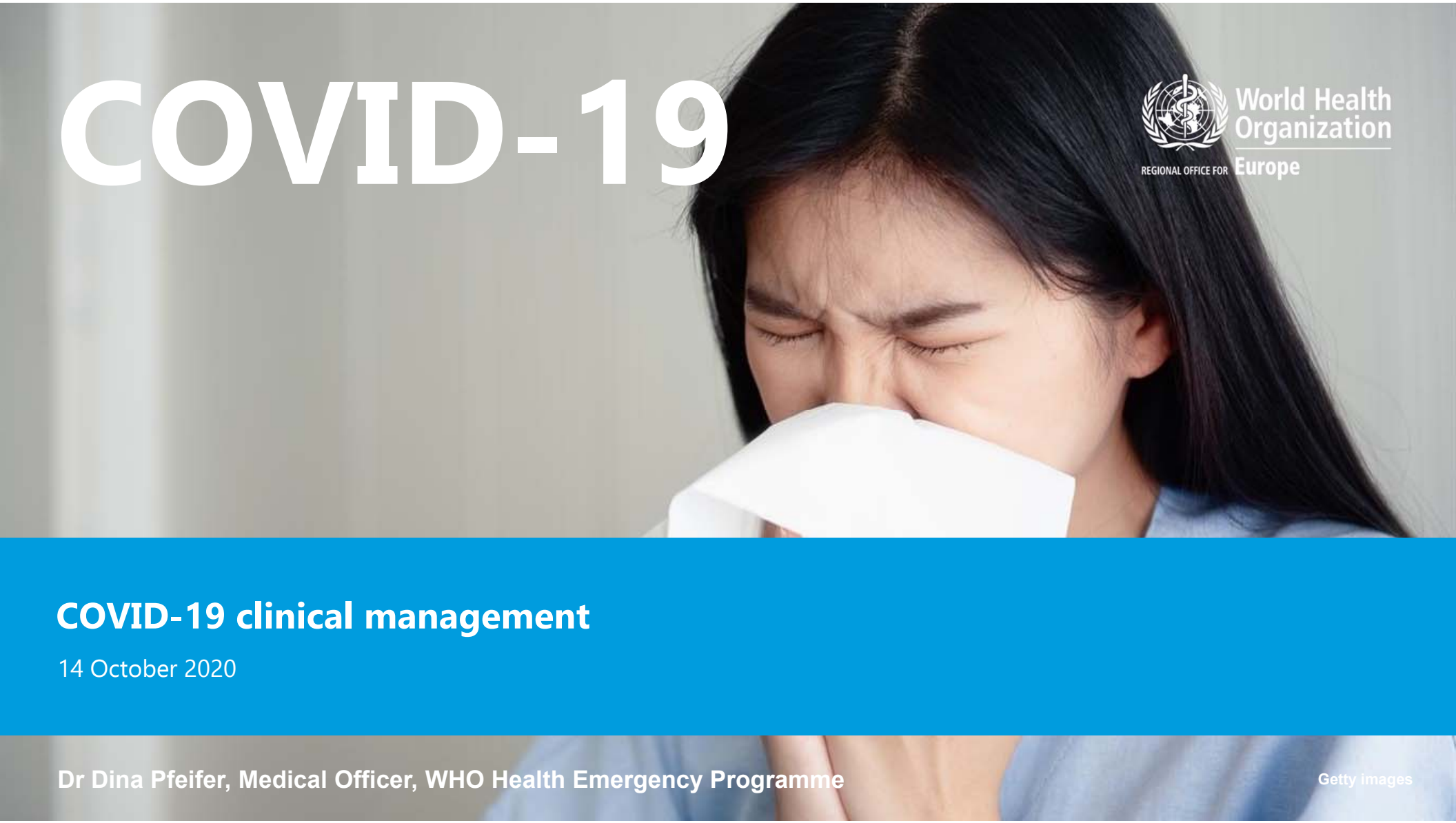


COVID-19 clinical management

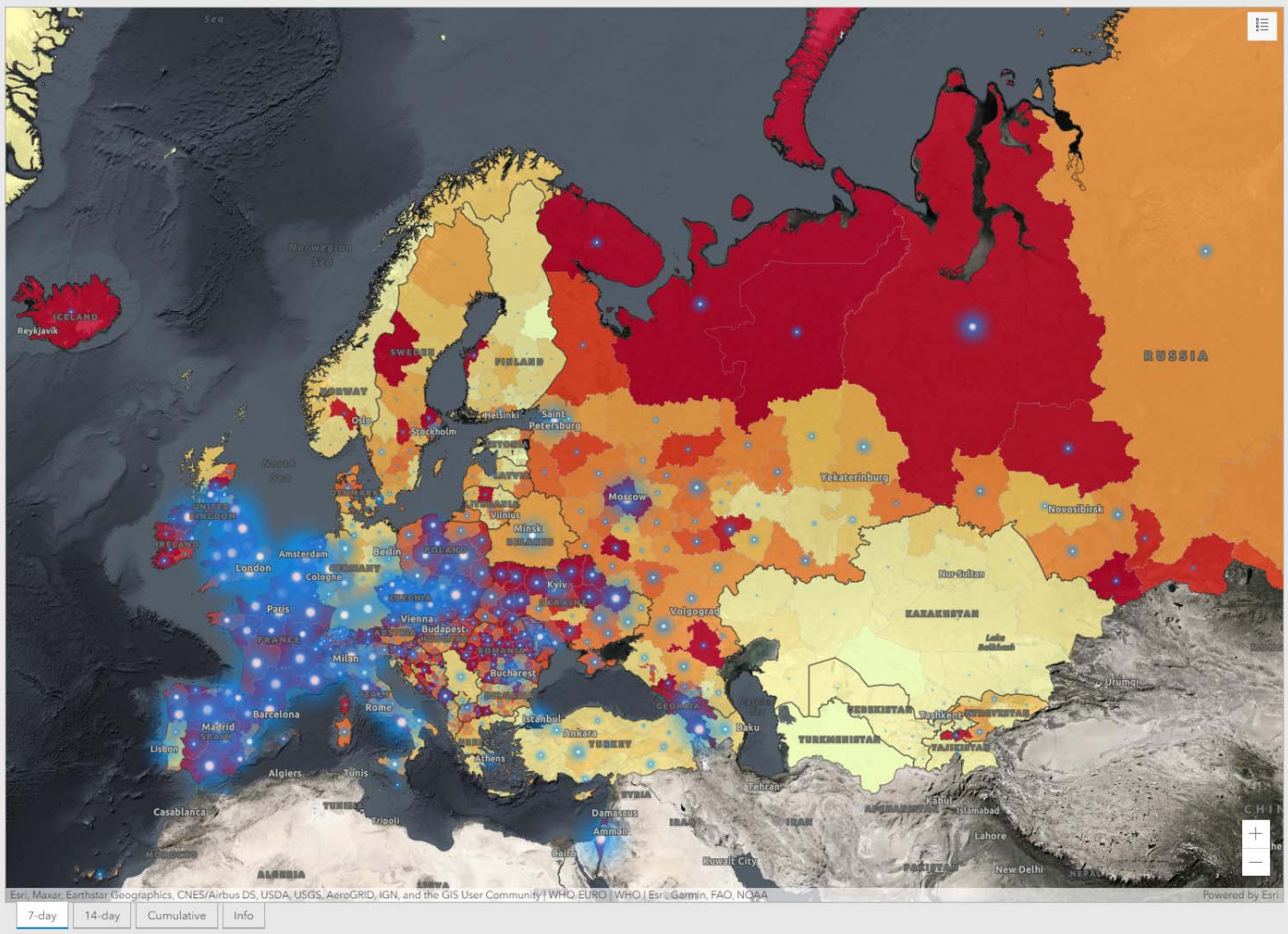
14 October 2020

Dr Dina Pfeifer, Medical Officer, WHO Health Emergency Programme

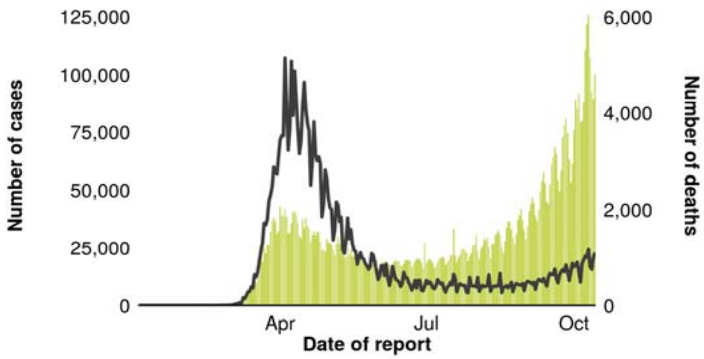
Getty images

WHO European Region Subnational Explorer (15 Oct 2020)

https://who.maps.arcgis.com/apps/opsdashboard/index.html#/ead3c6475654481ca51c248d52ab9c61

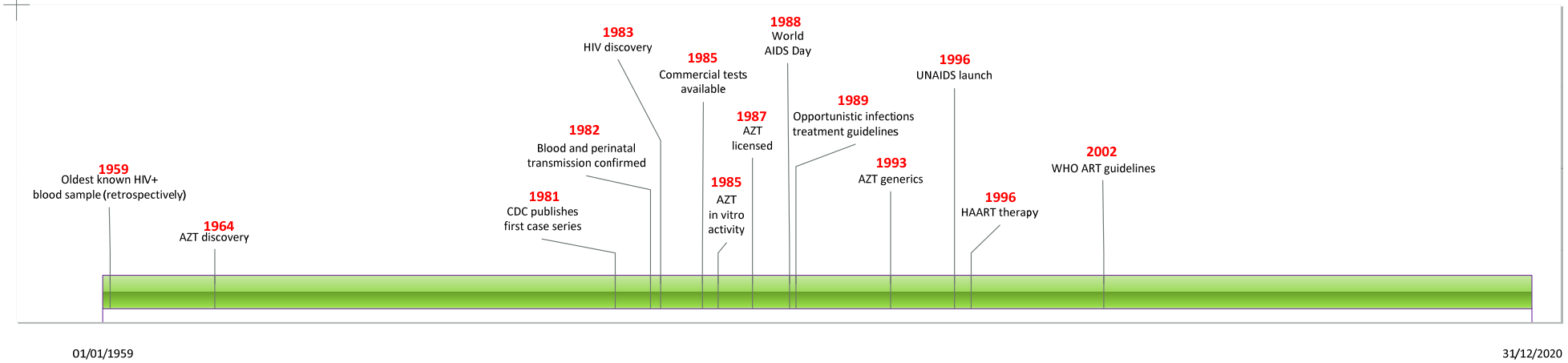


Cases and deaths by date of report



Preamble

Are we expecting too much?



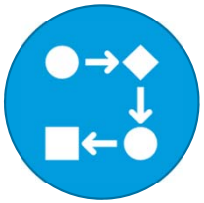
We stand nakedly in front of a pandemic as mortal as any pandemic there has ever been'

Halfdan Theodore Mahler, WHO Director General, Aug 1986

Scope of presentation

Guidelines and guidance

Methodology, availability and quality



SARS-CoV-2 and COVID-19

Pathogenesis and immunity

Novel & fast evolving conditions

Effective and affordable choice of interventions

Way forward …

Monitoring and evaluation

Clinical guidelines

Definition

Systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances

Institute of Medicine. 1990. *Clinical Practice Guidelines: Directions for a New Program*. Washington, DC: The National Academies Press. https://doi.org/10.17226/1626.

