



Wellcome Trust COBIT 19 Conference Call

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Participants

Nick Moakes – Chief Investment Officer

Jeremy Farrar – Role

Operator: Hello and welcome to the Wellcome Trust COBIT 19 conference call. My name is Monique and I'll be your coordinator for today's event. Please note this conference is being recorded and for the duration of the call your lines will be on listen-only. However, you will have the opportunity to ask questions throughout the call. This can be done by pressing star one on your telephone keypad to register your question. If you require assistance at any point, please press star zero and you'll be connected to an operator. I will now hand you over to your host, Nick Moakes to begin today's conference. Thank you.

Nick Moakes: Thank you very much indeed and welcome to everybody. Good afternoon for those of you on this side of the Atlantic. Good morning for those of you in the States. This is the second of these calls that we've done. The first one, many of you will have heard at the end of January. Given recent developments, we thought it would be helpful to reach out to our embassy network once again and give you another briefing. So, this will be delivered by our director, Professor Jeremy Farrar. Jeremy, as many of you will know, is a world expert in infectious tropical diseases. He was based in Vietnam for many years where he ran the Oxford University clinical research unit. He was responsible for research and response to the outbreaks of Swine flu of bird flu of SARS, and since being at Wellcome has been closely involved with the response to Ebola. So, with that, I'm going to pass it over to Jeremy. Jeremy?

Jeremy Farrar: Thanks so much, Nick, and welcome to everybody. As Nick said, thank you very much for all you do for what we do. What you do allows us to do what we can do. So, thank you very much for the partnership with Wellcome on all of these methods. What I'll do is I'll start with about 10 or 12 minutes of an update. Much of this I suspect you'll know from reading the newspapers and other media, but some of it you may not. I'll divide it also, and I think it should be clear when I'm sharing what are essentially facts, what are essentially modeling and estimates, particularly for the future, and then what a personal view. And I hope it's always clear which of those three it is. But if there's any doubt, then just ask me. Some of you have sent in some questions, which I'll answer specifically after the 10 or 12 minutes and then we'll open it up for any questions. Hope that is okay.

So, where are we? We can assume that this epidemic started at the beginning of December and the epicenter clearly is in Wuhan in China. The virus came across from an animal reservoir. Certainly, bats were involved, but bats were not the intermediate hosts between the animal world and humans, but essentially, although it is important for us to work out and it's a piece of tremendous work, a big work that we are doing to try own work out that animal source. In essence, this is now just a human infection and we should treat it as such. The infection coming

across from humans is beautifully adapted to the human population such that it transmits very beautifully between one person and another. That's known as the infectiousness of this virus.

And to give you a sort of quantification of that, if I had the infection today, I would pass it on to approximately three other people. That doesn't sound a very big number until you think that those three pass it onto three others and those people pass it on to three others. So, this is put together in something called the Arnot and to, again, give you some sort of context of that, influenza has an Arnot of about 1.4, 1.5. So, this is double that and the 1.4 to 1.5 to three is not a linear relationship, it's a much steeper curve as you go up the Arnot quantification. Wuhan is probably at the very peak at the moment or just coming off the peak of the epidemic, and that is to be celebrated of course, but that has taken extraordinary measures in Wuhan itself.

The city of 11 million people as essentially being in lockdown. As you know, all workplaces have essentially been closed, schools have been closed and most people have actually been quarantined voluntary or otherwise in their houses and apartments. And so, the draconian public health measures that China has been able to implement in Wuhan have undoubtedly reduced the peak of the epidemic and the epidemic in Wuhan in fact probably is coming off the peak now and down the other side of that epidemic curve. It's totally unclear what happens when China and the authorities in Wuhan inevitably have to loosen those restrictions. Clearly the whole population of Wuhan has not been infected and I would be very cautious about whether in fact when those restrictions are lifted, whether Wuhan didn't actually then go on to see a second or subsequent wave of this epidemic.

The other cities in China have not instituted yet the same draconian measures as the Hubei province has, but nevertheless, they are all going through some sort of epidemic curve. And it's very difficult to interpret the data coming out from China at the moment. The testing has not been able to keep up with the number of cases and inevitably there's been some chaotic scenes. There's been limited access to diagnostic testing and inevitably there's been some degree of political overlay on top of the testing and the results. So, the figures of confirmed case in China at the moment are about 80,000, modeling estimates would suggest that's an underestimate probably by almost an order of magnitude across the country of China at the moment. And some of that data inevitably comes now from outside China, and there are countries as mostly you would have predicted from flow of travel, from Wuhan and from China itself, are increasingly being infected. Singapore, Korea, Japan, you'll have followed all of those.

But I want to focus a little bit perhaps on two others, which are slightly surprising, but I think which gives us a sort of in some ways greater insight into where this epidemic is going. Iran, which does not have extensive links with China, has probably certainly had 15 deaths and maybe significantly more than that. And if you just think about that for a minute, it takes about two to three weeks to die after being infected with this virus. So, the 15 deaths that you see in Iran were infected probably two to three weeks ago. If you assume that one person in 100 dies of this infection, the case fatality rate of 1%, then three weeks ago there were approximately 15 times 100 people infected in Iran. The doubling time in any situation that we've seen is about seven days. So, in three weeks, you can do the sums better than I can, that's 1,500, 3,000. There may be 6,000 people infected in Iran today as an estimate of the total population burden. Probably significantly more than that.

Similarly, with Italy, Italy has seven deaths now. Those individuals would have been affected about three weeks ago. So therefore, there would have been about 700 cases three weeks ago,

700 doubles, 15, 1,400, now 2,800, now 5,600. So, you can probably assume that in Italy, and this is now modeling and personal view, that there's probably between five or 6,000 infected individuals in Northern Italy as of today. The measures that would be imposed in China are obviously specific to the social context of China and it actually is very difficult to imagine that other jurisdictions with other societal pressures would be able to impose the same sorts of public health restrictions that China has been able to do. And there is no doubt that those restrictions in China have led to a blunting of the epidemic curve and has certainly bought time for the rest of the world to prepare.

