Manejo Clínico – COVID-19

Virtual, 16 de abril de 2020

Organización Panamericana de la Salud
Organización Mundial de la Salud
Oficina Regional para las Américas

OPS

COVID-19 – los cuellos de botella

- Propagación similar a la influenza.
- Sin inmunidad de grupo

Transmisibilidad

- Más severo en ciertas poblaciones.
- Ausencia de medidas farmacológicas

Severidad

Impacto

OMS GIP, Evaluación de la Gravedad de Influenza Pandémica (PISA), 2017

Organización Panamericana de la Salud
Organización Mundial de la Salud
Américas
OPS

El Desafío Fundamental

- Gestionar el aumento potencial de los casos por COVID-19
  - No existen tratamientos comprobados
  - No existe una vacuna
- Limitación de la transmisión
- Continuar brindando servicios esenciales para los demás

Globally, as of **2:00am CEST, 16 April 2020**, there have been **1,995,983 confirmed cases** of COVID-19, including **131,037 deaths,** reported to WH

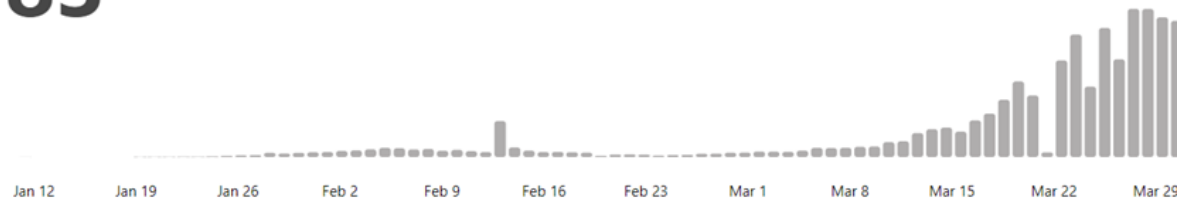
Confirmed Cases Over Time

Daily

1,995,983

confirmed cases

Source: World Health Organization



Deaths Over Time

Daily

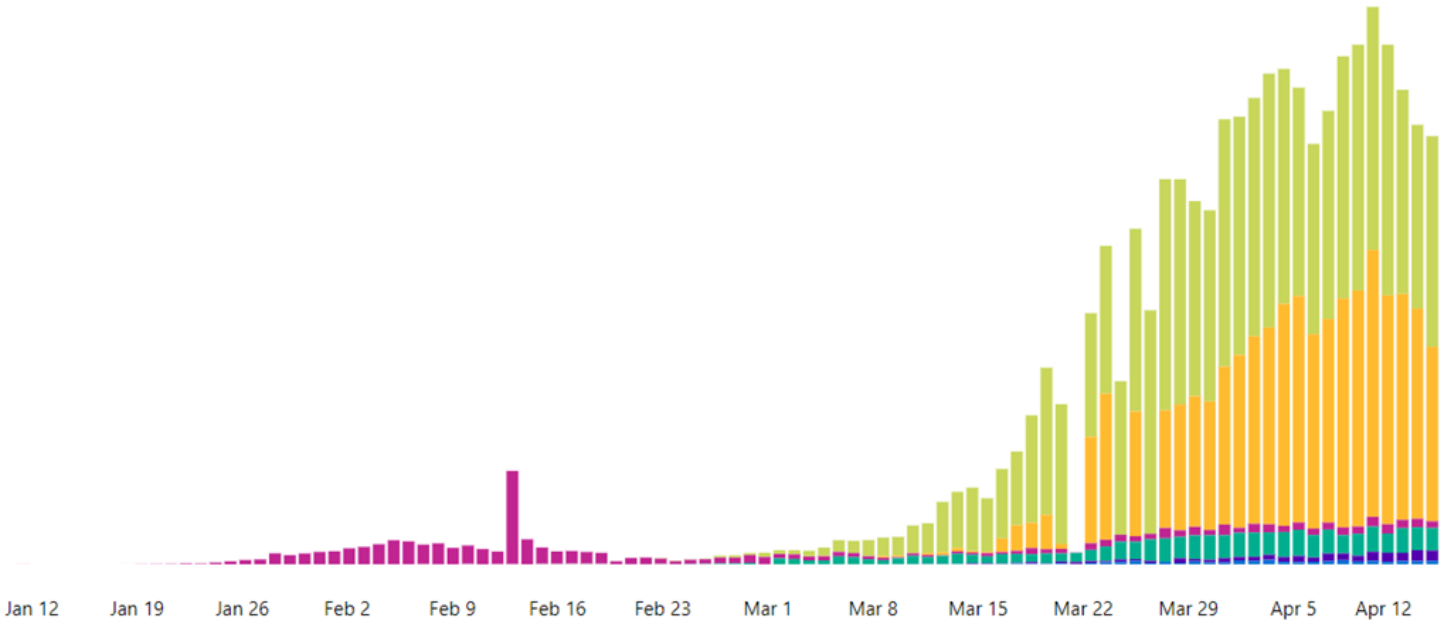
131,037

deaths

Source: World Health Organization

Estado actual de la pandemia (I)

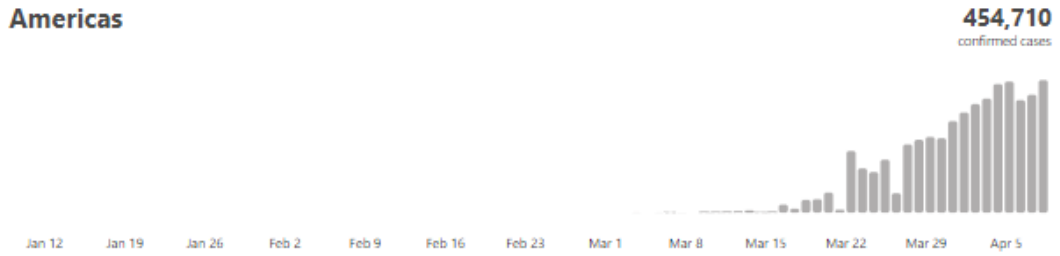
Estado actual de la pandemia (II)



https://who.sprinklr.com/

Estado actual de la pandemia (III)

https://who.sprinklr.com/



¿Quién está en mayor riesgo de complicaciones?

Distribución por edad de pacientes confirmados y muertes por COVID-19, China

Edad (años)	Casos confirmados	Muertes	Tasa de Letalidad
0–9	416 (0.9%)	0 (0.0%)	0.0%
10–19	549 (1.2%)	1 (0.1%)	0.2%
20–29	3,619 (8.1%)	7 (0.7%)	0.2%
30–39	7,600 (17.0%)	18 (1.8%)	0.2%
40–49	8,571 (19.2%)	38 (3.7%)	0.4%
50–59	10,008 (22.4%)	130 (12.7%)	1.3%
60–69	8,583 (19.2%)	309 (30.2%)	3.6%
70–79	3,918 (8.8%)	312 (30.5%)	8.0%
≥80	1,408 (3.2%)	208 (20.3%)	14.8%
Total	44,672 (100.0%)	1,023 (100.0%)	2.3%

Condiciones pre-existentes de pacientes confirmados con COVID-19 — China

Condición	Casos confirmados	Muertes	Tasa de letalidad
Hipertensión	2,683 (12.8%)	161 (39.7%)	6.0%
Diabetes	1,102 (5.3%)	80 (19.7%)	7.3%
Enfermedad cardiovascular	873 (4.2%)	92 (22.7%)	10.5%
Enfermedad respiratoria crónica	511 (2.4%)	32 (7.9%)	6.3%
Cáncer (cualquiera)	107 (0.5%)	6 (1.5%)	5.6%
Ninguno	15,536 (74.0%)	133 (32.8%)	0.9%
No disponible	23,690 (53.0%)	617 (60.3%)	2.6%

