



COVID-19 RESEARCH AND INNOVATION ACHIEVEMENTS

APRIL 2021



Contents

Acknowledgements	3
Acronyms and abbreviations	4
1. Executive summary	5
2. Introduction	6
3. The research response to COVID-19: global, collaborative, fast & effective	7
4. Achievements	18
1. Virus natural history, transmission and diagnostics	20
2. Animal and environmental research on the virus origin, and management measures at the human-animal interface	22
3. Epidemiological studies	25
4. Clinical management	28
5. Infection prevention and control, including health care workers' protection	31
6. Candidate therapeutics R&D	35
7. Candidate vaccines R&D	39
8. Ethics considerations for research	46
9. Social sciences in the outbreak response	48
5. SARS-CoV-2 variants	52
6. Regulatory science	54
7. Lessons learned	57
8. Publications and further resources	58

Acknowledgements

This document is a reflection of the collaborative nature of global research and a demonstration of the vast and extraordinary community behind each and every research action and study that is helping combat COVID-19.

We wholeheartedly thank the hundreds of thousands of patients and volunteers and their families who participated in all the research studies that we have cited and the thousands of staff and researchers who conducted the studies and cared for those patients, volunteers and families.

We also gratefully acknowledge the critical role of the national institutions and research centers

across the globe that have provided, and continue to provide, critical support in the implementation of priority research.

If we name one, we will need to name them all; and there are just too many. So we salute the global effort and all who are participating in it.

We thank all partners and funders without whose support none of this work would be possible.

And finally, we remember all those who have lost lives and loved ones to this devastating disease.

Acronyms and abbreviations

ACT Accelerator Access to COVID-19 Tools Accelerator

ACTIV Accelerating COVID-19 Therapeutics Interventions and Vaccines

ACTT US Adaptive COVID-19 Treatment Trial

ADE antibody-mediated disease

AGP airborne-generating procedure

AMR antimicrobial resistance

CAB community advisory board

CDC US Centers for Disease Control and Prevention

COVID-19 Coronavirus Disease 2019

CEPI Coalition for Epidemic Preparedness Innovations

CRF Case Record Form

DeMaND Development of Materials for Mask and N95 Decontamination (study and consortium)

ECDC European Centre for Disease Prevention and Control

EDCTP European and Developing Countries Clinical Trials Partnership

EPI-WIN WHO's epidemic information network

ERC WHO Research Ethics Review Committee

EUL emergency use listing

FAO Food and Agricultural Organization

FFX first few X cases and contacts

FIND Foundation for Innovative New Diagnostics

GLOPID-R Global Research Collaboration for Infectious Disease Preparedness

GOARN Global Outbreak Alert and Response Network

GPP good participatory practice

GRP good regulatory practice

GReIP good reliance practice

HIC high-income country

HW health care worker

ICMRA International Coalition of Medicines Regulatory Authorities

ICU intensive care unit

IFR infection fatality rate

IFRC International Federation of Red Cross and Red Crescent Societies

INN International Nonproprietary Names

IPC infection prevention and control

IS international standard

IVD in-vitro diagnostic

LMIC low- and middle-income country

LLMIC low- and lower middle-income country

NEJM New England Journal of Medicine

NIBSC UK National Institute for Biological Standards and Control

NIH US National Institutes of Health

OECD Organisation for Economic Cooperation and Development

OIE World Organisation for Animal Health

PCR polymerase chain reaction

PHE public health emergency

PHEIC public health emergency of international concern

PHSM public health and social measure

PPE personal protective equipment

RCCE risk communication and community engagement

RCT randomized controlled trial

R&D Research and Development

REACT Real-time Assessment of Community Transmission

RECOVERY UK Randomised Evaluation of COVID-19 Therapy (trial)

REMAP-CAP Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia

RNA Ribonucleic Acid

SAGE WHO Strategic Advisory Group of Experts in Immunization

SARS-CoV-2 severe acute respiratory syndrome coronavirus 2

SOP standard operating procedure

SRH sexual and reproductive health

ST Solidarity Trial

STV Solidarity Trial Vaccines

STT Solidarity Trial Therapeutics

TDR WHO Special Programme for Research and Training in Tropical Diseases

TPP Target Product Profile

UKCDR UK Collaborative on Development Research

UN United Nations

UNF UN Foundation

UNDRR United Nations Office for Disaster Risk Reduction

UNICEF United Nations Children's Fund

VAERD vaccine-associated enhanced respiratory disease

VOC variant of concern

WFP World Food Programme

WHA World Health Assembly

WHO World Health Organization

WHO AFRO WHO Regional Office for Africa

WHO EURO WHO Regional Office for Europe

1. Executive summary

This report provides a summary of global research initiatives and achievements to tackle COVID-19 agreed at the outset of the pandemic.

In March 2020, within a few weeks of the World Health Organization (WHO) declaring COVID-19 to be a public health emergency of international concern (PHEIC), a coordinated global research roadmap was published by WHO.

It was a pivotal document and represented a transparent and globally agreed pathway through which all individuals and organizations involved in the research response could act, and be held to account.

It identified and recorded:

- eight immediate research actions needed in the emergency response to COVID-19
- nine broader research priorities and actions with selected knowledge gaps for each area
- a timeline for implementation of research actions, as well as immediate, midterm and longer-term priorities

Fourteen months later, research on most of the knowledge gaps has been initiated and is progressing.

Progress against all research targets within the global roadmap are reflected in Figures 4 and 5.

New COVID-19 research challenges emerge everyday but scientific achievements have already provided answers to several of the knowledge gaps identified in the roadmap and priority research has been done with some achievements.

Most notably, Research and Development (R&D) has delivered safe and efficacious COVID-19 vaccines at an unprecedented speed; this is a triumph for modern science although equitable access remains a challenge.



Istock.com/PeopleImages

Research and innovation work has also helped us deliver:

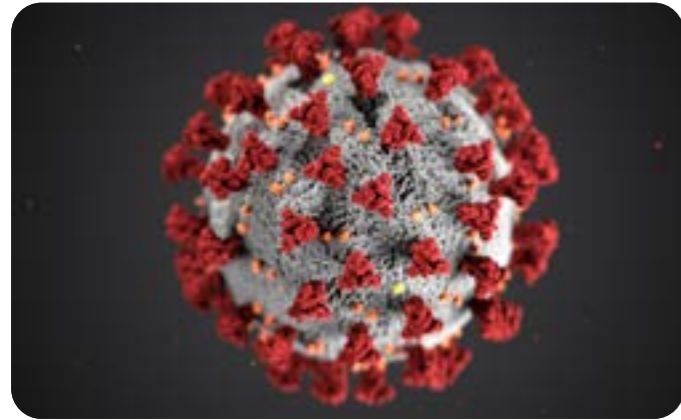
- Rapid diagnostics for use in community settings.
- The identification of optimal protective equipment (PPE) to protect health care staff and the public across the world.
- Evidence-based infection prevention and control (IPC) measures such as mask-wearing and social distancing in health care and community settings.
- Better understanding of likely animal host(s) for the virus. This will help in future efforts to prevent continued spillover to humans.
- Major clinical trials for the evaluation of candidate therapeutics, evaluating a dozen drugs, some of which have proven not to be effective in reducing mortality, and a handful of which have had positive results on cutting deaths.

These are just a selection of R&D achievements. But we cannot be complacent. R&D must continue to be flexible and innovative, adapting to the changing nature of the virus and its impact.

In this report, we measure research progress and identify key R&D achievements and the gaps that still exist. We now look forward to setting new research priorities for the next phase.

2. Introduction

The immense toll of COVID-19 on individuals, communities and countries across the world will be felt for many years to come.



The Centers for Disease Control and Prevention (CDC).

And yet in the midst of tragedy we have seen the best of humanity.

The response of the research and scientific communities across the world has been an outstanding example of this. The speed of mobilization of the R&D community and the collaborative and high-quality work of thousands of researchers and research institutions is unprecedented.

The pandemic has also been an opportunity to develop new ways of working: WHO and partners have facilitated hundreds of interactions and scientific consultations among researchers who have rapidly convened. The speed, depth and breadth of these interactions, and the participation of hundreds of researchers from across the world would not have been possible before.

A central and historic responsibility for the WHO has been the management of the global regime for the control of the international spread of disease. As part of this imperative, in May 2015 the Sixty-Eighth World Health Assembly (WHA) at the request of its 194 Member States asked WHO to create a broad global coalition to develop the WHO Research and Development (R&D) Blueprint for action to prevent epidemics.

The R&D Blueprint is both a convening mechanism to bring the global research community together and an instrument to provide technical guidance

for R&D preparedness and support research during epidemics.

In response to the current COVID-19 pandemic, the WHO R&D Blueprint rapidly assembled world scientists and stakeholders on COVID-19 at WHO's Geneva headquarters on 11-12 February 2020.

Their brief was to assess the current level of knowledge about the new virus, agree on critical research questions that needed to be answered urgently, and to find ways to work together to accelerate and fund priority research to curtail this outbreak and prepare for those in the future.

The Global Research Forum deliberations led to an agreement on two main goals: the first was to accelerate innovative research to help contain the spread of the epidemic and facilitate care for those affected; the second was to support research priorities that contribute to global research platforms with the hope of learning from the current pandemic response to better prepare for the next unforeseen epidemic.

Thereafter, WHO and partners have maintained a network of global researchers and experts that has produced a Global Research Roadmap to focus research efforts on COVID-19, debated research priorities, developed methods and critically appraised emerging evidence via hundreds of virtual scientific consultations with thousands of scientists around the world.

The processes and platforms that have since been developed will serve as the foundations for the research response in the event of any future public health emergencies of international concern (PHEICs) or pandemics.

This global coordination and support for the world's leading scientists and experts does not always make the headlines. But it has proven to be essential in advancing research and innovation which has underpinned some of the remarkable initiatives and breakthroughs detailed in this report.

3. The research response to COVID-19: global, collaborative, fast and effective

The following section describes how the research response to COVID-19 has been global, collaborative, fast and effective.

Global collaboration at an unprecedented scale

Across all key research areas there has been immense and unprecedented global collaboration among scientists and other experts.

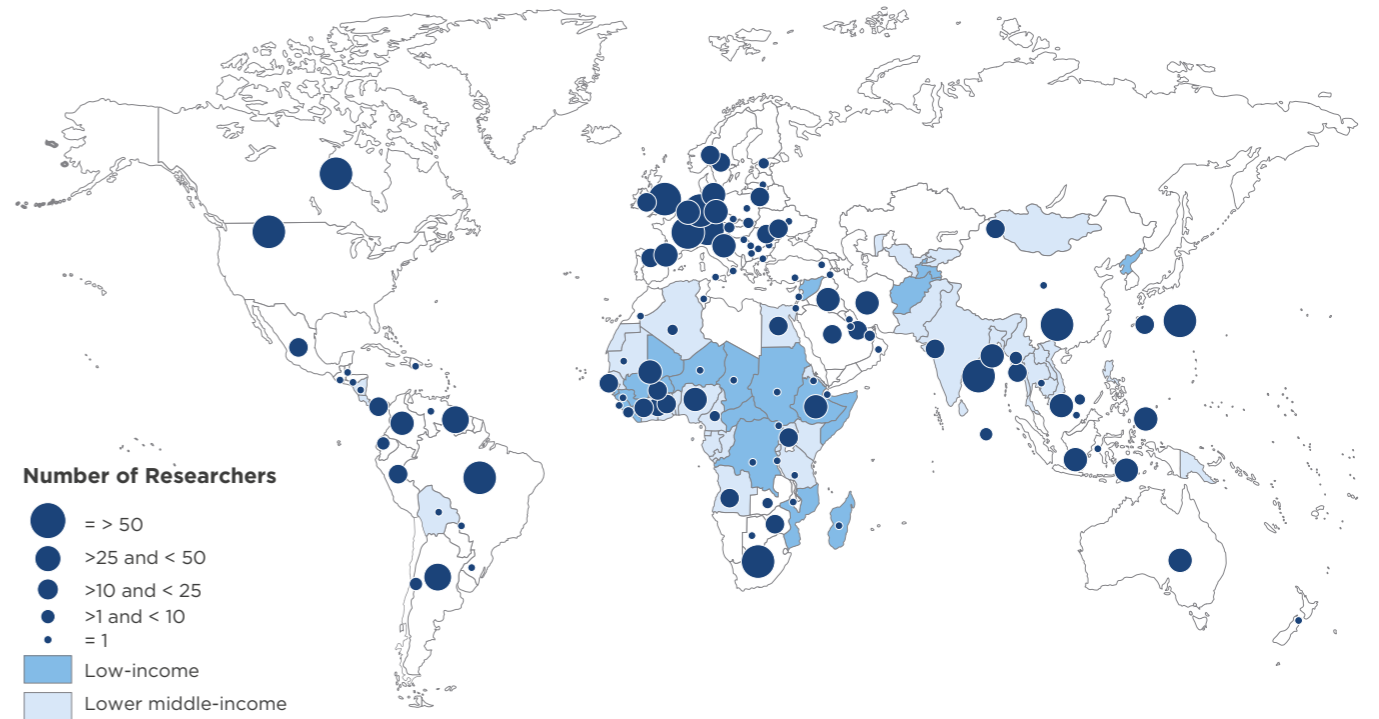
Figure 1 shows the extent of collaboration in COVID-19 research across the world. More than 3,000 researchers from 134 countries are

collaborating on the implementation of research and innovation activities and 40% of researchers are from low- and lower middle-income countries (LLMICs). They form WHO's Research and Innovation Collaborative Platform – a tool that can be activated to save lives now and in the event of future disease threats/pandemics.

FIGURE 1

COVID-19 Research and Innovation Collaborative Platform

Over 3000+ researchers from 134 countries collaborating with the implementation of the research roadmap (40% from LLMICs)



Disclaimer

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement. World Health Organization. WHO. 2020. All rights reserved.

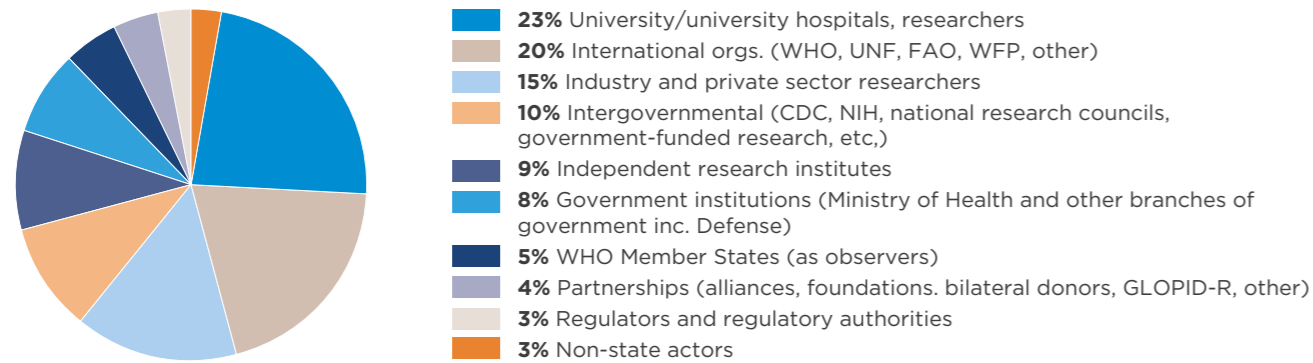
Bringing together the best minds from various perspectives

Figure 2 illustrates the collaboration across numerous research institutions for the implementation of the global roadmap. It shows the best minds and diverse perspectives brought together on this worldwide effort from global

partnerships, WHO Member States, government institutions, industry and private sector, university/hospital research departments and intergovernmental organizations, to name a few.

FIGURE 2

COVID-19 Research and Innovation Collaborative Platform Bringing together the best minds from various perspectives



How global R&D expertise has been coordinated and utilized

WHO has convened a broad global coalition of experts to develop and implement the R&D Blueprint to help accelerate research and development.

The Scientific Advisory Group (SAG) provides strategic and scientific advice on research priorities. It has reviewed the progress made and given advice to WHO on additional prioritization of research actions.

During the pandemic the multidisciplinary contributions of hundreds of scientists and institutions worldwide have been structured in main working parties called “Thematic Areas”.

Within each Thematic Area, specialized ad hoc independent expert groups are created to address each research priority – see Figure 3.

Given the interdependence of the various research areas and the need for a multidisciplinary approach there has been ongoing collaboration between experts in the various Thematic Areas. Each has more than one chair and reports regularly to the SAG on progress and challenges – see Figure 3.

FIGURE 3

Key R&D thematic areas and working groups.

R&D thematic area	Working Groups	Approx number attending meetings
Vaccines	Working Group – Vaccine R&D for COVID-19 vaccines	300
	Assays and standardization (official name: Virus, Reagents and Immune Assays).	120
	Animal models	
	Working Group on vaccine prioritization	30
	Working Group on clinical trial designs	100
Therapeutics	Working Group on monitored challenge model of experimental COVID-19 infection and illness (a.k.a. human challenge studies working group)	250
	Solidarity Trial Therapeutics (STT)	
Diagnostics	Therapeutics prioritization for COVID-19	30
	Coronavirus reference laboratory network	50-75
Ethics	Virus Evolution Working Group	25
	Ethics and COVID-19: resource allocation and priority-setting	
Social Science	COVID-19 Social Science working group	30
Clinical management	Management research working group with sub-working groups on: <ul style="list-style-type: none"> • Corticosteroids PMA • IL6 Blockers PMA • Heparin PMA • Respiratory studies • Post-COVID core outcome set • COVID-19 severity scores 	
	IPC, including HWs	
Epidemiological studies	WHO COVID-19 IPC R&D Expert Group	40

Aligning funding with research gaps across research priorities

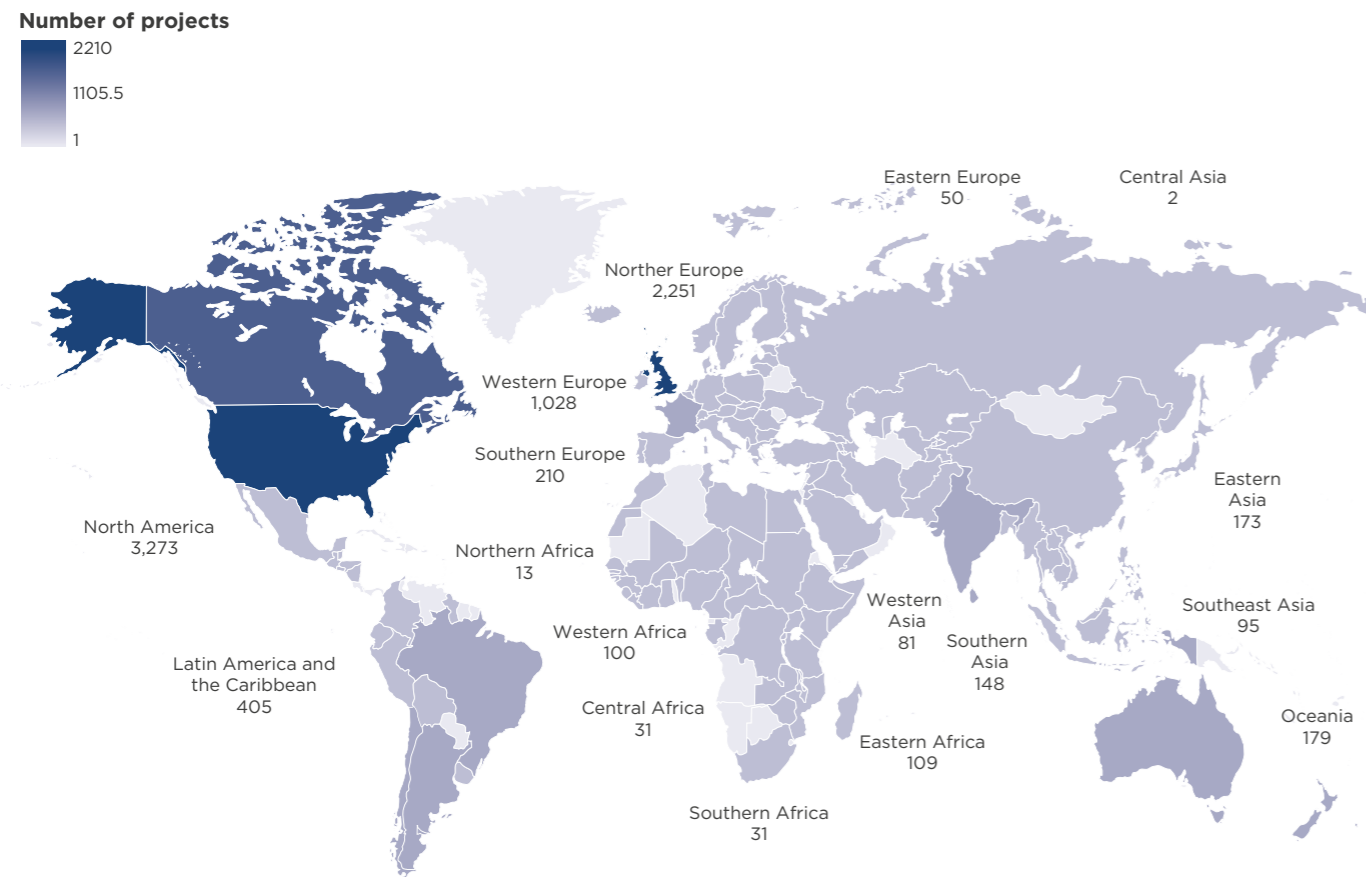
Underpinning the speed, effectiveness and focus of global research efforts against COVID-19 has been improved global coordination of funding for pandemic research. This has been led by the Global Research Collaboration for Infectious Disease Preparedness (GloPID-R).

Primarily, GLoPID-R identifies funding gaps to align funding with research needs, especially in low and middle-income countries (LMICs).

There remain massive discrepancies in how funding is distributed across the world, necessitating a collaborative effort to support LMICs. This is reflected in figure 4 below:

FIGURE 4

Location of Coronavirus Disease 2019 (COVID-19) research projects by country, WHO sub-region



Norton A, Bucher A, Antonia E et al. A living mapping review for COVID-19 funded research projects: six-month upstate [version 3]. Wellcome Open Res 2021, 5:209 (doi:10.12688/wellcomeopenres.16259.3)

ACT Accelerator partnership

Since April 2020, the COVID-19 Tools Accelerator (ACT) Accelerator partnership, launched by WHO and partners, has supported the fastest, most coordinated, and successful global effort in history to develop tools to fight a disease. With significant advances in research and development by academia, private sector and government initiatives, the ACT Accelerator is on the cusp of securing a way to end the acute phase of the pandemic by deploying the tests, treatments and vaccines the world needs.

The Facilitation Council provides high-level political leadership and enabling advice on global advocacy and resource mobilization to facilitate the work of the ACT Accelerator, its global collaborative framework, and its

partnerships to ensure the realization of the ACT-A vision: the rapid development, scale-up and equitable distribution of COVID-19 vaccines, therapeutics and diagnostics, underpinned by the strengthening of health systems.

Formally launched on 10 September 2020, the Council is currently co-chaired by Norway and South Africa.

The global partners are WHO, CEPI, Gavi, the Vaccine Alliance, the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Funds), Unitaid, FIND, the Wellcome Trust, the World Bank Group, and the Bill & Melinda Gates Foundation.



Funding for research and innovation

There is an urgent need for funders to focus their efforts on specific COVID-19 research areas in LMICs. Specific deficit areas in research funding that have been highlighted in the last year include: viral transmission and social science research; long COVID, and research in LMICs.

One of the tools to facilitate GLoPID-R's work is the COVID-19 Research Project Tracker – see

Figure 5 below - a live database of funded research projects which monitors progress on funding against the global roadmap. It is instrumental in reaching global funding decisions. During 2020/21 it has tracked 9,102 projects funded by 132 organizations taking place across 136 countries.

FIGURE 5

Global picture of research funding aligned to WHO Research Roadmap

Roadmap research thematic area	WHO priority sub-area							Total funding amount (\$)
	a	b	c	d	e	f	N/A	
1. Virus: natural history, transmission	823	605	170	598	123	85	49	821.4M
2. Animal and environmental research	72	6	7				3	16.9M
3. Epidemiological studies	611	259	72	258			132	370.5M
4. Clinical characterization and management	466	767	11	651	27	7	182	1,207.9M
5. Infection prevention and control	186	311	457	308			193	288.1M
6. Candidate therapeutics R&D	796	93	17	231	43		82	629.7M
7. Candidate vaccines R&D	219	41	34	8	17		80	1,618.5M
8. Ethics considerations for research	36	15	30	47	16		25	32.4M
9. Social sciences in the outbreak response	978	168	497	170	22	38	1,634	732.8M
Unallocated							725	0.0M

Credit: UKCDR and GLoPID-R COVID-19 Research Project Tracker, 2020

COVID Circle, a joint initiative between UKCDR and GLoPID-R is seeking to align and strengthen the global efforts on COVID-19 in resource-limited

settings. GLoPID-R is also currently in the process of growing its membership, especially in LMICs in Latin America, Asia and Africa.

Delivering immediate research actions at the start of the pandemic

The Global Research Forum identified eight immediate research actions “as immediate steps to contribute to the control of the outbreak”.