So, I've talked about the Arnot, I think it's still coalescing around where I predicted a week or two ago for those who are on the call of three, a case fatality rate of somewhere between 0.5 and 1% and an attack rate, and this is the denominator and this is perhaps the more important figure in a way, an attack rate which would suggest somewhere between 25 and 40% of our population would get infected. Again, to put that into context, in 2009 of the pandemics of H1N1 swine flu, as Nick suggested and talked about earlier, 16% of the world's population there were infected. And I think we can assume that that would be close to double that.

The other challenge of this infection as well as it being very infectious between one person and another is that you are infectious very early after getting infected. So, if I was infected last night, by this morning, I would maybe not have symptoms or if so, very mild, sore throat, cough, probably no fever at that stage, but I may be very infectious even 12 to 24 hours after gaining that infection. And I would remain infectious probably for up to 10 to 14 days through mild, moderate, and even when I became severe. As you can imagine, that's very well, that's very different to SARS, which is why I think although there are obvious analogies to SARS. It's a similar virus and it started in China. I don't think other public health or economic modeling that suggests this will follow the SARS epidemic bears any scientific scrutiny. SARS lasted nine months and infected 8,000 people. With this infection, we got to 8,000 people probably in about two and a half to three weeks after it emerged. So, you're dealing with a totally different epidemic curve and a totally different challenge to the public health systems.

We'd been working very hard on modeling that data, much of which I've just shared, but I can go into more details if anybody is interested, but also in ensuring that there are diagnostic tests, that there are drugs. We've been very involved in the two I think most robust clinical trials that are going on in China at the moment and we've supported the development of eight vaccines now, which are all now in development. But on the vaccine side, just to absolutely be transparent and honest with everybody, the first patient, the first volunteer will be dosed with the vaccine in the first week of March. That's a remarkable achievement to achieve that within six weeks of starting. But there won't be a vaccine of public health use during 2020. So, during 2020, we will be dependent on public health measures, non-pharmacological interventions, washing hands, potentially wearing masks.

And it won't be at least until 2021 until we have a vaccine that we can use as a public health measure. And that will assume good luck and good fortune all along the way. Just to again, underline the fact we've been trying to make a vaccine for SARS for 15 years, for Murs for seven years, and the common cold for about 50. And we've failed in each of those so far. So, although I'm more optimistic that science can deliver a vaccine now that it's not going to impact in 2020 on the public health outcomes of this. So, I think the way I frame this is an incredibly challenging, certainly something that I've not witnessed in my career, public health challenge

to the world. But I think we have to also now consider the broader societal implications of this. And there will be broader societal implications, particularly economic, logistics, supply chains and the rest. And China is now 17% of world GDP, as you know better than I do. But also, I think we're going to see increasing political tensions rise, particularly as we go into an election year in the United States. And there will inevitably be tensions that rise as part of the existing tensions that are dominating trade talks and other things. And I think all those three health economics and politics will increasingly come to bear on this epidemic as we go forward.

So perhaps pause there. Some have sent in some questions, which I can I think fairly quickly address and then we'll open it up to everybody else. First question is to what extent warmer weather will reduce our whole spread of the virus and when will this happen, and does it vary by country? It's a great question. The honest answer is we don't know. Many of these respiratory infections, influenza, the common cold are seasonal and they tend to have their biggest impact during the winter seasons in the Northern and Southern hemisphere with a very eclectic spread during, in the tropical areas where, which seemed to have annual epidemics of this rather than any seasonality. I wouldn't bet on this being seasonal. The virus does persist on surfaces for many days. It doesn't disappear in the cold weather. And actually, with China is indeed warming up at the moment. So, I don't think we can assume this will be seasonal.

Another question is, are there any symptoms, are there any other symptoms than fever, shortness of breath and cough? The only other two I would add would be sore throat and the general sense of tiredness and essentially, it's not distinguishable from normal flu. The incubation period is somewhere between, this is the period after you get infected until you start to have symptoms, probably the median guess of that is seven days, but the range is somewhere between one and 14 days and you seem to be infectious throughout that period, which is making control so very difficult. There are no privately available tests that you can purchase at the moment, although obviously many companies are trying to develop a rapid test that you could use and, but there is not one available today, which is the recommended mask. And 95 is good enough for this. If you want to purchase, if you can mask and 95 would be the one people would advise. The role of masks in preventing infection also is unknown. And there is some evidence that actually is they get wet, they increase transmission by increasing the droplets.

Any countries you'd be particularly worried about yet that is not yet announced? India with a population of 1.2 billion seems slightly odd, but it's only had three infections. I find that difficult to believe, but I think you can probably assume that this is essentially everywhere now. There's nothing special about Iran in terms of its connection to China. There's nothing special about Northern Italy and its connections. They don't have higher volumes of flow of people from infected areas. So, I think we can sort of assume now that if it's not there today, within the coming days and in the next couple of weeks it will be essentially in every country. And each country will go through its own epidemic curve. And that curve will be determined by a number of things, population density, but mostly by what the public health authorities are capable of doing in terms of restricting social distancing and other things as demonstrated in Wuhan. So, I think that answers all of the obvious questions we've come to that have come to us. So perhaps, Nick, open it up to any questions people want to ask.

Nick Moakes: Thanks, Jeremy. Just before I hand it back to Monique on the conference side, just to remind people that this is under Chatham house rules. So, you're very welcome to use

what you hear, but please don't attribute it. So, with that, we'll open up the floor to questions and I'll hand you back to your operator.

Operator: As a reminder, if you'd like to ask a question or make a contribution on today's call, please press star one on your telephone keypad. Please ensure your line remains un-muted locally. I will then speak to you individually, take your full name and introduce you to the call. Again, as a reminder, if you'd like to ask a question, please press star one on your telephone keypad now. We have questions submitted in the queue. Please stand by while I gather the first caller's details. Okay. All right, so we have our first question. Are you ready?

Nick Moakes: Yup.

Operator: All right, perfect. Our first question comes from the line of Byron Ween. Byron, go ahead with your question.

Speaker: Yes. There are a number of vaccines and pills that are being talked about. One from Gilead, one from Moderna. Are we anywhere near an antidote to Coronavirus or is that still a long way away?

