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Interview with Otmar Kloiber by WMJ Editor Peteris Apinis

The Covid-19 pandemic has created a globally troubling situation. In the whole world, governments and politicians, more or less in consultation with specialists of infectious diseases and epidemiologists, take controversial decisions both – on restrictions and on patient diagnosis and treatment. Although the situation is different in different countries, it seems that thanks to politicians and the media the world forgets about other diseases. In many countries of the world, people do not go to hospital or do not receive medical assistance for cardiovascular diseases, oncology diseases, endocrine disorders and other ailments because patients are afraid of either overburdening doctors or getting sick with Covid-19 and therefore do not visit hospitals and outpatient facilities. What is the viewpoint of the World Medical Association on it?

This is indeed a very serious phenomenon. We all know, not everything that is being presented at a medical appointment, is an illness, an injury or a condition that needs medical attention. However, we have seen reduction of "hard cases" like, for instance, significantly fewer patients with heart infarction and strokes show up in emergency rooms and that is troubling. There may, indeed, be fewer cases – a positive interpretation by itself – but it is more likely that patients with milder symptoms have not shown up. And that is worrying because they would have profited from an immediate diagnosis and treatment. We must expect an increase in the number of delayed and more serious cases. Pandemic preparedness is a solution. It must be planned, continuously trained and executed.

Proceeding from this point of view, I would like to ask you: why can't patients listen to the warning for timely careful treatment of their chronic diseases? We know that chronic cardiovascular diseases, endocrine disorders, high blood pressure, overweight are the main reasons for a severe course of the Covid–19 disease and mortality from it. At the moment, the need to treat chronic diseases in parallel with Covid-19 is focused on inadequately.

Your question gives the impression as if these problems are the responsibility of our patients. Many patients, especially those with chronic conditions, have learned to master their conditions quite well. For many others, the deterioration of their health starts later in life and sometimes it is diagnosed very late. Then, changing habits is difficult and needs assistance. The challenges of the Covid-19 pandemic are certainly not to be attributed to patients. They have been caused by lack in pandemic preparedness, wrong political decisions and, first of all, confusing communication. The fact that some conditions turned out to be aggravating factors is nothing patients could have rectified at the time of the pandemic.

Global vaccination against Covid–19 has started now. A number of vaccines are new and can be considered a completely new step in medical science. However, the attitude towards vaccination is very different in different countries. Worldwide, distrust in vaccination increases and anti-vaccination materials are disseminated. Has this problem been caused to a large extent by national politicians and officials intervening in the vaccination process?

Indeed, some politicians have been more part of the problem than the solution. In general, we observe several problems in the vaccine rollout and it is true for all kinds of vaccinations. First – and this is still the biggest problem – there are not enough resources to vaccinate all people. Covid-19 has made this very visible, but the problem exists concerning all vaccinations. Second, there is political distrust in vaccination in some developing countries. Third, there is vaccination hesitancy in affluent countries. These are mainly educated people who believe that pandemics won't affect them because they have been raised in what we believed were post-pandemic societies. They are not aware of the dreadful consequences of pandemics and they have kind of pseudo-scientific knowledge that makes them susceptible to misinterpretation, fake news and lies. Fourth, there are anti-vaxxers who live in their own universe of alternative facts.

During the Covid-19 pandemic many people have been confused with inconsistent, partly chaotic, information by some of the companies and some of the politicians. That did not help.

We know that the world moves toward universal health coverage. The view of the World Medical Association about it differs from that of the World Health Organization, but especially from the point of view of bankers and financiers. Unfortunately, Covid–19 has brought its own corrections as regards the introduction of coverage – both in developing and developed countries. What is your opinion: how is the universal coverage model developing now?

Let us hope that your optimism is correct that we are moving towards Universal Health Coverage (UHC). To be very clear: We do not disagree with the World Health Organization on UHC – not at all! We support the WHO call for UHC wholeheartedly and we see this as the most important strategic aim. Anybody who still believes that UHC is luxury has not understood the message from this pandemic. The human and economic price we pay for the pandemic is extremely high, but it is much higher for those countries which have no UHC.

Achieving UHC is not only a humanitarian challenge, it is also an absolute economic necessity. The pandemic has given proof of this.

Will the current errors and difficulties in organising vaccination leave any traces in terms of vaccination against influenza, diphtheria, papillomatosis and other diseases, the cases when vaccination should become even more important?

Let's be optimistic and hope we still can learn from mistakes ourselves.

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The most important document of the World Medical Association is the Helsinki Declaration that highlights very accurately the attitude of doctors to medical research. Unfortunately, there is a tendency to blame both vaccine developers and doctors taking various preparations against Covid–19 and see it as a clear inconsistency with the Helsinki position. Is the World Medical Association also prepared to discuss the issue: Covid–19 and the Declaration of Helsinki (DoH)?

The development, testing, production and authorization of the new vaccines have been the highlight during this pandemic. Compliments to scientists, the industry and the regulators and thanks to all who have participated as volunteers and researchers in their development!

Concerning the ethics of the trials, we have not seen or heard of violations of the ethical principles in those studies that have been duly published. The problem may lie with those developments that have been hidden, where clinical trials and their results are not completely transparent.

There are serious questions about placebo-controlled studies for additional Covid-19 vaccines as now we have effective vaccines. Those are discussions which we follow carefully. Prevention research will be an issue in the discussion of the next DoH revision.

If there is anything during the pandemic that has really gone well, it is the development of the vaccines. Our challenge now is equitable access to it.

A complementary question: Covid-19 has raised the issues declared by the WMA Declaration of Taipei on Ethical Considerations Regarding Health Databases and Biobanks. Intensive database building is taking place around the world, particularly with patient material produced for the diagnosis and treatment of Covid-19. Is this work worldwide fully in line with the principles of the Taipei Declaration?

Good question! There is still a lot of uncertainty about how to deal with health data. The Declaration of Taipei offers a very practical approach to use health data in an ethical manner and at the same time to maintain individual autonomy and protection. Like the DoH, it is a very realistic set of principles that can facilitate research and at the same time protection for the participants.

Covid-19 has brought new emphasis into global health communication. It is on the need to isolate, keep a distance, wear masks, stay at home, not to meet friends and relatives. At the same time, rhetoric on healthy lifestyles, physical activities, the need to prevent alcohol consumption and tobacco smoking has faded significantly. Should the World Medical Association and national medical associations remind people more of the need to take care of their health by reducing weight, eating healthily, taking care of their psychosocial well-being?

There certainly has been that shift and it was necessary at that time. When somebody is walking on thin ice, you probably don't warn that person not to smoke. But it is likewise correct that we have to refocus on the risks that cause ill-health and disability. And indeed, , the WMA, the World Health Organization and other partners are engaged in it. This is even more important as the pandemic has shown us that pre-conditions – many of which are avoidable – increase the risk of serious damage or even death.

It is precisely the Covid-19 pandemic that has highlighted the global problems Sir Michael Gideon Marmot highlighted at the World Medical Association a few years ago. In different countries of the world the poorest and poorly educated people suffer more from severe morbidity and mortality from Covid-19. Should we not organise a meeting on Covid-19 and social determinants at the World Medical Association?

We will have to accumulate our knowledge and we will have to rework our strategy to improve pandemic preparedness. The Social Determinants of Health are a key point in this process, no doubt.

How has the Covid-19 pandemic affected the work of doctors in the world? We know that many doctors have been severely ill with Covid-19, many have died. But even more doctors have burned out, encountering depression and anxiety. What should the national medical associations do at this time? How has the Covid-19 pandemic affected the work of the World Medical Association? We were used to meet in person, discuss and debate. Will it not be another WMA with completely different aims and agendas, other people and other priorities?

This is a bundle of questions. Many of us, of the health professions and other care givers have carried an extreme burden of the disease. Many have died. And it is a shame that in many countries health professionals and other health workers have not been protected when it was the time to equip them with the right protective material and, even worse, they or their remaining families are often still left alone with their sufferings. Medical Associations in many countries around the world are is struggling with the problems. Covid-19 must be accepted as an occupational disease for health professionals.

Like many others, the WMA has changed its way of working. We were lucky that much of our work, if not most of it, was already telework. The gatherings of our workgroups, the executive committee and many of our informal discussions were based on virtual meetings long before Covid-19. And last year, very successfully, we had our first General Assembly online. And that despite quite complicated weighted voting procedures. Thanks to the software platform created by young physicians – many thanks to them!

Virtual meetings have been necessary, and they will stay with us as will hybrid work patterns. But I doubt that they are a complete replacement of personal meetings. International work is about knowing and trusting one another. It is about sitting face to face and there is a lot of non-verbal communication in a meeting room and a lot of talking in the lobby. Online meetings, even with good video, don't deliver this.

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WMA 2021 Council Report

Seoul (Virtual), April 20–23, 2021

Nigel Duncan

The WMA's 217th Council meeting was due to be held in Seoul, South Korea. But regrettably because of the pandemic, the meeting had to be held online, as was the case in 2020. From April 20–23 the WMA organised a four-day virtual conference, with more than 100 delegates from 40 national medical associations registering for the committee meetings, and the Council sessions.

Tuesday 20 April

Council

The Council meeting was opened by the Secretary General, Dr. Otmar Kloiber, and began with a short video from the Korean Medical Association about Seoul and the KMA's history in the WMA. The President of the KMA, Dr. Choi Dae zip, then welcomed delegates.

He said: 'To all the medical professionals around the world who are fighting fearlessly against Covid-19 with devotion and sacrifice to protect the life and safety of humanity, I wish to express my respect and gratitude. I also grieve for the victims of Covid-19 and extend my deepest condolences to the bereaved families. Each country has a different set of medical environments, standards, public health policies and systems. As such, for the growth of medicine and medical services, it is critical to co-operate and exchange with overseas experts. In times like these, with billions suffering globally due to Covid-19, our communication and co-operation is required more than ever. Thus, our four-day Council session is a precious and meaningful time for such a cause, as a reliable guideline for global medical professionals. I also hope we can establish the basis for another WMA leap forward and for encouraging exchanges between members, committing ourselves to the mutual goal practising compassion for patients'.

Korea's Minister of Health and Welfare, Gwon Deok cheol, also welcomed the meeting. He said: 'In the face of this public health crisis we are deeply grateful to the dedication and hard work of medical professionals around the world who are committed to your responsibilities. We also thank you for the effort of organising this important international event. Although it has been more than a year since the spread of Covid-19, the global pandemic continues to this day. With the dedication of medical professionals and the proactive cooperation of citizens, the entire nation of Korea is striving to respond to Covid 19.

'As you have been ceaselessly combating the pandemic at the forefront, despite several crises, the Republic of Korea has been able to manage this public health crisis relatively stably. Once again, we wish to sincerely convey our respect and gratitude for your service. Since February we have begun vaccinations. Thanks to your active participation in this process, we expect to achieve herd immunity by November, our target deadline.

Until the day we overcome Covid-19 the Government will mobilise all of our capabilities for co-operating with you to respond to the pandemic situation'.

Dr. Kloiber read out a list of apologies and welcomed new Council members.

Council

Elections

Dr. Frank Ulrich Montgomery (Germany) was nominated for a second two-year term as Chair of Council. He was nominated by Dr. Zion Hagay, President of the Israeli Medical Association, who praised him for his leadership and for ensuring that the WMA's voice had been widely heard during the pandemic.

Dr. Montgomery was re-elected unopposed and took the Chair.

Vice-Chair of Council

Dr. Kenji Matsubara (Japan) was re-elected unopposed as Vice Chair of Council.

Treasurer

Dr. Ravindra Sitaram Wankhedkar (India) was re-elected unopposed as Treasurer.

Resumed Socio-Medical Affairs Committee

Recommendations from the resumed session of the Socio-Medical Affairs Committee, held online in January 2021, were considered.

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Taiwan

A proposed revision of the Council Resolution on Observer status for Taiwan to the World Health Organisation was tabled for approval by the Council and for forwarding to the General Assembly for adoption. The Resolution called for Taiwan's participation in all the WHO's health programs based on a substantive, timely and professional basis, as well as a full participating party to the International Health Regulations, allowing Taiwan's critical contribution to the global health protection network.

However, the Chinese Medical Association objected to the Resolution and proposed an amendment to withdraw it, arguing that it was factually wrong. It said that on the precondition the one China principle was observed, a number of measures had been taken to promote cross-Straits health co-operation. And it said there was no barrier to the participation of Taiwan, China in global health affairs, including the WHO.

The Taiwan Medical Association responded, saying that the Covid pandemic had posed a serious threat to all human beings, and Taiwan was helping the international community in combating the virus. It had shared its findings with the world. It would be a great loss to the international community if Taiwan was not included in the international partnership.

In a vote, Council rejected the Chinese amendment by 20 votes to 4, with two abstentions.

The Chinese Medical Association continued to express its strong opposition to the vote, saying that it would never recognize the Resolution.

On a further vote, the Resolution was adopted by 22 votes to one with two abstentions for forwarding to the General Assembly.

Plain Packaging of Cigarettes

The Council considered a proposed revision of the Resolution on Plain Packaging of Cigarettes. This strongly encourages national governments to support the introduction of initiatives that break brand recognition, including plain packaging of cigarettes and other tobacco products. It also deplores strategies from the tobacco industry to oppose the adoption and implementation of such a policy.

The South Africans asked for e cigarettes to be included as well, as these were now being attractively packaged, particularly to children. The committee heard that many young children were using these products. They looked harmless, cool and high tech, but they were in fact very dangerous.

An amendment to this effect was approved and the Council agreed that the Resolution, as amended, be forwarded to the General Assembly for adoption.

The Council also agreed that the proposed Statement on Photoprotection and a paper on Disaster/pandemic Preparedness be forwarded to the General Assembly for adoption.

President's Report

Dr. David Barbe (American Medical Association), in his written report, said his first six months as President had been both unusual and unprecedented. Essentially all meetings had been held virtually and there had been fewer of them. Invitations had been fewer and presentations shorter. But the WMA had continued to have a significant impact on the global discussion on health care and he had participated in several very important international meetings and events. The efforts of the WMA on the Covid virus and physicians around the world had not gone unnoticed.

The highlight of the year was the presentation to the WMA of the "Golden Arrow" award at the 18th Vienna Congress in late January. The WMA was the first organization to receive this very prestigious award. Previous recipients had all been individuals, including presidents of countries and Nobel laureates. The WMA on behalf of all physicians had received the award due to the extraordinary efforts and sacrifices physicians had made on behalf of their patients and their communities during the coronavirus pandemic.

Dr. Barbe thanked all the Council and Committee members and the NMAs for their work during these difficult and unprecedented times and said that physicians and their patients needed their NMAs and the WMA now more than ever. Because of the limitations caused by the pandemic, it would take extra effort by all of them to have that positive impact that was desperately needed in each of their countries. He also reported on the support that the WMA had given to the Turkish Medical Association during the year.

Secretary General's Report

An extensive written report was tabled, detailing to Council all the activities of the Secretariat since the last meeting.

Chair of Council's Report

Dr. Montgomery gave a brief oral report, expressing his disappointment about not being able to meet face to face.

Items of Urgency

Myanmar

Dr. Joseph Heyman, Chair of the Associate Members, reported to the meeting about the current situation in Myanmar, where doctors were being forced by the military to stop delivering care. Doctors working

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in clinics were being arrested, beaten and killed by the military for attempting to save lives. He suggested that the meeting should issue a statement supporting Myanmar doctors. The Indian Medical Association reported that it had close relations with the Myanmar Medical Association and was in contact with doctors in Myanmar.

The Chair suggested that an emergency resolution would be welcome.

The Council meeting was then adjourned.

Finance and Planning Committee

The committee was called to order by the Chair of the Council.

Election

Dr. Jung Yul Park (Korea) was re-elected Chair of the Committee.

Membership Dues Payments

The committee received a Report on Membership Dues Payments for 2021 and considered a Report on Membership Dues Arrears

The Treasurer, Dr. Ravi Wankhedkar, and the financial adviser, Mr Adolf Hällmayr reported that the membership dues status in 2021 was solid and in a comfortable position, as in the previous year. Two new members (Paraguay and the Netherlands) and some Constituent Members (Azerbaijan, Guinea and Haiti) had paid their dues as new additions. The Treasurer expressed gratitude to some members for the valuable contributions they had made by increasing their dues.

The Council approved the Report.

Financial Statement for 2020

The committee considered the interim Financial Statement for 2020 to be audited in June 2021. The Treasurer provided an in-depth analysis of the contents of the document, saying they represented a very solid basis. Dr. Kloiber explained that the audited version would be shared with all members before the General Assembly. In addition, the summary balance sheet had been published in the annual report.

The Council approved the Report.

Strategic Plan

The committee heard an oral report from the Secretary General on the Strategic Plan for 2020–2025. He said the plan was still valid and no change or adaptation was needed. The achievements and activities on the three major strategic areas – Universal Health Coverage, medical ethics and human rights and health – were continuing.

Future Meetings

The Committee considered the planning and arrangements for future WMA meetings:

- it was agreed that the 229th Council Session be held from 24–26 April 2025 and that the 76th General Assembly be held from 8–11 October 2025.
- an invitation from the Royal Dutch Medical Association to host the 77th General Assembly in 2026 in one of four cities – Amsterdam, Rotterdam, The Hague or Utrecht – was accepted.
- it was agreed that "Medical Ethics in a Globalized World" be accepted as the theme of the Scientific Session at the General Assembly, Berlin 2022. It was suggested that the meeting could also discuss the revision of the International Code of Medical Ethics.

The Spanish Medical Association invited all members to participate in the postponed Scientific Session in Cordoba on 17 September 2021, which would take place either in-person, in a hybrid format or online.

The British Medical Association expressed its regret that the BMA had had to convert the October General Assembly into a virtual format due to the uncertainty of the pandemic situation.

Dr. Kloiber reported that the 13th Geneva Conference on Person Centred Medicine, organised by the International College of Person Centred Medicine, was successfully held on 5–7 April 2021. Some WMA Past Presidents actively participated as part of the organising committee. He also reported on the International Symposium on Vaccination, which was originally planned as in-person meeting in the Vatican in 2020 but had to be postponed to 1–2 July this year. It was now planned to hold a small in-person meeting and reconsider holding an in-person meeting in larger format next year. He said the WMA would try to continue regional discussions on the International Code of Medical Ethics, which had proved very fruitful. It was also planning a series of webinars in the second half of this year to look into the consequences and lessons learned from the pandemic, as well as to discuss the outlook and preparation for pandemic situations.

Associate Membership

A report was received from the Associate Members for 2020.

The total number of Associate Members in good standing was 1,487. The regional breakdown was Japan with 605 members in good standing, all other countries 882 members in good standing, made up of 370 paid members, 29 life members, 326 junior doctors and 157 medical student members in free membership. Online applications for the different member types had been implemented on the WMA website.

The Associate Members and the World Continuing Education Alliance were offering its Associate Members free access to a new education platform to help accelerate

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the learning of physicians. This benefit had been available since June 2019.

The committee received the report.

The Chair of the Associates Members, Dr. Joseph Heyman, reported on the group's work on restructuring the membership rules. Volunteers from 29 countries had now drafted proposals for consideration. Their aim was to make the associate membership more valuable to the Association.

The Associates Members' Google group had grown to 422 members, and they reviewed all documents that were circulated for comment by the Council.

Junior Doctors Network Dr. Yassen Tcholakov, Chairperson of the Junior Doctors Network, gave an oral report on the Network's activities. A new management team had taken office in October 2020 and had operated completely virtually since then. But there had been many new members and a strong member engagement had been maintained during this period. The JDN was currently working on streamlining its membership process, creating a virtual newcomer session to introduce members who had recently joined to the activities and modes of work. The Network had three active working groups on Medical Exchange, Education, and International Mobility, Primary Health Coverage (PHC) and Medical Ethics. This year, the JDN planned to complete the two regular biannual editions of the *JDN Newsletter* in April and October 2021. It was also working on maintaining strong links with other health professionals' associations, and was currently working with other youth organizations and the World Health Organization on the establishment of a WHO Youth Council to advise the Director General.

Past Presidents and Chairs of Council Network

The Past Presidents and Chairs of Council Network had continued its work. Dr. Yoram Blachar had been playing an active role on the official relationship with the International Chair of Bioethics. Past President Dr. Jón Snaedal served as President of the International College for Person Centred Medicine, which had been cooperating with the WMA on organising its annual Geneva conference on person centred medicine since 2006. Drs Ardis Hoven and Jón Snaedal had continued on the Steering Committee of WMA Associate Members and had participated in the discussion on ideas for improving the membership activities and engagement.

The meeting was adjourned.

Wednesday 21 April

Finance and Planning Committee

The committee resumed with Dr. Park in the Chair.

He proposed that because of shortage of time yesterday, four items on the agenda should be deferred until the Council meeting on Friday – JDN Terms of Reference, reports on the World Medical Journal, Public Relations and Cooperative Relations, and three items should be deferred to the next meeting in October – LGBTQ Equity in Venues Hosting WMA Meetings and Functions, Green Guidelines for WMA meetings and Guideline for WMA Workgroup Operations.

This was agreed

Bylaws Amendments

The Committee considered two proposed amendments to the WMA Bylaws, both from the Nigerian Medical Association.

The first proposal related to the issue of Presidential voting in the General Assembly, where the Nigerians proposed an amended rule on notifying candidates about the number of votes cast. After a brief debate, the Nigerians agreed to a friendly amendment from the Israeli Medical Association that candidates may request to be notified of the number of votes cast following an election. Only the candidates would be informed of the votes scored by each candidate.

This was agreed by the committee to be sent to the Council for forwarding to the General Assembly for adoption.

The second proposal from the Nigerians related to the number of seats on Council. It proposed an amendment that the Pacific, Latin American and the Caribbean, and African regions should have one extra Council seat to be rotated between those NMAs that had no Council seats each Council term. The allocation of the seat should be decided by majority vote among those regional NMAs unrepresented in Council, after election results were announced by the Secretariat.

This proposal, which prompted a lengthy debate, was introduced with the aim of ensuring better representation and enhancing participation from underrepresented regions.

The Secretary General explained the cost implications and consequences of additional council seats. He reminded the committee about previous proposals for changing the membership of Council and suggested that more discussion was needed on the options of modality and how to implement the proposal.

Several NMA delegates commented on the proposal. Some supported the idea of expanding the Council, others advised caution, suggesting that the amendment could create unintended imbalances on the Council.

The committee agreed that further discussion of the amendment be postponed

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until the Finance and Planning Committee meeting in April 2022 in Paris, which is planned to be an in-person meeting.

Legal Seat of the WMA

The committee considered a report from the Secretary General on the legal seat of the WMA. He explained the problem of the organization being legally domiciled in New York, while its headquarters were in France. He proposed moving the legal seat back to France where the Association had been situated for the past 40 years.

This was agreed by the committee for recommending to the Assembly.

Rules Applicable to WMA Associate Membership

The committee considered a proposed revision of the Rules Applicable to WMA Associate Membership.

Dr. Joseph Heyman, Chair of the Associate Members, explained the background to changing the rules. The changes would ensure that activities of the group were no longer determined by a single person. Term limits would be imposed on officers of the Associate membership, there would be an increase in the number of people who participated in leadership by setting up a steering committee and an increase in democracy by allowing everyone to vote on issues. At the moment, medical students and junior doctors were not allowed to vote. They were increasing engagement and getting rid of some arcane rules.