Aim – to promote “best practices” that improve outcomes of treatment

→ outcomes identified in clinical trials are reproducible in normal practice
→ rapid and universal adoption of an effective treatment leads to optimal treatment for the whole population
→ an option for improving the quality of care

Problems and limitations

→ scientific evidence about what to recommend is often lacking, misleading, or misinterpreted

→ recommendations are influenced by the opinions and clinical experience as well as composition of the guideline development group

→ patients' needs may not be the only priority in making recommendations

Novel and fast evolving outbreaks

Research in emergencies

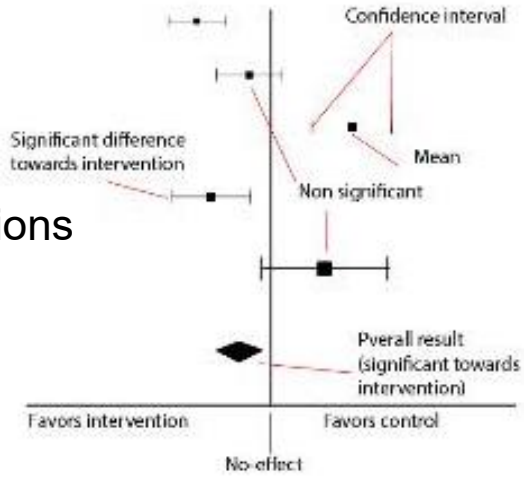
Why are randomized controlled trials so important?

Observational study
Observed effect = True effect + Selection effect

Randomized trial
Observed effect = True effect

Research vs. Care

Requires research integrated with care
Expended access
Ethical principles need to guide the interventions
Aim to addresses uncertainty about the safety and efficacy of the interventions
Prioritization of candidate interventions
Choosing appropriate design and sample size
Standardized approach with broad outreach to address heterogeneity



Cognitive biases

Systematic pattern of deviation from norm or rationality in judgment

Type	Context	Example in COVID-19
Ambiguity (risk) aversion	Inclination to adopt off-label therapies when other strategies (prone positioning, conservative fluid management) do not result in rapid, observable improvements in clinical condition	Prophylactic vs. therapeutic anticoagulation
Action (commission) bias	Decision to use an unproven medication as part of treatment plan because… ***"doing something is better than doing nothing"***	Hydroxychloroquine Azithromycin, Ribavirin
Availability bias	Easily recalled information incorrectly guides decision making … ***"It's a cytokine release syndrome!"*** therefore >>>> Prescribe anticytokine drugs	Tocilizumab, Anakinra, Sarilumab

https://doi.org/10.1016/j.chest.2020.05.548

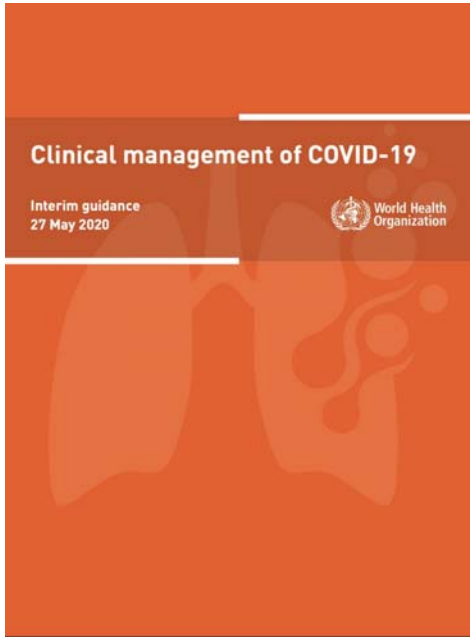
Cognitive biases (…cont'd)

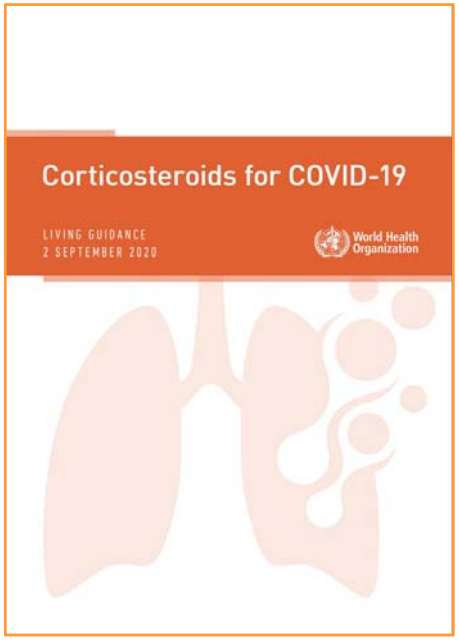
Systematic pattern of deviation from norm or rationality in judgment

