

1

If anything happens to me, this is what you need to know ...

30 DECEMBER 2019

Known cases: 4

I WAS IN AN AIRPORT lounge on New Year's Eve 2019 when my mobile rang. I was heading back to England from Rwanda and the Democratic Republic of Congo, where I had been visiting the Ebola vaccination centres in Rwanda across the politically fraught border region of North Kivu. I'd spent around a week going around the clinics and I'd had the vaccine myself in Prefegitura ya Cyangugu, a village in Rwanda. I was absolutely knackered and looking forward to a couple of days at home in Oxford before heading back to the office.

I was scanning my phone when I saw a report of a mystery pneumonia spotted by doctors at a hospital in China. I sent a short text message to George Gao, head of the Chinese Center for Disease Control and Prevention (China CDC) in Beijing, and an old friend. George is a very likeable character, as well as a respected scientist, a brilliant impressionist and a karaoke enthusiast. My message was short and simple, just asking if he was OK and that he should reach out if he needed anything.

He phoned me back. Very soon, George told me, the world would be hearing about a cluster of cases of a new pneumonia from Wuhan in China. The cases had already been reported to the World Health

Organization. It was, essentially, a courtesy call from one scientist to another. I remember him telling me that we wouldn't need to worry because it wasn't severe acute respiratory syndrome (SARS), and that we must keep in touch.

It was a relief to hear him rule out SARS, a deadly disease that features on the world's worry list and for which there is no vaccine or cure. It first appeared in 2002 – and one of its victims, Carlo Urbani, was a good friend of mine. He died while investigating an outbreak in Hanoi, Vietnam. He was just 46 and had a young family.

Carlo's work helped to identify SARS as a new coronavirus. Most importantly, he spotted that cases of severe pneumonia were being passed on from patients to health workers, who were falling sick and dying. Carlo organised the hospital's closure, alerted the world and, essentially, saved Vietnam. His legacy is honoured, if that is the right word, in the naming of the Urbani strain of the virus. This was the dominant strain that spread across South East Asia in 2003, before being contained, infecting more than 8,000 people and killing nearly one in ten of them.

Having spent eighteen years running an infectious diseases research facility in Ho Chi Minh City, I was badly shaken by Carlo's death. I know what it is like to deal with the science and politics of a new disease. I helped to alert the world to a potentially serious outbreak of H5N1 bird flu in Vietnam in 2004, along with colleagues Tran Tinh Hien, Nguyen Thanh Liem and Peter Horby, then an epidemiologist working for the World Health Organization in Hanoi and now an Oxford University scientist.

Both SARS and H5N1 had a profound psychological impact on me, because of the fear that comes with unknown diseases. They took me back to being a young doctor in London at the start of the HIV epidemic: as medical students and junior doctors we rarely stopped to question the power of medicine, believing unerringly that we could treat people and cure them. But when HIV came along in the early 1980s we could do nothing. Young people would come in to die. The West had not seen deaths from untreatable infectious diseases for many years.

When SARS came, it was the same. You don't know what you're dealing with, you're frightened, friends are dying and it's spreading around the world. Six months later, SARS was finished because it did not transmit readily between people: also, people were most infectious when they were symptomatic. There was little or no asymptomatic transmission, meaning that isolating people with symptoms brought a chain of transmission to an end. Despite lasting only six months, and causing 'only' 774 deaths, the epidemic was estimated to have cost around US \$40 billion.

The next year, bird flu struck Vietnam. It never got beyond about 100 cases but it killed roughly 60 per cent of people who caught it. We got lucky because, again, the disease fizzled out. These episodes, along with the emergence and reemergence of other diseases over the last twenty years such as the deadly bat-borne Nipah and Middle East respiratory viruses, and the mosquito-borne Zika virus, were the warnings for what would inevitably come.



When I went back to work on Friday 3 January 2020, I emailed two of my most senior colleagues: Eliza Manningham-Buller, the Chair of the Wellcome Trust and former director general of the UK intelligence agency MI5, and Mike Ferguson, her deputy. I would not normally trouble them about a small, distant outbreak – but this one in China felt different. If it turned out to be different, the Wellcome Trust, where I have been director for eight years, would be called upon for its expertise and money. The charity has long worked in the field of infectious diseases, with researchers all over the world; it played a key role in the research response to the Ebola outbreaks of 2014 and 2018, including funding vaccine research and clinical trials.