Dr. Kloiber said Associate membership had been revived. He recommended that the proposals should be circulated before reaching a decision in October.

This was agreed by the committee to recommend to the Council.

Medical Ethics Committee

The Medical Ethics Committee was called to order by the Chair of Council.

Election

Dr. Marit Hermansen (President of Norwegian Medical Association) was elected Chair in a contest with Dr. René Héman (Netherlands).

International Code of Medical Ethics

The committee received a written report on the International Code of Medical Ethics workplan, including a draft of the proposed changes to the code. Dr Ramin Parsa-Parsi, Chair of the workgroup, said that the group had held two very productive video conferences to continue discussing the draft revision. The draft was now ready to be opened up to external review in the form of a public consultation, which would be held in May. It was proposed that the draft should be made available on the website and circulated to ethics experts worldwide.

The committee agreed to forward to the Council the proposed draft for public consultation.

Reproductive Technologies

An oral report was received from the South African Medical Association Chair of the workgroup. The group was tasked with addressing the large and growing number of reproductive technology options and working further on the proposed revision of a Statement on Reproductive Technologies in coordination with the workgroup on Genetics and Medicine, given the number of cross-cutting issues. The committee was told that a number of key ethical and moral issues needed to be elaborated, including multiple pregnancies and termination of pregnancies.

The committee received the report.

Physicians Treating Relatives

The committee considered the proposed Statement on Physicians Treating Relatives submitted by the South African Medical Association. The Statement declared that physicians should not treat relatives, except in an emergency, for short term health problems or in a setting where there was no other qualified physician available.

The draft Statement had been circulated and NMA comments had been included. It was now proposed to include an amendment relating to the duty of the physician to refer a relative patient' in the event of any doubt or conflict with the health care of the patient, or in the situation taking a sensitive history and performing a physical examination may be difficult or uncomfortable for the patient or the physician'. A further friendly amendment was agreed to include the word 'emotionally' before the words 'difficult or uncomfortable'.

However, the view was put forward that the document was not yet ready to be approved. One speaker spoke of the need for some nuancing in the document on the issue of primary care, where what constituted a prescribable prescription differed from one country to another.

The committee voted on a proposal that the document, as amended, be sent to the Council for forwarding to the Assembly. When the vote ended in a tie, it was decided to re-circulate the document for further discussion.

Organ Donation in China

The German Medical Association gave an oral report on organ donation in China, saying that the Chinese Medical Association and German Medical Association had agreed to postpone this issue until October and would continue their discussions in the meantime.

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Declaration of Venice

The committee received an oral report from the American Medical Association on its work revising the Declaration of Venice on Terminal Illness. The committee was told that the Review Committee had now suggested that the Declaration be combined with the Declaration on End-of-Life Medical Care. The AMA said that as a result of this, it would be submitting a further report to the October meeting.

The committee received the report.

Women's Right to Health Care

The South African Medical Association presented a proposed major revision of the Resolution on the Women's Right to Health Care and How that Relates to the Prevention of Mother-to-Child HIV Infection. It suggested that the document be split into two policies – a Statement on Access of Women and Children to Health Care and a Statement on Women's rights to Health Care and How that relates to the Prevention of Mother-to-child HIV infection.

The Statement on Access proposed measures to combat centuries of gender inequality and gender bias on access to health care.

The Swedish Medical Association proposed amending the Statement on Access to include calls for the provision of preconception, prenatal and maternal care and post-natal care, including immunization, nutrition for proper growth and healthcare development for children. In addition, a paragraph was suggested on advocating for educational, employment and economic opportunities for women. These were accepted as a friendly amendments.

The committee agreed to recommend to Council splitting the original Resolution into two Statements, one on HIV and the other on access to health care.

Health Care for Sports Medicine

The American Medical Association submitted a proposed major revision of the Declaration on Principles of Health Care for Sports Medicine. The revised document recommends ethical guidelines for sports medicine physicians and says that the use of anabolic agents and performance enhancing drugs and methods is a threat to the health of athletes and is in conflict with the principles of medical ethics.

The committee was told that the revised document included a reference to the International Association of Athletics Federation regulations that had been opposed by the WMA. Consideration had also been given to the increasing use of anabolic steroids in non-professional athletes and adolescents.

The committee approved the document for sending to Council for adoption by the General Assembly.

Medical Ethics in the Event of Disasters

The committee received an oral report on the revision of policies on health emergencies in relation to natural disasters, epidemics and pandemics. It was told that a draft document would shortly be sent out for consideration.

Classification of Policies

As part of the Association's policy to review all documents that were 10 years old, the committee considered three policy statements and agreed that:

- the Declaration on End-of-Life Medical Care undergo a major revision and be merged with the Declaration of Venice;
- the Statement on the Professional and Ethical Use of Social Media undergo a major revision;
- that the WMA Recommendation on the Development of a Monitoring and Reporting Mechanism to permit Audit of Adherence of States to the Declaration of Tokyo be reaffirmed with a minor revision.

The committee agreed to recommend these proposals to the Council.

Human Rights

The committee was referred to the written activity report, in which details were given about action taken during the year to assist doctors in Turkey, Israel, Iran, Azerbaijan, Myanmar, Singapore and Sri Lanka. Among many other activities, work had continued with the International Committee of the Red Cross on the 'Health Care in Danger' project.

Thursday 22 April

Socio-Medical Affairs Committee

The Chair of Council called the meeting to order.

Election

Dr. Osahon Enabulele (Nigeria) was re-elected Chair of the Socio-Medical Affairs Committee by acclamation.

Health and Environment

The committee heard an oral report on the Environment Caucus meeting that had been held earlier that month. There had been an exchange with the Director of the Global Health and Climate Alliance, who had highlighted current activities. These included the *#HealthyRecovery* initiative launched by the *WHO-Civil Society Working Group to Advance Action on Climate Change and Health*. Through this successful initiative, more than 350 organisations representing 40 million medical and health professionals, raised their collective voice to G20 leaders, calling for a healthy recovery from the COVID-19 pandemic.

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The committee was also told about the global survey on climate change launched in October by the Global Climate and Health Alliance and George Mason University's Center for Climate Change Communication, in collaboration with WHO. The survey aimed to assess the perspectives of health professionals from countries in the six WHO regions around the world and about climate change and its impacts on health.

Medical Technology

The Israeli Medical Association gave an oral report on the workgroup on medical technology. The group had met to consider its remit, which was to examine all WMA policies and recommend those areas where the WMA should voice its opinion, where there should be policy and decide overall how the WMA should work in the area of medical technology. It was agreed that the group should work on a glossary to detail what the word 'technology' covered.

The report was received.

Disaster/pandemic preparedness

The committee received an oral report on the revision of WMA policies related to disaster/pandemic preparedness.

It was proposed to streamline policies to ensure they remained applicable and enabled the WMA to react quickly in the event of a pandemic/epidemic or disaster. Among the actions proposed were to archive both Ebola-specific documents and to have a major revision of the *WMA Statement on Medical Ethics in the Event of Disasters* to ensure that it captured ethics in emergencies in one document. The Statement should touch on new therapies, vaccines, emerging technologies, triage, priority criteria for hospitalization, the role of primary care and ethics of research. In addition, the Declaration on Disaster Preparedness and Medical Response in its current form was outdated and would benefit from a major revision.

The report was received.

Availability, Quality and Safety of Medicines

The committee considered a proposed Statement in support of Ensuring the Availability, Quality and Safety of All Medicines Worldwide. The Statement urges national governments to improve the availability of medications and calls on national governments to establish a national body charged with gathering information about the demand for and supply of medicines, to avoid shortages.

The committee was told by the French rapporteur that there had been a discussion about splitting the draft document into two parts and he thought this was logical. It was important that the text addressed countries all over the world, including wealthy countries. There was also the question as to whether the document should refer to the current pandemic that might no longer be relevant in a few years' time. The pandemic had exacerbated medicine shortages and vaccine shortages in particular. Delegates needed to talk about these issues and address all of the shortages they had seen in relation to Covid. The virus was here to stay for a few years and it might well continue to give them problems for many years.

In the debate that followed it was suggested that the document might benefit from including more global references, and several friendly amendments were accepted.

The issue of vaccine equity was raised, in particular shortages in India, and the fact that countries were not exporting vaccines. It was said that every country should have access, not only to vaccines, but to a range of central medicines.

Dr. Kloiber said that several statements on vaccine equity had been made by the WMA over the past year.

The Statement, as amended, was approved by the committee for sending to the Council for forwarding to the General Assembly.

Medical Liability & Defensive Medicine

The Israeli Medical Association introduced a proposed revision of the WMA Statement on Medical Liability. The Statement calls for an end to frivolous medical liability claims and warns that the increasing culture of blame could lead to defensive medicine. The committee was told that NMAs had been consulted and their comments had been included in the document.

The British Medical Association suggested that delegates should look at this document not in isolation but as part of a wider discussion, with the possibility of a White Paper on patient safety and medical regulation. The BMA had conducted a survey in which 95 per cent of the doctors responding said they were afraid of making medical errors, and many of them said this was a worry they had every day of their working lives. They said this was due to lack of resources, work force shortages and other constraints. Doctors were working in an environment where the system resulted in error rather than doctors as individuals. What was now needed was a discussion about systemic factors, systems of liability and no fault compensation.

The committee approved the revised Statement for sending to Council and forwarding to the General Assembly for adoption.

Access to surgery and anaesthesia care

The Junior Doctors Network presented a proposed Statement on Access to Surgery and Anesthesia Care, which it said had undergone significant changes. The committee was told that access to surgery care had for many years been neglected. The need for improvements were critical for reaching universal health care coverage. This was not about a single specialty, but could cover ob-

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stetrics, pain control, gynaecology, trauma care and primary care.

There was a suggestion that this paper did not fall within the WMA's core business and the paper should be much broader than just anesthesia.

However, the committee agreed to send the proposed Statement to Council for forwarding to the General Assembly for adoption.

Trade Agreements and Public Health

A proposed revision of the Council Resolution on Trade Agreements and Public Health was presented by the JDN. The document represented an update. But the Danish Medical Association suggested that the document failed to find the right balance between the advantages of international trade and the potential side effects on the healthcare sector. It focused too much on the disadvantages of trade. As a result, it was suggested that the document should be recirculated to evaluate the benefits of trade and to strengthen the document.

The proposal to recirculate the document was agreed and the committee recommended this to Council.

Migration and Health

The Norwegian Medical Association proposed a revision to the Statement on Medical Care for Refugees, including Asylum Seekers, Refused Asylum Seekers and Undocumented Migrants, and Internally Displaced Persons. The Statement reminds physicians of their duty to provide appropriate medical care to all refugees, including asylum seekers, undocumented migrants and internally displaced people and that they should do this based solely on clinical necessity, regardless of the civil or political status of the patient.

The Norwegian Medical Association, who had acted as rapporteur for the revision, said that most of the comments and amendments received from constituent members had been included in the consolidated document.

The committee agreed to forward the document, as amended, to the Council for forwarding to the General Assembly for adoption.

Family Violence

A revision to the Statement on Family Violence, which calls for zero tolerance for all forms of violence against women, was presented by the Nigerian Medical Association.

The German Medical Association referred to the preamble which stated that family violence was 'a grave universal public health and human rights problem that affected individuals, regardless of age, gender, racial/ethnic background, culture, religion, socioeconomic status or any other factor'. It wanted to include the words 'sexual orientation', arguing that this was a very prevalent reason for family violence. The change was agreed as a friendly amendment.

The document, as amended, was approved for sending to Council for adoption by the General Assembly.

Use of Telehealth for the Provision of Health Care

A proposed revision to the Statement on Guiding Principles for the Use of Telehealth for the Provision of Health Care was presented by the Chinese Medical Association with the new title of Statement on Digital Health. The Statement, which merges three WMA policies, urges patients and physicians to be discerning in their use of digital health and to be aware of the potential risks and implications.

The British Medical Association talked about the effect that Covid-19 had had on this issue. As a result, they believed this paper needed to be reframed. The word telehealth encompassed such a broad range of means of communication. The BMA had surveyed doctors on this issue and they did not want to return to the old normal. They wanted remote technology to continue. They had all seen the benefits of remote consultations, not a substitute but an adjunct, such as the monitoring of oxygen levels remotely. They needed to redefine what good care could look like. It was no longer appropriate to say, as the Statement did, that face to face consultations were the gold standard. Blood pressure monitoring, for instance, was better done at home. Also, telehealth could improve equity of access.

Several amendments to the document were suggested, such as the deletion of the sentence 'At present, face-to-face consultation should remain the gold standard of clinical care'. These were agreed by the committee.

However, the committee decided to recommend that the document, as amended, be recirculated for consideration.

Rights of Patients and Physicians in the Islamic Republic of Iran

The Kuwait Medical Association proposed a major revision to the WMA Resolution Supporting the Rights of Patients and Physicians in the Islamic Republic of Iran. The revised Resolution now declared that physicians in the Islamic Republic of Iran had reported deliberate denial of medical care in detention, withholding of essential and readily available medications by physicians and other health professionals and a lack of appropriate and functioning medical equipment. They had also reported widespread use of torture and ill-treatment in detention, denial of the rights of hunger strikers, and physicians' complicity in facilitating the death penalty for juveniles in assault on children's rights.

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The German Medical Association proposed an amendment to add a new sentence at the end of the document that the WMA 'stresses that physicians who adhere to the professional and ethical obligations outlined in the aforementioned declarations must be protected'. It argued that in many cases, physicians who adhered to their professional and ethical codes became victims of coercion, punishment, or executions themselves. It was therefore very important to stress the protection of physicians who fulfilled their duty and respected their professional and ethical obligations.

The amendment was accepted as a useful addition.

The committee agreed that the document, as amended, should be recirculated for further consideration.

Patient Safety and Medical Regulation

The British Medical Association proposed revisions to the WMA Declaration on Patient Safety. The committee was told that discussion on medical liability could not be separated from the issues around improving patient safety. They should change the paradigm of how they looked at regulation of the profession. It was often not the individuals who were negligent, it was the system. The fear of blame resulted in defensive practice and there was little learning. Many doctors would not even raise patient safety concerns.

The BMA was suggesting that the WMA should widen the definition of professional regulation to say that it must regulate the system and not just the individual. That would require the WMA to redefine its statements on professional regulation. The first question should be what went wrong, not who got it wrong. What was required now was a White Paper to set out these issues and make recommendations.

This led to a lengthy debate, with delegates discussing the need to improve systemic failures. It was argued that significant numbers of medical errors occurred within the context of wider systemic factors and failings, especially where doctors were working within pressurised environments. A narrow focus on regulating the acts and omissions of individual doctors without first fully considering these wider contributory factors resulted in the inappropriate and unfair targeting of individuals. This in turn resulted in a toxic culture of fear and blame, in which doctors were less likely to be open about errors and safety concerns and were more likely to practice defensively. This ran counter to the aim of improving patient safety through openness, learning and addressing root causes of error. Action was therefore required to foster a supportive health service culture in which medical regulation.

and investigations of errors appropriately examined and took into account any systemic pressures and systems failures.

The BMA proposed a review of the WMA Statement on Patient Safety to address systemic factors and pressures that could lead to medical error, and a document broadening the scope of medical regulation. This was supported by several speakers and the view was expressed that regulation was currently being used to fix the question of patient safety from the wrong side by just a blaming and shaming approach.

The committee approved the proposals for the BMA to continue work on the revision.

Classification of Policies

The committee considered recommendations from members, which was that five policies should undergo major revision:

- *Statement on Health Hazards of Tobacco Products and Tobacco-Derived Products*
- *Declaration of Edinburgh on Prison Conditions and the Spread of Tuberculosis and Other Communicable Diseases;*
- *Statement on the Global Burden of Chronic Disease;*
- *Statement on the Protection and Integrity of Medical Personnel in Armed Conflicts and Other Situations of Violence;*
- *Resolution on Occupational and Environmental Health and Safety.*
- It was recommended that four policies should undergo minor revision
- *Declaration on Leprosy Control around the World and Elimination of Discrimination against persons affected by Leprosy;*
- *Resolution on North Korean Nuclear Testing;*
- *Resolution on Child Safety in Air Travel;*
- *Resolution on Implementation of the WHO Framework Convention on Tobacco Control.*
- *It was recommended that two policies should be rescinded:*
- *Resolution on the Protection of Health Care Facilities and Personnel in Syria;*
- *Resolution on Zika Virus Infection.*

The German Medical Association said it would rather see the Syria Resolution undergo a minor revision to keep it alive. Attacks on medical personnel were still being reported in the tenth year of the war.

The committee agreed that this Resolution should undergo a minor revision and that the remainder of the recommendations should be accepted.

The Socio Medical Affairs Committee meeting was then adjourned.

Friday 23 April

Plenary Council

Emergency Motions

Alexei Navalny

The Council considered an emergency Resolution in support of Alexei Navalny.

The Resolution was moved by the Chair of Council.

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The Chinese Medical Association said that caution should be exercised on this matter. The Council was told there was no Russian representative present at the meeting and the content of the Resolution had not been verified. It was suggested that the secretariat should write to the National Medical Chamber of Russia to consult about the actual situation and their opinions before the proposed Resolution was submitted for consideration. A motion was proposed that the Resolution be delayed. But in the absence of a seconder, the motion fell.

A number of minor textual amendments were proposed and accepted.

On a vote, the Council approved the Resolution by 19 votes to one.

Myanmar

A proposed emergency Resolution in support of Medical Personnel and Citizens of Myanmar was submitted by the Chair of Council. After a brief debate, during which several textual amendments were accepted, the Council approved the emergency Resolution without a vote.

Covid-19

The BMA presented an emergency Resolution in support of the countries worst affected by the Covid-19 crisis. It was argued that it was time for proper global co-operation. Countries owed a debt to countries, such as India, which had manufactured and exported vaccines. No-one was safe until everyone was safe.

There was a debate about whether the Resolution should refer specifically to particular countries, such as India and Brazil. The Council was divided, with some speakers opposing the idea of mentioning specific countries, preferring to use the word 'worldwide', and others arguing that it was essential to include them by name. The Council was told that more than 100 nations had not received any vaccines.

On a vote it was decided by 12 votes to 11, with one abstention, to name India and Brazil in the Resolution.

Several friendly amendments, such as adding the need to strengthen 'health service resilience', were accepted without a vote and the Council approved the Resolution, as amended.

Medical Ethics Committee Report

The Council approved the following recommendations:

- That the current policy draft of the International Code of Medical Ethic be approved for the workgroup's ongoing work and that it be made available for a public consultation starting in May 2021;
- That the proposed revision of the Statement on Physicians Treating Relatives, as amended, be re-circulated to constituent members for comment;
- That the Declaration of Venice be merged with the Declaration on End-of-Life Medical Care;
- That the proposed Declaration on Principles of Health Care for Sports Medicine be approved with the recommendation that it be forwarded to the General Assembly for adoption;
- That the policy Medical Ethics in the Event of Disaster, once received, be circulated to constituent members for comment;
- That the Declaration on End-of-Life Medical Care undergo a major revision and be merged with the Declaration of Venice;
- That the Statement on the Professional and Ethical Use of Social Media undergo a major revision;
- That the WMA Recommendation on the Development of a Monitoring and Reporting Mechanism to Permit Audit of Adherence of States to the Declaration of Tokyo be reaffirmed with a minor revision.

Access of Women and Children to Health Care

The Council considered the proposed Statement on Access of Women and Children to Health Care, as amended, and the recommendation that it be approved, pending a compromise amendment between the South African and British Medical Associations on artificial intelligence algorithms.

The South African Medical Association said it had agreed with the BMA to add the following paragraph to the document: 'In order not to amplify any gender inequalities, information being programmed into artificial intelligence algorithms being created to inform medical diagnoses and management must take into account the specific health considerations of women, for example women may present with different symptoms to men'.

A further addition was proposed reading: 'Governments have an obligation to ensure that the information being programmed into artificial intelligence algorithms being created to inform medical diagnoses and management must include a representative sample of data from women to ensure the gender inequality gap is not amplified further'.

The Council approved the document as amended for forwarding to the General Assembly for adoption.

It also approved the proposed Statement on Women's Right to Health Care and How that Relates to the Prevention of Mother-to-Child HIV Infection, as amended, also for forwarding to the General Assembly for adoption.

Finance and Planning Committee Report

The Council approved the Report on Membership Dues Arrears, the Financial Statement for 2020 and moving the legal seat of the WMA back to France.

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Future Meetings

The Council accepted the committee's recommendation that:
- the 229th Council Session be held from 24–26 April 2025;
- the 76th General Assembly be held from 8–11 October 2025;
- the invitation from the Royal Dutch Medical Association for one of the cities Amsterdam, Rotterdam, The Hague or Utrecht to host the 77th General Assembly in 2026;
- "Medical Ethics in a Globalized World" be the theme of the Scientific Session of the General Assembly, Berlin 2022;
- the proposed revision of the Rules Applicable to WMA Associate Membership be circulated.

The Council agreed to defer to the next committee meeting in October three items:
- proposed Resolution on LGBTQ Equity in Venues Hosting WMA Meetings and Functions;
- proposed Green Guidelines for WMA Meetings;
- proposed revision of the Procedures and Operating Policies on the Workgroup.

Bylaws Amendments

The Council considered the proposed amendments to the WMA Bylaws relating to Presidential voting in the General Assembly and to the number of seats on Council. The American Medical Association said these were very important issues for the WMA and should be considered by a workgroup rather than during an online meeting. A report could then be made to the next meeting in October.

The Council approved the setting up of a workgroup.

JDN Terms of Reference

The Council approved the proposed revision of the Junior Doctors Network Terms of Reference.

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The Council considered a report from the Editor in Chief of the World Medical Journal. In his written report, he said the Covid–19 pandemic had impacted significantly on communication, discussions and contacts. Four Journals had been published during 2020, both in paper and digital format. In his oral report, he said that this year they would focus on articles about Covid–19, doctors' problems, sickness and burnout during the pandemic, and mental health. He said they would be interested in articles describing how national medical associations had coped during the pandemic, what difficulties they had suffered, and how they saw the future of the WMA and medicine, including issues relating to vaccination.

Public Relations

The Council received a report on the Association's public relations. The WMA had continued to maintain a good profile in the media over the past six months. The media's attention had naturally focused on Covid-19. The Association had issued a number of press releases on the pandemic, and the Chair of Council had continued to field a large number of media requests from around the world, ensuring a high global profile for the WMA.

The number of WMA twitter followers had increased to 14,000 and the WMA had increased its visibility by publishing periodically visual quotes of its latest policies that could be easily shared by its followers. The *WMA Facebook* account had more than 13,400 followers. The Association had also increased its online presence during the pandemic with a series of interviews with health leaders from around the world.

Cooperative Relations

The Council considered the proposed Appointment of the International Chair in Bioethics as WMA Cooperating Center.

The Council agreed that the Secretary General sign the proposed Memorandum of Understanding with the "International Chair in Bioethics" ICB and to list the ICB as WMA Cooperating Center.