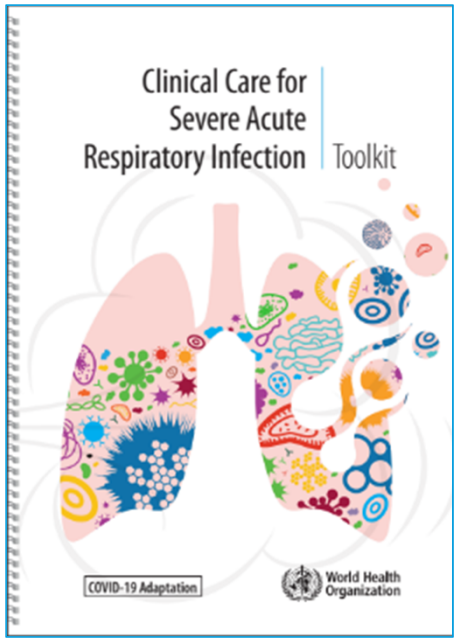
Type	Context	Example in COVID-19
Framing effect	Need to consider information independently (is medication A with 90% cure rate superior to medication B with 5% failure rate ???)	ACE inhibitors, ARBs, NASIDs
Overconfidence	Realization that physicians can often be wrong, despite best intentions	High vs. lower PEEP, failure to consider lung recruitability
Representativeness bias	Fatalistic attitudes regarding outcomes while COVID-19 base rates, true prevalence of disease, residual morbidity and mortality is still evolving	Access to care – elderly or individuals with underlying conditions

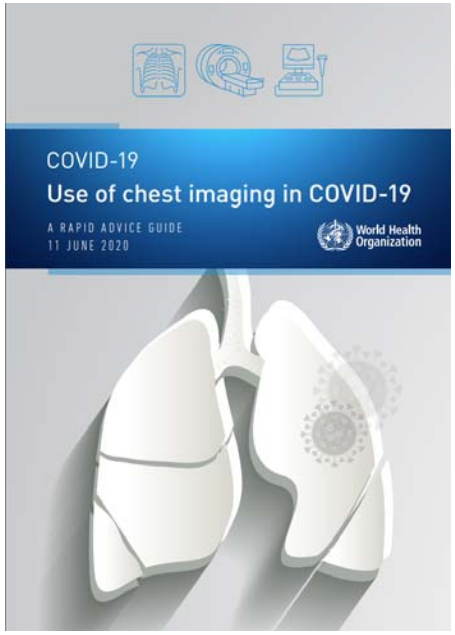
https://doi.org/10.1016/j.chest.2020.05.548

WHO clinical guidance - global





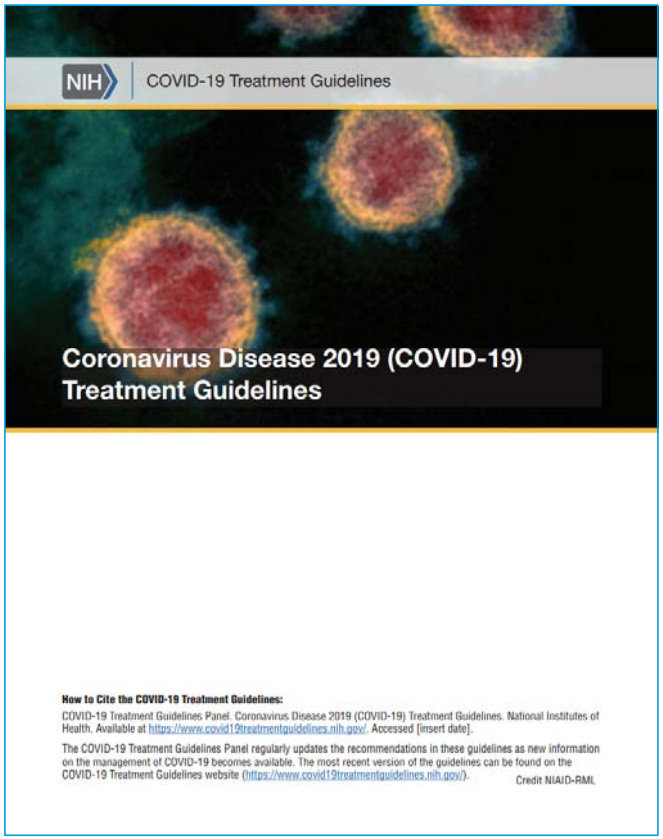


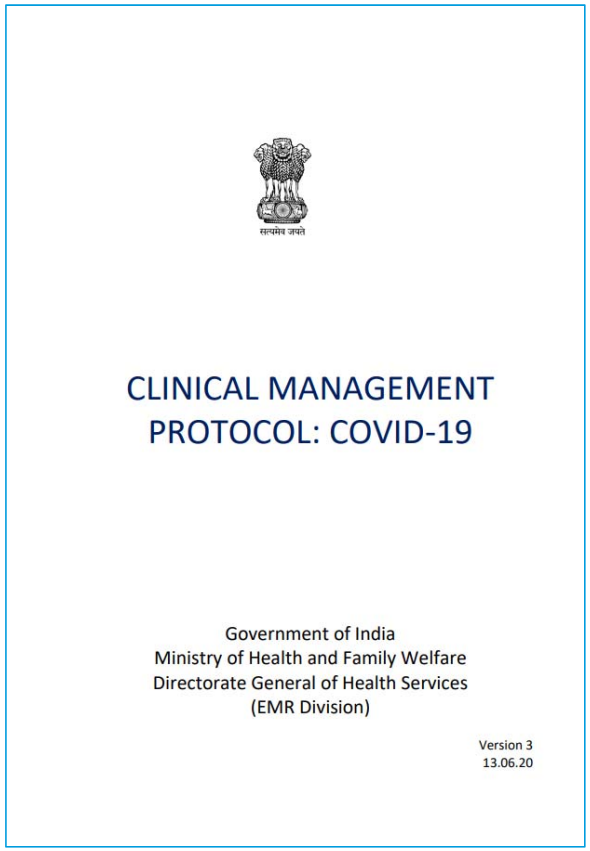


https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/patient-management

COVID-19 national guidance

World Health Organization
REGIONAL OFFICE FOR Europe





https://static-0.rosminzdrav.ru/system/attachments/attaches/000/050/584/original/03062020_%D0%9CR_COVID-19_v7.pdf https://www.covid19treatmentguidelines.nih.gov/ https://www.mohfw.gov.in/pdf/ClinicalManagementProtocolforCOVID19.pdf

