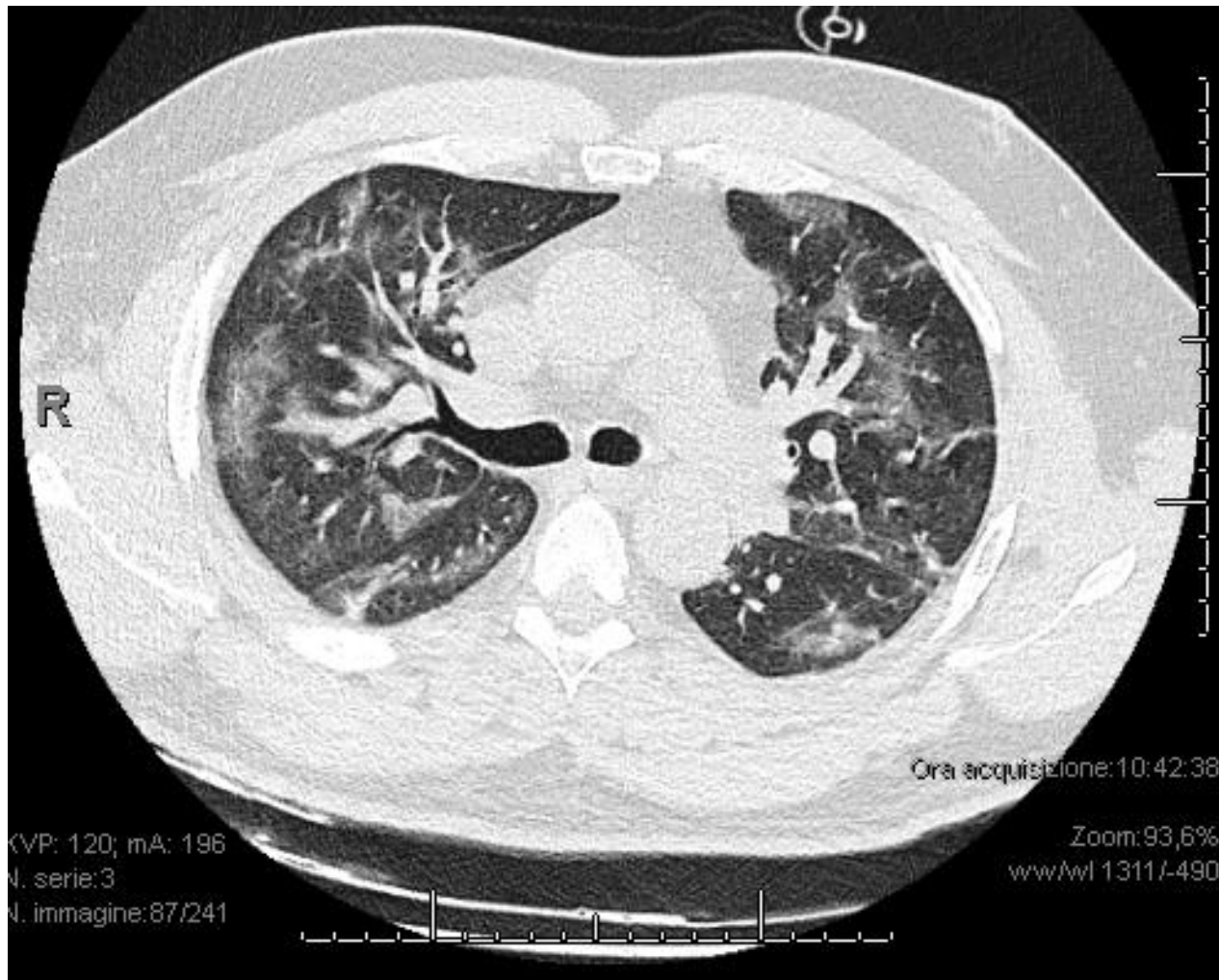
1. manifestazioni cliniche della malattia
2. modalità di trasmissione
3. procedure assistenziali a rischio
4. indagini diagnostiche
5. trattamenti terapeutici

- 1. manifestazioni cliniche della malattia**
2. modalità di trasmissione
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# La storia naturale







# La ventilazione assistita

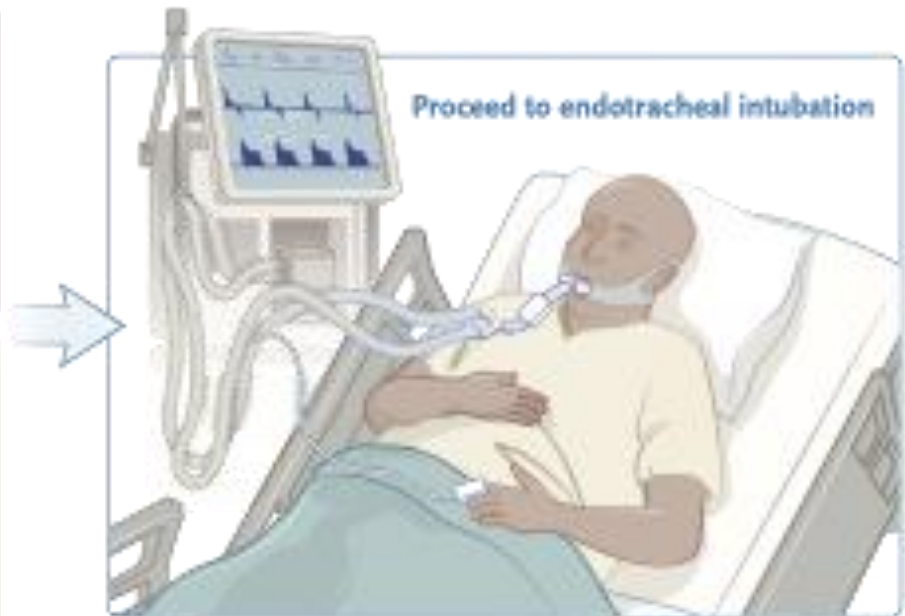
## A Determination of Need for Endotracheal Intubation for Covid-19–Related Respiratory Failure

### Possible Clinical Indications for Endotracheal Intubation

- Impending airway obstruction
- Signs of unsustainable work of breathing
- Refractory hypoxemia
- Hypercapnia or acidemia
- Encephalopathy or inadequate airway protection

### Additional Considerations

- Does illness trajectory predict deterioration?
- Are difficulties in endotracheal intubation anticipated?
- Is there hemodynamic instability?
- Will intubating now improve the safety of a planned procedure or transportation?
- Will intubating now improve infection control and staff safety?



# Trombosi venosa profonda

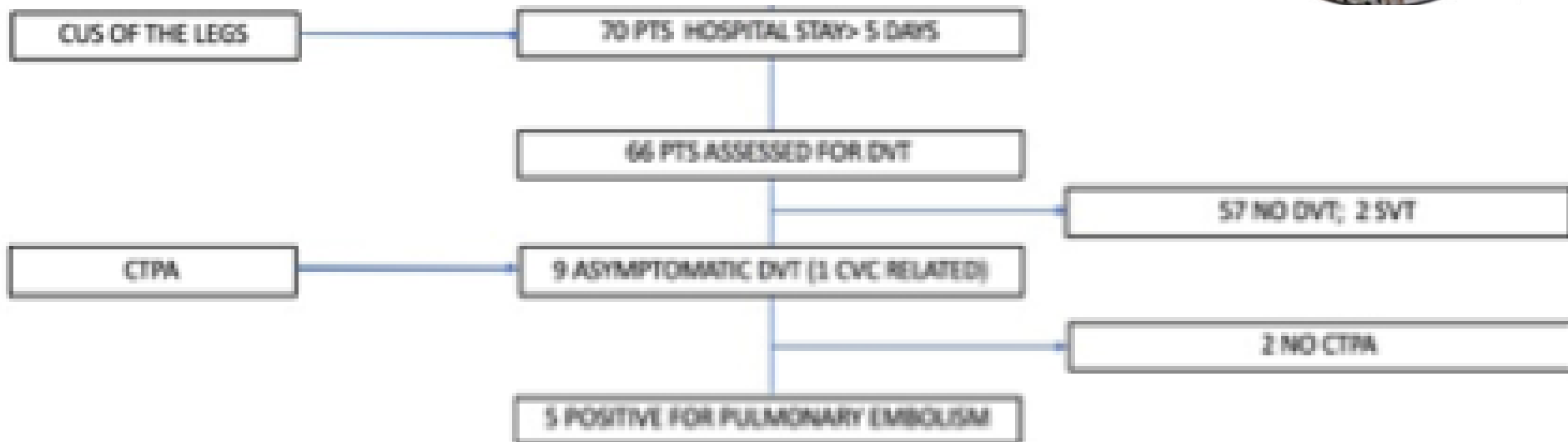
Internal and Emergency Medicine  
<https://doi.org/10.1007/s11739-020-02472-3>