China CDC Semanal, 17 Febrero 2020

Experiencia Italiana (I)

- 1.Crear **cohorte en UCIs** para pacientes con COVID-19
- **Organizar un área de triaje** donde pueda ocurrir ventilación mecánica mientras se espera el diagnóstico
- **Protocolos locales de intervención** para identificar aquellos con síntomas respiratorios y obtener diagnóstico
- **Garantizar la disponibilidad de EPP** adecuado
- **Reportar todo paciente positivo o sospechoso** críticamente enfermo al centro de coordinación regional

Opinion

VIEWPOINT

Critical Care Utilization for the COVID-19 Outbreak in Lombardy, Italy

Early Experience and Forecast During an Emergency Response

Giacomo Grasselli, MD
Department of Pathophysiology and Transplantation, University of Milan, Italy; and Dipartimento di Anestesia, Rianimazione ed Emergenza-Urgenza, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.

Antonio Pesenti, MD
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Maurizio Cecconi, MD
Dipartimento Anestesia e Terapie Intensive, Humanitas Rozzano, Milan, Italy.

Supplemental content

Corresponding Author: Antonio Pesenti, MD, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Università degli studi di Milano, Via F. Sforza 35, 20122 Milan, Italy (antonio.pesenti@unimi.it).

On February 20, 2020, a patient in his 30s admitted to the intensive care unit (ICU) in Codogno Hospital (Lodi, Lombardy, Italy) tested positive for a new coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19). He had a history of atypical pneumonia that was not responding to treatment, but he was not considered at risk for COVID-19 infection.[1] The positive result was immediately reported to the Lombardy health care system and governmental offices. During the next 24 hours, the number of reported positive cases increased to 36. This situation was considered a serious development for several reasons: the patient ("patient 1") was healthy and young; in less than 24 hours, 36 additional cases were identified, without links to patient 1 or previously identified positive cases already in the country; it was not possible to identify with certainty the source of transmission to patient 1 at the time; and, because patient 1 was in the ICU and there were already 36 cases by day 2, chances were that a cluster of unknown magnitude was present and additional spread was likely.

On February 21, an emergency task force was formed by the Government of Lombardy and local health authorities to lead the response to the outbreak. This Viewpoint provides a summary of the response of the COVID-19 Lombardy ICU network and a forecast of estimated ICU demand over the coming weeks (projected to March 20, 2020).

Setting the Priorities and the Initial Response

In Lombardy, the precrisis total ICU capacity was approximately 720 beds (2.9% of total hospital beds at a total of 74 hospitals); these ICUs usually have 85% to 90% occupancy during the winter months.

The mission of the COVID-19 Lombardy ICU Network was to coordinate the critical care response to the outbreak. Two top priorities were identified: increasing surge ICU capacity and implementing measures for containment.

Increasing ICU Surge Capacity

The recognition that this outbreak likely occurred via community spread suggested that a large number of COVID-19–positive patients were already present in the region. This prediction proved correct in the following days. Based on the assumption that secondary transmission was already occurring, and even with containment measures that health authorities were establishing, it was assumed that many new cases of COVID-19 would occur, possibly in the hundreds or thousands of individuals. Thus, assuming a 5% ICU admission rate,[2] it would not have been feasible to allocate all critically ill patients to a single COVID-19 ICU. The decision was to cohort patients in 15 first-responder hub hospitals, chosen because they either had expertise in infectious disease or were part of the Venous-Venous ECMO Respiratory Failure Network (RESPIRA).[3]

The identified hospitals were requested to do the following:

1. Create cohort ICUs for COVID-19 patients (areas separated from the rest of the ICU beds to minimize risk of in-hospital transmission).
2. Organize a triage area where patients could receive mechanical ventilation if necessary in every hospital to support critically ill patients with suspected COVID-19 infection, pending the final result of diagnostic tests.
3. Establish local protocols for triage of patients with respiratory symptoms, to test them rapidly, and, depending on the diagnosis, to allocate them to the appropriate cohort.
4. Ensure that adequate personal protective equipment (PPE) for health personnel is available, with the organization of adequate supply and distribution along with adequate training of all personnel at risk of contagion.
5. Report every positive or suspected critically ill COVID-19 patient to the regional coordinating center.

In addition, to quickly make available ICU beds and available personnel, nonurgent procedures were canceled and another 200 ICU beds were made available and staffed in the following 10 days. In total, over the first 18 days, the network created 482 ICU beds ready for patients.

Containment Measures

Local health authorities established strong containment measures in the initial cluster by quarantine of several towns in an attempt to slow virus transmission. In the second week, other clusters emerged. During this time, the ICU network advised the government to put in place every measure, such as reinforcing public health measures of quarantine and self-isolation, to contain the virus.

ICU Admissions Over the First 2 Weeks

There was an immediate sharp increase in ICU admissions from day 1 to day 14. The increase was steady and consistent. Publicly available data indicate that ICU admissions (n = 556) represented 16% of all patients (n = 3420) who tested positive for COVID-19. As of March 7, the current total number of patients with COVID-19 occupying an ICU bed (n = 359) represents 16% of currently hospitalized patients with COVID-19 (n = 2217).

https://jamanetwork.com/journals/jama/fullarticle/2763188

Experiencia Italiana (I)

D1-D14: aumento inmediato de admisiones en la UCI

- 1.Constante y exponencial
- 1.12% del total identificado por COVID-19 + pacientes
- 1.16% de todas las admisiones por COVID-19
- 1.Saturación temprana de la capacidad de laboratorio
- 1.Necesidad de redes regionales de UCI

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jama.com

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Experiencia en E.E.U.U. - Hospitalización

TABLE. Hospitalization, intensive care unit (ICU) admission, and case–fatality percentages for reported COVID–19 cases, by age group — United States, February 12–March 16, 2020

Age group (yrs) (no. of cases)	%*		
	Hospitalization	ICU admission	Case-fatality
0–19 (123)	1.6–2.5	0	0
20–44 (705)	14.3–20.8	2.0–4.2	0.1–0.2
45–54 (429)	21.2–28.3	5.4–10.4	0.5–0.8
55–64 (429)	20.5–30.1	4.7–11.2	1.4–2.6
65–74 (409)	28.6–43.5	8.1–18.8	2.7–4.9
75–84 (210)	30.5–58.7	10.5–31.0	4.3–10.5
≥85 (144)	31.3–70.3	6.3–29.0	10.4–27.3
Total (2,449)	**20.7–31.4**	**4.9–11.5**	**1.8–3.4**

* Lower bound of range = number of persons hospitalized, admitted to ICU, or who died among total in age group; upper bound of range = number of persons hospitalized, admitted to ICU, or who died among total in age group with known hospitalization status, ICU admission status, or death.

Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020

CDC COVID-19 Response Team

On March 18, 2020, this report was posted as an MMWR *Early Release on the* MMWR *website (http://www.cdc.gov/mmwr).*

Globally, approximately 170,000 confirmed cases of coronavirus disease 2019 (COVID-19) caused by the 2019 novel coronavirus (SARS-CoV-2) have been reported, including an estimated 7,000 deaths in approximately 150 countries (*1*). On March 11, 2020, the World Health Organization declared the COVID-19 outbreak a pandemic (*2*). Data from China have indicated that older adults, particularly those with serious underlying health conditions, are at higher risk for severe COVID-19–associated illness and death than are younger persons (*3*). Although the majority of reported COVID-19 cases in China were mild (81%), approximately 80% of deaths occurred among adults aged ≥60 years; only one (0.1%) death occurred in a person aged ≤19 years (*3*). In this report, COVID-19 cases in the United States that occurred during February 12–March 16, 2020 and severity of disease (hospitalization, admission to intensive care unit [ICU], and death) were analyzed by age group. As of March 16, a total of 4,226 COVID-19 cases in the United States had been reported to CDC, with multiple cases reported among older adults living in long-term care facilities (*4*). Overall, 31% of cases, 45% of hospitalizations, 53% of ICU admissions, and 80% of deaths associated with COVID-19 were among adults aged ≥65 years with the highest percentage of severe outcomes among persons aged ≥85 years. In contrast, no ICU admissions or deaths were reported among persons aged ≤19 years. Similar to reports from other countries, this finding suggests that the risk for serious disease and death from COVID-19 is higher in older age groups.

Data from cases reported from 49 states, the District of Columbia, and three U.S. territories (*5*) to CDC during February 12–March 16 were analyzed. Cases among persons repatriated to the United States from Wuhan, China and from Japan (including patients repatriated from cruise ships) were excluded. States and jurisdictions voluntarily reported data on laboratory-confirmed cases of COVID-19 using previously developed data collection forms (*6*). The cases described in this report include both COVID-19 cases confirmed by state or local public health laboratories as well as those with a positive test at the state or local public health laboratories and confirmation at CDC. No data on serious underlying health conditions were available. Data on these cases are preliminary and are missing for some key characteristics of interest, including hospitalization status (1,514), ICU admission (2,253), death (2,001), and age (386). Because of these missing data, the percentages of hospitalizations, ICU admissions, and deaths (case-fatality percentages) were estimated as a range. The lower bound of these percentages was estimated by using all cases within each age group as denominators. The corresponding upper bound of these percentages was estimated by using only cases with known information on each outcome as denominators.

As of March 16, a total of 4,226 COVID-19 cases had been reported in the United States, with reports increasing to 500 or more cases per day beginning March 14 (Figure 1). Among 2,449 patients with known age, 6% were aged ≥85, 25% were aged 65–84 years, 18% each were aged 55–64 years and 45–54 years, and 29% were aged 20–44 years (Figure 2). Only 5% of cases occurred in persons aged 0–19 years.

Among 508 (12%) patients known to have been hospitalized, 9% were aged ≥85 years, 36% were aged 65–84 years, 17% were aged 55–64 years, 18% were 45–54 years, and 20% were aged 20–44 years. Less than 1% of hospitalizations were among persons aged ≤19 years (Figure 2). The percentage of persons hospitalized increased with age, from 2%–3% among persons aged ≤19 years, to ≥31% among adults aged ≥85 years. (Table).

Among 121 patients known to have been admitted to an ICU, 7% of cases were reported among adults ≥85 years, 46% among adults aged 65–84 years, 36% among adults aged 45–64 years, and 12% among adults aged 20–44 years (Figure 2). No ICU admissions were reported among persons aged ≤19 years. Percentages of ICU admissions were lowest among adults aged 20–44 years (2%–4%) and highest among adults aged 75–84 years (11%–31%) (Table).

Among 44 cases with known outcome, 15 (34%) deaths were reported among adults aged ≥85 years, 20 (46%) among adults aged 65–84 years, and nine (20%) among adults aged 20–64 years. Case-fatality percentages increased with increasing age, from no deaths reported among persons aged ≤19 years to highest percentages (10%–27%) among adults aged ≥85 years (Table) (Figure 2).

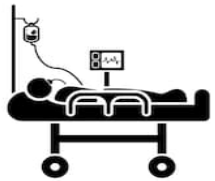
Discussion

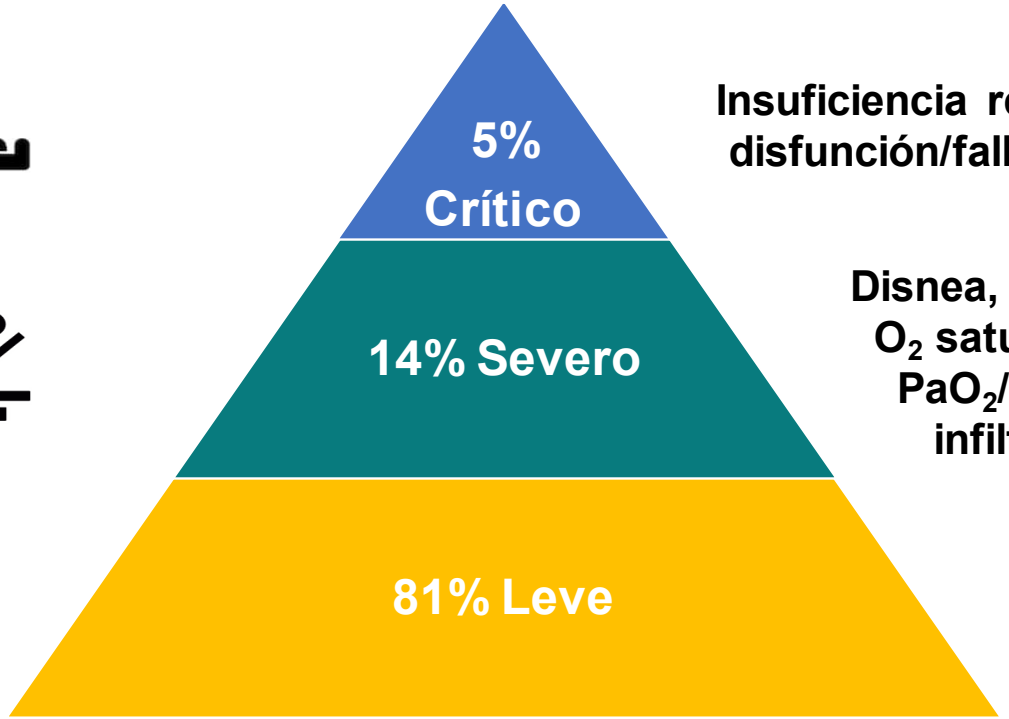
Since February 12, 4,226 COVID-19 cases were reported in the United States: 31% of cases, 45% of hospitalizations, 53% of ICU admissions, and 80% of deaths occurred among adults

https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6912e2-H.pdf

¿Qué se puede esperar?