Socio-Medical Affairs Committee Report

The Council agreed that the following proposed documents be forwarded to the General Assembly for adoption:
- Statement in Support of Ensuring the Availability, Quality and Safety of All Medicines Worldwide;
- Statement on Medical Liability;
- Statement on Family Violence;
- Statement on Access to Surgery and Anesthesia Care;
- Statement on Medical Care for Migrants and that the *Resolution on Global Refugee Crisis*, the *Resolution on Refugees and Migrants* and the *Resolution on Migration* be rescinded and archived;

It was agreed that the following documents be circulated for comments:
- Resolution on Trade Agreements and Public Health;
- *Statement on Guiding Principles for the Use of Telehealth for the Provision of Health Care*;
- Resolution Supporting the Rights of Patients and Physicians in the Islamic Republic of Iran;

Patient Safety
- It was agreed that the British Medical Association be tasked with preparing a proposed Statement on broadening the scope of medical regulation and with revising the Statement on Patient Safety.

Classification of Policies

The Council agreed with the committee's recommendations on the classification of policies that were 10 years old and that five policies should undergo major revision:

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- *Statement on Health Hazards of Tobacco Products and Tobacco-Derived Products;*
- *Declaration of Edinburgh on Prison Conditions and the Spread of Tuberculosis and Other Communicable Diseases;*
- *Statement on the Global Burden of Chronic Disease;*
- *Statement on the Protection and Integrity of Medical Personnel in Armed Conflicts and Other Situations of Violence;*
- *Resolution on Occupational and Environmental Health and Safety.*

That five policies should undergo minor revision:

- *Declaration on Leprosy Control around the World and Elimination of Discrimination against persons affected by Leprosy;*
- *Resolution on North Korean Nuclear Testing;*
- *Resolution on Child Safety in Air Travel;*
- *Resolution on Implementation of the WHO Framework Convention on Tobacco Control;*
- *Resolution on the Protection of Health Care Facilities and Personnel in Syria.*

And that one policy should be rescinded:

- *esolution on Zika Virus Infection.*

Advocacy and Communication

An oral report was given from the Chair of the Advocacy and Communications Workgroup on refocusing the Association's advocacy work. The Council was told this was a new plan to engage with a group of people from the constituent members to reach out on communications.

World Health Organization

The Secretary General reported on the forthcoming World Health Assembly which would be discussing the pandemic and how to improve international health regulations. A WHO group had been looking at how the organisation had performed during the pandemic and what had to be changed.

Vaccine Hesitancy

The meeting ended with a comment from Nigeria, complaining about vaccine hesitancy being encouraged on You Tube by doctors, the majority of whom came from the western world and the United States. He said that the messages were very discouraging, confusing and worrying for people when they made statements about the Covid-19 vaccines not being acceptable. It was suggested that a statement should be prepared on the issue. The Chair of Council said this was a very important issue. The WMA was aware of the problem of both fake information on social media and the activities of anti-vaxxers. He suggested that a paper should be prepared on the issue.

After final thanks from the Secretary General to the meeting's organisers, the Council meeting was brought to a close.

Mr. Nigel Duncan
Public Relation Consultant, WMA

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WMA Council Resolution in Support of the Countries Worst Affected by the Covid-19 Crisis

Adopted by the 217th WMA Council Session, Seoul (online), April 2021

The World Medical Association is deeply concerned to see the alarming and worsening Covid crisis in many countries worldwide, such as currently in India and Brazil. We recognise the huge challenges doctors and other healthcare professionals are facing in maintaining healthcare systems in such harrowing conditions. The WMA calls on the international community and governments to urgently prioritise support and aid to these the worst affected nations, including oxygen, drugs, vaccines, Personnal Protective Equipment (PPE) and other equipment as needed, and to strengthen healthcare system resilience in the face of future pandemics. The pandemic will not end until we tackle Covid in every nation and this is a time for global cooperation, solidarity and support for one another.

WMA Council Resolution in Support of Medical Personnel and Citizens of Myanmar

Adopted by the 217th WMA Council Session, Seoul (online), April 2021

The World Medical Association notes with alarm the continuing actions of the current police and Myanmar security forces including arbitrary arrests and detention of health personnel and other citizens, attacks against physicians and other health personnel and facilities, and continuing harassment and intimidation of protesters, human rights defenders and journalists. The WMA and its members are seriously disturbed by their terrorizing, arresting, kidnapping and murdering health care workers for treating protesters.

These activities are in total opposition to the international recommendations in the *WMA Declaration on the Protection of Health Care Workers in situation of Violence*, the *WMA Statement on the Protection*

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and Integrity of Medical Personnel in Armed Conflicts and Other Situations of Violence as well as the *United Nations Declaration on Human Rights Defenders*.

Thus, the WMA and its members demand that the Myanmar security forces take immediate action to:

- Guarantee, in all circumstances, the physical and psychological integrity of protesters, including health personnel who are arrested;
- Release protesters and personnel immediately and unconditionally, and drop all charges against them since their detention is arbitrary as it only aims at preventing freedom of expression and their human rights activities;
- Put an urgent end to attacks against health personnel and facilities and ensure their protection to provide adequate health care provisions to all.
- Stop all acts of harassment, intimidation, and killing, against protesters, human rights defenders and journalists and comply with all the provisions of the *United Nations Declaration on Human Rights Defenders*;
- Ensure in all circumstances respect for human rights and fundamental freedoms in accordance with international human rights standards and international instruments, including the International Covenant on Economic, Social and Cultural Rights.
- Cooperate with international fact-finding commissions.

WMA Council Resolution in Support of Alexei Navalny

Adopted by the 217th WMA Council Session, Seoul (online), April 2021

The World Medical Association notes with alarm the critical health condition of the Russian opposition activist Alexei Navalny detained in Moscow since January 2021.

Navalny has been on a hunger strike since 31 March and was transferred to a prison hospital on Monday 21st of April. Corroborating information indicates that he is facing denial of adequate medical care and threatened to be force-fed by the prison authorities.

The WMA recalls its *Declaration of Malta on Hunger Strikers* laying down the medical ethical principles governing hunger strikes, in particular the respect of the individual's autonomy and dignity. Force-feeding and any other forms of coercion constitute a form of torture and is contrary to medical ethics.

The WMA recalls the standards of international human rights law, including the International Covenants on Civil and Political Rights and on Economic, Social and Cultural Rights, guaranteeing, amongst other matters, the freedom of expression, access to adequate healthcare as well as the prohibition of torture or cruel, inhuman or degrading treatment. The Russian Federation ratified the covenants in 1973 and is held accountable for its commitments.

Thus, the WMA and its members call on the Russian authorities to ensure full respect for its human rights obligations, and demand immediate action to ensure that Alexei Navalny be treated with humanity and with respect for the inherent dignity of the human person, in particular:

- That he be urgently examined by independent and qualified medical experts,
- That the Russian authorities take all the required measures to provide adequate conditions in line with the Malta Declaration to respect his decision to hunger strike and to ensure that he is not force-fed,
- That he be released immediately as he is a prisoner of conscience deprived of his liberty for his peaceful political activism and exercising free speech.

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Current Research and Future Direction of Haematology in China

Wei Sun

Xiao-Jun Huang

Overview

Haematological diseases are a heterogeneous group of malignancies that affect people's health worldwide such as leukaemia, lymphoma and multiple myeloma. Based on *Global Cancer Statistics 2020*, it is an estimated of 474,519 newly diagnosed leukaemia worldwide, with 311,594 of new death in 2020 [1]. Its high mortality and long treatment cycle seriously hinders quality of patients' life and social and economic development. Treatment options for leukaemia include chemotherapy, hematopoietic stem cell transplantation (SCT), small molecular targeted drugs, monoclonal antibodies, CAR-T cell therapy etc. The development of treatments for haematological malignancies leads to the new era of precise targeted therapy, which benefit from stratified and individualized treatment. The treatment innovation on haematological malignancies from Chinese researchers and clinicians has enriched to the development of global leukaemia precise therapy. In the following paragraphs, we will discuss the exploration of precision therapy, current research and future direction of haematology in China.

Allogeneic stem cell transplantation

Allogeneic stem cell transplantation (allo-SCT) is a method for the therapeutic cure of haematological malignancies [2–4]. However, donor limitations restrict the wide use of allo-SCT. In the past two decades, researchers have established several haplo-SCT protocols based on different approaches to induce immune tolerance [5–7]. Those approaches include 1) ex vivo graft T cell depletion (TCD) in combination with mega doses of CD34+ cells and/or anti-third-party CD8 T cells, in vitro CD3αβ/CD19 depletion, 2) granulocyte colony stimulating factor (G-CSF) plus anti-thymocyte globulin (ATG)-based regimens with unmanipulated T cell replete graft, which originated from the Peking group, China [8, 9], and 3) post-transplantation cyclophosphamide (PT/CY) for tolerance induction [10–12].

In a series of pilot studies on G-CSF-induced immune tolerance by Huang's group, bone marrow T cell hypo-responsiveness could be induced by the upregulation of monocytes and plasmacytoid dendritic cells and the downregulation of co-stimulatory signals during *in vivo* G-CSF administration. The polarization of T cells from Th1 to Th2 could be maintained after *in vitro* mixture of G-CSF-mobilized peripheral blood grafts (G-PB) and G-CSF primed bone marrow grafts (G-BM) [13, 14]. Combinations of G-CSF and ATG were proposed to play a fundamental role in overcoming HLA barriers [15] through the action of regulatory B cell, regulatory T cell, Th17/Tc17, and myeloid-derived suppressor cells [16–22].

Based on the mechanistic research on cytokine-induced immune tolerance, in 2000 Huang and colleagues at Peking University initiated a pilot study investigating unmanipulated haplo-SCT without in vitro TCD for the treatment of acute leukaemia. The study mainly included mixed grafts of G-PB and G-BM, modified busulfan/cyclophosphamide (Bu/Cy) plus ATG for myeloablative conditioning, and cyclosporine A + methotrexate + mycophenolate mofetil for intensified graft-versus-host disease (GvHD) prophylaxis. All patients (n = 58) in the pilot cohort achieved sustained, full donor-type engraftment with an acceptable incidence of grades II–IV acute GvHD (aGvHD, 37.9%) and chronic GvHD (cGvHD, 65.4%). The 2-year disease-free survival (DFS) rates for standard- and high-risk patients were 77.6% and 63.2%, respectively [23, 24]. The cohort was updated [9, 25–27] and expanded to 756 cases in 2010, with 99.5% sustained myeloid engraftment, 43% grades II–IV aGvHD, and 53% cGvHD. The three-year DFS for standard- and high-risk patients was 68% and 49%, respectively [28]. Based on T cell tolerance induced by G-CSF, the

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Peking University group established a novel G-CSF-primed haploidentical blood and marrow transplantation system (The Beijing Protocol) [5, 6], including individualized conditioning regimens, the combination of unmanipulated G-CSF primed blood and marrow as allografts, donor selection based on non-human leukocyte antigen (HLA) systems, risk-directed strategies for GVHD and relapse [29].

HLA match plays a predominant role in the selection of the best donor among unrelated transplants but does not influence the outcomes in haplo-SCT [30, 31]. A given patient might have multiple choices for a haplo-donor, raising the question, "who is the best haplo-donor?" Based on a large sample size and relative consistency of transplant variables, young male non-inherited maternal antigen mismatched donors were suggested to reduce the risk of severe GvHD or relapse. As recommended, transplants from older mothers and non-inherited paternal antigens mismatched donors should probably be avoided [32].

According to a prospective study by Huang et al., unmanipulated haplo-SCT with G-CSF and ATG was proven superior to chemotherapy as a post-remission treatment for intermediate- or high-risk AML or ALL in CR1. The cumulative relapse incidence for haplo-SCT was 12.0% vs. 57.8% for chemotherapy, and the four-year DFS for haplo-SCT was 73.1% vs. 44.2% for chemotherapy. Additionally, in multi-centre studies, Wang et al. reported that haplo-SCT had outcomes comparable to matched sibling donor (MSD)-SCT for adults with intermediate- or high-risk AML in CR1. Similar results were achieved in Philadelphia-negative high-risk ALL in CR1 and MDS [33–36]. Haplo-SCT may also improve outcomes for children compared with umbilical cord blood transplantation [37]. Accordingly, haplo-SCT was adopted as the first-choice alternative donor to HLA-identical sibling donor (ISD). Based on these outcomes, this unique system was named the "Beijing Protocol." As Kodera et al. from the Worldwide Network for Blood and Marrow Transplantation (WBMT) commented, "The Beijing Protocol was shown to be a reliable treatment strategy for patients without a suitable HLA-matched donor" [38].

The "Beijing Protocol" was adopted in the majority of Chinese SCT centres (n > 90). The number of haplo-SCT cases increased to approximately 2500 per year, making it the largest source of allo-SCT donors (37.6%–51.5%) in China since 2013. The "Beijing Protocol" was also reproduced successfully in Italy, Israel, Korea, and Japan [39-41]. The European Society for Blood and Marrow Transplantation reported that G-CSF + ATG-based regimens comprise 43%–45% of haplo-SCT compared with PTCy, which comprises 27%–57% of haplo-SCT in Europe [42–44]. As R. Handgretinger commented, "more than half of the HLA haplotype mismatched transplantations performed worldwide will follow similar protocols (to the Beijing Protocol)" [45]. Correspondingly, haplo-SCT has been a global phenomenon as the frequency of haplo-SCT has grown steadily from 3% to 5% to more than 10% of allo-SCT in Europe and USA [46]. The global contribution of the "Beijing Protocol" and PT-CY thus heralds a new era where "everyone has a donor".

Acute promyelocytic leukaemia

Acute promyelocytic leukaemia (APL) was associated with a severe bleeding tendency and an extremely poor prognosis in history [47]. In the last thirty years, the therapeutic outcomes of APL have markedly improved. The combination of all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) is reported to result in complete remission (CR) rates exceeding 90% and overall survival (OS) rates of 85–99% [48, 49].

In the evolution of therapeutic approaches for APL, the first historical milestone was chemotherapy based on anthracyclines [50]. In the pre-ATRA period, anthracycline-based chemotherapy regimen with or without cytosine arabinoside (Ara-C) was applied in newly diagnosed APL patients. The use of daunorubicin in induction therapy improved CR rate from 13 to 55% in APL [50]. However, the median duration of remission remained poor, ranging from 11 to 29 months [51, 52]. The adoption of ATRA and ATO as treatments constituted a landmark in the development of targeted therapy for APL. In the 1980s, leukemic promyelocytes were found to possess the unique capability to undergo differentiation when exposed to ATRA [53]. Later, ATO was found to be capable of eradicating APL-initiating cells, resulting in a curative effect [54]. The introduction of the ATRA/ATO combination as a synergistic therapy created new possibilities for the treatment of APL. In the initial attempt, combined ATRA/ATO for the induction of remission followed by consolidation chemotherapy resulted in a CR rate of 95.2% and a DFS rate of 100% with a median follow-up of 18 months [55].

In China, the study of oral arsenic formulations has a long history. Beginning in the 1970s, arsenic oxide (As2O3) was used to treat APL [47]. Realgar-Indigo naturalis formula (RIF) is a drug compound containing 30 mg of realgar, 125 mg of Indigo naturalis, 50 mg of Radix salviae miltiorrhizae, 45 mg of Radix pseudostellariae, and 20 mg of garment film in one pill. Based on its clinical results and the anti-APL activity *in vitro* and *in vivo* [56], RIF has been approved by the Chinese FDA and has been commercialized and commonly available in China since 2009.

Huang et al. conducted a single-centre pilot study to evaluate the efficacy of oral arsenic and ATRA without chemotherapy in newly diagnosed non-high-risk APL patients. All patients achieved haematologic CR after a median time of 29.5 days. The rate of complete molecular remission was 65% at 3 months and 100% at 6 months [57]. This preliminary result is encouraging and

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provides initial evidence for the success of a largely home-based treatment protocol for the treatment of non-high risk APL. Subsequently, these findings were confirmed by a multicentre, non-inferiority, open-label, randomized, controlled phase 3 trial at 14 centres in China [58]. This study has suggested that non-high risk APL can be cured using oral arsenic plus ATRA without conventional chemotherapy.

Huang's group has tried to extend the outpatient model to newly diagnosed high-risk APL patients [59]. With a median follow-up of 33 months, 20 patients (100%) achieved a CR after a median time of 30 days. The 3-year estimated OS and EFS were 100% and 89.4%, respectively. Thus, oral arsenic formulations can be administered outside the hospital, which reduces the need for hospital visits, resulting in a superior quality of life than that associated with intravenous ATO.

Chimeric antigen receptor-T cell therapy

Chimeric antigen receptor (CAR) – T cell therapy is one of the most promising treatments of tumor immunotherapy. As of December 2019, a total of 593 clinical trials in Oncology have been registered in ClinicalTrials.gov database, of which 48% of trials are from China and 39% from the USA. Research on CAR-T cell therapy in China focus on not only newly diagnosed haematological malignancies, relapsed or refractory haematological malignancies, but also bridging to allo-SCT and relapse prevention after allo-SCT.

Newly diagnosed haematological malignancies & relapsed or refractory haematological malignancies

Xu KL et al. reported using humanized CD19-specific CAR-T (hCART19) to treat two newly diagnosed untreated adults with B-cell ALL. CR was achieved after CAR-T infusion. No recurrence was observed with follow up for 31 and 21 months, respectively [60]. A series of clinical studies have demonstrated that CAR-T cell therapy shows favourable response rate (CR rate ranging from 54.5% to 88.7%) in relapsed or refractory (r/r) B-ALL and lymphoma [61]. Multi-specific target CAR-T and humanized CD19 CAR-T showed high efficacy for preventing relapse [62, 63]. As for r/r multiple myeloma (MM), Chen SY et al. demonstrated that BCMA CAR T-cell product LCAR-B38M displayed safety and durable responses in r/r MM, with 88.2% of CR rate [64]. Zhou JF et al. treated r/r MM with humanized BCMA-specific CAR-T cells, with 72.2% of the patients achieving CR or sCR [65]. Xu KL et al. reported that 22 patients with r/r MM were infused humanized anti-CD19 CAR T cells and murine anti-BCMA CAR T cells, with 95% of ORR, including 43% sCR, 14% CR, 24% VGPR, and 14% PR [66]. Taken together, BCMA CAR-T cell therapy shows impressive efficacy in r/r MM. However, CAR-T for r/r AML hindered by additional challenges. The central problem of potent, antigen-specific immunotherapy for AML is the absence of truly AML-specific surface antigens. Myeloid ablation should occur with the use of potent CAR T cells directed against CD33 and pan-myeloablation could occur if anti-CD123 CAR T cells were used. Chinese researchers found that CLL1 is highly expressed on AML leukaemia stem cells and blasts cells, but not on normal hematopoietic stem cells. A secondary AML patient was treated with anti-CLL1 CAR-T therapy and achieved morphological, immunophenotypic and molecular complete remission for over 10 months [67]. Ongoing early clinical studies are still being performed in patients with AML who have relapsed/refractory disease.

Bridging to allo-SCT & relapse prevention after allo-SCT

In recent years, more and more researchers focus on allogeneic CAR-T therapies. As for allo-SCT donor-derived CAR-T, allo-CAR-T can be used as a bridge to SCT, as conditioning regimen, and as a powerful means in preventing relapse after allo-SCT. Pan J et al. described an approach for "CAR-T bridging to allo-SCT" in r/r B-ALL, with 90% of r/r patients achieving CR or CRi, 85% of CR/CRi patients bridged to allo-HCT remained in MRD – with a median follow-up time of 206 days [68]. Therefore, CAR-T bridging to SCT in r/r B-ALL shows high response rate and safety. Similarly, allo-SCT donor-derived CAR-T can be also used as the conditioning regimen under the circumstances of allo-SCT. A group of Chinese researchers reported a case, whom was a 12-year-old girl with CD19 r/r ALL preparing to underwent allo-SCT. The patient received Flu, Bu, and Cy combined with the same haplo- donor-derived CD19-CAR-T cells as the conditioning regimen. No blast cells were detected on day +22 after transplantation, suggesting that treatment of r/r ALL with RIC including CD19-CAR-T cells followed by haplo-SCT was safe and effective [69]. As a powerful means in preventing relapse after allo-SCT, CAR-T can be used for patients with relapsed B-ALL, for patients with MRD positive but no response to DLI, and for prophylactic infusion in patients with high risk B-ALL. For example, Peking University Institute of Hematology reported 83.3% of MRD-negative CR rate after allo-SCT donor-derived CAR T-cell infusion in patients with relapsed B-ALL after haplo-SCT [70]. Coincidentally, the team also confirmed that donor-derived CAR-T was effective for patients with MRD no response to DLI in B-ALL after allo-SCT with 83.33% of MRD-negative remission, half of the patients currently alive without leukemia (Huang et al. 2019). A study conducted by Huang XJ et al. also confirmed that despite the CR rates is relatively high for relapsed patients after all-SCT, cumulative recurrence rate at 18 months was 68.3%, the OS rate for the CR patients was 30.0% at 18 months, with a median OS of 12.7 months [71]. CAR-T cell therapy shows significant short-term effect

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and favourable response in patients with B-ALL that relapse. Therefore, CAR-T is another platform following chemotherapy and allo-SCT, which is beneficial to comprehensive therapy.

Future direction

Precise treatment of haematological malignancies is the mission and direction of Chinese haematology oncologists in the new era. Chinese scholars should work together to develop new therapeutic targets for leukaemia, starting with the pathogenesis of leukaemia, immune cells and hematopoietic microenvironment. We should establish a perfect clinical system and commit to high-level clinical research. Meanwhile, it is the precise treatment needs to build a stem cell transplantation platform that changes the current status from everyone can transplant to everyone will receive personalized transplantation.

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Covid-19 in Spain: Health System Response and 2021 Perspective with the Vaccination Plan

Tomás Cobo Castro

The Pandemic in Spain

COVID-19 has been and continues to be, a pandemic with devastating effects due to its morbidity and mortality and the supervening situation caused by the saturation of the health services and blocking of social and economic activity across the world. No similar references exist in our recent past; the professional and scientific world has risen to the global challenge with an enormous investment in talent and resources that has made it possible to create instruments and methods for its diagnosis, clinical management and treatment, and now, vaccines to fight it.

The COVID-19 pandemic has had a particularly high incidence and mortality rate in Spain. Compared to other countries, the adjusted excess deaths per 100,000 inhabitants in 2020 rank Spain occupies a pitiful fifth place in the 29 countries with the highest incomes worldwide [1].

The death rate has been high, albeit unequal in Spain, and has followed a temporal dynamic of four "waves" (with the last one being much smaller), with widely different profiles; said evolutionary profiles are shown in Figure 1.

The incidence curves are compared to the mortality curves; as shown in Figure 2, the cumulative 14-day notification rate is lower at the start of the pandemic, while the mortality rate is extremely high during the early phases.

The first wave (March and April 2020) had an early and dramatic development in Spain, with increasing exponential morbidity and extremely high mortality, especially among institutionalised elderly people. Health and social workers were greatly affected by the lack of personal protective equipment and the rapid exhaustion (due to use and hoarding) of the available international stock of coveralls, gloves and face masks. The uncertainty of a new disease whose characteristics were unknown posed an added difficulty in facing it. The epidemic quickly spread to nursing homes, in which the particular vulnerability of the residents produced very high mortality rates.

A radical lockdown was established, and it was necessary to declare the State of Alarm: the first one through RD 463/2020 of 14 March, which was extended until it ended on 21 June, when the first wave had been clearly overcome).

The emergence from the first wave posed new challenges. On 15 April, the EU, which had maintained a low profile and been subject to criticism for its inability to guarantee supplies of materials and medicines, marked out a "common road map" to lift the restrictions (which, in particular, affected the movement of people and border control). In Spain, the Council of Ministers Agreement of 28 April 2020 approved the Plan for the Transition to the New Normal [2] , which set out the "reopening" process.