Jeremy Farrar: Yeah, so deal with both of those separately. The Gilead is remdesivir, which we've been very involved with the doctors in Wuhan conducting a randomized controlled trial actually against placebo. They've done a remarkable job anticipated that recruitment for that would go on until April or May. In fact, they've recruited patients far faster. So, I think we have 450 or 500 patients now randomized and we would anticipate seeing a result of that within the next few weeks. On the Moderna, Moderna, again, we've been working very closely with Sepi and with the national institutes of health in United States, they will be the first vaccine into human trials in the first week of March as a preventative vaccine.

So, both Gilead and Moderna have been absolutely at the forefront. And then following on from that is all of the usual pharmacological pharma companies and ourselves through Sepi on the vaccines and also on the therapeutics. In China at the moment there are about 70 clinical trials going on. Some of them don't make much sense scientifically and some of them do make sense. And I would hope we would have a result of that within the next, some of those, within the next month. There is no specific therapy available today that we know treats this infection or, and there is no vaccine that prevents it.

Speaker: Thank you.

Nick Moakes: Yeah. The next question please.

Operator: Our next question comes from the line of Robert Nelson. Robert, go ahead with your question.

Robert Nelson: Hi Jeremy. I was just wondering what you think about the dangers of enhancement or, and how would you design these trials and what do you think the potential risks are there?

Jeremy Farrar: Thanks. So, what is getting out there is there are some infections. They're relatively red, just happens to be one. I've spent much of my career working on, which is Denki where we're infect after one infection, you're more exposed to more severe disease later. That's something called enhancements and where vaccines have been known in the last five years to increase the risk of severe disease for some people. So, it is a real worry of. The data on

enhancement per Coronaviruses does only come from animal models. There's been no evidence of that in any vaccine trials for SARS or indeed for Mers. And so, whilst I think it's absolutely right to be cautious of it on the vaccine side, not the therapeutic side, I would worry less. It's got to be looked at, but I would worry much less than I would for Denby and other infections. The animal model that it comes from, that it's not a particularly good model and we've seen no evidence in the preclinical studies to date of any enhancement.

Robert Nelson: Okay. Thanks.

Operator: Our next question comes from the line of Sicilia [inaudible]. Sicilia, go ahead with your question.

Speaker: Thank you. Hi Jeremy. I was just wondering if you have any information about why the CDC isn't testing more people in the US? I've heard of cases in San Francisco where there are symptomatic patients who are being told they cannot be tested unless they've had a direct presence or contact in China.

Jeremy Farrar: Tricky one. As you know as well, CDC, as everybody has done, it's not just CDC, has struggled a little bit with the diagnostic testing, struggled in two ways. One is to make sure it's sensitive and specific and secondly that they can produce it at the scale that is required given particularly in the United States just how many people do have direct contact to China. The links to China in many parts of the world now is becoming obviously less relevant than it was even two or three weeks ago. And in many parts of the United States, as in Northern in Western Europe at the moment, obviously you're also going through your influenza season. And so, both CDC and the United States and public health England here and European CDC have been very reluctant to go out and test everybody because there just has not been the capacity of diagnostic testing to be done for that.

I think that will change. In fact, I think it's changed already. Access to those tests has become more available. Their sensitivity and specificity are increased and I think, well I know, that the United States are planning to very significantly increase the amount of testing they're doing in critical care facilities, in care homes and in other settings where respiratory infections are going to be very common. The UK has also just announced it's going to ramp up the testing it's doing.

Speaker: Thank you.

Operator: Our next question comes from the line of Kevin Berry. Kevin, go ahead with your question.

Speaker: Yeah, thanks for taking my question, Jeremy. Is it surprising to you at all that no cases have been reported in Mexico or South America, for example?

Jeremy Farrar: Yeah, I mean, absolutely. I mean, I think if this is not now present in every country, it's in Afghanistan. If it's in Afghanistan, it's very difficult to imagine it's not in Mexico. So, I think we will be moving, we are moving into a new phase. I think that's obvious from everybody's questions, but also reading the media we're entering a new phase where we are seeing this in essentially every continent and increasingly in every country. The big question, and I think it sometimes people are getting stuck on this, whether this is an epidemic or a pandemic. I mean there is a subtle difference between the two, but I think it's largely semantic.

I mean, you're talking about a pandemic really just meaning there is sustained community transmission in multiple continents.

Are you there yet or not is a judgment call. It's not making a slightest bit of difference to what we do at Wellcome, whether somebody calls it an epidemic or pandemic, our assumption is this is now in every continent and will continue to spread in every country. And will come to an end at some point, but we will see epidemic curves, whilst we hope not like Wuhan, we will see increasing number of cases over the coming days and weeks in essentially every jurisdiction.

Operator: Our next question comes from the line of Alex Torrance. Alex, go ahead with your question.

Speaker: Hi, Jeremy. Thank you for making the time for the call. A couple of questions for me please. So firstly, you mentioned a critical care rate for those infected last time of around 20%. any update on that?

Jeremy Farrar: Yeah. I can take a little bit. It's probably a little bit, sorry, the question is all of the total number of people infected, how many would require critical care? Is that their question?

Speaker: Correct.

Jeremy Farrar: Yeah, I think that 20% is probably a bit lower than that now. But that is driven, as I said earlier, by the size of the denominator. As we appreciate just how extensive the attack rate is in this, 25 to 40% of the world's population being affected, it's a very, very large number. So I would probably dial that back in terms of the need access to critical care, but it will only drop back to, if you ask top of my head, and this is a personal view now, not even - it's certainly not fact and not really on modeling, would be to about 12%. But if you do it again, run through the numbers and that's a very significant number if the denominator is that big.

It obviously also does depend on the demographic as the population you're talking about. Clearly this does have a bigger impact, as you'd expect, on people with other illnesses with age. And although we have seen adults getting severe disease, everything up from early twenties, through until people in their eighties, we have not seen as many children as we might've expected. But I think you can assume that overall 10 to 12% of people would need some degree of critical care if not necessarily on a ventilator and things, but some degree of enhanced critical care. Those are the figures that essentially US governments are working on in terms of case scenario planning.