Espectro de Manifestaciones Clínicas de COVID-19





Insuficiencia respiratoria, shock séptico disfunción/falla multiorgánica

Disnea, RR ≥ 30/min, O_2 saturación ≤93%, PaO_2/FiO_2 ratio <300, y/o pulmón infiltrados >50% dentro de 24–48 horas

No neumonía & casos de neumonía leve

China CDC Semanal 17 Febrero 2020

Organización Panamericana de la Salud
Organización Mundial de la Salud
Américas
OPS

Symptoms near the time of presentation in various cohorts

	Guan et al. NEJM (largest cohort)	Shi et al Lancet	Yang et al. Lancet (critically ill pts)	Chen et al.	Huang et al.	Xu et al. BMJ
Constitutional						
Fever	473/1081 (43%)	18/21 (86%)	46/52 (88%)	82/99 (83%)	40/41 (98%)	48/62 (77%)
Myalgia	164/1081 (15%)		6/52 (12%)	11/99 (11%)		
Headache	150/1081 (14%)	2/21 (10%)	3/52 (6%)	8/99 (8%)	2/38 (8%)	21/62 (34%)
Upper respiratory						
Rhinorrhea	53/1081 (5%)	5/21 (24%)	3/52 (6%)	4/99 (4%)		
Sore throat	153/1081 (14%)			5/99 (5%)		
Lower respiratory						
Dyspnea	205/1081 (19%)	9/21 (43%)	33/52 (64%)	31/99 (31%)	22/40 (55%)	2/62 (3%)
Chest tightness		5/21 (24%)				
Cough	745/1081 (68%)	15/21 (71%)	40/52 (77%)	81/99 (82%)	31/41 (76%)	50/62 (81%)
Sputum	370/1081 (34%)	3/21 (14%)			11/39 (28%)	35/62 (56%)
Hemoptysis	10/1081 (1%)				2/39 (5%)	2/62 (3%)
Gastrointestinal						
Nausea/Vomiting	55/1081 (5%)	2/21 (10%)	2/52 (6%)	1/99 (1%)		
Diarrhea	42/1081 (4%)	1/21 (5%)		2/99 (2%)	1/38 (3%)	3/62 (8%)

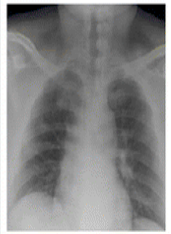
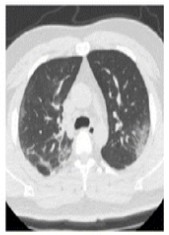
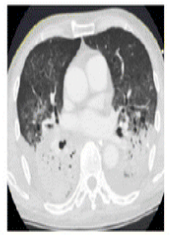
Admission laboratory pattern in patients with COVID-19

	Guan et al NEJM (largest cohort)	Shi et al Lancet	Chen et al Lancet	Huang et al. Lancet	Xu et al. BMJ
WBC count	4.7 (3.5-6)	7.8 (2.5)	7.5 (4)	6.2 (4-10.5)	4.7 (3.5-5.8)
Platelet count	168 (132-207)	213 (100)	214 (79)	164 (132-263)	176 (136-215)
Lymphocyte count (normally >1)	1 (0.7-1.3)	1 (0.3)	0.9 (0.5)	0.8 (0.6-1.1)	1 (0.8-1.5)
Hemoglobin	13.4 (12-15)	12.7 (1.3)	13 (1.5)	12.6 (11.8-14)	13.7 (12.9-15.2)
ALT (U/L)		51 (25)	39 (22-53)	32 (21-50)	22 (14-34)
AST (U/L)		48 (21)	34 (26-48)	34 (26-48)	26 (20-32)
Bilirubin uM/L (normal range 5-22 uM/L)		14 (4)	15 (7)	12 (10-14)	
Creatinine (normal range up to ~80-100 uM)		68 (15)	76 (25)	74 (58-86)	72 (61-84)
Prothrombin time (normal range ~12.7-15.4)		10.5 (0.4)	11 (2)	11 (10-12.4)	
APTT (normal range ~21-37 seconds)		34 (7)	27 (10)		
Thrombin time (normal range ~15-18.5)		32 (8)			
Fibrinogen mg/dL		192 (350)			
D-dimer (mg/L) – (NI range seems to vary?)		6.9 (1.1)	0.9 (0.5-2.8)	0.5 (0.3-1.3)	0.2 (0.2-0.5)
Creatinine kinase			85 (51-184)		
LDH (normal range up to 250 U/L)			336 (260-447)	286 (242-408)	205 (184-260)
C-Reactive Protein mg/L		61 (40)	51 (42)		
Procalcitonin	<0.5 in 95% patients		0.5 (1)	0.1 (0.1-0.1)	0.04 (0.03-0.06)
Erythrocyte sedimentation rate (ESR)			50 (23)		
Ferritin			808 (490)		

Laboratory findings are generally nonspecific. Substantial *deviation* from these values might argue *against* a diagnosis of COVID-19. However, in most cases, laboratory findings are unlikely to be tremendously helpful.

Curso clínico "típico"

Bouadma L. Intensive Care Med

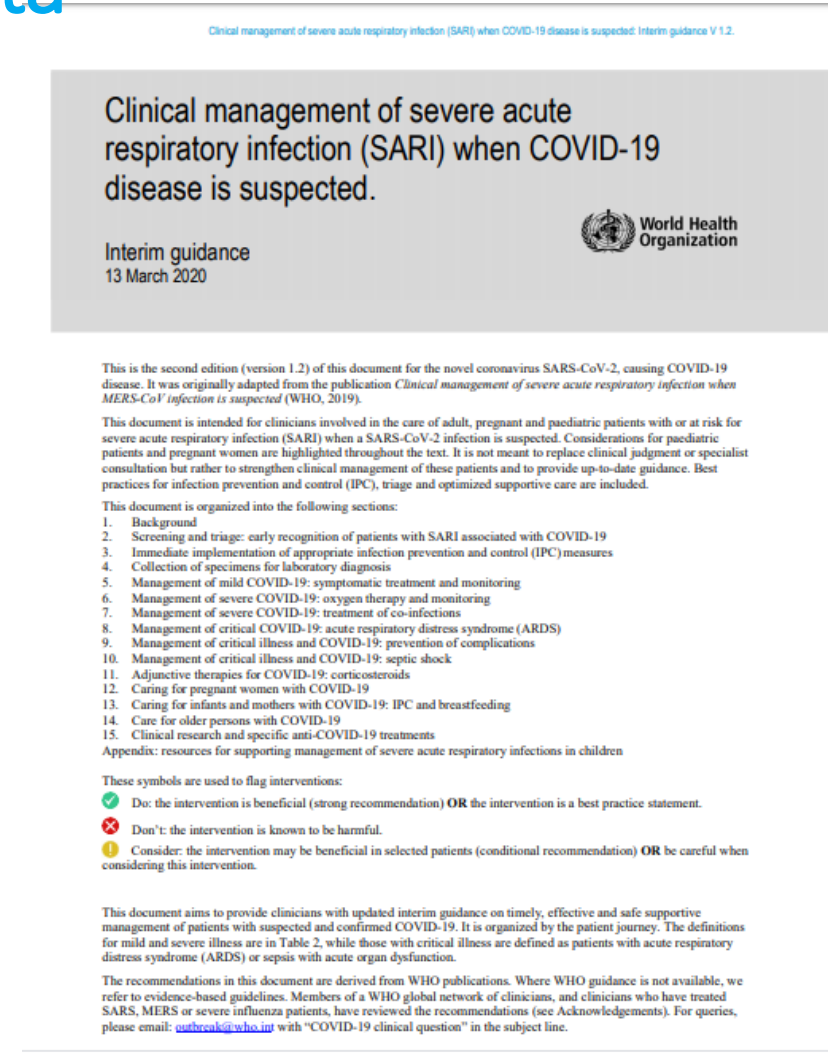
Typical features according to current publications Age Mean (SD) 55,5 (13·1), Male (68%) Exposure to Huanan seafood market in Wuhan, China (49%) Chronic medical underlying illness (51%) Admission to Intensive Care Unit (23%)									
INCUBATION PERIOD and ONSET OF SYMPTOMS 3 DAYS AGO		FIRST WEEK				SECOND WEEK			LONG TERM INFO PENDING
	SETTING	WARD Illness day 4	WARD Illness day 5	WARD Illness day 6	WARD Illness day 7	WARD/ICU Illness day 8	ICU Illness day 9	ICU Illness day 10	ICU Illness day 11
	REPEATED SAMPLING OF THE NASOPHARYNX AND TRACHEAL ASPIRATES (IF INTUBATED) BY rRT-PCR FOR THE COVID-19	Initial important viral shedding		Decrease of the viral shedding sometimes associated with transient respiratory deterioration		Respiratory failure, increase of the viral shedding and viremia or Decrease of the viral shedding, and superinfections			Duration of viral excretion unknown
	OXYGEN THERAPY AND MECHANICAL VENTILATION	NO		Consider oxygen support	FNC	FNC followed by MV	MV		MV
	ORGAN FAILURE	**Typical signs according to current publications** Fever, cough, and shortness of breath (15%) bilateral pneumonia (75%), lymphopenia (35%), thrombocytopenia (12%), prothrombin time decreased (30%), elevated liver enzyme levels (about 30%)		Deterioration of respiratory status with most often spontaneous recovery		ARDS If shock beware of superinfections ⚠ Possible renal failure Neurological failure unlikely Hemostasis disorders			YES
	CO-INFECTION/SUPERINFECTION	NOT LIKELY				Consider a possible HAP/VAP and other nosocomial infections (see text for diagnostic procedures)			Profound immune paralysis and late onset infections
	ANTIBIOTICS	NO				Consider antibiotic therapy			YES