Examples of additional resources

Ständiger Arbeitskreis der Kompetenz- und Behandlungszentren für Krankheiten durch hochpathogene Erreger am Robert Koch-Institut

Hinweise zu Erkennung, Diagnostik und Therapie von Patienten mit COVID-19

Stand: 09.10.2020

Für den STAKOB erarbeitet von:
Torsten Feldt, Wolfgang Guggemos, Katrin Heim, Bettina Klug, Regine Lehnert, Christoph Lübbert, Michaela Niebank, Frieder Pfäfflin, Katja Rothfuss, Stefan Schmiedel, Miriam S. Stegemann, August Stich, Isabel Trebesch, Timo Wolf

Unter Mitwirkung von:

Deutsche Gesellschaft für Pädiatrische Infektiologie e.V. (DGPI)
Deutsche Gesellschaft für Infektiologie e.V. (DGI)
Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin e.V. (DGP)
Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)
Paul-Ehrlich Institut (PEI)

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STAKOB

2

Zusammenfassung der letzten Änderungen

Änderung vom 09.10.2020
Anpassung der Kriterien zur klinischen Einteilung, Ergänzungen zur Antikoagulation, zur Anwendung von Remdesivir und Dexamethason, Ergänzung der Hinweise zu Kindern

Änderung vom 06.08.2020
Anpassung der Informationen über Tocilizumab

Änderung vom 22.07.2020
Aktualisierung der Informationen über Dexamethason, redaktionelle Anpassungen

Änderung vom 16.07.2020
Ergänzung der Informationen über Remdesivir, Grafik zu Remdesivir und Dexamethason

Änderung vom 09.07.2020
Therapiehinweise für Remdesivir und Dexamethason

Änderung vom 04.07.2020
Ergänzung der Informationen über antivirale Therapien (Remdesivir)

Änderung vom 02.07.2020
Ergänzung der Informationen über antivirale Therapien (Lopinavir/r)

Änderung vom 24.06.2020
Anpassung der Informationen über Dexamethason

Änderung vom 18.06.2020
Ergänzung der Informationen über Dexamethason

Änderung vom 10.06.2020
Ergänzung der Informationen über antivirale Therapien (Rekonvaleszenten-Plasma)

Änderung vom 29.05.2020
Aufnahme der Warnhinweise zu Hydroxychloroquin

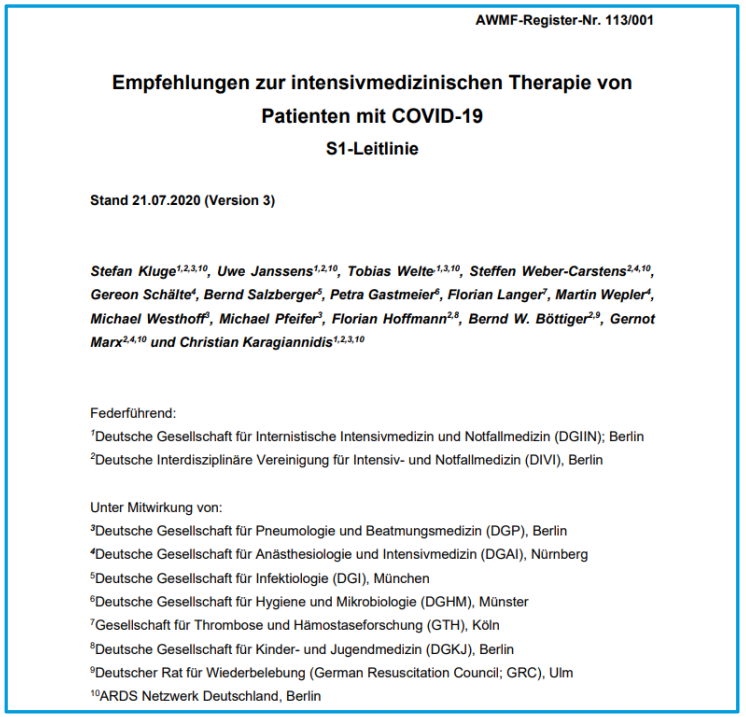
Änderung vom 19.05.2020
Anwendungshinweise zu Remdesivir

Änderung vom 07.05.2020
Aktualisierung der Symptomliste und redaktionelle Änderungen

Änderung vom 17.04.2020
Einzelne Aktualisierungen und redaktionelle Änderungen

Änderung vom 08.04.2020
Aufnahme von Hinweisen zu thromboembolischen Ereignissen, allgemeinen Hinweisen zu antiviraler Therapie und Erläuterungen zu individuellem Heilversuch, off-label-use, Härtefall-Programm

STAKOB



AWMF-Register-Nr. 113/001

Empfehlungen zur intensivmedizinischen Therapie von Patienten mit COVID-19

S1-Leitlinie

Stand 21.07.2020 (Version 3)