IM - ORIGINAL



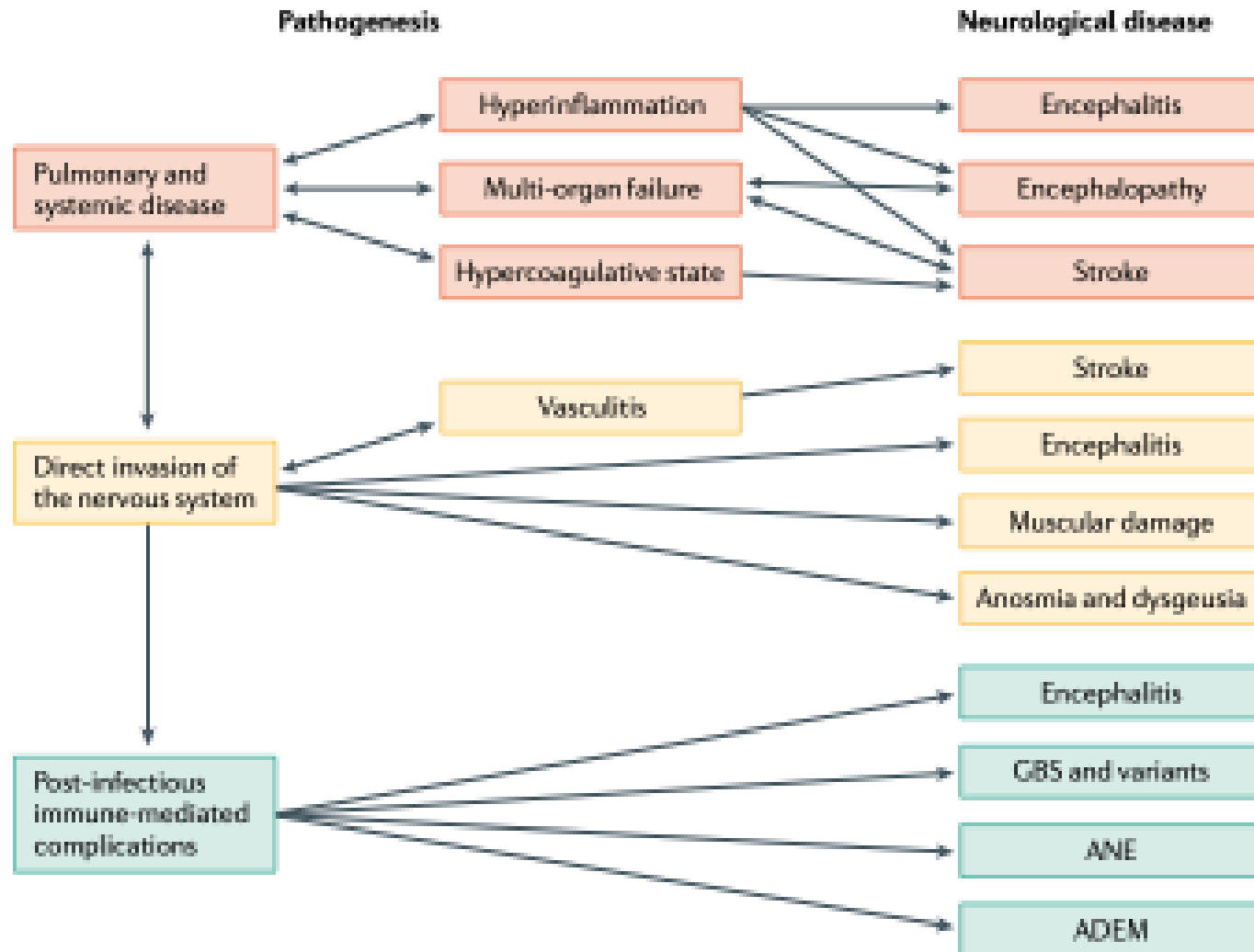
## Prevalence of asymptomatic deep vein thrombosis in patients hospitalized with SARS-CoV-2 pneumonia: a cross-sectional study

Matteo Giorgi-Pierfranceschi<sup>1</sup> · Oriana Paoletti<sup>2</sup> · Angelo Pan<sup>3</sup> · Fabio De Gennaro<sup>1</sup> · Anna Laura Nardecchia<sup>1</sup> · Rossella Morandini<sup>2</sup> · Claudia Dellanoce<sup>2</sup> · Samuele Lombi<sup>1</sup> · Maurizio Tala<sup>2</sup> · Vanessa Cancelli<sup>2</sup> · Silvia Zambelli<sup>2</sup> · Giancarlo Bosio<sup>4</sup> · Laura Romanini<sup>3</sup> · Sophie Testa<sup>2</sup>



# Lifting the mask on neurological manifestations of COVID-19

Alessandro Pezzini  and Alessandro Padovani

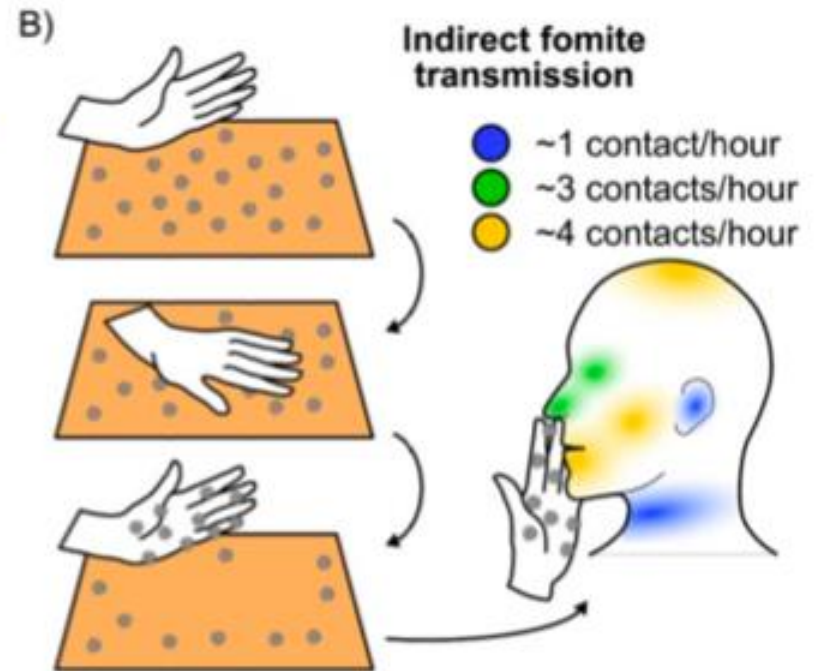
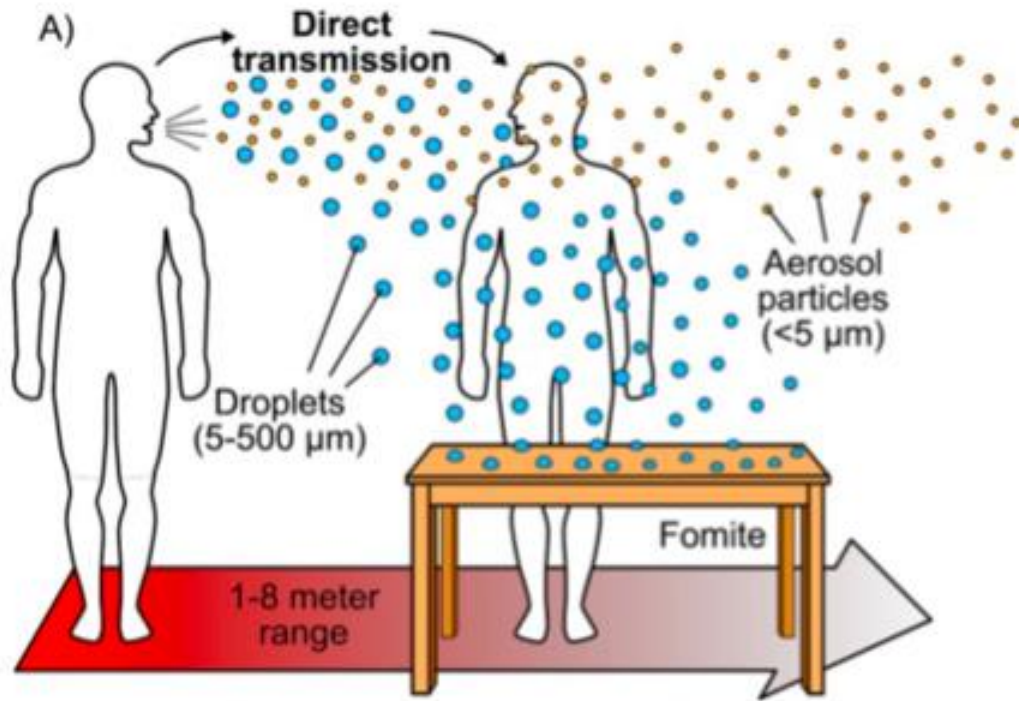


