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Webinar

Stand on the Same Side – Preventing a Second Wave of Covid-19's Outbreak

This document is the direct transcription of a Webinar organized by Prof. L. Corbetta of the University of Florence on April 19th, 2020.

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"STAND ON THE SAME SIDE" Videoconferences

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"Implementing a science-based lockdown exit strategy is essential to sustain containment of COVID-19. China's experience will be watched closely, as other countries start considering—and, in some cases, implementing—their own exit strategies"

The Lancet, Volume 395, Issue 10232, 18–24 April 2020, Pages 1305-1314

This phrase expresses the purpose of this program called "Stand on the Same Side against Covid-19" that takes advantage of the new and rapid digital technologies to put together several experts worldwide. It's a global space were many countries hit by SARS -COV-2 can share only scientific information in order to face the pandemic.

APR, 29th 2020,
CHINA-EUROPE VIDEOCONFERENCE

"STAND ON THE SAME SIDE AGAINST COVID-19 - PREVENTING A SECOND WAVE OF COVID-19'S OUTBREAK"

Shiyue Li: Hi, everyone. Welcome to the webinar. This meeting is the second China/Europe seminar on fighting COVID-19. Last meeting was about one month ago.
Before this webinar, many thanks to Dr. Corbetta for organising this meeting. Today, the topic for this webinar is preventing a second wave COVID-19 outbreak. We have doctors from Europe and China to join together to exchange our opinions on this topic. So, I have just a brief opening speech and then I'd like to invite Dr Corbetta to give some words. Please, Professor Corbetta.

Lorenzo Corbetta: Okay, professor. Hello, everyone. Professor Jing Li, if you want to introduce the speakers, please.

Jing Li: Okay. It's my honour to introduce all the speakers one by one. Today, we have seven outstanding speakers, talking about various topics on when the second wave of COVID-19 outbreak will be. There is German speaker, UK speaker, Italian speakers, Chinese speakers. I'm happy to introduce the first one that is from China, Professor Guo Shuliang.
Professor Guo is the Head of Department of Respiratory and Critical Care Medicine at the First Affiliated Hospital of Chongqing Medical University. He's also the leader of the international group of the Committee into the Intervention of Respiratory Diseases. He is also Vice President of the Respiratory Endoscope Society of the World Endoscope Physicians Association. His topic today will be a strategy in the community, in hospitals, with the second wave of outbreak in China.

Shuliang Guo: Okay. Thank you for your introduction, Professor Li. Hello, everyone. It's my great pleasure to introduce a strategy in communities and hospitals to prevent a second wave of outbreak in Chongqing, China.
China has had great success in fighting against the COVID-19 until now. We began to restore normal economic and social order.

However, some experts expressed their concern on a second wave of outbreak. Even in China, there is a high-probability event. So, after the first wave, is there going to be a second wave? The answer is probably. In the Spanish Flu pandemic in 1918, there were multiple waves and here shows the second wave of SARS, and the second wave of COVID-19 in Singapore recently. So, China has a potential risk of a second wave epidemic because China is far from herd immunity and they're under a great pressure of imported infections and emerging asymptomatic transmissions. The recent epidemic rebound, here, you can see in Heilongjiang province due to the dramatic increase of imported cases and the recent local chain and cross provincial spread in Harbin due to dining, gathering and cross infection in hospital intensifying these concerns.
So, how to prevent a second wave of outbreaks. We introduce some strategies for communities and hospitals in Chongqing.

- The first one is the risk- and the region-specific resumption and reopening. We resume and reopen based on the risk rating. The risks are ranked as low, medium, high risk regions. For example, the low-risk regions means administrative regions with no confirmed cases and without new confirmed cases in the past consecutive fourteen days. Here, on March 20th, all districts in Chongqing were declared no risk and the emergency response had adjusted to the third level. So, in different risk regions, there are different strategies. For example, in low-risk regions, the main strategy is to prevent imported cases. In medium-risk regions, the principal strategy is to prevent imported cases and domestic rebound and re-infections meanwhile. We focus on the strategy at city and community level here. We demand staying alert constantly and we resume and re-open gradually and dynamically.
- For example, the graduating class begins schooling first, the class is divided into smaller ones, we prefer remote teaching and large entertainment are still closed.
- We also want to control by taking temperature at ports and stations. Also, we scan the health coding before entry, as shown here. If the code is blue, you can pass, but if it is yellow or red, it's not permitted entry.
- We continue to wear masks, keep a one-metre distance and avoid gathering.
- We expand PCR and detection, and this testing, to find out asymptomatic persons. All of the three groups that

should be tested including their close contacts, people from Hubei and Wuhan to Chongqing, and the person inbound to Chongqing within fourteen days. This people will be isolated for fourteen days in different designated hospitals or home.

- So, at a hospital level, we have careful entry control. We scan a health code, like here shows, and we check temperature and face recognition. We do pre-check triage and fever clinic control. The patient will be admitted only after the PCR (Polymerase Chain Reaction) and the CT (Computer Tomography) Scan examination. Besides above, the anti-epidemic agencies, measures and isolation wards remain unchanged. We strengthen internet medical services to reduce patient gathering. For all hospitalized patients and high-risk operations, PCR testing should be done firstly. We continue personnel training and remain vigilant. We protect medical workers with PPE (Personal Protective Equipment) in high-risk departments during diagnosis and treatment. We do escort testing. Emergency isolation sections have been set up in each ward and we do strictly terminal disinfection.
- To deal with a second outbreak, the government in Chongqing strengthen the construction and storage of the epidemic emergency system. The government are now building four new public health emergency hospitals with a capacity of 5,000 beds in Chongqing. Here, we can see they're located in the central, in the west, in the north east and the south east district. That covers the whole of Chongqing city. China is accelerating the research and development of vaccines and specific drugs. As director of CDC (Center of Diseases Control) in China, Gao Fu, mentioned the China vaccine may be available for emergency use in September. So, all of the strategies and measures worked well.
- Here, from February 25th, there were no confirmed cases, and all the asymptomatic cases are imported with zero to five cases per day. However, globally, more than 200,000 people have died of COVID-19 and the American CDC director warned that the second wave could be even more devastating. So, we must join hands, do more efforts, stand on the same side, to fight against COVID-19 and to prevent a second wave. So, thanks for your attention. Thanks.

Jing Li: Thank you very much, Professor Guo for his intensive introduction. He introduced different waves of the COVID-19 outbreak in several cities in China, and also raised some risks of the second outbreak, and introduced some strategy, including some vaccines, very nice. Now, we move to the second one. The second speaker will be Professor Paolo Bonanni. He is the professor of hygiene, University of Florence, and director of the Specialisation School in Hygiene and Preventive Medicine, University of Florence. He's going to give us a talk on control strategies outside the hospital to prevent a second spike of COVID-19. Let's welcome Professor Bonanni.

Paolo Bonanni: Thanks a lot for the second invitation to this second webinar. The situation has changed, obviously, since the last webinar, because of course the epidemic has progressed.