Tempestade de citoquinas

Elevacion de PCR, ferritina, LDH, IL-6, dímero-D

La investigación es un componente integral importante de la respuesta

- **Muchas incógnitas**
- Enfermedad y su manejo óptimo
- Reservorios de virus (¿el origen?)
- Evolución del virus
- Transmisión y epidemiología
- Necesidad urgente de desarrollar contramedidas seguras y eficaces que puedan estar disponibles, accesibles y adecuadas para su uso en las poblaciones más necesitadas



Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: Interim guidance V 1.2.

Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected.

World Health Organization

Interim guidance
13 March 2020

This is the second edition (version 1.2) of this document for the novel coronavirus SARS-CoV-2, causing COVID-19 disease. It was originally adapted from the publication *Clinical management of severe acute respiratory infection when MERS-CoV infection is suspected* (WHO, 2019).

This document is intended for clinicians involved in the care of adult, pregnant and paediatric patients with or at risk for severe acute respiratory infection (SARI) when a SARS-CoV-2 infection is suspected. Considerations for paediatric patients and pregnant women are highlighted throughout the text. It is not meant to replace clinical judgment or specialist consultation but rather to strengthen clinical management of these patients and to provide up-to-date guidance. Best practices for infection prevention and control (IPC), triage and optimized supportive care are included.

This document is organized into the following sections:

1. Background
2. Screening and triage: early recognition of patients with SARI associated with COVID-19
3. Immediate implementation of appropriate infection prevention and control (IPC) measures
4. Collection of specimens for laboratory diagnosis
5. Management of mild COVID-19: symptomatic treatment and monitoring
6. Management of severe COVID-19: oxygen therapy and monitoring
7. Management of severe COVID-19: treatment of co-infections
8. Management of critical COVID-19: acute respiratory distress syndrome (ARDS)
9. Management of critical illness and COVID-19: prevention of complications
10. Management of critical illness and COVID-19: septic shock
11. Adjunctive therapies for COVID-19: corticosteroids
12. Caring for pregnant women with COVID-19
13. Caring for infants and mothers with COVID-19: IPC and breastfeeding
14. Care for older persons with COVID-19
15. Clinical research and specific anti-COVID-19 treatments

Appendix: resources for supporting management of severe acute respiratory infections in children

These symbols are used to flag interventions:

Do: the intervention is beneficial (strong recommendation) **OR** the intervention is a best practice statement.

Don't: the intervention is known to be harmful.

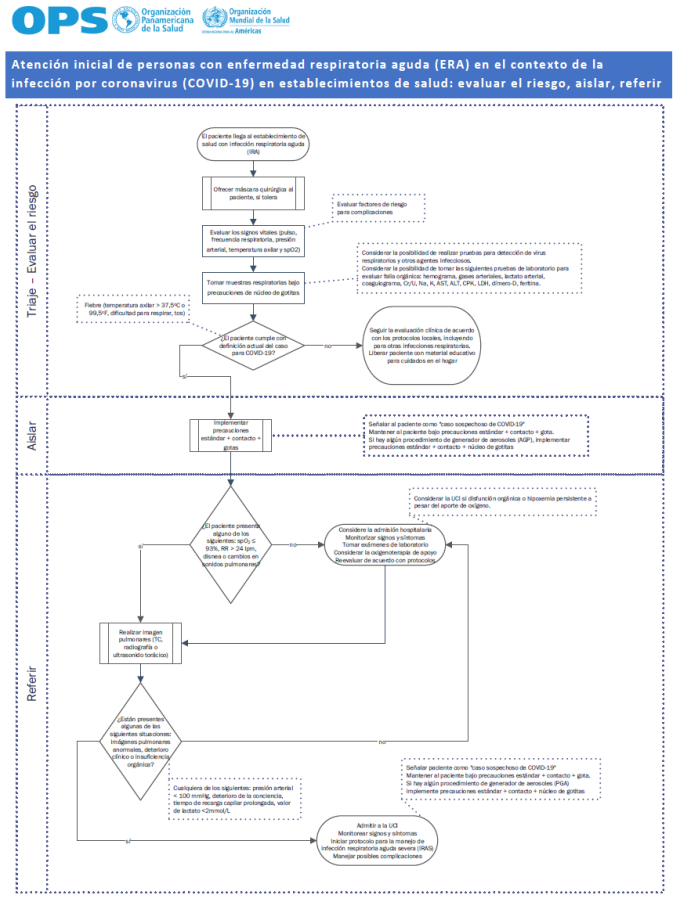
Consider: the intervention may be beneficial in selected patients (conditional recommendation) **OR** be careful when considering this intervention.

This document aims to provide clinicians with updated interim guidance on timely, effective and safe supportive management of patients with suspected and confirmed COVID-19. It is organized by the patient journey. The definitions for mild and severe illness are in Table 2, while those with critical illness are defined as patients with acute respiratory distress syndrome (ARDS) or sepsis with acute organ dysfunction.

The recommendations in this document are derived from WHO publications. Where WHO guidance is not available, we refer to evidence-based guidelines. Members of a WHO global network of clinicians, and clinicians who have treated SARS, MERS or severe influenza patients, have reviewed the recommendations (see Acknowledgements). For queries, please email: outbreak@who.int with "COVID-19 clinical question" in the subject line.

https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected

Atención al paciente con COVID-19: triaje / aislar / referir



Atención inicial de personas con infección respiratoria aguda (IRA) en el contexto de la infección por coronavirus (COVID-19) en establecimientos de salud: evaluar el riesgo, aislar, referir.

(recomendaciones provisionales, versión 1 – 12 de Abril de 2020)

Objetivo

- Brindar recomendaciones sobre la atención inicial de personas con enfermedad respiratoria aguda (ERA) en el contexto de la infección por coronavirus (COVID-19) en establecimientos de salud basado en flujograma de toma de decisiones.

Estas recomendaciones son preliminares y están sujetas a revisión a medida que se tengan nuevas evidencias.* Las recomendaciones proporcionadas en este documento se aplican a adultos mayores de 18 años. Audiencias específicas, como los bebés, los niños y las mujeres embarazadas, se abordarán en un documento separado.