1. manifestazioni cliniche della malattia
- 2. modalità di trasmissione**
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# Fattori importanti per la trasmissione

- Infettività relativamente elevata ( $R_0 = 2,5 - 3$ ) -  
Morbillo  $R_0 = 18$
- Trasmissione attraverso le alte vie respiratorie (e anche per contatto)
- Periodo di incubazione relativamente lungo
- Lungo periodo di eliminazione del virus
- Attuali abitudini di viaggio globali

# La trasmissione

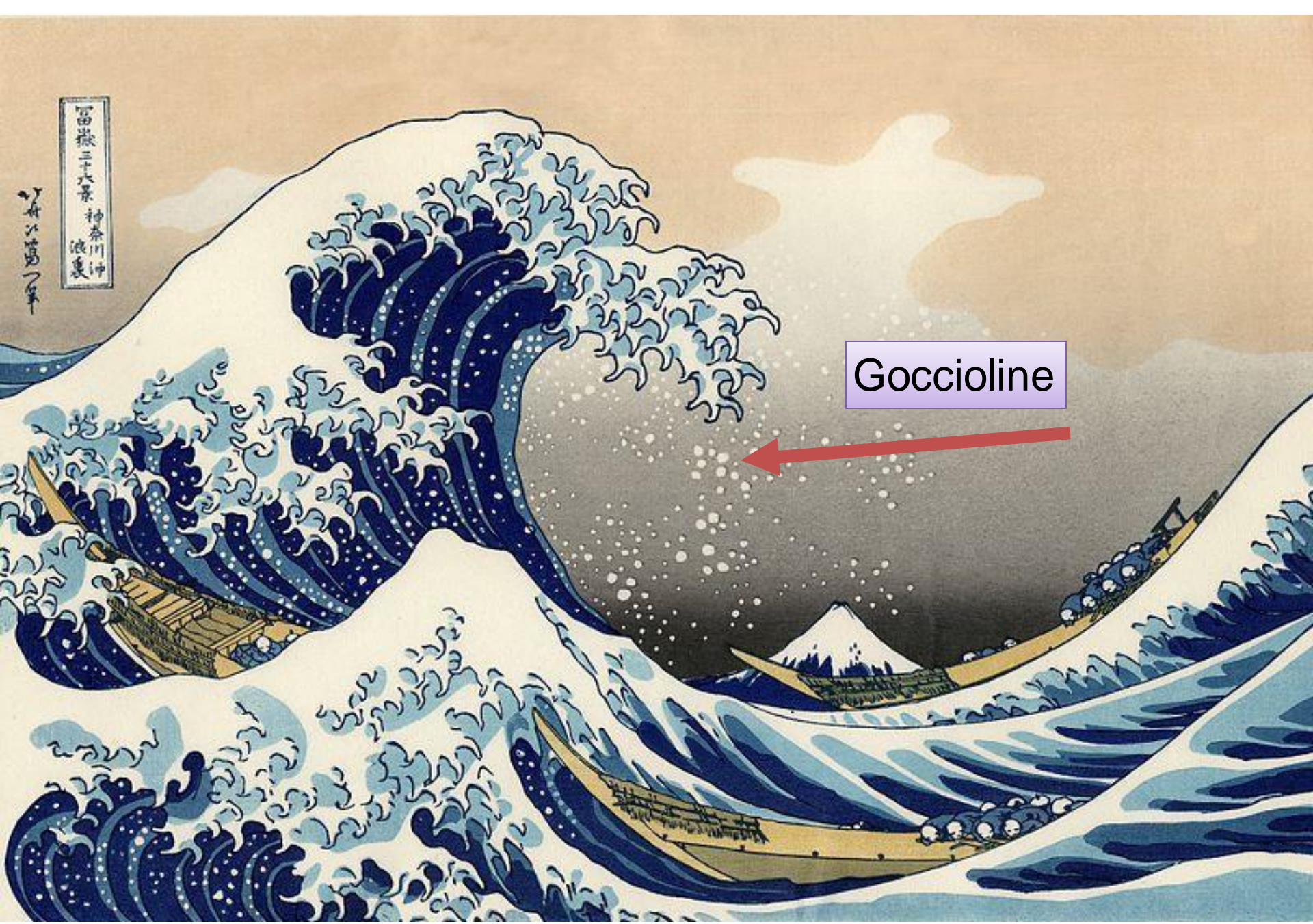






La grande onda di Kanagawa. Katsushika Hokusai 1830-1831 <sup>15</sup>





Goccioline

La grande onda di Kanagawa. Katsushika Hokusai 1830-1831 <sup>16</sup>

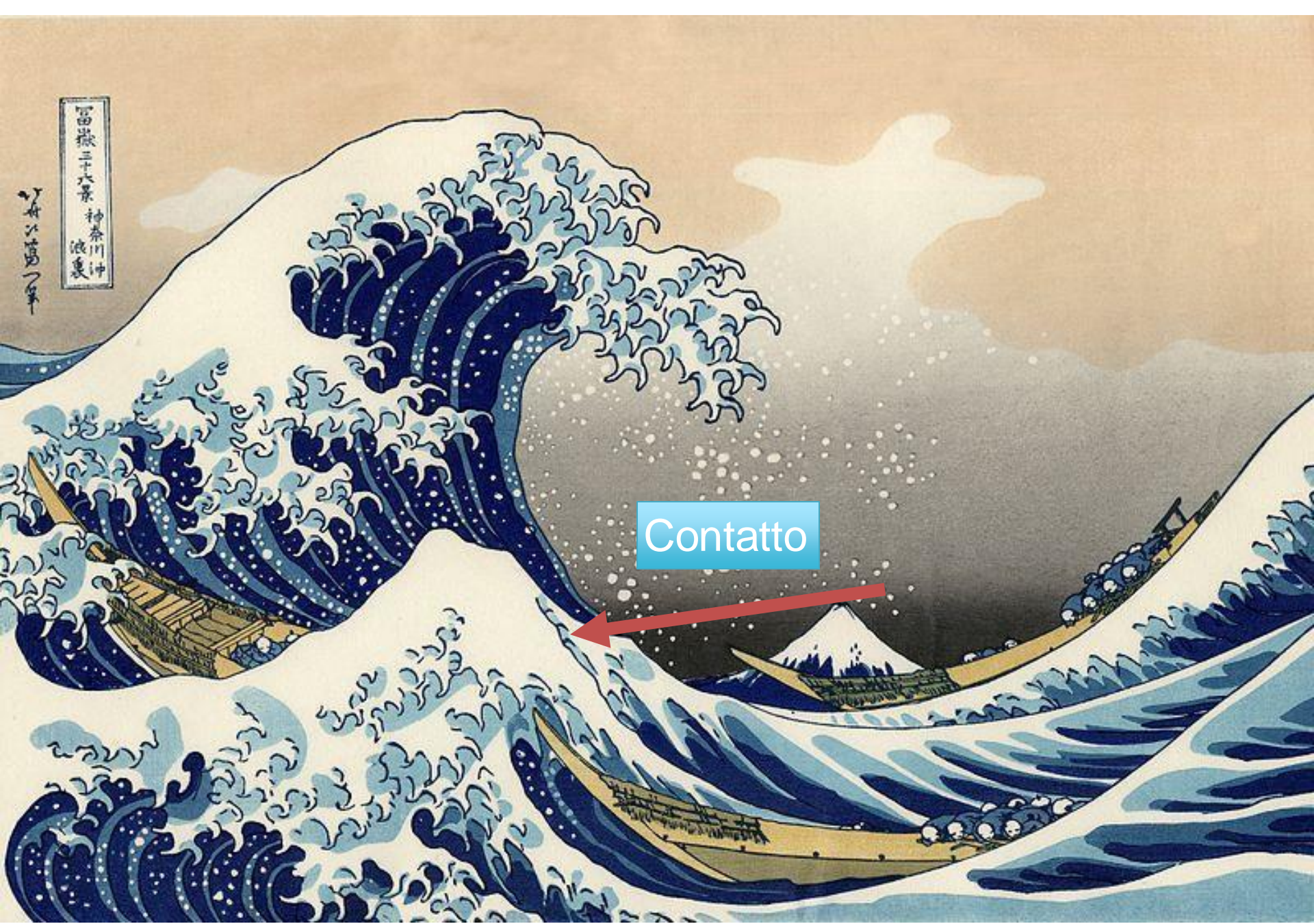




Aerosol

La grande onda di Kanagawa. Katsushika Hokusai 1830-1831 <sup>17</sup>





Contatto

La grande onda di Kanagawa. Katsushika Hokusai 1830-1831 <sup>18</sup>

# Aspetti centrali nella trasmissione di SARS-CoV-2

1. Contatto ravvicinato: <2 metro
2. Contatto prolungato: >15 minuti
3. Contatti ripetuti
4. Procedure a rischio di produrre aerosol