Speaker: Okay. Thank you for that. And then the second question kind of going the other way was, I think you're talking about an infected population very materially higher than what you were talking about last time. And also, fatality rate very materially higher. So, I think you said something like 0.1, 2.5% for fatality and now saying 0.5 to 1%. So, I just wondered if you could give a bit more color on the drivers for those two assumptions that you're working with now.

Jeremy Farrar: I'd perhaps have overstated that just at a median, and of course there will be a range around this because it depends on your access to healthcare. If you're in the very best healthcare system in the world, you would anticipate that mortality case fatality rates for those needing care would be lower than they would be in South Sudan, for instance. So, I think there is a range around case fatality. Case fatality in Wuhan is still around between two and 4%. I

would stick to an overall case fatality of about 0.5. Now in some jurisdictions, that will go up to 1% and might even go higher than that if there's no access to critical care. And in some places, it might be lower than that, but I would stick to about a 0.5 case fatality rate. Overall attack rate of the population, I would, again, I may have misled you and I apologize for that. I would still stick with an attack rate of a median of about 30% of the world's population that would get infected with this on a range somewhere between 25 and 40.

There are others. The Hong Kong modeling group have estimated that figure is 60%. That seems quite high to me. And being optimistic, I would say it'd be less than that, but it's going to be 20, 25, 30%. It's not it's going to be significantly higher than influenza in 2009. So just to, sorry, answer that just to make clear, everyone sort of gets what I'm saying there. I think the attack rates will be between 25 and 40% of the world's population will see this infection and I think the case fatality rate will be 0.5.

Speaker: Thanks very much, Jeremy.

Operator: Our next question comes from the line of Phillip Fan. Phillip, go ahead with your question.

Speaker: Hello professor. Thank you for your time. I have a couple of questions here. One is that you mentioned it's going to be a second and third wave. Can you describe how that works? Is it just more people getting infected, longer durations? I just want to know how that manifests, and then a second question is, based on your experience, how do you think governments should react and how do you think government will react around the world? Thank you.

Jeremy Farrar: Okay. So, the series of waves, so when an infection comes into a population at the beginning of it, nobody has any immunity, and so therefore everybody is equally susceptible to that infection. After a while, a certain percentage of the population has now seen the infection and probably they have some degree of immunity to subsequent re-infection. And so that is a group of people who are no longer susceptible. If you assume that in Wuhan, let's say today, 30% of the Wuhan population has now seen the virus, that 30% cannot be reinfected. And so, you're left with 70% of the population that are still susceptible. As you remove the public health measures that have been unprecedented in the last 100 years, then that 70% remains susceptible. And so, you would anticipate that some of that 70% will be infected in a second wave.

Does that answer the question? In the end, you run out of susceptibles, but thankfully not all of us are equally susceptible and therefore some people survive. Otherwise we would all finished in the middle ages with plague. So, it depends on the ratio of people that are still susceptible and then the people that are now immune to this infection. And the probability I think is that you will see second waves even in Wuhan as you reduce the draconian public health measures that have been implemented and have undoubtedly reduced the peak of the epidemic.

Speaker: Yeah. Sorry, can I just follow up? So, is there a time lag between the first and second or did you just go hand in hand?

Jeremy Farrar: Yeah, that's a great question. I mean, it depends on a number of variables. It depends on how quickly or slowly you reduce, you lessen the public health intervention measures. It depends how many people are infected at the time you do that. It will not be zero, but you can imagine if it was then let's say 1% of the population are then still having the virus

up their nose, it'll take that 1% a little bit of time to infect the 70% of the population that's still susceptible. So, it does take a little bit of time. If you asked me to guess, I'd say there'd be a gap of two to three months before you might see the epidemic going up again. But of course, in that two or three months, other things have changed. The seasons have changed in China, and so if there is any seasonality to this, you might anticipate that that would push it out further. It might even push it out into the next autumn or winter in the Northern China, in the Northern hemisphere. But I think if you look back to every influenza or another epidemic of the last 100 years, you've always seen second or third waves. In fact, in 1918, which is the one of course everybody goes back to, the second and third waves killed more people than the first wave did. And in fact, in 2009 with the influenza pandemic, far more people died in the UK in the second wave in 2010 than they did in 2009.

Speaker: Right. Thank you for that.

Jeremy Farrar: The second question was about how governments have responded. Again, tensely sort of political sensitivity here. China has, I don't know any other country really on earth that could have done what China has done in terms of essentially locking down the city of 11 million people. And largely it seems that that population of mostly accepted that, remarkable. I'm not sure that would be possible in central London or San Francisco or New York with quite the same degree of acceptance. And one of the conversations I was very involved in this morning is just thinking through the behavioral aspects and societal aspects and what would tip society over into something slightly less accepting than perhaps what Wuhan has done.

But with this infection, with the amount, the degree of how infectious this is, the measures even in Wuhan can dampen the peak of the epidemic and they can spread out and delay the time to the epidemic. But given how infectious this is, you cannot prevent an epidemic with this level of infectiousness. So, the containment strategies of the moment are absolutely right and they've essentially bought other cities in China and the rest of the world time, but they will not be able to prevent it completely. And you can see that from the church in Korea, from the cruise ships in Japan and indeed what's happening in Italy today and Iran, you get a sense of just how infectious this is. So, your public health measures can dampen the peak. They can buy you time, but they can't prevent the epidemic altogether.

Speaker: Thank you for that.

Operator: All right. Our next question comes from the line of Chris Hansen. Chris, go ahead with your question.

Speaker: Hey Jeremy, thank you for doing this. I really appreciate it. My question is really around the confidence interval of both the mortality rate and the severe case rate. And a lot of the initial data was coming out of China, which probably is a little more suspect than what we're seeing around the rest of the world now. So, if you could just talk about that as we get more data points, do you think those will change or are you pretty confident in them now? And then the second part of that is what is the severe case rate? What does that mean? Is this 10 to 15%, does that mean people hospitalized or just having bad symptoms? And then what should we expect if we're talking about 25 to 30% of the world or 40% of the world getting this, what does that mean?