In Italy and in Europe, we are lagging behind China regarding the number of cases, because you showed that you had no longer cases in some provinces since February 25th, when we were starting. So, the phase two is just starting now in Europe and in Italy, and I would like to highlight some points of discussion regarding the control strategies outside the hospital to prevent a second spike. The first slide I want to show is a little bit crowded-, I apologise for this, but this is the official data from Italy from two days ago. I want to draw your attention to the number of cases here. We have almost 200,000 cases. We surpassed that amount in the last two days. But, of course, this number is an underestimate, because I would like to remind you that in Italy, for a long time, only cases who were strongly symptomatic and who accessed the hospital were for sure tested for PCR. So, probably, the real number will be much higher than these figures. You see this, also, from the number of deaths that we've had, that puts us with a case fatality rate which is much higher than in other countries. This is not, probably, due to different characteristics of the virus or differences in Italy compared to cases in other countries, but the problem is that we are underestimating the denominator of these numbers. The other important thing is that many healthcare workers were infected. You see here that around 10% of the overall cases were healthcare workers. The other important part is the case fatality rate, which despite this being probably overestimated, all the same you can see here that people from 60 to 69 have a case fatality rate, provisional fatality rate, of almost 10%, much higher in the elderly population.

But this is putting a special focus, because there was a discussion in the country saying that we shouldn't prevent people from 60 to 69 years going back to work in the first phase two weeks, because there might be a danger for them if they get infected. My contribution to today's webinar is mainly of questions rather than answers, because we ask ourselves a lot of questions in this preparation for the phase two. So, we are starting our phase two on May 4th and there was a lot of discussion in the country, because many people who are waiting to go back to work were a little bit deluded by the progressive opening that the Italian government decided to do. So, we are opening little by little, and some elements of consideration for the progressive reopening of work activities. Of course, in all the companies and fabrics, people will be tested for temperature. If they are over 37.5 degrees, they will not be let in the industry or the office. But the questions I want to raise are the following ones.

What is the real number of infected subjects still unknown? And what is the proportion of the overall population which is still spreading the virus?

So, of course, we have a question mark on the number of asymptomatic subjects that are going around, without being

aware of being a person who can infect other people. Then, how long an infected subject carries the virus in saliva, this clinically healed subjects who still test PCR-positive three weeks later. So, three weeks after they were considered healed from a clinical point of view. So, it's difficult to understand how long the spread of the virus can be sustained by people who are clinically okay.

The other problem is, is the virus shed in faeces? We know yes, but how long? This is also a problem for the management of toilets in the companies and offices. Are face masks always needed outdoors and in the workplace? Which masks should be worn, and should that be compulsory?

Also, here, there is a lot of discussion. Probably, in some companies, they are trying to avoid the permanent masking of people who work there if they can keep a distance of more than two metres. But, the other question is, how frequent is aerosol production from an infected subject? Is this substantially contributing to virus spread or not? Again, we are going towards summer and, of course, there is a lot of air conditioning foreseen for the next months. The question is, is air conditioning dangerous? Should its maintenance be different from normal times? My last question here is, can serological tests be useful to manage re-admission at work or not? I tried to make some consideration on what I asked ourselves. So, we need to test people twice, and they need to be negative to PCR with at least 24 hours of distance between the first and second test, for re-admission in the community. Because, otherwise, we are risking them to spread the virus.

If PCR is not performed and people are not confirmed cases, but only suspected COVID-19 cases, I suggested to the people who ask me, for the reopening of work facilities, to leave the subject at home for two or three weeks more if this is possible. If this is not possible, they should compulsorily wear the masks anywhere and at all times outside their home when they go to work. We need to provide the careful sanitisation of toilets, handles, taps, and we should have different toilets for internal and external workers in workplaces. We should keep 1.8 metres between workers whenever possible. If not, surgical masks should be worn when the distance is less. We need to exchange air.

So, window opening whenever possible. Air conditioning does not seem, from the evidence we have, to contribute to virus spread. So, normal maintenance for them. The only suggestion is to keep humidity at a higher level, because this probably makes the possible drop that's containing the virus be bigger and fall down. So, the spread is mainly through big droplets and, in this sense, hand hygiene is crucial and to be very much stressed.

Some considerations and suggestions

- Need to test twice negative to PCR (24-hour interval) for re-admission in community.
- If PCR not performed by suspected COVID-19 case, leave subject at home for 2-3 weeks after healing is possible - if not, compulsory wearing of surgical mask at any time.
- Careful sanitization of toilets, handles, taps, different toilets for internal and extenal workers.
- Keep 1.8 meters between workers whenever possible. Surgical masks must be worn if distance less.
- Exchange air (window opening) whenever possible. Air conditioning does not seem to contribute to virus spread, normal maintenance, humidity not too low.
- Spread mainly thorough big droplet, hand hygiene crucial.
- Serological tests: different types (rapid strip; ELISA; chemiluminescence), different sensitivity and specificity; unclear role of IgG in virus clearance.
- Are antibodies long lasting? Protective? How long? *Still to be proven.*

Regarding serological tests, we have a lot of adaptations. So, there are different types. Rapid strips, ELISA, chemiluminescence. They have different sensitivity and specificity, and we don't know yet the role of IgG in virus clearance. So, I think that we must go on testing these tests-, let me say it like this, but we don't have definitive answers on the role of the serological testing. Also, because, how long are antibodies lasting? Are they protective and if they are protective, how long? All of this needs to be proven. I just want to highlight an interesting paper from China that should be published in the next month, showing that in restaurant in Guangzhou, there was a way to show that in a restaurant, before the closing, people who are under the air conditioning machine spread the virus to the closer tables, but not to the tables here, E and F. So, air conditioning is probably not contributing to the distribution of the virus through the machine, but creating an air flow might bring the droplets from the table of infected subjects to the nearby tables. So, this is also interesting for the management of restaurants and bars in the near future. This is an example of something we're doing with companies here in Italy.
The original article can be found here:
https://wwwnc.cdc.gov/eid/article/26/7/20-0764_article

This is an example of management of face masks in an Italian mechanical company. So, they wrote guidelines for their workers, saying that, for distribution criteria, for activities with an interpersonal distance of less than two metres, they should stop work, evaluate with a responsible for the work management, if there can be another way to work with a distance of more than two metres. But, if there is no possibility to work without this distance, they should ask for an FFP2 mask if this work is short-lasting. But, if this is needed for a long time, they should ask for a surgical mask.

The disposal of masks is in dedicated bins as special waste, and bins should also be located near changing rooms and infirmaries. Masks are also supplied by the company, for people who travel from home to workplace and back, and the preference for mask-wearing at any time during work. So, if there are some people who want to wear this mask for all the entire duration of work, they can be provided with these masks. So, I want to close my presentation. We still have to learn much also on effective containment in the phase of lockdown release.

An example of management of face masks in an Italian mechanical company

Use of face masks in accordance with WHO recommendations:

Distribution criteria

- For activities with interpersonal distance < 2 meters the following criteria apply:
- Stop Work - To evaluate with the responsible of work management
- Identify Hazard - Identify phases which require a distance < 2 m
- Control Hazards & Verify barriers - Identify together with the responsible alternative ways of performing tasks which allow a distance > 2 m
- If not possible - (i,e, 3-4 times per turn, few minutes) ask for a FFP2 mask
- If continuously < 2 m for the entire turn - (i.e. mounting the same component closely), ask for a surgical mask

Disposal

- Masks must be disposed of in dedicated bins as "special waste (CER 180103*)"
- Bins should also be located near to changing rooms and infirmaries

Masks are also supplied by the company for

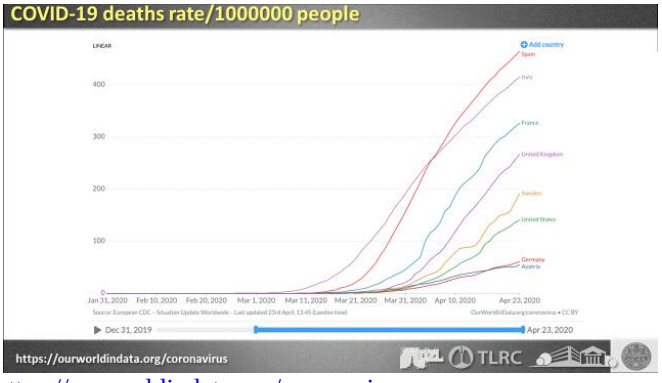
- Travel home/workplace and back
- Preference for mask wearing at any time during work

We do hope that this can be done successfully and with limited need of new selective closures of activities and communities in the next phase. But we must be very careful and we must be able to close the places where new contagion occurs, if this should be the case in the next few weeks. Thank you very much for your attention.