Estructura del flujograma

- El flujograma presentado en este documento está estructurado en tres pasos:
  - **Triaje** – evaluación de riesgo de los pacientes que llegan a los establecimientos de salud con enfermedades respiratoria aguda en el contexto de COVID-19.
  - **Aislamiento** – aplicación de precauciones estándares y basadas en mecanismos de transmisión para casos sospechosos y confirmados.
  - **Referir** – evaluación del nivel de insuficiencia respiratoria y manejo de complicaciones; derivación a niveles más altos de complejidad de atención.

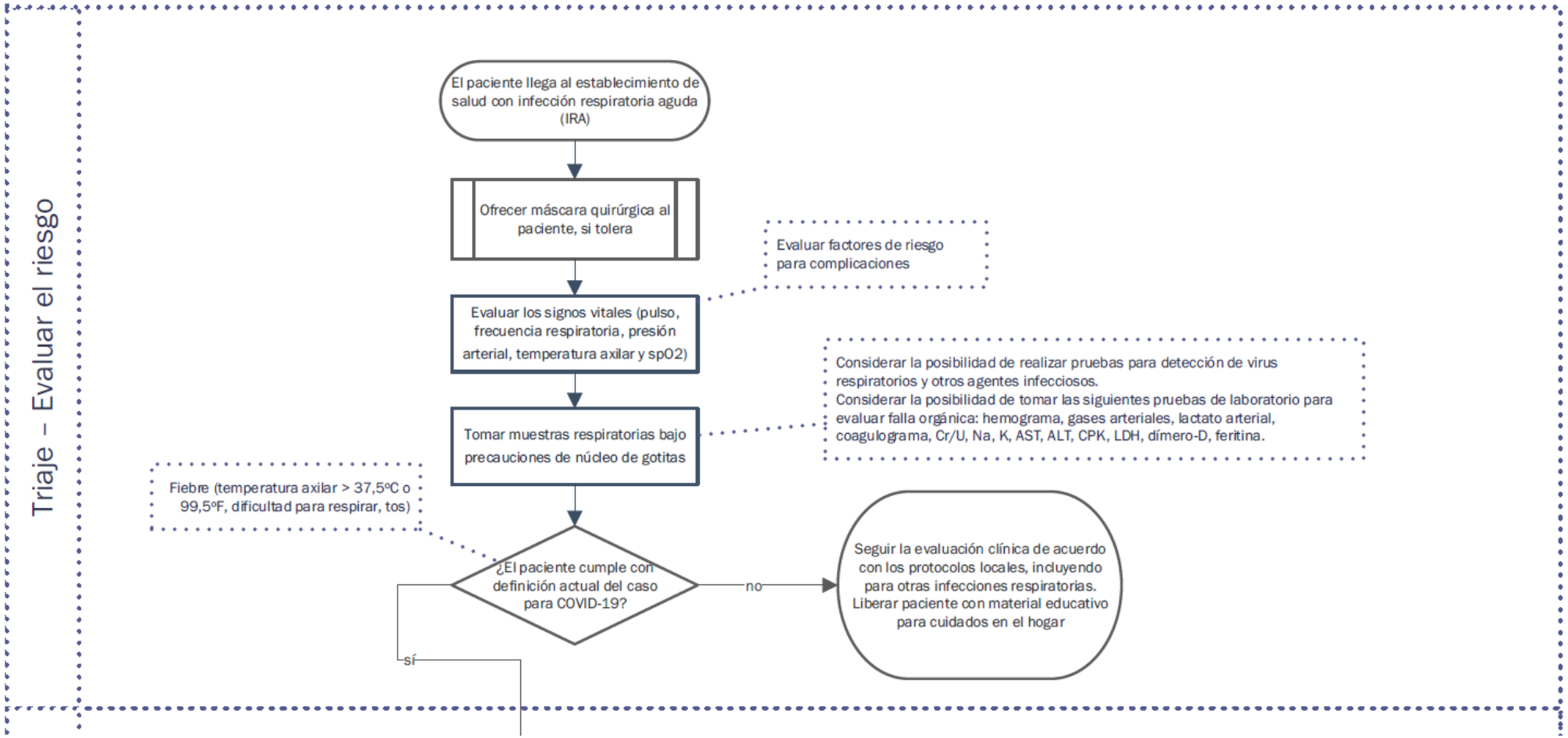
Documentos clave

- Para cada uno de los pasos del flujograma, se recomienda consultar los siguientes documentos:

Paso	Documentos claves
Triaje	• Recomendaciones técnicas para configuración de una zona de triaje de pacientes con síntomas respiratorios • Planos y flujos EMT-Triaje y Planos y flujos EMT-IRAG • Recomendaciones técnicas para configuración de un Equipo Médico de Emergencia (EMT) especializado de tratamiento de Infección Respiratoria Aguda Grave (IRAG) • Requerimientos para uso de equipos de protección personal (EPP) para el nuevo coronavirus (2019-nCoV) en establecimientos de salud • Vigilancia mundial de la infección humana por el nuevo coronavirus (2019-nCoV)
Aislamiento	• Prevención y control de infecciones durante la atención sanitaria de casos en los que se sospecha una infección por el nuevo coronavirus (nCoV) • Uso racional de equipos de protección personal para infección por coronavirus (COVID-19)
Referir	• Manejo clínico de la infección respiratoria aguda grave (IRAG) en casos de sospecha de COVID-19 • Guía para el cuidado crítico de pacientes adultos graves con Coronavirus (COVID-19) en las Américas: versión larga y versión corta

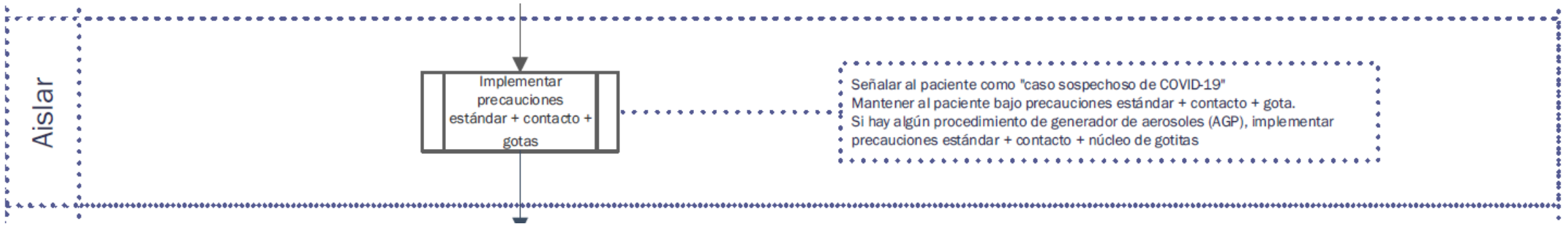
https://www.paho.org/en/topics/coronavirus-infections/coronavirus-disease-covid-19