These actions were reflected in the Global Research Roadmap which:

- pointed to the responsibility of the global community to provide the best evidence to inform public health interventions to curtail the current epidemic

- highlighted the need to strike the right balance between stopping transmission now and preparing for the future

- underlined the imperative for research to focus on actions that can save lives now

For all eight immediate research areas identified in the roadmap, research activities were promptly initiated (see Figure 6):

FIGURE 6

Immediate research actions	Action-started	When did research start?
1. Mobilize research on rapid point of care diagnostics for use at the community level	✓	February 2020
2. Immediately assess available data to learn what standard of care approaches from China and elsewhere are the most effective	✓	February 2020
3. Evaluate as fast as possible the effect of adjunctive and supportive therapies	✓	March 2020
4. Optimize use of personal protective equipment and other infection prevention and control measures in health care and community settings	✓	March 2020
5. Review all evidence available to identify animal host(s), to prevent continued spill over and to better understand the virus transmissibility in different contexts over time, the severity of disease and who is more susceptible to infection	✓	March 2020
6. Accelerate the evaluation of investigational therapeutics and vaccines by using “Master Protocols”	✓	March 2020
7. Maintain a high degree of communication and interaction among funders so that critical research is implemented	✓	February 2020
8. Broadly and rapidly share virus materials, clinical samples and data for immediate public health purposes	✓	March 2020

Research and Innovation actions by thematic area Feb 2020 - Feb 2021

Over the past year multiple studies in nine thematic areas have been carried out by researchers all around the world. More recently, global research collaboration has focused on a tenth issue - the emergence of SARS CoV-2 variants of concern (VOCs).

Figure 7 shows how the vast majority of research areas are on track timing-wise benchmarked against the proposed delivery date in the global roadmap.

FIGURE 7

Thematic area of research	Proposed target delivery date in Roadmap	Activity description	Status of research
Candidate therapeutics	February 2020	Master Protocol for evaluation of candidate therapeutics is available.	✓
Candidate therapeutics		Data on Safety and efficacy of candidates (RCTs) are produced and analysed.	✓
Data sharing		Monitor compliance with research data sharing norms.	✗
Ethics considerations for research		Expedited evaluation of protocols.	✓
Candidate therapeutics		Promote adequate supply of therapeutics showing efficacy with overview of available supply and production capacity. Negotiate agreements with manufacturers to facilitate access and long-term availability on reasonable/equitable terms.	✓
Candidate vaccines		Global TPP building on experience from MERS and Disease X.	✓
Ethics considerations for research		4-pager on WHO ethics guidance for COVID-19.	✓
Social sciences in the outbreak response		Establish mechanisms for dialogue and input into all relevant thematic areas (key focus areas: public health, clinical care and health systems, media and communications, engagement, sexual and reproductive health, international coordination)	✓
Data sharing		Develop repository list of entities holding isolated novel corona viruses and other relevant materials, and related data and information.	✗
Clinical management		March	Agree core clinical outcomes to be reported to WHO from all clinical datasets.
Ethics considerations for research	Four brief papers on key explanations of ethical values for COVID-19 (equity, solidarity, trust, vulnerability).		✓
Virus natural history	Establish appropriate controls and EQA systems.		✓
Candidate therapeutics	Candidate therapeutics identified for clinical studies		✓
Candidate therapeutics	Master Protocol for prophylaxis is available.		✗
Candidate vaccines	Prioritization criteria for vaccine evaluation.		✓
Candidate vaccines	Trial design synopsis for vaccine evaluation.		✓
Ethics considerations for research	Trial design synopsis for vaccine evaluation.		✓
Candidate therapeutics	Repository of data from in vitro/in vivo testing available to refine work of global community assumes continuous updates.		✓

✓ Initiated ✓ Planned ✗ Not yet initiated

Thematic area of research	Proposed target delivery date in Roadmap	Activity description	Status of research	
Epidemiological studies	March 2020	Modeling studies to consider measures to protect HCWs and other critical societal functions.	✓	
Clinical management		Preliminary data collection on aerosolization with high flow O2.	✓	
Clinical management		RCTs for steroids and high flow O2 - initiation.	✓	
Epidemiological studies		Cohort studies to clarify pre-symptomatic/asymptomatic transmission.	✓	
Epidemiological studies		Retrospective review of hospital admissions to identify risk factors for severe disease.	✓	
Candidate vaccines	April	Animal models for both efficacy and disease enhancement-landscape and way forward.	✓	
Clinical management		Observational cohorts with viral sampling to better understand pathophysiology, risk factors for severe disease, shedding, explore best options for triage processes, and optimal specimen sampling strategies.	✓	
Virus natural history, transmission and diagnostics		Development and validation of kits meeting TPPs.	✓	
Candidate therapeutics		Prioritized potential combinations identified.	✓	
Candidate therapeutics		In vitro and In vivo combination testing data are available.	✓	
Candidate vaccines		Assay development and validation required for vaccine R&D.	✓	
Candidate vaccines		Vaccine Phase 2b/3 Master Protocol.	✓	
Candidate therapeutics		June	Adequate animal models available (mapping first then models testing).	✓
Virus natural history, transmission and diagnostics			Distribution of kits meeting TPPs.	✓
Virus natural history, transmission and diagnostics			Point of care testing available.	✓
Virus natural history, transmission and diagnostics	Multiplex detection assays available.		✓	
Virus natural history, transmission and diagnostics	Shedding and replication compartment studies - results.		✓	
Virus natural history, transmission and diagnostics	Support to sequence sharing platforms including GISAID.	✓		
Virus natural history, transmission and diagnostics	Harmonization/standardization or EQA system for ELISA.	✓		

✓ Initiated ✓ Planned ✗ Not yet initiated

Thematic area of research	Proposed target delivery date in Roadmap	Activity description	Status of research
Animal and environmental research on the virus origin, and management measures at the human-animal interface	June 2020	Animal serological screening.	✓
Animal and environmental research on the virus origin, and management measures at the human-animal interface		Inventory of banked animal samples for coronaviruses in bats and other wildlife in southern Asia.	✓
Animal and environmental research on the virus origin, and management measures at the human-animal interface		Data on diversity, number and origin of animals sold in live markets in China and South-East Asia.	✓
Animal and environmental research on the virus origin, and management measures at the human-animal interface		Animal-human-environment related risk awareness and information campaigns.	✓
Epidemiological studies		Household transmission studies to determine role of different age groups in transmission.	✓
Epidemiological studies		Prospective studies in different settings to estimate effects of alternate social distancing measures, and comparative analysis of impact of interventions.	✓
Candidate therapeutics	July	Standard protocols for in vitro testing/in vivo testing	✓
Candidate therapeutics		Data on safety and efficacy of prophylaxis are available.	✓
Data sharing		Promote sustainable sequence sharing platforms including public domain and public access models (such as GISAID).	✓
Clinical management		Agree core clinical outcomes to be reported to WHO from all clinical datasets	✓
Ethics considerations for research		Four brief papers on key explanations of ethical values for COVID-19 (equity, solidarity, trust, vulnerability).	✓
Animal and environmental research on the virus origin, and management measures at the human-animal interface		Options for improved biosafety in live animal markets identified.	✓
Virus natural history, transmission and diagnostics		High throughput and automation.	✓
Infection prevention and control, including health care workers' protection		Effectiveness of movement restrictions determined through systematic reviews, surveys, ecological studies.	✓
Candidate therapeutics		Data on safety and efficacy of combination therapies (RCTs).	✓
Data sharing		Establish an evaluation of new model of information sharing including use of preprints to determine if new norms require modification case studies.	✗

✓ Initiated ✓ Planned ✗ Not yet initiated

Thematic area of research	Proposed target delivery date in Roadmap	Activity description	Status of research	
Animal and environmental research on the virus origin, and management measures at the human-animal interface	August 2020	Options for improved biosafety in live animal markets piloted.	✓	
Virus natural history, transmission and diagnostics		Devices available to measure prognostic markers.	✓	
Animal and environmental research on the virus origin, and management measures at the human-animal interface		Description of wildlife trade and its drivers in China and SE Asia.	✓	
Animal and environmental research on the virus origin, and management measures at the human-animal interface.		Risk factors for animal-human infection identified.	✓	
Infection prevention and control, including health care workers' protection		Effectiveness of specific PPE determined through systematic reviews, observational studies, case-control studies.	✓	
Infection prevention and control, including health care workers' protection		Effectiveness of activities to minimize the role of the environment.	✓	
Infection prevention and control, including health care workers' protection		Collaboration with social science groups on increasing compliance with evidence-based IPC measures through qualitative approaches to determine possible interventions.	✓	
Ethics considerations for research		Activate PHE Ethics network for COVID-19 - case studies.	✓	
Animal and environmental research on the virus origin, and management measures at the human-animal interface		November - February 2021	Animal model studies on origin/routes of transmission.	✓
Animal and environmental research on the virus origin, and management measures at the human-animal interface			Additional sampling to identify animal reservoir.	✓
Animal and environmental research on the virus origin, and management measures at the human-animal interface	Options for improved biosafety in live animal markets implemented with training.		✓	

✓ Initiated ✓ Planned ✗ Not yet initiated

4. Achievements

Summary

Following the development of the Coordinated Global Research Roadmap for COVID-19 in March 2020, research activities worldwide have been carried out in nine thematic areas and in three cross cutting areas to support all research endeavours.

These have filled many of the key knowledge gaps identified in the roadmap, providing greater clarity on the prevalence of COVID-19, supporting the development of safe and effective COVID-19 vaccines in record time, and evaluating potential COVID-19 therapeutics.

Over the past year, multiple activities have been carried out under each theme to support globally coordinated responses to COVID-19. More recently, global collaboration has focused on a tenth key issue – the emergence of SARS-CoV-2 VOCs.

Theme 01: Origin of the virus and COVID-19 at the human-animal interface: Studies have been carried out to explore the ability of SARS-CoV-2 to infect multiple animals in a range of countries, and to assess the potential for SARS-CoV-2 transmission through the food chain. An international multidisciplinary WHO mission in China has investigated the possible origins of SARS-CoV-2.

Theme 02: Virology, transmission and diagnostics: Multiple activities have been undertaken to facilitate the use of antigen-based rapid diagnostic tests to provide data on COVID-19 infections to inform national and global decision-making. The largest ever implementation study, likely to involve up to one million participants, is ongoing in four low- and middle-income countries (LMICs).

Theme 03: Epidemiological studies: The Unity initiative has provided a suite of materials to support high-quality sero epidemiological studies in different settings and among different populations. These have been used in more than 70 countries, including many LMICs, and in humanitarian settings. Epidemiology has provided deeper knowledge of routes of transmission and of settings that facilitate spread and understanding the effectiveness of public health and social measures. Research has also underpinned ongoing assessment of the impact of SARS-CoV-2 variants and of the impact of COVID-19 vaccination programmes.

Theme 04: Clinical characterization and management: A global COVID-19 Clinical Data Platform has been developed and includes anonymized patient records from more than 40 countries. Rapid evidence appraisals have fed into ‘living guidelines’ for COVID-19 therapeutics. There have been extensive efforts to enhance oxygen supply and distribution. Research studies are being carried out on approaches for respiratory support, and discussions are underway to develop a rigorous clinical definition of long COVID.

Theme 05: Infection prevention and control (IPC): Multiple studies have been done to improve understanding of SARS-CoV-2 transmission in clinical and community settings and to assess the impact of control measures. Studies have also focused on optimizing the use of personal protective equipment (PPE).

Theme 06: Therapeutics R&D: We have now proven that platform trials are feasible. These large simple trials can generate actionable data on effective therapies (e.g. steroids, IL6 inhibitors) and identification of ineffective ones (e.g. hydroxychloroquine, lopinavir/ritonavir, interferon beta 1-a SC, convalescent plasma, azithromycin).

Theme 07: Vaccines: Over ten major trials have delivered strong efficacy data - with many vaccines now being deployed in different parts of the world. TPPs and study designs have guided evaluation (including in the context of variants)

Theme 08: Ethics: Essential guidance was developed collaboratively: including a rapid review of research during pandemics, and guidance on ethics for allocation and priority setting of interventions.

Theme 09: Social science: Good participatory practice for emerging pathogens (GPP-EP) and a community-centred

The three cross-cutting areas to support research have had strong results:

Regulatory science

Regulatory science work has facilitated, through emergency use listing, deployment of 28 diagnostic tests, seven vaccines and two therapeutics for COVID-19 - as well as the streamlining of regulatory processes and alignment.

Framework to assess the impact of variants

WHO has established a SARS-CoV-2 Risk Monitoring and Evaluation Framework to identify,

monitor and assess variants of concern (VOCs). It involves surveillance, research on VOCs, and evaluation of the impact on diagnostics, therapeutics and vaccines.

Infodemics

At the WHA in May 2020, a key resolution (WHA73.1) calls on Member States to provide reliable COVID-19 content, take measures to counter mis- and disinformation and leverage digital technologies across the response. The provision of clear evidence-based information is a critical area of WHO work.



© WHO / Blink Media / Juliana Tan

1. Virus natural history, transmission and diagnostics

Summary

Important and critical research was carried out to advance our understanding on the key work done to facilitate the use of rapid diagnostic tests to assess COVID-19 epidemiology and to inform national COVID-19 control measures.

Aim

A key aim of the virology R&D thematic area of the global roadmap has been to improve understanding of the SARS-CoV-2 natural history, transmission dynamics and diagnostics to increase access to rapid near-patient testing and to support national and global decision-making on COVID-19 control.

The following objectives underpinned the research agenda:

- **Objective 1:** Support development of products to improve clinical processes.
- **Objective 2:** Research how the virus spreads, its shedding and the natural history of disease in support of clinical management and development of interventions.
- **Objective 3:** Develop tools and studies to monitor phenotypic change and potential adaptation.
- **Objective 4:** Immunity – Support public health measures, clinical management and development of interventions vital for tracing the spread of the virus and to inform vaccine development.
- **Objective 5:** Disease modelling to support clinical management and development of interventions by researching transmission dynamics and diagnostics.

Achievements

1. **Diagnostics:** Multiple global meetings have been organized to coordinate various aspects of rapid diagnostic test development and implementation including: the creation of target product profiles (TPPs) for existing and new test methods; the development of an

implementation guide for antigen-based rapid diagnostic tests; and the development of a set of training resources for antigen-based rapid diagnostic tests. By March 2021 over 1,000 tests were developed: 177 antigen rapid diagnostic tests are commercially available. Of those, 26 tests—including two antigen, 23 molecular and one antibody test—have been granted WHO emergency use listing by WHO.

2. **Advancing the research agenda:** WHO and the Foundation for Innovative New Diagnostics (FIND) co-hosted a meeting to define a research agenda for the development and use of antigen-based rapid diagnostic tests. FIND is hosting a COVID-19 test directory and pipeline. FIND is tracking the current status of SARS-CoV-2 tests commercialized and in development. For immunoassays and molecular tests for COVID-19, they have compiled a fully searchable directory that includes performance data (sensitivity and specificity).
3. **Implementation guide:** WHO and FIND have developed an implementation guide and checklist for antigen-based rapid diagnostic tests, which provides a summary of the key issues that must be considered before, during and after the introduction of such tests.
4. **Capacity-building:** WHO and FIND have developed a comprehensive set of resources to support the training of HWs in the use of antigen-based rapid diagnostic tests. Materials can be adapted and customized based on national guidelines and target group of participants. In addition, multiple webinars have been organized in different regions to train scientists and health professionals in various COVID-19 procedures, including polymerase chain reaction (PCR) testing, genomic sequencing, and use of antigen-based rapid diagnostic tests.

5. **Implementation projects:** A large-scale implementation project has been launched in Kenya, Mozambique, Sri Lanka and Tajikistan, following an open call for proposals, to gather data on operationalization of antigen-based rapid diagnostic testing and impacts on local health systems. This is the largest monitored implementation project to date, with up to one million patients likely to be tested. An additional project in Pakistan is investigating the use of ELISpot assays to detect post-infection cellular immunity.

Benefits

Work in this theme has helped to generate evidence on the value of antigen-based rapid diagnostic tests, and has built capacity for their use globally. The results from the global implementation study will provide key data to support their effective and efficient implementation into national health systems.

Outputs

Two Antigen Rapid Diagnostic Tests [approved by WHO](#) for emergency use

[Performance evaluations ongoing](#), with data published on a rolling basis

Resources now available: Virtual biobank directory, [Test tracker](#), [Diagnostic implementation simulator](#)

To secure equitable access to tests, ACT-A has procured over 27 million molecular tests and 12 million rapid antigen tests for LMICs

To stimulate rapid and effective country uptake, catalytic funding in over 15 countries for Ag RDT roll-out Developed COVID-19 Ag RDT [implementation guide](#), [Online training](#) was deployed for over 23,000 participants in almost 200 countries; FIND developed [Ag RDT modular training package](#) with WHO and published [PCR test development guide](#) with ASLM

Other outputs include:

Target product profiles: www.who.int/publications/m/item/covid-19-target-product-profiles-for-priority-diagnostics-to-support-response-to-the-covid-19-pandemic-v.0.1

Implementation guide: www.who.int/publications/i/item/9789240017740

Training package: <https://extranet.who.int/hslp/content/sars-cov-2-antigen-rapid-diagnostic-test-training-package>

Laboratory testing strategy recommendations for COVID-19. World Health Organization 2020; Available from: <https://apps.who.int/iris/handle/10665/331509>.

Laboratory assessment tool for laboratories implementing COVID-19 virus testing. World Health Organization 2020 8 April 2020 7 July 2020; Available from: <https://apps.who.int/iris/handle/10665/331715>.

Laboratory biosafety guidance related to coronavirus disease (COVID-19). World Health Organization 2020; Available from: <https://apps.who.int/iris/handle/10665/332076>

Advice on the use of point-of-care immunodiagnostic tests for COVID-19. World Health Organization 8 April 2020; Available from: <https://apps.who.int/iris/handle/10665/331713>.

Antigen detection in diagnosis of SARS-CoV-2 infection using rapid immunoassays, interim guidance. World Health Organization 2020. Available from: <https://apps.who.int/iris/handle/10665/334253>

COVID-19 diagnostic testing in the context of international travel <https://www.who.int › Publications › i › item>

SARS-CoV-2 antigen-detecting rapid diagnostic tests: An implementation guide. <https://www.who.int/publications/i/item/9789240017740>

COVID-19 diagnostic testing in the context of international travel <https://www.who.int › Publications › i › item>

2. Animal and environmental research on the virus origin, and management measures at the human-animal interface



Istock.com/LeArchitecto

Important and critical research was carried out to advance our understanding of the origins of the virus and management measures at the human-animal interface, developing strategies to prevent transmission between animals and humans, including future spillover.

Aim

A key aim of the this thematic area of the global roadmap has been to improve understanding of SARS-CoV-2 in animals and the environment in order to provide knowledge of potential routes through which the virus could transmit between animal and humans. Infection of animal hosts also creates opportunities for the formation of novel animal reservoirs and for SARS-CoV-2 variants to evolve and re-infect humans. In addition, understanding the original spillover event of SARS-CoV-2 can inform the prevention of future zoonotic disease outbreaks.

Three specific objectives underpinned the research agenda:

- ➔ **Objective 1:** Identify animal source and route of transmission (hosts, any evidence of continued spill over to humans and transmission between animals and humans).

- ➔ **Objective 2:** Improve understanding of socioeconomic and behavioural risk factors for spillover and transmission between animals and humans (identify the risks linked to trade and consumption of potentially infected animal species and the communities or occupational groups more at risk across different interfaces).
- ➔ **Objective 3:** Design and test suitable risk reduction strategies at the human-animal environment interface, accordingly (limit infection in high-risk areas and for at-risk populations and the public).

Achievements

1. **Origins of SARS-CoV-2:** Critical research on the source of the virus was undertaken. Investigation in animal populations explored the infection with SARS-CoV-2 or related coronaviruses in multiple wild, domestic and

companion animal species, and in multiple countries. Until now, no animals sampled before December 2019 have been found to be infected with SARS-CoV-2.

2. **Joint WHO-China study:** An international multidisciplinary WHO mission visited China early in 2021. Its findings have shed light on the possible origins of SARS-CoV-2 and the areas where further investigation should be focused. The investigation was carried out on the zoonotic source of SARS-CoV-2 and the route of its introduction to the human population in China, including the possible role of intermediate hosts. Based on these studies, the beginning of SARS-COV-2 circulation in the human population was estimated to be most likely mid-November to early December 2019. As of now, the zoonotic source has not been identified, but SARS-COV-2 susceptible (farmed) wild animals and products from regions that are bat SARS-related CoV hotspots were sold at the Huanan market and genomic data suggests there is likely to be an intermediate host between bats and humans.
3. **Susceptibility of animals to SARS-CoV-2 infection:** Evaluations were carried out on the susceptibility of multiple animal species to SARS-CoV-2 infection in controlled conditions, both in vivo and in vitro; characterization of the efficiency of cell receptors of candidate species for SARS-CoV-2; and analysis of genotype and phenotype variations (expression pattern of host proteins) in the course of infection. This included the validation of diagnostic tools for animal samples (incl. serological tests); development of guidance material for safe sampling and testing; and transfer of technology in multiple countries hosting potentially susceptible animals.
4. **Diversity of variants:** Important laboratory studies have been done assessing the potential of SARS-CoV-2 variants to infect different species. Host responses to variants and impacts on the severity of disease have also been explored. In addition, an outbreak in European mink farms was intensively studied. New variants were identified and tracked in human and mink populations. These variants were not thought to still be circulating. Emerging from the outbreak in mink farms, risk assessment at the global level and development of biosafety guidance were done.

5. **Food chain contamination:** Important studies have been carried out to explore the persistence, survival and infectivity of SARS-CoV-2 in food-associated environments. Other work has examined the risk of transmission to food animals and transmission along the food chain, including in traditional markets, in a variety of global settings. Other achievements include the development of methods to quantify infectious particles of SARS-CoV-2; evaluation of virus persistence and infectivity during food processing; quantification in water and food matrices on various products and under variable environmental conditions; guidance for competent authorities responsible for national food safety control systems; and guidance for the development of communication and awareness campaigns in at-risk areas, including traditional markets. This strand of work has involved close collaboration with key global bodies in animal health and food safety, particularly the World Organization for Animal Health (OIE) and the UN Food and Agriculture Organization (FAO).
6. **Impacts on nutrition and anaemia:** A global multi-agency team was established to assess the impact of COVID-19 on nutrition. Various monitoring tools have been adapted so information on COVID-19 can be incorporated. Other work has focused on supporting global and national bodies addressing anaemia, as COVID-19 has had significant impacts on food security and disrupted the work of anaemia prevention programmes.
7. **Risk associated with wildlife value chain and trade:** The risk associated with fur animal farming was assessed.
8. **Animal COVID-19 detection:** The ability of dogs to detect COVID-19 infections was explored to provide a possible complementary approach to diagnostic tools being currently used. Early results have been promising.

Benefits

In addition, research was conducted to understand how SARS-CoV-2 behaves in animals and food systems to inform national and global control measures. Further surveillance will be essential to detect cross-species transmission and novel animal reservoir formation, particularly given the potential for viral evolution in other animal hosts.

This research agenda continues to be primordial to: i) limit the risk of recurrent transmission of SARS-CoV-2 and related variants from established animal reservoir to human, as well as formation of novel animal reservoirs through human-to-animal transmission; ii) reduce selection pressure associated with spillover and genomic variations of the circulating viruses; iii) counter illegal trading of wildlife and undetected movement of traded animals, thanks to improved regulation of the associated food chain; and iv) reduce the risk of future spillover of zoonotic pathogens from domestic and/or wild animals through a better understanding of the dynamic of the COVID-19 outbreak and improved biosafety and monitoring at the human-animal-environment interface.

Process

The WHO COVID-19 HAI R&D Expert Group worked in concert with the WHO Secretariat, the OIE Ad-hoc group on COVID-19 and the human-animal interface, the OIE advisory group for animal health surveillance during the COVID-19 events, the FAO experts and other COVID-19 research pillars and working groups, with the purpose of facilitating coordination and collaboration of research and innovation, and boosting synergy in the field of HAI during the response to the COVID-19 pandemic.

Outputs

Mink-associated SARS-CoV-2: <https://www.who.int/csr/don/03-december-2020-mink-associated-sars-cov2-denmark/en/>

Origins of SARS-CoV-2: <https://www.who.int/health-topics/coronavirus/origins-of-the-virus>

Serological investigation of SARS-CoV-2 related coronavirus infection in animals, South East Asia/ Thailand <https://www.nature.com/articles/s41587-020-0631-z>

WHO-convened Global Study of Origins of SARS-CoV-2: China Part. Joint WHO-China Study <https://www.who.int/publications/i/item/who-convened-global-study-of-origins-of-sars-cov-2-china-part>

Exposure of humans or animals to SARS-CoV-2 from wild, livestock, companion and aquatic animals <http://www.fao.org/3/ca9959en/CA9959EN.pdf>

GLEWS+ Risk assessment - SARS-CoV-2 in animals used for fur farming <https://www.who.int/publications/i/item/WHO-2019-nCoV-fur-farming-risk-assessment-2021.1>

COVID 19 and food safety: guidance for competent authorities responsible for national food safety control systems https://www.who.int/publications/i/item/WHO-2019-nCoV-Food_Safety_authorities-2020.1

A rapid review of evidence on managing the risk of diseases emergence in the wildlife trade https://www.oie.int/fileadmin/Home/eng/International_Standard_Setting/docs/pdf/WGWildlife/OIE_review_wildlife_trade_March2021.pdf

Reducing public health risks associated with the sale of live wild animals of mammalian species in traditional food markets https://cdn.who.int/media/docs/default-source/food-safety/ig--121-1-food-safety-and-covid-19-guidance-for-traditional-food-markets-2021-04-12-en.pdf?sfvrsn=921ec66d_1&download=true

3. Epidemiological studies



© WHO / Blink Media / Gilliane Soupe

Important and critical research was carried out to advance our understanding of SARS-CoV-2 transmission dynamics and COVID-19 severity and susceptibility through high-quality epidemiological studies across the globe.

Aim

A key aim of the epidemiological studies thematic area of the global roadmap has been to develop and implement eight standardized epidemiological protocols within the Unity initiative portfolio as well as generating essential epidemiological data to support public health decision-making. Use of standardized protocols has ensured the comparability of findings across studies. In addition, the Solidarity II, which is a global research forum of partners coordinated by WHO, aims to help standardize serological testing to enable comparability between studies, as well as identifying and bridging research gaps, sharing cutting-edge scientific findings and creating collaborations to progress the research of serological epidemiology of SARS-CoV-2.