Jeremy Farrar: So, I think you're absolutely right, and we should just remind ourselves, we're only on about day 55 or 60 now of this epidemic. I mean, it probably started very early in December. The first cases were picked up at the end of December and we're only in mid-February now. So, we are, data points are coming in all of the time. And with each data point you become more confident about the estimates you're making. You're also absolutely right that the data coming out of yes, Japan, particularly Singapore, Korea, Italy now, those in some ways are even more informative than what's happening in Wuhan because Wuhan is just totally overwhelmed with what is happening. And having been in those situations, it's chaotic and frightening and the last thing on your mind is gathering data when you're trying to deal with that situation.

So, what you learn from Singapore, Korea, Japan, Italy, other places are now absolutely critical in terms of understanding the questions that you pose. I think the best estimates on the questions you ask, and I've just pulled this up on my computer. So, this comes from working treating with the United States and this is from data from the cruise ships, from Korea, Japan, and everywhere else. What it estimates here is, and I think these figures to me pass the common sense test, is that of the total population infected, let's say that is for argument's sake, 30% of the world's population. You can anticipate that about 12% would need hospitalization. Now obviously who gets hospitalized in which country varies hugely. Americans tend to get hospitalized far easier than you do in Britain just because we haven't gotten the facilities here.

But assuming, so this is US data and estimates, of the total population affected, 12% would hospitalization, 3% would require intensive care and a case fatality rate of about 0.5 to 1%. What that translates to in the US with a population of 325 million people and an attack rate of 30% is you'd have about 100 million people who would get ill over the course of, let's say six to 12 months, you'd require about 15 million people to be hospitalized. You'd have about two, two and a half million people requiring intensive care and you'd have somewhere between 500,000 and a million additional deaths.

Speaker: And just one follow-up on that, is there a clear delineation between, let's say, age in the severe case rate, would it be like 30 or 40%, say, about people about 50 or much lower amongst people under 50. Is that the right way to think about it or not?

Jeremy Farrar: Yeah, it is. Age is certainly a factor, but I think it's probably not age that's important. I think it's probably co-morbidities. That is not just having this, but having this on top of other illnesses. And of course, those illnesses increase with age. So, I think although age is being pulled out, I suspect it's related to other illnesses that compound the problem. But of course, in the demographic of most of Western Europe and North America now, the number of people who are above a certain age and the number of people with other illnesses is significantly higher, and so it's not particularly comforting I think that that it's a predominantly affecting people with other illnesses because that's just such a common feature of our societies today.

Where I would be particularly concerned, particularly in Western Europe, North America, the data from prisons in China has been startling. Effectively prisons, cruise ships have demonstrated one introduction leads to 400 cases. That's what happened in the prisons in China. And it's what's happened essentially on the cruise ship. And if you think of prisons and cruise ships in other environments, then you're thinking about care homes. You're thinking about people in schools or in military camps or in any sort of closed environment. And there I think you can anticipate this one case leading to many, many other cases as we saw on the

cruise ships and in the prisons in China. And around the rest of the world that's a big worry just because the number of people living in refugee camps and others.

Operator: All right, we have eight more questions left in the queue. Our next question comes, I'm sorry, as a reminder, if you'd like to ask a question on today's call, please press star one on your telephone keypad. Our next question comes from the line of Bob Culture. Bob, go ahead with your question.

Speaker: Thank you so much for this incredibly interesting conversation. By shutting down Wuhan and the graft soccer city is in the future in China economic output is clearly going to be lower. I'm curious, when you mentioned the economic implications, what are the products that you would say are not going to be made? And for healthcare I've heard that many of the antibiotics and small molecules that used to come from, can you speak to that? [inaudible] orders as we shouldn't dissipate, as we hospitalize millions of people around the world.

Jeremy Farrar: Yeah, so in the healthcare setting, and these are guesses, but I think they're pretty accurate, but you can get this from any website. Western Europe, North America about 60%, I think I'm right in saying, 60% of pharmaceutical products are either manufactured or put together or packaged in China. And about 70% of vaccines, that is a higher figure in Sub-Saharan Africa where 70 to 80% of drugs come at some point, have some link to China, and now they may be put together in India, but they're coming from basic raw materials that are assembled in China. So, the supply chain on therapeutic drugs and vaccines depends hugely on China. And that is true in Western Europe, North America as well as even more so in Sub-Saharan Africa actually.

But it's beyond that, it's also the personal protective equipment. It's things like gloves in surgery. It's spare parts for ventilators in the health care setting. So much of this is now either manufactured or assembled in China and then obviously shipped around the world and you'll be aware of the falloff in trade, both flight but also increasingly shipping. And I think that's just a reflection of the downturn in the Chinese manufacturing capacity. In the non-pharma sector of course, I'm less knowledgeable about that, but you will all be in terms of the supply chains that depend on China, and I think this will inevitably when eventually this does come to an end, it'll have to force companies to rethink their focus on a single country as being such a critical part of the global supply chain. So that's why I think and stress that this is currently a health issue of course, but it will be increasingly an economic issue and I think as economics gets a bit tighter, it will become a political issue as well.

Speaker: Thank you.

Operator: Our next question comes from the line of Bunco. Go ahead with your question.

Speaker: Hi. Yeah, thanks again for doing this call, it's been great. I had a couple of questions. First, you said once people have this, you can remove them. So, is the thinking this is not like the flu and there's going to be a different strain every year, or is this a relatively stable virus? Like how are people thinking in terms of -

Jeremy Farrar: Yeah, it's a great question. So, we have in, I mean, SARS disappeared 15 years ago and we've not seen another human infection with SARS. So, it's difficult to know, to take, to take much knowledge from the SARS epidemic. Mars, which is the Middle East respiratory syndrome, which is caused by Coronavirus as well, has been circulating in camels

and some humans for the last seven years. That has not changed dramatically. Flu, and we have not seen any dramatic changes in this Coronavirus in the two months that it's been circulating in humans. Coronaviruses can change, but they don't tend to change in the same way that flu viruses do. They don't change their proteins quite as much as influenza does. So, my guess, and this is now a guess, it's not based really on any facts, would be that you would see peaks of this in future seasons driven by that susceptible population I talked about rather than particularly changes in the virus itself driving new ways, but that's a personal opinion rather than a factually based.