Jing Li: Thank you very much, Professor Bonanni, for your very interesting talk on the prevention of the outbreak outside hospital. You have very important three points and I want to have a summary. You mentioned the unknown proportion of the population that it's still spreading the virus on the probability of the second outbreak, and you introduced some elements of the consideration for the progressive reopening of work activities. The third, I would like to thank you again, you mentioned a very interesting paper from China for the restaurant management.
Also, you mentioned the face mask selection on certain situations. Thank you very much.
Now, we come to the next speaker, Professor Felix JF Herth. Professor Herth of Thorax University in Heidelberg in Germany. He also is the head of department of internal medicine pulmonology and critical care. Also, the chief of the European Committee for Bronchology and Interventional Pulmonology. He's going to give us the talk with a topic of role of hospital reorganisation and testing capabilities to achieve the best outcome. Now, Professor Herth, please.

Felix Herth: Yes. Thanks a lot for giving me the opportunity to share with you what we did in Germany in the past and how Germany is handling the COVID situation. To be honest, I can tell you what we did, I have no idea what we have to do next, because nobody knows if a second wave is coming and when. Just to give you a brief update, this is the actual situation in Germany. We have about 160,000 cases and we lost about 6,000 patients. Lorenzo asked me to show our real data. This is our reproduction rate. DIAPO Since fourteen days, we are now below one. So, that means that only one patient is infecting one other. Yesterday, we have had a little peak: we have to upgrade to 1.00. Before, we have been 0.94. So, actually, the situation in Germany is quite stable regarding the infection rate. As you see here, we have had a couple of patients on the ICU (Intensive Care Unit) like everybody else in the world. But many patients reached a level of entering an ICU with a mortality of 30%. So, that means, in the severe population, dealing with COVID, we have to compare the mortality rate to the other parts of the world.

I've just put here a couple of other European countries on the table. Germany was actually quite successful to keep the mortality of COVID-19 really on the lower limits. We had a range of 2%. Austria has the same results published, but all other countries are really above us. So, the question is-, maybe this is the reason why Lorenzo asked me to participate today, the question was why Germany did it a little bit, or it seems, did it a little bit better than the rest of the world. Now, here are my explanations for that.



https://ourworldindata.org/coronavirus

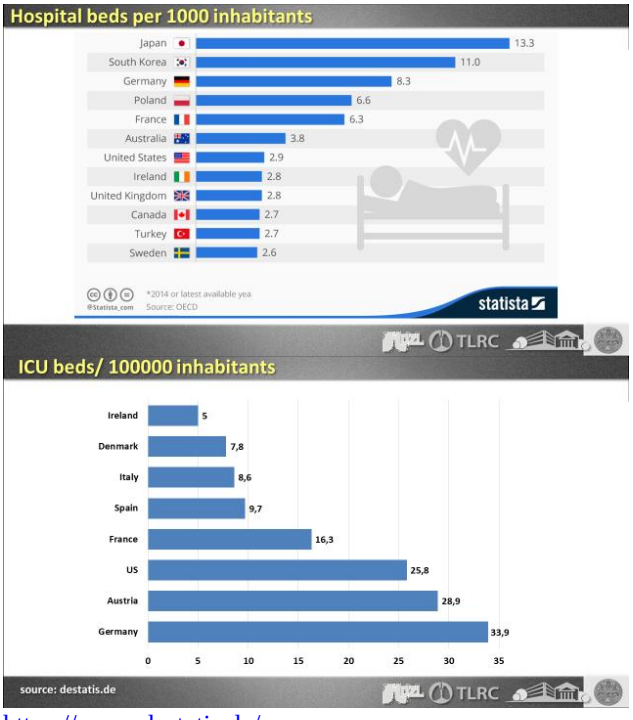
This is the timeline of how we shut it down. The first patient in Germany we have at the end of January, and at least in March 13th, the decision was made for Angela Merkel to shut down Germany.

We closed schools, we closed universities, nobody was able to enter Germany anymore. So, this has been a timeline of shutting down. What was decided on March 13th for the hospitals, we postponed all elective procedures, the outpatient clinics have been closed, and only 50% of the beds from the hospitals are occupied by normal patients. So, the reserve of

COVID patients have been 50% of the whole hospital capacities in Germany.

From March 13th, we didn't allow any visitors in the hospital and any patient who entered the hospital have had to answer a couple of questions. If they have contact with COVID patients, if they're coming from a risk area, and we measured all patients' fever from the beginning. In the case the patient developed fever, they were directly transferred to COVID unions that have been received this way. A couple of additional reasons why Germany is quite successful at the moment to handle COVID-19 is the handling of its hospital beds. Again, this is a comparison. Japan and South Korea, they even have more hospital beds for people in their country, but when you compare it to the other European areas and also to the United States, **we have three times more hospital beds than the UK has**. So, the capacity for the hospital is bigger than in other areas.

Also, not looking at hospital beds, looking to the ICU beds, we have more ICU beds per inhabitants compared to other areas in the world. So, therefore, the hospital capacity is quite high, so we were able to handle the patients maybe in a better situation than perhaps the colleagues in north Italy, or in France, where they really reached the limits of what the hospitals can offer.



https://www.destatis.de/

I put the data up, measured at March 2020, when the peak really came. In Germany, **we really have the opportunity to do a lot of PCR tests.**

So, actually, we're doing about 300,000 PCR tests per week in Germany. So, that might be that we're detecting more patients at an earlier stage. This is one explanation from me why we have had, from the beginning, a low mortality rate, that we have a huge capacity for PCR tests which allow us to even offer tests to patients with mild symptoms. This is also one of the major reasons why we still are lucky with the mortality rate. A couple of days after the shutdown, we opened so-called drive-in testing. So, patients were able to come to bigger areas.

They just opened the window of their car, we did the swab, they got a QR code and we sent the test result from the patient data to the QR code of the patient. But the contact between patient and medical-healthcare providers have been very limited. See, this is one of the pictures from our drive-in testing.

So, we offered a lot of testing, even not inside the hospitals What we also did, we established so-called corona taxis. We are knowing that the patient has a positive swab and, often, quite mild symptoms, but we're knowing that seven is the critical day, so all patients would be sent home. Home quarantine have been visited by a doctor at the five and six. We measured, at that time, the situation. We looked at a patient and in the case the patient developed symptoms, we directly hospitalised them. So, the corona taxis, which have been mentioned here in the New York Times, have been quite successful to identify mild patients who are on their way **to getting a severe illness at an earlier stage**, so we brought them into the hospital system and we started the treatment with various medication. So, last slide. This has been the first wave of Germany. You see, this is our timeline, this is the actual data. So, it looks like we survived the first wave-, actually, we're doing similar things we just heard from Paolo.

We're giving a lot of recommendations and a lot of information to the population, and we're hoping that the second wave, if a second wave appears, would be a little bit smaller and hopefully the Germans can handle their patients in the way we handled the first wave here in Germany. Thanks for your attention.