Prefaced with the line 'Just for info in confidence', I told Eliza and Mike about my phone conversation with George Gao and included a link to a news item on the BBC website about the mystery viral pneumonia from Wuhan. Just before signing off, I speculated that China CDC would make an announcement within 48 hours. I assumed that's what George had meant by his phone call. I

reassured Eliza and Mike that ‘it is not SARS, although probably a known “relative”. Nothing for Wellcome to do at the moment.’

I turned out to be wrong. The cases of unexplained and untreatable pneumonia in Wuhan kept growing, matched later by reports of crowded hospital wards and overflowing mortuaries. Social media and online chat rooms in China hummed with rumours of a strange new illness spreading in Wuhan, including among hospital workers; reports began filtering in of police crackdowns on those trying to get information out over the heavily monitored internet.

By the second week of January, I was beginning to realise the scale of what was happening. I was also getting the uncomfortable feeling that some of the information needed by scientists all around the world to detect and fight this new disease was not being disclosed as fast as it could be. I did not know it then, but a fraught few weeks lay ahead.

In those weeks, I became exhausted and scared. I felt as if I was living a different person’s life. During that period, I would do things I had never done before: acquire a burner phone, hold clandestine meetings, keep difficult secrets. I would have surreal conversations with my wife, Christiane, who persuaded me we should let the people closest to us know what was going on. I phoned my brother and best friend to give them my temporary number. In hushed conversations, I sketched out the possibility of a looming global health crisis that had the potential to be read as bioterrorism.

‘If anything happens to me in the next few weeks,’ I told them nervously, ‘this is what you need to know.’



The process of reporting a new disease to the wider world is quite informal and not at all glamorous. It often starts with a brief notice on ProMED-mail, an online repository collating short descriptions of outbreaks of animal and human diseases in different countries, as well as other news snippets relating to diseases, such as grant announcements. That is where I had picked up the information on the Wuhan cases that George Gao and I spoke about. The descriptions

of outbreaks are clipped from official sources, such as health authorities, but also from social media and local newspapers. Every outbreak that becomes a global headline begins as a local rumour.

ProMED stands for 'Program for Monitoring Emerging Diseases' and is run by the International Society for Infectious Diseases, which boasts more than 80,000 members in 201 countries. It is not sustained by any government or the World Health Organization but by volunteers operating a non-profit initiative on a shoestring budget. It is also far more respected – and critical to global health – than the informal setup would imply. I first became aware of ProMED in 1999, while investigating a mysterious brain infection striking down pig farmers in Malaysia. That turned out to be the first known outbreak of Nipah virus, regarded ever since as one of the world's deadliest disease threats.

The ProMED alert that had caught my eye was dated 30 December 2019, next to a line reading simply: 'Undiagnosed pneumonia – China (HU):RFI'. 'HU' refers to Hubei, the central province in which the city of Wuhan is located: 'RFI' signals a request for further information. The first signs of SARS were cases of undiagnosed pneumonia.



Nobody knew it then but that single line marked the debut of a new disease, one that would come to be called Covid-19 and cause the biggest upheaval to the global order since the Second World War. The line clicks through to an imperfect machine translation of a story relating to 'an urgent notice on treatment of pneumonia of unknown cause' originally posted that evening by the Medical Administration of Wuhan Municipal Health Committee, concerning four patients with an unknown form of pneumonia.

A report appended underneath that urgent notice adds worrying detail gleaned on 31 December: 27 people were in various hospitals in Wuhan with viral pneumonia or pulmonary (lung) infection. Two were recovering but seven were critical. Flu and bacterial diseases

had been ruled out – but not SARS. Citizens were being urged not to panic.

All the patients apparently had links to the Wuhan South China Seafood Wholesale Market (also known as the Huanan Seafood Market). That market link would have worried scientists like me: crowded and cramped ‘wet markets’, named for the melting ice that keeps meat and seafood fresh, often sell wild and domestic animals alongside meat and fish. The messy overlap provides contact between species, a common feature in the emergence of new diseases because it opens avenues for microbial traffic. That exchange can be between different animal species and between animal species and humans. The report added: ‘At present, related virus typing, isolation treatment, public opinion control, and terminal disinfection are underway.’

Public opinion control. Underneath the news reports, a ProMED moderator made an astute observation. Having been involved in publishing early information about SARS, the anonymous moderator wrote, ‘the type of social media activity that is now surrounding this event is very reminiscent of the original “rumors” that accompanied the [SARS] outbreak.’ Weibo, the Chinese social media channel, was also buzzing with speculation.