# Mercato cinese del cibo

## *Wet market*



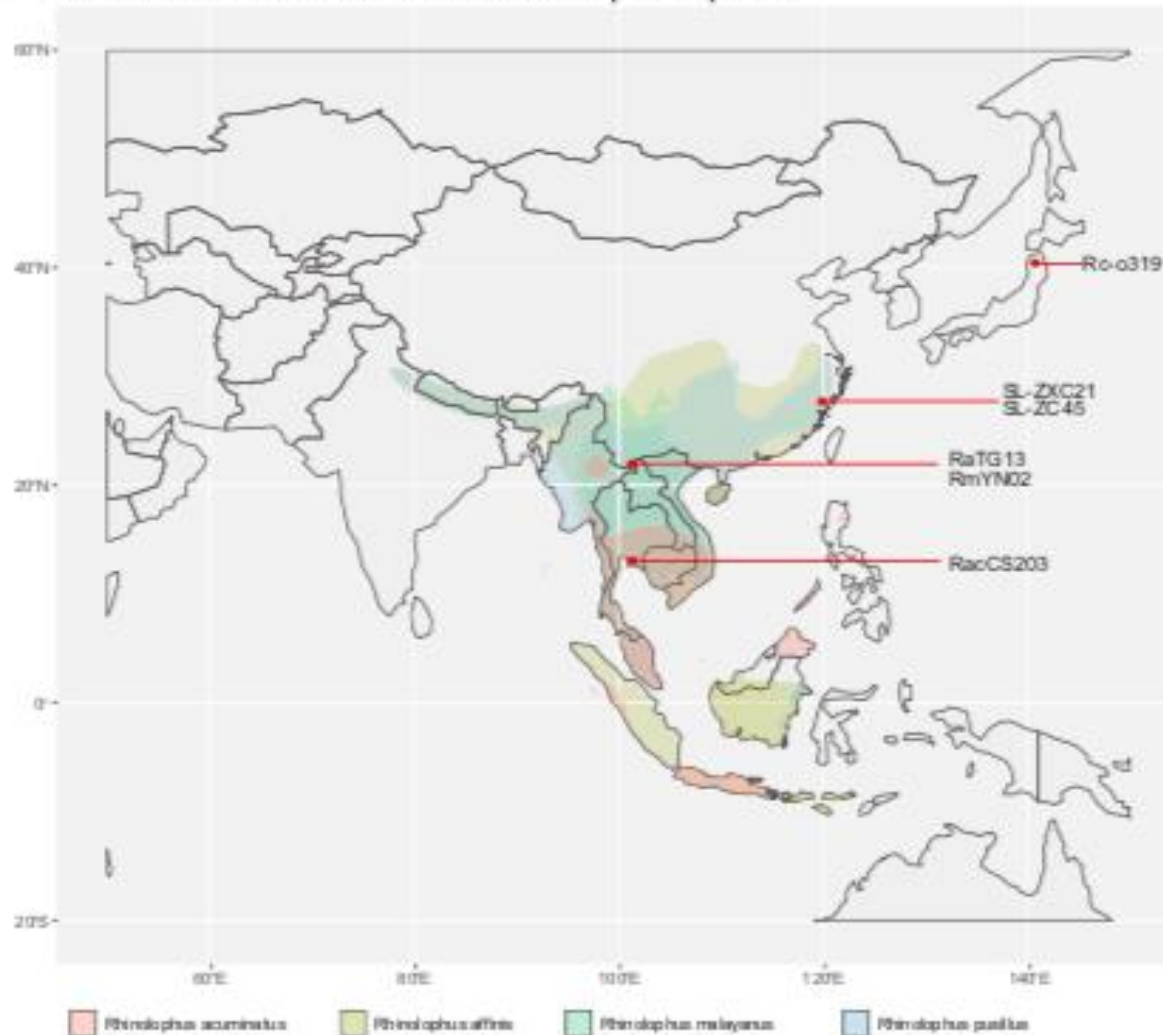


# Pipistrelli

- I pipistrelli (Chiroptera) sono il secondo più grande ordine di mammiferi dopo i roditori
- 1400 specie
- Presenti in tutto il globo

# Presenza di pipistrelli che ospitano Coronavirus

**a** Distribution of SC2r-CoV host *Rhinolophus* species



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# Procedure che generano aerosol

- Rianimazione cardiopolmonare,
- **Intubazione ed estubazione** con le relative procedure come ventilazione manuale e aspirazione aperta del tratto respiratorio,
- **Broncoscopia**,
- Induzione di espettorato,
- Terapie in grado di generare nebulizzazione\*,
- **NIV, BiPAP, CPAP**, ventilazione ad alta frequenza oscillatoria, ossigenazione nasale ad alto flusso\*,
- **Tampone nasofaringeo**
- Procedure correlate alla tracheotomia/tracheostomia,
- Chirurgia e procedure autoptiche che includono apparecchiature ad alta velocità\*,
- Alcune procedure dentistiche (es. trapanazione ad alta velocità)\*,
- Procedure endoscopiche (es. gastrointestinale dove è presente aspirazione aperta del tratto respiratorio superiore)\*

# Transmission of SARS-CoV-2: implications for infection prevention precautions

Scientific brief  
9 July 2020



- Use of **contact and droplet precautions** by health workers caring for suspected and confirmed COVID-19 patients, and use of airborne precautions when aerosol generating procedures are performed;
- Continuous use of a **medical mask** by health workers and caregivers working in all clinical areas, during all routine activities throughout the entire shift;
- At all times, practice frequent **hand hygiene**

# I fondamentali



**Sempre**





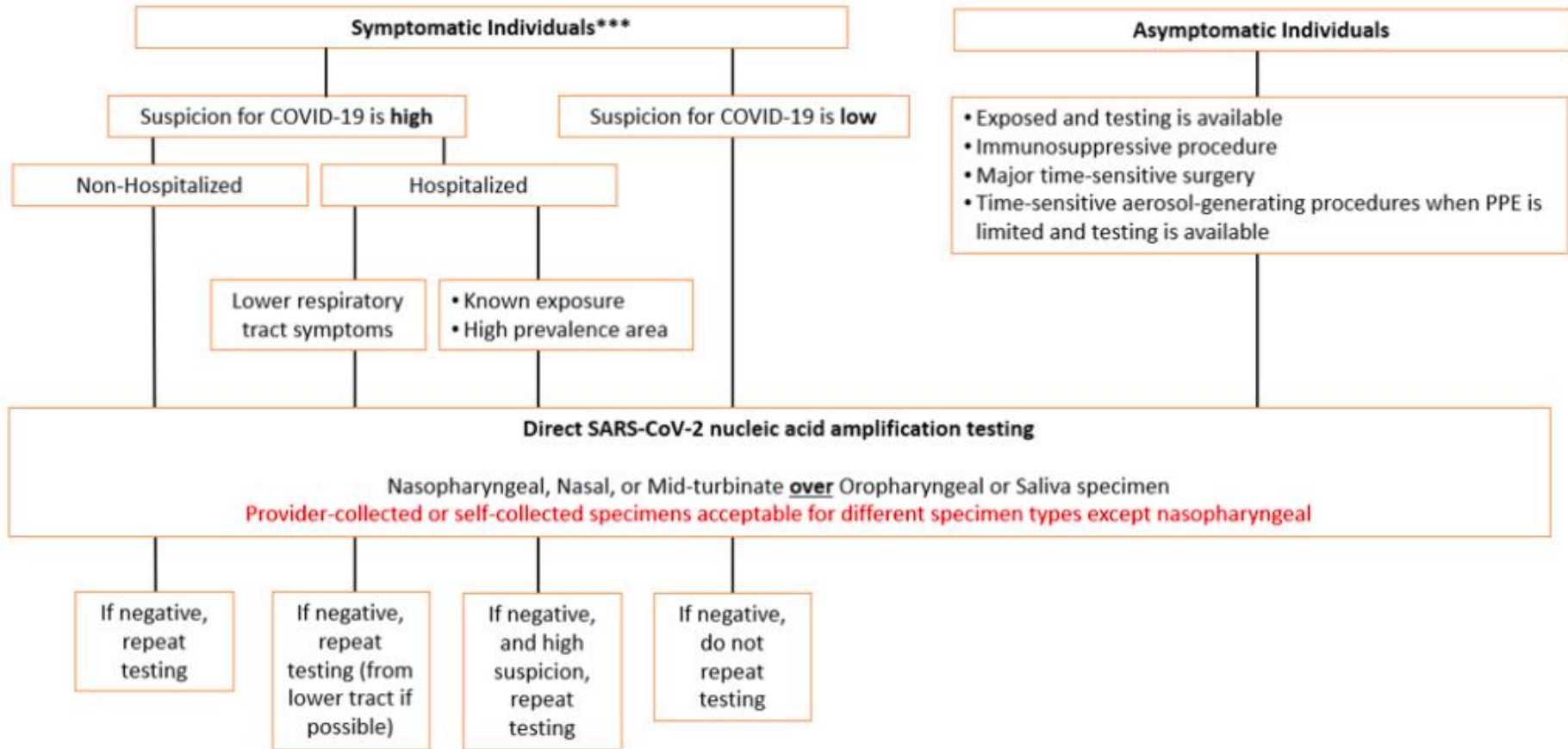
1. manifestazioni cliniche della malattia
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# Diagnosi