Jing Li: Thank you. Thank you very much for this explanation of the Germany strategy on the prevention and treatment of COVID-19. You introduce the prevalence of COVID-19 and even the ICU and administration. Very impressive. Also, the mortality rate is very low in Germany in a tight line. Also, you have some very successful strategies for the patients administration in the hospital and also the ICU bed capacities. It's highest among the European countries. Also, the testing's available in every way. Yes, very

impressive.

Thank you very much. Then we go to the next speakers, Professor Javier Flandes. He's the Director of the Bronchoscopy and Interventional Pulmonology Unit and Section Head of Pulmonary Medicine. University Hospital Foundacion Jimenez Diaz in Madrid, Spain. President of the Spanish Association for Bronchoscopy and Interventional Pulmonology. Also, he is the governor of Spain American College of Chest Physicians, Association for Bronchology and Interventional Pulmonology.

He's going to give us the topic on how to manage people under investigation and probably COVID-19.

Javier Flandes: Okay. Good morning. Thank you for inviting me to do this webinar. My topic is about the management of patients with suspected COVID-19. In the initial part of my lesson, I want to show the management of the programme to any potential suspicious cases.

This is the situation during the lockdown period, which started here in Spain in March and has been extended to the 9th May in Spain.

Madrid is the region with the highest rate of infections in all the country. I want to show you, the differences in-between countries. Sorry, I don't put Germany. That's a pity, because Germany is very successful in their position. But it's very similar, the curve that we have, in Italy. In Spain, and also the United States with a different plateau. It is very different from the Chinese curve, and also we can discuss with Dr Guo this point of view. We can see the new cases per day in the time. This is data from Spain. It's very bad.

It's worse than other countries. But we are very similar to Italy, as Dr Paolo Bonanni showed us. We have, now, at this moment, a total-, in the blue line, you can see the infected patients. More than 200,000 patients.
In the grey line, you can see the patients who are recovering. More than 100,000. In the black line, deceased people.
About 23,000. The data is very similar to Italy. But I have this data from Spain about the mortality rate of coronavirus by age group. People older than 80, the mortality is about 20-21%, all these people will die. We count a cut of-, in people older than 70 years old, they have a high possibility to die with this disease.

Unfortunately, we have a special situation is the infection of the healthcare workers, and Spain is the country with the highest number of healthcare workers infected. We have now, at this moment, more than 40,000. In Italy, I hear now, from my friend, the number is 20,000. It's twice. The nurses are 60% of all the affected healthcare workers. But, apparently, this result is because we started our country with all the indispensable safety issues.

We are overflowing facilities and we are not prepared for this pandemic. Focusing on the main topic of the lesson, one question comes out. Do all patients need to be tested? Well, today, the agreement is, we need to sample all the patients with suspected infection with moderate or severe symptoms. And also, of course, all the patients are witnessing that is the rule. These are their symptoms. But, in the case of the patients without any risk factors, without co-morbidities, they don't need to be hospitalised. Patients have to take an active role in their treatment and follow carefully an indication of healthcare authorities. We must perform PCR test, regardless of when the symptoms have started and, of course, at least twice. When the PCR test is negative, we need to consider testing from another respiratory-tract site.

But, in this moment, we can question the role of the bronchoscopy. The bronchoscopy has four indications. But, when it's possible, we need to avoid the bronchoscopy procedures and I think it's a paradox because, apparently, Madrid is the place where we perform more bronchoscopies in the world to the COVID patients. Only in my institution, we perform more than 500 bronchoscopies in the ICU for COVID patients. But in some situations, it's mandatory. Definitely, in the Journal of Thoracic Disease there's the indication of the bronchoscopy procedures in five steps. Emergent, urgent, acute, subacute and elective. This group permit to organise in their timing for a schedule. But I think, and I prefer the suggestion, the presentation, the stratification made by the American Association for Bronchology and IP. In patients with suspected or confirmed COVID infection, they separate in three groups. Emergent bronchoscopy, people with severe or moderate symptomatic tracheal or bronchial stenosis, airway obstruction, massive haemoptysis or a stent that's migrated. Urgent bronchoscopy, oncology indication, whole lung lavage and also foreign body aspiration.

Stratification Bronchoscopy Procedures

Emergent Bronchoscopy	Urgent Bronchoscopy	Non Urgent Bronchoscopy
Severe or moderate symptomatic Tracheal or Bronchial Stenosis	Lung mass suspicious for cancer	Mild tracheal or bronchial stenosis
Symptomatic central airway obstruction (endotracheal or endobronchial mass or mucus plug)	Mediastinal or hilar adenopathy suspicious for cancer	Clearance of mucus
Massive hemophysis	Whole long lavage	High suspicion of sarcoidosis with no immediate need to start therapy
Migrated stent	Foreign object aspiration	Chronic interstitial lung disease
	Mild to moderate hemoptysis	Detection of chronic infection (MAI)
	Suspected pulmonary infection in immunocompromised patients	Chronic cough
		Tracheobronchomalacia evaluation
		Bronchial thermoplasty
		Bronchoscopic lung volume reduction

Most of the procedures are performed in the ICU units with patient under medical ventilation. This is our situation in our hospital. We perform about 95% of the bronchoscopy in the ICU and only 5% in the bronchoscopy suite, at this moment, in the last six weeks.

For the diagnostic purposes, we've had three indications. First, when an alternative diagnosis is suspected. Second, in case of an infection. Three, in neoplastic scenarios. Generally lavage should be avoided in severe patients because it could it can be worse.

Weeks ago, this article appeared in Respirology (Colt H, April 11, 2020) is summarizing the recommendations for different medical associations about bronchoscopies, in this period of pandemia. I think we can consult the protect measures for the patients and the doctors, but in general, it's more about the personal protective equipment that we use.
Answering the question of where to place the COVID patients, we can see symptomatic positive patients, so they would be hospitalised of course, in isolation rooms. **Also, patients with a negative swab but high-clinical suspicions should be admitted like COVID, also in the same area**.

The treatment, you have no definite treatment. Also, supportive depends on the state of the infection, but there is no definitive therapy. Finally, about the antiviral therapy, if there are different therapeutic treatments, it depends on the hospitals. Or it depends, also, on the countries. But the only drug that we say is the antivirus. We must use it as soon as possible, in the early stages of this disease. That's all I have. Thank you very much.

Jing Li: Thank you for your talk. Very interesting cover from the pre-runs to the indication
the testings and the decision to certain kinds of patients in the hospitals and PCR testings. Also, your indications for the therapeutic and diagnosing, safety considerations of bronchoscopy in COVID-19 patients. Also, you mentioned some treatment and support of antivirus for COVID-19 patients. Very interesting talk.

Then, we go to the next one. Now, for Professor Lorenzo Corbetta.

Lorenzo Corbetta is an associate professor of respiratory disease in the University of Florence. He is also a Director of the educational programme in Interventional Pulmonology. Also, he is the Scientific and Website Director the European Association for Bronchology and Interventional Pulmonology. He is the National Regent of the Association of Bronchology and Interventional Pulmonology. He's going to give us a talk on the risks and benefits of aerosol-producing procedures in the area of COVID-19.

Lorenzo Corbetta: Thank you very much, Professor Li Jing. Good morning to everyone and good evening to our Chinese and Asiatic colleagues.

This is Florence, now the squares are completely empty under the lockdown.

After 4th of May, we will unlock, but only the manufacturing companies, but not the museums, churches and shops. They will be closed. So, the landscape will remain the same for the next month. Much of the information I will show comes from the statements of the main associations, mainly British Thoracic Society, American Academy, WHO, Chinese Statement- that was their first one. The most recent is the statement from the Society for Advanced Bronchoscopy and they are all posted in our website on the European Association of Bronchology and Interventional Pulmonology (EABIP) where there are other updated articles. The last one is also in Italian, the AIPO position paper.