The first wave had exposed many structural problems in the National Health System; the weakened public health system, the lack of investment in primary care, the lack of resources and access to strategic supplies and problems in the cohesive operation of the National Health System, with its highly decentralised structure divided among 17 Autonomous Communities made it difficult to provide a coordinated response. On 7 May the House of Representatives set up the Commission for the Economic and Social Reconstruction which, in just over two months, approved a decision; its 71 recommendations relating to the "health and public health" received strong political backing and have a notably reformist content, which could be a road map for updating and revitalising the National Health System [3]. The idea of "reconstruction" was somewhat relegated to the agenda when the growing incidence of COVID-19 led to a new wave.

This second wave was very quick to arrive and started its ascent in July. It worsened in October and it was not until November that it started to fall slightly. On 22 October a document was published with "Actions for a Coordinated Response to control transmission" [4], approved by the National Health System Inter-territorial Council which established in great detail the levels of alert and indicators that would determine the risk assessment. Furthermore, on 25 October, in the middle of the second wave, a new State of Alarm was declared (RD 926/2020) which, shortly afterwards, was extended for a maximum of six months (it ended on 9 May).

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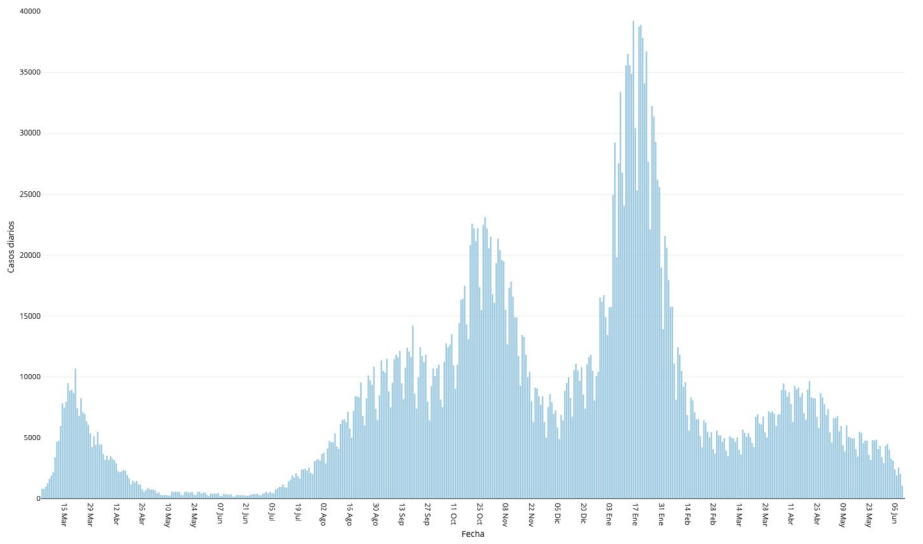

Figure 1. Daily number of confirmed cases of COVID-19 in Spain. Source: Ministry of Health Website https://cnecovid.isciii.es/covid19/#ccaa

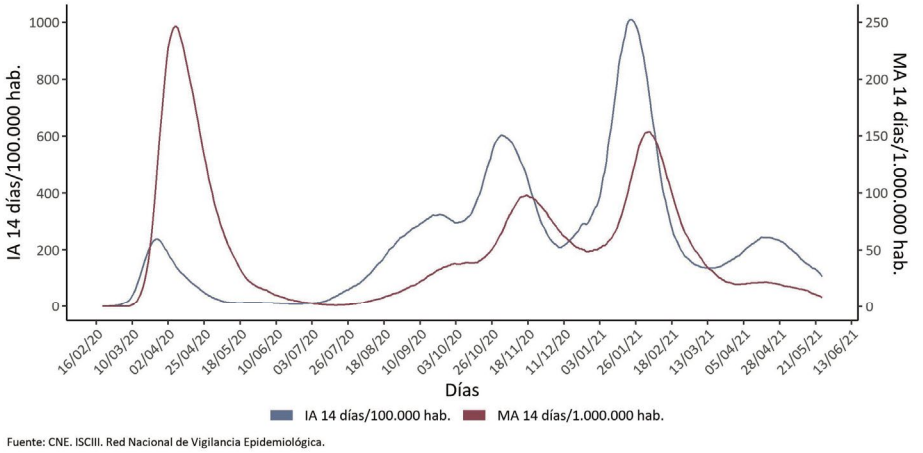

Figure 2. Comparison of Incidence and Mortality in cumulative 14-day notification rate. Source: RENAVE-Centro Nacional de Epidemiología, Instituto de Salud Carlos III (Figure 9 of the text). https://www.isciii.es/QueHacemos/Servicios/VigilanciaSaludPublicaRENAVE/EnfermedadesTransmisibles/Paginas/InformesCOVID-19.aspx

The prolongation of measures to restrict movement (closing of regional borders and curfews), restrictions on the number of people who could meet, capacity limitations and restrictions and the closing of restaurants, bars and nightclubs had a growing effect on the morale of the population (what is known as pandemic fatigue). As well as on the economy in general (2020 witnessed an unprecedented fall in the GDP of 11%), and on certain sectors, in particular. The eager promise of funds from the EU (which wanted to regain its role in the crisis) led to the creation of an extensive programme to protect employment (financial aid and subsidies for unemployed workers), but the prolongation of the pandemic has tended to reduce the sustainability of such measures.

The third wave began in December 2020, reaching a maximum number of cases on 15 January, as a result of the increase in population movements and family and commercial interactions at Christmas. During this third wave, political tension and institutional rivalry have played a greater than desirable role, both due to the perceived contradiction between health and the economy and the competition aroused by the distribution and administration of the first vaccines (18 January 2021) and the distribution criteria.

Vaccination strategy and process

On 18 December the National Health System Inter-territorial Council (the body that coordinates the central health authorities and those of the 17 Autonomous Communities) drafted a Vaccination Strategy [5] that required enormous flexibility and management capacity. The initial slowdown in supply and the idea of not being able to "save the summer" had a negative effect on the collective morale while controlling the third wave also took its toll by saturating hospitals and UCIs in many Autonomous Communities.

The COVID-19 vaccines are now the decisive factor in controlling the pandemic in 2021. The EU went one step further with its centralised approach [6] which, despite the problems (related to production and fulfilment of contracts), has permitted a stable flow and prevented even greater problems. Because it should be considered that the European member states continue to be

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united in relation to the negotiation, contracting and distribution, thus preventing what might have been an inefficient and embarrassing struggle between countries to obtain as many vaccine doses as possible for their citizens.

The Vaccination Strategy in Spain was updated on seven occasions, until 11 May [7]. The challenge was to combine the progressive availability of vaccines with the establishment of priorities. On 7 May the EU had four vaccines authorised by the European Commission: The Pfizer/BioNTech Comirnaty vaccine, authorised on 21 December2020; the Moderna vaccine, authorised on 6 January 2021; the AstraZeneca Vaxzevria vaccine, authorised on 29 January 2021 and the Janssen/Johnson & Johnson vaccine, authorised on 11 March 2021.

On 24 May, 17.2 million Pfizer vaccines, 5 million Astra-Zeneca vaccines, 2.1 million Moderna vaccines and 0.3 million Janssen vaccines had been administered in Spain. A total of 8 million Spaniards have now received two doses (17.1% of the population) and 16.7 million have received at least one dose (35.2%).

The strategy has experienced complications due to problems of availability; in addition to delays or failure to honour production commitments which, in the case of the Astra-Zeneca vaccine, has led to litigation between the European Commission and the laboratory, the pharmacovigilance system raised the alarm between March and April 2021 in relation to thromboembolic events in the AZ and Janssen vaccines (particularly among people under 60). In Spain, the Vaxzevria vaccination programme was suspended between 16 and 23 March. On 24 March it was resumed, increasing the age of those eligible to receive this vaccine to 65 years. From 8 April, following the assessment report drafted by the European Medicines Agency (EMA), the use of this vaccine was confined to people over 60 years of age.

Since the end of April and in May, the vaccine supply and administration rate has rapidly increased, making it feasible to achieve the Government's goal of having 70% of the population immunised before the end of the summer.

The defining of priorities in administering the vaccine has been based on 10 groups with 9 additional subgroups, taking into consideration criteria related to severity of the disease, the capacity to become infected and workers performing essential jobs.

The risk-benefit balance of the vaccines is extremely positive; the medicine regulation agencies (EMA and FDA) have endorsed the use of the vaccines being administered in Spain. Nonetheless, many European governments have established recommendations combining the type of vaccine with the age of the persons receiving it.

Managing a vaccination programme with so many age groups and criteria has proved to be extremely complicated; public debate about adverse reactions, the age of the persons receiving the vaccine and priority groups have given rise to much distrust, which has increased with the doubts and difficulties in explaining the changes in strategy. At all events, the fact that the vaccination process is now progressing at a very fast rate is now resolving many of the problems related to priority.

The idea of reducing the use of Vaxzevria due to the adverse effects detected has taken precedence, despite their low frequency (up to 25 April, out of a vaccinated population of 5 million, 11 cases of thromboembolic events have been detected in Spain, causing three deaths). This has led the central health authorities to recommend the administering of the second dose of an ARNm vaccine (Pfizer or Moderna), but this has not been included in the summary of product characteristics due to not having been tested in clinical trials. Instituto de Salud Carlos III has conducted a rapid study on reactogenicity and immunogenicity in administering a second dose of Pfizer, with positive results For this reason, the use of guidelines is being considered, but accepting that people can voluntarily ask to receive Vaxzevria as the second dose by signing a consent form.

In Spain, the number of people who refuse to be vaccinated is very small, but in the case of Astra-Zeneca, a considerable number of people have asked to change to another in some Autonomous Communities, following the news about the adverse effects. The prospect of implementing the EU-COVID-19 digital certificate (approved on 20 May 2021) to allow vaccinated persons to travel will no doubt help to encourage vaccination among those who are more likely to refuse it.

The perspective of the medical profession

The pandemic has taken a heavy toll on Spanish doctors. 112 of our colleagues were among the first to die and many have fallen ill, as a result of their commitment and dedication to treating patients, especially during the first phases, in which there was a shortage of personal protective equipment. And also, as second victims, since we had to assume the enormous effort of taking on heavy workloads and witnessing human suffering for more than one year; fatigue and the physical and psychological consequences will continue to accompany us for quite some time.

We have criticised both governments and the health authorities [8]. We were insufficiently prepared to deal with the pandemic and furthermore, in the previous decade, the National Health System suffered heavy cutbacks due to the economic crisis from which we have not yet recovered; public health and primary care were in very precarious conditions and were underfunded.

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Nonetheless, we have also been supported by citizens, who have recognised the effort and commitment of all the health and social workers to their patients. It has been comforting to see how we have honoured our Hippocratic Oath and how all doctors have joined forces in the common task of saving the lives of patients, regardless of their speciality or rank. It has been an emotional re-encounter with the finest of the medical profession, which has continued to exist beneath the cold and impersonal surface of technomedicine.

And today, we hope that, through the vaccines, the fruit of science and medical technology will control this pandemic that has caused so much harm.

In all cases, from the perspective of the medical profession, what is relevant here and now is to make headway in the vaccination programme, and to do this, it is important to generate trust among citizens and ask institutions to behave with caution and clearly maintain the priority of immunising those who are most vulnerable (an objective that to a great extent already been achieved).

Encouraging vaccination and strengthening the role of the Public Health authorities; even though new scientific information may exist that generates uncertainty, we are in need of a firm collective decision maker. It is necessary to find mechanisms for participating in decisions that do not entail generating distrust and erode the credibility of the technical bodies whose duty is to establish the measures to be taken, normally with great uncertainty and variables that need to be taken into consideration. Without forgetting that to control the pandemic, it is essential to encourage vaccination in all countries as soon as possible, to guarantee collective immunity. As the vaccination progresses, it will be more important to strengthen resources to investigate outbreaks, perform systematic tracking procedures and ensure that isolation and quarantine processes are complied with; only by doing this will we be able to extinguish the embers and apply our best efforts to the prevention of avoidable morbidity and mortality.

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The Czech Strategy of the Controlled Establishment of Herd Immunity Ended in Disaster

Politicians made a false dilemma of whether to protect the health or the economy. We wanted to outsmart the virus, but we lost everything. More than 30,000 dead and a ruined economy – this is the result of the worst catastrophe in our recent history.

The Czech Republic has a population of 10,5 million and is one of the countries most affected by Covid-19. Last year, due to an increase in the number of deaths, the population decreased, and the average life expectancy shortened. This happened for the first time since World War II.

1 March 2020 was the day when the first case of Covid-19 was confirmed in the Czech Republic. There were no anti-epidemic plans, and no personal protective equipment was available to health professionals. Fortunately, the government initiated a swift response by implementing effective anti-epidemic measures, and the spread of the epidemic halted. People monitored horror situation in more af-

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Milan Kubek

fected countries and were disciplined and helped each other. The symbol of our successful fight against the epidemic became homemade masks, which substituted a lack of protective equipment. In the first half of 2020, only 347 patients died from Covid-19 in the Czech Republic.

After successfully managing the first wave of the epidemic, a sense of self-complacency and false security prevailed in our country. With the participation of leading politicians, a common picnic of thousands of people took place on the Charles Bridge in Prague on 1 June 2020, and it became a symbol of foolishness. In the summer of last year, in contrast to many other countries, there were practically no anti-epidemic measures applied. The government did not use the *relaxation period* – given by the summertime – to prepare for the autumn wave of the epidemic, which experts warned against.

The situation began to worse at the end of August – after people returned from holidays abroad, and the critical point came in early September after children returned to school. It was not mandatory to wear a mask, testing was insufficient, and the numbers of infected began to increase rapidly. Given that the regional elections took place in early October, politicians did not dare to implement unpleasant but effective anti-epidemic measures. That turned to be a catastrophic mistake.

Popular but incompetent Minister of Health, Vojtěch, was dismissed on 21 September, and he was replaced by a firm professor of epidemiology and a former soldier, Prymula. The government declared a state of emergency. However, the epidemic was already burst out. The most affected group of people were the elderly, especially residents of retirement homes and social facilities, who were dying by the hundreds.

Before the result of the anti-epidemic measures could reveal, Minister Prymula was forced to abdicate due to compromising photographs showing him not observing the rules he had ordered. Paediatrician Blatný, at that time unknown to the public, became the third minister. However, he did not take the epidemic seriously enough. For example, the Czech Medical Chamber has repeatedly (and vainly) appealed to him to take more effective anti-epidemic measures so we can bring the epidemic under control before people run out of patience and stop respecting restrictions.

The second wave of the epidemic culminated in early November. An average of 250 people died of Covid-19 a day, and the disease became the most common cause of death (140 people die of cardiovascular disease, and 75 people die of cancer every day in the Czech Republic). At the beginning of November, overall mortality doubled compared to the five-year average. At that time, on a per capita basis, the Czech Republic had the highest number of people who died of Covid-19. To handle the epidemic, elective care had to be drastically reduced, and most hospital wards were transformed into so-called *Covid units*.

After the situation began to improve in the second half of November, the government – under constant pressure from the opposition requiring loosening anti-epidemic measures or the protest demonstrations – made another fatal mistake. Three weeks before Christmas, they opened restaurants and shops. Nobody listened to the warnings of experts or disproval of the Czech Medical Chamber. Free antigen testing turned to be counterproductive, too. People who received a negative result thought they could not infect others. However, this was not the case due to the low sensitivity of these tests.

During Christmas, people were visiting their relatives and at the beginning of this year, the third wave of the epidemic started. Vaccination became a ray of hope, although in the first months there was a lack of vaccines. The elderly were the first group to be vaccinated. The Czech Medical Chamber enforced priority vaccinations for all health professionals who were the most affected professional group. At a critical time, we had almost 10,000 infected health professionals, including 1,200 physicians. In total, we had 77,000 infected health professionals, among them 12,000 physicians. The saddest thing is that 88 health professionals died, including 34 physicians.

In January 2021, hospitals in the most affected regions started to collapse, and patients had to be distributed throughout the country. Due to insufficient sequencing of PCR tests, we did not know that the more contagious so-called British (alpha) mutations of the virus began to prevail in our country sooner than at the beginning of February. At that time, after a slight improvement, the implemented anti-epidemic measures occurred to be insufficient, and the fourth wave of the epidemic – the most massive one – began to unfold. Health professionals fought for human lives while politicians argued over whether, or not, a state of emergency should stay declared and whether, or not, closure of schools, restaurants and shops was legal. It is sad that, in addition to some politicians, the epidemic

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Covid-19 in the Czech Republic – numbers

	Currently infected		Hospitalized		In critical condition		Daily deaths	
1. wave	11.4.2020	4 570	8.4.2020	423	12.4.2020	100	8.4.2020	15
2. wave	28.10.2020	122 539	5.11.2020	8 141	3.11.2020	1203	3.11.2020	261
3. wave	6.1.2021	118 468	7.1.2021	7 513	12.1.2021	1 155	8.1.2021	196
4. wave	14.3.2021	159 922	15.3.2021	9 458	16.3.2021	2 061	15.3.2021	236

Source: The Institute of Health Information and Statistics of the Czech Republic

	Cases per million inhabitants (cumulative)	Deaths per million inhabitants (cumulative)
Czech Republic	155 600	2 827
Hungary	83 600	3 100
Poland	76 000	1 975
Austria	72 100	1 185
Slovenia	71 700	2 285
Germany	44 500	1 078

Source: John Hopkins University (22.6.2021)

https://ourworldindata.org

was downplayed, and the anti-epidemic measures were questioned also by some physicians, including the rector of Charles University. Various fake news regarding the safety of vaccination and another questioning of Covid-19 seriousness spread through the internet, too.

During the epidemic, our government, whose credibility in the eyes of the Czech population gradually fell to a historical minimum, unfortunately, did not venture to close factories or reduce all economic activities except for the critical infrastructure. In the winter, however, at least antigen testing at regular intervals became mandatory for all employees.

In mid-March, more than 200 patients died of Covid-19 per day again. Some elderly have already been vaccinated, though there were still casualties within the younger population. In critical weeks, the total number of deaths in the Czech Republic (for all causes) increased by up to 60% compared to the five-year average. There were 10,000 patients with Covid-19 in hospitals, of whom more than 2,000 were in critical condition. Thanks to the enormous effort of health professionals, the Czech healthcare system withstood this huge pressure, while in some of the neighbouring countries, it collapsed even with the smaller numbers of infected people. At the peak of the epidemic, 160,000 patients were infected in our country.

The decline of the epidemic was too slow, and people's discontentment grew. Vaccination was slow, too. On 7 April 2021, Minister Blatný was recalled and replaced by renowned dermatologist Professor Arenberger. He initiated the gradual anti-epidemic measures loosening but was recalled within a month due to his unclear property situation. Prime minister Babiš appointed a lawyer, Vojtěch, to the post of the Minister of Health for the second time – he already held this post at the beginning of the second wave of the epidemic. As if to show that the epidemic is over, and we are to forget both more than 30,000 deaths (the total number of deaths during the epidemic has exceeded the average of the past five years by more than 40,000) and the ruined economy.

Covid-19 has been confirmed in more than 1,700,000 people, with probably another 1 million patients not confirmed by tests. At present, the epidemic situation is favourable, but the Czech Republic remains below the EU average in terms of vaccination rates. At the end of June, only 25% of the population has been vaccinated with both doses. Although children from the age of 12 will be vaccinated from the beginning of July, politicians focus on their campaigns before the October parliamentary elections, rather than on vaccination-promoting campaigns.

A year ago, we celebrated *a victory* over Covid-19 in the Czech Republic. That was before another 30,000 patients died of this disease. It is hard to avoid *a déjà vu* feeling when most people are now only interested in how to enjoy their holidays again, we have the same minister again, and at the beginning of October, elections will take place again. Before this event, politicians will compete in populism. We hope for the best, but we should prepare for the worst. Wish us luck.

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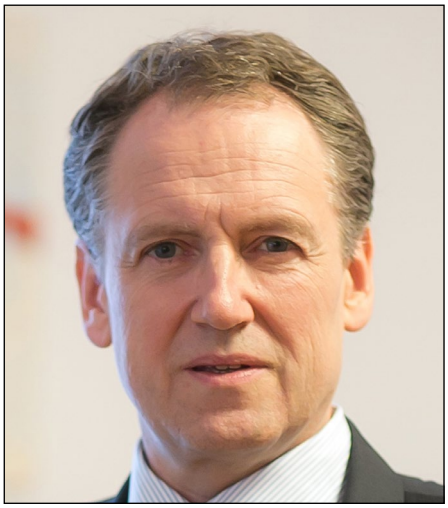
Austria's Approach to Combatting Covid-19



Herwig Lindner

By the start of the first lockdown on 16 March 2020 at the latest, the pandemic was present in everybody's life. Schools switched to distance learning, non-essential shops shut down and intensive care beds started to fill up. Within a few days, the number of infected people doubled. Fortunately, however, the "near overload" in Austria's hospitals never occurred, partly due to the country's shutdown with following lockdowns and the willingness of the general population to comply with the necessary measures (mouth/nose protection, ventilation, hand hygiene, social/physical distancing, etc.) [1], but also due to the well-equipped hospitals in regards to the number of available hospital beds and the relatively high capacities in intensive care units. This put Austria in the favourable situation of being able to support other European countries by supplying respirators and offering hospital beds with respirator access to some of their patients in Austrian ICUs. One important step to relieve the Austrian health care system, especially the intensive care units, was the approval of safe and effective vaccines. However, it wasn't long until demand became higher than supply. This was due to the initial reluctance to procure vaccines, which meant that there was not enough vaccine available for a rapid vaccination campaign. To date, more than 6 million vaccinations have been administered, with more than 2 million people already having full vaccination protection [2]. Although the government's target of administering vaccinations to all those willing and eager to be vaccinated by the end of June will not be reached, we are now well on our way [3].

Challenges of the COVID Pandemic in Austria

A week after the global spread of the disease was declared a pandemic by the World Health Organization (WHO), a nationwide lockdown was imposed as a quick and rigorous response to help flatten the curve in Austria. Despite growing case numbers in late summer 2020, a second lockdown wasn't ordered until mid-November. In the beginning of the pandemic, suspected infected persons were ordered to quarantine at home, while attempts were made to locate any contact persons so that, if necessary, home quarantine could also be imposed on them. However, contact tracing became more and more difficult due to the rising number of cases. Early on, Austria's government relied on testing to quickly identify infected individuals and break the spread of the virus by isolating them. The Austrian testing strategy for the detection of SARS-CoV-2 has three main objectives: Testing-Tracing-Isolation (TTI), transmission prevention and information gathering. In order to best contain transmission, it is necessary to regularly test as many asymptomatic individuals as possible in addition to TTI, which specifically targets symptomatic individuals [4]. Willingness to be tested has increased in Austria, albeit slowly. Thus, despite the rather unsuccessful mass testing efforts, which were modelled after previous experiences in South Tyrol and Slovakia, it was decided to provide free access for all citizens to antigen testing, as well as to PCR testing for those experiencing symptoms. This offer is to remain in place at least until the end of summer 2021, especially since the group of 12- to 15-year-olds probably won't be vaccinated until July or August [5].

The pandemic has made undesirable developments in the health system clearly visible. Too little investment in the health sector over the years has led to a lack of training opportunities, vacant positions and poor remuneration. The challenging work that doctors do on a daily basis is often ignored and not sufficiently rewarded [6]. Together with complications in the non-transparent procurement of the vaccine and the rapid spread of negative coverage in the media, debates and uncertainties arose in the population, which now need to be resolved and clarified.

