COVID-19: Lessons for Public Health and Clinical Practice

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Global Situation (as of 19 October 10H CEST)

- **Previous 24 hours:**
  - 338,096 new confirmed cases.
  - 4,556 new deaths.

- **Cumulative:**
  - 39,944,882 confirmed cases.
  - 1.1 million deaths.

### Countries with the highest number of new cases in previous 24 hours

<table>
<thead>
<tr>
<th>Country</th>
<th>New Cases</th>
<th>Total Cases</th>
<th>New Deaths</th>
<th>Total Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>55,722</td>
<td>7,550,273</td>
<td>579</td>
<td>114,610</td>
</tr>
<tr>
<td>United States of America</td>
<td>52,508</td>
<td>8,019,237</td>
<td>588</td>
<td>217,659</td>
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<tr>
<td>France</td>
<td>29,833</td>
<td>867,978</td>
<td>85</td>
<td>33,204</td>
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<tr>
<td>Brazil</td>
<td>24,062</td>
<td>5,224,362</td>
<td>461</td>
<td>153,675</td>
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<tr>
<td>United Kingdom</td>
<td>16,981</td>
<td>722,413</td>
<td>67</td>
<td>43,646</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>15,982</td>
<td>1,415,316</td>
<td>179</td>
<td>24,366</td>
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<tr>
<td>Argentina</td>
<td>13,510</td>
<td>979,119</td>
<td>384</td>
<td>26,107</td>
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<tr>
<td>Italy</td>
<td>11,705</td>
<td>414,241</td>
<td>69</td>
<td>36,543</td>
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<tr>
<td>Poland</td>
<td>8,536</td>
<td>175,766</td>
<td>49</td>
<td>3,573</td>
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<tr>
<td>Netherlands</td>
<td>8,439</td>
<td>228,234</td>
<td>23</td>
<td>6,751</td>
</tr>
</tbody>
</table>
COVID-19 deaths reported in the last 7 days per 1 million population
(From 12 October 2020, 10:00AM to 18 October 2020, 10:00AM (CEST))
COVID-19: currently facing different transmission situations

Avoided large outbreaks

Major outbreak brought under control

Major outbreak brought under control, but having eased restrictions, are now seeing resurgence

Intense transmission
COVID-19 Challenges and Lessons Learned
Health systems facing COVID-19 outbreak

- Huge stress posed by increasing demand for care of people with COVID-19
- Lack of supplies and equipment
- Burden on health care workers
- Disruption of essential health services

Dilemma: balance the demands of responding to COVID-19 with strategic planning and coordinated action to maintain quality essential health services
Pulse survey on continuity of essential health services during the COVID-19 pandemic

- 80% of countries had a defined essential health services package prior to the outbreak
- 66% of all countries had identified a core set of services to be maintained during the COVID-19 pandemic
- The Eastern Mediterranean Region was the most affected, followed by the African and the South-East Asia Regions. Essential health services in the countries in the European and the Western Pacific Regions were least affected
- Most frequently disrupted Essential health services were routine immunization services – outreach services (70%) and facility-based services (61%) – noncommunicable disease diagnosis and treatment (69%), family planning and contraception (68%), treatment for mental health disorders (61%), antenatal care (56%) and cancer diagnosis and treatment (55%).
Countries reporting disruptions (partially or completely) across 25 essential health services

Service disruptions reported by countries (n=52)

- Routine immunization (outreach)
- Dental services
- Rehabilitation services
- Implementation of planned ITN campaigns
- NCD diagnosis and treatment
- Implementation of seasonal malaria campaigns
- Routine immunization (health facilities)
- Implementation of planned IRS campaigns
- Family planning and contraception
- Treatment for mental health disorders
- Cancer diagnosis and treatment
- Antenatal care
- Sick child services
- Management of malnutrition
- Palliative services
- Malaria diagnosis and treatment
- Outbreak detection and control (non-COVID)
- TB case detection and treatment
- Facility based births
- Continuation of established ARV treatment
- Urgent blood transfusion services
- Inpatient critical care services
- 24-hour emergency room/unit services
- Emergency surgery
- Others*