Speaker: Great. And we haven't really heard much about young children being affected. Is there something about the immune system there or children that is useful learning here? Or is this too early to tell?

Jeremy Farrar: Yeah, it's really important to know this because this has huge implications for public health measures. There's little point closing down schools which are very disruptive economically if children themselves are not particularly contributing to this epidemic. And it has been very stark how children have been less, seemingly less affected by this than have adults. That could be because of the idea of enhancement we heard about earlier, I personally doubt that. It could be because the children express less of the protein that the virus binds to. That's possible. It's possible that this virus prefers people that smoke or live in polluted areas or whatever. There's all sorts of reasons why it might affect adults more than children, but it's something we have to understand in order to design the right public health intervention measures.

I will send a paper just this morning actually from the New England Journal, which will come out soon, which looked at children between the seventh and the 14th of January. And actually, at that time, in the first two or three weeks of this epidemic, as many children as adults were being admitted to hospitals in Wuhan. And in fact, if you go back and talk to the doctors and nurses in Wuhan at the moment that many of the schools were reporting 25 to 30% absenteeism in the last few weeks of December, which suggests that actually this does circulate in children. Maybe they don't get such severe disease, so they're not coming to a critical care facility. But I think at the moment we can't assume children are somehow protected from this epidemic.

Speaker: Great. Thank you. And then my last question is what does the rate of explosion like in the diamond princess in South Korea call? Like what does that tell you about how it spreads? Are air slides really how people are thinking versus they're not really anything to do?

Jeremy Farrar: Yeah, it does. It tells you an awful lot. I mean, the cruise ships will go down in history as something that provided incredible information, but also how not to manage a crisis by locking people up on a ship. But that's for another day. I think at the moment we have to assume this has spread by the spiritual roots. So, coughing, sneezing, but also touching surfaces. When you cough into your hands and you then touch a surface or a coffee cup or something, clearly the virus can persist on that surface and actually probably for some considerable time days rather than hours and then can be picked up by somebody else later. There are suggestions that it might be spread by the gastrointestinal system. That's not proven yet, but I think we have to assume the biggest method of transmission is by respiratory roots. So, coughing and sneezing and then coughing into your hands, et cetera. Very, very similar to influenza.

Speaker: Great. Thank you.

Operator: Our next question comes from the line of Eureka Whitalin. Eureka, go ahead with your question.

Speaker: Thank you very much. This is super helpful. I had a couple of specific questions with regards to company policy on travel and events. I'm curious to whether you have any advice as to battling company travel altogether at this point? Traveling on the tube and in busy cities and sort of bigger events where we're bringing together people from different countries, even if they haven't been on the restricted just yet.

Jeremy Farrar: Yeah. And obviously we're thinking about this on a daily basis and I do think this is something you just have to keep under constant review. I mean, a week ago we would not have been restricting travel to Italy, for instance, but now we would, certainly to Northern Italy. So, I think it does need to be looked at almost on a daily basis. At the moment, what we're advising is we're advising against travel to the hardest hit countries. So obviously that's China, it's Singapore, it's Korea, it's Japan, it's Vietnam, and it's Northern Italy. I think the best advice on that probably though, and this is what we follow, is to follow either the US CDC guidance on this or if in Europe, the European CDC or the UK public health authorities rather than trying to make it up ad hoc.

We are looking at all travel. We're restricting it where it makes sense. Sometimes in fact, not because of fears of getting infected, but actually concerns about people getting stuck somewhere and then having to be quarantined when they come back or flights being canceled or postponed, et cetera. So, for me, it's both about picking up the infection somewhere and the duties of care for that, but also there's the responsibility of people getting stuck or quarantined when they come back, which can sometimes be incredibly disruptive to people's lives and their work.

Speaker: And a follow-on question to that. Would you advise against traveling on the tube at this point?

Jeremy Farrar: No. Tube is unpleasant at the best of times, but I wouldn't, I was on the tube this morning and I wouldn't have any - I wouldn't at the moment not travel on the tube in London. If I was in Wuhan, as I said last time, I wouldn't necessarily go on holiday to move home tomorrow, but I probably wouldn't travel on public transport in Wuhan, but the rest of the world I still would, yes.

Speaker: And I guess one last question. Thank you so much. What would make you change that? What is the tipping point? So, something suddenly you have this sort of an explosion of cases in Italy.

Jeremy Farrar: Yeah. That and that is the million-dollar question really. Everybody knows that we're going through this period of containment at the moment. We're essentially trying to mitigate the worst and we're buying ourselves time, time to make sure that the health system is set up for the surge capacity that is probably going to follow. Trying to make sure we can work out if drugs work or vaccines could be developed with, essentially buying ourselves time at the moment. And there is just an outside hope that we might be able to contain it. Singapore seems to be doing a pretty good job on that, but my view, and this is now the personal view, I think it's going to be extraordinary difficult to contain it forever. And I think you will reach

tipping points and I think Italy tells us a great deal about the number of cases that are going to happen and how that has spread across, albeit Northern Italy at the moment, but how it will spread quite dramatically when it comes.

And I think when that happens, when you start to see clustering of cases, when you start to see community cases as well as the more severe end of the spectrum, and there is always an iceberg effect here with a small number of severe cases in a very large community infected behind it, then you have to revisit all that advice. And if Northern Italy today was London tomorrow, then I think we at Wellcome would be moving towards people working from home, advising against traveling on public transport and making sure we had contingency plans in place that people could work from home. And we're testing those at the moment. We're not there yet in London. I don't believe you're there anywhere in the United States at the moment. You might be there in Italy, Northern Italy at the moment, but you're not there in London or any other country in Western Europe.

Operator: All right. Our next question comes from the line of Adam Radishack. Adam, go ahead with your question.

Speaker: Thanks, Jeremy. Could you walk us through how you get to your numerator and denominator when calculating a fatality rate given that the number of cases and the therefore the number of deaths are both being underreported?