But my presentation will follow the true story of our colleague, *MP from overseas, 50 years old, interventional pulmonologist like many of us, with no co-morbidities and he tells his story in a social network.*
For some reason, he went to work last Tuesday morning as

usual, he did what is considered a high-risk bronchoscopic procedure on a patient with lung cancer. This is considered a high-risk procedure, because the procedures generate aerosol.

But, we have to do it, because unfortunately cancer doesn't seem to care about a pandemic. It's very dangerous, this procedure, because it generates small particles, smaller than ten microns. The aerosol that reaches down lungs with the COVID-19 produces pneumonia and more. Not only bronchoscopy but also tracheotomy and aspiration, lung aspiration are very risky.

But, our colleague did the right thing because we know that we have to reduce the number of bronchoscopy, but as Flandes showed before, there are some emergent, urgent and acute diseases that require a bronchoscopy in few time and what is recommended by the Society for Advanced Bronchoscopy is within two weeks. So, he did a bronchoscopy for a patient that can't wait. And he told in his story that his hospital provided all the proper protection. What are the proper protection, appropriate protection?

They are recommended by the WHO since 19th March, that is a complete protection, like you can see in this picture of one of my colleagues. And in every aerosol generating procedures performed on COVID-19 patients, not only but also suspected, we must wear respirator N95 or FFP2 better, FFP3, gown, gloves, eye protection and apron.

And better, especially in some procedures, like bronchoscopy, Powered Air Purifying Respirators. Because they protect better and they are more comfortable because avoids breathing resistance, suffocation and moisture.

Powered Air purifying Respirators (PAPR)

A PAPR is a battery-powered blower that provides positive airflow through a filter, cartridge, or canister to a hood of face piece.

Advantages of using a PAPR kit during COVID-19 pandemic:

- Most of the PAPR kits **use HEPA filters** which give a greater level of respiratory protection than N95 masks.
- Extremely useful for doctors who are performing prolonged surgical procedures and health care workers posted in COVID19 isolation areas as it **avoids breathing resistance/suffocation and moisture** build up associated with using N95 mask along with goggles/face shield.
- Provides head and neck protection.

Approved for people with facial hair and it does not require fit testing because of a full hood.

But our patient, when arrived at home that evening didn't feel right and he had a fever and short of breath. So, he called the infectious disease colleague, who recommended to go to the ER.

He said goodbye to his wife and his daughter and this is a very sad situation because, in this situation, there are no visitors allowed and sometimes it's the last time that you can say goodbye to your family. This is very, very sad so, so being he a doctor, he cried all the way to the ER in his car. In ER, the shortness of breath got worse and he had a nasal swab for COVID-19, that was negative, he had a CT scan and was moved to the ICU because of the concern for possible quick decompensation that, in COVID, is very frequent. The infectious disease colleague considered some strange

"My hospital provided my staff and me with all the proper PPE, as they throughout"

Rational use of personal protective equipment (PPE) for coronavirus disease (COVID-19)
WHO Interim guidance
19 March 2020

Recommended personal PPE during the outbreak of COVID-19, according to the setting, personnel, and type of activity.

Setting	Target personnel or patients	Activity	Type of PPE or procedure
Health care facilities			
Inpatient facilities			
Patient room	Health care workers	Providing direct care to COVID-19 patients	Medical mask Gown Gloves Eye protection (goggles or face shield)
		Aerosol-generating procedures performed on COVID-19 patients	Respirator N95 or FFP2 standard or equivalent. Gown Gloves Eye protection Apron

infectious disease being swab negative, like, for example, malaria, brucellosis, leptospirosis and others, putting him in treatment with the doxycycline. He did another swab and that was negative again. But despite two negative tests, he remained in isolation as we know there are many false negative tests and the clinical situation was very suspected for COVID. The question is, is it COVID? What other test do we have to do?

We know that the swab is the primary and preferred method for diagnosis and we know that a bronchoscopy should have an extremely limited role in diagnosis of COVID-19 and only be considered in intubated patients and only for upper respiratory symptoms where negative and if other diagnosis considered that would significantly change clinical management.
But we know also, that it's more sensitive because this study demonstrated 93% of positivity versus 63% of the nasal or pharyngeal swabs 32%.

In this study, SARS-CoV-2 was detected in specimens from multiple sites of 205 patients with **COVID-19, with lower respiratory tract samples most often testing positive for the virus (93%)**.
The original article can be found here:
https://jamanetwork.com/journals/jama/fullarticle/2762997

And another study, demonstrated that endotracheal aspiration from the deep lung had demonstrated an higher viral load in every phase of the disease and persisted more than nasal swab. The link to the original article is: https://www.atsjournals.org/doi/10.1164/rccm.202003-0572LE.

For this reason, the guidelines said that, as Flandes showed before, although bronchoscopy has to be limited, it has potential diagnostic indications but the recommendations are very generic.

Additional testing patient with suspected COVID-19 is very, very generic after negative nasal swabs. This slide is in Italian but you can understand that in our hospital, we perform BAL for the diagnosis of COVID only after two negative swabs and indeterminate CT scan. If you have typical CT scan, also after two negative swabs, we consider the patient as positive. *And our patient, our colleague, fortunately he was feeling better after three days but because there is still a very rare possibility of having COVID-19, he had to be quarantined for two weeks.* He asked himself, do I have COVID-19? He doesn't know and we don't know, he maybe close to 50/50 and also, the antibody testing doesn't resolve the problem, doesn't answer it. And the problem is that he had no symptoms before the fever and he was at work with colleagues and patients. So, this is the story, now our colleague is better, this is the story of a colleague like us that performed bronchoscopies every day.

So, we have to consider this and the recommendation for performing bronchoscopy procedures during COVID-19 are now, for the moment, that bronchoscopy is not considered as a diagnostic modality for COVID because the primary preferred method is the nasopharyngeal, oropharyngeal swab and sputum analysis.

And we have to evaluate the need for bronchoscopy in every bronchoscopy that we perform. Better to perform bronchoscopy procedures under general anaesthesia and not awake or under conscious sedation in order to limit the dissemination of aerosols. For this, some tricks recommended by the Chinese Thoracic Society are to ensure that the patient wears a cap that also covers the eyes. Place a suction catheter in the patient's oral cavity, cover the patient's mouth with a surgical mask and if the patient is ventilated, use the access port to limit the production of circulation.
Precautions provided by the Chinese Thoracic Society for bronchoscopy to avoid aerosol spreading during bronchoscopy:

- Ensure the patient wears a cap that also covers the eyes, place a suction catheter in the patient's oral cavity and cover the patient's mouth with a surgical mask.
- Use the access port in the patient's mask/the mount during noninvasive/invasive mechanical ventilation.

See also:
https://www.ers-education.org/publications/european-respiratory-review.aspx

It's mandatory to use a disposable bronchoscope, especially in an ICU care setting and also to use a sampler that's easier to use.

Again, perform the bronchoscopy possibly in negative pressure isolation rooms, minimize the staff for bronchoscopic procedures and avoid training fellows, at least in this period. And personal protective equipment should be used and it's very important donning and doffing protocols, especially doffing protocols. Standard disinfection for all equipment and be careful during the rigid bronchoscopy and better to wear a Powered Air Purifying Respirator kit and be wise in choosing any bronchoscopy procedure.

Thank you very much for your attention and I hope to see you soon for the next webinars 19th May and 29th May, focused on diagnosis and treatment of COVID-19. Thank you very much.