* Includes postnatal care, school-based programmes, elective surgery, and medicine supply chains

Partially disrupted: 5% to 50% of patients not treated as usual
Completely disrupted: more than 50% of patients not treated as usual
Approaches for overcoming health services disruptions

- Triaging to identify priorities: 76%
- Telemedicine deployment to replace in-person consultations: 63%
- Task shifting/role delegation: 57%
- Novel supply chain and/or dispensing approaches for medicines through other channels: 54%
- Community outreach to provide information on service disruptions and changes: 53%
- Redirection of patients to alternative health care facilities: 52%
- Others: 24%
- Government removal of user fees: 14%
Digital Health technologies

- Telemedicine
- Global Learning Collaborative Platforms (eg ECHO)
- Electronic, portable health records
- What technologies can be considered public health goods?
- **WHO Digital Health Clearing House** *(A digital platform that connects Ministries of Health with providers of assessed digital health solutions that can best support countries’ response to COVID-19 and other health domains)*
A new paradigm
- (Virtual) Shared Medical Appointments

**BENEFITS FOR PATIENTS**

- Improved patient engagement
- Higher patient knowledge & satisfaction
- Shorter waits for appointments
- Higher compliance to medications
- Higher follow-up rates over time as patients form bonds with their peers
- Improved clinical outcomes
- Reduced flare-ups and emergency room visits

**BENEFITS FOR PROVIDERS**

- Higher productivity
- Expanded access
- Reduced cost of no shows
- Reduced long-term patient costs
- Reduced repetition → higher quality interactions
- Greater doctor satisfaction
- Lower environmental footprint
COVID-19 Country Case Studies

- **Strong political leadership and successful mobilization of resources using a whole-of-society approach**
  - Gain the trust of the public and ensure public compliance with public health measures
  - Whole-of-Government response to the pandemic

- **Government cash assistance** to people unemployed by the lockdown

- Early activation of a strong response system

- Long-term country investment to strengthen the health emergency response after previous epidemics and essential public health services

- Early contact tracing, quarantine and travel restriction measures

- Assessment of risks (existing and projected) at all levels of healthcare facilities

- Identifying extra ‘surge’ capacity each healthcare facility needs to cope with COVID-19 and non-COVID-19 related health emergencies

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**Figure:** The message of the King of Bhutan on the website’s homepage of the Royal Government of Bhutan.

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**Figure:** Mobile COVID-19 testing laboratory, Morocco.

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**COVID-19: THAILAND**

Suvarnabhumi International Airport

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Doctors and nurses of a major hospital in Vietnam, Bach Mai hospital, expressed their commitment and solidarity with the rest of the world in the fight against COVID-19. Photo credit: WHO Viet Nam
WHO COVID-19 Database of scientific publications

- 90,000 citations and growing since March 2019
- Extended scope with inclusion of preprints and clinical trials
- More powerful software for screening and generating backbone of content
- 3000+ active users/day
- User feedback on one-stop convenience

WHO’s normative function: leading policy & technical guidance

Steering policy through:
- HQ-Regional leadership
- 45 Global Health Leaders
- STAG-IH

Convening experts for guidance development:
- Technical guidance published by WHO

- Surveillance
- Clinical management
- Laboratory
- Supply & logistics
- Modeling
- Infection prevention & control

- Critical preparedness, readiness and response actions for COVID-19
- Surveillance, rapid response teams, and case investigation
- Surveillance, rapid response teams, and case investigation
- Country-level coordination, planning, and monitoring
- Clinical care
- Infection prevention and control/WASH
- The Unity Studies: Early Investigations Protocols
- Essential resource planning
- Guidance for schools, workplace and institutions
- Risk communications and community engagement
- Virus origin/Reducing animal-human transmission
- Points of entry/mass gatherings

As of 12 May 2020
Update on published SARS-CoV-2 seroepidemiology

As of end September 2020:

• >140 peer-reviewed publications and pre-print manuscripts plus >10 government reports

Available results

• Most study results suggest <10% seroprevalence
• Few studies suggest >20% in areas of higher transmission intensity and/or among frontline workers
• Serial sampling studies show an increasing fraction of the population has been exposed to SARS-CoV-2
• Few studies have stratified results by age or by the same age categories;
  — available studies suggest that younger children appear to have lower rates of infection when compared to adults; adolescents appear to have similar seroprevalence to adults
• Longitudinal cohort and individual studies are limited, so there is currently limited information on persistence of immunity
Full genome tree derived from all outbreak sequences 2020-10-20

Notable changes:
138,569 full genomes (+2,864) (excluding low coverage, out of 148,257 entries)

Updated clades:
S clade 6,417 (+59)
L clade 4,214 (+33)
V clade 5,258 (+7)
G clade [5477X] 32,192 [101] [+1,221 [+9]]
GR clade [5477X] 54,064 [7,337] [+887 [+6]]
GH clade [5477X] 32,574 [671] [+644 [+13]]
Other clades 3,850 (+13)

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.
Real-time data sharing is not achieved by governmental Regulations ... it is incentivized by the confidence in transparent sharing mechanisms.
Genomic sequence data is important for the response

- Development of **first diagnostics kits** and refinement through ongoing surveillance for mutations
- Identification of potential **drug and vaccine targets** through repurposing
- Genomic epidemiology allows analysis of the exportation and importation events of viruses between countries, contact-tracing in countries, or identification of nosocomial transmission chains
- Evidence that the **virus has not drifted to significant strain difference**, with in particular the cell receptor binding pocket appearing stable
- Identification of **animal precursors** (in bats and pangolins)
GISAID was ready for Disease X ==> newly emerging coronavirus

Viral pneumonia cases reported in central China

Whole genome sequences for the novel #coronavirus (2019-nCoV) from the Chinese authorities were shared with WHO and have also been submitted by Chinese authorities to the GISAID platform so that they can be accessed by public health authorities, laboratories and researchers.

Complete genomes sequenced

Less than 48 hours

Shared with the world via GISAID
COVID-19 Therapeutics, Diagnostics and Vaccines
ACT Accelerator

- Accelerate the development of diagnostics, therapeutics and vaccines
- Ensure fair and equitable access across the world
- Led by WHO with countries and many global partners
- Covax the vaccine pillar
- Over 200 vaccines in development, 40 in clinical trials
- 60 to 70% of the world’s population will need to be immunized
- Public health and social measures needed till 2022
Development of diagnostics for COVID-19 has followed an accelerated timeline

- 31 Dec 2019: Cluster of "pneumonia of unknown cause" identified in Wuhan
- 11 Jan: Genetic sequencing shared
- 12 Jan: WHO first teleconference with Dx and lab network
- 13 Jan: WHO first protocol for PCR assay released
- 20 Jan: WHO screened manufacturers to produce requested kits
- 24 Apr: COVID-19 ACT Accelerator launched
- 2 Feb: First dispatch of PCR Dx kits to Regional and Country Offices
- 28 Feb: WHO Emergency Use Listing (EUL) procedure for PCR assays launched
- 15 Apr: First purchase orders under the Dx Consortium issued
- 13 Jan: WHO first protocol for PCR assay released
- 29 Jan: Production for requested kits started
- 28 Feb: WHO Emergency Use Listing (EUL) procedure for PCR assays launched
- 15 Apr: First purchase orders under the Dx Consortium issued

To date: 23 million tests procured across partners (Global Fund, GDF/StopTB, PAHO, UNDP, Unicef, WHO) with over 18 million in transit or delivered
SARS-CoV-2 Diagnostics

• Nucleic Acid Amplification Test (e.g. rRT-PCR)
  o Reference method for diagnosis of active infection
  o More sensitive than viral culture
  o Limited access globally, especially outside major cities

• Antigen detection (Ag RDT)
  o Simple-to-use lateral flow format, relatively inexpensive, fast
  o Detects most infectious individuals
  o Sensitivity and specificity lower than PCR

• Antibody detection
  o Reliably sensitive only after 2nd to 3rd week of illness
  o Useful in epidemiologic studies, not for acute patient management
Who can be detected with an Ag RDT?