Jeremy Farrar: Yeah, so that is a combination of trying to sort of cobble together a few like data points from various places. So just to sort of take you through that, obviously there's data coming out of China itself from Wuhan, but we know how overwhelmed they are and we know how they've restricted testing to focus, for instance, on moderate and severe disease. So, that doesn't give you a great idea of the total denominator, but you can add other data points to that. You know how many people six, two months ago flew from Wuhan to other parts of China. You know how many people got on a plane and flew to other countries. And you can work out by pretty simple math and modeling how many people there would have to be number of people infected in Wuhan to have that number of people arrive in Hong Kong or Singapore or whatever.

And you can do those sums. You can imagine doing those estimates. And that's how you get to the total number of people that you believe to be infected now. So, in order to have the number of deaths that are occurring, you must have a certain number of people, the denominator, in the community to give you those deaths. And that's where the modeling data would suggest that there is about a 10-fold underestimate of the total number of cases in China. And because of that working out of case fatality rates, let's say it's 1% in Italy, and Italy has now has 10 deaths, then you can assume that there are 1,000 cases in Italy to give you 10 deaths bearing in mind that those deaths were infected three weeks ago because it takes three weeks to die. So therefore, you can assume that three weeks ago there were 1,000 deaths and you know the doubling rate from China is approximately six or seven days. So, you can just play that those numbers through to you see today.

Really important to appreciate that deaths always lag behind cases because it takes people time to die. And the first deaths you see will always be in the most vulnerable and you'll see the people dying later who have more resilience and capacity to withstand this infection. So that's why you tend to see older people dying early in an epidemic and you see the deaths occurring

in a broader spectrum of age, which is what we see now because younger people tend to survive longer than older people. Sorry, that's all a bit morbid, but that's the truth.

Operator: Okay. Our next question comes from the line of Thomas Daniel. Thomas, go ahead with your question.

Thomas Daniel: Thank you so much for this discussion. Invaluable. I'm curious about the persistence of acquired immunity to Coronavirus. In some I'm reading it appears that patients in fact may not have persistent immunity. Do you have any perception or inferences to be made from SARS or from other Coronavirus infections relevant to this?

Jeremy Farrar: Yeah, it's a great question because if there is no immunity after natural infection, then trying to make a vaccine for this will be almost impossible. And so, the question you ask is really important and also of course, drives that susceptible population two months from now. If I was infected today and in two months' time I'm susceptible again, then the world is not in a great place in terms of this epidemic because you're continuously have a huge population that that is susceptible. My working assumption is that after an infection you will have immunity to this Coronavirus. How long that lasts? I don't know. Nobody knows, but I would imagine that you would have immunity, you would be less susceptible to a second infection and that may last some time. And if you ask me how long, I would say years rather than months, and even if it doesn't protect you necessarily from being infected, it may protect you from getting more severe disease and it may protect you from dying and it may protect you from passing it onto somebody else. Those three things are critical in terms of understanding the epidemiology. So, I'm an optimist and I think after infection you'll have some degree of protective immunity.

Thomas Daniel: Thanks.

Operator: The next question comes from the line of Mark Damha. Mark, go ahead with your question.

Speaker: Thanks for your time. You've probably answered the question already, but I wanted to know, do you think will start limiting things like flights and from not just the company aspect, but from a tourism aspect, do you see holidays being cancelled? Do you think that's a wise idea if you're saying that this is now probably across the world, do you actually want to travel too far?

Jeremy Farrar: Well yeah, I think you're already seeing a downturn in tourism and you're seeing a downturn in airline industry volumes. I mean, you've probably seen that beautiful graphic of the number of flights across China and if you haven't yet, I'll send it to you. So, people are voted with their feet already and essentially not flying today. And I think it will have a huge impact over the next 12 months on the tourist and trade travel industry including hotels and everything else that goes with that. I think in fact governments will do the opposite of what you've described. I think in this space, which we still call containment, then governments are rightly or wrongly restricting travel. They are - Austria closed its border to trains with Italy for short time. Iraq has closed its border with Iran, et cetera.

I think countries will do that at this stage. But actually, when you move from containment into mitigation, which I assume we will at some point in the coming days or weeks, then actually there's no point doing that. There's no point stopping flights when actually it's just as prevalent

in your country as it is in the country you're flying to. So, I think you're going through a phase now, whether a travel restriction imposed by countries, they'll come a time when everyone just drops out because there's no purpose to it.

Speaker: Okay. Thanks very much.

Operator: We have three final questions in the queue. As a heads up, the question queue is now closed and we'll take these final three questions. Our next question comes from the line of Eric Dan Dean. Eric, go ahead with your question.

Speaker: Thank you, Jeremy for the call, very informative. You were pretty emphatic that we would not have a vaccine until the end of 2020. Can you help us understand what the bottlenecks and timetable would be for vaccine development and is there any way to fast track that development?

Jeremy Farrar: Yeah, I mean there is a way to fast track that. I mean we were very involved in the fast track of the Ebola vaccine, which we managed to get done in, well effectively a year. But that was for a vaccine that actually was very easy to develop. In fact, I mean I wouldn't have said that at the time, but in retrospect the vaccine was able to produce very, very strong immunity, protected 99% of people that received it. And it was just an extremely good vaccine that was actually relatively easy to develop. The Coronaviruses are a completely different challenge. And as I said, we don't have a vaccine for SARS, for MERS or indeed for the common cold. And so, the ability to make a vaccine and a strong immune response, the response that would protect you is a much bigger challenge in Coronavirus than it is in Ebola.

We are fast tracking. I mean to go from the sequence of the virus, which is what we needed in the first few days of January to having the first person received the vaccine in the first week of March has never been done in history before. I mean that process from sequence to first person would normally take somewhere between three and five years. So, we've brought that down to about five weeks. The other of course is when you're giving a vaccine, particularly to a disease, which for the vast majority of people will be mild, then you have to be absolutely sure of the safety of that vaccine. With Ebola I was much more gung ho. If you get Ebola, you've got a 70 to 80% chance of dying. And therefore, you'd take a pretty big risk to receive a vaccine that you hope would prevent you getting it.

With this Coronavirus you've got a less, in my view, less than 1% chance of dying. And therefore, you've got to be absolutely sure that that vaccine is safe before you roll it out to 350 million Americans or seven billion people around the world. So, the safety requirements and the threshold that you need to go through to prove that what you have is safe, let alone effective is very significant. And actually, rightly so. So, there are some bottlenecks. We've worked very hard with the FDA and the European medicines agency and all other agencies around the world to make sure there is not a complex regulatory pathway to this, but it will go through a single approval process effectively. And we very much hope that of the eight vaccines we've supported, and probably there's another five or six on top of that from companies and other groups around the world, that one or two of those would show to be safe and protective.