The moderator turned out to be Marjorie Pollack, an American epidemiologist who has worked in 50 countries for the US Centers for Disease Control and Prevention. She noted that the bubonic plague, which had cropped up the month before in Inner Mongolia, was sometimes accompanied by unusual pneumonia but assumed this had been already ruled out in Wuhan (plague is caused by *Yersinia pestis*, a bacterium, while the Wuhan pneumonia bore the hallmarks of a viral infection). She appealed for more information, and for the results of any tests.

On 31 December, the WHO requested information from China on the Wuhan cluster of atypical pneumonias.



On 3 January 2020, ProMED posted an update pulled from the *South China Morning Post*. The unexplained disease was spreading: 44 patients in Wuhan, up from 27; 11 seriously ill with breathing difficulties and lesions, or scarring, on both lungs. There was another unwelcome development: five people had shown up in Hong Kong with unexplained fever after visiting Wuhan. Yet the Chinese authorities had not yet found – or not yet chosen to disclose – the cause.

By 5 January 2020, the WHO, guided by the official information it was receiving from Wuhan, was reporting that there was no significant evidence of human-to-human transmission. Contact tracing was underway to find those linked to the Wuhan patients, many of whom had been stallholders at the seafood market. The persistent market link, the WHO reported, ‘could indicate an exposure link to animals’.

That tight case definition resulted in an Escher’s loop of misguided circular reasoning: testing only those people with a link to the market created the illusion that the market was the source of disease, because everyone testing positive had been there. In reality, the net should have been cast wider – and the continually growing casualties should have immediately prompted suspicions of human-to-human transmission rather than infections from a single source, such as a contaminated animal carcass.

The WHO also reported that no healthcare workers seemed to have come down with symptoms: illnesses among nurses and doctors act like a canary in the coalmine for new contagious diseases, because infection takes place before nurses, ambulance drivers and other healthcare staff know what they are dealing with.

But, to any outside observer familiar with China as a scientific superpower, second only to the US in research spending, the ignorance was peculiar. Why did nobody seem to know what Wuhan medics were dealing with? The authorities kept insisting that SARS, influenza and bacterial causes had been ruled out – and yet had not pronounced on what could be ruled in. It was baffling: samples would have been sent from those first patients to laboratories for urgent

testing and analysis. There was even a top-level biosafety laboratory in Wuhan, a coincidence that would later fuel theories about the virus's origins. Why had that information, potentially crucial to global public health, not yet been released?

ProMED reported: 'The Chinese Center for Disease Control and Prevention is expected to make an announcement of its findings in the coming days, a person familiar with the matter said. The CDC couldn't be reached for comment late Tuesday [7 January 2020].' The report went on to remind readers that China had covered up SARS when it emerged in 2002, reporting it to the WHO only after it began spreading across and beyond southern China.

Just a week into the new year, the unknown disease was no longer wreaking havoc just in Wuhan, a city of 11 million people and a major travel hub in central China. Authorities in neighbouring Hong Kong and Singapore, having already experienced the unwanted gift of SARS nearly two decades earlier, were now monitoring their borders for passengers with fever. A lot of people were becoming anxious – and for good reason. A week is an unsettlingly long time in the world of infectious diseases.

By Friday 10 January it was clear that the Chinese authorities knew more than they were letting on. Colleagues at the World Health Organization discovered that two scientific papers about this new viral pneumonia were in the pipeline at *Nature* and the *New England Journal of Medicine*, two prestigious journals. Maria Van Kerkhove, an epidemiologist in the WHO's Health Emergencies Programme, alerted me.

It was time to send out a signal. I tweeted:

If rumours of publications on the Wuhan Pneumonia situation are being prepared and submitted to @nature @NEJM are true & that critical health information is not being shared immediately with @WHO – something is very wrong

Within minutes, the tweets attracted a private message on Twitter and a phone call from the other side of the world. Something was, indeed, very wrong.



Scientists track how viruses relate to each other by drawing family trees, in much the same way that people can trace their own origins back by following the trail of births, deaths and marriages. Instead of surnames and family records, viruses reveal their origins in their genetic sequences. Genetic overlap pinpoints the similarities between different viruses, signposting when they potentially share a common ancestor. Likenesses between human viruses and animal ones can also narrow down which animal might have transferred a virus across the species barrier to us.

Scientists can then construct a 'phylogenetic tree' that accords the newbie pathogen its rightful place in the viral hierarchy by establishing how closely related it is to other known viruses. This helps virologists to decide whether an emerging virus is a variation on a known virus or a fresh addition to a particular family of viruses. A tree for a virus can be drawn in different ways but often looks like a collection of fork prongs (or tines).