- Symptom onset
- Most contagious cohort
- Viral load

Time

RDT detection cut-off

PCR detection cut-off

Viral load
Repurposed antiviral drugs for COVID-19
Interim WHO SOLIDARITY trial results

Results submitted to the
New England Journal of Medicine,

and posted on MedRxiv on October 15, 2020
https://www.medrxiv.org/content/10.1101/2020.10.15.20209817v1

DISCLAIMER: interim SOLIDARITY trial results does not necessarily represent the views of the WHO.
WHO SOLIDARITY randomised trial of 4 drugs for hospitalised COVID

- Remdesivir (intravenous)
  - Day 0, 200mg; days 1-9, 100mg.

- Hydroxychloroquine (oral)

- Lopinavir-ritonavir (oral)

- Interferon ß1a (mainly subcutaneous)
WHO Solidarity COVID therapeutics trial

>400 hospitals in >30 countries (purple: already started) enrolling >12,000 inpatients
Little effect of the 4 study drugs on 28-day mortality

(a) Remdesivir vs its control
- 12.7% Control
- 12.5% Remdesivir
- Stratified rate ratio, 0.95 (95% CI 0.81-1.11)
- p=0.50 by log-rank test

(b) Hydroxychloroquine vs its control
- 10.2% Hydroxychloroquine
- 8.9% Control
- Stratified rate ratio, 1.19 (95% CI 0.89-1.59)
- p=0.23 by log-rank test

(c) Lopinavir vs its control
- 10.3% Control
- 9.7% Lopinavir
- Stratified rate ratio, 1.00 (95% CI 0.79-1.25)
- p=0.97 by log-rank test

(d) Interferon vs its control
- 12.9% Interferon
- 11.0% Control
- Stratified rate ratio, 1.18 (95% CI 0.96-1.39)
- p=0.11 by log-rank test
Solidarity Trials Therapeutics: Conclusions

Combining data from all 4 trials, the Remdesivir vs not death rate ratio (RR) is 0.91 (95% CI 0.79-1.05), p=0.20

- This slightly favourable Remdesivir result could have arisen just by chance if Remdesivir does nothing and the real death rate ratio is 1 in all trials.
- Narrower confidence intervals would be helpful (particularly for Remdesivir), but the main need is for better treatments.

- There could be a small benefit in lower-risk patients, but not a big one. More evidence is needed, but BETTER DRUGS are needed even more.
COVID-19 vaccine accelerated development

Normal vaccine development performs each step in sequence
To accelerate COVID-19 vaccine development, steps are done in parallel

• All usual safety and efficacy monitoring mechanisms remain in place; such as adverse event surveillance, safety data monitoring & long-term follow-up
• Phase IV post-marketing surveillance for side effects is critical and essential
COVID-19 vaccine candidates in Phase III trials

- As of 02 October 2020 there are 42 COVID-19 candidate vaccines in clinical evaluation of which 10 in Phase III trials
- There are another 151 candidate vaccines in preclinical evaluation
- Phase III trials usually require 30,000 or more participants
- All top candidate vaccines are for intra-muscular injection
- Most are designed for a two-dose schedule (exceptions with a * in table are single dose)