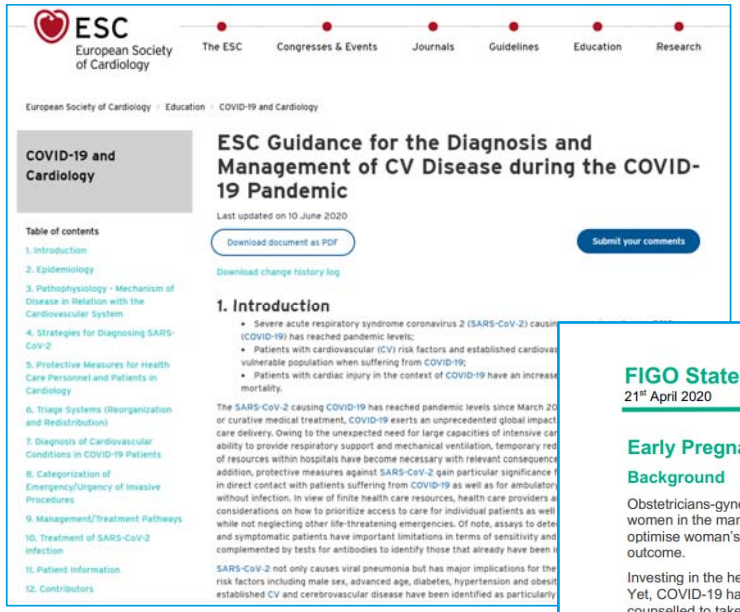
Stefan Kluge[1,2,3,10], Uwe Janssens[1,2,10], Tobias Welte[1,3,10], Steffen Weber-Carstens[2,4,10], Gereon Schälte[4], Bernd Salzberger[5], Petra Gastmeier[6], Florian Langer[7], Martin Wepler[4], Michael Westhoff[8], Michael Pfeifer[3], Florian Hoffmann[2,8], Bernd W. Böttiger[2,9], Gernot Marx[2,4,10] und Christian Karagiannidis[1,2,3,10]

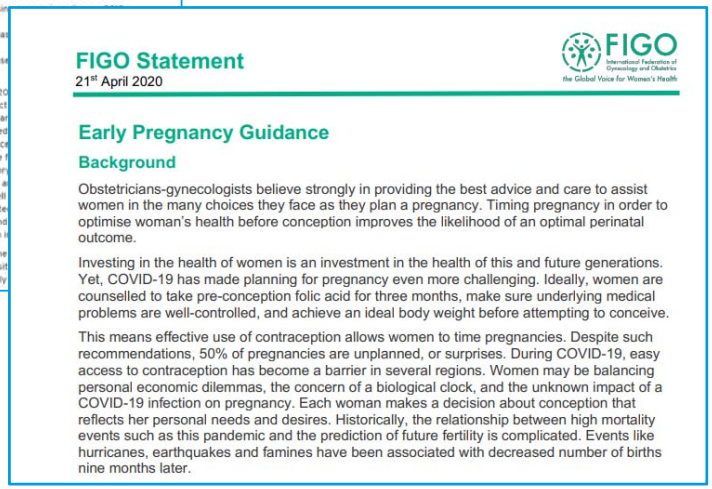
Federführend:
[1]Deutsche Gesellschaft für Internistische Intensivmedizin und Notfallmedizin (DGIIN); Berlin
[2]Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin (DIVI), Berlin

Unter Mitwirkung von:
[3]Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin (DGP), Berlin
[4]Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin (DGAI), Nürnberg
[5]Deutsche Gesellschaft für Infektiologie (DGI), München
[6]Deutsche Gesellschaft für Hygiene und Mikrobiologie (DGHM), Münster
[7]Gesellschaft für Thrombose und Hämostaseforschung (GTH), Köln
[8]Deutsche Gesellschaft für Kinder- und Jugendmedizin (DGKJ), Berlin
[9]Deutscher Rat für Wiederbelebung (German Resuscitation Council; GRC), Ulm
[10]ARDS Netzwerk Deutschland, Berlin

https://www.rki.de/DE/Content/Kommissionen/Stakob/Stellungnahmen/Stellungnahme-Covid-19_Therapie_Diagnose.pdf?__blob=publicationFile

COVID-19 professional societies guidelines

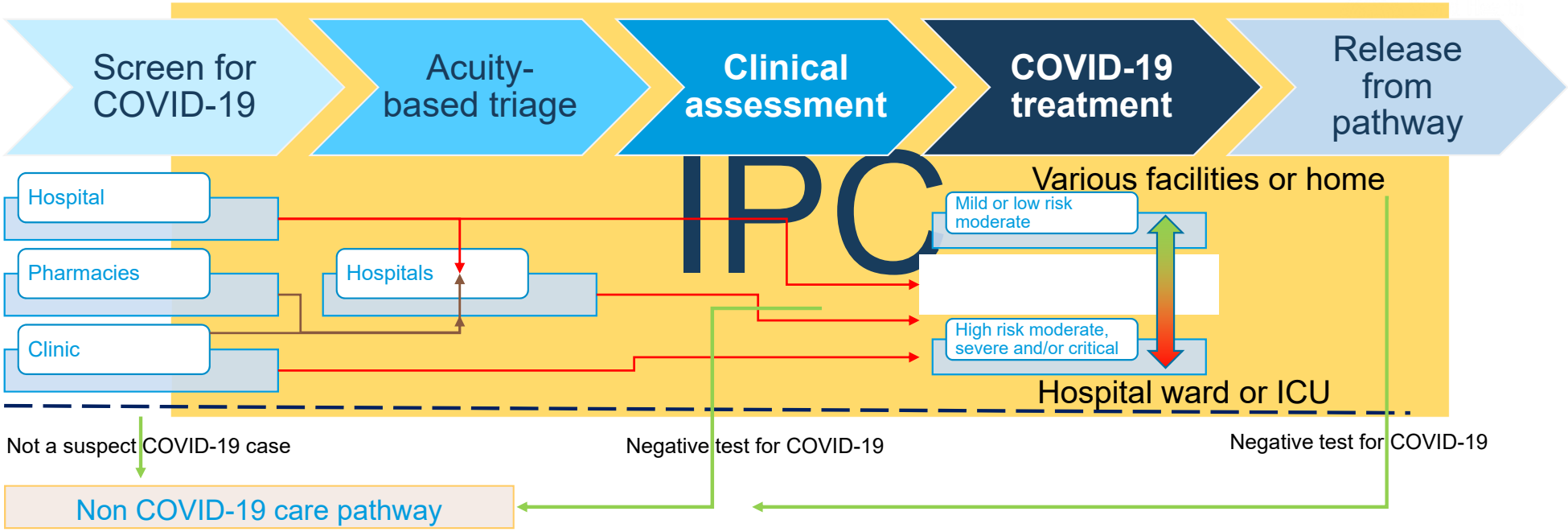




https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/ https://www.escardio.org/Education/COVID-19-and-Cardiology/ESC-COVID-19-Guidance/ https://www.figo.org/resources/covid-19-resources