Three specific objectives underpinned the epidemiological studies research agenda:

➔ **Objective 1: Describe transmission dynamics of SARS-CoV-2.** Develop eight protocols covering key issues such as population-based, age-stratified seroepidemiological

investigations, assessing household transmission, assessing risk factors for infection of health care workers (HWs), and the design of prospective cohorts studies to determine maternal, pregnancy and neonatal outcomes for women and neonates with SARS-CoV-2 infections.

➔ **Objective 2: Describe disease severity and susceptibility.** Implement the Unity initiative and bring partners together under the Solidarity II as a global forum which promotes the implementation of serological studies for estimating the exposure to SARS-CoV-2 in the population. This facilitates collaboration between public health agencies, academic institutions and philanthropic foundations.

➔ **Objective 3: Evaluate control and mitigation measures.** Promote, facilitate and support epidemiological studies in countries with limited resources and expertise and build capacity in COVID-19 epidemiology.

Achievements

- 1. Coordination:** Regular contact has been maintained with key partners working on seroepidemiological initiatives, including the Pasteur Institute and the US Centers for Disease Control and Prevention (CDC), to share experience and ensure close alignment of activities, optimizing the use of limited resources.
- 2. Unprecedented and rapid data and material sharing across the seroepidemiological community.**
- 3. Capacity-building:** Countries in all regions have received technical support to build epidemiological capacity. As well as support for study design, protocol development and statistical analysis, scientific writing workshops have also been organized in different regions. To facilitate studies, some low-income countries have been provided with laboratory equipment, serology reference panels and WHO International Standards (antibody). Equipment for whole-genome sequencing has also been introduced into countries that previously lacked the capacity for such analyses.
- 4. Data analysis:** The WHO Regional Office for Europe (WHO EURO) and the European Centre for Disease Prevention and Control (ECDC) have collaborated on a systematic review and meta-analysis of published and unpublished data from sero-epidemiological studies. This has provided important insights into the severity of COVID-19 infections and SARS-CoV-2 transmission dynamics. In addition, WHO has worked with several partners in Australia, Thailand, Japan, and the Occupied Palestinian Territory to study the impact of public health and social measures (PHSMs), and has commissioned a modelling study to explore the impact of point-of-entry testing and quarantine.
- 5. Networking:** Several regions have established shared platforms to support the exchange of knowledge and standardization of methodologies. For example, a joint WHO EURO/ECDC seroepidemiology network involving more than 300 public health professionals has been established. In addition, a regular WHO AFRO seroepidemiology webinar series has been running since October 2020. Solidarity II calls are held on a weekly basis and allow partners across the globe

to share findings, methodology and raise challenges faced.

- 6. Vaccine effectiveness:** As vaccine rollout gains pace, mechanisms are being put in place to monitor vaccine effectiveness. Multiple factors related to target populations or vaccine schedules could influence vaccine performance and need to be monitored. The WHO Regional Office for Africa (WHO AFRO) has established a working group to develop guidance and standardized procedures for evaluating vaccine effectiveness, and collaborations with partners are exploring the potential for a region-wide vaccine effectiveness network.

Benefits

Standardization of approaches is widely recognized to be vital for quality assurance and ensuring the comparability of results. Epidemiological studies are essential for assessing COVID-19 disease burdens and patterns of infection to guide evidence-based control measures. A global picture of COVID-19 is vital for tracking COVID-19 hotspots and for identifying variants of concern (VOCs). Suppressing or controlling transmission through the implementation of effective and probable and confirmed cases; measures to protect high-risk groups; and vaccination, will reduce infection and disease and ultimately mortality.

Process

In collaboration with technical partners, WHO – through the Unity initiative - has developed eight, standardized epidemiological protocols. The Unity initiative has also assisted with the implementation of these studies in WHO Member States, facilitating coordination between key partners working on seroepidemiological initiatives, technical support to build epidemiological capacity, laboratory equipment and serology reference panels, data analysis and network-building.

In addition, the Solidarity II has established weekly calls between partners, provided materials (e.g. WHO international standards, reference panels, viral antigen plasmids) and training webinars for standardizing serological testing, sharing the latest scientific findings and fostering collaborations to progress the research on the seroepidemiology of SARS-CoV-2.

Outputs

Deeper knowledge of the routes of transmission of SARS-CoV-2 and when people are able to transmit the virus to others

- The virus mainly spreads between people in close contact through infected droplets and aerosols and at or around the time an infected person develops symptoms.
- Infection occurs through inhalation or inoculation through the eyes, nose and mouth.
- Long range aerosol/airborne transmission can occur in specific settings where aerosol generating procedures are conducted and in indoor settings where there is poor ventilation.
- People with and without symptoms can transmit the virus.
- Studies suggest that approximately 10%-20% of cases are responsible for 80% of transmission events.

Understanding of settings that appear to facilitate transmission

- Outbreaks and super-spreading events have been noted in several settings including, but

not limited to, (mass) social and religious gatherings, bars and nightclubs, some work places, and long-term living facilities.

- Closed settings, prolonged close contact and/or in indoor settings with inadequate ventilation facilitate transmission.

Better understanding of severity

- Infection fatality ratio estimates have been generated: 0.16 to 1.6 with all age groups considered; infection fatality rate (IFR) increases by age and is higher for people with underlying conditions.

Understanding effectiveness of public health and social measures (PHSMs)

- Timely and early implementation of a combination of measures is critical in relation to transmission dynamics.
- Gathering prospective data on social contact patterns is a useful complement to surveillance and PHSMs data to better understand the impact of interventions.
- Data on adherence/coverage and acceptability of measures are very useful but remain scarce.

Unity studies

WHO Unity studies are a global research initiative that seeks to increase evidence-based knowledge for action through standardized seroepidemiological (blood-based) and environmental research.

The initiative promotes standardized epidemiological, molecular and serological methods to facilitate international comparisons and cooperation so that both countries and the global community can collectively address knowledge gaps and inform an evidence-based COVID-19 response.

More than 100 countries have signalled their intention to implement one or more Unity protocols and studies are underway in over 50 countries.

The studies can be adapted to local settings and implemented rapidly to collect robust data on key epidemiological parameters to understand, respond to and control the COVID-19 pandemic.

Finally, Unity studies enable countries, regardless of their income, to conduct local investigations and are thus an invaluable tool for research equity.

4. Clinical management

Under this thematic area important and critical research was carried to advance our understanding of COVID-19 clinical characterization and management (CCM) including a large clinical research network led by WHO that advanced on our major work areas: clinical characterization, clinical research tools, rapid evidence appraisal of COVID-19 therapeutics, and a package of respiratory studies. Over time, this has expanded to include the new variants of concern (VOCs) and the appearance of post-COVID-19 condition (long COVID).

Aim

A key aim of the this thematic area of the global roadmap has been to fill gaps in knowledge to advance and optimize the safe supportive care of COVID-19 patients.

Five specific objectives underpinned the social sciences research agenda:

- **Objective 1:** Define the natural history of COVID-19 infection.
- **Objective 2:** Determine interventions that improve the clinical outcome of COVID-19-infected patients
- **Objective 3:** Determine optimal clinical practice strategies to improve the processes of care.
- **Objective 4:** Determine how best to link key research questions with researchers in affected regions who are able to recruit patients.
- **Objective 5:** Develop platform(s) to maximize commonality of data collection across trials and collaborations between trials.

Achievements

Clinical characterization:

1. **Launch of WHO Global Clinical Data Platform:** This global data platform includes anonymized patient records from more than 40 countries and continues to grow. A dashboard is in development to provide real-time visualization

of data to inform public health decision making. To date, the platform includes over 100,000 anonymized patient records from over 40 countries.

2. **Oxygen scale-up:** WHO led technical consultations with experts to address oxygen supply chain bottlenecks in support of adequate access worldwide, and to develop operational guidance on the scale-up of oxygen production at production facilities. In addition, technical support was provided to 18 countries to enhance oxygen supply systems. Throughout 2020, WHO has been coordinating the global multi-partner biomedical consortium, which has been working to expedite the supply of oxygen and related products for COVID-19 treatment. WHO is now leading the oxygen operations pillar of the Access to COVID Tool (ACT) Accelerator Oxygen Emergency Taskforce. A key aim will be to support the development of comprehensive applications from countries for support to scale up oxygen supplies.
3. **Oxygenotherapy** An observational study was done to define the availability and use patterns of oxygen therapy at COVID-19 facilities around the world, with a protocol under ethical review.
4. **Long COVID:** WHO led expert consultations on the long-term effects of COVID-19 infections in order to develop a clear definition of long COVID. A core outcome set was developed and a community consultation exercise is underway to finalize a definitive clinical description. A statistical analysis plan has been further developed for long COVID data in the global COVID-19 Clinical Data Platform.

5. **Evidence appraisals:** Through the WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACTS) initiative, expert groups have been established to undertake systemic evidence appraisals of IL-6 blockers. This may reduce the risk of severe inflammatory reactions, and anti-coagulants, which may in turn help prevent the development of harmful blood clots. The studies follow a common methodology and findings are being used to update 'living guidelines' for COVID-19 therapeutics.
6. **Respiratory studies:** A global expert working group has been established to develop a protocol for COVID-19 respiratory studies, including an interventional study to compare non-invasive respiratory interventions and their impacts on mortality. To underpin an interventional study, observational studies are being undertaken at 24 sites in six regions to better understand current oxygen and respiratory support practices.
7. **Clinical network:** A COVID-19 Clinical Network has been established to facilitate exchange of information and discussion of real-life challenges. This network has made important contributions to the development of enhanced case management for COVID-19.
8. **Clinical Characterization and Management Research Working Group:** This network meets once a week. Three sub-groups have been established to work on the two evidence appraisals and the respiratory studies. New sub-groups are being established to revise the COVID-19 severity classification and to oversee work on long COVID.
9. **A respiratory expert panel meets weekly to discuss innovations:** This panel is developing a compendium of innovations and a series of educational videos on use of medical equipment for COVID-19 treatment.
10. **Living Systematic Review of Pregnancy and COVID-19:** see publication.
11. **Observational cohort study of pregnant women with COVID-19:** Master Protocol.
12. **Observational cohort study of children with COVID-19.**
13. **Minimum common core outcome set for COVID-19** see publication.

14. **Case Record Forms (CRFs)** see above on Clinical Data Platform can be used for clinical trials.

15. **Prospective meta-analysis, WHO Rapid Evidence Appraisal of Therapeutics (REACTS) and COVID-19**

- Corticosteroids PMA.
- IL6 Receptor Antagonist PMA: see published protocol.
- Anticoagulation PMA: see published protocol.

Benefits

Better understanding of COVID-19 in sub-populations will help to target health interventions to these populations. Common metrics (severity definitions) and tools (clinical progression scale) will facilitate international data collection and aggregation.

Better understanding of the VOCs will support the planning of health systems in management of these patients, as well as understanding if there will be a differential impact with therapeutics (specifically antivirals). Conducting prospective meta-analysis allows for more rapid aggregation of published and unpublished data to inform timely production of WHO Living Guideline on Therapeutics and COVID-19.

Conducting research on oxygen use and availability and respiratory support interventions has the ability to advance and standardize the provision of safe care to patients with severe and critical COVID-19 in resource-limited settings. Sharing of data and experience has led to marked improvements in outcomes for COVID-19 patients. Multiple activities have helped to increase oxygen supplies to countries in need, and to identify the most effective ways to use oxygen therapy.

Process

We have a large global clinical research network that meets on a regular basis to advance on our major work areas: clinical characterization, clinical research tools, rapid evidence appraisal of COVID-19 therapeutics, and a package of respiratory studies to advance safe supportive care of COVID-19 patients.

Outputs

- a. <https://www.who.int/teams/health-care-readiness-clinical-unit/covid-19/data-platform/>. Four CRFs: core, pregnant women, Multisystem Inflammatory Syndrome in Adults (MIS-A), and post-COVID follow-up
- b. HIV sub-population report under review in PRC
- c. Dashboard under development (launch likely in one week, will add link)
- d. Living Systematic Review of Pregnancy and COVID-19: see publication <https://www.bmj.com/content/370/bmj.m3320>
- e. Cohort study of pregnant women with COVID-19 - Master Protocol: see website for more information: <https://www.who.int/reproductivehealth/topics/emergencies/COVID-19-SRH-Research/en/>
- f. Several guidelines and publications were produced cohort study of children with COVID-19 (see Appendixes)
- g. Minimum common core outcome set for COVID-19: see publication [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30483-7/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30483-7/fulltext)
- h. Case Record Forms (see above on Clinical Data Platform) can be used for clinical trials
- i. Corticosteroids PMA: see publication <https://jamanetwork.com/journals/jama/fullarticle/2770279>
- j. IL6 Receptor Antagonist PMA: see published protocol. https://www.who.int/publications/i/item/WHO-2019-nCoV-PMA_protocols-anti-IL-6-2021.1
- k. Anticoagulation PMA: see published protocol: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=213461
- l. Observational cohort study of children with COVID-19: see publications
 - m. Minimum common core outcome set for COVID-19 [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30483-7/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30483-7/fulltext)
 - n. Case Record Forms (see above on Clinical Data Platform) can be used for clinical trials. <https://www.who.int/teams/health-care-readiness-clinical-unit/covid-19/data-platform/>
 - o. Therapeutic evaluation: Prospective meta-analysis, WHO Rapid Evidence Appraisal of Therapeutics and COVID-19 (REACT) (Corticosteroids PMA; IL6 Receptor Antagonist PMA; Anticoagulation PMA)
 - p. Corticosteroids PMA: see publication <https://jamanetwork.com/journals/jama/fullarticle/2770279>
 - q. IL6 Receptor Antagonist PMA: see published protocol. https://www.who.int/publications/i/item/WHO-2019-nCoV-PMA_protocols-anti-IL-6-2021.1
 - r. Anticoagulation PMA: see published protocol: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=213461
 - s. Respiratory studies in COVID-19
 - t. Observational study to define the availability and use patterns of oxygen therapy at COVID-19 facilities around the world
 - u. Interventional study to evaluate efficacy of the various non-invasive respiratory devices.
 - v. Post-COVID-19 condition: meeting report <https://www.who.int/news-room/events/detail/2021/02/09/default-calendar/webinar-post-covid-19-condition>
 - x. Delphi survey for post-COVID-19 clinical case definition (in development)
 - aa. Delphi survey for post-COVID-19 core outcome set (in development)

5. Infection prevention and control, including health care workers' protection

Important and critical research was carried out to better understand infection prevention and control (IPC) measures required to inform recommendations and to optimize the effectiveness of personal protective equipment (PPE), in order to minimize the risk of SARS-CoV-2 transmission in both health care workers (HWs) and the community.

Aim

A key aim of the IPC thematic area of the roadmap has been to address knowledge gaps related to SARS-CoV-2 modes of transmission to identify effective countermeasures and to optimize the effectiveness of PPE.

Three specific objectives underpinned the IPC research agenda:

- ➔ **Objective 1:** Understand the effectiveness of public health and social measures (PHSMs) (movement control, mask-wearing, physical distancing, etc.) and IPC strategies to prevent secondary transmission in health care and community settings.
- ➔ **Objective 2:** Optimize the effectiveness of PPE and its usefulness in reducing the risk of transmission in health care and community settings.
- ➔ **Objective 3:** Identify the role of the environment in transmission.

Achievements

1. **Understanding HW infections:** WHO is leading an international multi-centre case control study assessing HW infections to identify risk factors associated with SARS-CoV-2 infections. The study involves over 20 countries and 130 sites, which have enrolled over 3,000 cases and controls to date has collected data on more than 3,000 health workers. The pooled data will provide a better insight into risk factors of HW infections from various countries, including stratifications by income level and geographical region.

2. Understanding modes of transmission:

Extensive systematic reviews were carried out on modes of transmission for SARS-CoV-2 and associated questions such as infectious dose, the distance that droplet can travel, the role of ventilation, and of the environment in transmission. Living systematic reviews were developed for five key modes of transmission (droplets/airborne, close contact, fomites, oro-faecal and vertical transmission).

3. Optimizing the usability and effectiveness of PPE and non-medical masks in real-world settings:

Multiple ongoing research projects aim to assess human factors and user preferences, contamination risks, and engineered textile considerations for protection/source control effect of PPE, and non-medical masks used in the community. A randomized controlled trial (RCT) is currently ongoing with the aim of comparing the effectiveness of medical masks and respirators at preventing SARS-CoV-2 infection during non-critical care of patients with COVID-19. A community study is ongoing to include a testing strip within face masks as a non-invasive way to obtain community surveillance samples, in particular persons with asymptomatic infections.

4. Improving PPE effectiveness and addressing shortages:

Multiple studies are underway to identify improvements to the design, performance testing, and reprocessing capacities for PPE and non-medical masks, in particular, a novel way to assess mask fit without the use of fit-testing. In the context of supply shortages and logistical concerns that continue to impact remote communities, innovative methods are being studied to inform guidance for reprocessing PPE during severe shortages (applicable in all resource settings) and transportation of PPE and other medical supplies by drone.

5. Implementing research to better understand SARS-CoV-2 transmission in hospital settings:

Multiple studies on SARS-CoV-2 transmission were carried out in hospital settings. These included work on hospital-based SARS-CoV-2 surveillance systems, as well as studies assessing the impact of COVID-19 on antimicrobial resistance (AMR) and the spread of hospital-acquired infections.

6. Building evidence for non-pharmaceutical interventions:

Ongoing comprehensive evidence syntheses were conducted on non-pharmaceutical interventions to reduce the spread of respiratory viruses, to inform the development of SARS-CoV-2 control measures and guidance.

7. Understanding the cost-effectiveness of IPC interventions:

WHO is working with the Organisation for Economic Cooperation and Development (OECD) to investigate cost-effectiveness of IPC interventions to prevent SARS-CoV-2 transmission and outbreaks in clinical settings.

8. Standardization of processes, protocols and tools:

The development of protocols and tools was a key part of the work undertaken, especially on reprocessing, decontamination and PPE design. An additional study explored the impact of decontamination on mask fit, and the human factors that may affect the willingness of HWs and the general public to use reprocessed masks.

9. Establishing IPC data monitoring platforms:

A global online resource and data portal for monitoring IPC at national and facility level has been developed and was launched on 5 May 2021. One tool for assessment of the minimum requirements for IPC programmes at the national level was made available for the launch; the portal will further include tools and indicators related to facility level assessments, including preparedness, readiness and response to COVID-19. This will help provide better insights into what countries are doing and where there may be gaps that need improvement.

Benefits

The evidence generated by this research has supported and will further inform measures and guidance to reduce the risk of SARS-CoV-2

transmission and provide protection of HWs and members of the general public. The activities aim to identify the factors influencing nosocomial transmission of SARS-CoV-2 and the most appropriate IPC measures for COVID-19, and to evaluate innovations to improve the design of PPE and optimize its use.

Process

IPC research is supported by a group of international experts named the WHO COVID-19 IPC R&D Expert Group. This group works in concert with the WHO Secretariat, other experts and other COVID-19 research pillars and working groups, with the purpose of facilitating coordination and collaboration of research and innovation, and boosting synergy in the field of IPC during the response to the COVID-19 pandemic.

The international expert group is focused on specific projects for stimulating and steering research and innovation, supporting timely generation and dissemination of research results, developing evidence-based recommendations and technical guidance, developing and improving access to relevant tools, investigating the impact on health care-associated infections, and ensuring that the needs of low- and middle-income health care settings and countries are taken into consideration in the development of protocols and designs. Moreover, it regularly contributes to the multidisciplinary research agendas, including other areas such as social science, environmental health science and epidemiology.

Outputs

While many studies are still ongoing, the areas of research described above, have generated the following outputs so far:

Objective 1: Understand the effectiveness of PHSMs (movement control, mask-wearing, physical distancing, etc.) and IPC strategies to prevent secondary transmission in health care and community settings. The COVID-19 IPC R&D Expert Group has led or participated in seven systematic reviews and 26 primary studies; WHO is leading a global multicentre case-control study assessing HW risk factors for SARS-CoV-2 infection and their clinical presentation through serologic responses over time, as well as the set-up of an IPC monitoring portal and the development of a research agenda for hand hygiene in the context of

COVID-19. Many of these studies are ongoing; here we present some highlights of available results:

- A study modelling European non-pharmaceutical intervention data found that prohibiting of mass gatherings and closure of education facilities and some non-essential businesses was associated with reduced incidence of SARS-CoV-2 infection, whereas stay at home orders and closure of all non-essential businesses was not associated with any additional protective impact.
- A Singapore study assessing asymptomatic attack rates and transmission among close contacts in the community found that the symptom-based testing strategy missed about 62% of cases. They also found that the risk of infection for household contacts increased by sharing a bedroom or speaking with an index case for more than 30 minutes. (Ng et al, 2020). Among non-household contacts, exposure to an index case by speaking for 30 minutes or longer and sharing a vehicle were associated with increased risks. The evidence from this study informed the guidance on physical distancing, mask use in the community, and home care recommendations.
- A systematic review which assessed the effects of physical distancing was conducted to inform guidance on the recommendation of physical distancing resulting in the reinforcement of WHO's guidance on distancing measures of at least one-meter distance.

A key aspect of this objective has been to address the burden of infection in HWs and related risk factors.

- A living systematic review of evidence on HWs has reported a prevalence of SARS-CoV-2 seropositivity among HWs ranging from 1.4% to 32.2%. It identified risk factors for HW infection such as involvement in high-risk procedures (e.g. intubations, direct or intense patient contact, or contact with bodily secretions). IPC training and education, as well as correct use of PPE were associated with decreased risk of infection. This review also found that universal masking policy in health care facilities was associated with decreased risk of SARS-CoV-2 infections in HWs.
- The WHO international multicentre case control study of risk factors for SARS-CoV-2 infections

in HWs started in May 2020 and is currently running in over 20 countries and 130 sites, which have enrolled over 3,000 cases and controls to date.

Additional studies have investigated the burden of hospital onset COVID-19 infection.

- Researchers in a UK university hospital developed a surveillance system to detect and investigate health care-associated SARS-CoV-2 transmission (nosocomial COVID-19). This research involved testing the system and its successful integration in the national surveillance, and understanding the relative weight of nosocomial COVID-19 transmission to the overall impact of the pandemic. Furthermore, researchers found that wards involved in admission pathways and in a high number of connections were at higher risk (representing hubs of transmission due to high frequency of movement through wards). These findings allowed targeting strengthening of IPC measures in specific risk areas.

Objective 2: Optimize the effectiveness of PPE and its usefulness in reducing the risk of transmission in health care and community settings. The R&D Blueprint has outlined priority research areas and open challenges associated with effectiveness, compliance and safety of PPE in health care and non-medical masks used in community settings, including: effectiveness of different types of PPE to prevent transmission, PPE decontamination methods with applicability in resource-limited settings, improved and innovative material/textile engineering for PPE and community masks, user-preferences and comfort, contamination risks during activities and procedures in health care and community settings, and surveillance of the relative infection prevention effect of various types of PPE in real-world settings. In this priority area, members of the COVID-19 IPC R&D Expert Group have led or participated in four systematic reviews and 20 primary studies.

- A consortium of 52 researchers and scientists involved in the 'Development of Methods for Mask and N95 Decontamination' (DeMaND) study across 13 university and laboratory research groups is actively contributing to a novel, low-cost, decontamination method using 'methylene blue dye' (an existing WHO essential medicine) plus a light source activation mechanism (ultraviolet, sunlight,

phosphorescent) to generate singlet-oxygen capable of deactivating SARS-CoV-2 and other pathogens on PPE. The DeMaND study includes robust multidimensional research aimed at assessing effectiveness against pathogens on a variety of PPE and community masks, optimal application and reapplication methods for methylene blue dye and light sources, and post-reprocessing evaluation of functional and inhalational safety for reuse of PPE after decontamination. An article by the DeMaND consortium, accepted for publication and available in pre-print, reported that the decontamination treatment using methylene blue and light robustly and consistently inactivated all three coronaviruses tested (including SARS-CoV-2) on respirators and medical masks with at least a four-log reduction, while maintaining their integrity and fit.

– Three primary studies by Ludwig-Begall et al. assessing decontamination of masks and respirators using various methods and treatments (vaporized hydrogen peroxide, ultraviolet germicidal irradiation, and dry heat) and their relative effect on the integrity and fit after multiple cycles have demonstrated that these methods can prove effective against a range of pathogens present in the health care setting, including norovirus and SARS-CoV-2 surrogates; however, each method has limitations in the number of cycles that can be performed before functional degradation of the mask or respirator is experienced.

– A study by Ong et al. assessed the potential for SARS-CoV-2 contamination on PPE but did not find any SARS-CoV-2 particles on any of the PPE sampled. Limitations to this study were that it was done in airborne isolation rooms and it may not be generalizable to other room configurations. Indeed, preliminary results from other investigators included in the COVID-19 IPC R&D Expert Group found widespread contamination using a respiratory particulate tracer surrogate of PPE and rooms where anaesthesia and airway procedures are undertaken.

➔ **Objective 3:** Identify the role of the environment in transmission. The role of the environment in SARS-CoV-2 transmission (including aerosol and fomite) has been addressed through 11 primary

studies. Some studies have provided evidence that was considered to inform guidance development:

– A study investigating the presence of SARS-CoV-2 on surfaces found virus contamination detected by polymerase chain reaction (PCR) in several surfaces in health care settings where COVID-19 symptomatic positive patients resided, in particular in bathroom settings (toilet bowl and sink samples), suggesting the presence of viral shedding in stool and that environmental contamination could play a role in transmission, although viral culture was not done to demonstrate virus viability (Ong et al., 2020). The study also found that current cleaning and decontamination recommendations are sufficient for eliminating surface contamination.

– A study by Ong et al. (2020) aimed to determine the extent of shedding of viable SARS-CoV-2 in respiratory aerosols from COVID-19 patients. SARS-CoV-2 particles could be found by PCR in aerosols using various air sampling methods; however, the same PCR-positive air samples were negative on viral culture, indicating no detectable viable virus in air particles. Environmental samples yielded the same type of results.