<table>
<thead>
<tr>
<th>10 CANDIDATE VACCINES IN PHASE III CLINICAL EVALUATION</th>
<th>VACCINE PLATFORM</th>
<th>LOCATION OF PHASE III STUDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinovac</td>
<td>Inactivated virus</td>
<td>Brazil</td>
</tr>
<tr>
<td>Wuhan Institute of Biological Products / Sinopharm</td>
<td>Inactivated virus</td>
<td>United Arab Emirates</td>
</tr>
<tr>
<td>Beijing Institute of Biological Products / Sinopharm</td>
<td>Inactivated virus</td>
<td>China</td>
</tr>
<tr>
<td>University of Oxford / AstraZeneca</td>
<td>Viral vector *</td>
<td>United States of America</td>
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<tr>
<td>CanSino Biological Inc. / Beijing Institute of Biotechnology</td>
<td>Viral vector *</td>
<td>Pakistan</td>
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<tr>
<td>Gamaleya Research Institute</td>
<td>Viral vector</td>
<td>Russia</td>
</tr>
<tr>
<td>Janssen Pharmaceutical Companies</td>
<td>Viral vector</td>
<td>USA, Brazil, Colombia, Peru, Mexico, Philippines, South Africa</td>
</tr>
<tr>
<td>Novavax</td>
<td>Protein subunit</td>
<td>The United Kingdom</td>
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<tr>
<td>Moderna / NIAID</td>
<td>RNA</td>
<td>USA</td>
</tr>
<tr>
<td>BioNTech / Fosun Pharma / Pfizer</td>
<td>RNA</td>
<td>USA, Argentina, Brazil</td>
</tr>
</tbody>
</table>

https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

* Single dose schedule
WHO Solidarity vaccine trial
Achieving rapid progress towards global objectives

- Evaluating several different candidate vaccines
- Expeditiously enrolling people at sites with high rates of COVID-19
- Eliminating inefficiency of design & conduct of separate trials
- International collaboration & country commitment

Increasing the likelihood of finding several effective vaccines
Rapid accumulation of data to support rigorous evaluation
Results within 3-6 months after each vaccine is ready for inclusion
Fosters international deployment with equity of access

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31821-3/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31821-3/fulltext)
Key ethical considerations during COVID-19 pandemic

• Build on preexisting guidance to develop guidance materials fit for purpose in COVID-19

• Identify principles for research and their application (SOPs, Solidarity trials, human challenge studies)

• Develop allocation principles for clinical management, vaccines, diagnostics, & therapeutics

• Ethics of AI based applications, contact tracing Apps, immunity passports etc
Global burden of diseases and injuries, 1990-2009 Findings

• Sustained improvements in health over the past 70 years

• Maternal and child mortality have decreased, as has the burden of TB, HIV, and malaria; All of these were part of the Millennium Development Goals

• But across the world there is rising exposure to crucial risk factors related to the noncommunicable diseases such as diabetes, heart and lung diseases and cancer, including such risks as high blood glucose and particulate air pollution.

Ref: GBD 2019 (https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30925-9/fulltext)
Identified Gaps

• Health systems are ill-prepared for the projected rapid rise in NCDs and disabilities

• Public health has failed to stop the increase in critical risk factors
  • There is a pressing need to tackle wider determinants of health
  • The rise in exposure to key risk factors and deaths from cardiovascular disease indicates a turning point in global life expectancy gains

• The pandemic in context raises difficult questions about the direction of global health:
  • We must pay more attention to the socio-demographic index—which is related to income, education, and fertility rates.

Ref: GBD 2019 (https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30925-9/fulltext)
It is not about a single pandemic

As Richard Horton, the editor of *The Lancet*, has written: “The pandemic is not the making of a single coronavirus, but the combination of three epidemics: the virus, the chronic conditions that make people more susceptible to it, and a situation of deepening poverty and inequality. A single pandemic is too simple a narrative to capture this reality. What we’re faced with in Britain,’ he says, is a ‘syndemic’—a synthesis of epidemics.”

The pandemic has shown us that we will only achieve health for all when we address all socioeconomic factors and widespread inequalities.
How are health and healthcare going to be transformed by the current crisis?

• Every government sector now has to be involved in outbreaks

• Early, widespread, accurate communication of information, including WHAT IS NOT KNOWN, is absolutely critical

• Communities must be engaged from the very beginning—bottom up, not top down

• We have to communicate early and often

• We must engage the entire range of experts working on outbreaks, including from the social and behavioural sciences, from the very beginning

• We must prepare now for the next pandemic!
Thank you!