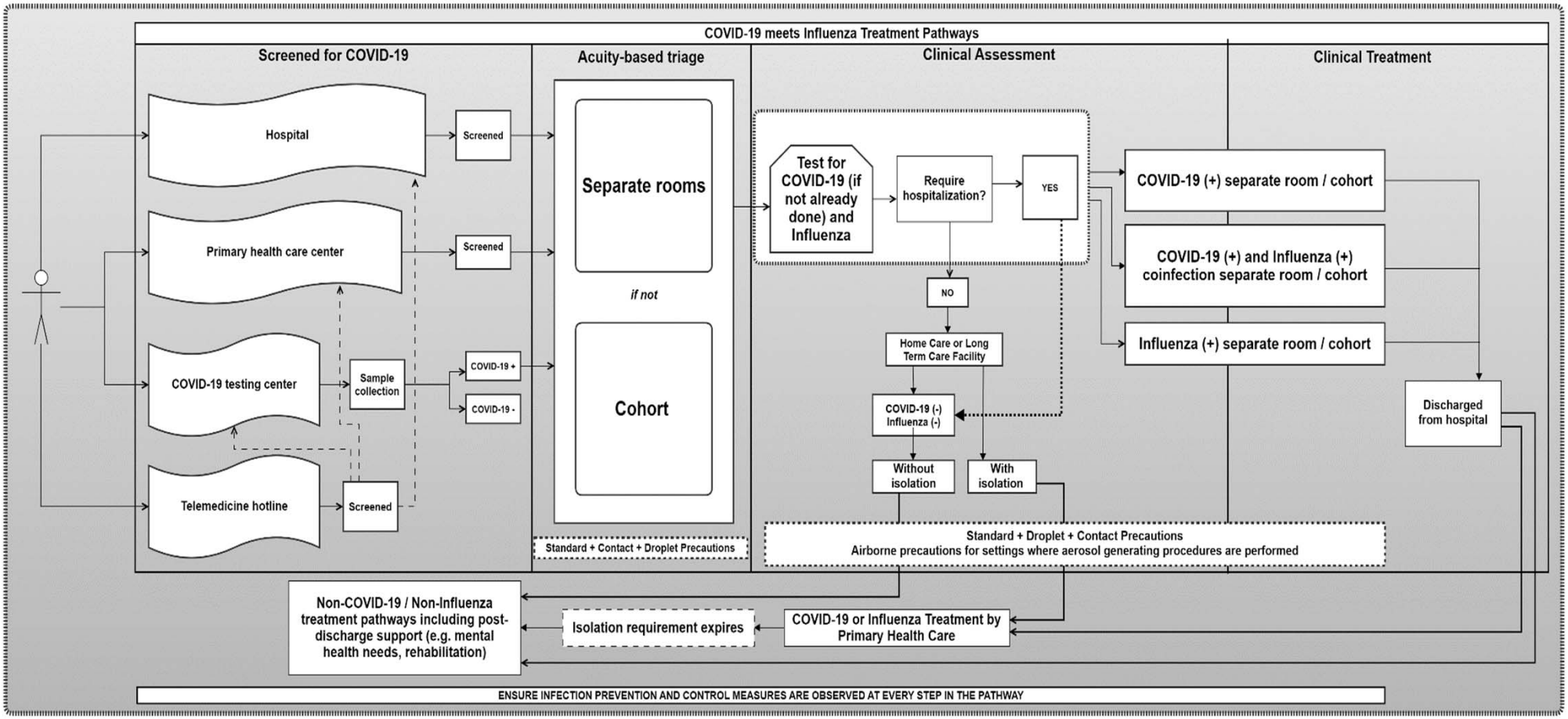
WHO COVID-19 care pathway

Version of 27 May 2020



COVID-19 meets influenza care pathway

World Health Organization
REGIONAL OFFICE FOR Europe



Clinical management of an adult with mild COVID-19

World Health Organization
REGIONAL OFFICE FOR Europe

General

→ No symptoms or mild upper respiratory tract symptoms or cough, new bout of myalgia or asthenia
→ No new shortness of breath or reduction in oxygen saturation
→ Epidemiological management until confirmed as COVID-19
→ Baseline assessment – (Is it a mild case?) address alternative diagnosis and underlying conditions
→ Determining setting of care

Therapy

→ Similar management to seasonal flu, advise to rest
→ Antipyretics generally not required, but paracetamol or ibuprofen may be considered for symptomatic relief
→ Do **NOT** prescribe:

~~Antibiotics~~ (unless there is evidence of concurrent community acquired (bacterial) pneumonia)
~~Dexamethasone~~ or other ~~corticosteroids~~
Any other experimental treatments outside of clinical trial (eg. ~~azithromycin~~, ~~favipiravir~~, ~~hydroxychloroquine~~, ~~inteferon~~, ~~redemsivir~~, ~~tocilizumab~~, etc)

→ Continue with therapy for preexisting conditions

Inhaled and oral steroids for asthma or COPD similar to its use in viral exacerbation, do not use nebuliser

Clinical management of an adult with mild COVID-19 …cont'd

Therapy

→ Continue with therapy for preexisting conditions

Conditions managed with immunosupressants – change or cease only with assessment of treating physician