– Another study in ICU settings by Ong et al. (2020) was able to detect SARS-CoV-2 at various particle sizes in air samples in ICU airborne isolation rooms suggesting risk of infection in settings where aerosol-generating procedures (AGPs) are performed. Viable virus was not found through cell culture from environmental samples.

– Another study by Chia et al. (2020) compared ICU settings with the general wards and was able to find particles of larger sizes in the ICU settings' air samples (1-4µm and >4µm), but was not able to capture smaller particles in these air samples (<1µm); additionally all rooms that had positive air samples also had PCR-positive surface contamination detected indicating the possibility for fomite transmission of SARS-CoV-2 virus. Both of these findings correlated with the day of illness and nasopharyngeal viral loads of COVID-19 patients suggesting the presence of SARS-CoV-2 in the air is possibly highest in the first week of symptomatic illness.

6. Candidate therapeutics R&D



© WHO / Blink Media / Hannah Reyes Morales

Core (Master) Protocols have been developed at an unprecedented rate This has significantly accelerated the evaluation of promising novel and repurposed therapeutics, in particular through a few large adaptive, platform trials, using innovative designs and rigorous methods, and enabling collaboration between multiple sites, countries and regions, as well as stimulating developer and manufacturer engagement. Meanwhile, screening and prioritization of compounds for preclinical and clinical evaluation was organized with a gradual but steady improvement in global dialogue and coordination.

Aim

Three specific objectives underpinned the therapeutics research agenda:

- ➔ **Objective 1:** Continuously identify candidates for clinical evaluation and scan the landscape of scientific evidence.
- ➔ **Objective 2:** Develop multicentre core protocols to evaluate efficacy and safety in randomized clinical trials.
- ➔ **Objective 3:** Coordinate and collaborate internationally to implement clinical trials for evaluation of the safety and efficacy of therapeutics.

Achievements

1. **Global coordination:** Multiple efforts have been made to enhance coordination of COVID-19 therapeutics research, to avoid unnecessary duplication of efforts, to promote standardized approaches that ensure the comparability of results, and to provide platforms for sharing of data. National, regional and global coordination has been essential to create the platforms able to carry out large-scale randomized studies. Support has included the development of a repository list of laboratories holding COVID-19 isolates, ensuring the availability of animal models, developing standardized protocols for virus propagation and testing, establishing a repository for in vitro and in vivo test data, and maintaining free online resources on drug interactions.

2. Discussion of research methods and emerging evidence:

The convening of experts and the facilitation of discussion forums were intense and multidisciplinary. Large-scale collaborations have been established through multiple expert working groups with global representation and covering key areas of COVID-19 therapeutic development including:

- Development of target product profiles (TPPs) for COVID-19 therapeutics
- In vitro and in vivo testing to support COVID-19 therapeutic development
- Clinical trial design and methodologies
- Development of the core protocols and standard operating procedures (SOPs)
- Clinical research coalitions, focusing on research in low- and middle-income countries (LMICs)

3. Research landscape: The COVID-19 living mapping of ongoing research shows where all registered treatment trials are currently being conducted and the nature of those studies. The map is an interactive online data visualization with a weekly update on the aggregation of emerging evidence generated from clinical trials on pharmacological and non-pharmacological treatment of COVID-19, as well as preventive interventions. This is intended to help researchers and funders plan for future trials, as well as regulatory authorities and guideline developers in evidence-based decision making.

The COVID-19 living evidence synthesis of trial results provides a constantly updated list of treatment comparisons and the evidence underlying such comparisons, including a detailed description of primary studies, an assessment of risk-of-bias, an analysis and a grading of the evidence. It is a living database with weekly updates of a comprehensive systematic review bringing into a single interactive tool all the trials with results in the R&D pipeline on COVID-19 treatment: this enables the user to explore a range of key data related to the treatment and this is intended to assist decision-makers.

The COVID-19 drug interactions provides information on the likelihood of interactions between the experimental agents used for the treatment of COVID-19 and commonly prescribed co-medications.

4. Evidence generation and synthesis: Initially focused on repurposed medicines, large platform trials, such as the UK Randomised Evaluation of COVID-19 Therapy (RECOVERY) Trial, the US Adaptive COVID-19 Treatment Trial (ACTT) and the Accelerating COVID-19 Therapeutics Interventions and Vaccines (ACTIV) networks, the global Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) network, and the Solidarity Trial Vaccines (STV) therapeutics were rapidly established to collect high-quality evidence on potential treatments.

These international platforms have generated vital data on the safety and efficacy of COVID-19 therapeutics, allowing for rapid adjustment of standards of care when appropriate. The inexpensive and widely available steroid dexamethasone has notably demonstrated strong evidence of clinical benefits, reducing deaths by up to one third in hospitalised patients with severe respiratory complications of COVID-19.

The benefits of immunomodulators targeting the IL-6 pathway such as tocilizumab or sarilumab have been reported to add to those of steroids. In contrast, unpromising overall findings have been reported on the use of other agents. The dosing regimens of remdesivir, hydroxychloroquine, lopinavir-ritonavir and interferon beta-1a had little or no effect on hospitalized patients with COVID-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay.

No convincing evidence of meaningful clinical benefit from convalescent plasma or azithromycin has been demonstrated in patients admitted to hospital with COVID-19 either.

There is a need for better treatments, and all these platforms are actively pursuing evaluation of further drugs, including combinations of treatments. Each trial platform has established mechanisms to prioritize of candidate drugs to be evaluated. These share common features, including open submission processes, assessment and triaging by independent expert groups, and final prioritization by overarching committees and triallists. Large amounts of data have been made available, although greater sharing of landscaping and evaluation material would be beneficial.

Benefits

From a global perspective, much has been achieved over the past year. There is global consensus on the importance of large, well-conducted trials delivering robust evidence, and that duplication of efforts wastes resources. The progress achieved by large platform trials show that large international trials are possible, even during a pandemic, and offers the promise of quickly and reliably answering critical public health questions concerning therapeutics. The evidence generated is ensuring that health care resources are reserved for treatments of known therapeutic benefit.

These trial platforms have the potential to be used to evaluate both repurposed medicines and newly developed therapeutics in a wide range of global settings. Trial data are also important to understand the mechanisms of COVID-19 disease and to identify biomarkers associated with disease progression and response to therapy, which will facilitate patient management as well as therapeutic development.

Outputs

In April 2021, 2,910 treatment trials were registered, of which 1,472 were recruiting patients. However, most of these trials were inconclusive and produced unreliable data:

- The COVID-NMA initiative: Living Mapping of Trials - a living mapping of all registered trials
- The COVID-NMA initiative: Living Synthesis of Published Trials - a living synthesis of trial results
- COVID-19 Drug Interactions - a drug interactions resource

In the current pandemic context where a single “quick fix” solution is unlikely, slight to moderate benefits would be significant and this requires large-scale randomized evidence that can be generated in large, ongoing platform trials. The main major platform trials underway are:

- UK Randomised Evaluation of COVID-19 Therapy (RECOVERY) Trial
- Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)
- Randomized Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP)
- ANTICOV adaptive platform trial
- Solidarity Trials of COVID-19 therapeutics and vaccines



© WHO / Blink Media / Hannah Reyes Morales

Solidarity Trial Therapeutics (STT)

Among the largest international randomized trial platforms for COVID-19 treatments

The rapid spread of COVID-19 led to a huge demand for effective treatments. In the absence of reliable data, many therapeutics were introduced, sometimes supported by far from robust scientific evidence. In response, on 18 March 2020, WHO launched the Solidarity Trial Therapeutics (STT) to fast-track research on treatments that worked.

The STT's innovative approach is based on:

- **Simplicity** by focusing on questions of public health importance, and simplifying procedures with a randomized control clinical trial (RCT) protocol and a paperless online data and randomization system allowing for rapid centralized analyses. The adaptive study design allows novel treatment arms to be added while the trial is in progress or discontinuing some treatment arms that are proven to be ineffective or unsafe.
- **Scale** by prioritizing counties at highest risk and hospitals that have the most number of adults hospitalized with definite COVID-19 symptoms and no contra-indication to any of the study drugs; this approach ensures the greatest level of enrollment and enables rapid generation of accurate results based on a large sample size.
- **Access and collaboration** by ensuring all countries can join the STT as cosponsors and receive WHO technical and financial support including free access to all trial drugs, thanks to donations negotiated with collaborating developers and manufacturers.

By the end of 2020, the therapeutics ST became one of the largest international randomized trial platforms for COVID-19 treatments. More than 30 countries from all WHO regions had joined the trial. These countries represented over over 500 hospitals worldwide and several thousands of clinicians that enrolled over 15,000 patients. Interim results on the first four repurposed drugs were published early December 2020:

“These remdesivir, hydroxychloroquine, lopinavir, and interferon regimens had little or no effect on hospitalized patients with COVID-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay.

For each of these four repurposed nonspecific antivirals, several thousand patients have now undergone randomization in various trials. The

unpromising overall findings from the regimens tested suffice to refute early hopes, based on smaller or nonrandomized studies, that any of these regimens will substantially reduce inpatient mortality, the initiation of mechanical ventilation, or hospitalization duration. Narrower confidence intervals would be helpful (particularly for remdesivir), but the main need is for better treatments. The Solidarity Trial has been recruiting approximately 2000 patients per month, and efficient factorial designs may allow it to assess further treatments, such as immune modulators or anti-SARS-Cov-2 monoclonal antibodies.”¹

“The quest for knowledge about the coronavirus is a global effort. The Solidarity Trial is an important part of the puzzle. I am proud that Norway will contribute by having the first patient included in the study. I would like to commend the WHO for the global leadership and its initiative in setting up the Solidarity Trial.” **Bent Høie**,
Minister of Health and Care Services, Norway

Although the results for the first four treatment options evaluated were unpromising, they were highly informative for policy makers and clinicians worldwide.

As of May 2021 the global platform of the STT has expanded to new countries and is getting ready to rapidly evaluate new treatment options in a second period, officially called “Solidarity Plus”. After careful considerations of newer antithrombotics, antivirals, immunomodulators, and anti-SARS COV-2 monoclonal antibodies, a number of new treatments have been recommended by an independent advisory group of experts.

The progress achieved by the STT of COVID-19 therapeutics shows that large international randomized trials are possible, even during a pandemic, and offers the promise of quickly and reliably answering critical public health questions concerning therapeutics. Trials have been vital in demonstrating the therapeutics impact or lack thereof, so that more lives can be saved, and health care resources can be used on treatments of proven efficacy. This global platform trial will continue to efficiently evaluate promising new treatment options.

¹ Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results | NEJM

7. Candidate vaccines R&D



© WHO / Blink Media / Andrew Quilty

Important and critical work was carried out to advance our understanding and research for safe and effective COVID-19 vaccines and to accelerate and coordinate the research, development and evaluation of candidate products. Core protocols have been developed at an unprecedented speed as duly committed under the eight immediate research actions agreed at the Global Research Forum 2020.

Aim

Three specific objectives underpinned the vaccines research agenda:

- ➔ **Objective 1:** Continuously identify candidates for clinical evaluation and scan the landscape of scientific evidence.
- ➔ **Objective 2:** Develop multicentre core protocols for a standardized approach to assess efficacy and safety in randomized clinical trials.
- ➔ **Objective 3:** Coordinate and collaborate internationally to implement clinical trials, for evaluation of the safety and efficacy of vaccines.

Achievements

- 1. Global coordination:** Multiple efforts have been made to enhance coordination of COVID-19 vaccine research, to avoid unnecessary duplication of efforts, to promote standardized approaches that ensure the comparability of results, and to provide platforms for sharing of data. Support has included development of a repository list of laboratories holding COVID-19 isolates, ensuring the availability of animal models and developing standardized protocols and preferred characteristics of a vaccine.
- 2. Discussion of research methods and emerging evidence:** Multiple expert working groups were established to promote greater coordination in COVID-19 vaccine-related R&D. These include groups focusing on:

- **Target product profiles (TPPs):** This group was developed through a broad and multidisciplinary consultation process with key stakeholders in human and animal health, with the aim of guiding and prioritizing the development of vaccines. It describes the preferred and minimally acceptable profiles for human vaccines for long term protection of persons at high ongoing risk of COVID-19 such as health care workers (HWs) and for reactive use in outbreak settings with rapid onset of immunity.
- **Animal models:** The working group on animal models was established on February 2020 and has been developing preclinical models of SARS-CoV-2 infection. Since its inception, the goal of this WHO COVID Modelling Group has been to accelerate the development of COVID-19 vaccines and therapeutics by rapid sharing of data among member scientists worldwide. In addition, another main focus of the group was to assess vaccine-associated enhanced respiratory disease (VAERD) and antibody-mediated disease (ADE enhancement) in animal models.

The group has identified a portfolio of models to assess pathogenesis, transmission and SARS-CoV-2 immunity; and to accelerate therapeutic and vaccine development. Unprecedented data sharing avoided unnecessary experiment repetition. Organs on chip technology surfaced as an alternative to animal modelling for several applications. In addition, immunology studies showed no evidence of VAERD and served to investigate biomarkers and vaccine correlates of protection. Remarkably, preclinical studies matched Phase I, II clinical data. The assessment of variants of concern (VOCs) transmission, pathogenesis and immune escape reinforced the importance of virus sharing and the identification of secondary reservoir and species tropism has been unprecedented.

Lastly, the importance of viral working stock propagation has been highlighted in several months of collaborative international work and data sharing. This has been summarized in a short publication under review. This publication provides a cautionary note about ensuring working stocks are not compromised by the accidental generation of mutations and/or deletions in laboratory working stocks.

- **Assay development:** The working group on assays was established on February 2020. The expert group that focuses on COVID-19 viruses, reagents and immune assays have been developing standardized assays for measuring immune responses to ensure comparability. Early topics of the group included status updates on the development and availability of SARS-CoV-2 viral isolates and other critical reagents and discussions of the potential for cross-reactivity between SARS-CoV-2, SARS-CoV-1 and MERS-CoV. Then transitioned to the development of immune assays, cross reactivity, duration of immunity, assay comparisons, and assay harmonization, based on antibody standards. Some of the key achievements from the group are listed below:
 - Viruses and other key reagents such as expression plasmids, proteins and antibodies have been made widely available through repositories such as BEI Resources, NIBSC and the European Virus Archive as well as directly from lab to lab, as well as commercial sources. Multiple assays have been developed to measure binding antibodies against full-length Spike protein, portions of the Spike protein such as RBD, or the N protein. This includes multiple formats such as ELISA and ECL assays. Wild-type virus neutralization assays, pseudovirus neutralization assays and surrogate neutralization assays are available and being used to assess neutralizing antibody titers. In many cases, good correlation is observed between binding assays and neutralization, although this is influenced by the format of the assay.
 - A WHO International Standard (IS) for anti-SARS-CoV-2 immunoglobulin was developed by NIBSC and approved by the WHO Expert Committee on Biological Standardization in December 2020.
 - wtVNA and psVNA have been established in multiple laboratories for the WHO Variants of Concern (VOC) as well as for several Variants of Interest (VOI) to assess changes in neutralization activity for convalescent and vaccine sera.
 - Assays to assess T cell responses to SARS-CoV-2 infection as well as vaccination have been established in multiple laboratories. These have also been applied to VOCs.

- Duration of binding antibody, neutralizing antibody and T cell responses to SARS-CoV-2 infection has been assessed in multiple studies. Conditions used to culture SARS-CoV-2 are critically important. Multiple passages in Vero cells can lead to the proliferation of mutations, especially of the Furin cleavage site in the Spike protein. In studies of antibody cross reactivity with other coronaviruses, there has been little cross reactivity observed with seasonal human betacoronaviruses, some cross reactivity with MERS-CoV and the most cross reactivity with SARS-CoV. Neutralizing antibody and Fc functional antibody responses were both found to correlate with protection from SARS-CoV-2 disease in re-infection, adoptive transfer and vaccine studies in non-human primates.
- **Clinical trial design:** A group of experts in clinical trials, regulatory, and outbreak management provided advice and considerations on appropriate phase 2b/3 trial designs to assess safety and efficacy of vaccines during public health emergencies (PHEs).
- **Core protocol development:** A group of multidisciplinary experts drafted a core protocol for the global platform trial, the vaccines ST, with the aim of rapidly evaluating multiple candidate vaccines and providing sufficient evidence of safety and efficacy against COVID-19 to support decision-making about vaccine deployment.
- **Vaccine prioritization:** The expert group established criteria for selection of vaccines for clinical trials and prioritizing the most promising candidates for inclusion. The group produced a table that outlines the criteria and the scoring system for assessing the inclusion of a candidate vaccine.
- **Human challenge studies:** The Advisory Group on Closely Monitored Challenge Models of Experimental COVID-19 Infection and Illness in Healthy Young Adult Volunteers developed a set of recommendations to inform the design and implementation of controlled human infection studies. Two groups have started human challenge studies with low-risk healthy individuals (aged 18-30) to initially determine through dose escalation the target dose of

challenge agent that will elicit an asymptomatic level of illness. The studies have received ethical approval and aim to assess antivirals and/or candidate vaccines and establish correlates of protection in previously infected individuals.

In addition, online research forums have been established to facilitate global discussions on key aspects of vaccine development and to encourage the sharing of data and experiences, with a focus on key issues such as:

- **Knowledge gaps and research priorities.** Discussing the current state of COVID-19 vaccine development and future research priorities and needs. Much remains unknown about current COVID-19 vaccines and there is a need to increase global manufacturing and capacity. There are questions remaining about the duration of protection and the impacts on viral transmission, long-term safety and activity against emerging variants. There is also a need for global collaboration, data sharing and standardized assays, and a clinical data repository to support research. Technical discussions will continue to support research groups towards ensuring the quality of challenge studies in terms of standards, norms and harmonization of the protocols.
- **SARS-CoV-2 variants: Knowledge gaps and research.** Developing and agreeing on an R&D agenda in response to existing and emerging SARS-CoV-2 variants. Assessing the implications of VOCs for vaccine development and developing mechanisms to track and respond to them. The following priority areas of research were identified: i) detection of variants and the need for a global surveillance strategy to detect and track new VOCs; ii) understanding the epidemiology and evolution of variants; iii) understanding variant biology and how mutations affect the biology of variant SARS-CoV-2 strains; iv) understanding clinical impacts and consequences of infection with variants; and (v) understanding the impacts on vaccine effectiveness. WHO is outlining the pathway for assessing vaccines in the context of variants for current, modified and new vaccines. Additionally, sharing, standardization, data integration, capacity-building, new diagnostic tools and leveraging trials and cohort studies, nomenclature, communication and global coordination were identified as important research facilitators.

- **Study designs:** Potential designs and methodological approaches for clinical trials and observational studies have been developed to assess the impact of variants on vaccine efficacy and effectiveness. Multiple vaccines are being rolled out globally and are seen as pivotal to COVID-19 control. However, SARS-CoV-2 is prone to mutation and multiple variant strains have been identified. The key outcomes from this forum where i) WHO must play a role in coordinating activities to identify the need for vaccines against new SARS-CoV-2 variants and the sequences that are most appropriate for global use; ii) as vaccines are deployed, it will be essential to gather data on their performance against evolving variants; iii) regulatory alignment at global level is important; iv) communication should be prioritized to raise awareness of challenges and ongoing activities.
- **Data and material sharing:** Encouraging more rapid sharing of data and virus samples for analysis.

Furthermore, an Agile Vaccine Research Working Group holds monthly meetings to provide updates of COVID-19 vaccine research progress with the ability to pivot, given dynamic research needs, and to facilitate rapid dissemination and open discussion of research protocols and emerging results. This forum provides space to vaccine developers and funders to share information on their research plans and priorities including those related to variants.

3. Research landscape: The COVID-19 living map is an interactive database that provides instant access to all registered clinical trials (both randomized and non-randomized) being conducted worldwide on novel COVID-19 vaccines. The COVID-19 living evidence synthesis of trial results provides a constantly updated list of vaccine comparisons where data are available, as well as the general characteristics of each trial with an assessment of risk-of-bias (evidence synthesis and profile for phase 2-3 trials; risk-of-bias assessment for safety outcomes only for phase 1-2 studies). The COVID-19 candidate vaccine landscape and tracker is a comprehensive COVID-19 vaccine landscape listing all the pre-clinical and clinical vaccine candidates being developed worldwide. Updated weekly, the landscape tracks the progress of each candidate vaccine from pre-clinical through to Phase 1, 2, 3 and 4

studies, as well as providing links to published reports on the safety, immunogenicity and efficacy data. The landscape of observational study designs on the effectiveness of COVID-19 provides an overview of observational studies which evaluate the effectiveness of COVID-19 vaccination in real-world settings, assessing endpoints on immunity, infection, transmission, efficacy and safety. It includes key features in terms of study design, sample size, study population, key outcomes measured and location of study.

4. Evidence generation and synthesis

Several living and interactive maps and evidence syntheses are available at the R&D Blueprint webpage. The COVID-19 living map provides instant access to all registered clinical trials being conducted worldwide. The landscape of observational studies focuses on the effectiveness of COVID-19 vaccination in real-world settings.

5. Vaccine safety: Guidance on the development of pharmacovigilance capacity to monitor vaccine safety, assessment of rare cases of side-effects in vaccinated people and actively reviewing emerging evidence in collaboration with regulatory authorities. WHO is also coordinating research to help understand the risk of any emerging safety concern, such as background rates, potential mechanisms of action and possible mitigating measures.

Solidarity Trial Vaccines (STV): Setting the stage for additional vaccine development and clinical evaluation, the ST of COVID-19 vaccines will be launched as a large, international, randomized clinical trial platform to rapidly and efficiently evaluate the efficacy and safety of multiple candidate COVID-19 vaccines and to ensure that as many of the vaccine candidates still in development have the best chance of success. Its aims are to evaluate efficiently and rapidly (within 3–6 months of each vaccine’s introduction into the study) the efficacy of multiple vaccines, helping to ensure that weakly effective vaccines are not deployed. High enrollment rates facilitated by flexible trial design and hundreds of study sites in high-incidence locations will yield results on short-term efficacy for each vaccine within just a few months of including that vaccine in the trial. Preparations are complete to initiate the trial in two countries in at least 15 trial sites with an anticipated enrollment rate of 200 patients per site per week.

Dates when information on efficacy for selected vaccines was first announced

Vaccine	Efficacy results	
	Date of first released information	Press release link
Pfizer-BioNTech	09 November 2020	https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-vaccine-candidate-against
Sputnik V	11 November 2020	https://sputnikvaccine.com/newsroom/pressreleases/the-first-interim-data-analysis-of-the-sputnik-v-vaccine-against-covid-19-phase-iii-clinical-trials/
Moderna	16 November 2020	https://investors.modernatx.com/news-releases/news-release-details/modernas-covid-19-vaccine-candidate-meets-its-primary-efficacy
AstraZeneca-University of Oxford	23 November 2020	https://www.astrazeneca.com/media-centre/press-releases/2020/azd1222hr.html
Sinopharm	29 December 2020	https://www.biospace.com/article/china-s-sinopharm-claims-covid-19-vaccine-has-79-percent-efficacy/
Sinovac Biotech	13 January 2021	https://www.bbc.com/news/world-latin-america-55642648
Novavax	28 January 2021	https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3
Johnson & Johnson	29 January 2021	https://www.inj.com/johnson-and-johnson-announces-single-shot-janssen-covid-19-vaccine-candidate-meets-primary-endpoints-in-interim-analysis-of-its-phase-3-ensemble-trial
CanSino Biologics	08 February 2021	https://www.bloomberg.com/news/articles/2021-02-08/pakistan-says-cansino-s-covid-vaccine-shows-65-7-efficacy In China, administered to military personnel since June 2020
Bharat Biotech	04 March 2021	https://www.pharmaceutical-technology.com/news/bharat-biotech-vaccine-efficacy/

Benefits

Safe and effective COVID-19 vaccines have been developed at unprecedented speed, with the first vaccinations taking place less than a year after SARS-CoV-2 was first identified. The speed of vaccine development has depended on extensive collaboration and cooperation between multiple stakeholders. Even so, further vaccines are still required to increase global manufacturing capacity, to provide products with additional desirable properties, and potentially to address SARS-CoV-2 VOCs.

Outputs

In April 2021, 235 randomized vaccine clinical trials and 90 non-randomized studies of vaccines were registered, of which 153 were recruiting patients. A total of 280 vaccines were in development: 183 in preclinical and 97 in clinical development.

- [WHO Target Product Profiles for COVID-19 Vaccines](#) - preferred characteristics of a COVID-19 vaccine
- [The COVID-NMA initiative: Living Mapping of Trials](#) - a living mapping of all registered vaccine trials

- [The COVID-NMA initiative: Living Synthesis of Published Trials](#) - a living synthesis of vaccine trial results
- [The COVID-19 candidate vaccine landscape and tracker](#) - a living compilation on vaccine candidates in development
- [The landscape of observational study designs on the effectiveness of COVID-19 vaccination](#) - a living compilation

Animal models

- [Global animal laboratories capacities to support vaccine and therapeutic evaluation, 13 August 2020.](#)
- [COVID-19 Animal Models Summary of progress made by the WHO COVID-19 modelling ad hoc Expert working Group, 26 March - 1 June 2020.](#)
- [COVID-19 Animal Models Summary of progress made by the WHO COVID-19 modelling ad hoc expert working group, 15 March - 26 March 2020](#)
- [COVID-19 Animal Models Summary of progress made by the WHO COVID-19 modelling ad hoc Expert working Group, 27 February - 15 March 2020](#)

Assay development

- [COVID-19 Summary of progress made by the WHO Reagents, Cross-reactivity and Immune Assays Working Group, 18 March - 1 April 2020](#)
- [WHO R&D Blueprint: novel Coronavirus: prospects for evaluating cross-reactivity of nCoV with SARS-CoV, 27 January 2020.](#)

- [WHO Consultation on Cross-Reactivity with other coronaviruses, 24 January 2020.](#)

Clinical trial design, core protocol development

- [An international randomised trial of candidate vaccines against COVID-19, 28 May 2020.](#)

Vaccine prioritization

- [Criteria for COVID-19 vaccine prioritization, 17 May 2020.](#)
- [WHO R&D Blueprint novel Coronavirus \(nCov\) Vaccine prioritization for clinical trials, 30 January 2020](#)

Human challenge studies

- [WHO Advisory Group Tasked to Consider the Feasibility, Potential Value and Limitations of Establishing a Closely Monitored Challenge Model of Experimental COVID-19 in Healthy Young Adult Volunteers, 7 December 2020](#)
- [Feasibility, Potential Value and Limitations of Establishing a Closely Monitored Challenge Model of Experimental COVID-19 Infection and Illness in Healthy Young Adult Volunteers, 2 December 2020.](#)

SARS-CoV-2 variants: Knowledge gaps and research.