Atención al paciente con COVID-19: triaje / aislar / referir



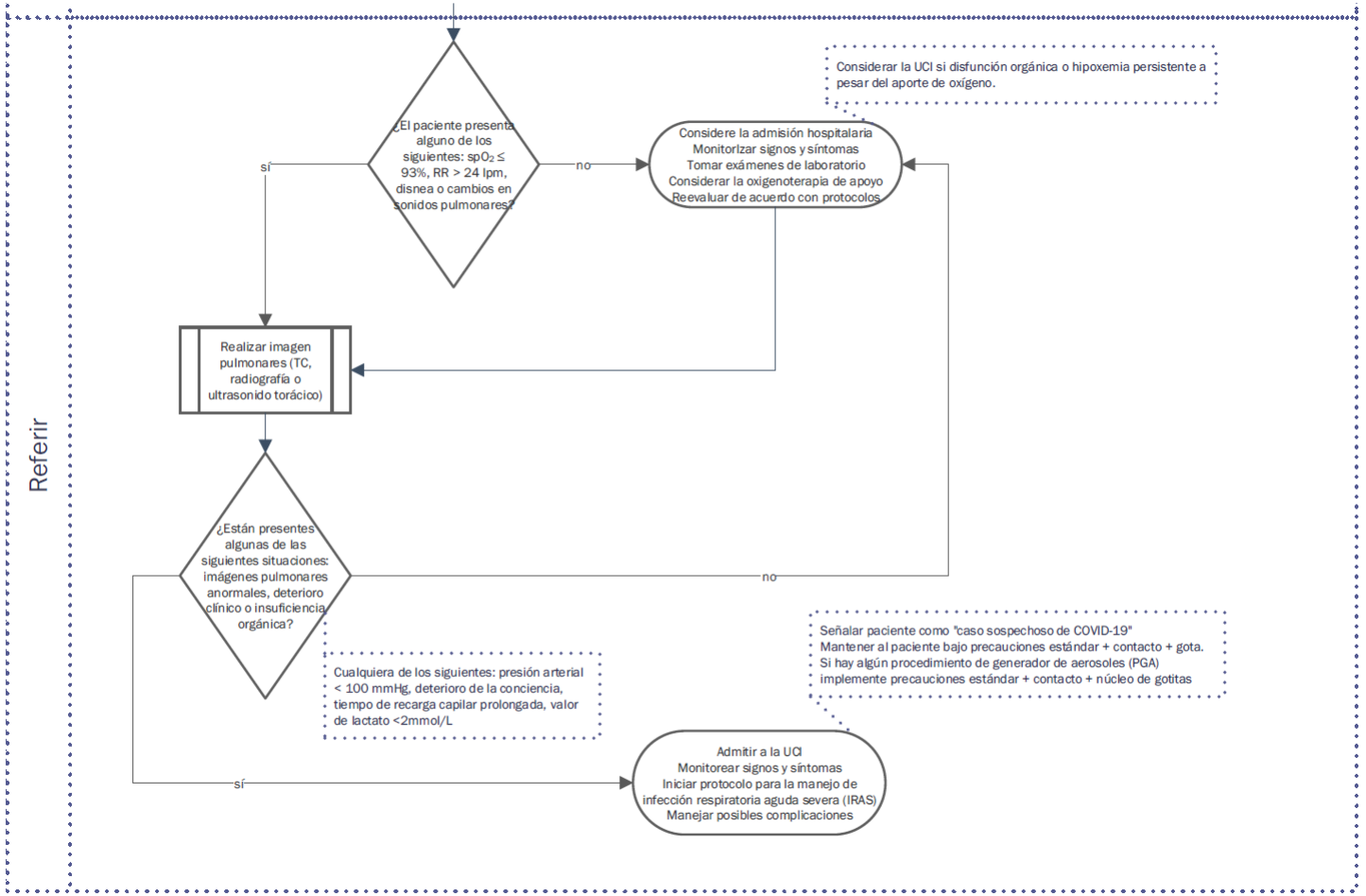
https://www.paho.org/en/topics/coronavirus-infections/coronavirus-disease-covid-19

Atención al paciente con COVID-19: triaje / aislar / referir



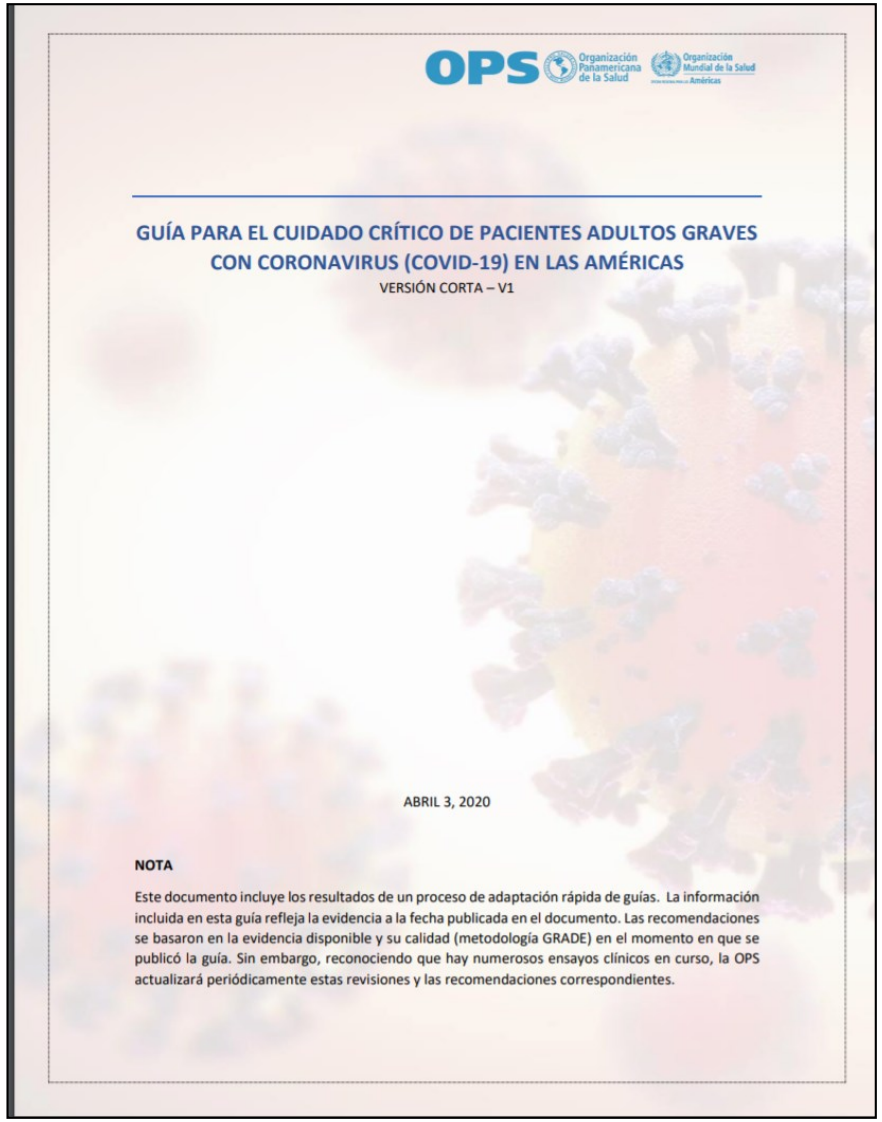
https://www.paho.org/en/topics/coronavirus-infections/coronavirus-disease-covid-19

Atención al paciente con COVID-19: triaje / aislar / referir



https://www.paho.org/en/topics/coronavirus-infections/coronavirus-disease-covid-19

Cuidado crítico



OPS Organización Panamericana de la Salud | Organización Mundial de la Salud Américas

GUÍA PARA EL CUIDADO CRÍTICO DE PACIENTES ADULTOS GRAVES CON CORONAVIRUS (COVID-19) EN LAS AMÉRICAS

VERSIÓN CORTA – V1

ABRIL 3, 2020

NOTA

Este documento incluye los resultados de un proceso de adaptación rápida de guías. La información incluida en esta guía refleja la evidencia a la fecha publicada en el documento. Las recomendaciones se basaron en la evidencia disponible y su calidad (metodología GRADE) en el momento en que se publicó la guía. Sin embargo, reconociendo que hay numerosos ensayos clínicos en curso, la OPS actualizará periódicamente estas revisiones y las recomendaciones correspondientes.

https://www.paho.org/es/documentos/guia-para-cuidado-critico-pacientes-adultos-graves-con-coronavirus-covid-19-americas-0

"Ninguna evidencia clínica apoya actualmente la eficacia y seguridad de un medicamento contra cualquier coronavirus en humanos."