Jing Li: Thank you Professor Corbetta for your very interesting story and come up to the introduction of the guideline for the bronchoscopy in COVID patients and also

your emphasis, the indication and also the strategy and safety procedure to perform bronchoscopy, thank you very much. And then, we come to the next speaker, Professor Mohammed Munavvar. Professor Mohammed Munavvar is a Consultant, Chest Physician, an Interventional Pulmonologist and works in the Lancashire Teaching Hospital. And he's also the Honorary Senior Lecturer in University of Manchester and also he's the President of British Thoracic Society, President of the European Association of Bronchology and Interventional Pulmonology. He's going to give us a talk with the topic of how the thoracic societies could lead the political position. Now Professor Munavvar, please.

Mohammed Munavvar: Wonderful, thank you so much Dr Li Jing, Dr Shiyue Li and the organising committee for inviting me to speak here today, it's an absolute delight, a pleasure, an honour to be here and interacting with so many friends and colleagues from around the world including Lorenzo, Javier, Felix. The title of my talk was slightly amended a couple of days ago by Lorenzo, so I'm showing you the up to date title and in my ten minutes that's been allocated, I'm going to give you a very brief introduction. Spend some time with regard to education, statement and guidelines, focus more on research and therapeutic trials and spend a minute concluding my presentation. That's the plan.

First of all, I do not have any conflict of interest with regard to this talk, my primary job is with the Lancashire Teaching Hospitals in Preston in the UK although I work with a number of other organisations, including BTS, EABIP. So, in the UK we've been hit very hard by COVID, as we've seen, colleagues in Italy, Spain, France, US and many other countries. As of yesterday, we've had 161,000 positive cases and very sadly we've lost more than 20,000 patients in the UK. The total number of cases has been going up although we are now seeing, fortunately, a slight flattening of the curve, thanks to the lockdown and various other measures.

As Javier mentioned, unfortunately, there have been a high percentage of infection amongst healthcare workers, one particular study from the Health Service Journal showed that more than 100 healthcare workers unfortunately passed away as a consequence of COVID. Our thoughts and prayers are indeed with each and every family that's been affected, not just the healthcare workers but around the country. So, moving to the next part of my talk on education, statement and guidelines, when this whole saga of COVID started, there was a great deal of confusion as to how we deal with this new disease. What do we do in specific situations related to COVID? And at British Thoracic Society, our main ethos is to work on high quality educational reviews, guidelines which can then be disseminated widely throughout the world, free of cost. And a whole machine of people, a whole team of people sprung into action and have produced, in a matter of about twenty days, what would have taken several months to create. That is a whole lot of statements and guidelines, trying to review literature and producing consensus statements and this is not just respiratory. We will see everything from oxygen use to Lorenzo and Javier spoke about bronchoscopy procedures, guidelines. Plural procedures, critical care, pulmonary rehabilitation, also Venous Thromboembolism in these patients, acute kidney injury in these patients, so unique problems that have arisen during this devastating pandemic.

So, all of this is available to you on the British Thoracic Society website, free of cost and besides all these collaborative work, we have also worked with NICE, National Institute of Clinical Excellence, NHSE, Royal College of Physicians and a host of other organisations to produce collaborative documents, guidelines to assist people at the frontline to be able to provide the bets possible care for these patients. There's a whole team and I'm enormously grateful to every member of BTS who has contributed, including the BTS board, the council, the specialist advisory groups, some renowned professors like Wei Shen Lim in Nottingham, the team behind BTS and the headquarters. All of them have worked 24/7 and remember that many of these respiratory physicians and the BTS, also are working day-to-day in the COVID wards, they are at the frontline providing care to these patients. A very simple statement which was produced, which is unique, I wish to highlight, and this is the brainchild of our chair of BTS, Professor John Bennett from Glenfield Hospital, Leicester and this is called SPACES.

This is totally unique, where a simple concept, sharing patient assessments cuts exposure to staff. Javier highlighted the 20% incidence of infection of our healthcare workers and this very simple principle that John initiated, where any healthcare worker, irrespective of their grade, attending to a patient suspected or proven COVID would then check everything that there needs to be checked rather than duplicating assessments and also, looking at possibility of remote consultations, phones, iPads, two way radios, intercoms etc.

So, this is, I think made an enormous difference and has been disseminated throughout the world. Education and guidance is at the top of what we do at BTS and you will see, only a couple of days ago, our Deputy Chief Executive, Sally Welham, informed me that over 200,000 documents have been downloaded from the BTS website, over 100,000 page views of COVID-19 guidance and a lot more. So, please do visit our website and make use of the documents that people have put together with so much effort. Okay, so moving to the second major part of my talk, third rather, is I'm going to focus on research and therapeutic trials.

If you type in COVID-19 studies on the database, on the WHO database you will see that there are about 915 studies and increasing every day, going on throughout the world, scientific studies. And if you type in on PubMed reference, there are more than 7,000 manuscripts that have already been written. However, there needs to be a coordinated effort to get robust evidence, systematic studies with systematic literature. The UK government pumped in millions of pounds, inviting applications for grants a couple of months ago, and as a consequence, a number of studies have been started in the UK, more than twenty major studies. Simple ones like PRINCIPLE, which is in primary care, the use of

hydroxychloroquine to reduce hospitalisation and eventually expedite recovery, to vaccine development.

You might have heard, vaccine development is the flavour of the month and last week, a couple of volunteers have already been injected with a new trial coronavirus vaccine at Oxford. We await the results with excitement, although unfortunately that's going to take quite a few months before we see any result. A number of other areas are also being tested, such as plasma transfusions in COVID and a huge number of other studies which are taking place, besides vaccine development, therapeutic trials, prophylaxis among healthcare workers, a very adaptive platform of REMAP CAP trial in intensive care. RECOVERY, which I hope will be a landmarkstudy and I'll come to that in a minute. Therapy development, antibody testing, population surveillance, behaviour and policy research, virology, transmission and mathematical modelling and a lot more. I just want to spend a few minutes describing the recovery trial, this is a randomised evaluation of COVID-19 therapy, initiated from Oxford, this is the chief investigator, Professor Peter Horby, we must congratulate this team for coming up with this idea. And this is, again, a very adaptive trial because they started off looking at people, patients who were eighteen years of age who are admitted to hospital, proven or suspected SARS-CoV-2 infection and divided them and separated them, randomised them in a two is to one is to one is to one fashion.

No additional treatment, just standard supportive therapy. Lopinavir-ritonavir, which is, as we know an anti HIV drug. Low dose Dexamethasone steroid. Hydroxychloroquine. Subsequently Azithromycin was added.

The idea, the outcome was primary outcome of 28 days of all-cause death, secondary outcome of duration of hospitalisation, need for ventilation and need for renal replacement therapy. As the recruitment has progressed, I was pleased to hear that more than 7,500 patients have been recruited. Under normal circumstances in any other study, this would be a huge number and would be called a success, yes it is a success, but because, if you look at the fact that we have multiple arms in this study, we need (TC 01.20.00) many more thousand patients and these studies taking place in multiple centres across the UK. Congratulations to every single site who are actively recruiting, including ours, there's a lot more to do, many more thousand patients need to be recruited before we can draw meaningful conclusions. Recently, a second randomisation has been added to the study wherein, if the patient becomes hypoxic or deteriorates with regard to inflammatory markers, despite the first randomisation and treatment, the assumption is that you might be heading towards a cytokine storm and therefore an anti-IL6 inhibitor, such as tocilizumab has been introduced.