- [COVID Vaccines. Methodological approaches to assess variants effect on vaccine efficacy, effectiveness and impact, 11 February 2021.](#)
- [COVID-19 new variants: Knowledge gaps and research, 12 January 2021.](#)

Solidarity Trial Vaccines (STV)

The Solidarity Trial: Vaccines (STV) is a large, international randomized clinical trial to rapidly and simultaneously evaluate the safety and efficacy of multiple candidate COVID-19 vaccines. This will increase the number of vaccines in circulation and thus enhance global vaccine availability.

The trial will seek to address the widening gap between rich and poor countries in their access to new and effective vaccines and redress the inequities in vaccine distribution.

The trial's innovative features are:

- **Scale:** It is can be run in multiple sites with sufficient incidence of COVID-19 to ensure rapid enrollment and generate data on vaccine safety and efficacy. All countries can participate and will receive WHO technical and financial support and access to trial vaccines.
- **Speed:** Simplified procedures with a randomized controlled clinical trial (RCT) protocol and use of a paperless good clinical practice (GCP)-compliant cloud-based randomization and data system allows for rapid enrollment at multiple sites and rapid results.
- **Adaptability:** Promising vaccines can be added to the trial, and/or others dropped if they prove ineffective. The trial design is responsive so it can respond to changes in

standards of prevention and care; different timings for the availability of candidate vaccines, and uncertainties that may arise about the course of the pandemic in various settings and populations.

Using standardized methodology to evaluate multiple COVID-19 vaccines means those vaccines that show weaker efficacy will not be deployed and will be rapidly dropped from the trial. Trial data will facilitate regulatory and informed deployment decisions, including through the ACT Accelerator and its vaccine arm, the COVAX facility.

Safe and effective vaccines are recognized as vital to controlling the COVID-19 pandemic. Several have recently been granted emergency use authorization in some countries. Their initial rollout has been cause for hope that vaccination will help bring the pandemic under control.

As well as increasing global manufacturing capacity, the development of more vaccines will expand our options, with the potential for better products with greater efficacy that offer longer protection or are easier to distribute and administer. Rapidly developing, evaluating and manufacturing vaccines at scale is a huge challenge.

It is vital that as many vaccines as possible are evaluated to ensure that the demands of all countries can be met and everyone everywhere can be vaccinated.

8. Ethics considerations for research



Extensive guidance material has been developed and implemented to ensure that ethical considerations are integrated into research planning and allocation of COVID-19-related resources, as well as into pandemic response more generally.

Aim

A key aim of the ethics R&D thematic area of the global roadmap has been to ensure that ethical considerations inform COVID-19-related research and pandemic responses.

Three specific objectives underpinned the ethics research agenda:

- ➔ **Objective 1:** Enable the identification of key knowledge gaps and research priorities.
- ➔ **Objective 2:** Formulate a clearly defined research governance framework which enables effective and ethical collaboration between multiple stakeholders, including WHO, the global research community, subject matter experts, public health officials, funders, and ethicists.
- ➔ **Objective 3:** Facilitate effective cross-working and collaboration across the other thematic areas of the WHO before R&D.

Achievements

1. **Ethics principles for COVID-19 research:** Multiple fit-for-purpose COVID-19-related ethics guidance documents have been developed. These include guidance related to ethical standards for research, for research ethics committees, on human challenge studies, resource allocation and priority-setting, and mandatory vaccination. As well as WHO documents, multiple articles have been published in the scientific literature to communicate this work to wider audiences.
2. **National ethics committees:** Several studies have looked at the key role of ethics committees and the ethics review process in COVID-19 from a country perspective. As well as studies in low- and middle-income countries (LMICs), the standard operating procedures (SOPs) for rapid review of research during public health emergencies (PHEs) have been widely adopted by (national) research ethics committees.

3. **Allocation and prioritization:** Principles for equitable allocation and prioritization for clinical management, vaccines, diagnostics and therapeutics have been developed.
4. **Ethics advice:** Significant inputs and contributions to WHO COVID-19-related initiatives have been made. These include guidelines on clinical management of COVID-19 patients; the Solidarity Trial (ST) protocols; Good Participatory Practice (GPP) guidance; the WHO Strategic Advisory Group of Experts in Immunization (SAGE) values framework for the allocation and prioritization of COVID-19 vaccination; and advising on diagnostics and allocation, palliative care, disability, ageing, the inclusion of pregnant women in research, as well as placebo use in COVID-19 vaccine trials.
5. **Outreach:** More than 15 seminars were organized through the Epidemic Ethics Platform. Presentations were also delivered across multiple platforms, and regional and global summits of national ethics committees organized.
6. **Data access:** A joint initiative was organized with the WHO Special Programme for Research and Training in Tropical Diseases (TDR) on creating an evidence base to inform guidance on sharing of COVID-19-related research data, with the aim of promoting data sharing and reuse.
7. **Use of evidence:** With the social sciences theme, a study is being conducted to capture learning related to evaluation, integration and the uptake of evidence in COVID-19 response and recovery decision-making.
8. **Preparedness:** Building is underway now for ethical considerations for subsequent waves and future infectious disease threats.

Benefits

Establishing an international consensus and WHO standards on key ethical issues, such as differential measures/restrictions for vaccinated and unvaccinated people, is a prerequisite for an effective response to COVID-19. The populations around the world will only have trust in and comply with the measures if they are perceived to be fair and just and in line with ethical norms. Furthermore, as the vaccine rollout continues to be very inequitable, despite best efforts of COVAX, there is a continuing need to emphasize the necessity for international solidarity and the moral obligations of the global community. It remains important to stress how important global solidarity is in the response to COVID-19, and the moral obligations of the international community.

Process

The Health Ethics and Governance Unit in WHO is supported by a group of international experts through the COVID-19 and Ethics Working Group to develop guidance materials fit for purpose in COVID-19; identify principles for research and their application (SOPs, STs, human challenge studies); develop allocation principles for clinical management, vaccines, diagnostics and therapeutics, and build ethical preparedness for the second wave and beyond.

Outputs

- Guidance for Research Ethics Committees for Rapid Review of Research During Public Health Emergencies
- Key Criteria for the Ethical Acceptability of COVID-19 Human Challenge Studies
- Ethical Considerations to Guide the Use of Digital Proximity Tracking Technologies for COVID-19 Contact Tracing
- Resource Allocation and Priority Setting Policy Brief
- R&D Ethics: www.who.int/publications/i/item/WHO-RFH-20.1

9. Social sciences in the outbreak response

Important and critical research was carried out by WHO and partners to strengthen public health and clinical responses to COVID-19, mitigate secondary impacts, and inform the design of COVID-19 research studies and interventions using evidence from the social science.

Aim

A key aim of the social science in outbreak response thematic area of the roadmap has been to bring technical expertise from social and behavioral sciences to integrate with biomedical understandings of the COVID-19 pandemic to strengthen the response at international, regional, national and local levels in order to stop the spread of COVID-19 and mitigate its social and economic impacts.

Three specific objectives underpinned the social science research agenda:

- ➔ **Objective 1:** Generate high-quality evidence to achieving the goals of the strategic public health response plan.
- ➔ **Objective 1:** Develop and employ strong methodologies and theoretical frameworks to tackle current epidemic challenges.
- ➔ **Objective 3:** Understand non-intended consequences of epidemic-control decisions.

Achievements

1. **Ad hoc global consultation: Community-centred approaches to health emergencies – progress, gaps and research priorities (31 March 2021):** This event aimed to promote a rethink of the role of communities in prevention, detection, response and recovery interventions during outbreaks of new and re-emerging infectious diseases. Drawing on experiences of COVID-19 and other disease control efforts, it signposted the vital role of trust, agency, social cohesion, plural forms of knowledge and resilience for inclusive, people and community-centred approaches across the health emergency cycle. A key outcome was to specify evidence needs to drive and better support community-led initiatives, programmes and responses.

2. **Good participatory practice (GPP):** A suite of tools to operationalize the WHO Good Participatory Practice Guidance for Emerging Pathogens (GPP-EP) is now available, which includes guidance on setting up and working with Community Advisory Boards (CABs). Tailored engagement and learning materials for standardized best practice across sites for the Solidarity Trial Vaccines (STV) have also now been developed. These include a practical, user-friendly handbook and content for online learning for GPPs at national level and on crisis communications. Additional materials include standardized communications tools (leaflets, FAQs etc), a short, animated explainer of the trial; a FlipBook for standardized information exchange during trial recruitment; a clinical trials explainer; engagement planning and budget templates; tools for tracking anxieties and rumours; and an evaluation framework for engagement with COVID-19 clinical trials.
3. **Social science to optimize infection prevention and control (IPC):** This joint initiative with the IPC thematic area developed tools and materials for rapidly assessing health workers (HWs)' views of IPC procedures in clinical settings. This work provides decision-makers with data-driven insights to understand how to optimize infection control procedures based on what HWs report as barriers and enablers following recommended procedures. These tools have been developed: a research protocol guidance document and data collection tool, grounded in behavioral theory, that includes a standardized measure of HW wellbeing, and a companion document based on implementation science to identify evidence-based strategies that translate outcomes of the study to action. The data collection tool has been digitalized for ease of implementation. These tools have been adapted and contextualized to deliver this research by 16 groups across 51 countries, capturing the views of over 10,000 HWs in different settings.

Additional question sets have been developed and digitalized for rapid research relative to new SARS-CoV-2 variants and to HW views of vaccination. To assist field-based practitioners working in humanitarian settings in low- and middle-income countries (LMICs), a short guide on how to develop and implement HW surveys in these settings was also developed.

4. **Social science and ethics:** This joint initiative with the ethics thematic area captured learning related to how key decision-makers evaluate, integrate and use evidence to make decisions to tackle COVID-19 response and recovery. Based on semi-structured interviews with 25 scientific advisers from 11 WHO Member States, the study highlighted: i) pressures with making decisions during times of intense uncertainty with incomplete or unavailable evidence, or evidence of variable quality and scientific rigor; ii) pressure with informing decisions when large amounts of new evidence were emerging very quickly; and iii) challenges with bringing together and weighing up different perspectives and different kinds of scientific evidence to inform decision-making. Key lessons from this work highlight: i) an urgent need for research, government and health care system capacity to meet emergent pandemic requirements, including the ability to produce and integrate contextually relevant evidence; ii) the importance of clear communication between scientists and decision-makers, and the vital role of risk and science communication with the general public; and iii) the need to engage wider stakeholder groups and scientific perspectives to determine what qualifies as evidence and how evidence is weighed in decision-making, and the societal implications of those decisions.
5. **Social science and sexual and reproductive health (SRH):** This joint initiative with the SRH department reviewed stakeholder perceptions of SRH services and a health systems analysis on its readiness and capacity in providing SRH services during the pandemic. Two generic protocols and associated documents were developed (available on request). Currently eight sites in Brazil, Burkina Faso, Ghana, Italy, Kenya, Pakistan, Thailand and United Kingdom are generating site-specific protocols and preparing for implementation. A research site in China has adapted both protocols, obtained local and WHO ethical approvals, conducted

a pilot of the study instruments, and are now preparing for study implementation.

6. **Rapid qualitative assessments in public health emergencies (PHEs):** The COVID-19 pandemic has highlighted the need for a suite of social science methodologies, tools and guidance to address the full range of complex social, health, political, economic and structural dimensions of a global pandemic. A sub-group of the COVID-19 Research Roadmap Social Science Working Group conducted a rapid evaluation of 138 published and unpublished sources to identify recommendations for best practices in conducting rapid qualitative assessments used in PHEs. This work contributes to setting standards for rapid social science evidence generation.
7. **Risk communication and community engagement (RCCE) among migrant workers:** An intervention package for RCCE among migrant workers in Singapore that viewed RCCE as a system level intervention for migrant worker populations living in closed settings, provided a grounded illustration of participatory practice and engagement as a core part of outbreak response. The outcome of this project was an intervention package for wider scale-up and spread, thereby contributing to the evidence base for RCCE approaches, and for promoting more standardized approaches to RCCE. This work aligns with the global RCCE strategy.
8. **Policy lessons from government responses to COVID-19:** In areas of the WHO Western Pacific Region first affected by the COVID-19 pandemic, an expert working group examined key government containment, control and mitigation policies and measures using the WHO's 'Critical Preparedness, Readiness and Response Actions for COVID-19' as a conceptual framework. Experts from the Hong Kong Special Administrative Region, China, Japan, Malaysia, The Republic of Korea, Shanghai/Mainland China and Singapore reviewed multiple source documents, discussed, analyzed and synthesized findings to highlight key policy lessons at different phases of the COVID-19 pandemic in these jurisdictions. These include the value of early interventions of border control, case identification, isolation and management, and contact tracing and quarantine that were

effective in averting the need for widespread community quarantine or lockdown when COVID-19 became dispersed in the community. There is also a need for a more precise risk assessment methodology that captures social costs calibrated with the effectiveness of interventions and the criticality of community and business engagement.

9. Review of implications of home care in a biological hazard: A technical report was produced that reviewed guidelines and practices of care delivered by formal and informal care providers with care recipients maintained in their homes to increase community surge capacity in response to COVID-19. Key findings from the report informed an update to the WHO guidance on home care for patients with suspected or confirmed COVID-19 and the management of their contacts, and the development of the technical advisory document, 'Integrating biological hazards (including pandemics) into disaster risk recovery planning' to inform the UN Office for Disaster Risk Reduction (UNDRR).

10. Triage critical care during COVID-19: During COVID-19, in many parts of the world, there are likely to be insufficient resources to provide care for critically ill patients. Rapid research was conducted in April 2020 to articulate ethical and context-specific considerations for practitioners needing to make decisions about triage of critically ill patients in high, middle, and low-income settings. Key findings based on 52 semi-structured interviews and 15 written responses collected from across all six WHO regions highlighted: i) in high-income settings, the value of a pragmatic approach guided by assessments of who is most likely to benefit from available resources (utilitarian approach), with the caveat that these decisions are highly complex and that HWs also need autonomy to make bedside in-person patient assessments based on evolving pandemic conditions; ii) anxiety, stress and resistance across all regions about fixed resource allocation decisions, particularly in the face of limited clarity on how and who was involved in developing best practices for resource allocation in their settings; iii) in low-income countries, emphasis on pre-existing inequalities (rather than resource allocation guidance) as key drivers for who gets access to or is prioritized for care. The report is published via the humanitarian health ethics research group.

Benefits

Work in this theme has made important contributions towards developing research tools and generating evidence to strengthen the response to COVID-19, mitigating secondary impacts of the pandemic, shaping interventions, and ensuring the success of research studies. This includes innovative, cross-cutting evidence generation that brings perspectives from social and behavioral sciences to multiple pillars of the strategic response including RCCE, IPC, and clinical management. An increased prominence and integration of evidence from social and behavioral sciences in decision-making at national levels is being observed. Likewise, tools and materials for contextually relevant and appropriate evidence generation at local and national levels to create an accessible evidence base for decision-makers has been crucial.

Process

The social science in outbreak responses thematic area draws technical advice from international experts through the COVID-19 Social Science Working Group. The theme works closely with the Global Outbreak Alert and Response Network (GOARN) social science research and the Risk Communication and Community Engagement (RCCE) Collective Service, a collaborative partnership supported by WHO, the International Federation of Red Cross and Red Crescent Societies (IFRC), the United Nations Children's Fund (UNICEF) and GOARN.

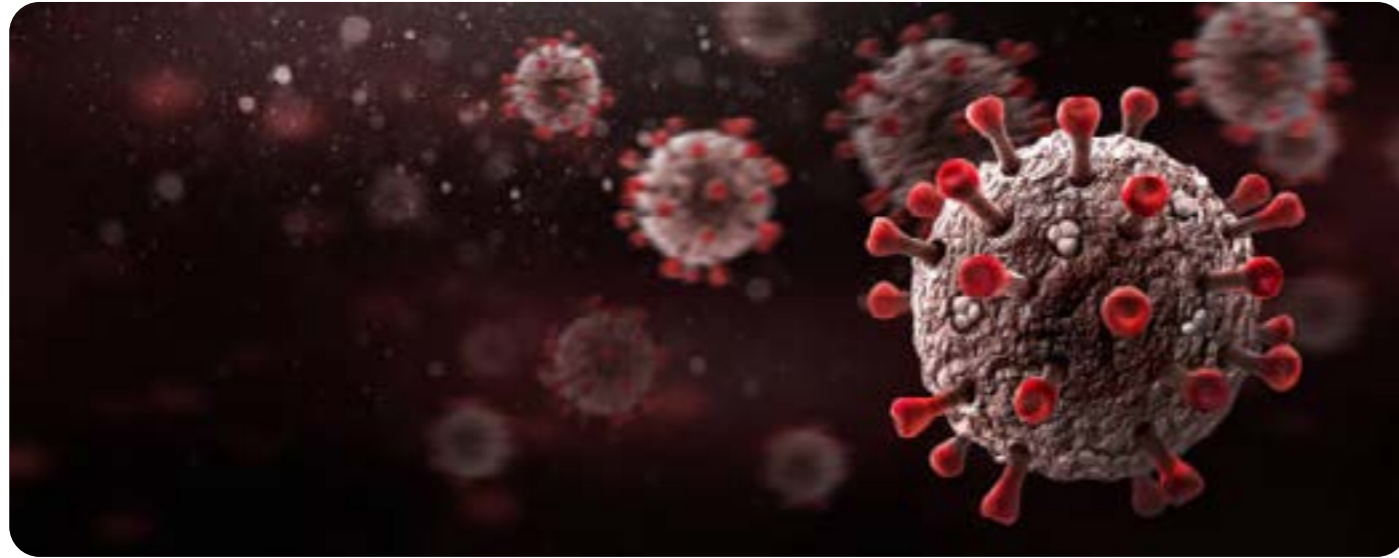
The group works closely with other COVID-19 operational social science research initiatives and networks, including the Risk Communication Community Engagement (RCCE) Collective Service and the GOARN Analytics for Operations Working Group. The group coordinates within WHO with the EPI-WIN (WHO's epidemic information network) team and Behavioral Insights Unit, as well as with colleagues working on different technical areas including, immunization, ethics, gender, maternal and child health, and SRH.

Joint initiatives have also been set up with other working groups of the COVID-19 Research Roadmap to advance the cross-cutting nature of the agenda put forward at the start of the COVID-19 pandemic. The group also works closely with the donor community via the GLOPID-R Social Science Working Group.

Outputs

- Tools for rapid research among HWs, including in humanitarian and fragile settings
- RCCE intervention package for vulnerable population groups exposed to outbreaks in closed settings for wider scale up based on COVID-19 rapid response
- Tools for implementing standardized best practices in Good Participatory Practice for Emerging Pathogens (GPP-EP) to operationalize WHO best practice guidance for engagement in clinical trials
- Standard recommendations/methodologies for rapid social science evidence generation
- Readily available protocol to study recovery decision-making and uptake of evidence in COVID-19
- Policy lessons and recommendations focused on preparedness plans and response actions and targeted towards governments at national and local level
- Network-building and coordination mechanism to rapidly convene social science expertise on a global scale in order to provide technical advice on implementation of the research roadmap
- Outcome of global consultation: evidence gaps to strengthen community-centred approaches in public health emergencies.

5. SARS-CoV-2 variants



Istock.com/Loops7

A global framework is being established to track, analyze and respond to SARS-CoV-2.

Aim

Specific research on SARS-CoV-2 variants was not an explicit thematic area of the global roadmap and has been pulled out with the aim of developing global systems to identify and track new SARS-CoV-2 variants, to assess their implications for diagnostics, treatments and control measures (including vaccines), and to recommend actions to safeguard public health.

Achievements

1. **Animal models:** Coordinated research on animal models is being carried out to shed light on key variant-related questions such as their impact on transmission, severity of disease, sensitivity to host immune responses and host range.
2. **Standardized assays:** Standardized methodologies and assays have been developed so that results obtained in different laboratories can be compared. Important studies have been done to assess how well sera from patients and vaccine recipients neutralize VOCs.

3. **Trials and observational studies:** Efforts are being made to incorporate analysis of variants into clinical trials and non-randomized observational studies. Techniques such as sieve analysis, which extracts data specific for particular genetic variants, can be used in either context to determine whether variants affect vaccine performance.
4. **Regulatory alignment:** Regulatory authorities and the WHO have agreed a set of principles to guide the evaluation and approval of modified first-generation vaccines targeting variants. Assuming certain criteria are met, developers will not need to provide new clinical efficacy data but must show that a modified vaccine elicits the equivalent immune response to a variant as their first-generation vaccine produced against the original SARS-CoV-2 strain.
5. **Modified vaccine development:** Although existing vaccines are likely to remain protective against known VOCs (as of April 2021), developers are creating and evaluating vaccines targeting variants, for use in primary immunization or as boosters.

6. **Correlates of protection:** Intensive research is being undertaken to identify correlates of protection. Although neutralizing antibodies are associated with protection against COVID-19, it is not known for certain that they are directly responsible for protection. An understanding of correlates of protection would facilitate studies extending licensed vaccines to additional populations (such as young people or pregnant women) and the development of new vaccines and variant-specific vaccines. A full understanding will require integration of clinical and experimental data.

Benefits

Work on VOCs has provided vital insights into their impacts on transmission, pathogenesis and immune evasion. As of April 2021, variants appear to show enhanced transmissibility but have little or no impact on disease severity. Antibody neutralization of variants is reduced to varying degrees, but first-generation vaccines still appear to protect against severe disease. Over the longer term, a global mechanism to detect and track variants will be essential to ensure that public health measures, including vaccination, are sufficient to control the virus. Rapid sharing of virus samples and data will be essential for ensuring swift detection and analysis of potentially problematic new variants.

6. Regulatory science

Summary

Important and critical activities were implemented by WHO to prequalify and/or emergency use list (EUL) urgently needed health products for the COVID-19 pandemic, namely in-vitro diagnostics (IVDs), treatments, vaccines, immunization devices and cold-chain equipment. In parallel, WHO coordinated the efficient regulatory authorization of COVID-19 vaccines worldwide through implementation of the regulatory reliance concept, and the rapid evaluation of emerging safety signals for COVID-19 vaccines.

Aim

A key aim of the regulatory science thematic area of the global roadmap has been to develop and implement efficient and effective product assessment mechanisms to evaluate quality, safety and efficacy of (urgently needed) investigational diagnostics, therapeutics and vaccines for COVID-19 based on WHO clinical guidelines and target product profiles (TPPs). In parallel, the regulatory preparedness work aims to assist COVAX-supported countries to efficiently authorize COVID-19 vaccines using the reliance concept to provide technical assistance to collect adverse events, identify key safety signals and take appropriate actions in coordination with regulatory agencies around the world. The development and updating of written and physical standards that are critical in product assessment has been accelerated for COVID-19 products.

These specific objectives underpinned the regulatory preparedness agenda:

- **Objective 1:** Assess quality, safety, efficacy and user-suitability of COVID-19 diagnostics, treatments and vaccines, including products that are under clinical trials.
- **Objective 2:** Develop and implement an efficient process for resource-limited countries to rapidly authorize vaccines that are either listed for EUL or authorized by stringent regulatory authorities for procurement.
- **Objective 3:** Continue developing and updating written guidance for evaluation of diagnostics, treatments, vaccines, PPEs and blood products, to develop International

Nonproprietary Names (INN) where appropriate, and international reference standards for assessments of diagnostics and vaccines.

- **Objective 4:** Extend the development of guidance and reference standards to variants of concern (VOCs).
- **Objective 5:** Promote information sharing and engage in dialogues with regulatory agencies around the world.

Achievements

1. **Quality assessment of IVDs, treatments, vaccines and other health products:** As of 7 May 2021, more than 138 IVDs had been assessed with 28 IVDs listed under EUL, while 32 were not recommended for procurement. Assessment of 78 IVDs is ongoing. For treatment, two dexamethasone finished pharmaceutical products and two dexamethasone active pharmaceutical ingredients have been prequalified. Assessments of monoclonal antibodies for treatments will be initiated as soon as WHO clinical guidelines are issued. Since December 2020, seven COVID-19 vaccines have been listed under EUL, and six accompanying 0.3 ml immunization devices have been prequalified, with two additional products currently being assessed. Four vaccines are under assessment and pre-discussions are ongoing with six additional vaccine manufacturers.
2. **Efficient process for resource-limited countries to approve COVID-19 vaccines:** Although the regulatory systems of over 70% of countries

around the world remain weak, underlying emergency preparedness work and adoption of the regulatory reliance concept allowed 101 out of 145 countries to successfully authorize the first EUL-listed COVID-19 vaccine within 15 days. This record-speed authorization was possible through a joint effort between WHO, the manufacturer and the reference regulatory agency supporting WHO. This collaboration allowed national regulatory agencies, with a confidentiality agreement signatory, to access WHO Assessment Reports.

3. **Regulatory guidance and international reference standards:** The WHO Expert Committee on Biological Standardization (ECBS) accelerated its efforts to develop and update written guidance for evaluation of vaccines and blood products, and for international reference standards for diagnostics and vaccines for COVID-19.