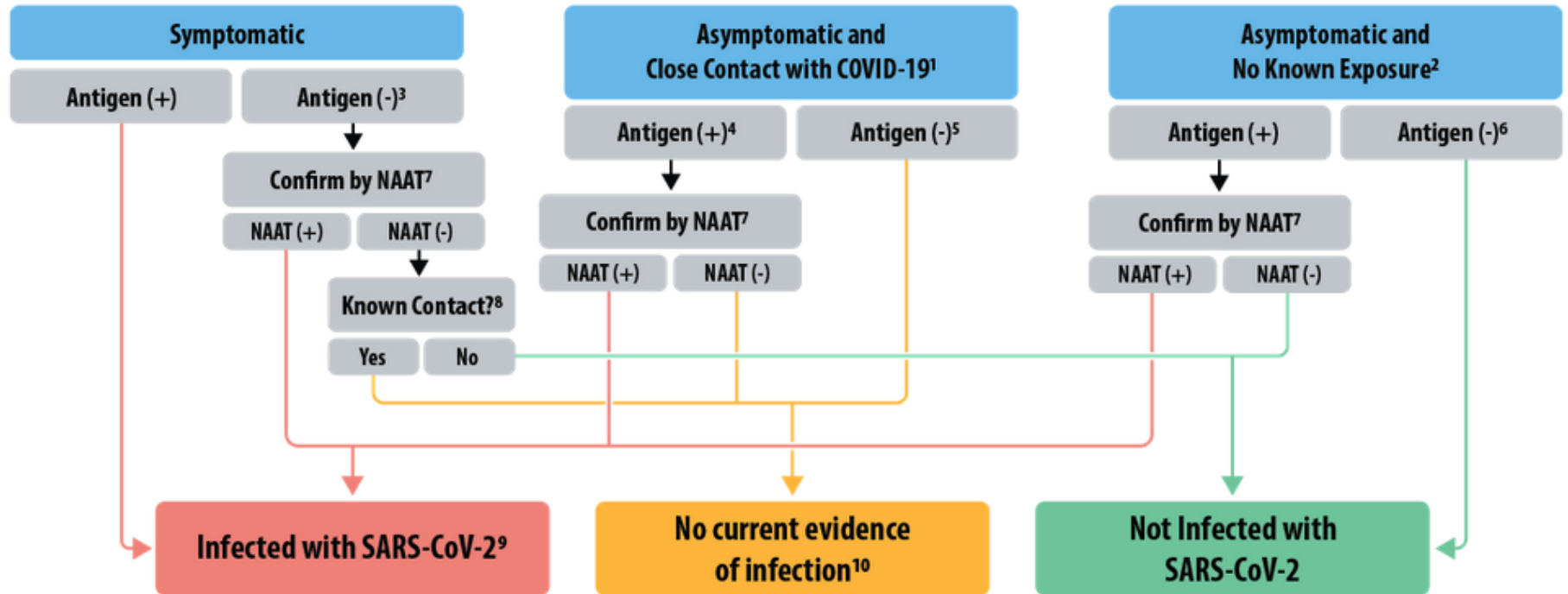
## Esecuzione dei tamponi per SARS-CoV-2