At the beginning of the pandemic, doctors had to struggle with the lack of protective equipment. As in other countries, in the first weeks of the pandemic there wasn't sufficient or adequate protective equipment – especially masks were scarce. Doctors worked under very difficult conditions during this period. This was further complicated by the global competition for masks and other protective equipment, even to the point of countries confiscating trucks carrying aid supplies and respirators, not letting the drivers cross the border to reach their destination country. In the Austrian federal system, some states provided their general practitioners with masks, while others unfortunately did not. As a result, doctors put themselves at risk in the fight against the pandemic and some fell ill or even succumbed to their infection while fulfilling their obligations as doctors.

To prevent medical collateral damage during the lockdown and shutdown periods,

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practices remained mostly open, especially for primary care and initial examinations and consultations. Telemedicine (especially telephone, videocalls, e-mail) was made possible for the period of the pandemic to drastically reduce direct patient contact. To what extent telemedicine was used in addition to or instead of personal patient consultations was up to the general practitioners themselves. A limit on the number of patients in waiting rooms prevented the accumulation of groups of people and ensured compliance with the distancing rules. Prescriptions can currently still be sent to patients or directly to a preferred pharmacy, where patients can pick up their medication. Challenges we are now facing more and more frequently are patients continuing to skip their check-ups and their reluctance to seek medical treatment. During the first lockdown, patients – partly with severe illnesses – avoided practices and clinics out of fear of contracting an infection. Many patients did not have their scheduled preventive check-ups, despite most practices and clinics being open. This trend must now be counteracted in order to increase the number of examinations again and to be able to detect diseases early and treat them quickly. Because, while COVID is undeniably a serious disease, it is not the only one.

Implementation of the Vaccination Strategy

On 27 December 2020, during Austria's second lockdown, the first few members of one of the "at risk groups" were chosen to be vaccinated by Dr. Thomas Szekeres, President of the Austrian Medical Chamber, and Dr. Ursula Wiedermann-Schmidt, President of the Austrian Society for Vaccinology and Chair of the Austrian Vaccination Commission, to herald the start of the Austrian vaccination program. This was seen as a historic day and a turning point after a months-long battle with the pandemic. At that time, the 3 phases of the Austrian government's vaccination strategy were to first immunize the "high-risk group", e. g. people over 80, followed by "older people and employees of the critical infrastructure", before all Austrians were to be vaccinated in the third and final phase [7]. Unfortunately, it became clear relatively quickly that due to delivery delays and the slow distribution of the vaccines, the vaccination program could not be carried out as planned. At that time, the Austrian Medical Chamber issued numerous press releases to urge those who were politically responsible to buy more vaccines. The Austrian Medical Chamber already called for vaccines to be obtained quickly and in sufficient quantities in the summer of 2020. Unfortunately, those remarks remained unheard. While supply shortages from and scepticism about AstraZeneca resulted in fewer people being vaccinated, increased supply from BioNTech/Pfizer accelerated the vaccination schedule. Nonetheless, many of those willing to be vaccinated still have to wait for their first shot to be administered [3].

The implementation of the vaccination strategy was further complicated by the different interpretations of the national vaccination strategy in Austrian federal states, resulting in varying implementations of the same strategy, with different "priority rules" and schedules throughout the country [8]. Perceived disadvantages and uneven distribution further fueled the debate around the vaccination strategy and its implementation, which increased uncertainty among the population.

Being a comparatively small country, Austria appreciates being part of the procurement and distribution process of the European Union. In regards to administering the vaccines, the authorities opted for a dual system early on – with vaccinations being administered in vaccination centres and practices of general practitioners. Unfortunately, as has been seen in many other countries, Austria is now struggling with an increasing number of people refusing to wear masks and opposing vaccinations altogether. Doctors play an important role in dispelling such doubts and gaining trust, especially since physicians in private practices know their patients best and can provide information and administer vaccines quickly [9].

Long COVID as a Lengthy Endeavour

Due to the global emergence of cases and enormous collection of data worldwide, COVID is now among the best-researched infectious diseases. It is mainly the rapid developments and investments in research, but above all the hard work of doctors all over the world, that has led to the development of vaccines to stop the spread of infectious disease in such a short amount of time. While the risk of contracting COVID for previously uninfected persons is decreasing as vaccination progresses, the number of Long COVID patients is expected to increase steadily. These patients face particularly difficult challenges since neither symptoms, therapies nor the length of impairment can be assessed at this point. Due to the varying duration, intensity and symptoms of the disease, it is often difficult to determine whether a patient is struggling with Long COVID at all. As this is an emerging and constantly evolving phenomenon, there is a lack of data as things stand. Therefore, information from psychosocial hotlines or survey data from the 'Austrian Corona Panel' is currently used as a basis for findings concerning the development and emergence of a growing number of Long COVID cases [10].

As the name already suggests, however, it can be assumed that Long COVID will keep us occupied for a longer period of time, especially given that an estimated 10-20% of COVID patients suffer long-term consequences from the disease. Since the existing range of care is far from sufficient and most expenses related to Long COVID are not covered by the health insurance funds,

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the first Long COVID outpatient clinic was recently established in Vienna [11]. This is a first step towards being able to treat patients with protracted courses more adequately, but more affordable and accessible treatment options are still needed [12]. Especially given the fact that in addition to physical difficulties, many patients also have to face psychological, neurological and psychiatric consequences. However, there still needs to be research on the connection between these and the patient's COVID infection. [10] With the continued rapid development in research and practice, it is hoped that it will be possible to quickly find out which therapies and drugs help and which do not – a ray of hope for patients affected by Long COVID.

Outlook

Currently, when entering cultural and catering facilities, sports stadiums and gyms, a certificate confirming a negative test result, an administered vaccination or recovery from infection has to be shown. The proof can be found on paper or in the form of the "green passport", which is valid within Austria in the first phase and EU-wide in July [13]. It was important to refrain from a quick implementation of an "Austrian green passport" and instead focus on an uncomplicated, Europe-wide solution [14]. Due to delays and technical difficulties, however, access to the green passport valid in Austria was only recently made possible. The respective certificates are to be mutually recognized by EU member states, whilst recognizing the different applicable rules of each member state. [15]

Thanks to the availability of vaccines and growing vaccination coverage, the situation this summer is not comparable to last summer when another wave was already imminent. What is important now is to use the summer months, which, as we know from experience, are less critical, to boost the pace of the vaccination program and take early action in autumn to prevent another new wave of rising cases. We need to take advantage of the calm situation – the "breathing space" – and low case numbers to counteract the infectious disease by implementing a strong vaccination program, not only in Austria but worldwide. We have to speed up the administration of vaccinations all over the world and push the COVAX program. Otherwise, the infection rate is set to yet again spike in countries with currently low infection rates, which must be prevented.

We do need to be aware of the fact that vaccinations will not bring us back to normality, but that we instead need to adjust to a new normality. According to current research, it can be expected that, in the near future, our lives will be affected by COVID in the same way as they are affected by annual influenza. For both, vaccinations offer good protection overall. We must hope that the spread of mutations will slow down sufficiently to give pharmaceutical companies the time to tailor effective vaccines and pharmaceutical drugs to them. At the same time, we have to keep in mind that the further course or even the end of the pandemic depends not only on the emergence of mutations and escape variations for which the currently available vaccine may have no effect but also on the willingness of the population to be vaccinated. Despite the steadily growing willingness of the Austrian population to be vaccinated, it must not be ignored that scepticism has prevailed since the beginning of the vaccination campaign, especially due to the broad media coverage of cases where individuals had to struggle with severe side effects. This must be counteracted with a broad-based information campaign involving health professionals and political representatives. What will contribute decisively to vaccination readiness and willingness is the cooperation of EU countries with regard to the green passport, the freedom to travel and the handling of tested, recovered and vaccinated persons. Only through transparent communication and cooperation can we cope well with the uniquely challenging situation we are currently experiencing.

Since the COVID-19 pandemic is a supranational challenge, tackling the pandemic requires supranational thinking and acting. During the establishment of rules and structures, the strengths and weaknesses of the federal system became apparent. Many lessons have been learned and many more lessons need to be learned to get better at combatting sooner, harder, and in a more orderly way together in the fight against the COVID-19 pandemic.

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Covid-19 Response Plan and Vaccination in Bangladesh

M Mushtuq Husain

Bangladesh, like any other country of the world, is fighting relentlessly against the COVID-19 pandemic. The fighting is spread on many fronts. Detecting the cases, preventing transmission, responding to pandemic, containment and mitigation of the pandemic – all the tasks are to be accomplished simultaneously. At the outset of the fight, a Pandemic Preparedness and Response Plan, BPRP, was formulated to steer whole-of-the government and the whole of the society [1]. Again, when the COVID-19 vaccine was available for deployment, Bangladesh joined the comity of nations to vaccinate its citizens. A National Vaccine Deployment Plan (NVDP) was formulated to conduct the mass vaccination [2]. However, we faced a challenge to keep the pace of vaccination due to a shortage of supply by the manufacturers.

Bangladesh has a good network of healthcare facilities (HCF), both government and private. Private HCF are more clustered around big cities. Bangladesh also developed a good network of public health service facilities, particularly in rural areas. But a robust public health system is lacking, particularly in largely populated big cities. Pandemic usually starts in densely populated urban areas, then spread to semi-urban and rural areas. But the very urban area is yet to develop public health system to combat public health emergencies, like the COVID-19 pandemic. To date, Bangladesh is struggling to contain and mitigate the pandemic with low resource, keeping the concentrated epidemic away from densely populated urban areas. It will be an acid test to keep the pandemic away from being explosive in the coming days.

COVID-19 pandemic situation in Bangladesh

Bangladesh identified the first COVID-19 case on 8th March 2020 and the first death was reported on 18th March 2020. According to the Directorate General of Health Servic-

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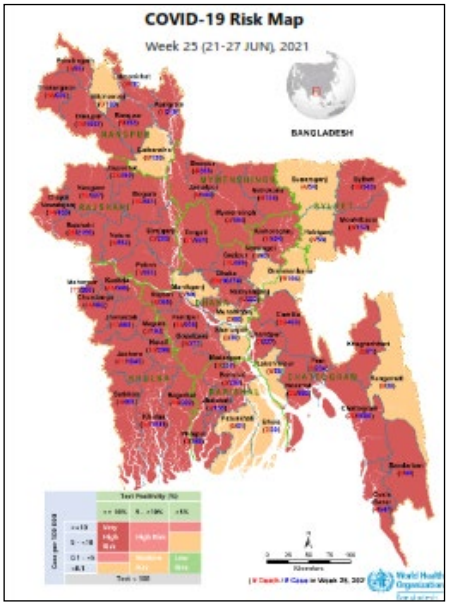
es (DGHS), as of 29 June 2021, there were 904,436 COVID-19 cases confirmed by RT-PCR (Real time polymerase chain reaction), GeneXpert, and Rapid Antigen tests including 14,388 related deaths (Case Fatality Rate 1.59%) [3]. Bangladesh stands among the top 30 countries in the world in terms of the total number of confirmed COVID-19 cases, and accounts for 0.45% cases of the world, while the country is among the top 40 countries in total death count.

A significant number of physicians and other healthcare professionals were infected and died. To date (as of 21 June 2021) 156 physicians, 3 dental surgeons died from COVID-19; while (as of 23 May 2021) 2,925 doctors, 2,003 nurses, and 3,297 other healthcare staff were infected with COVID-19 [4].

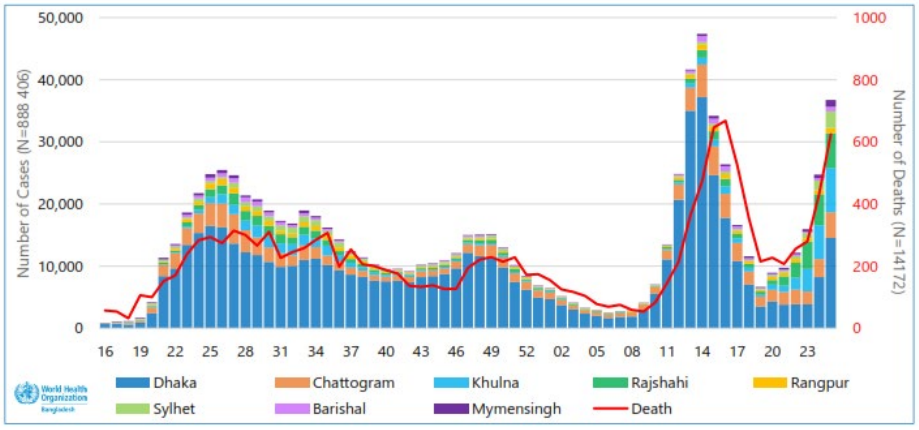
Bangladesh is witnessing the third wave of a pandemic now. In the epidemiological week 25, 2021 number of new cases in Bangladesh was 36,378; a 48.5% increase compared to the week before; the case per 100 000 population per week was 21.6. The country reported 624 new deaths, a 45.1% increase; death per 100 000 per week was 0.4. The weekly new test was 179 047 (daily average: 25 578), a 17.3% increase than the week before; tests per 100 000 per week was 105; the weekly average test positivity rate (TPR) is 20.5%, TPR increased by 26.5% from last week.



Bangladesh Preparedness and Response Plan (BPRP) for COVID-19

Bangladesh is responding to the pandemic following a Preparedness and Response Plan (BPRP). The country is implementing the response activities through committees from the national level down to the upazila level with multi sectoral involvement representing the relevant ministries, the United Nations agencies, national and international organizations including Bangladesh Medical Association (BMA) and development partners through a pillar-based multi sectoral coordination mechanism. The plan includes mechanisms for developing surge capacity to manage the patients, sustain essential services and reduce social impact. The response strategy and actions are continuously reviewed and adjusted as necessary to ensure efficient use of financial and human resources for the effective response to the pandemic, and to be reflective of any new information, operational research advances, good practices internationally and updated recommendations from WHO. Disease surveillance alongside response is an important component for prevention and control of the transmission. The country is screening at points of entry (PoE) and quarantines a large number of persons. The Rapid Response Teams (RRT) from national to upazila level are responding to the outbreak and overseeing quarantine and isolation at home, facilities or community. With established community transmission, high dependence health services along with Intensive Care Units (ICU) facilities are being strengthened. Emphasis is given to prevent hospital-acquired infections and protection of the caregiver both at the health care facility, at home and within the community. Emphasis is given also to prevent catastrophic health expenditure with the principle of 'No One is Left Behind' and social and gender inclusion. Strong concerted efforts have been taken for communication and advocacy nationally and locally using all media and means of risk communication and community engagement. In case of quarantine, especially during community-based quarantine, measures are taken to ensure the basic needs of the people are met and the security of people's property is ensured through active involvement of the law enforcing agency. Sufficient budget allocation along with a political commitment from the highest level is of paramount importance for the successful implementation of the plan.

The figure below is showing the trend of COVID-19 cases, Deaths as of 27 JUN (epi-week 25) 2021



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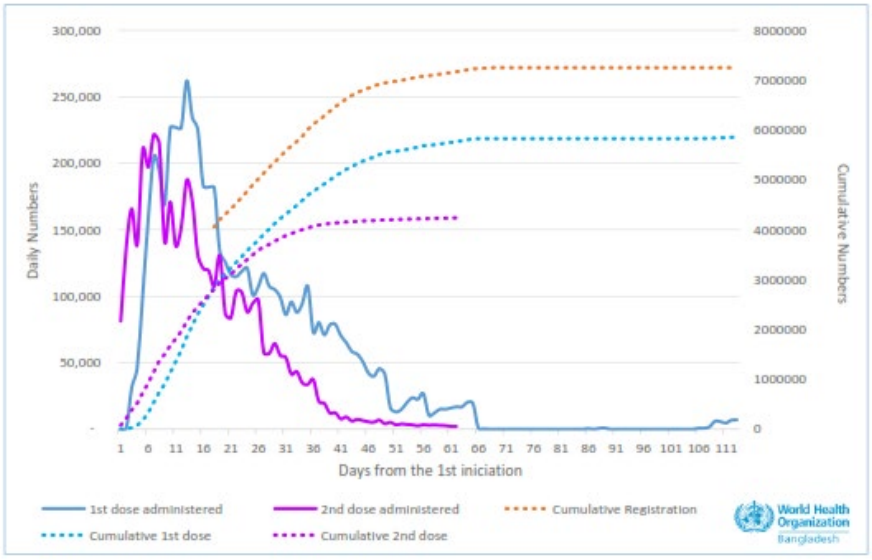
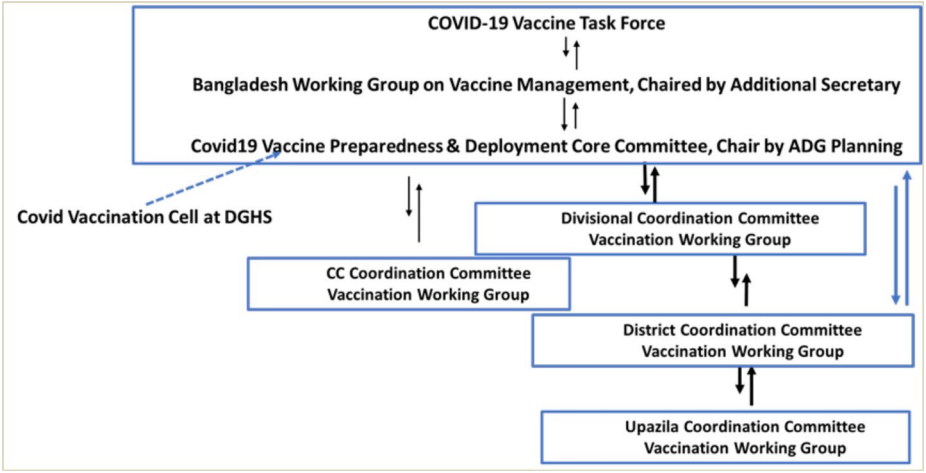
The figure below shows a comparison between the number of COVID-19 vaccines administered as of 27 JUN 2021



The overall coordination of different committees and working groups shown below



National Vaccine Deployment Plan (NVDP)

The NVDP document aims to present Bangladesh's plans for the deployment, implementation, and monitoring of potential COVID-19 vaccine(s). Due to the current uncertain environment for COVID-19 vaccine development, the document is based upon key assumptions and will likely need to be reviewed and revised over time.

Vaccine situation in Bangladesh

Oxford/AstraZeneca (COVISHIELD) 2nd dose vaccination has been continuing with remaining balance doses only in very few health facilities in the country. Since the beginning, as of 29 June 2021, a total of 10,107,884 doses of COVISHIELD vaccine were administered, out of which 5,820,015 population received their 1st dose and 4,287,869 competed for their two doses schedule.

Sinopharm vaccine (BIBP) vaccination has been continuing from the selected 67 centres in the whole country. As of 29 June 2021, a total of 55,590 target population received 1st jab and 1329 finished their two doses schedule. The government has decided to expand the centres in another 41 health facilities in Dhaka North and South City Corporations and some of the sites in the different Districts to expedite the consumption of 1.1 million Sinopharm vaccines. Vaccinators and other related health staff of those facilities receive training on 29 and 30 June 2021.

The first run of COVID-19 Pfizer–BioNTech COVID-19 vaccine has launched in three government hospitals in Dhaka City Corporation on 21 June. Total 240 target population age >40 years of age who registered earlier have received their 1st jab on that day. The government decided next week for wide inoculation of Pfizer vaccine. However, it is decided the Pfizer vaccine will be given from the selective health facilities of Dhaka City Corporation to consume 100,620 doses from the COVAX Facility.

Vaccination: Planning and coordination

The government of Bangladesh has established Planning and Coordination Committees at all levels to facilitate, coordinate and support the development of the COVID-19 vaccine deployment plan, and to oversee the planning, implementation and monitoring of the deployment and introduction of COVID-19 vaccine(s) in the country.

A separate Committee has also been established to coordinate and support planning, implementation and monitoring and evaluation of COVID-19 vaccination among Forcibly Displaced Myanmar Nationals (FDMNs), who are popularly known as Rohingya.

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Vaccine: regulatory preparedness

In Bangladesh, the national regulatory authority in respect to vaccine is the Directorate General of Drug Administration (DGDA). There are three main objectives for regulatory preparedness for COVID-19 vaccines in Bangladesh: (1) specify regulatory pathways of the Directorate General of Drug Administration (DGDA) to approve market access for COVID-19 vaccines; (2) put in place required regulatory instruments and resources in advance to ensure timely decision-making; and (3) put in place required regulatory instruments to ensure reporting on vaccine safety.

The import requirements will vary based on the origin of the vaccines and the purchase method. The registration time is expected to take 2-3 days for vaccines purchased through the COVAX facility, 12-15 days for other imported vaccines and 12-15 days for locally produced vaccines, assuming the registration requirements have been met.

The DGDA is not performing testing on vaccines procured from assured sources, such as WHO prequalified vaccines, vaccines listed as Emergency Use Listing (EUL) or approved by stringent regulatory authorities. In this case, review of the summary lot protocols is conducted, and vaccine release is expedited through the review of the minimum documents as advised by WHO. In contrast, laboratory testing of the first three batches will be required for locally produced vaccines or vaccines imported from non-WHO prequalified sources. Additional batches may be tested at the discretion of DGDA for monitoring, pharmacovigilance and post-marketing surveillance.

A risk management plan (RMP) is in place to safeguard against any harm associated with the use of the products. In case of any harm occurring while using the products there should be a clear understanding between the COVAX facility, national authorities and the manufacturer(s) regarding liability and indemnity.

Vaccine: Advocacy, Communication and Demand Promotion

Three activity areas have been identified, namely social mobilisation and community engagement, multimedia and Information & Communication Technology (ICT) Initiatives and policy and advocacy dialogue. The objectives are: (1) to create awareness and improve knowledge among the general population about the COVID-19 Vaccination Campaign. (2) to contribute towards the maximum participation of the priority target groups in the vaccination campaign. (3) to mobilize and engage communities and individuals through accurate and timely information. (4) to mitigate and manage the media impact of potential AEFIs and other negative events among the general population and target groups. A crisis communication plan have been developed and links has been created with the Risk Communication and Community Engagement (RCCE) team of COVID-19 pandemic response.

Vaccine deployment

Bangladesh has developed a plan, together with its National Immunization Technical Advisory Group (NITAG), to ensure the equitable allocation of limited doses. This plan was informed by WHO Strategic Advisory Group of Experts (SAGE)'s recent guidance on the allocation and prioritization of COVID-19 vaccination.

A phased rollout of the COVID-19 vaccine(s) is anticipated in Bangladesh, initially focused on high-risk groups (including health workers directly involved in COVID-19 response, front line workers and immunocompromised patients, etc.) and eventually extended to other groups (including older adults, adults with co-morbidities, education staff, public transport workers, migrant workers, etc.), according to the principles of health and equity.

The vaccines are deployed in a nationwide campaign using teams made up of six people (two vaccinators and four volunteers) at a variety of vaccination sites. The target population are registered by electronic voluntary registration using a national identity card (NID)/Birth registration card/Passport or by requesting different departments to provide list of staff (through format) or by the first-line health care providers. Ultimately every vaccinee is being registered electronically and their vaccine records are in the database of DGHS. The vaccinee is able to download the vaccine certificate from the website any time providing her/his identification number.