Development of new guidance for evaluation of Ribonucleic Acid (RNA)-based vaccines and for monoclonal antibodies for infectious diseases and the assignment of INN to well-defined vaccine substances are ongoing. SARS-CoV-2 antibody and nucleic acid international reference standards were prepared in collaboration with a WHO collaborating centre, and development of additional standards are ongoing. To mitigate potential bottlenecks and unnecessary wastage of vaccines, WHO prepared an operational tool for efficient and effective lot release of COVID-19 vaccines.

WHO also produced the COVID-19 vaccine safety guidance manual to enhance and harmonize surveillance systems, and ensure transparent data collection, analyses and sharing of data to support evidence-based decision-making at local, national, regional and global levels, and collaboration.

4. **Guidance and reference standards for variants:** WHO published a 'points to consider' guidance for evaluation of modified COVID-19 vaccines to ensure scientifically sound, ethically acceptable, efficient, prompt and reliable evaluation of modified versions of monovalent vaccines. The WHO guidance was developed in consultation with regulatory authorities that had already developed guidance to evaluate modified vaccines, to ensure a harmonized

approach and alignment in the requirements for evaluation. Whether additional international reference standards for variants are needed is being investigated.

5. **Working with regulatory agencies around the world:** WHO aims to facilitate implementation of regulatory reliance, especially by regulatory agencies with limited capacity and expertise. To support countries, WHO has developed guidance for Good Regulatory Practices (GRPs) and Good Reliance Practices (GRlPs). The principles presented in the GRlPs guidance promote an efficient approach by leveraging the output of other regulators while focusing on value-added national regulatory activities. Also in collaboration with the International Coalition of Medicines Regulatory Authorities (ICMRA), joint statements were issued on i) the need for improved global regulatory alignment on COVID-19 medicines and vaccines (November 2020); and ii) transparency and data integrity (7 May 2021).

Benefits

Procurement agencies and WHO Member States have been provided with authoritative and trusted guidance on urgently needed quality-assured diagnostics, treatments, vaccines and other health products to address COVID-19. Practical, collaborative ways of working with regulators around the world have been developed that have enabled timely regulatory decision-making without compromising the independent evaluation of quality, safety and efficacy of these essential COVID tools. This has enabled these products to be used in populations worldwide and continues in gathering post-approval clinical and safety data in a standardized manner.

The work continues to i) identify additional needed health products with assured quality, safety and efficacy; ii) build regulatory efficiency through the reliance concept which allows products to rapidly reach countries and people; iii) engage in dialogues with regulatory agencies, manufacturers, and other relevant stakeholders to minimize bottlenecks; iv) strengthen regulatory systems and build capacity to prepare for future public health emergencies (PHEs); and v) continue developing guidance to evaluate products that use innovative technologies and platforms.

Outputs

- Urgently needed IVDs and vaccines assessed for EUL and relevant treatments and immunization devices prequalified.
- EUL on COVID-19 relevant IVDs: <https://extranet.who.int/pqweb/vitro-diagnostics/coronavirus-disease-covid-19-pandemic-%E2%80%94-emergency-use-listing-procedure-eul-open>
- EUL on COVID-19 vaccines: <https://extranet.who.int/pqweb/vaccines/covid-19-vaccines>
- Prequalification of medicines: <https://extranet.who.int/pqweb/medicines>
- Prequalification of immunization devices: <https://extranet.who.int/pqweb/immunization-devices>
- COVID-19 vaccines: safety surveillance manual and training materials developed together with e-training materials and conducted webinars and trainings for countries and health care professions to collect and identify key safety signals and take appropriate actions in coordination with regulatory agencies around the world.
- Covid-19 vaccines: safety surveillance manual and training materials http://www.who.int/publications/i/item/10665_338400
- The Global Advisory Committee on Vaccine Safety on COVID-19 vaccines reviewed concerned safety signals and provided its analytical statements. <https://www.who.int/groups/global-advisory-committee-on-vaccine-safety/>
- Guidance on GRiPs finalized and encourages all national regulatory authorities to apply its concept to streamline approvals of urgently needed COVID-19 vaccines. <https://www.who.int/news/item/29-04-2021-who-publishes-new-guidance-to-promote-strong-efficient-and-sustainable-regulatory-systems>
- SARS-CoV-2 antibody and nucleic acid international reference standards developed to ensure standardized measurements and evaluations. <https://www.who.int/news-room/feature-stories/detail/standardization-of-vaccines-for-coronavirus-disease-covid-19>
- Joint statements issued with International Coalition of Medicines Regulatory Authorities to streamline regulatory processes and to highlight the importance of sharing clinical trial results.
- Joint statement on the need for improved regulatory alignment on COVID-19 medicines and vaccines (06 November 2020) <https://www.who.int/news/item/06-11-2020-who-icmra-joint-statement-on-the-need-for-improved-global-regulatory-alignment-on-covid-19-medicines-and-vaccines>
- Joint statement on transparency and data integrity (07 May 2021) [https://www.who.int/news/item/07-05-2021-joint-statement-on-transparency-and-data-integrityinternational-coalition-of-medicines-regulatory-authorities-\(icmra\)-and-who](https://www.who.int/news/item/07-05-2021-joint-statement-on-transparency-and-data-integrityinternational-coalition-of-medicines-regulatory-authorities-(icmra)-and-who)
- Innovative mechanism developed to facilitate and speed up regulatory approval of COVID-19 vaccines by resource-limited NRAs through sharing WHO EUL assessment reports under confidentiality agreement https://extranet.who.int/pqweb/sites/default/files/documents/CA_NRA_English_20210204.pdf
- INN for Variant COVID-19 Vaccine Active Substances developed to facilitate tracking of variant COVID-19 vaccines and to enhance standardized safety data collection and surveillance systems. <https://www.who.int/teams/health-product-and-policy-standards/inn/> <https://www.who.int/publications/i/item/inn-21-520>
- Surveillance, detection and protective actions strengthened to mitigate health impact from substandard and falsified COVID-19 related products in the market. https://www.who.int/health-topics/substandard-and-falsified-medical-products#tab=tab_1

7. Lessons learned

No one is safe until we are all safe.

The pandemic is not over and together we recognize the need to strengthen our collaborative efforts to achieve the fair access and equity principles that are the foundations of all of our work.

More than one year into the pandemic we are at a juncture where we can review R&D progress and look to the challenges that still exist.

The emergency response and contributing research areas have been delivered at high speed and the lessons learned are numerous.

All of us who have played our part in this extraordinary endeavor have been learning at every stage; necessarily we have implemented, tested and evaluated the effectiveness of our preparedness and response strategies.

The following are some of the key lessons that will inform our future actions:

Studies addressing public health concerns

We need to advocate for a focused effort to conduct studies that are large enough and robust enough to answer the critical questions that are outstanding, with a concerted move away from conducting many small-scale often inconclusive and potentially duplicative studies.

There is an emerging consensus that platform trials addressing public health questions should become the preferred approach. Large, simple trials can provide reliable estimates on even moderate effects, are opportunities to engage existing capacity from all countries, and can become an integral part of response actions.

The global contribution of researchers worldwide sets the foundations for fair and equitable access.

On research with fair and equitable access at the outset

Research should help reduce uncertainty on issues that will help inform public health actions. Studies that contribute to fair and equitable access should be prioritized and research agreements should include defined access clauses from the outset.

Scaling up manufacturing should be part of the initial planning; intellectual property and technology transfer issues should not be an afterthought.

On investments on research priorities with a long term outlook

Coordination of donors and alignment with defined priorities must continue. Reliable global financing to ensure end-to-end approaches should be earmarked from the start.

Access to opportunities for researchers around the world to contribute their capacities to global research is the way forward, rather than capacity-building only.

It is time to broaden the scope, update the priorities and maintain focus.

Especially considering the emerging variants, it is essential to support global monitoring efforts and strengthen linkages. Close collaborations with expert groups and partners must continue and expand. Large platform trials should be continued and further promoted.

Building on the identified weaknesses and areas for improvement, the global roadmap must be further consolidated in an end-to-end approach to ensure efficiency and global equity.

8. Publications and further resources

Key WHO research related documents and guidance

Cross-cutting themes:

1. World Health Organization. COORDINATED GLOBAL RESEARCH ROADMAP: 2019 NOVEL CORONAVIRUS (March 2020). Available from: <https://www.who.int/publications/m/item/a-coordinated-global-research-roadmap>
2. World Health Organization. Statement of the WHO Working Group on COVID-19 Animal Models (WHO-COM) about the UK and South African SARS-CoV-2 new variants, 23 December 2020. Available from: [https://www.who.int/publications/m/item/statement-of-the-who-working-group-on-covid-19-animal-models-\(who-com\)-about-the-uk-and-south-african-sars-cov-2-new-variants](https://www.who.int/publications/m/item/statement-of-the-who-working-group-on-covid-19-animal-models-(who-com)-about-the-uk-and-south-african-sars-cov-2-new-variants)
3. World Health Organization. Global animal laboratories capacities to support vaccine and therapeutic evaluation, 13 August 2020. Available from: <https://www.who.int/publications/m/item/global-animal-laboratories-capacities-to-support-vaccine-and-therapeutic-evaluation>
4. World Health Organization. COVID-19 Animal Models - Summary of progress made by the WHO COVID-19 modelling (27 February - 15 March 2020). Available from: <https://www.who.int/publications/m/item/covid-19-animal-models-summary-of-progress-made-by-the-who-covid-19-modelling-27-february-15-march-2020>
5. World Health Organization. COVID-19 Animal Models - Summary of progress made by the WHO COVID-19 modelling (15-26 March 2020). Available from: <https://www.who.int/publications/m/item/covid-19-animal-models-summary-of-progress-made-by-the-who-covid-19-modelling-15-26-march-2020>
6. World Health Organization. COVID-19 Animal Models - Summary of progress made by the WHO COVID-19 modelling (March-04 June 2020). Available from: [https://www.who.int/publications/m/item/covid-19-animal-models-summary-of-progress-made-by-the-who-covid-19-modelling-\(march-04-june-2020\)](https://www.who.int/publications/m/item/covid-19-animal-models-summary-of-progress-made-by-the-who-covid-19-modelling-(march-04-june-2020))

Origins of the virus - Human to animal interface

1. World Health Organization. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19), 16-24 February 2020. Available from: [https://www.who.int/publications/i/item/report-of-the-who-china-joint-mission-on-coronavirus-disease-2019-\(covid-19\)](https://www.who.int/publications/i/item/report-of-the-who-china-joint-mission-on-coronavirus-disease-2019-(covid-19))
2. World Health Organization. Origin of SARS-CoV-2, 26 March 2020. Available from: https://apps.who.int/iris/bitstream/handle/10665/332197/WHO-2019-nCoV-FAQ-Virus_origin-2020.1-eng.pdf
3. World Health Organization. Consultation on the use of trained dogs for screening COVID-19 cases, 8 March 2021. Available from: <https://www.who.int/publications/m/item/consultation-on-the-use-of-trained-dogs-for-screening-covid-19-cases>
4. World Health Organization. Human-Animal-Environment Interface Research, 8 January 2021. Available from: <https://www.who.int/publications/m/item/human-animal-environment-interface-research>
5. World Health Organization. Reducing public health risks associated with the sale of live wild animals of mammalian species in traditional food markets; Interim guidance, 12 April 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-Food-safety-traditional-markets-2021.1>
6. World Health Organization. WHO-convened Global Study of Origins of SARS-CoV-2: China Part Joint WHO-China Study 14 January-10 February 2021. Available from: <https://www.who.int/publications/i/item/who-convened-global-study-of-origins-of-sars-cov-2-china-part>
7. World Health Organization. WHO-convened Global Study of the Origins of SARS-CoV-2, 5 November 2020. Available from: <https://www.who.int/publications/m/item/who-convened-global-study-of-the-origins-of-sars-cov-2>
8. World Health Organization. SARS-CoV-2 in animals used for fur farming; GLEWS+ Risk assessment, 20 January 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-fur-farming-risk-assessment-2021.1>

9. World Health Organization. COVID-19 and Food Safety: Guidance for competent authorities responsible for national food safety control systems Interim guidance, 22 April 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Food_Safety_authorities-2020.1

10. World Health Organization. COVID-19 and food safety: guidance for food businesses Interim guidance, 7 April 2020. Available from: <https://www.who.int/publications/i/item/covid-19-and-food-safety-guidance-for-food-businesses>

11. World Health Organization. WHO recommendations to reduce risk of transmission of emerging pathogens from animals to humans in live animal markets or animal product markets, 26 March 2020. Available from: <https://www.who.int/publications/i/item/10665332217>

Transmission dynamics - Virology

1. World Health Organization . (2020). COVID-19 diagnostic testing in the context of international travel: scientific brief, December 16, 2020. Available from: <https://apps.who.int/iris/handle/10665/337832?locale-attribute=de&>
2. World Health Organization. (2020). Diagnostic testing for SARS-CoV-2: interim guidance, 11 September 2020. World Health Organization. Available from: <https://apps.who.int/iris/handle/10665/334254>
3. World Health Organization . (2020). Laboratory biosafety guidance related to coronavirus disease (COVID-19): interim guidance, 13 May 2020. Available from: <https://apps.who.int/iris/handle/10665/332076>
4. World Health Organization. (2020). Laboratory testing for coronavirus disease (COVID-19) in suspected human cases: interim guidance, 19 March 2020. Available from: <https://apps.who.int/iris/handle/10665/331501>
5. World Health Organization. (2020). Laboratory testing of human suspected cases of novel coronavirus (nCoV) infection: interim guidance, 10 January 2020. Available from: <https://apps.who.int/iris/handle/10665/330374>

6. World Health Organization. (2020). Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases: interim guidance, 14 January 2020. Available from: <https://apps.who.int/iris/handle/10665/332300>

7. Laboratory testing of 2019 novel coronavirus (2019-nCoV) in suspected human cases: interim guidance, 17 January 2020. Interim Guidance, 17 January 2020. Available from: [https://www.who.int/publications/i/item/laboratory-testing-of-2019-novel-coronavirus-\(2019-ncov\)-in-suspected-human-cases-interim-guidance-17-january-2020](https://www.who.int/publications/i/item/laboratory-testing-of-2019-novel-coronavirus-(2019-ncov)-in-suspected-human-cases-interim-guidance-17-january-2020)

8. World Health Organization. Statement of the WHO Working Group on COVID-19 Animal Models (WHO-COM) about the UK and South African SARS-CoV-2 new variants, 23 December, 2020. Available from: [https://www.who.int/publications/m/item/statement-of-the-who-working-group-on-covid-19-animal-models-\(who-com\)-about-the-uk-and-south-african-sars-cov-2-new-variants](https://www.who.int/publications/m/item/statement-of-the-who-working-group-on-covid-19-animal-models-(who-com)-about-the-uk-and-south-african-sars-cov-2-new-variants)

9. World Health Organization. Definition and categorization of the timing of mother-to-child transmission of SARS-CoV-2; Scientific brief, 7 February 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-mother-to-child-transmission-2021.1>

10. World Health Organization. Contact tracing in the context of COVID-19; Interim guidance, 1 February 2021. Available from: <https://www.who.int/publications/i/item/contact-tracing-in-the-context-of-covid-19>

11. World Health Organization. Online global consultation on contact tracing for COVID-19, 9-11 June 2020. Available from: <https://www.who.int/publications/i/item/online-global-consultation-on-contact-tracing-for-covid-19-9-11-june-2020>

12. World Health Organization. A prospective cohort study investigating maternal, pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2: Generic protocol, 2 December 2020. Available from: <https://www.who.int/publications/m/item/a-prospective-cohort-study-investigating-maternal-pregnancy-and-neonatal-outcomes-for-women-and-neonates-infected-with-sars-cov-2>

13. World Health Organization. Transmission of SARS-CoV-2: implications for infection prevention precautions: Scientific Brief, 9 July 2020. Available from: <https://www.who.int/publications/i/item/modes-of-transmission-of-virus-causing-covid-19-implications-for-ipc-precaution-recommendations>

Surveillance – EPI studies

1. World Health Organization. Regional Office for Europe. (2021). Estimating COVID-19 vaccine effectiveness against severe acute respiratory infections (SARI) hospitalisations associated with laboratory-confirmed SARS-CoV-2: an evaluation using the test-negative design: guidance document. Available from: <https://apps.who.int/iris/bitstream/handle/10665/341111/WHO-EURO-2021-2481-42237-58308-eng.pdf?sequence=1&isAllowed=y>
2. World Health Organization. Operational considerations to expedite genomic sequencing component of GISRS surveillance of SARS-CoV-2, 16 February 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-genomic-sequencing-GISRS-2021.1>
3. World Health Organization. SARS-CoV-2 in animals used for fur farming GLEWS+ Risk assessment, 20 January 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-fur-farming-risk-assessment-2021.1>
4. World Health Organization. Genomic sequencing of SARS-CoV-2: a guide to implementation for maximum impact on public health, 8 January 2021. Available from: <https://www.who.int/publications/i/item/9789240018440>
5. World Health Organization. SARS-CoV-2 genomic sequencing for public health goals: Interim guidance, 8 January 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-genomic-sequencing-2021.1>
6. World Health Organization. WHO COVID-19 Case definition: Updated in Public health surveillance for COVID-19, 16 December 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Surveillance_Case_Definition-2020.2

7. World Health Organization. Public health surveillance for COVID-19: Interim guidance: Interim guidance, 16 December 2020. Available from: <https://www.who.int/publications/i/item/who-2019-nCoV-surveillanceguidance-2020.8>

8. World Health Organization. Corrigenda – Maintaining surveillance of influenza and monitoring SARS-CoV-2, 3 December 2020. Available from: <https://www.who.int/publications/m/item/corrigenda>

9. World Health Organization. Maintaining surveillance of influenza and monitoring SARS-CoV-2 – adapting Global Influenza surveillance and Response System (GISRS) and sentinel systems during the COVID-19 pandemic, 19 November 2020. Available from: <https://www.who.int/publications/i/item/maintaining-surveillance-of-influenza-and-monitoring-sars-cov-2-adapting-global-influenza-surveillance-and-response-system-gisrs-and-sentinel-systems-during-the-covid-19-pandemic>

10. World Health Organization. Considerations in the investigation of cases and clusters of COVID-19: Interim guidance, 22 October 2020. Available from: <https://www.who.int/publications/i/item/considerations-in-the-investigation-of-cases-and-clusters-of-covid-19>

11. World Health Organization. Status of environmental surveillance for SARS-CoV-2 virus: Scientific brief, 5 August 2020. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-sci-brief-environmentalSampling-2020-1>

12. World Health Organization. Estimating mortality from COVID-19: Scientific brief, 4 August 2020. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-Sci-Brief-Mortality-2020.1>

13. World Health Organization. Considerations for implementing mass treatment, active case finding and population-based surveys for neglected tropical diseases in the context of the COVID-19 pandemic: Interim guidance, 27 July 2020. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-neglected-tropical-diseases-2020-1>

14. World Health Organization. Global COVID-19 Clinical Platform: Rapid core case report form (CRF), 13 July 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Clinical_CRF-2020.4

15. World Health Organization. Medical certification, ICD mortality coding, and reporting mortality associated with COVID-19, 7 June 2020. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-mortality-reporting-2020-1>

16. World Health Organization. Digital tools for COVID-19 contact tracing, 4 June 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Contact_Tracing-Tools_Annex-2020.1

17. World Health Organization. Surveillance protocol for SARS-CoV-2 infection among health workers, 28 May 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-HCW_Surveillance_Protocol-2020.1

18. World Health Organization. Assessment of risk factors for coronavirus disease 2019 (COVID-19) in health workers: protocol for a case-control study, 26 May 2020. Available from: [https://www.who.int/publications/i/item/assessment-of-risk-factors-for-coronavirus-disease-2019-\(covid-19\)-in-health-workers-protocol-for-a-case-control-study](https://www.who.int/publications/i/item/assessment-of-risk-factors-for-coronavirus-disease-2019-(covid-19)-in-health-workers-protocol-for-a-case-control-study)

19. World Health Organization. Population-based age-stratified seroepidemiological investigation protocol for coronavirus 2019 (COVID-19) infection, 26 May 2020. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-Seroepidemiology-2020.2>

20. World Health Organization. WHO reference laboratories providing confirmatory testing for COVID-19, 19 April 20. <https://www.who.int/publications/m/item/who-reference-laboratories-providing-confirmatory-testing-for-covid-19>

21. World Health Organization. COVID-19 Early Epidemiologic and Clinical investigations for public health response: Technical focus, 24 February 2020. Available from: <https://www.who.int/publications/m/item/covid-19-early-epidemiologic-and-clinical-investigations-for-public-health-response>

Clinical Management

1. World Health Organization. Target product profiles for priority diagnostics to support response to the COVID-19 pandemic v.1.0, 28 September 2020. Available from: <https://www.who.int/publications/m/item/covid-19-target-product-profiles-for-priority-diagnostics-to-support-response-to-the-covid-19-pandemic-v.0.1>
2. World Health Organization. Informal consultation on the potential role of interleukin-6 blockers in the clinical management of COVID 19 infection, 11 April 2020. Available from: <https://www.who.int/publications/m/item/informal-consultation-on-the-potentialrole-of-interleukin-6-blockers-in-theclinical-management-of-covid-19infection---11th-april-2020>
3. World Health Organization. COVID-19 Clinical management Living guidance, 25 January 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1>
4. World Health Organization. (2021). Therapeutics and COVID-19: living guideline, 31 March 2021. Available from: <https://apps.who.int/iris/bitstream/handle/10665/340374/WHO-2019-nCoV-therapeutics-2021.1-eng.pdf?sequence=1&isAllowed=y>
5. World Health Organization. Corticosteroids for COVID-19, 2 September 2020. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-Corticosteroids-2020.1>
6. World Health Organization. (2021). WHO living guideline: drugs to prevent COVID-19: interim guidance, 2 March 2021. Available from: <https://apps.who.int/iris/bitstream/handle/10665/339877/WHO-2019-nCoV-prophylaxes-2021.1-eng.pdf?sequence=13&isAllowed=y>
7. World Health Organization. Maintaining a safe and adequate blood supply and collecting convalescent plasma in the context of the COVID-19 pandemic: Interim guidance, 17 February 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-BloodSupply-2021-1>

8. World Health Organization. Home care for patients with suspected or confirmed COVID-19 and management of their contacts: Interim guidance, 12 August 2020. Available from: [https://www.who.int/publications/i/item/home-care-for-patients-with-suspected-novel-coronavirus-\(ncov\)-infection-presenting-with-mild-symptoms-and-management-of-contacts](https://www.who.int/publications/i/item/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts)

9. World Health Organization. Biomedical equipment for COVID-19 case management - inventory tool: Interim guidance, Harmonized health service capacity assessments in the context of the COVID-19 pandemic, 25 June 2020. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCov-biomedical-equipment-inventory-2020.1>

10. World Health Organization. Clinical care of severe acute respiratory infections - Tool kit: Interim guidance, 11 April 2020. Available from: <https://www.who.int/publications/i/item/clinical-care-of-severe-acute-respiratory-infections-tool-kit>

11. World Health Organization. Severe Acute Respiratory Infections Treatment Centre: Interim guidance, 28 March 2020. Available from: <https://www.who.int/publications/i/item/10665-331603>

12. World Health Organization. Operational considerations for case management of COVID-19 in health facility and community: Interim guidance, 19 March 2020. Available from: <https://www.who.int/publications/i/item/10665-331492>

13. World Health Organization. Technical specifications for invasive and non-invasive ventilators for COVID-19: Interim guidance 15 April 2020. Available from: https://apps.who.int/iris/bitstream/handle/10665/331792/WHO-2019-nCoV-Clinical-Ventilator_Specs-2020.1-eng.pdf

14. World Health Organization. Oxygen sources and distribution for COVID-19 treatment centres: Interim guidance 4 April 2020. Available from: <https://www.who.int/publications/i/item/oxygen-sources-and-distribution-for-covid-19-treatment-centres>

15. World Health Organization. WHO COVID-19 Clinical care bundle, 23 April 2021. Available from: <https://www.who.int/publications/m/item/who-covid-19-clinical-care-bundle>

16. World Health Organization. Interim recommendations for use of the ChAdOx1-S [recombinant] vaccine against COVID-19 (AstraZeneca COVID-19 vaccine AZD1222, SII Covishield, SK Bioscience), 21 April 2021. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.2

17. World Health Organization. Annexes to the interim recommendations for use of the ChAdOx1-S [recombinant] vaccine against COVID-19 (AstraZeneca COVID-19 vaccine AZD1222, SII Covishield, SK Bioscience): Grading of evidence - Evidence to recommendations tables, 21 April 2021. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-annexes-2021.2

18. World Health Organization. Asthma and COVID-19: scientific brief, 19 April 2021. Available from: <https://www.who.int/publications/i/item/who-2019-ncov-sci-brief-asthma-2021.1>

19. World Health Organization. Background document on the Janssen Ad26.COV2.S (COVID-19) vaccine: Background document to the WHO Interim recommendations for use of Ad26.COV2.S (COVID-19) vaccine, 17 March 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE-recommendation-Ad26.COV2.S-background-2021.1>

20. World Health Organization. How to monitor and report COVID-19 vaccine side effects, 15 March 2021. Available from: <https://www.who.int/publications/m/item/how-to-monitor-and-report-covid-19-vaccine-side-effects>

21. World Health Organization. Monitoring COVID-19 vaccination: Considerations for the collection and use of vaccination data; Interim guidance, 3 March 2021. Available from: <https://www.who.int/publications/i/item/monitoring-covid-19-vaccination-interim-guidance>

22. World Health Organization. Health worker communication for COVID-19 vaccination flow diagram, 1 March 2021. Available from: <https://www.who.int/publications/m/item/health-worker-communication-for-covid-19-vaccination-flow-diagram>

23. World Health Organization. AstraZeneca ChAdOx1-S/nCoV-19 [recombinant], COVID-19 vaccine; COVID-19 vaccine explainer, 26 February 2021. Available from: <https://www.who.int/publications/m/item/chadox1-s-recombinant-covid-19-vaccine>