# Algoritmo per il test molecolare per SARS-Cov-2



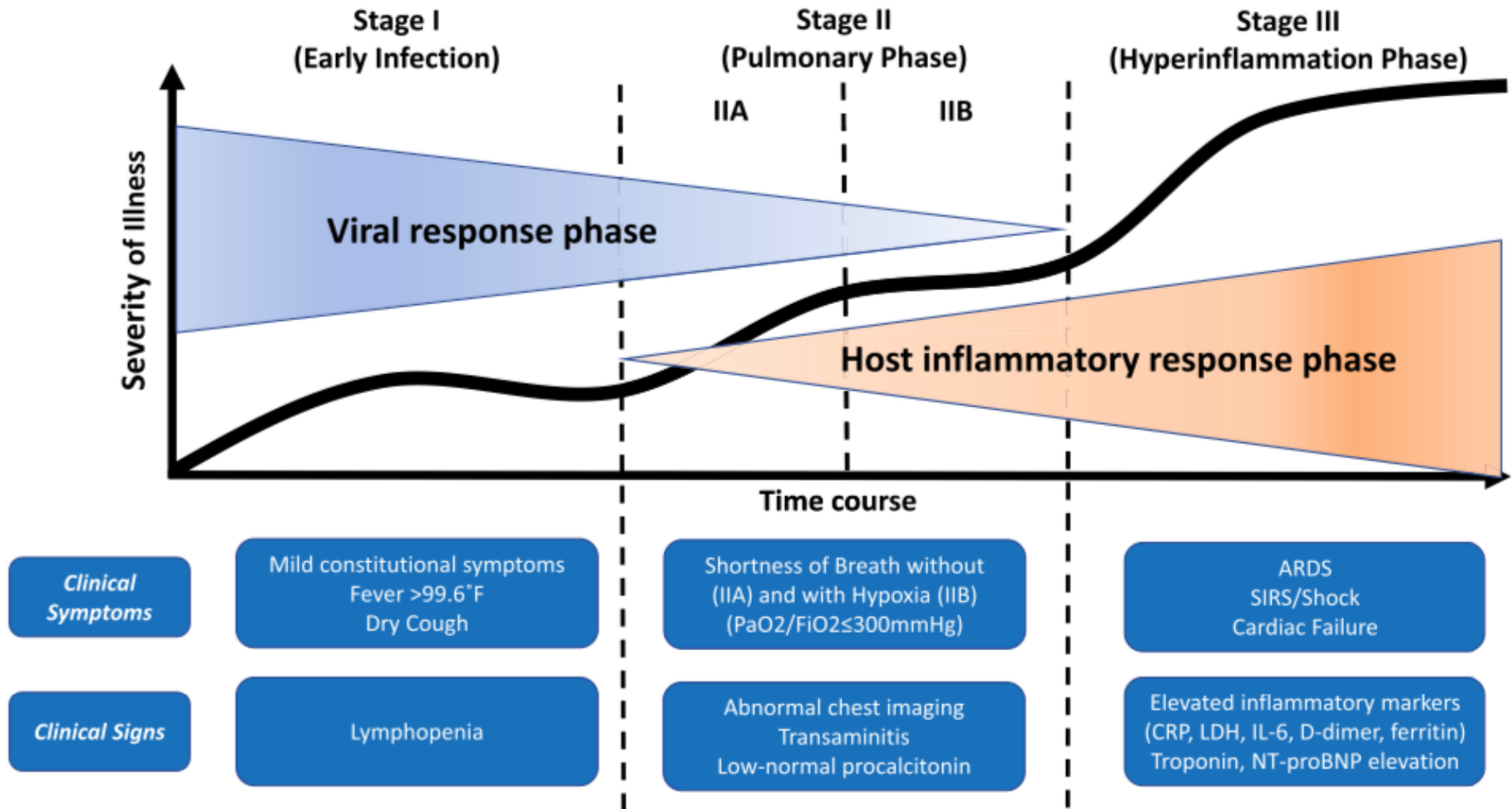
# Test antigenici



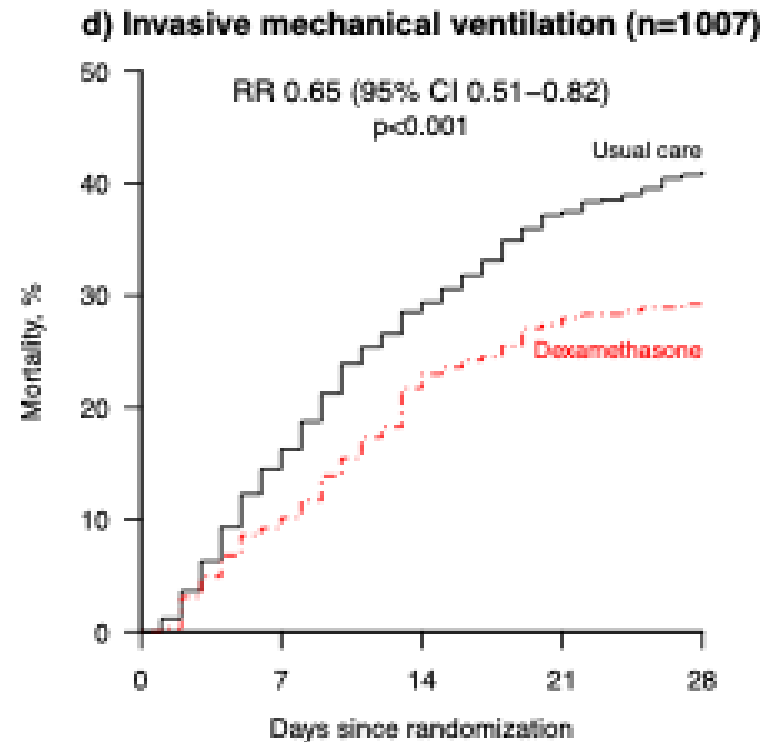
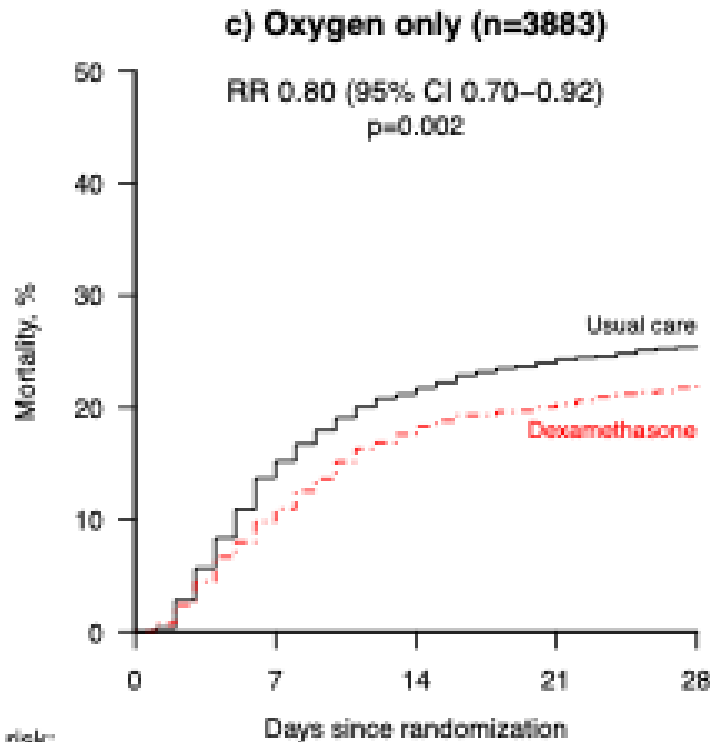
<https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html>

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# La storia naturale



# Corticosteroidi



Number at risk:		Days since randomization				
		0	7	14	21	28
Dexamethasone	1279	1107	1004	971	940	
Usual care	2604	2162	1965	1880	1832	

Number at risk:		Days since randomization				
		0	7	14	21	28
Dexamethasone	324	290	246	230	224	
Usual care	683	569	474	418	389	

# Profilassi/Terapia anticoagulante

Internal and Emergency Medicine

<https://doi.org/10.1007/s11739-020-02331-1>

IM-POINT OF VIEW



## Switch from oral anticoagulants to parenteral heparin in SARS-CoV-2 hospitalized patients

Sophie Testa<sup>1</sup> · Oriana Paoletti<sup>1</sup> · Matteo Giorgi-Pierfranceschi<sup>2</sup> · Angelo Pan<sup>3</sup>

Received: 25 March 2020 / Accepted: 30 March 2020

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# Terapia IDSA

		Setting and severity of illness			
		<i>Ambulatory care: mild-to-moderate disease</i>	<i>Hospitalized: mild-to-moderate disease without need for suppl. oxygen</i>	<i>Hospitalized: severe but non-critical disease (spO<sub>2</sub> &lt;94% on room air)</i>	<i>Hospitalized: critical disease (e.g., in ICU needing MV, or septic shock, ECMO)</i>
<b>1</b>	Hydroxy-chloroquine (HCQ)*	NA	Recommend against use ⊕⊕⊕○	Recommend against use ⊕⊕⊕○	Recommend against use ⊕⊕⊕○
<b>2</b>	HCQ* + azithromycin	NA	Recommend against use ⊕⊕○○	Recommend against use ⊕⊕○○	Recommend against use ⊕⊕○○
<b>3</b>	Lopinavir + ritonavir	NA	Recommend against use ⊕⊕⊕○	Recommend against use ⊕⊕⊕○	Recommend against use ⊕⊕⊕○
<b>4-6</b>	Corticosteroids	NA	Suggest against use ⊕○○○	Suggest use ⊕⊕⊕○ R: If dexamethasone is unavailable, equivalent total daily doses of alternative glucocorticoids may be used.**	Recommend use ⊕⊕⊕○ R: If dexamethasone is unavailable, equivalent total daily doses of alternative glucocorticoids may be used.**

Setting and severity of illness					
<i>Ambulatory care: mild-to-moderate disease</i>		<i>Hospitalized: mild-to-moderate disease without need for suppl. oxygen</i>		<i>Hospitalized: severe but non-critical disease (spO<sub>2</sub> &lt;94% on room air)</i>	<i>Hospitalized: critical disease (e.g., in ICU needing MV, or septic shock, ECMO)</i>
<b>7</b>	<i>Tocilizumab</i>	NA	NA	<p><b>Suggest use</b> ⊕○○○</p> <p>R: Patients, particularly those who response to steroids alone, who put a high value on avoiding possible adverse events of tocilizumab and a low value on the uncertain mortality reduction, would reasonably decline tocilizumab. In the largest trial on the treatment of tocilizumab, criterion for systemic inflammation was defines as CRP ≥75 mg/L</p>	<p><b>Suggest use</b> ⊕○○○</p> <p>R: Patients, particularly those who response to steroids alone, who put a high value on avoiding possible adverse events of tocilizumab and a low value on the uncertain mortality reduction, would reasonably decline tocilizumab. In the largest trial on the treatment of tocilizumab, criterion for systemic inflammation was defines as CRP ≥75 mg/L</p>
<b>8</b>	<i>Convalescent plasma</i>	NA	Recommended only in the context of a clinical trial (knowledge gap)	Recommended only in the context of a clinical trial (knowledge gap)	Recommended only in the context of a clinical trial (knowledge gap)
<b>9-11</b>	<i>Remdesivir</i>	NA	<p><b>Suggest against routine use</b> ⊕○○○</p>	<p><b>Suggest use</b> ⊕⊕○○</p> <p>R: In patients on mechanical ventilation or ECMO, the duration of treatment is 10 days.</p>	<p><b>Suggest use</b> ⊕⊕⊕○</p> <p>R: For consideration in contingency or crisis capacity settings (i.e., limited remdesivir supply): Remdesivir appears to demonstrate the most benefit in those with severe COVID-19 on supplemental oxygen rather than in patients on mechanical ventilation or ECMO.</p>

Setting and severity of illness			
<i>Ambulatory care: mild-to-moderate disease</i>	<i>Hospitalized: mild-to-moderate disease without need for suppl. oxygen</i>	<i>Hospitalized: severe but non-critical disease (spO<sub>2</sub> &lt;94% on room air)</i>	<i>Hospitalized: critical disease (e.g., in ICU needing MV, or septic shock, ECMO)</i>

12	<i>Famotidine</i>	NA	Suggests against use except in a clinical trial ⊕○○○	Suggests against use except in a clinical trial ⊕○○○	Suggests against use except in a clinical trial ⊕○○○
13	<i>Bamlanivimab + etesevimab</i>	<b>Suggest use</b> ⊕⊕○○ R: Patients with mild to moderate COVID-19 who are at high risk of progression to severe disease admitted to the hospital for reasons other than COVID-19 may also receive bamlanivimab/etesevimab. For patients at high risk for progression to severe disease, the data are strongest for bamlanivimab/etesevimab. Bamlanivimab monotherapy or casirivimab/imdevimab may have similar clinical benefit, but data are more limited. There are limited data on efficacy of bamlanivimab/etesevimab in high-risk patients between 12 and 18 years of age.	NA	NA	NA
14	<i>Bamlanivimab monotherapy</i>	NA	NA	Recommend against use ⊕⊕⊕○	NA