Again, as a randomised fashion, randomisation with control, for each of these arms. The outcomes will be mortality at 38 days and need for ventilation. As I mentioned earlier, that is going to be a massive trial and I think will hopefully be a game changer in the field of COVID treatment. I just want to briefly mention my own hospital's involvement. There's a very dynamic research team, clinical research facility who have been working round the clock with a number of studies, and this number is going up every day. More than 400 patients have been recruited. A number of local studies also being planned including immunity levels and antibody testing among healthcare workers, RECOVERY trial is certainly up and running in our hospital at the Preston Lancashire Teaching Hospital. I'm very grateful to each and every person at Lancashire Teaching Hospital research department who are involved with this.

So, in conclusion, what is the future plan with COVID? We spoke about another wave, pandemic, flattening of the curve, further low incidence with waves, are we looking at number of waves? Or are we moving to an endemic phase? We have all got to be vigilant and do not take the foot off the pedal. We will also have to restructure, adapt, reorganise services, both in the hospital and primary care.

We'll have to progressively, we've already started this, progressively move to digital healthcare, telehealth, minimise face to face consultation, everybody coming to the hospital or any interaction will need to be tested, screened, isolated prior to any intervention as Lorenzo and Javier have eluded to. Maybe we need novel, quicker methods for assessment, including non-invasive methods, speedy, accurate tests, effective tests, even therapy will need to be planned on a remote basis. Virtual Pulmonary Rehabilitation has been started. But research is going to be pivotal to our success in the war against this condition. Vaccines, without a doubt, but what about prophylaxis for these patients? What about effective therapy? I've mentioned one trial but there may be similar trials around the world that will help. But more than ever before, we need to have a truly collaborative approach across borders, across countries and continents and fight in a collective, consistent fashion because the reality is, nobody is safe until everyone is safe, with regards to this condition. We need to make the dream come true to overcome COVID. Many thanks indeed for your very kind attention. Take care, stay safe, stay well, god bless you, hope to meet you again.

Jing Li: Thank you Professor Munavvar, very sophisticated talk on the introduce the strategy of the treatment and prevention and future challenge that we face. Also you introduced a very nice clinical trial and research carrying on now in the UK, very, very nice talk. Yes, maybe we need to discuss the topic later and very impressed with your statement that no one is safe until everyone is safe. Yes, very nice.

Okay, now we move on to the next one, Professor Li Qiang, he's the Director of Respiratory department and chief physician. Professor, doctoral supervisor and he's also Director of World Association for Bronchology and Interventional Pulmonology and he's a Member of Chinese Thoracic Society and also the Deputy Director of Interventional Pulmonology Group of Chinese Thoracic Society and also the Standing Committee of Committee of Minimally Invasive Therapy in Oncology, okay? And he's going to give us the talk with the topic of application of mesenchymal stem cells in the treatment of severe COVID-19 patients.

Now, please Professor Li.

Qiang Li: Okay, thank you the Professor Li Jing and many of the old friends, the Professor Herth and Professor Corbetta and Professor Guo and Professor Shiyue how are you? Today, I would introduce my recent research for the use of stem cell, it's the element that would treat the COVID-19. Now, I want to invite my colleague, Dr Wang Na to introduce that.

Na Wang: Right, it is my great honour to have this opportunity, give us all the lecture about the mesenchymalstem- cell therapy for COVID-19 pneumonia and first I would like to introduce our hospital first.

The Shanghai East Hospital is located in the Lujiazui Pudong New Area, which is very developed nowadays and we have two major campus, one is Lujiazui and the other one is World Expo in campus of our hospital and we are very welcoming for all of our friends including all of the professors today, coming to our hospital and sharing, and exchange different thoughts and experience based on both pulmonology as well as critical care medicine. So, today we're going to take about viral sepsis and ARDS secondary COVID-19 cases and also we would like to talk about the current situation of Mesenchymal Stem Cell Therapy in terms of the COVID-19 disease. And also, we would like to share some of our own experience in the treatment of Mesenchymal Stem Cell.

First I would like to share two of the studies which was run by Professor Bin Cao from China, these two articles were published in March, they shared the data about the risk factors and also some epidemic characteristics, based on the large patient population. The data showed that around 15.7% patients would develop to severe cases and among them, the mortality was over 50% among the patients.

And also, several risk factors associated with ARDS, including elder age, over 65 and higher fevers, and also on the risk of factors (inaudible 01.29.54) associated with that score and the higher level of D-dimer. So, and also, this is another article shared (TC 01.30.00) about the complication of COVID-19 as we saw that sepsis is one of the most common complications and the second one would be the respiratory failure and ARDS. And followed by heart failure and septic shock, also including coagulopathy. This slide shows the time course about the COVID-19 disease's evolution. We saw that, on average, day nine and ten, people can develop sepsis and after one or two days, the ARDS would come out. So, we found, the data showed that the ARDS always happened after the sepsis onset, so we think about them. Maybe this ARDS was secondary to the sepsis, and also, as shown in the lower chart, among the known survivors, we saw that after the sepsis and ARDS onset, there were several secondary organ dysfunctions including kidney and cardiac injury, secondary infection, as well as even death. And in terms of the current management strategies, we have several medications talked about a lot, including Remidesivir, hydrochloroquine or arbidols but actually, on all these medications are showed a limited get us support in the treatment aspect.

And also, for the corticosteroids, which is recommended in our Chinese guidelines with a low dosage within the short term usage to suppress the inflammatory reaction, and there were several traditional medicine. And beside the medications we have several respiratory support, including oxygen therapy, high flow and NPPV and mechanical ventilation and ECMO. But actually, there were no very promising treatments, so we were thinking about, how can we modulate the viral sepsis to prevent the disease progress of COVID-19? We came up with an idea about the Mesenchymal Stem Cell Therapy so, I would like to talk about it. Current teams in China, we have four teams, the biggest, which is led by Professor Wang Fusheng from PLA Medical Center. And the second is led by Professor Zhou Qi from Harbin Medical University and also, Zhao Chunhau Professor from Shanghai University. And the fourth one is our team, headed by Professor Liu Shongmin and Li Qiang. This is a review article about Mesenchymal Stem Cell, talking about how it works in the COVID-19 treatment. MSC could release cytokines and have some immunomodulatory effect, it can suppress the inflammation reaction and stimulate the recovery process at the same time. As a result, it could protect the alveoli epithelial cells, reclaim the pulmonary microenvironment and can prevent the pulmonary fibrosis as well as cure the lung dysfunction.

This is a recently published article from Zhao Chunhau's team on the agent and the disease. They talk about the transplantation of ACE2-negative Mesenchymal Stem Cell. They enrolled ten patients in total and three of them were assigned to the control group and the seven of them were assigned in the treatment group and the result showed that, this is the mass cytometry profile about them, plus more cell properties. We can see that, let's say, the right figure, this is we're seeing in normal people. Different part of the cells were marked as different colour and labelled as different numbers. This is from the normal people, and the left two figures were COVID-19 infected patients. Before the treatment of stem cells, we found that several clusters of cells, such as CD4 and CD8 T cell and K cell and endocentric cells, which were marked as purple, blue and brown, were overreacted in our blood. Then after the stem cell therapy, all these overreacted immune cells subsided and the other part of the normal cells increased after the treatment. As we can see, the different colours shown in the left figure. And for the immune cytokine levels, we saw that for the some anti-inflammatory cytokines, including IL-10, VEGF and IP-10, which were increased after the stem cell treatment and for TNF alpha, which is known as the pro inflammatory cytokine, was decreased after the treatment.