Diabetes and cardiovascular disease – continue ACE inhibitors/ARBs unless new contraindication develops, continue use (no change of dose) of insulin, other diabetic therapies or statins

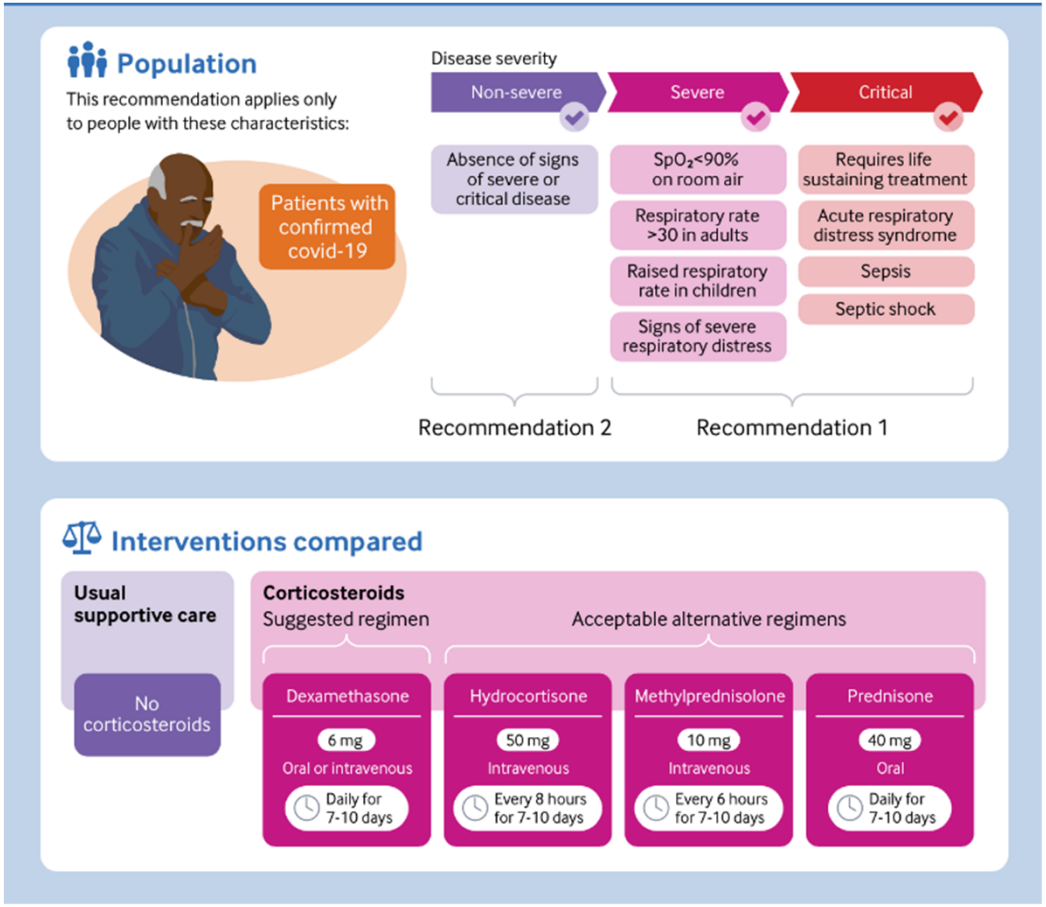
Monitoring

→ Infection prevention and control measures for patients managed at home
→ Instruct patient and family members to watch for signs of deterioration
→ Deploy pulse oximetry devices if feasible
→ Monitor for symptoms persisting longer that 4 weeks

Escalation of care

→ Transfer if patient develops symptoms or signs of moderate or severe COVID-19

Corticosteroid treatment for severe and critical cases



Recommendation 1)
We recommend systemic corticosteroids rather than no corticosteroids for the treatment of patients with severe and critical COVID-19 (strong recommendation, based on moderate certainty evidence)

Recommendation 2)
We suggest not to use corticosteroids in the treatment of patients with non-severe COVID-19
(conditional recommendation, based on low certainty evidence)

https://www.who.int/publications/i/item/WHO-2019-nCoV-Corticosteroids-2020.1
https://app.magicapp.org/#/guideline/4446

Global COVID-19 Clinical Data Platform

World Health Organization

Contribute your COVID-19 hospitalized patient data and help inform the development of optimum clinical management strategies

Email us at: covid_clinplatform@who.int to request further information or login credentials.
Website: https://www.who.int/teams/health-care-readiness-clinical-unit/covid-19/data-platform

Curing COVID-19

How to implement change in clinical management of novel and emerging infections?

Supportive care

→ Apprise performance and ensure minimal standards of care are met
→ Ensure equity in quality care delivery – utilize Hawthorne effect across the health care system
→ Engage in advancing supportive care – search for better or more effective solutions

Refresh understanding of underlying concepts

→ Pathophysiology, patho- and immuno- genesis
→ Get abreast with therapeutics modes of action
→ Consider limits of diagnostic tests
→ Understand capacity and mode of operation of equipment used
→ Reconsider ethical principles

Novel conditions require novel solutions

→ Avoid loosing time and resources generating poor quality evidence – massive research effort is needed
→ Embrace paradigm that clinical medicine is based on well designed research

Governance

→ Clinicians adequately represented in decision making of preparedness and response activities
→ Avoid politicization and conflicting interests

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youtube.com/user/whoeuro

World Health Organization
REGIONAL OFFICE FOR Europe

Weltgesundheitsorganisation
REGIONALBÜRO FÜR Europa

Organisation mondiale de la Santé
BUREAU RÉGIONAL DE L' Europe

Всемирная организация здравоохранения
Европейское региональное бюро