24. World Health Organization. Global COVID-19 Clinical Platform Case Report Form (CRF) for Post COVID condition (Post COVID-19 CRF), 25 February 2021. Available from: [https://www.who.int/publications/i/item/global-covid-19-clinical-platform-case-report-form-\(crf\)-for-post-covid-conditions-\(post-covid-19-crf-\)](https://www.who.int/publications/i/item/global-covid-19-clinical-platform-case-report-form-(crf)-for-post-covid-conditions-(post-covid-19-crf-))

25. World Health Organization. Diagnostic testing for SARS-CoV-2: Interim guidance, 11 September 2020. Available from: <https://www.who.int/publications/i/item/diagnostic-testing-for-sars-cov-2>

26. World Health Organization. Considerations for the provision of essential oral health services in the context of COVID-19, 3 August 2020. Available from: <https://www.who.int/publications/i/item/who-2019-nCoV-oral-health-2020.1>

27. World Health Organization. Smoking and COVID-19: Scientific Brief, 30 June 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Sci_Brief-Smoking-2020.2

28. Multisystem inflammatory syndrome in children and adolescents with COVID-19 Scientific brief, 15 May 2020. Available from: <https://www.who.int/publications/i/item/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19>

29. World Health Organization. (2020). Priority medical devices list for the COVID-19 response and associated technical specifications: interim guidance, 19 November 2020. Available from: <https://apps.who.int/iris/bitstream/handle/10665/336745/WHO-2019-nCoV-MedDev-TS-O2T.V2-eng.pdf?sequence=1&isAllowed=y>

30. World Health Organization. COVID-19 and the use of angiotensin-converting enzyme inhibitors and receptor blockers: Scientific Brief, 7 May 2020. Available from: <https://www.who.int/publications/i/item/covid-19-and-the-use-of-angiotensin-converting-enzyme-inhibitors-and-receptor-blockers>

31. World Health Organization. Bacille Calmette-Guérin (BCG) vaccination and COVID-19: Scientific brief, 12 April 2020. Available from: [https://www.who.int/publications/i/item/bacille-calmette-gu%C3%A9rin-\(bcg\)-vaccination-and-covid-19](https://www.who.int/publications/i/item/bacille-calmette-gu%C3%A9rin-(bcg)-vaccination-and-covid-19)

Infection prevention and control incl. HCW protection

1. World Health Organization. Infection prevention and control (IPC) pillar Achievements, February 2020 - January 2021. Available from: [https://www.who.int/publications/m/item/who-covid-19-infection-prevention-and-control-\(ipc\)-pillar](https://www.who.int/publications/m/item/who-covid-19-infection-prevention-and-control-(ipc)-pillar)

2. World Health Organization. COVID-19: Occupational health and safety for health workers Interim guidance 2 February 2021. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-HCW_advice-2021.1

3. World Health Organization. Laboratory biosafety guidance related to coronavirus disease (COVID-19): Interim guidance, 28 January 2021. Available from: <https://www.who.int/publications/i/item/WHO-WPE-GIH-2021.1>

4. World Health Organization. Aide-memoire: Infection prevention and control (IPC) principles and procedures for COVID-19 vaccination activities, 15 January 2021. Available from: <https://www.who.int/publications/i/item/who-2019-ncov-vaccination-IPC-2021-1>

5. World Health Organization. Infection prevention and control guidance for long-term care facilities in the context of COVID-19 update: Interim guidance, 8 January 2021. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC_long_term_care-2021.1

6. World Health Organization. Infection prevention and control health-care facility response for COVID-19: Interim guidance, 20 October 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-HCF_assessment-IPC-2020.1

7. World Health Organization. Rational use of personal protective equipment for coronavirus disease (COVID-19) and considerations during severe shortages: Interim guidance, 23 December 2020. Available from: [https://www.who.int/publications/i/item/rational-use-of-personal-protective-equipment-for-coronavirus-disease-\(covid-19\)-and-considerations-during-severe-shortages](https://www.who.int/publications/i/item/rational-use-of-personal-protective-equipment-for-coronavirus-disease-(covid-19)-and-considerations-during-severe-shortages)

8. World Health Organization. Mask use in the context of COVID-19: Interim guidance, 1 December 2020. Available from: [https://www.who.int/publications/i/item/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-\(2019-ncov\)-outbreak](https://www.who.int/publications/i/item/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak)

9. World Health Organization. Technical specifications of personal protective equipment for COVID-19, 13 November 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-PPE_specifications-2020.1

10. World Health Organization. Prevention, identification and management of health worker infection in the context of COVID-19, 30 October 2020. Available from: <https://www.who.int/publications/i/item/10665-336265>

11. World Health Organization. Infection prevention and control for the safe management of a dead body in the context of COVID-19: Interim guidance, 4 September 2020. Available from: <https://www.who.int/publications/i/item/infection-prevention-and-control-for-the-safe-management-of-a-dead-body-in-the-context-of-covid-19-interim-guidance>

12. World Health Organization. Advice on the use of masks for children in the community in the context of COVID-19, 21 August 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC_Masks-Children-2020.1

13. World Health Organization. Considerations for quarantine of contacts of COVID-19 cases: Interim guidance, 19 August 2020. Available from: [https://www.who.int/publications/i/item/considerations-for-quarantine-of-individuals-in-the-context-of-containment-for-coronavirus-disease-\(covid-19\)](https://www.who.int/publications/i/item/considerations-for-quarantine-of-individuals-in-the-context-of-containment-for-coronavirus-disease-(covid-19))

14. World Health Organization. Water, sanitation, hygiene, and waste management for SARS-CoV-2, the virus that causes COVID-19: Interim guidance, 29 July 2020. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC-WASH-2020.4>

15. World Health Organization. Infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed: Interim guidance, 29 June 2020. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC-2020.4>

16. World Health Organization. Breastfeeding and COVID-19: Scientific Brief, 23 June 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Sci_Brief-Breastfeeding-2020.1

17. World Health Organization. Overview of Public Health and Social Measures in the context of COVID-19, 18 May 2020. <https://www.who.int/publications/i/item/overview-of-public-health-and-social-measures-in-the-context-of-covid-19>

18. World Health Organization. Cleaning and disinfection of environmental surfaces in the context of COVID-19, 16 May 2020. Available from: <https://www.who.int/publications/i/item/cleaning-and-disinfection-of-environmental-surfaces-in-the-context-of-covid-19>

19. World Health Organization. Considerations for public health and social measures in the workplace in the context of COVID-19, 10 May 2020. Available from: <https://www.who.int/publications/i/item/considerations-for-public-health-and-social-measures-in-the-workplace-in-the-context-of-covid-19>

20. World Health Organization. Preparedness, prevention and control of coronavirus disease (COVID-19) for refugees and migrants in non-camp settings: Interim guidance, 17 April 2020. Available from: [https://www.who.int/publications/i/item/preparedness-prevention-and-control-of-coronavirus-disease-\(covid-19\)-for-refugees-and-migrants-in-non-camp-settings](https://www.who.int/publications/i/item/preparedness-prevention-and-control-of-coronavirus-disease-(covid-19)-for-refugees-and-migrants-in-non-camp-settings)

Treatments R&D

1. World Health Organization. COVID 19 Landscape of experimental treatments, 27 April 2020. Available from: <https://www.who.int/publications/i/item/covid-19-landscape-of-experimental-treatments>

2. World Health Organization. WHO Target Product Profiles for COVID-19 Therapeutics, 27 July 2020. Available from: <https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-therapeutics>

3. World Health Organization. COVID-19 WHO Target Product Profiles for COVID-19 Therapeutics in Hospitalized Patients, October 2020. Available from: <https://www.who.int/publications/m/item/covid-19-therapeutics-target-product-profile-for-hospitalized-patients>

4. World Health Organization. WHO Target Product Profiles for COVID-19 Therapeutics for non-hospitalized patients, December 2020. Available from: <https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-therapeutics-for-non-hospitalized-patients>

5. World Health Organization. Covid-19 - living NMA initiative on studies of treatments. Available from: <https://www.covid-nma.com/dataviz/>

6. World Health Organization. Covid-19 Living synthesis of study results - List of treatment comparisons, a summary of the evidence for that comparison, and a detailed description of primary studies, including a risk of bias assessment. Available from: https://covid-nma.com/living_data/index.php

7. World Health Organization. COVID-19 Therapeutic Trial Synopsis, 18 February 2020. Available from: <https://www.who.int/publications/i/item/covid-19-therapeutic-trial-synopsis>

8. World Health Organization. World Health Organization COVID-19 core protocol; An international randomised trial of additional treatments for COVID-19 in hospitalised patients who are all receiving the local standard of care, 22 March 2020. Available from: <https://www.who.int/publications/m/item/an-international-randomised-trial-of-additional-treatments-for-covid-19-in-hospitalised-patients-who-are-all-receiving-the-local-standard-of-care>

9. World Health Organization. Targeted Update: Safety and efficacy of hydroxychloroquine or chloroquine for treatment of COVID-19, 11 June 2020. Available from: <https://www.who.int/publications/m/item/targeted-update-safety-and-efficacy-of-hydroxychloroquine-or-chloroquine-for-treatment-of-covid-19>

10. World Health Organization. COVID 19 Experimental Treatments, 28 April 2020. Available from: <https://www.who.int/publications/m/item/covid-19-candidate-treatments>

11. World Health Organization. Outline of designs for experimental vaccines and therapeutics, 17 January 2020. Available from: <https://www.who.int/publications/m/item/outline-of-designs-for-experimental-vaccines-and-therapeutics>

12. World Health Organization. Informal consultation on the potential inclusion of Sofosbuvir/Daclatasvir in a clinical trial, 19 June 2020. Available from: <https://www.who.int/publications/m/item/informal-consultation-on-the-potential-inclusion-of-sofosbuvir-daclatasvir-in-a-clinical-trial---19-june-2020>

13. World Health Organization. Informal consultation on the potential inclusion of Immunomodulators in a clinical trial, 6 May 2020. Available from: <https://www.who.int/publications/m/item/informal-consultation-on-the-potential-inclusion-of-immunomodulators-in-a-clinical-trial---6-may-2020>

14. World Health Organization. Clinical Trial Design Protocol - consultation on Immunomodulators, 7 May 2020. Available from: <https://www.who.int/publications/m/item/clinical-trial-design-working-group-consultation-on-immunomodulators---7th-may-2020>

15. World Health Organization. Informal consultation on the potential inclusion of Immunomodulators in a clinical trial, 13 May 2020. Available from: <https://www.who.int/publications/m/item/informal-consultation-on-the-potential-inclusion-of-immunomodulators-in-a-clinical-trial---13-may-2020>

16. World Health Organization. Informal consultation on the dose of chloroquine and hydroxychloroquine for the SOLIDARITY Clinical Trial, 8 April 2020. Available from: <https://www.who.int/publications/m/item/informal-consultation-on-the-dose-of-chloroquine-and-hydroxychloroquine-for-the-solidarity-clinical-trial--8-april-2020>

17. World Health Organization. Informal consultation on the role of therapeutics in COVID-19 prophylaxis and post-exposure prophylaxis - Post-exposure prophylaxis studies (PEP) subgroup, 10 April 2020. Available from: <https://www.who.int/publications/m/item/informal-consultation-on-the-role-of-therapeutics-in-covid-19-prophylaxis-and-post-exposure-prophylaxis--10-april-2020>

18. World Health Organization. Informal consultation on the role of therapeutics in COVID-19 prophylaxis and post-exposure prophylaxis - Prophylactic studies (PrEP) subgroup, 15 April 2020. Available from: <https://www.who.int/publications/m/item/informal-consultation-on-the-role-of-therapeutics-in-covid-19-prophylaxis-and-post-exposure-prophylaxis---15-april-2020>

19. World Health Organization. Informal consultation on the role of therapeutics in COVID-19 prophylaxis and post-exposure prophylaxis, 16 April 2020. Available from: <https://www.who.int/publications/m/item/informal-consultation-on-the-role-of-therapeutics-in-covid-19-prophylaxis-and-post-exposure-prophylaxis---16-april-2020>

20 World Health Organization. Informal consultation on the role of therapeutics in COVID-19 prophylaxis and post-exposure prophylaxis, 1 May 2020. Available from: <https://www.who.int/publications/m/item/informal-consultation-on-the-role-of-therapeutics-in-covid-19-prophylaxis-and-post-exposure-prophylaxis---1-may-2020>

21. World Health Organization. Informal consultation on the potential role of IL6/IL-1 antagonists in the clinical management of COVID 19 infection, 25 March 2020. Available from: <https://www.who.int/publications/i/item/informal-consultation-on-the-role-of-il-6-il-1>

22. World Health Organization. Informal consultation on the potential role of chloroquine in the clinical management of COVID 19 infection, 13 March 2020. Available from: <https://www.who.int/publications/i/item/informal-consultation-on-the-potential-role-of-chloroquine-in-the-clinical-management-of-covid-19-infection>

23. World Health Organization. (2020). WHO R&D Blueprint: informal consultation on prioritization of candidate therapeutic agents for use in novel coronavirus 2019 infection, Geneva, Switzerland, 24 January 2020. Available from: <https://apps.who.int/iris/bitstream/handle/10665/330680/WHO-HEO-RDBlueprint%28nCoV%29-2020.1-eng.pdf?sequence=1&isAllowed=y>

24. World Health Organization. Outline of designs for experimental therapeutics, 20 January 2020. Available from: <https://www.who.int/publications/i/item/outline-of-designs-for-experimental-vaccines-and-therapeutics-20-january-2020>

25. World Health Organization. Outline of trial designs for experimental therapeutics, 27 January 2020. Available from: <https://www.who.int/publications/i/item/outline-of-trial-designs-for-experimental-therapeutics>

26. World Health Organization. (2021). Anti-interleukin-6 therapies for hospitalized patients with COVID-19: a protocol for a prospective meta-analysis of randomized trials, February 19, 2021. Available from: <https://apps.who.int/iris/bitstream/handle/10665/339775/WHO-2019-nCoV-PMA-protocols-anti-IL-6-2021.1-eng.pdf?sequence=1&isAllowed=y>

27. World Health Organization. (2020). Clinical care for severe acute respiratory infection: toolkit: COVID-19 adaptation. Available from: https://apps.who.int/iris/bitstream/handle/10665/331736/WHO-2019-nCoV-SARI_toolkit-2020.1-eng.pdf?sequence=1&isAllowed=y

28. World Health Organization. WHO Working Group - Solidarity core protocol for therapeutics, 26 April 2020. Available from: <https://www.who.int/publications/i/item/who-working-group-core-protocol-for-therapeutics-against-covid19>

29. World Health Organization. The use of non-steroidal anti-inflammatory drugs (NSAIDs) in patients with COVID-19: Scientific brief, 19 April 2020. Available from: [https://www.who.int/publications/i/item/the-use-of-non-steroidal-anti-inflammatory-drugs-\(nsaids\)-in-patients-with-covid-19](https://www.who.int/publications/i/item/the-use-of-non-steroidal-anti-inflammatory-drugs-(nsaids)-in-patients-with-covid-19)

30. World Health Organization. Off-label use of medicines for COVID-19: Scientific Brief, 31 March 2020. Available from: <https://www.who.int/publications/i/item/off-label-use-of-medicines-for-covid-19-scientific-brief>

Vaccine R&D

1. World Health Organization. Landscape of observational study designs on the effectiveness of COVID-19 vaccination. Available from: https://cdn.who.int/media/docs/default-source/2021-fair-pricing-forum/observational-studies-on-covid19-vaccine-effectiveness_draft-landscape_29.03.2021.xlsx.zip?sfvrsn=512896f7_3&download=true

2. World Health Organization. The COVID-19 candidate vaccine landscape and tracker. Available from: https://cdn.who.int/media/docs/default-source/blue-print/06.04.2021-novel-coronavirus_landscape_covid-19.xlsx033cfc8f-b99b-4edf-aedb-765a272e9eb5.zip?sfvrsn=d6471b19_3&download=true

3. World Health Organization. Feasibility, Potential Value and Limitations of Establishing a Closely Monitored Challenge Model of Experimental COVID-19 Infection and Illness in Healthy Young Adult Volunteers, 2 December, 2020. Available from: <https://www.who.int/publications/m/item/feasibility-potential-value-and-limitations-of-establishing-a-closely-monitored-challenge-model-of-experimental-covid-19-infection-and-illness-in-healthy-young-adult-volunteers>

4. World Health Organization. WHO Advisory Group Tasked to Consider the Feasibility, Potential Value and Limitations of Establishing a Closely Monitored Challenge Model of Experimental COVID-19 in Healthy Young Adult Volunteers, 7 December 2020. Available from: <https://www.who.int/publications/m/item/report-of-the-who-ag-on-human-challenge-studies>

5. World Health Organization. COVID-NMA initiative, A living map of on-going research showing studies per country, study design, type of vaccine, study phase and type of patients. Available from: <https://covid-nma.com/vaccines/mapping/>

6. World Health Organization. An international randomised trial of candidate vaccines against COVID-19, 28 May 2020. Available from: <https://www.who.int/publications/i/item/an-international-randomised-trial-of-candidate-vaccines-against-covid-19>

7. World Health Organization. Criteria for COVID-19 vaccine prioritization, 17 May 2020. Available from: <https://www.who.int/publications/m/item/criteria-for-covid-19-vaccine-prioritization>

8. World Health Organization. WHO Target Product Profiles for COVID-19 Vaccines, 29 April 2020. Available from: <https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-vaccines>

9. World Health Organization. Overview of the types/classes of candidate vaccines against MERS-CoV, 5 February 2020. Available from: <https://www.who.int/publications/m/item/overview-of-the-types-classes-of-candidate-vaccines-against-mers-cov>

10. World Health Organization. Overview of the types/classes of candidate vaccines against SARS-CoV, 5 February 2020. Available from: <https://www.who.int/publications/m/item/overview-of-the-types-classes-of-candidate-vaccines-against-sars-cov>

11. World Health Organization. WHO R&D Blueprint novel Coronavirus (nCoV) Vaccine prioritization for clinical trials, 30 January 2020. Available from: <https://www.who.int/publications/i/item/who-r-d-blueprint-novel-coronavirus-ncov-vaccine-prioritization-for-clinical-trials>

12. World Health Organization. WHO R&D Blueprint: novel Coronavirus: prospects for evaluating cross-reactivity of nCoV with SARS-CoV, 27 January 2020. Available from: <https://www.who.int/publications/i/item/who-r-d-blueprint-novel-coronavirus-prospects-for-evaluating-cross-reactivity-of-ncov-with-sars-cov>

13. World Health Organization. WHO Consultation on Cross-Reactivity with other coronaviruses, 24 January 2020. Available from: <https://www.who.int/publications/i/item/who-consultation-on-cross-reactivity-with-other-coronaviruses>

14. World Health Organization. COVID-19 new variants: Knowledge gaps and research, 13 January 2021. Available from: <https://www.who.int/publications/m/item/covid-19-new-variants-knowledge-gaps-and-research>

15. World Health Organization. COVID Vaccines Methodological approaches to assess variants effect on vaccine efficacy, effectiveness and impact, 11 February 2021. Available from: <https://www.who.int/publications/m/item/methodological-approaches-to-assess-variants-effect-on-vaccine-efficacy-effectiveness-and-impact>

16. World Health Organization. COVID-19 Animal Models Summary of progress made by the WHO COVID-19 modelling ad hoc Expert working Group, 27 February – 15 March 2020. Available from: <https://www.who.int/publications/m/item/covid-19-animal-models-summary-of-progress-made-by-the-who-covid-19-modelling-27-february-15-march-2020>

17. World Health Organization. COVID-19 Animal Models ad hoc working group: Summary of progress made by the WHO COVID-19 modelling ad hoc Expert working Group, 26 March – 1 June 2020. Available from: [https://www.who.int/publications/m/item/covid-19-animal-models-summary-of-progress-made-by-the-who-covid-19-modelling-\(march-04-june-2020\)](https://www.who.int/publications/m/item/covid-19-animal-models-summary-of-progress-made-by-the-who-covid-19-modelling-(march-04-june-2020))

18. World Health Organization. COVID-19 Reagents, Cross-reactivity and Immune Assays Working Group, 18 March – 1 April 2020. Available from: [https://www.who.int/publications/m/item/summary-of-progress-made-by-the-who-assays-for-vaccines-group-of-experts-\(18-march-1-april\)](https://www.who.int/publications/m/item/summary-of-progress-made-by-the-who-assays-for-vaccines-group-of-experts-(18-march-1-april))

19. World Health Organization. Evaluation of COVID-19 vaccine effectiveness; Interim Guidance, 17 March 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccine-effectiveness-measurement-2021.1>

20 World Health Organization. AZD1222 vaccine against COVID-19 developed by Oxford University and Astra Zeneca: Background paper (draft), 10 February 2021. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-background-2021.1

21. World Health Organization. Background document on the mRNA-1273 vaccine (Moderna) against COVID-19, 3 February 2021. Available from: [https://www.who.int/publications/i/item/background-document-on-the-mrna-1273-vaccine-\(moderna\)-against-covid-19](https://www.who.int/publications/i/item/background-document-on-the-mrna-1273-vaccine-(moderna)-against-covid-19)

22. World Health Organization. Interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19, 25 January 2021. Available from: <https://www.who.int/publications/i/item/interim-recommendations-for-use-of-the-moderna-mrna-1273-vaccine-against-covid-19>

23. World Health Organization. mRNA-1273 vaccine (Moderna) against COVID-19 Background document (draft), 19 January 2021. Available from: [https://www.who.int/publications/i/item/mrna-1273-vaccine-\(moderna\)-against-covid-19-background-document-\(draft\)](https://www.who.int/publications/i/item/mrna-1273-vaccine-(moderna)-against-covid-19-background-document-(draft))

24. World Health Organization. Pfizer/BioNTech COMIRNATY®, COVID-19 vaccine, 18 January 2021. Available from: <https://www.who.int/publications/m/item/comirnaty-covid-19-mrna-vaccine>

25. World Health Organization. Evidence to recommendations for COVID-19 vaccines: Evidence framework, 10 December 2020. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-SAGE-Framework-Evidence-2020-1>

26. World Health Organization. WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination, 13 September 2020. Available from: <https://www.who.int/publications/i/item/who-sage-values-framework-for-the-allocation-and-prioritization-of-covid-19-vaccination>

27. World Health Organization. Immunization in the context of COVID-19 pandemic, 15 May 2020. Available from: <https://www.who.int/publications/i/item/immunization-in-the-context-of-covid-19-pandemic>

28. World Health Organization. COVID-19 Vaccine Checklist, 22 February 2021. Available from: <https://www.who.int/publications/m/item/covid-19-vaccine-checklist>

Social Science

1. World Health Organization. Perceptions of Healthcare Workers regarding local infection prevention and control procedures for COVID-19: Research protocol, 29 April 2020. Available from: <https://www.who.int/publications/m/item/perceptions-of-healthcare-workers-regarding-local-infection-prevention-and-control-procedures-for-covid-19-research-protocol>

2. World Health Organization. Working with Community Advisory Boards for COVID-19 related clinical studies, 23 April 2020. Available from: <https://www.who.int/publications/m/item/working-with-community-advisory-boards-for-covid-19-related-clinical-studies>

3. World Health Organization. Good Participatory Practice for COVID-19 clinical trials: a toolbox, 23 April 2020. Available from: <https://www.who.int/publications/m/item/r-d-good-participatory-practice-for-covid-19-clinical-trials-a-toolbox>

4. World Health Organization. Data for action: achieving high uptake of COVID-19 vaccines, 1 April 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccination-demand-planning-2021.1>

5. World Health Organization. Community needs, perceptions and demand: community assessment tool, 5 February 2021. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccination-community_assessment-tool-2021.1

6. World Health Organization. Conducting community engagement for COVID-19 vaccines: Interim guidance, 31 January 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccination-community-engagement-2021.1>

7. World Health Organization. Acceptance and demand for COVID-19 vaccines: Interim guidance, 31 January 2021. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccination-demand_planning-tool-2021.1

8. World Health Organization. COVID-19 Global Risk Communication and Community Engagement Strategy: Interim guidance, December 2020 – May 2021. Available from: <https://www.who.int/publications/i/item/covid-19-global-risk-communication-and-community-engagement-strategy>

9. World Health Organization. Considerations for implementing and adjusting public health and social measures in the context of COVID-19: Interim guidance, 4 November 2020. Available from: <https://www.who.int/publications/i/item/considerations-in-adjusting-public-health-and-social-measures-in-the-context-of-covid-19-interim-guidance>

10. World Health Organization. Behavioural considerations for acceptance and uptake of COVID-19 vaccines: WHO technical advisory group on behavioural insights and sciences for health, meeting report, 15 October 2020. Available from: <https://www.who.int/publications/i/item/9789240016927>

11. World Health Organization. Gender and COVID-19: Advocacy Brief, 14 May 2020. Available from: <https://www.who.int/publications/i/item/gender-and-covid-19>

12. World Health Organization. A guide to preventing and addressing social stigma associated with COVID-19, 24 February 2020. Available from: <https://www.who.int/publications/m/item/a-guide-to-preventing-and-addressing-social-stigma-associated-with-covid-19>

Ethics

1. World Health Organization. Ethical considerations to guide the use of digital proximity tracking technologies for COVID-19 contact tracing, 28 May 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Ethics_Contact_tracing_apps-2020.1

2. World Health Organization. Guidance for research ethics committees for rapid review of research during public health emergencies, 28 May 2020. Available from: <https://www.who.int/publications/i/item/9789240006218>

3. World Health Organization. Key criteria for the ethical acceptability of COVID-19 human challenge studies, 6 May 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Ethics_criteria-2020.1

4. World Health Organization. Ethical standards for research during public health emergencies: Distilling existing guidance to support COVID-19 R&D, 29 March 2020. Available from: <https://www.who.int/publications/i/item/WHO-RFH-20.1>

5. World Health Organization. COVID-19 and mandatory vaccination: Ethical considerations and caveats, 13 April 2021. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-Policy-brief-Mandatory-vaccination-2021.1>

6. World Health Organization. Emergency Use Designation of COVID-19 candidate vaccines: Ethical considerations for current and future COVID-19 placebo-controlled vaccine trials and trial unblinding, 18 December 2020. Available from: <https://www.who.int/publications/i/item/emergency-use-designation-of-covid-19-candidate-vaccines-ethical-considerations-for-current-and-future-covid-19-placebo-controlled-vaccine-trials-and-trial-unblinding>

7. World Health Organization. Evidence to recommendations: Methods used for assessing health equity and human rights considerations in COVID-19 and aviation, 23 December 2020. Available from: <https://www.who.int/publications/i/item/evidence-to-recommendations-methods-used-for-assessing-health-equity-and-human-rights-considerations-in-covid-19-and-aviation>

COVID-19 Diagnostics and assays

1. World Health Organization. Advice on the use of point-of-care immunodiagnostic tests for COVID-19: scientific brief: Scientific brief, 8 April 2020. Available from: <https://www.who.int/publications/i/item/advice-on-the-use-of-point-of-care-immunodiagnostic-tests-for-covid-19-scientific-brief>

2. World Health Organization. Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays: Interim guidance, 11 September 2020. Available from: <https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2-infection-using-rapid-immunoassays>

3. World Health Organization. SARS-CoV-2 antigen-detecting rapid diagnostic tests: An implementation guide, 21 December 2020. Available from: <https://www.who.int/publications/i/item/9789240017740>

Selected peer-reviewed publications relevant to the various research thematic areas

Transmission dynamics – Virology

1. Mayigane LN, de Vázquez CC, Vente C, Charles D, Copper FA, Bell A, Njenge HK, Schmidt T, Samhuri D, Htike MM, Kato M. The necessity for intra-action reviews during the COVID-19 pandemic. *The Lancet Global Health*. 2020 Dec 1;8(12):e1451-2.