"La administración de cualquier droga no probada como "último recurso" asume erróneamente que el beneficio será más probable que el daño".

El "cementerio" de las drogas contra el ébola utilizadas en el África occidental y los Estados Unidos/Europa que no funcionaron:

- Cloroquina
- Hidroxicloroquina
- Favipiravir
- Brincidofovir
- Plasma de convalencencia

Opinion

VIEWPOINT

Treating COVID-19—Off-Label Drug Use, Compassionate Use, and Randomized Clinical Trials During Pandemics

Andre C. Kalil, MD, MPH
Division of Infectious Diseases, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, Nebraska.

Viewpoint
Audio

In the 2014 Ebola outbreak, close to 30 000 individuals developed Ebola viral disease (EVD), and numerous therapies were tested against this virus, including chloroquine, hydroxychloroquine, favipiravir, brincidofovir, monoclonal antibodies, antisense RNA, and convalescent plasma, among many others. With such a large number of therapeutic interventions given to affected patients, the goal was to determine which was efficacious against Ebola. Ultimately, none proved to be efficacious or safe.

Why were new therapies not discovered? One reason is because virtually all studies were single-group interventions without concurrent controls, which led to no definitive conclusion related to efficacy or safety. Despite much resistance and controversy regarding asking patients with EVD to participate in a randomized clinical trial (RCT),[1] the National Institutes of Health (NIH) conducted the first and only RCT during that outbreak. It took several months to design the trial, but it was implemented and successfully launched during the outbreak; however, it was too late for the RCT to be completed.[2] This tragedy of not discovering new therapies during an outbreak cannot be repeated.

> The rapid and simultaneous combination of supportive care and RCTs is the only way to find effective and safe treatments for COVID-19 and any other future outbreak.

The world is now facing a pandemic of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2, the cause of COVID-19), for which no proven specific therapies are available, other than supportive care. In China, and now Italy, France, and Spain, a large number of patients have received off-label and compassionate use therapies such as chloroquine, hydroxychloroquine, azithromycin, lopinavir-ritonavir, favipiravir, remdesivir, ribavirin, interferon, convalescent plasma, steroids, and anti–IL-6 inhibitors, based on either their in vitro antiviral or anti-inflammatory properties. These therapies have been mostly given without controls, except for a few randomized trials started in China, and more recently in the US.[3]

Although many drugs have in vitro activity against different coronaviruses, no clinical evidence currently supports the efficacy and safety of any drug against any coronavirus in humans, including SARS-CoV-2. Numerous drugs that have been highly promising in vitro for other infectious diseases have failed in clinical studies. If in vitro activity automatically translated into clinical activity, more antimicrobial drugs for all kinds of infectious diseases would be available. Yet, there are published case reports of old and new drugs with in vitro activity against SARS-CoV-2 that have been given to patients but without a comparison control group. The administration of any unproven drug as a "last resort" wrongly assumes that benefit will be more likely than harm. However, when a drug with unknown clinical effects is given to patients who have severe illness from a new disease (like COVID-19), there is no way to know whether the patients had benefited or were harmed if they were not compared to a concurrent control group. A common interpretation of off-label use and compassionate use of drugs is that is that if the patient died, they died from the disease, but if the patient survived, they survived because of the given drug. This is not true.

As a practical example, chloroquine/hydroxychloroquine, azithromycin, and lopinavir-ritonavir have a variety of adverse effects, including QT prolongation, torsades de pointes, hepatitis, acute pancreatitis, neutropenia, and anaphylaxis. Considering that most patients who have died from COVID-19 were elderly and had cardiovascular comorbidities and that affected patients frequently have cardiac arrhythmias,[4,5] chloroquine/hydroxychloroquine, azithromycin, and lopinavir-ritonavir could potentially increase the risk of cardiac death. Additionally, hepatitis and neutropenia are clinical manifestations of COVID-19, and both hepatic and bone marrow dysfunction could be made worse by the off-label use of these drugs; thus, it would be impossible to differentiate the drug-related adverse effects from the disease manifestations in the absence of a control group.

Compassionate use of drugs that have not been previously approved for clinical use (eg, remdesivir) could cause serious adverse effects that were not previously detected because of the very small number of exposed patients. With respect to anti-inflammatory therapy, the use of intravenous steroids has been associated with delayed coronavirus clearance in both blood and lungs with MERS-CoV[6] and SARS-CoV,[7] and steroids were associated with significantly increased risk of mortality and secondary infections in patients with influenza.[8] Furthermore, even low-dose steroids have shown harm in patients with sepsis, and IL-6 inhibitors may cause even more profound immunosuppression than steroids, increasing the risk of sepsis, bacterial pneumonia, gastrointestinal perforation, and hepatotoxicity.[9,10] Yet, despite substantial evidence of potential harm, steroids and IL-6 inhibitors are now being given to patients with

Corresponding Author: Andre C. Kalil, MD, MPH, Department of Internal Medicine, University of Nebraska Medical Center, 95400 Nebraska Medical Center, Omaha, NE 68135 (akalil@unmc.edu).

Kalil AC. JAMA 24 Marzo 2020.

Tratamientos – Numerosos ensayos en curso o planificados

- Cloroquina/hidroxicloroquina – recent FDA EUA
- Antivirales
  - Remdesivir
  - Lopinavir/Ritonavir
- Plasma de covalecencia
- Inmunomoduladores/Anticuerpos monoclonales
  - IL-6 Inhibidores: e.g. Sarilumab, Tociluzumab - RA/JRA
  - JAK Inhibidores e.g. Baricitinib
- Inhalación:
  - Inhalación de óxido nítrico
  - Cánula nasal de alto flujo

Clinical Trials.gov

Emergencia de salud pública
Protocolo básico de SOLIDARIDAD

Objetivo	• Comparar los efectos en los principales resultados en el hospital • Comparar el estándar local de atención (SOC) *versus* SOC + 1 de 4 agentes antivirales
Objetivo principal	• Estimar los efectos en mortalidad hospitalaria en enfermedad moderada y grave por COVID-19
Objetivos secundarios	• Evaluar los efectos sobre la duración del hospital, recepción de ventilación o cuidados intensivos, e identificar reacciones adversas graves.

Estándar local de atención, O estándar local MÁS uno de

1. **Remdesivir**
2. **Cloroquina**
3. **Lopinavir, o**
4. **Lopinavir + Interferón**

R&DBlueprint

Powering research to prevent epidemics

Organización Panamericana de la Salud
Organización Mundial de la Salud
Américas

OPS

Resumen

- Amplia gama de enfermedades
  - Mayor riesgo para los ancianos y las personas con comorbilidades
- Los gravemente enfermos podrían sobrecargar los recursos disponibles
  - Camas de UCI
  - Oxígeno
  - Respiradores
  - EPP, otros suministros
  - Personal
- El impacto puede ser mitigado con reconocimiento precoz de casos, aislamiento y oxígenoterapia

¿Comentarios/Preguntas?