Setting and severity of illness					
		<i>Ambulatory care: mild-to-moderate disease</i>	<i>Hospitalized: mild-to-moderate disease without need for suppl. oxygen</i>	<i>Hospitalized: severe but non-critical disease (spO<sub>2</sub> &lt;94% on room air)</i>	<i>Hospitalized: critical disease (e.g., in ICU needing MV, or septic shock, ECMO)</i>
<b>15</b>	<i>Baricitinib + Remdesivir</i>	NA	NA	<b>Suggest use****</b> ⊕⊕○○ R: For hospitalized patients who cannot receive corticosteroids because of a contraindication. Baricitinib 4 mg daily dose for 14 days (or until hospital discharge). The benefits of baricitinib plus remdesivir for persons on mechanical ventilation are uncertain.	
<b>16</b>	<i>Baricitinib + remdesivir + corticosteroids</i>	Recommended only in the context of a clinical trial (knowledge gap)	NA	NA	NA
<b>17-18</b>	<i>Ivermectin</i>	<b>Suggests against use except in a clinical trial</b> ⊕○○○	NA	<b>Suggests against use except in a clinical trial</b> ⊕○○○	NA

# Plasma convalescente

## FDA NEWS RELEASE

# FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID-19 Treatment, Another Achievement in Administration's Fight Against Pandemic

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**For Immediate Release:** August 23, 2020

Content current as of:



# Plasma convalescente

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More Press Announcements for Immediate Release: August 23, 2020

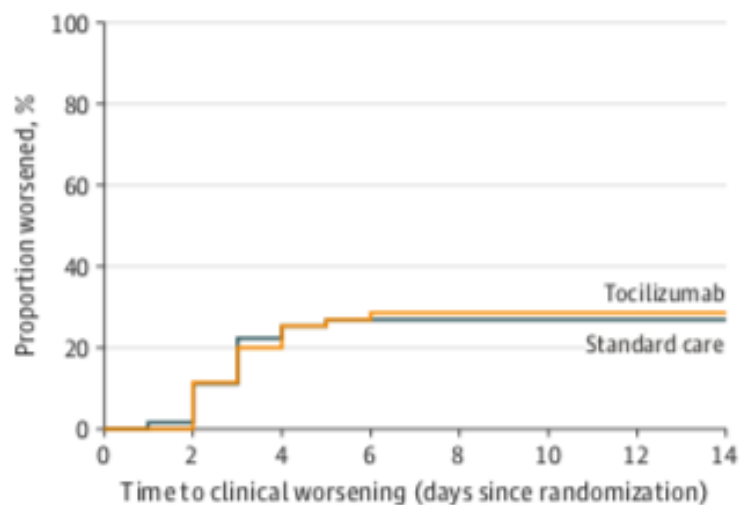
Content current as of:

Detailed description: This is a screenshot of a news article from the FDA website. The main image shows Donald Trump at a political rally, speaking into a microphone and gesturing with his right hand. Behind him, a crowd of supporters is visible, many holding red signs that say 'MAKE AMERICA GREAT AGAIN'. Some people are also holding up smartphones to record the event. The website's navigation bar is at the top, featuring the FDA logo and 'U.S. FOOD & DRUG ADMINISTRATION'. On the left, there are navigation links for 'Home / News & Events' and 'FDA Issues Emergency'. On the right, there are 'Search' and 'Menu' buttons. Below the image, there is a section for 'More Press Announcements for Immediate Release' dated 'August 23, 2020'. At the bottom right, it says 'Content current as of:'.

# Tocilizumab - TCZ-RCT

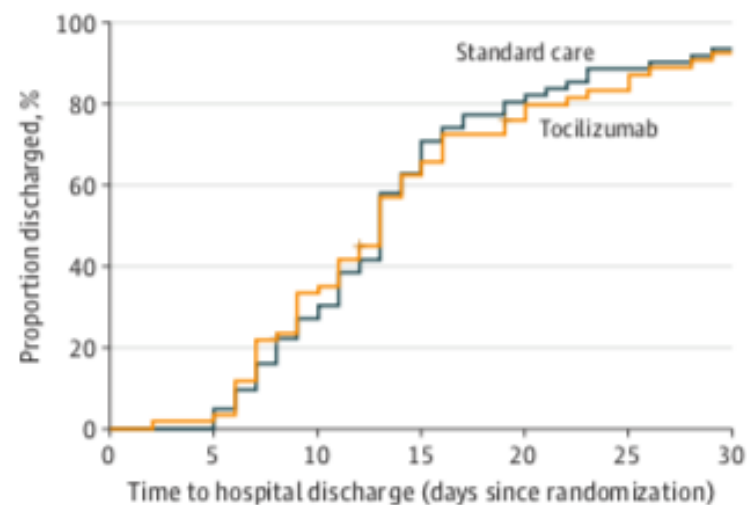
- PaO<sub>2</sub>/FIO<sub>2</sub> ratio between 200 and 300 mm/Hg
- temperature > 38 °C during the last 2 days
- serum C-reactive protein (CRP) > 100 mg/L or greater and/or CRP level increased to at least twice the admission measurement

**A** Cumulative clinical worsening



No. at risk	0	2	4	6	8	10	12	14
Tocilizumab	60	53	45	43	43	43	43	43
Standard care	63	56	47	46	46	46	46	46

**B** Hospital discharge rates



No. at risk	0	5	10	15	20	25	30
Tocilizumab	60	58	39	20	11	7	4
Standard care	63	60	43	18	11	7	4

Kaplan-Meier estimates of cumulative clinical worsening (A) and hospital discharge (B).

# Tocilizumab



## *Roche provides an update on the phase III COVACTA trial of Actemra/RoActemra in hospitalised patients with severe COVID-19 associated pneumonia*

- ◆ **COVACTA trial did not meet its primary endpoint of improved clinical status in patients with COVID-19 associated pneumonia, or the key secondary endpoint of reduced patient mortality**
- ◆ **The study is the first global, randomised, double-blind, placebo-controlled phase III trial investigating Actemra/RoActemra in this setting**
- ◆ **Roche remains committed to continuing the Actemra/RoActemra clinical trial programme in COVID-19 to further explore Actemra/RoActemra in other treatment settings, including in combination with an antiviral**

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### *Additional information*

- ⬇ [29072020\\_MR\\_COVACTA](#)



# Tocilizumab



## Services

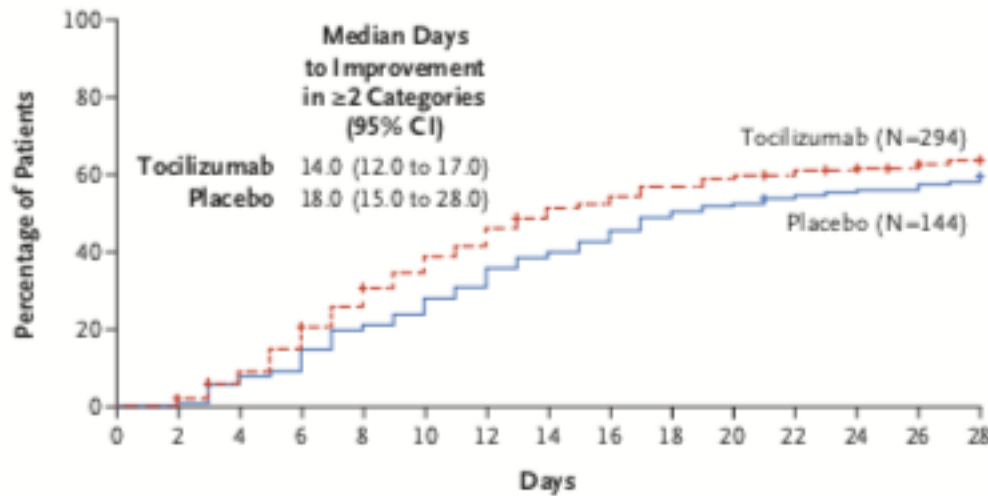
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information  
OVACTA

*Roche provides an update on the phase III COVACTA trial of Actemra/RoActemra in hospitalised patients with severe COVID-19 associated pneumonia*

- ◆ COVACTA trial did not show a statistically significant difference in status in patients with severe COVID-19 associated pneumonia
- ◆ The study is the first global phase III trial investigating the use of tocilizumab in hospitalised patients with severe COVID-19 associated pneumonia
- ◆ Roche remains committed to its COVID-19 treatment programme in COVID-19 hospitalised patients with severe COVID-19 associated pneumonia in other treatment settings