2. Memish ZA, Perlman S, Van Kerkhove MD, Zumla A. Middle East respiratory syndrome. *The Lancet*. 2020 Mar 28;395(10229):1063-77.

Surveillance – EPI studies

1. Biggerstaff M, Cowling BJ, Cucunubá ZM, Dinh L, Ferguson NM, Gao H, Hill V, Imai N, Johansson MA, Kada S, Morgan O. Early insights from statistical and mathematical modeling of key epidemiologic parameters of COVID-19. *Emerging infectious diseases*. 2020 Nov;26(11).

2. Extraordinary-meeting-Advisory-Forum-17-March-2020.pdf. (n.d.). Retrieved May 12, 2021, from <https://www.ecdc.europa.eu/sites/default/files/documents/Extraordinary-meeting-Advisory-Forum-17-March-2020.pdf>

Clinical Management

1. Agarwal, A., Basmaji, J., Muttalib, F., Granton, D., Chaudhuri, D., Chetan, D., ... & Vandvik, P. O. (2020). High-flow nasal cannula for acute hypoxemic respiratory failure in patients with COVID-19: systematic reviews of effectiveness and its risks of aerosolization, dispersion, and infection transmission. *Canadian Journal of Anesthesia/ Journal canadien d'anesthésie*, 67(9), 1217-1248.

2. Agarwal, A., Fernando, S. M., Honarmand, K., Bakaa, L., Brar, S., Granton, D., ... & Vandvik, P. O. (2021). Risk of dispersion or aerosol generation and infection transmission with nasopharyngeal and oropharyngeal swabs for detection of COVID-19: a systematic review. *BMJ open*, 11(3), e040616.

3. America, S., & Asia, S. (2020). COVID 19 and the oxygen bottleneck. *Bull World Health Organ*, 98, 586-587.

4. Carson, G. (2021). Research priorities for Long Covid: refined through an international multi-stakeholder forum. *BMC medicine*, 19(1), 1-4.

5. Group, I. C. C., Pritchard, M. G., & Olliaro, P. L. (2020). Symptoms at presentation for patients admitted to hospital with Covid-19: results from the ISARIC prospective multinational observational study. *medRxiv*.

6. Marshall, J. C., Murthy, S., & Diaz, J. (2020). Fungal infections should be part of the core outcome set for COVID-19—Authors' reply. *The Lancet Infectious Diseases*.

7. Marshall, J. C., Murthy, S., Diaz, J., Adhikari, N., Angus, D. C., Arabi, Y. M., ... & Zhang, J. (2020). A minimal common outcome measure set for COVID-19 clinical research. *The Lancet Infectious Diseases*.

8. Pritchard, M. G. (2020). COVID-19 symptoms at hospital admission vary with age and sex: ISARIC multinational study. *medRxiv*.

9. Sterne, J. A., Diaz, J., Villar, J., Murthy, S., Slutsky, A. S., Perner, A., ... & Marshall, J. C. (2020). Corticosteroid therapy for critically ill patients with COVID-19: A structured summary of a study protocol for a prospective meta-analysis of randomized trials. *Trials*, 21(1), 1-3.

10. Sterne, J. A., Murthy, S., Diaz, J. V., Slutsky, A. S., Villar, J., Angus, D. C., ... & Marshall, J. C. (2020). Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. *Jama*, 324(13), 1330-1341.

11. Talisuna, A. O., Bonkoungou, B., Mosha, F. S., Struminger, B. B., Lehmer, J., Arora, S., ... & Moeti, M. R. (2020). The COVID-19 pandemic: broad partnerships for the rapid scale up of innovative virtual approaches for capacity building and credible information dissemination in Africa. *The Pan African Medical Journal*, 37.

Infection prevention and control incl. HCW protection

1. Al-Ansary, L., Bawazeer, G., Beller, E., Clark, J., Conly, J., Del Mar, C., ... & Jones, M. (2020). Physical interventions to interrupt or reduce the spread of respiratory viruses. Part 2-Hand hygiene and other hygiene measures: systematic review and meta-analysis. medRxiv.
2. Bahrs, C., Kimmig, A., Weis, S., Ankert, J., Hagel, S., Maschmann, J., ... & Pletz, M. W. (2020). Seroprevalence of SARS CoV-2 antibodies in healthcare workers and administration employees: a prospective surveillance study at a 1,400-bed university hospital in Germany. medRxiv.
3. Blaak, M. J., Fadaak, R., Davies, J. M., Pinto, N., Conly, J., & Leslie, M. (2021). Virtual tabletop simulations for primary care pandemic preparedness and response. *BMJ Simulation and Technology Enhanced Learning*, bmjstel-2020.
4. Brainard, J. S., Jones, N., Lake, I., Hooper, L., & Hunter, P. (2020). Facemasks and similar barriers to prevent respiratory illness such as COVID-19: A rapid systematic review. MedRxiv.
5. Brainard, J. S., Rushton, S., Winters, T., & Hunter, P. R. (2020). Introduction to and spread of COVID-19 in care homes in Norfolk, UK. medRxiv.
6. Chia, P. Y., Coleman, K. K., Tan, Y. K., Ong, S. W. X., Gum, M., Lau, S. K., ... & Marimuthu, K. (2020). Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients. *Nature communications*, 11(1), 1-7.
7. Chou, R., Dana, T., Buckley, D. I., Selph, S., Fu, R., & Totten, A. M. (2020). Epidemiology of and risk factors for coronavirus infection in health care workers: a living rapid review. *Annals of internal medicine*, 173(2), 120-136.
8. Chou, R., Dana, T., Jungbauer, R., Weeks, C., & McDonagh, M. S. (2020). Masks for prevention of respiratory virus infections, including SARS-CoV-2, in health care and community settings: a living rapid review. *Annals of internal medicine*, 173(7), 542-555.
9. Chou, R., Dana, T., Jungbauer, R., Weeks, C., & McDonagh, M. S. (2020). Update alert: masks for prevention of respiratory virus infections, including SARS-CoV-2, in health care and community settings. *Annals of internal medicine*, 173(5), W86.
10. Chu, D. K., Akl, E. A., Duda, S., Solo, K., Yaacoub, S., Schünemann, H. J., ... & Reinap, M. (2020). Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. *The Lancet*, 395(10242), 1973-1987.
11. Fadaak, R., Davies, J. M., Blaak, M. J., Conly, J., Haslock, J., Kenny, A., ... & Leslie, M. (2021). Rapid conversion of an in-patient hospital unit to accommodate COVID-19: An interdisciplinary human factors, ethnography, and infection prevention and control approach. *Plos one*, 16(1), e0245212.
12. Harrigan, S. P., Tsang, V. W., Spiegel, J. M., & Yassi, A. (2020). Health and safety of health workers in the context of COVID-19: A global survey.
13. Hopman, J., Allegranzi, B., & Mehtar, S. (2020). Managing COVID-19 in low-and middle-income countries. *Jama*, 323(16), 1549-1550.
14. Hunter, P. R., Colon-Gonzalez, F., Brainard, J. S., & Rushton, S. (2020). Impact of non-pharmaceutical interventions against COVID-19 in Europe: a quasi-experimental study. MedRxiv.
15. Jefferson, T., Foxlee, R., Del Mar, C., Dooley, L., Ferroni, E., Hewak, B., ... & Rivetti, A. (2008). Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. *Bmj*, 336(7635), 77-80.
16. Lendvay, T. S., Chen, J., Harcourt, B. H., Scholte, F. E., Kilinc-Balci, F. S., Lin, Y. L., ... & Chu, M. C. (2020). Addressing Personal Protective Equipment (PPE) Decontamination: Methylene Blue and Light Inactivates SARS-CoV-2 on N95 Respirators and Masks with Maintenance of Integrity and Fit. medRxiv.
17. Leslie, M., Fadaak, R., Davies, J., Blaak, J., Forest, P. G., Green, L., & Conly, J. (2020). Integrating the social sciences into the COVID-19 response in Alberta, Canada. *BMJ Global Health*, 5(7), e002672.
18. Ng, O. T., Marimuthu, K., Koh, V., Pang, J., Linn, K. Z., Sun, J., ... & Lee, V. J. (2021). SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: a retrospective cohort study. *The Lancet infectious diseases*, 21(3), 333-343.
19. Nussbaumer-Streit, B., Mayr, V., Dobrescu, A. I., Chapman, A., Persad, E., Klerings, I., ... & Gartlehner, G. (2020). Quarantine alone or in combination with other public health measures to control COVID 19: a rapid review. *Cochrane Database of Systematic Reviews*, (9).
20. Ong, S. W. X., Lee, P. H., Tan, Y. K., Ling, L. M., Ho, B. C. H., Ng, C. G., ... & Marimuthu, K. (2020). Environmental contamination in a coronavirus disease 2019 (COVID-19) intensive care unit—What is the risk?. *Infection Control & Hospital Epidemiology*, 1-9.
21. Ong, S. W. X., Tan, Y. K., Coleman, K. K., Tan, B. H., Leo, Y. S., Wang, D. L., ... & Marimuthu, K. (2021). Lack of viable severe acute respiratory coronavirus virus 2 (SARS-CoV-2) among PCR-positive air samples from hospital rooms and community isolation facilities. *Infection Control & Hospital Epidemiology*, 1-6.
22. Ong, S. W. X., Tan, Y. K., Sutjipto, S., Chia, P. Y., Young, B. E., Gum, M., ... & Ng, O. T. (2020). Absence of contamination of personal protective equipment (PPE) by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Infection Control & Hospital Epidemiology*, 41(5), 614-616.
23. Paludan-Müller, A. S., Boesen, K., Klerings, I., Jørgensen, K. J., & Munkholm, K. (2020). Hand cleaning with ash for reducing the spread of viral and bacterial infections: a rapid review. *Cochrane Database of Systematic Reviews*, (4).
24. Peters, A., Lotfinejad, N., Guitart, C., Simniceanu, A., Padoveze, M. C., Borzykowski, T., ... & Pittet, D. (2020). “Nurses and midwives: clean care is in your hands”: the 5th May 2020 World Health Organization SAVE LIVES: Clean Your Hands campaign. *Antimicrobial Resistance & Infection Control*, 9(1), 1-3.
25. Price, J. R., Mookerjee, S., Dyakova, E., Myall, A., Leung, W., Weiße, A. Y., ... & Holmes, A. H. (2021). Development and delivery of a real-time hospital-onset COVID-19 surveillance system using network analysis. *Clinical Infectious Diseases*, 72(1), 82-89.
26. Rawson, T. M., Ming, D., Ahmad, R., Moore, L. S., & Holmes, A. H. (2020). Antimicrobial use, drug-resistant infections and COVID-19. *Nature Reviews Microbiology*, 18(8), 409-410.
27. Rawson, T. M., Moore, L. S., Castro-Sanchez, E., Charani, E., Davies, F., Satta, G., ... & Holmes, A. H. (2020). COVID-19 and the potential long-term impact on antimicrobial resistance. *Journal of antimicrobial chemotherapy*, 75(7), 1681-1684.
28. Rawson, T. M., Moore, L. S., Zhu, N., Ranganathan, N., Skolimowska, K., Gilchrist, M., ... & Holmes, A. (2020). Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. *Clinical Infectious Diseases*, 71(9), 2459-2468.
29. Rawson, T. M., Wilson, R. C., & Holmes, A. (2021). Understanding the role of bacterial and fungal infection in COVID-19. *Clinical Microbiology and Infection*, 27(1), 9.
30. Rawson, T. M., Wilson, R. C., & Holmes, A. (2021). Understanding the role of bacterial and fungal infection in COVID-19. *Clinical Microbiology and Infection*, 27(1), 9.
31. Tartari, E., Hopman, J., Allegranzi, B., Gao, B., Widmer, A., Cheng, V. C. C., ... & Voss, A. (2020). Perceived challenges of COVID-19 infection prevention and control preparedness: A multinational survey. *Journal of Global Antimicrobial Resistance*.
32. Tartari, E., Saris, K., Kenters, N., Marimuthu, K., Widmer, A., Collignon, P., ... & International Society of Antimicrobial Chemotherapy Infection and Prevention Control (ISAC-IPC) Working Group. (2020). Not sick enough to worry? “Influenza-like” symptoms and work-related behavior among healthcare workers and other professionals: Results of a global survey. *PloS one*, 15(5), e0232168.
33. Tartari, E., Tomczyk, S., Pires, D., Zayed, B., Rehse, A. C., Kariyo, P., ... & Allegranzi, B. (2021). Implementation of the infection prevention and control core components at the national level: a global situational analysis. *Journal of Hospital Infection*, 108, 94-103.
34. Temkin, E., Schwaber, M. J., Solter, E., Vaturi, A., Hen, D., Lugassy, C. G., ... & Carmeli, Y. (2021). Extremely low prevalence of asymptomatic COVID-19 among healthcare workers caring for COVID-19 patients in Israeli hospitals: a cross-sectional study. *Clinical Microbiology and Infection*, 27(1), 130-e1.

35. Tomczyk, S., Aghdassi, S., Storr, J., Hansen, S., Stewardson, A. J., Bischoff, P., ... & Allegranzi, B. (2020). Testing of the WHO Infection Prevention and Control Assessment Framework at acute healthcare facility level. *Journal of Hospital Infection*, 105(1), 83-90.

36. Tomczyk, S., Storr, J., Kilpatrick, C., & Allegranzi, B. (2021). Infection Prevention and Control (IPC) Implementation in Low-Resource Settings: A Qualitative Analysis.

37. Zhao, M., Liao, L., Xiao, W., Yu, X., Wang, H., Wang, Q., ... & Cui, Y. (2020). Household materials selection for homemade cloth face coverings and their filtration efficiency enhancement with triboelectric charging. *Nano letters*, 20(7), 5544-5552.

38. Zhou, J., Otter, J. A., Price, J. R., Cimpeanu, C., Garcia, D. M., Kinross, J., ... & Barclay, W. S. (2020). Investigating SARS-CoV-2 surface and air contamination in an acute healthcare setting during the peak of the COVID-19 pandemic in London. *Clinical Infectious Diseases*.

Treatments R&D

1. Dean, N. E., Gsell, P. S., Brookmeyer, R., Crawford, F. W., Donnelly, C. A., Ellenberg, S. S., ... & De Gruttola, V. (2020). Creating a framework for conducting randomized clinical trials during disease outbreaks.

2. Moorthy, V., Henao- Restrepo, A. M. H., Preziosi, M. P., & Swaminathan, S. (2020). Data sharing for novel coronavirus (COVID-19). *Bulletin of the World Health Organization*, 98(3), 150.

3. Moorthy, V., Restrepo, AMH, Preziosi, MP and Swaminathan, S., 2020. *Global Health Observatory. Boletín de la Organización Mundial de la Salud*, 98, p.150.

4. Muñoz-Fontela, C., Dowling, W. E., Funnell, S. G., Gsell, P. S., Riveros-Balta, A. X., Albrecht, R. A., ... & Barouch, D. H. (2020). Animal models for COVID-19. *Nature*, 586(7830), 509-515.

5. Rochweg, B., Agoritsas, T., Lamontagne, F., Leo, Y.S., Macdonald, H., Agarwal, A., Zeng, L., Lytvyn, L., Appiah, J.A., Amin, W. and Arabi, Y., 2020. A living WHO guideline on drugs for covid-19. *bmj*, 370(m3379), p.518.

6. Soto, A., Quiñones-Laveriano, D. M., Garcia, P.

J., Gotuzzo, E., & Henao-Restrepo, A. M. (2020). Rapid responses to the COVID-19 pandemic through science and global collaboration: The solidarity clinical trial. *Revista Peruana de Medicina Experimental y Salud Publica*, 37(2).

7. WHO Solidarity Trial Consortium. (2021). Repurposed antiviral drugs for COVID-19—interim WHO SOLIDARITY trial results. *New England journal of medicine*, 384(6), 497-511.

Vaccine R&D

1. Dean, N. E., Gsell, P. S., Brookmeyer, R., Crawford, F. W., Donnelly, C. A., Ellenberg, S. S., ... & De Gruttola, V. (2020). Creating a framework for conducting randomized clinical trials during disease outbreaks.

2. Fleming, T. R., Krause, P. R., Nason, M., Longini, I. M., & Henao-Restrepo, A. M. M. (2021). COVID-19 vaccine trials: The use of active controls and non-inferiority studies. *Clinical Trials*, 1740774520988244.

3. Krause, P. R., Fleming, T. R., Ellenberg, S. S., Henao-Restrepo, A. M., Krause, P. R., Fleming, T., ... & Sommerfelt, H. (2020). Maintaining confidentiality of emerging results in COVID-19 vaccine trials is essential. *The Lancet*, 396(10263), 1611-1613.

4. Levine, M. M., Abdullah, S., Arabi, Y. M., Darko, D. M., Durbin, A. P., Estrada, V., ... & Restrepo, A. M. H. (2020). Viewpoint of a WHO Advisory Group Tasked to Consider Establishing a Closely-monitored Challenge Model of Coronavirus Disease 2019 (COVID-19) in Healthy Volunteers.

5. Krause, P. R., Fleming, T. R., Ellenberg, S. S., Henao-Restrepo, A. M., Krause, P. R., Fleming, T., ... & Sommerfelt, H. (2020). Maintaining confidentiality of emerging results in COVID-19 vaccine trials is essential. *The Lancet*, 396(10263), 1611-1613.

6. Krause, P. R., Fleming, T. R., Longini, I. M., Peto, R., Beral, V., Bhargava, B., ... & Swaminathan, S. (2020). Placebo-Controlled Trials of Covid-19 Vaccines-Why We Still Need Them. *The New England journal of medicine*.

7. Krause, P., Fleming, T. R., Longini, I., Henao-Restrepo, A. M., Peto, R., Dean, N. E., ... & Henao-Restrepo, A. M. (2020). COVID-19 vaccine trials should seek worthwhile efficacy. *The Lancet*, 396(10253), 741-743.

Social Science

1. Atkinson, P., Gobat, N., Lant, S., Mables, H., Pilbeam, C., Solomon, T., ... & Sheard, S. (2020). Understanding the policy dynamics of COVID-19 in the UK: Early findings from interviews with policy makers and health care professionals. *Social Science & Medicine*, 266, 113423.

2. Bielicki, J. A., Duval, X., Gobat, N., Goossens, H., Koopmans, M., Tacconelli, E., & van der Werf, S. (2020). Monitoring approaches for health-care workers during the COVID-19 pandemic. *The Lancet Infectious Diseases*.

3. Carter, S. E., Gobat, N., Zambruni, J. P., Bedford, J., Van Kleef, E., Jombart, T., ... & Ahuka-Mundeke, S. (2020). What questions we should be asking about COVID-19 in humanitarian settings: perspectives from the social sciences analysis cell in the Democratic Republic of the Congo. *BMJ Global Health*, 5(9), e003607.

4. Carter, S. E., Gobat, N., Zambruni, J. P., Bedford, J., Van Kleef, E., Jombart, T., ... & Ahuka-Mundeke, S. (2020). What questions we should be asking about COVID-19 in humanitarian settings: perspectives from the social sciences analysis cell in the Democratic Republic of the Congo. *BMJ Global Health*, 5(9), e003607.

5. Carter, S., Moncrieff, I. S., Bayugo, Y., Hickler, B., Gobat, N., Singh, N., ... & Niederberger, E. (2020). Guidance for health care worker surveys in humanitarian contexts in LMICs.

6. Chan, E. Y. Y., Gobat, N., Kim, J. H., Newnham, E. A., Huang, Z., Hung, H., ... & Wong, S. Y. S. (2020). Informal home care providers: the forgotten health-care workers during the COVID-19 pandemic. *The Lancet*, 395(10242), 1957-1959.

7. Chan, E. Y., Lo, E. S., Huang, Z., Kim, J. H., Hung, H., Hung, K. K., ... & Gobat, N. (2020). Characteristics and well-being of urban informal home care providers during COVID-19 pandemic: a population-based study. *BMJ open*, 10(11), e041191.

8. Collis, A., Garimella, K., Moehring, A. V., Rahimian, M. A., Babalola, S., Gobat, N., ... & Aral, S. (2021). Global survey on COVID-19 beliefs, behaviors, and norms.

9. Pilbeam, C., Malden, D., Newell, K., Dagens, A., Kennon, K., Michelen, M., ... & Sigfrid, L. (2021). Accessibility, inclusivity, and implementation of COVID-19 clinical management guidelines early in the pandemic: a global survey. *medRxiv*.

10. Sigfrid, L., Maskell, K., Bannister, P. G., Ismail, S. A., Collinson, S., Regmi, S., ... & Carson, G. (2020). Addressing challenges for clinical research responses to emerging epidemics and pandemics: a scoping review. *BMC medicine*, 18(1), 1-15.

11. Silverberg, S. L., Puchalski Ritchie, L. M., Gobat, N., Nichol, A., & Murthy, S. (2020). Clinician-researcher's perspectives on clinical research during the COVID19 pandemic. *PLoS one*, 15(12), e0243525.

12. van der Westhuizen, H. M., Kotze, K., Tonkin-Crine, S., Gobat, N., & Greenhalgh, T. (2020). Face coverings for covid-19: from medical intervention to social practice. *bmj*, 370.

13. van der Westhuizen, H. M., Kotze, K., Tonkin-Crine, S., Gobat, N., & Greenhalgh, T. (2020). Authors' reply to Kolstoe and Hanna and colleagues. *bmj*, 371.

14. van Hout, D., Hutchinson, P., Wanat, M., Pilbeam, C., Goossens, H., Anthierens, S., ... & Gobat, N. (2020). The experience of European hospital-based health care workers on following infection prevention and control procedures for COVID-19. *medRxiv*.

15. Verberk, J. D., Anthierens, S. A., Tonkin-Crine, S., Goossens, H., Kinsman, J., de Hoog, M. L., ... & Gobat, N. H. (2021). Experiences and needs of persons living with a household member infected with SARS-CoV-2: A mixed method study. *PLoS one*, 16(3), e0249391.

16. Voo, T. C., Reis, A. A., Thomé, B., Ho, C. W., Tam, C. C., Kelly-Cirino, C., ... & Munsaka, S. (2021). Immunity certification for COVID-19: ethical considerations. *Bulletin of the World Health Organization*, 99(2), 155.

17. Voo, T. C., Reis, A. A., Thomé, B., Ho, C. W., Tam, C. C., Kelly-Cirino, C., ... & Munsaka, S. (2021). Certificación de inmunidad para la COVID-19: Consideraciones éticas. *Bulletin of the World Health Organization*, 99(2), 155-161.

Ethics

1. Jamrozik, E., Littler, K., Bull, S., Emerson, C., Kang, G., Kapulu, M., ... & Selgelid, M. J. (2021). Key criteria for the ethical acceptability of COVID-19 human challenge studies: Report of a WHO Working Group. *Vaccine*, 39(4), 633-640.

2. Köhler, J., Reis, A. A., & Saxena, A. (2021). A survey of national ethics and bioethics committees. *Bulletin of the World Health Organization*, 99(2), 138.

3. Soll, D., Guraiib, M. M., Rollins, N. C., & Reis, A. A. (2020). Improving assent in health research: a rapid systematic review. *BMC medical research methodology*, 20, 1-10.

4. Voo, T. C., Reis, A. A., Thomé, B., Ho, C. W., Tam, C. C., Kelly-Cirino, C., ... & Munsaka, S. (2021). Immunity certification for COVID-19: ethical considerations. *Bulletin of the World Health Organization*, 99(2), 155.

5. Singh, J.A., Kochhar, S., Wolff, J. et al. Placebo use and unblinding in COVID-19 vaccine trials: recommendations of a WHO Expert Working Group. *Nat Med* 27, 569–570 (2021). <https://doi.org/10.1038/s41591-021-01299-5>

WHO Headquarters in Geneva

Avenue Appia 20

1202 Geneva

Telephone: +41-22-7912111



**World Health
Organization**



R&D Blueprint

Powering research
to prevent epidemics