Now, we think about, how is the safety and efficiency of Mesenchymal Stem Cell Therapy in the treatment of severe COVID-19 patients? So, we came at this idea and started all the preparation process in early February, including study design, cooperation, IRB approvement, sort of, like this. But actually, due to the limited patient population in Shanghai, we actually have less than 300 patients in total in Shanghai, we don't think that's sufficient for us to recruit in this study, so we decided to move to Wuhan and are recruiting patients there. So, we left Shanghai and headed to Wuhan or March 5th. I

would like to show you several photos of our team and this is Professor Li and this is Professor Li, this is our whole team, we have eight physicians together, including pulmonary department and radiology department as well as pharmacology department. But initially, after we arrived at Wuhan, there were several issues that we've met, first, most of the critical patients, they have already lived through the acute inflammatory and the cytokine storm stage and most of the patients are already in the recovery process of the disease. And also, a lot of patients present as different severity of pulmonary fibrosis which present as dyspnea and decreased exercise capacity, clinically.

Here are some CT scan features shown up on our patients, we can see there was a predominant pulmonary fibrosis, noticed in the recovery process. Then we were thinking that, how can the Mesenchymal Stem Cell help with the recovery process? This is also a review article that showed that MSC may have many therapeutic effects on the fibrosis, based on the different mechanism, including immunomodulation and decreased inflammatory reaction and anti-apoptosis and scarring effect. On the other hand, it can stimulate angiogenesis and chemotaxis, which are pretty critical in the tissue recovery progress. So, we made our protocols, we decided to give the umbilical cord Mesenchymal Stem Cell on day zero, day five and day ten, for three times in total, with a dosage of one times six power of ten per kilogram and through the IV line within one to two hours.

Before the infusion of the cells, we used a Promethazine for prophylaxis of the allergic reaction and the follow up date will be day fifteen, 30, 60 and 90. And we would like to observe several parameters including the PEF ration, inflammation status, CT chest or CT evolution and also symptom improvements which was measured by the mMRC score and the fatigue score.

For the safety aspect, we collected if there were any adverse effect onset, how's the liver enzyme level, as well as a creanine level as for the kidney function and the D gamma level for coagulation function. We start our first case enrolled on March 5th, in the first week we have ten patients in total from Wuhan Sixth Hospital and from the second week we have 36 patients in total from Wuhan Taikang Tongji Hospital. And after almost 30 days, on March 30th, we moved back to Shanghai. Here are several photos during our study process, this is the moment we were enrolling our applicants based on the criteria of selection and execution. And this is the moment Professor Li and the faculty of the hospital, they were talking about the protocols as IRB discussions with the hospital. And this is the moment before we go into the critical care unit and the quarantine ward to give the patients the stem cells. This is our stem cell, and this is the moment we were rounding with the patients. So, for the baseline characteristics of our patients, we have nine patients assigned in the control group and eleven patients had only one infusion of stem cells, and ten patients had two times and sixteen patients have three times together.

And for the parameters including gender, age, allergic history, surgery history as well as medication history, there were no differences noticed among these groups. Next we, about the results, first we analyzed the safety about the MSC treatment, there was no significant differences between the control and experimental group, along with the time course, including D-Dimer, creanine level, AST and ALT level which means that there was no significant change in the liver, kidney function as well as the coagulation. And as for the inflammation status, we compared the CRP level between these two groups and also, we didn't notice any differences. Next, we collected the mMRC score and the fatigue score according to different symptoms and signs of our patients, we can see that, along with the time course, all these Q scores were decreased but no differences was noticed between these two groups. We also compared the PF ratio to assess the oxygenation function of our patients, the data showed that, compared with the control group, the PF ratio was significantly improved seven days after the treatment of MSC. The P value was less than 0.05. We also compared the lymphocytes and the neutrophil levels before and after the stem cell treatment and also, we didn't find any significant differences between these two groups.

As for the CT scan features, we used a CT score calculation which was published earlier for the assessment of COVID-19 severity, compared with the control group, the CT score was significantly improved seven days after the treatment and P value was less than 0.05. Here I would like to show you several of the CT scans, this is one of our patients in our team, we've had the CT follow up on March 13th, 22nd and 27th, we saw that there's significant improvement on pulmonary fibrosis. So, for our conclusions, we firstly found that MSC therapy had a greater safety, including liver function, renal function and the coagulation change and we found that MSC (mesenchymal stem cells) therapy might have the therapeutic effect for severe COVID-19 patients, based on the improvement of PF (PaO_2/FiO_2) ratio as well as the CT (Computed Tomography) scan evolution. But there were also several limitations of our study, first, most of our patients were under the recovery process in pulmonary fibrosis, the change of the inflammation stage was a lack of our study. And second, we just had a very short term follow up, as long as less than 30 days. We still need the more long term data to have a better conclusion of our MSC therapy.

So, the highlight of our speech today, there are several studies that show MSC might have the potential role in the modulation of inflammation during the acute stage of COVID-19. There were several academic clinical trials running in China and though our study mainly focused on the anti-fibrous effect of MSC in COVID-19.

And there were very limited data that showed the relative promising results of MSC, in terms of the inhibition of inflammation, improvement on both clinical symptoms and the CT features but we do need a long term follow up and analysis to have a comprehensive conclusion of MSC therapy. So, this is pretty much our lecture today. Thank you for all your listening.

Jing Li: Thank you very much for your very clear introduction of your clinical trial as I can say, of the application of the Mesenchymal Stem Cells in the treatment

of severe COVID-19 patients and the design and the location of the patients, and the observation of efficacy and the safety of this kind of treatment. We look forward for your further, comprehensive results.

Now, we've finished with all the talks and then we come to the discussion and I would like to invite Professor Corbetta and to join me to chair the discussion.

Lorenzo Corbetta: Yes, thank you, unfortunately we have no time, because our connection lasts until 2:30PM. We have a lot of questions but we can answer all of one or two questions. The other will be posted on the website, we and answer in the next video conferences. One question that is repeated, I share with you, is if the temperature and the hot season will change the viral answer of the COVID. If you have experience in China where you had these changes of climate? Shiyue Li or Professor Guo?

Shuliang Guo: I will try. I will try. This is a question for America this morning, for California, and in my opinion, there is no proven evidence to support the temperature effect on the COVID and these worries. In a research from Hong Kong University, they are comparing the temperatures, different temperature and humidity effect on the various symptoms. They found when the temperature reach to 68 degrees, the virus will be active less for than five minutes. However, when the temperature is between 22 to 25 degrees, with humidity of 40% to 60%, the virus will survive longer than 14 days. But this is research involved with SARS but not SARS-CoV-2 and another research from Hong Kong University is they're using temperature up to 70 degrees and the virus has been killed quickly. We need more evidence, maybe after this summer we can get some answers and we need more laboratory simulation to make sure. And for clinical practice, as we know, the patient, the confirmed patient in the southern hemisphere is smaller than those in the northern hemisphere, for example, the patients in Australia, Indonesia and New Zealand is reported as only around 10,000 per country so maybe a large indicator shows the higher temperature has slowed down the transmission of the virus. However, this data should be due to the, maybe, the poor testing conditions. So, we need more data to make clear, okay, thank you.

Lorenzo Corbetta: Okay, we have hundreds of questions and I ask you to answer to them in the next time, the next days I can send you and we will post on the website so we can give the answer to our connections.
So, I invite you, all of you, and the other people to the next video conference on diagnostic tools for the screening and diagnosis of COVID that will be happening on 19th May and the other on treatment for intensive care and pharmacology treatment and clinical management on 29th May. I thank all of you and I hope to see you soon in the next video conferences, thank you very much.