Vaccine: Human Resources

DGHS has the infrastructure and human resources across the country that is capable of deploying and administering the COVID-19 vaccine(s). Vaccination implementation is done with technical support from DGHS and administrative support from MoHFW along with other relevant administrative bodies, including law enforcement agencies.

Phases of the COVID-19 vaccine rollout in Bangladesh

Phase	Stage	Population %	Population number
1	Ia	3%	5,184,282
	Ib	7%	**12,096,657**
2	II	11-20%	17,280,938
3	III	21-40%	34,561,877
	IV	41-80%	69,123,754
		TOTAL	**138,247,508**

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A Training Plan is being implemented to address the training needs, considering interpersonal communication skills and the need for infection prevention and control. In the context of COVID-19, remote training is preferred to in-person training. Training materials developed by WHO has been adapted and translated and additional training materials have been also created.

The standard operating procedure (SOP) for infection prevention and control measures such as hand hygiene, wearing a mask and physical distance has been ensured before, during and after the vaccination session. Human resources have been provided with adequate personal protection equipment (PPE) to minimize exposure risk during immunization sessions.

Vaccine, Cold Chain and Logistics Planning

The following table shows different options of storage capacity needed national level if the COVID-19 vaccines come in several tranches. The required space calculation will be revised/updated once the exact volume of the COVID vaccine is announced.

The analysis estimates that there is currently a shortfall of approximately 6m^3 of space in cold rooms and 2.40m^3 of free space in freezer rooms at the national level. The additional storage requirements for COVID-19 vaccines can be met by hiring cold rooms from other sources at the national level, as implemented for the recent Measles-Rubella vaccination campaign. Additional cold chain equipment would be required at district and upazila levels. The estimated cost of the additional ice-lined refrigerators/freezers, cold boxes, vaccine carriers, Fridge Tag-2s, Freeze Indicators is USD 8 million.

To store few particular types of vaccine, ultra-low temperature freezers is needed. There are several facilities in Dhaka City, but it is far from adequate. Therefore, if an ultra-low cold chain were required for COVID-19 vaccines at a national scale, the National Expanded Programme of Immunization (EPI) would need to procure around 1095 ultra-low freezers to cover all levels (upazila to national) which would take substantial resources and time.

Safety boxes are used to keep sharps (syringes) produced from the COVID-19 vaccination. Used vials will be counted before disposal. While the transportation of vaccine and logistics and waste management activities are not expected to pose challenges, they require additional resources, such as the hiring of vehicles and labour.

In the routine immunization program, there is no security concern for vaccination session or any campaign activities with routine vaccine. But for COVAX-19 there is a need of special security at store, during transportation and during vaccination session which is provided by the law enforcing agencies.

Vaccine Safety

The routine immunization programme in Bangladesh currently uses passive surveillance in a paper-based system with both facility-based and community-based surveillance. Following the introduction of COVID-19 vaccines, it is likely that there may be higher rates of Adverse Effect following Immunization (AEFI)s and Adverse Events of Special Interest (AESIs). However, there is no such serious incident reported to date. The vaccination campaign will have to go a long way, we have to remain alert for any serious adverse effects. The surveillance system is extended to include:

- **Passive surveillance**: Existing paper-based reporting by health care workers (HCW) at 792 sites.
- **Stimulated passive surveillance**: HCWs to report and follow-up vaccinated people through different channels, e.g., home visit report AEFIs, phone call.
- **Active surveillance**: having designated staff visiting in the specified health care facilities
- **Active vaccine surveillance and monitoring (AVSM):** Using pharmacoepidemiologic methods to monitor a cohort of vaccine recipients for AESIs.

AEFIs during the COVID-19 vaccination program is reviewed and implemented through the existing AEFI committees at

Cold chain capacity requirements of COVID-19 vaccines by the number of doses

Scenario	Total number of doses for single doses	Space required in m^3 considering 3.5 cm^3 per dose (single dose vial)	Total number of doses for two doses	Space required in m^3 considering 3.5 cm^3 per dose (two dose vial)
If it comes 2% of the total doses	3,836,368	13.43 m^3	7,672,736	26.85 m^3
If it comes 3% of the total doses	5,754,552	20.14 m^3	1,15,09,104	40.28 m^3
If it comes 5% of the total doses	9,590,921	33.57 m^3	1,91,81,842	67.14 m^3
If it comes 10% of the total doses	19,181,842	67.14 m^3	3,83,63,684	134.28 m^3
If 20% of vaccine come altogether (single supply)	38,363,684	134.28 m^3	7,67,27,367	268.55 m^3

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national and districts/City Corporation levels. A specific AEFI report and line listing form is used and data entered into the existing DHIS2 system. This is facilitating the collection, collation, transmission, analysis and feedback of the country's vaccine safety data. AEFI's is investigated as required.

Monitoring and Evaluation (M&E)

The M&E framework of the COVID-19 vaccination programme aims to assess performance and to provide recorded information to support the analysis of progress against the vaccination programme and the related strategy update. The specific objectives are as follows:

1. To develop and implement electronic data management systems for monitoring COVID-19 vaccination activities (resources, service delivery, supply chain, vaccine wastage, cold chain, surveillance, AEFI, injection safety and waste management etc.).
2. To develop and implement an online monitoring mechanism for assessing readiness progress and programme performance against key milestones.
3. To integrate the COVID-19 surveillance system.
4. To evaluate the COVID-19 vaccine implementation programme to understand programme efficiency, as well as vaccine efficacy and safety.

A Results Framework has been developed to define the indicators and an evaluation framework prepared that outlines how country preparedness, programme implementation, the impact of COVID-19 vaccination and vaccine efficacy and safety will be evaluated over time. For example, the Vaccine Introduction Readiness Assessment Tool [VIRAT (WHO)] and the Vaccine Readiness Assessment Framework [VRAF (World Bank)] tools have been customized according to the country context to support the readiness assessments.

Vaccine: Resources

Bangladesh has joined COVAX Advance Marketing Commitment (AMC) countries to secure COVID-19 vaccine(s). As per the COVAX allocation, Bangladesh expects to receive vaccine doses equal to 20% of its population (34,561,877) followed by additional doses equal to at least 40% of its population (69,123,754) based on availability of vaccine and weighted allocation. Bangladesh will share vaccine cost of USD 1.6-2 per dose with COVAX. It is estimated that it may cost USD 2 per person to support operation. A total of $179.8-$207.4m is required for vaccine and operational cost for the first 20% of the population, whereas for 40% it is estimated that cost would be $290.4m-345.7m for vaccine and operational cost. But the COVAX commitment to Bangladesh is yet to speed into full swing.

Bangladesh government purchased vaccine by its own arrangement through trilateral negotiation with Serum Institute of India (SII). The government planned to purchase doses equal to 9% of its population. The estimated cost of the vaccines was USD 5 per dose. A total of $150m and $ 37.5m is required for vaccine and operational cost for 9% of the population. But a surge of the COVID-19 pandemic in India temporarily halted vaccine supply from SII. The government is exploring other sources to procure vaccine bilaterally. To support the vaccine preparedness and deployment activities, a budget of USD 97.6 million is requested.

Bangladesh is exploring various funding sources to support COVID vaccine deployment in the country. Several international development partners already offered technical support for vaccine procurement.

Conclusion

Bangladesh is facing the challenge of the COVID-19 pandemic through enforcing public health and social measures (PHSM), detection and isolation of cases and contacts, clinical management, preventive measures including mass vaccination. The BPRP and NVDP are in the process of updating since a new scenario emerges since the unfolding of the pandemic and beginning of vaccination. New and newer scientific evidence is coming to light which is changing existing guidelines and action plans. Community engagement is an important prerequisite for pandemic control. Community empowerment through mobilization of community resources has been proved successful in several urban and rural clusters of infection. The suffering of the disadvantaged population may be minimized in this way of community partnership.

In the paucity of COVID-19 vaccine, more emphasis on public health and social measures at community, institution, family and personal level is the way to fight the pandemic. No single type of measure may not be effective, a combination of all the measures are the key to success. It is evident from the experience of the pandemic that, no single person may remain safe until everybody is safe. Similarly, no country may become safe until every country of the world become safe.

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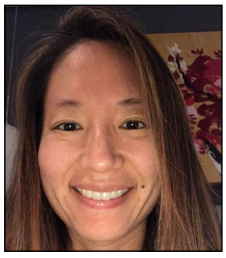
Covid-19: Brazilian Medical Association (AMB)

Summary Recommendations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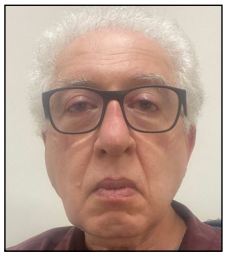
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Brazilian Epidemiologic Situation

The impact of the COVID-19 epidemic in Brazil is one of the most important in the world, since the first case described in February 2020, 18 million Brazilian people were infected (8.500/100 thousand inhabitants) and more than half a million died by the disease (240/100 thousand inhabitants) [1]. In terms of COVID-19 total deaths, Brazil is the second country in the world most affected, very close to U.S. that had registered 600.000 fatal cases, despite the Brazilian population is just about 2/3 of U.S. [2].

Due to underdiagnosis, the fatality rate is imprecise (2.8%), but the absolute number of daily deaths today varies between 2 and 4 thousand, and the number of new cases between 40 and 100 thousand. There is no idea about the variables of the population profiles involved, including a lot of speculation regarding the variants. Related to vaccination for COVID 19 we have about 11% of the population immunized. The disease remains out of control.

Brazil emerged as a global epicentre of the COVID-19 epidemic in the beginnings of 2021, starting a second wave of high increase of new cases and deaths (the first one occurred in the middle of 2020), while other countries achieved some success in reducing the impact of the pandemic adding prevent strategies, as mass vaccination, public policies to avoid agglomeration and educational campaigns stimulating the use of masks, social distance and hands hygiene [3, 4].

Objective of this Article

This article aims to briefly summarize the recommendations of the BMA in relation to prophylaxis (prevention) and treatment of mild COVID (outpatients).

Description of the Etiology of Covid-19

Covid-19 has as causal agent the virus SARS-CoV2, order Nidovirales, family Coronaviridae, genus Betacoronavirus. Other viruses already described as disease agents are part of this genus: OC43 and HKU4 that cause the common cold, SARS-CoV and MERS-CoV, both potential agents of serious diseases but with limited epidemic action. Coronaviruses are the largest RNA-viruses and can invade human cells through the protein S that forms its envelope, which can couple to the ACE2 receptor of human cells A [5-7].

CoVs infect humans and a variety of avian and mammalian species worldwide. There are six CoVs known to infect humans, including two a-CoVs (229E and NL63) and four b-CoVs (OC43, HKU1, severe acute respiratory syndrome [SARS]-CoV, and Middle East respiratory syndrome [MERS]-CoV). All human CoVs are zoonotic as a distinguishing characteristic. In particular, bats are regarded as a key reservoir of CoVs, and many human CoVs are believed to have originated from bats. Since the beginning of this century, two zoonotic CoVs, SARS- CoV and MERS-CoV, have been identified to cause severe human diseases. The outbreak of SARS-CoV in 2003 was responsible for 8096 cases and 774 deaths world- wide. Since its discovery in Middle Eastern countries in 2012, MERS-CoV has infected 2494 people with a current case fatality rate of 34.4%. These outbreaks have raised public health concerns about the potential for the emergence of another novel zoonotic CoV [8].

SARS-Cov2 is a previously unknown bat-origin CoV causing severe and fatal pneumonia in five patients from Wuhan, China. Sequence results revealed that this virus, harboring a single open reading frame gene 8 (ORF8), is phylogenetically closest to bat SARS-like CoV, but is in a separate lineage. Furthermore, the amino acid sequence of the tentative receptor-binding domain (RBD) of this new CoV resembles that of SARS-CoV, indicating that they might use

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the same receptor. These findings highlight the urgent need for regular surveillance of the interspecies transmission of bat-origin CoV to human populations [8].

Classification and Definition of Mild Disease

The disease (COVID 19) can be classified by its severity as follows [9]:

Mild illness [9]

Patients with uncomplicated upper respiratory tract viral infection may have non-specific symptoms such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, or headache. Rarely, patients may also present with diarrhoea, nausea, and vomiting. Older and/or immunosuppressed patients may present with atypical symptoms. Symptoms due to physiological adaptations of pregnancy or adverse pregnancy events (e.g., dyspnea, fever, gastrointestinal symptoms, fatigue) may overlap with COVID-19 symptoms.

Pneumonia [9]

Adults: pneumonia with no signs of severe pneumonia and no need for supplemental oxygen. Children: pneumonia with cough or difficulty breathing plus fast breathing (i.e., <2 months of age: ≥60 breaths/minute; 2-11 months of age: ≥50 breaths/minute; 1-5 years of age: ≥40 breaths/minute) and no signs of severe pneumonia.

Severe pneumonia in adults and adolescents [9]

Fever or suspected respiratory infection plus one of the following: Respiratory rate >30 breaths/minute; Severe respiratory distress; SpO_2 ≤93% on room air.

Severe pneumonia in children [9]

Cough or difficulty breathing plus at least one of the following: Central cyanosis or SpO_2 <90%; Severe respiratory distress (e.g., grunting, very severe chest indrawing); Signs of pneumonia with a general danger sign (i.e., inability to breastfeed or drink, lethargy or unconsciousness, or convulsions); Other signs of pneumonia may be present in children including chest indrawing or fast breathing (i.e., <2 months of age: ≥60 breaths/minute; 2-11 months of age: ≥50 breaths/minute; 1-5 years of age: ≥40 breaths/minute); While the diagnosis is made on clinical grounds, chest imaging may identify or exclude some pulmonary complications [9].

Diagnosis of Covid-19

Clinical (signs and symptoms)

COVID-19 affects many organs of the body, so people with COVID-19 may have a wide spectrum of symptoms. Symptoms and signs of the illness may be important to help them and the healthcare staff they meet to know whether they have the disease [10].

Symptoms: people with mild COVID-19 might experience cough, sore throat, high temperature, diarrhoea, headache, muscle or joint pain, fatigue, and loss or disturbance of the sense of smell and taste. Signs are obtained by clinical examination. Oxygen, people with mild symptoms consult their doctor (general practitioner). People with more severe symptoms might visit a hospital outpatient or emergency department. Depending on the results of a clinical examination, patients may be sent home to isolate, may receive further tests or be hospitalized [10].

In 26.884 participants the prevalence of COVID-19 varied from 3% to 71% with a median of 21%, without discrimination of mild from severe COVID-19. A greater proportion included participants who presented to outpatient settings, which is where most clinical assessments for COVID-19 take place [10].

Only cough and fever had a pooled sensitivity of at least 50% but specificities were moderate to low. The cough had a sensitivity of 67.4% and as specificity of 35.0%. The fever had a sensitivity of 53.8% and a specificity of 67.4%. Anosmia alone, ageusia alone, and anosmia or ageusia had sensitivities below 50% but specificities over 90%. Anosmia had a pooled sensitivity of 28.0% and a specificity of 93.4%. Ageusia had a pooled sensitivity of 24.8% and a specificity of 91.4%. Anosmia or ageusia had a pooled sensitivity of 41.0% and a specificity of 90.5%. The presence of anosmia or ageusia may be useful as a red flag for COVID-19. The presence of fever or cough, given their high sensitivities, may also be useful to identify people for further testing [10].

Patients with symptoms meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia. Presenting signs and symptoms of COVID-19 vary: Most people experience fever (8% to 99%), cough (59% to 82%), fatigue (44% to 70%), anorexia (40% to 84%), shortness of breath (31% to 40%), myalgias (11% to 35%). Other non-specific symptoms, such as sore throat, nasal congestion, headache, diarrhoea, nausea, and vomiting, has also been reported.

Loss of smell (anosmia) or loss of taste (ageusia) preceding the onset of respiratory symptoms have also been reported [11].

Additional neurological manifestations reported include dizziness, agitation, weakness, seizures, or findings suggestive of stroke including trouble with speech or vision, sensory loss, or problems with balance when standing or walking. Older people and immunosuppressed people may present with atypical symptoms such as reduced alertness, reduced mobility, diarrhoea, loss of appetite, confusion and absence of fever. Symptoms such as dyspnea, fever, gastro-

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intestinal symptoms, or fatigue because of physiological adaptations in women who are pregnant, adverse pregnancy events or other diseases such as malaria, may overlap with symptoms of COVID-19. Children may report fever or cough less frequently than adults [11].

Laboratory tests

Universal access to accurate SARS-CoV-2 nucleic acid testing is critical for patient care, hospital infection prevention and the public response to the COVID-19 pandemic. Information on the clinical performance of available tests is rapidly emerging, but the quality of evidence of the current literature is considered moderate to very low. Recognizing these limitations, the Infectious Diseases Society of America (IDSA) panel weighed available diagnostic evidence and recommends nucleic acid testing for all symptomatic individuals suspected of having COVID-19. In addition, testing is recommended for asymptomatic individuals with known or suspected contact with a COVID-19 case. Testing asymptomatic individuals without known exposure is suggested when the results will impact isolation/quarantine/personal protective equipment (PPE) usage decisions, dictate eligibility for surgery, or inform solid organ or hematopoietic stem cell transplantation timing. Ultimately, prioritization of testing will depend on institutional-specific resources and the needs of different patient populations [12].

Diagnostic testing will help in safely opening the country, but only if the tests are highly sensitive and validated under realistic conditions against a clinically meaningful reference standard. Measuring test sensitivity in asymptomatic people is an urgent priority. It will also be important to develop methods (e.g., prediction rules) for estimating the pretest probability of infection (for asymptomatic and symptomatic people) to allow the calculation of post-test probabilities after positive or negative results. Negative results even on a highly sensitive test cannot rule out infection if the pretest probability is high, so clinicians should not trust unexpected negative results (i.e., assume a negative result is a "false negative" in a person with typical symptoms and known exposure) [13].

Nucleic acid amplification tests (NAAT)

Routine confirmation of cases of COVID-19 is based on detection of unique sequences of virus RNA by NAAT such as real-time reverse-transcription polymerase chain reaction (rRT-PCR) with confirmation by nucleic acid sequencing when necessary. The viral genes targeted so far include the N, E, S and RdRP genes. One or more negative results do not rule out the possibility of COVID-19 virus infection. Several factors could lead to a negative result in an infected individual, including poor quality of the specimen, containing little patient material (as a control, consider determining whether there is adequate human DNA in the sample by including a human target in the PCR testing); the specimen was collected late or very early in the infection; the specimen was not handled and shipped appropriately; technical reasons inherent in the test, e.g. virus mutation or PCR inhibition [14].

Considering the findings that more than half of individuals with positive PCR test results are unlikely to have been infectious, RTPCR test positivity should not be taken as an accurate measure of infectious SARS-CoV-2 incidence. The results confirm the findings of others that the routine use of "positive" RT-PCR test results as the gold standard for assessing and controlling infectiousness fails to reflect the fact "that 50-75% of the time an individual is PCR positive, they are likely to be post-infectious". Asymptomatic individuals with positive RT-PCR test results have higher cut-off (Ct) values and a lower probability of being infectious than symptomatic individuals with positive results. Although Ct values have been shown to be inversely associated with viral load and infectivity, there is no international standardization across laboratories, rendering problematic the interpretation of RT-PCR tests when used as a tool for mass screening [15].

Rapid point-of-care tests [16]

Rapid point-of-care tests aim to confirm or rule out COVID-19 infection in people with or without COVID-19 symptoms. They are portable, so they can be used wherever the patient is (at the point of care); are easy to perform, with a minimum amount of extra equipment or complicated preparation steps; are less expensive than standard laboratory tests; do not require a specialist operator or setting; and provide results 'while you wait'. The interest is two types of commercially available, rapid point-of-care tests: antigen and molecular tests. Antigen tests identify proteins on the virus; they come in disposable plastic cassettes, similar to pregnancy tests. Rapid molecular tests detect the virus's genetic material in a similar way to laboratory methods but using smaller devices that are easy to transport or to set up outside of a specialist laboratory. Both test nose or throat samples [16].

In people with confirmed COVID-19, antigen tests correctly identified COVID-19 infection in an average of 72% of people with symptoms, compared to 58% of people without symptoms. Tests were most accurate when used in the first week a-er symptoms first developed (an average of 78% of confirmed cases had positive antigen tests). This is likely to be because people have the most virus in their system in the first days a-er they are infected. In people who did not have COVID-19, antigen tests correctly ruled out infection in 99.5% of people with symptoms and 98.9% of people without symptoms [16].

Although overall results for diagnosing and ruling out COVID-19 were good (95.1% of infections correctly diagnosed and 99% correctly ruled out), some antigen tests are

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accurate enough to replace RT-PCR when used in people with symptoms. This would be most useful when quick decisions are needed about patient care, or if RT-PCR is not available. Antigen tests may be most useful to identify outbreaks, or to select people with symptoms for further testing with PCR, allowing self-isolation or contact tracing and reducing the burden on laboratory services. People who receive a negative antigen test result may still be infected [16].

Image exams

Results from 1.834 patients reported the diagnostic accuracy of both CT and RT-PCR, in the same set of patients. Sensitivity estimates for CT scan ranged from 0.69 to 1.00 and for RT-PCR varied ranging from 0.47 to 1.00. The pooled estimates of sensitivity for CT and RT-PCR were 0.91 and 0.84, respectively. On subgroup analysis, pooled sensitivity of CT and RT-PCR was 0.95 and 0.91 ($p< 0.05$). The pooled specificity of CT and RT-PCR was 0.31 and 1.00. CT is more sensitive than RT-PCR in detecting COVID-19 infection but has a very low specificity. Since the results of a CT scan are available quickly, it can be used as an adjunctive initial diagnostic test for patients with a history of positive contact or epidemiological history [17].

The findings indicate that chest CT is sensitive and moderately specific for the diagnosis of COVID-19. Chest X-ray is moderately sensitive and moderately specific for the diagnosis of COVID-19. Ultrasound is sensitive but not specific for the diagnosis of COVID-19. Thus, chest CT and ultrasound may have more utility for excluding COVID-19 than for differentiating SARS-CoV-2 infection from other causes of respiratory illness [18].

Chest CT [18]

Pooled results showed that chest CT correctly diagnosed COVID-19 in 87.9% of people who had COVID-19. However, it incorrectly identified COVID-19 in 20% of people who did not have COVID-19.

Chest X-ray [18]

Pooled results showed that chest X-ray correctly diagnosed COVID-19 in 80.6% of people who had COVID-19. However, it incorrectly identified COVID-19 in 28.5% of people who did not have COVID-19.

The evidence suggests that chest CT is better at ruling out COVID-19 infection than distinguishing it from other respiratory problems. So, its usefulness may be limited to excluding COVID-19 infection rather than distinguishing it from other causes of lung infection [18].

Non-Drug Prevention and Management

Mask

The available preclinical findings limited clinical and indirect evidence suggests biological plausibility that face masks may reduce the spread of SARS-CoV-2. The available clinical trial evidence shows no significant difference in limiting transmission respiratory viral illnesses, but the evidence is of poor quality. All current evidence focuses on protection for the wearer not on controlling spread [19].