But then you've got to also manufacture the thing. And as you probably know, there are not large-scale manufacturing plants around the world doing nothing at the moment. And so, you have to build that manufacturing capacity and you have to do that at risk because you may not ever get to a manufacturing stage. So those are all discussions that we're having. I spoke to

the world bank this morning about them releasing a \$10 billion to get this going so that there's manufacturing capacity the regulatory alignment so that we're not doing it three or four times, but just once and making sure that this is both a protective but also safe. And we will do that as quickly as we can. I just think we have to be honest and open about the timeframe, the realistic timeframes to that.

Speaker: Thank you. Just a quick follow-up, presumably China is not managed or regulated in any way by some of these bodies like FDA, et cetera. Are you aware of any types of vaccine development that's going on in China where perhaps they're less stringent and be able to fast track that at a greater rate?

Jeremy Farrar: Yeah, there are. I mean, there's a number of vaccines. There's a number of very good Chinese companies that are making vaccines. And yes, the Chinese regulatory authority is not as stringent as the FDA or the EMA, but actually, with the reforms of the FDA and the EMA over the last say five years I don't think there's very much difference in timescale from a regulatory hurdle that is different between the FDA and the United States or the Europeans or the Chinese actually. And that's probably the regulatory hurdles are probably not the bottleneck. The bottleneck is developing a vaccine that creates an immune response in you or me, which offers protection. That's a scientific challenge at the moment rather than a regulatory one. I think we've sorted out the regulatory pathway. It's the science to make an immunogenic and safe protective vaccine that's the challenge of the moment.

Speaker: Thanks so much.

Operator: Our next question comes from the line of Stacy Garber. Stacy, go ahead with your question.

Speaker: Hello. I believe Orika asked very similar questions. So, I'll ask a follow on to her question about travel and events. We're struggling with this idea should we suspend group gatherings prophylactically so to eliminate a potential place where people gather for infection even in relatively unaffected areas like the US. And we're just struggling with that responsibility and we'd love your opinion on that.

Jeremy Farrar: Yeah. Again, I think this does need, if not day to day, certainly week to week assessment. As I said earlier, I mean, we would not even have considered Northern Italy even a week ago and yet now, clearly Northern Italy is struggling with what is probably a very major cluster of epidemic of cases. I think this does just need looking at on a day to day, week to week basis. I can tell you what I mean, now this is personal opinion of what I think we would do at Wellcome, I would have no problem in us having a gathering here in London at the Wellcome building. I'd have no problem us going to the United States and having a meeting today with people. We would not do that in China, would not do that in Singapore at the moment. I would keep to the 10 or 12 countries around the world that are really going through epidemics at the moment that we really do know about. And I wouldn't cancel everything, otherwise the world does come to a complete standstill and I don't think at the moment that's justified. And I think it just has to be a pragmatic decision. If you're planning meetings now, as I'm sure you are, and we are, I was supposed to go to Singapore in April or May and we've postponed that for just sensible pragmatic both for getting infected and getting stuck somewhere. But I wouldn't call off a meeting in middle of March in Chicago for instance. I think that's going too far.

Speaker: Wonderful. Thank you.

Operator: Our final question comes from the line of Banco bong. Go ahead with your question.

Speaker: All right, thanks for the follow-up questions. Can you comment on the severity of this disease relative to flu, and generally what is the capacity of the US or UK systems to handle that? And then the other question is which comorbid illnesses are most susceptible? Are the respiratory ones like asthma or COPD or is it just general level of wellness?

Jeremy Farrar: Yeah, So, most influenza seasons, one of a better phrase, have an overall case fatality rate of about 0.1, perhaps a little bit less than that in countries with good health systems, but if you say a 0.1. And most seasonal influenza periods give you an attack rate of let's say maybe five or 10% of the population. So, if you compare that with where we are on this, where I would conservatively estimate that the case fatality rate is 0.5%, so at least five times higher than normal flu. And certainly, in China and in places with perhaps less good health systems that'll be higher than that, but you've got an attack rate which is considerably higher. So, again, your denominator is so much bigger. So, I would be less reassured by a low case fatality rates because it's in effect in terms of health systems, it's all about the absolute numbers rather than the rates. So, attack rate of 30% and a case fatality rate of 0.5 or 1%, that gives you a very large number.

I can't really comment on the US system. I don't know it nearly as well as say I do the UK system. I think the UK system, if there was an epidemic here like Italy at the moment, would really struggle. Critical care facilities in the UK are running at about 98 to 102% capacity on any one day, and so the number of the surge capacity there is quite limited. And so, the capacity, that's one reason why trying to delay this for as long as possible is so important because we will be out of our peak flu season in another two or three weeks in the UK and that will reduce the burden on the health system generally. And that will be true in North America as well. But every country including the United States is looking through these contingency plans and thinking, what would we do if we were faced with 1,000 patients in Chicago tomorrow that required some degree of critical care and every country, if they're not doing this, they should be doing it now.

Speaker: Right. And then comorbid illnesses?

Jeremy Farrar: Sorry. Yeah, it's really important. The most common have been, as you say, chronic lung disease, chronic obstructive lung disease, heart failure, diabetes and smoking. Those have been the risk factors that have most come out in the Chinese large series that have been published. So, and they probably go together as well. And they won't come as any surprise, I'm sure.

Speaker: Thank you.

Nick Moakes: Excellent. Well, thank you all very much indeed for taking part this afternoon. We really value your partnership and if you have any follow-up questions, please don't hesitate to ask us in the investment division here at Wellcome. We will be more than happy to seek the right answers from somebody who actually knows what he's talking about. And on that note, Jeremy, thank you very much indeed.

Jeremy Farrar: Yep, pleasure. Thank you all.

Operator: Thank you for joining today's call. You may now disconnect. Hosts, please stay on the line and await further instruction.

[END OF TRANSCRIPT]