A Improvement in Ordinal Clinical Status

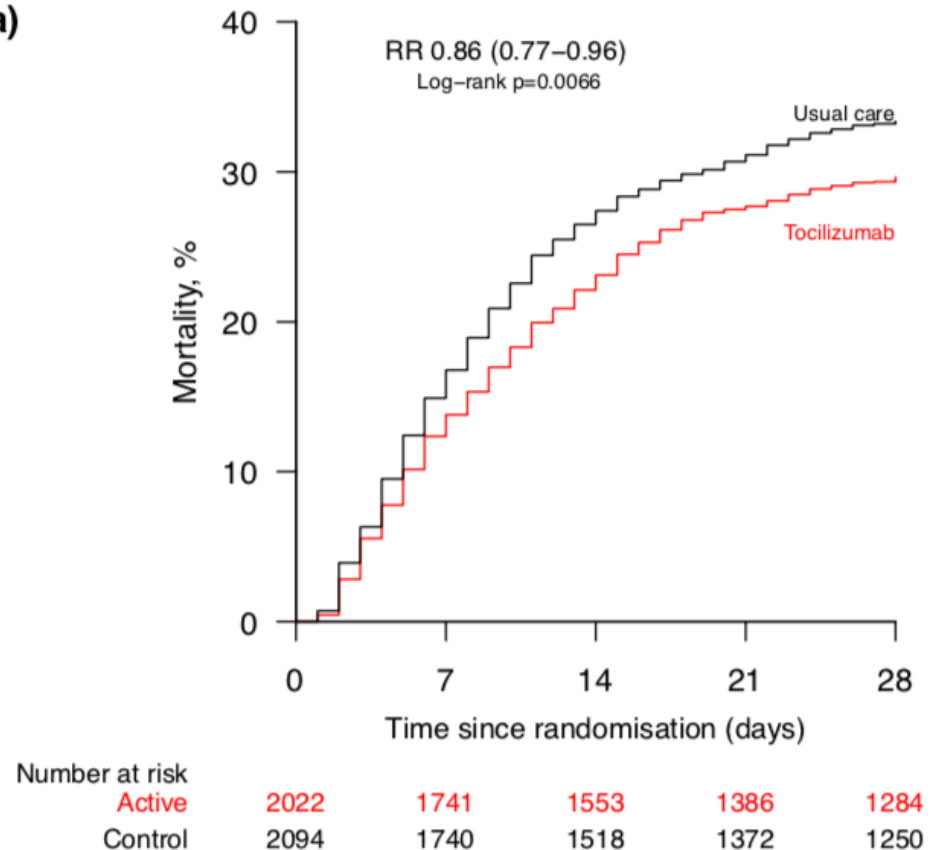


No. at Risk

Tocilizumab	294	294	275	248	216	189	169	148	137	124	118	115	110	107	99
Placebo	144	144	135	130	115	109	99	88	82	73	69	65	63	62	59

# Tocilizumab Recovery

- evidence of progressive COVID-19
- oxygen saturation <92% on room air or receiving oxygen therapy,
- serum C-reactive protein (CRP)  $\geq 7$  (a)
- 4116 patients
- glucocorticoid: 82%
- Death: 33% vs. 29%
- CI 0.77 - 0.96 (p= 0.007)

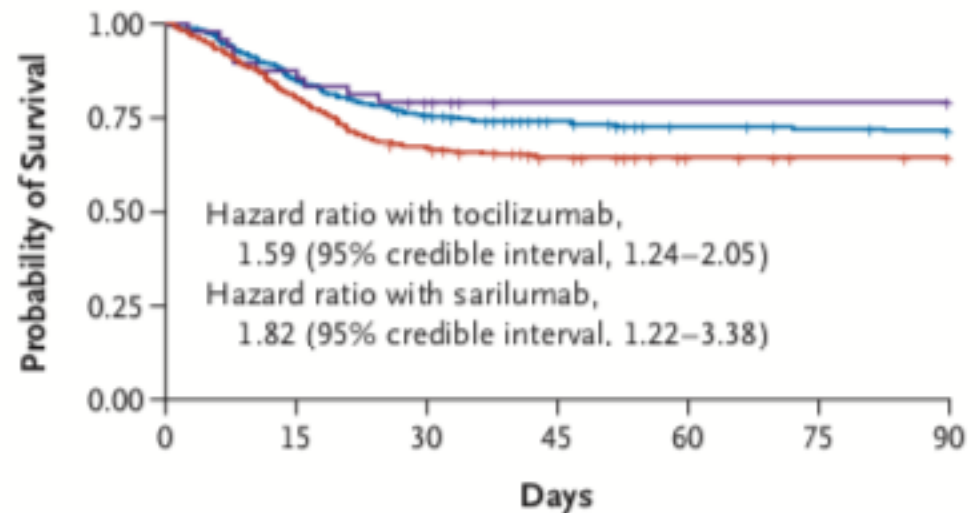


# Tocilizumab/Sarilumab Remap-Cap

- severe disease: ICU patient
- invasive or non invasive ventilation (>30 L/min FiO2 >40%),
- intra-venous infusion of any vasopressor or inotrope

A

- 803 patients
- glucorticoid: 93%
- Death: 36% vs. 27%
- OR TCZ: 1.64 (1.14-2.35)
- OR SLM: 2.01 (1.14-4.71)



No. at Risk

	0	15	30	45	60	75	90
Sarilumab	48	42	37	31	31	31	31
Tocilizumab	353	300	266	242	230	226	224
Control	402	323	268	242	231	226	225

Remap-Cap, NEJM 2021

Saper identificare il corretto momento delle terapie

Since interleukin-6 and other cytokines are potentially critical for both a healthy response to SARS-CoV-2 and a detrimental cytokine storm, it is particularly **important that the right subgroups of patients with Covid-19 are selected for treatments at the right time.**

# Conclusioni

1. Clinica: non solo respiratoria. Forme croniche
2. Trasmissione: per goccioline e contatto
3. Procedure a rischio: attenti alla produzione di aerosol. Corretto uso DPI. Igiene mani
4. Diagnostica: raffinata in evoluzione
5. Terapie ...

E quindi uscimmo a rivedere le stelle



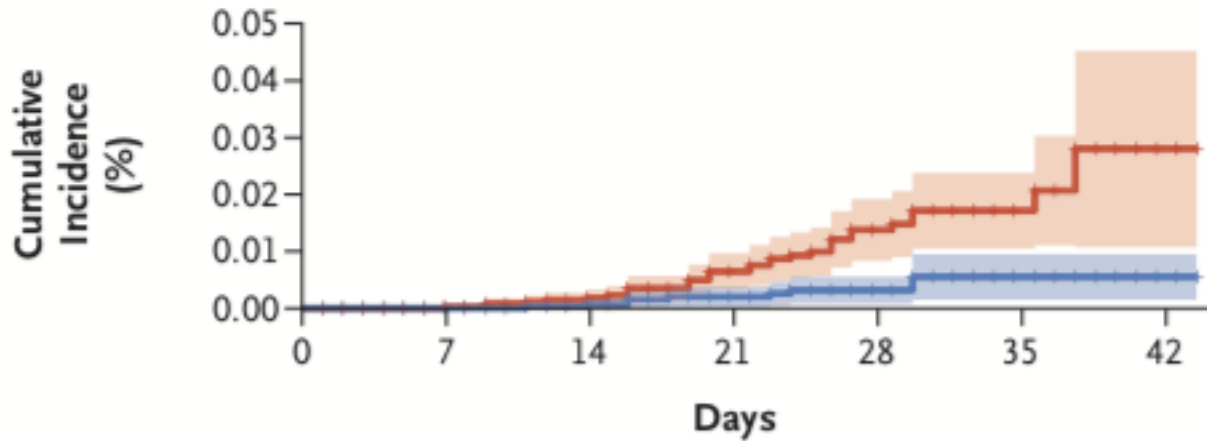
Dante, Divina commedia, Inferno, canto XXXIV, verso 139

ORIGINAL ARTICLE

BNT162b2 mRNA Covid-19 Vaccine  
in a Nationwide Mass Vaccination Setting

Noa Dagan, M.D., Noam Barda, M.D., Eldad Kepten, Ph.D., Oren Miron, M.A.,  
Shay Perchik, M.A., Mark A. Katz, M.D., Miguel A. Hernán, M.D.,  
Marc Lipsitch, D.Phil., Ben Reis, Ph.D., and Ran D. Balicer, M.D.

# Morte per Covid-19



**No. at Risk**

Unvaccinated	596,618	414,909	264,479	189,950	110,008	38,510	4316
Vaccinated	596,618	414,938	264,538	190,032	110,101	38,575	4322

**Cumulative No. of Events**

Unvaccinated	0	1	6	16	27	30	32
Vaccinated	0	0	2	5	7	9	9