The evidence regarding the effectiveness of medical face masks for the prevention of COVID-19 in the community is compatible with a small to moderate protective effect, but there are still significant uncertainties about the size of this effect. Evidence for the effectiveness of non-medical face masks, face shields/visors and respirators in the community is scarce and of very low certainty. Although the evidence for the use of medical face masks in the community to prevent COVID-19 is limited, face masks should be considered as a non-pharmaceutical intervention in combination with other measures as part of efforts to control the COVID-19 pandemic [20].

Taking into account the available evidence, the transmission characteristics of SARS-CoV-2, the feasibility and potential harms associated with the use of various types of face masks, the following options are proposed [20]:

- In areas with community transmission of COVID-19, wearing a medical or non-medical face mask is recommended in confined public spaces and can be considered in crowded outdoor settings;
- For people vulnerable to severe COVID-19, such as the elderly or those with underlying medical conditions, the use of medical face masks is recommended as a means of personal protection in the above-mentioned settings;
- In households, the use of medical face masks are recommended for people with symptoms of COVID-19 or confirmed COVID-19 and for the people who share their household.

Based on the assessment of the available scientific evidence, no recommendation can be made on the preferred use of medical or non-medical face masks in the community. When non-medical face masks are used, it is advisable that masks that comply with available guidelines for filtration efficacy and breathability are preferred [20].

The very limited scientific evidence regarding the use of respirators in the community does not support their mandatory use in place of other types of face masks in the community. Although respirators would not be expected to be inferior to non-medical or medical face masks, the difficulties to ensure their appropriate fitting and use in community settings as well as potential adverse effects related to lower breathability should be considered [20].

The use of face masks in the community should complement and not replace other

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preventive measures such as physical distancing, staying home when ill, teleworking, if possible, respiratory etiquette, meticulous hand hygiene and avoiding touching the face, nose, eyes, and mouth. The appropriate use of face masks and promoting compliance with their use when recommended as public health measures are key to the effectiveness of the measure and can be improved through education campaigns [20].

Face mask use could result in a large reduction in risk of infection (n=2.647; aOR 0.15, RD −14.3%; low certainty), with stronger associations with N95 or similar respirators compared with disposable surgical masks or similar (eg, reusable 12–16-layer cotton masks; p =0 090; posterior probability >95%, low certainty). Eye protection also was associated with less infection (n=3.713; aOR 0.22, RD −10.6%; low certainty) [21].

Distance

A systematic review retrieved 172 observational studies across 16 countries and six continents, with no randomized controlled trials and 44 relevant comparative studies in healthcare and non-health-care settings (n= 25.697 patients) Transmission of viruses where lower with the physical distancing of 1 m or more, compared with a distance of less than 1 m (n=10.736, pooled adjusted odds ratio [aOR] 0.18; risk difference [RD] −10.2%; moderate certainty); protection was increased as the distance was lengthened (change in relative risk [RR] 2.02 per m; p =0.041; moderate certainty) [21].

Current rules on safe physical distancing are based on outdated science. The distribution of viral particles is affected by numerous factors, including airflow. Evidence suggests SARS-CoV-2 may travel more than 2 m through activities such as coughing and shouting. Rules on distancing should reflect the multiple factors that affect risk, including ventilation, occupancy, and exposure time [22].

How should infection control practice be changed if we provisionally accept that aerosols have an important role in viral transmission? The inhalational risk may be reduced by social distancing, limiting interaction indoors, avoiding air recirculation, improved natural and artificial ventilation, and innovative engineering solutions which collect and neutralise aerosols to provide clean air in personal and community spaces. The infection risk associated with deep breathing, talking, and singing indoors is underappreciated and urgently needs attention. Since the 2003 SARS outbreak, research in aerobiology, physics, and computational fluid dynamics has advanced our understanding of the aerosol generation and the carriage and fate of respiratory particles. Airborne transmission of Covid-19 is now the plausible cause of superspreading events in a call centre in Korea, a choir practice in Skagit County, US, and a restaurant in Guangzhou, China. The pandemic is at a critical juncture, and these strong signals should not be ignored by politicians and public health leaders [23].

Isolation

The studies consistently reported the benefit of quarantine, contact tracing, screening, and isolation in different settings. Model estimates indicated that quarantine of exposed people averted 44 to 81% of incident cases and 31 to 63% of deaths. Quarantine along with others can also halve the reproductive number and reduce the incidence, thus, shortening the epidemic period effectively. Early initiation of quarantine, operating large-scale screenings, strong contact tracing systems, and isolation of cases can effectively reduce the epidemic. However, adhering only to screening and isolation with lower coverage can miss more than 75% of asymptomatic cases; hence, it is not effective. Quarantine, contact tracing, screening, and isolation are effective measures of COVID-19 prevention, particularly when integrated together. To be more effective, quarantine should be implemented early and should cover a larger community [24].

General strategies

Two fundamental strategies are possible: (a) mitigation, which focuses on slowing but not necessarily stopping epidemic spread – reducing peak healthcare demand while protecting those most at risk of severe disease from infection, and (b) suppression, which aims to reverse epidemic growth, reducing case numbers to low levels and maintaining that situation indefinitely. Each policy has major challenges. We find that that optimal mitigation policies (combining home isolation of suspect cases, home quarantine of those living in the same household as suspect cases, and social distancing of the elderly and others at most risk of severe disease) might reduce peak healthcare demand by 2/3 and deaths by half. However, the resulting mitigated epidemic would still likely result in hundreds of thousands of deaths and health systems (most notably intensive care units) being overwhelmed many times over. For countries able to achieve it, this leaves suppression as the preferred policy option [25].

The optimal control of COVID-19 with the help of Non-Pharmaceutical Interventions (NPIs). On the basis of sensitivity indices of the parameters we apply Non-Pharmaceutical Interventions (NPIs) to control the sensitive parameters and hence formulate the optimal control model. The major NPIs are, stay home, sanitiser (wash hands), early case detection (PCR test) and face mask. These NPIs helps in mitigation and reducing the size of the outbreak of the disease [25].

Non-pharmacological interventions, such as lockdown and mass testing, remain as the mainstay of control measures for the outbreak. Based on one modelling study, mass testing reduced the total infected

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people compared to no mass testing. For lockdown, ten studies consistently showed that it successfully reduced the incidence, onward transmission, and mortality rate of COVID-19. Limited evidence showed that a combination of lockdown and mass screening resulted in a greater reduction of incidence and mortality rate compared to lockdown only. However, there is not enough evidence on the effectiveness of mass testing only [26].

Our results suggest that exposure in settings with familiar contacts increases SARS-CoV-2 transmission potential. Additionally, the differences observed in transmissibility by index case symptom status and duration of exposure have important implications for control strategies such as contact tracing, testing and rapid isolation of cases. There was limited data to explore transmission patterns in workplaces, schools, and care-homes, highlighting the need for further research in such settings [27].

Monitoring

Use the following signs and symptoms to help identify people with COVID-19 with the most severe illness [11]:

- severe shortness of breath at rest or difficulty breathing
- reduced oxygen saturation levels measured by pulse oximetry
- coughing up blood
- blue lips or face
- feeling cold and clammy with pale or mottled skin
- collapse or fainting (syncope)
- new confusion
- becoming difficult to rouse
- reduced urine output.

When pulse oximetry is available in primary and community care settings, to assess the severity of illness and detect early deterioration, use: pulse oximetry in people 18 years and over with COVID-19 oxygen saturation levels below 91% in room air at rest in children and young people (17 years and under) with COVID [11].

Criteria for discharging patients from isolation (i.e., discontinuing transmission-based precautions) without requiring retesting: For symptomatic patients: 10 days after symptom onset, plus at least 3 additional days without symptoms (including without fever and without respiratory symptoms). For asymptomatic cases: 10 days after a positive test for SARS-CoV-2. The initial recommendation of two negative PCR tests at least 24 hours apart can be used. Some patients may experience symptoms beyond the period of infectivity. Care of COVID-19 patients after acute illness. Discharge criteria from clinical care need to consider the patient's condition, disease experience and other factors. Release from the COVID-19 care pathway is not the same as clinical discharge from a facility or from one ward to another [9].

Patients with mild and moderate illness may not require emergency interventions or hospitalization; however, isolation is necessary for all suspect or confirmed cases to contain virus transmission. The decision to monitor a suspect case in a health facility, community facility or home should be made on a case-by-case basis. This decision will depend on the clinical presentation, requirement for supportive care, potential risk factors for severe disease, and conditions at home, including the presence of vulnerable persons in the household [9].

Early identification of patients at risk for and with severe disease allows for rapid initiation of optimized supportive care treatments and safe, rapid referral to a designated destination in the COVID-19 care pathway (with access to oxygen and respiratory support). Known risk factors for rapid deterioration, severe disease, and/or increased mortality are: older age (> 60 years) and NCDs such as cardiovascular disease, diabetes mellitus, chronic lung disease, cancer and cerebrovascular disease. Patients with one or more of these risk factors should be monitored closely for deterioration, preferably in a health facility. As described above, the decision to monitor in a health facility, community facility or home should be made on a case-by-case basis. This decision will depend on the clinical presentation, requirement for supportive care, risk factors and conditions at home, including the presence of additional vulnerable persons in the household. Risk factors for severe disease in pregnancy include increasing maternal age, high BMI, non-white ethnicity, pre-existing comorbidities, and pregnancy-specific conditions such as gestational diabetes and pre-eclampsia [9].

Some patients develop severe pneumonia and require oxygen therapy and minority progress to critical disease with complications such as respiratory failure or septic shock. COVID-19 confirmation needs to be made prior to determining severity; particularly in children, for whom the differential diagnosis for respiratory distress is particularly important. Children with suspected or confirmed COVID-19 infection should be kept together with caregivers wherever possible (if caregivers also have suspected or confirmed COVID-19 infection), and cared for in child-friendly spaces, considering specific medical, nursing, nutritional, and mental health, and psychosocial support needs of children [9].

Shared decision making [29]

With the patient, family, and community some principal information can be shared:

- That the key symptoms are cough, fever, breathlessness, anxiety, delirium, and agitation, but they may also have fatigue, muscle aches, and headache;
- That they and people caring for them should follow the guidance on self-isolation and the UK guidance on protecting vulnerable people;
- That if the symptoms are mild, they are likely to feel much better in a week;

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- Who to contact if their symptoms get worse.

Minimise face-to-face contact by [29]:
- Offering telephone or video consultations;
- Cutting non-essential face-to-face follow up;
- Using electronic prescriptions rather than paper;
- Using different methods to deliver medicines to patients.

When possible, discuss the risks, benefits, and possible likely outcomes of the treatment options with patients with COVID-19, and their families and carers, so that they can express their preferences about their treatment and escalation plans. Put treatment escalation plans in place because patients with COVID-19 may deteriorate rapidly and need urgent hospital admission. For patients with pre-existing advanced comorbidities, find out if they have advance care plans or advance decisions to refuse treatment, including do not attempt resuscitation decisions. Document this clearly and take account of these in planning care [29].

Be aware that older patients or those with comorbidities, frailty, impaired immunity, or a reduced ability to cough and clear secretions are more likely to develop severe pneumonia. This could lead to respiratory failure and death. If possible, encourage patients with a cough to avoid lying on their back because this makes coughing ineffective [29].

Be aware that, on average, fever is most common five days after exposure to the infection. Advise patients to drink fluids regularly to avoid dehydration (no more than 2 litres per day). Do not use antipyretics with the sole aim of reducing body temperature. Advise patients to take paracetamol if they have fever and other symptoms that antipyretics would help treat. Tell them to continue only while the symptoms of fever and the other symptoms are present. Until there is more evidence, paracetamol is preferred to non-steroidal anti-inflammatory drugs (NSAIDs) for patients with COVID-19 [29].

Prognosis

Re-infection

In this study during the first surge, 533.381 people were tested, of whom 11.727 were PCR positive, and 525 339 were eligible for follow-up in the second surge, of whom 11.068 had tested positive during the first surge. Among eligible PCR positive individuals from the first surge of the epidemic, 72 tested positive again during the second surge compared with 16.819 of 514.271 who tested negative during the first surge (adjusted RR 0.195). Protection against repeat infection was 80.5%. The alternative cohort analysis gave similar estimates (adjusted RR 0.21), estimated protection 78.8%. In the alternative cohort analysis, among those aged 65 years and older, observed protection against repeat infection was 47.1%. Evidence of waning protection over time (3–6 months of follow-up 79.3% vs ≥7 months of follow-up 77.7% [29].

Immunity

Using sequential samples from SARS-CoV-2 infected individuals collected up to 94 days demonstrated declining neutralizing antibodies (nAb) titres in the majority of individuals. For those with a low nAb response, titres can return to baseline over a relatively short period. Further studies using sequential samples from these individuals are required to fully determine the longevity of the nAb response and studies determining the nAb threshold for protection from re-infection are needed [30].

SARS-CoV-2-specific memory T cells will likely prove critical for long-term immune protection against COVID-19. It was mapped the functional and phenotypic landscape of SARS-CoV-2-specific T cell responses in a large cohort of unexposed individuals as well as exposed family members and individuals with acute or convalescent COVID-19. Acute phase SARS-CoV-2-specific T cells displayed a highly activated cytotoxic phenotype that correlated with various clinical markers of disease severity, whereas convalescent-phase SARS-CoV-2-specific T cells were polyfunctional and displayed a stem-like memory phenotype. Importantly, SARS-CoV-2-specific T cells were detectable in antibody-seronegative family members and individuals with a history of asymptomatic or mild COVID-19. This collective dataset shows that SARS-CoV-2 elicits robust memory T cell responses akin to those observed in the context of successful vaccines, suggesting that natural exposure or infection may prevent recurrent episodes of severe COVID-19 also in seronegative individuals [31].

Long COVID [32]

COVID-19 can cause persistent ill-health. Around a quarter of people who have had the virus experience symptoms that continue for at least a month but one in 10 are still unwell after 12 weeks. This has been described by patient groups as “Long COVID”. Our understanding of how to diagnose and manage Long COVID is still evolving but the condition can be very debilitating. It is associated with a range of overlapping symptoms including generalized chest and muscle pain, fatigue, shortness of breath, and cognitive dysfunction, and the mechanisms involved affect multiple system and include persisting inflammation, thrombosis, and autoimmunity. It can affect anyone, but women and health care workers seem to be at greater risk. Long COVID has a serious impact on people’s ability to go back to work or have a social life. It affects their mental health and may have significant economic consequences for them, their families and society.

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Policy responses need to take account of the complexity of Long COVID and how what is known about it is evolving rapidly. Areas to address include [32]:

- The need for multidisciplinary, multispecialty approaches to assessment and management;
- Development, in association with patients and their families, of new care pathways and contextually appropriate guidelines for health professionals, especially in primary care to enable case management to be tailored to the manifestations of disease and involvement of different organ systems;
- The creation of appropriate services, including rehabilitation and online support tools;
- Action to tackle the wider consequences of Long COVID, including attention to employment rights, sick pay policies, and access to benefit and disability benefit packages;
- Involving patients both to foster self-care and self-help and in shaping awareness of Long COVID and the service (and research) needs it generates; and
- Implementing well-functioning patient registers and other surveillance systems; creating cohorts of patients, and following up on those affected as a means to support the research which is so critical to understanding and treating Long COVID.

Methods

Clinical Questions

In patients without a diagnosis of COVID 19, but submitted to environments with the possibility of contagion, does the use of Hydroxychloroquine or Ivermectin or Antibiotics or Antivirals or Steroids or Anticoagulants or Monoclonal Antibodies or Plasm or Nitazoxanide or Colchicine prevent illness? Or in patients with mild COVID 19, do these drugs reduce hospitalization or mortality, and does not increase the risk of adverse events?

Eligibility criteria for studies to be included

PICO

Patient: without COVID confirmed by PCR (prophylaxis) or with mild COVID 19 (treatment)

Interventions: Drugs studied (Hydroxychloroquine or Ivermectin or Antibiotics or Antivirals or Steroids or Anticoagulants or Monoclonal Antibodies or Plasm or Nitazoxanide or Colchicine)

Comparison: Standard treatment or placebo

Outcome: occurrence of illness, hospitalization (infirmary or ICU), mortality and adverse events

Study design: Phase 3 randomized clinical trials (RCTs) and phase 3 RCTs systematically reviewing the PICO. No consulted period, language, or full text availability limits.

Bases consulted with their respective strategies

The individual drug strategies included the synonyms, however, in order not to extend the content too much, the drugs will be generically mentioned in the search strategy of this article. The complete strategies are available on the AMB website (project guidelines).

Medline, EMBASE, Central Cochrane and Clinical Trials

#1 = COVID OR COV OR CORONAVIRUS OR SARS
#2 = (Hydroxychloroquine or Ivermectin or Antibiotics or Antivirals or Steroids or Anticoagulants or Monoclonal Antibodies or Plasm or Nitazoxanide or Colchicine)
#3 = #1 AND #2
#4 = #3 AND Random*

Data Extracted

Data regarding authorship, year of publication, description of patients, interventions (drugs studied), outcomes and follow-up time will be extracted from the studies.

Bias risk and Quality of evidence

The risk of bias will be assessed using the items in Rob 2 [33], plus other fundamental elements, and expressed as very serious, serious, or non-serious. The quality of the evidence will be extrapolated from the risk of bias obtained from the study (s) (if there is no meta-analysis) using the GRADE terminology [34] in very low, low, and high, and through the GRADEpro software [34] (if there is meta-analysis) in very low, low, moderate, and high.

Analysis and Summary of Outcomes

The outcomes when categorical will be expressed by group (drugs studied and comparisons) and through the number of events and the calculated risk (%) for each group (a division of the number of events by the total number of patients in each group). If the risk difference (RD) between the groups is significant (95% confidence) it will be expressed with the 95% confidence interval (95% CI) and the Number needed to treat (NNT) or to produce damage (NNH).
If there is more than one study included with common outcomes, it will be aggregated through meta-analysis using RevMan 5.4 software [35].

Results

The results presented will follow the following sequence: total articles retrieved and selected, Hydroxychloroquine or Ivermectin or Antibiotics or Antivirals or Steroids or Anticoagulants or Monoclonal Antibodies or Plasm or Nitazoxanide or Colchicine.

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Total results

A number of 2.674, 1.073 and 1.045 studies were retrieved from Medline, Embase, and Clinical Trials, respectively. Eliminating duplicates and meeting the eligibility criteria, 174 studies were selected so that their full texts could be accessed, from which 158 papers were excluded. Then, available to support this assessment in accordance with the eligibility criteria adopted, there are 16 randomized trials [Hydroxychloroquine (n:9); Ivermectin (n:1); Antibiotics (n:0); Antivirals (n:1); Steroids (n:0); Anticoagulants (n:0); Monoclonal Antibodies (n:2); Plasm (n:1); Nitazoxanide (n:1); Colchicine (n:1)], whose characteristics, results, risk of bias, quality of evidence and synthesis of evidence are described below [36-51].

Hydroxychloroquine (HCQ)

Description of the included studies of HCQ in covid-19 prophylaxis

In health professionals in two hospitals in the USA, 132 patients were randomized (out of 139 evaluated), 66 for the group. Patients were randomized before taking the COVID-19 positivity tests, as they were excluded from the use of the drug (HCQ dose 600 mg/day for 8 weeks). The main outcome was measured by RT-PCR nasal swab at 4 and 8 without or if symptoms of COVID-19 infection were present. The secondary outcome was to assess modification of the QT interval, but it was added as a subsequent amendment to the protocol. Information on adverse effects was collected, where 64 patients in the HCQ group and of these 52 swabs and 54 swabs were tested in the 4 and 8 weeks respectively. In the placebo group, there were 52 and 54 swabs at 4 and 8 weeks [(PATCH) Investigators NCT04329923] [36].

In subjects with up to 96 h of exposure to high risk to HCQ: 400 mg was used for 3 days followed by 200 mg/day for 11 days, with the vitamin C placebo. The outcome of infection was measured at 14 days and 28 days with RT-PCR (NCT04328961) [37].

A study was carried out on people at high risk of contamination due to exposure at work and who had exposure to index cases in 9 health centres in Spain. Open study, which allowed cross-over, HCQ dose of 800 mg in D1 and 600 mg of D2-D6. The outcome was a 14-day RT-PCR swab measurement. Monitored adverse events were assessed. Total of 672 index cases reflected in 2485 contact persons, being randomized in 1206 for HCQ and 1279 for standard treatment. There were 171 missing data in the main result [(BCN-PEP-CoV2) NCT04304053] [38].

Individuals at high risk of contamination (healthcare professionals) were randomized to use HCQ 400 mg once/week for 12 weeks, HCQ 400 mg twice/week for 12 weeks or placebo (folic acid). The outcomes have a problem of detection if you consider the possible or probable symptom criterion of COVID-19, as not all individuals underwent the RT-PCR test [NCT04328467 (PEP TEAM)] [39].

Individuals at high risk of contamination were evaluated in a selected population in the USA and Canada by media notices within 4 days after having a positive index. People were asymptomatic. HCQ was used at the loading dose of 800 mg, followed by 600 mg in 6-8 hours after the attack, followed by 600 mg for another 4 days. The analyzed outcome was positive RT-PCR at D14. Hospitalization rate and adverse events were observed (NCT04308668) [40].

Description of included studies of HCQ in the treatment of mild COVID-19

A randomized study with HCQ arm, Lopinavir-ritonavir, and placebo. The HCQ dose was 800 mg of attack followed by 400 mg/day for 9 days. Out-of-hospital population, symptomatic with positive RT-PCR (TOGETHER) [41].

A study in two health units in Qatar evaluated patients with COVID-19 with mild and out-of-hospital symptoms. Triple blind study with the primary endpoint of viral load at treatment D6. One arm used HCQ 600 mg/day for one week and the other placebo arm (had an arm with the addition of azithromycin). Adverse event with ECG to measure QT. The secondary outcome is a description of hospitalization. There were 152 randomized patients in the HCQ group with ITT in 150, 152 in the placebo group with 147 for ITT (NCT04349592) [42].

Open study with symptoms of covid-19 less than 5 days with positive RT-PCR. The dose of HCQ was 800 mg in D1 followed by 400 mg/day for 6 days. Outcomes were viral load, hospitalization [(BCN-PEP-CoV2) NCT04304053] [43].

American Canadian group, using treatment protocol in mild symptomatic patients with onset of symptoms within 4 days. HCQ dose was 800 mg of attack, followed by 600 mg in 6-8 hours after and followed by 600 mg/day for 4 days (total days in treatment was 5 days). Control was with folic acid (NCT04308668) [44].

Result of included HCQ studies on COVID-19 prophylaxis

Incidence of COVID-19 (positive RT PCR)

There is no difference in the incidence of COVID (RT PCR +) in patients with prophylactic use compared between HCQ and control, in the follow-up period between 2 and 8 weeks. Moderate quality of evidence.

Hospitalization

There is no difference in the incidence of hospitalization in patients with prophylactic

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use compared between HCQ and control, in the follow-up period between 2 and 8 weeks. Quality of moderate evidence.

Adverse events

The use of prophylactic HCQ increases the risk of adverse events by 12% (95% CI 6 to 8%) – NNH: 9, when compared to the control in 2-to-8-week follow-up. Very low quality of evidence.

Serious adverse events

There is no difference in the incidence of serious adverse events in patients with prophylactic use when comparing HCQ and control, in the follow-up between 2 and 8 weeks. Very low quality of evidence.

Deaths

There is no difference in the incidence of deaths in patients with prophylactic use when comparing HCQ and control, in the follow-up between 2 and 8 weeks. Quality of moderate evidence.

Result of included HCQ studies on the treatment of mild COVID-19

Hospitalization

There is no difference in hospitalization, when compared to HCQ and control, in the treatment of patients with mild COVID. High quality of evidence.

Adverse events

There is no difference in adverse events, when compared to HCQ and control, in the treatment of patients with mild COVID. Very low quality of evidence.

Serious adverse events

There is no difference in serious adverse events, when compared to HCQ and control, in the treatment of patients with mild COVID. High quality of evidence.

Deaths

There is no difference in deaths, when compared to HCQ and control, in the treatment of patients with mild COVID. High quality of evidence.

Risk of bias and quality of the evidence of HCQ (included studies)

The risk of bias in the included studies to support the conclusions about prophylaxis is serious due to methodological limitations related to losses, prognostic characteristics, intention-to-treat analysis (ITT) and sample calculation.

The risk of bias in the included studies to support the conclusions about treatment is not serious.

The quality of the evidence in the prophylaxis analysis varied according to the outcome analyzed: diagnosis of COVID (moderate), hospitalization (moderate), adverse events (very low), serious adverse events (very low) and deaths (moderate).

The quality of the evidence in the treatment analysis varied according to the outcome analyzed: hospitalization (high), adverse events (very low), serious adverse events (high) and deaths (high).

Summary of the evidence

HCQ in the prophylaxis or treatment of patients with mild COVID

There is no difference in the incidence of COVID (RT PCR +), hospitalization, serious adverse events and deaths in patients with prophylactic use comparing HCQ and controls without HCQ, in the 2 to 8 week follow-up. The use of prophylactic HCQ increases the risk of adverse events by 12% (95% CI 6 to 8%) – NNH: 9, when compared to controls without HCQ, in the 2-to-8-week follow-up. The quality of the evidence varied between very low or moderate.

There is no difference in hospitalization, adverse events, serious adverse events, and deaths when comparing HCQ and controls without HCQ, in the treatment of patients with mild COVID. The quality of the evidence varied between very low or high.

Ivermectin

Studies were not selected (meeting the eligibility criteria) that allowed analyzing the use of Ivermectin prophylactically in patients without the disease.

Description of included studies of Ivermectin in the treatment of mild COVID

The study tested the use of Ivermectin at a dose of 300 µg/kg for 5 days (N: 238), compared to placebo with a similar regimen of use (N: 238). The studied patients had mild COVID (home or hospitalized), with onset of symptoms in the last 7 days. The analyzed outcomes were death, hospitalization, and adverse events within 3 weeks [45].

Result of included Ivermectin studies on the treatment of mild COVID-19

The results regarding the outcomes in the comparison of Ivermectin and placebo showed no differences in hospitalization [DR 0.84% (95%CI -4.25 to +5.93)], in mortality [DR -0.42% (95%CI -1.24 to +0.40)] and in adverse events [DR -2.94% (95%CI -11.44 to 5.55) [45]. Meta-analysis was not performed because only one study was included.

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Risk of bias and quality of the evidence of Ivermectin (included studies)

The risk of bias was considered severe due to the absence of appropriate primary or secondary intermediate outcomes (relevant outcomes through posthoc analysis only) and the absence of intention-to-treat analysis. The quality of extrapolated evidence of the risk of bias considered is low [45].

Summary of the evidence. Ivermectin in the treatment of patients with mild COVID

There is no consistent evidence available to support the use of Ivermectin, either in patients at risk for COVID 19 or in patients with mild disease. There is no difference in the risk of hospitalization, mortality or adverse events when compared to the use of a placebo. The quality of available evidence is low.

Antibiotics

Studies were not selected (meeting the eligibility criteria) that allowed analyzing or indicating the use of antibiotics prophylactically or in the treatment of COVID patients with mild disease.

Summary of the evidence. Antibiotics in the prophylaxis or treatment of patients with mild COVID

There is no RCT-based evidence currently available to support the indication of prophylactic antibiotic therapy or specific therapy for patients with mild COVID 19.

Antivirals

Description of included studies of Antivirals in the treatment of mild COVID

In non-hospitalized adult patients with COVID, the use of lopinavir-ritonavir (800 mg and 200 mg, respectively, every 12 hours, followed by 400 mg and 100 mg, respectively, every 12 hours for 9 days) was compared in 244 patients, with placebo (n: 227). The analyzed outcomes of interest were hospitalization, mortality and adverse events [46].

Result of included Antivirals studies on the treatment of mild COVID-19

The results (outcomes) will be expressed in relation to the antiviral treatment (lopinavir-ritonavir) in patients with mild COVID-19: hospitalization, mortality, adverse events, and serious adverse events.

Hospitalization: there is no difference in the risk of hospitalization between the two groups compared (antiviral and placebo).

Mortality: there is no difference in mortality between the two groups compared (antiviral and placebo).

Adverse events: the risk of adverse events in the compared antiviral and placebo groups was 37.7% and 21.2%, respectively. Therefore, there is an increase in the risk of adverse events of 16.5% (95% CI 8.3 to 24.6%) with the use of antivirals in these patients (NNH: 6; 95%CI 4 to 12).

Serious adverse events: The risk of serious adverse events in the compared antiviral and placebo groups was 37.7% and 20.2%, respectively. Therefore, there is an increase in the risk of adverse events of 17.4% (95%CI 9.4 to 25.4%) with the use of antivirals in these patients (NNH: 6; 95%CI 4 to 10).

Risk of bias and quality of the evidence of Antivirals

The risk of bias from the included study to support the treatment conclusions is not serious. The quality of evidence can be considered high.

Summary of the evidence. Antivirals in the treatment of patients with mild COVID

There is an increased risk of adverse events and serious adverse events in out-of-hospital patients with mild COVID-19 treated with an antiviral (lopinavir-ritonavir).

Steroids

Studies were not selected (meeting the eligibility criteria) that allowed analyzing or indicating the use of steroids prophylactically or in the treatment of COVID patients with mild disease.

Summary of the evidence. Steroids in the prophylaxis or treatment of patients with mild COVID

There is no evidence-based on randomized clinical trials evaluating the use of steroids (VO, IV, IM) in patients with mild COVID.

Anticoagulants

Studies were not selected (meeting the eligibility criteria) that allowed analyzing or indicating the use of anticoagulants prophylactically or in the treatment of COVID patients with mild disease.

Summary of the evidence. Anticoagulants in the prophylaxis or treatment of patients with mild COVID

There is currently no RCT-based evidence available to support the indication of prophylactic or therapeutic anticoagulation for patients with mild COVID 19. Several randomized trials are ongoing evaluating the use of prophylactic anticoagulation in COVID-19.

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Monoclonal Antibodies

Description of included studies of Monoclonal Antibodies in the treatment of mild COVID

A study [47] evaluated the use of neutralizing antibodies in patients with mild COVID-19 and outpatients with a positive test for COVID-19 in the first three days of symptom onset. This study had five arms: placebo (n: 156), 700 mg bamlanivimab (n: 101), 2.8 g bamlanivimab (n: 107), 7.0 g bamlanivimab (n: 101), 2.8 g bamlanivimab with 2.8 g of etesevimab (n: 112) [47].

Another study determined the effect of bamlanivimab on the incidence of COVID-19 among residents and skilled nursing staff and assisted living facilities (residents and staff of 74 skilled nurses) with exposure to at least one confirmed case of SARS-CoV-2. A total of 1175 participants were randomized to receive a single intravenous infusion of bamlanivimab, 4200 mg (n = 588) or placebo (n = 587). The primary outcome was the incidence of COVID-19, defined as detection of SARS-CoV-2 by PCR, or progression to mild or severe COVID within 21 days of detection [48].

Result of included Monoclonal Antibodies studies on the treatment of mild COVID-19 [47]

The results (outcomes) will be expressed in relation to treatment with neutralizing antibodies in patients with mild COVID-19: hospitalization, mortality and adverse events.

Hospitalization: the risk of hospitalization with the use of neutralizing antibodies was 0.9% (in combination with bamlanivimab and etesevimab, and at doses of 700mg and 7.0g of bamlanivimab) and 5.7% for placebo. With these treatment regimens there was a 4.8% reduction in the risk of hospitalization (NNT: 20).

Mortality: there is no difference in mortality between the two groups compared (neutralizing antibodies in the treatment of mild COVID and placebo).

Adverse events: there is no difference in the risk of adverse events between the two groups compared (neutralizing antibodies in the treatment of mild COVID and placebo).

Result of included Monoclonal Antibodies studies on prophylaxis of mild COVID-19 [48]

The results (outcomes) will be expressed in relation to prophylaxis with neutralizing antibodies in individuals exposed to patients with COVID-19: infection (PCR +), mortality and adverse events.

Infection (PCR+): bamlanivimab was associated with a significantly lower incidence of SARS-CoV-2 infection compared to placebo (17.9% vs. 23.3%; P = 0.02), with a difference an absolute risk of −5.4% (95% CI, −10.5% to −0.3%). NNT: 20.

Mortality: there is no difference in mortality between the two groups compared (neutralizing antibodies in COVID prophylaxis and placebo).

Adverse events: there is no difference in the risk of adverse events between the two groups compared (neutralizing antibodies in COVID prophylaxis and placebo).

Risk of bias and quality of the evidence of Monoclonal Antibodies

The risk of bias from the mild COVID treatment study [47] and the prophylaxis study [48] is "non-severe" in both. And the quality of evidence related to the outcomes where there was a difference (hospitalization in the treatment of mild COVID and infection in the prophylaxis) can be considered high.

Summary of the evidence. Monoclonal Antibodies in the prophylaxis and treatment of patients with mild COVID

There is a reduction in the risk of hospitalization in patients with mild COVID-19 treated with neutralizing antibody (bamlanivimab associated or not with etesevimab). There is a reduction in the risk of SARS-Cov-2 infection with the prophylactic use of monoclonal antibody (bamlanivimab) in individuals exposed to patients with COVID.

Convalescent Plasm

Description of included studies of Plasm in the treatment of mild COVID

In this selected study [49], 160 patients with up to 48 h of onset of symptoms related to COVID-19 (mild) were randomized. Patients over 75 years of age, regardless of the presence of comorbidities, and those aged 65 to 74 years with comorbidities were considered eligible. The intervention considered the use within 72 h of symptom onset of 250 ml of convalescent plasma with IgG titres greater than 1:1000 against the spike of SARS-CoV-2, compared with 250 ml of 0.9% saline in the placebo group. The study outcome was the development of a severe respiratory condition with a respiratory rate > 30 mpm or pulse oximetry <93% in room air 15 days after the intervention infusion. Data on non-invasive ventilation, mechanical ventilation, shock, and death were collected [49].

Result of included Convalescent Plasm studies on the treatment of mild COVID-19 [49]

The results (outcomes) will be expressed in relation to Convalescent Plasma treatment in patients with mild COVID-19: evolution to severe respiratory condition, non-invasive or mechanical ventilation and deaths.

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Severe respiratory condition: the risk of severe respiratory condition in the plasma and placebo groups was, respectively, 16.2% and 31.2%, with a significant reduction in this risk of 15.0% (95%CI 2.0 to 27.9%) with the use of plasma (NNT: 7 – 95%CI 4 to 50).

Mortality: there is no difference in mortality between the two groups compared (plasma and placebo).

Noninvasive and mechanical ventilation: there is no difference in the risk of noninvasive or mechanical ventilation between the two groups compared (convalescent plasma and placebo).

Risk of bias and quality of the evidence of Convalescent Plasm

The risk of bias from the included study to support the treatment conclusions is not serious. The quality of evidence can be considered moderate due to the imprecision of the outcome in which there was a benefit (worsening of the respiratory condition).

Summary of the evidence. Convalescent Plasm in the treatment of patients with mild COVID

There is a reduction in the risk of developing a severe respiratory condition with the use of convalescent plasma (IV) in elderly patients (aged > 75 years or aged between 65 and 74 years, associated with comorbidities) not hospitalized with mild COVID-19.

Nitazoxanide

Description of included studies of Nitazoxanide in the treatment of mild COVID

In this selected study [50] 1575 were evaluated, of these 475 had positive RT-PCR for COVID-19, symptoms starting up to 3 days and were randomized to intervention with nitazoxanide 500 mg oral solution (20mg/ml) 3 times a day for 5 days or placebo group that received a similarly coloured solution. The primary outcome was the resolution of the symptoms of interest (dry cough, fever and/or fatigue) after the 5th day of therapy. The hospitalization rate after drug therapy, adverse effects on the 14th day of follow-up was also evaluated.

Result of included Nitazoxanide studies on the treatment of mild COVID-19 [50]

The results (outcomes) will be expressed in relation to the treatment of Nitazoxanide in patients with mild COVID-19: adverse events and deaths.

Mortality: there is no difference in mortality between the two groups compared (Nitazoxanide and placebo).

Adverse events: there is no difference in the risk of adverse events between the two groups compared (Nitazoxanide and placebo).

Risk of bias and quality of the evidence of Nitazoxanide

The risk of bias from the included study to support the treatment conclusions is not serious. The quality of evidence can be considered low due to the imprecision of the results and in the intermediate and primary outcomes.

Summary of the evidence. Nitazoxanide in the prophylaxis and treatment of patients with mild COVID

There is no benefit in terms of reduced mortality or increased risk of adverse events with the use of Nitazoxanide in patients with mild COVID.

Colchicine

Description of included studies of Colchicine in the treatment of mild COVID [51]

Patients aged 40 years and over diagnosed with COVID-19 within 24 h and who were not being treated in hospital underwent treatment with Colchicine (0.5 mg twice a day for the first 3 days and then one once daily for 27 days thereafter) compared to placebo. A total of 4,488 patients were included, divided into two groups: Colchicine (2.235) and placebo (2.253).

The primary efficacy endpoint was a composite of death or hospital admission due to COVID-19 infection within 30 days of randomization. Secondary outcomes consisted of the components of the composite primary outcome and the need for mechanical ventilation within 30 days of randomization. Pneumonia, and other serious adverse events and non-serious adverse events were also collected.

Result of included Colchicine studies on the treatment of mild COVID-19 [51]

The results (outcomes) will be expressed in relation to Colchicine treatment in patients with mild COVID-19: hospitalization, mechanical ventilation, adverse events, serious adverse events, deaths.

Hospitalization: the risk of hospitalization in the Colchicine and placebo groups was, respectively, 4.1% and 5.4%, with a significant reduction in this risk of 1.3% (95%CI 0.04 to 2.5%) with the use of Colchicine.

Mortality: there is no difference in mortality between the two groups compared (Colchicine and placebo).

Adverse events: there is no difference in the risk of adverse events between the two groups compared (Colchicine and placebo).

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Serious adverse events: the risk of serious adverse events in the Colchicine and placebo groups was, respectively, 4.8% and 6.1%, with a significant increase in this risk of 1.3% (95%CI 0.004 to 2.6%) with the use of Colchicine.

Risk of bias and quality of the evidence of Colchicine

The risk of bias from the included study to support the treatment conclusions is not serious. The quality of the evidence due to the imprecision of the results should be considered moderate.

Summary of the evidence. Colchicine in the treatment of patients with mild COVID

There is a reduction in the risk of hospitalization and an increase in the risk of serious adverse events with the use of Colchicine in non-hospitalized patients with mild COVID-19.

Discussion

This document is to endorse medical recommendations about the pharmacological treatment to prophylaxis and mild COVID-19 based on the best scientific evidence in the literature.

This article evidences the lack of pharmacological treatment to be used as a prophylactic to COVID-19. For the mild COVID-19, we could demonstrate that most clinical randomized studies failed to show benefits to control the progression of the disease. On the other hand, we observed that maybe there exists a specific population that has the benefits of early use of convalescent plasma. However, more RCTs are needed to confirm the efficacy of convalescent plasma in older people.

In the mild presentation of covid-19, the available and effective therapeutic options blocking the disease's poor clinical course are scarce. At the same time, we do not have safe clinical or laboratory markers to assess the prognosis of disease progression. In about 85% of cases, the evolution is benign, but in the remaining 15%, it may present with rapid deterioration, with clinical and respiratory worsening. Thus, it is essential to follow all initial outpatient cases of the disease. It is necessary to monitor general symptoms, temperature, heart rate, and oxygen saturation. Patients with covid-19 should be ensured easy and fast access to information resources, clinical, laboratory, and radiological controls when indicated.

Indeed, the importance of disposing of a systematic review using only RCT phase III is essential during the pandemic crisis, that exists a thousand disconnected information related to the disease. In this context, this document can support the choice of the best medical practice using a robust method.

Furthermore, scientific societies are too dynamic to post new evidence daily and have never worked as they do now to bring this information in a way that can be safely replicated and used. Controversies in medical treatment have always been constant in the literature. This is part of the construction of medical knowledge, that can be fragmented, but the principle is to assess the probability of finding the correct choice. However, after more than one year of pandemic, we still find the dualism in some situations, such as in this context of prophylaxis and mild COVID-19 treatment. We always should prevent the misuse and misinterpretation of information, because it can be harmful.

Unfortunately, we continue without miracle pharmacological treatment to prevent disease severity or prophylaxis. We still recommend the masks use, vaccination for all population, avoid agglomeration and perform diagnostic tests as a control tool of dissemination. For future studies, is important to consider the variabilities of risk COVID-19 infection and it is necessary large trials to detect the benefit of the user's other pharmacological treatment.

Drugs Prescription in Covid Prophylaxis or Mild Covid Treatment Recommendations

1. The use of Hydroxychloroquine in the prophylaxis of COVID or treatment of patients with mild COVID is not recommended.
2. The use of Ivermectin in the prophylaxis of COVID or treatment of patients with mild COVID is not recommended.
3. The use of antibiotics in the prophylaxis of COVID or treatment of patients with mild COVID is not recommended.
4. The use of antivirals in patients with mild COVID is not recommended because, in addition to not producing benefit, it causes harm.
5. The use of steroids in the treatment of patients with mild COVID is not recommended.
6. The use of anticoagulants in the prophylaxis of COVID or treatment of patients with mild COVID is not recommended.
7. The use of neutralizing monoclonal antibodies can be used in patients with mild COVID (bamlanivimab associated or not with etesevimab) or prophylactic (bamlanivimab) in individuals exposed to COVID.
8. The use of plasma (IV) in elderly patients with mild COVID (not hospitalized) can be a therapeutic option to reduce the risk of worsening the respiratory condition. However, its restricted application or favorable to the hospital environment can act as a barrier to its applicability, and this recommendation is not appropriate for pre-hospital use.
9. The use of nitazoxanide in the prophylaxis of COVID or treatment of patients with mild COVID is not recommended.
10. The use of Colchicine in the treatment of patients with mild COVID is not recommended due to a null (1) ratio between benefit (hospitalization)/harm (serious adverse events).

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Obituary

Tribute to ***Padma Shri Dr. K. K. Aggarwal***
5 September 1958–17 May 2021

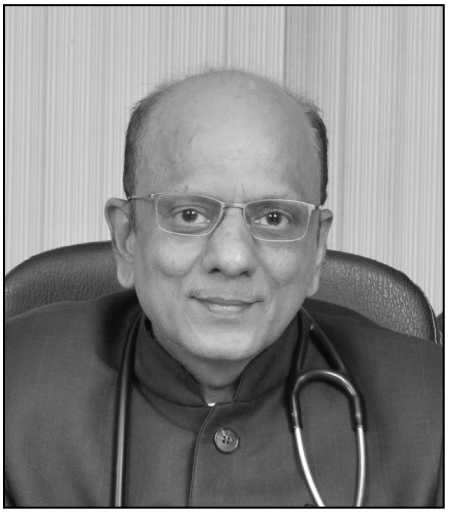
Dr. Ravi Wankhedkar
Treasurer, World Medical Association
Past National President Indian Medical Association

Dr. K. K. Aggarwal, a great teacher of medical science and a doyen of public health, breathed his last on 17 May 2021 at All India Institute of Medical Sciences, New Delhi. A true champion from the scientific and medical fraternity, he was an Indian physician and cardiologist who was President Confederation of Medical Associations in Asia and Oceania (CMAAO), President of the Heart Care Foundation of India, the Past National President of Indian Medical Association, Secretary General, Indian Medical Association, President of Delhi Medical Association and Indian Medical Association, New Delhi Branch. Until 2017, he served at Moolchand Medcity, New Delhi, as a Senior Consultant, Physician and Cardiologist, and Dean, Board of Medical Education. He received Dr. BC Roy National Award in 2005 which is given for outstanding service in the field of Socio-Medical Relief. The government of India honoured him in 2010 with the Padma Shri, India's fourth-highest civilian award, for his contributions to the field of medicine.

His contributions in public health during Covid 19 times was very noteworthy. He was the first person in India to warn the medical fraternity and general public about Covid. His daily educative mails to update physicians were highly useful. For the lay persons his daily "KK Meditalks" were extremely informative. It was indeed a great irony that he himself succumbed to Covid.

Dr KK Aggarwal, MBBS, MD, Gold Medalist, had a very keen sense of clinical research and was one of the pioneers of streptokinase therapy for heart attacks in India who also introduced the technique of Colour Doppler Echocardiography in India. Being the first to use clot busters in patients with acute myocardial infarction in 1984, he introduced colour Doppler echocardiography in North India in 1987. He was also a Limca Book of World Record Holder for the maximum people trained in the life-saving technique of Hands-only CPR. A legend of Cardiology, Dr Aggarwal worked tirelessly to establish connections between technology and the tradition. He also used alternative medicine – Yoga and Ayurveda – to treat his patients. Dr. Aggarwal saved countless lives with his undeterred efforts of reaching out to the masses to raise awareness amidst the raging pandemic.

Department of Science & Technology conferred upon him the National Award for Outstanding Efforts in Science & Technology Communication in 2013. He was a reputed science and health education communicator, with a social media following of more than 10 million people, who did phenomenal work for creating mass awareness on the SARS COV-2 virus. He also worked hard through annual Perfect Health Melas which became a huge success among school children and various other stakeholders. He published many books on health, including Alloveda – in which he combined ancient Vedic Medicine with modern Allopathy. He is credited with six textbook chapters on echocardiography and thousands of articles in the national and international press. Dr. Aggarwal will be remembered for his indomitable dedication towards public health, medical science, science communication and public welfare during his 30 years of medical and social presence.



His pursuit of excellence continued in the diverse roles of physician-scientist, Researcher, academic teacher, writer, editor, administrator, Meditation teacher and public health activist. A recipient of Delhi Hindi Sahitya Sammelan – Sahitya Shree Award 2007 as a doctor and philosopher of Indian Culture, he also received Vishwa Hindi Samman in 2015. He was decorated with FICCI Health Care Personality of the Year Award 2016, Dr D S Mungekar National IMA Award, Indira Gandhi Priyadarshini Award 2003, and the Rajiv Gandhi Excellence Award 1993, along with numerous other awards and recognitions. It is noteworthy that he was also a member of Ethics Committee, Medical Council of India, and Chairman Ethics Committee Delhi Medical Council. Dr Aggarwal also served as Group Editor in Chief IJCP Group of Publications and eMedinews- the first national daily medical newspaper. A holder of Three Limca Book of World Records and a TEDx Speaker, he was a prolific writer, an eloquent columnist and also a TV Anchor. Championing the cause of medical professionals, health & human rights, medical ethics, he was keenly interested in revamping the medical education in India. His untimely passing away is a loss to the whole scientific community and human kind.

His last do message from the hospital bed with O2 on, that the "Show must go on" will remain an everlasting directive for the entire India.

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