At the tip of each tine lies the name of a virus designed to showcase something of its origins. The pandemic virus that causes Covid-19 is now called SARS-CoV-2: severe acute respiratory syndrome coronavirus-2. The original SARS virus to which it bears significant genetic resemblance used to be called SARS-CoV and has now been renamed SARS-CoV-1.

Eddie Holmes is a British-born virologist and professor at the University of Sydney who does exactly this sort of viral detective work. He is, in my book, the outstanding evolutionary biologist of his generation, with an extraordinary brain when it comes to pattern recognition.

Eddie belongs to a research consortium which includes the Shanghai Public Health Clinical Center and School of Public Health at Fudan University, Shanghai, where he holds an honorary professorship. Since 2012, Eddie has worked closely with Professor Yong-Zhen Zhang, a professor at Fudan University, on finding and identifying new animal viruses, and Wuhan is a familiar locale in their virus-hunting network.

‘We have this little routine,’ Eddie says of his work with Zhang trying to document the diversity and evolution of animal viruses. ‘His team collect samples – they can be spiders or fish or anything – and then I go over there once or twice a year and help analyse the data.’

They don’t normally study samples from humans but genomic sequencing, the method used to place viruses in their family trees, can also be used as a diagnostic, to help identify mystery viruses found in hospital patients. Over the past eight years, Eddie and Zhang, more used to collecting virus samples from cave-dwelling bats than from city dwellers, have built up contacts with Wuhan doctors. As Eddie says, rather honestly: ‘The animal stuff is great but everyone wants to find a new human virus. It was obvious that Zhang was going to be one of the first people to get hold of samples.’

On 3 January 2020, Zhang struck viral gold: a sample taken from a pneumonia patient hospitalised in Wuhan on 26 December 2019 arrived at his lab packed in dry ice in a metal box. By 2am on 5 January, after a 40-hour shift in the lab, Zhang and colleagues had worked out its genetic sequence. It was a coronavirus that looked suspiciously like SARS-CoV-1, the virus responsible for the 2002/3 outbreak. Coronaviruses are named for their similarity in appearance to a crown: under powerful microscopes, the virus particles look like tiny spheres covered in small spiky protrusions. Those spikes help the virus get into cells to infect people; most vaccines target the spikes to disrupt the process.

Eddie still remembers the phone call (Sydney is three hours ahead of Shanghai): ‘We agreed that he should tell the Ministry of Health in China immediately. Zhang did it the same day.

‘Zhang told them it was clearly very closely related to the first SARS virus and that it was very likely to be respiratory because of its relatedness. He also told the ministry that people should take precautions.’

That phrase – ‘people should take precautions’ – was a direct warning that this new virus, like its dangerous predecessor, might be able to spread from one person to another. Eddie says this should have been interpreted back then as a warning of human-to-human

transmission. In the end, China did not confirm this publicly until 20 January, more than two weeks later.

While Zhang informed Beijing, some of the sequence was deposited on 5 January 2020 on GenBank, an online collection of publicly available gene sequences run by the National Institutes of Health in the US. But it takes a while for those deposited sequences to be checked, edited and put through the system in a way that others can use. There was an imperative to post the entire sequence more publicly. Anyone, anywhere, could then use that published information to develop a diagnostic test. The world would, at a stroke, have eyes on the virus.

There was, though, a major hitch: Zhang was told in no uncertain terms not to publish anything. The gagging order, Eddie understood, came from Beijing. The warnings to stay silent were real: medics had already been disciplined by the Chinese Communist Party (CCP) for discussing hospital cases online. One of the earliest whistleblowers, ophthalmologist Dr Li Wenliang, became a potent symbol of China's mismanagement of the emerging crisis: he was admonished for warning hospital colleagues of a dangerous new infection, became infected and died aged just 33. The Chinese government later apologised to his family, including his pregnant wife.

Eddie and Zhang hit on a loophole to get round the gagging order: the government ban on publishing information about the outbreak did not preclude them from writing and submitting a scientific paper. Holmes contacted the journal *Nature*; one of its editors, Clare Thomas, urged them to submit something as soon as possible. By 7 January 2020, Zhang's paper, with Eddie as one of the co-authors, reached *Nature's* offices in London.

Things began moving quickly and chaotically. On 8 January, rumours began circulating that the new virus was a coronavirus, putting it in the same family as SARS. A day later, the Chinese authorities confirmed the fact. But, otherwise, and especially on the genome sequence of the virus, they were silent. Not only had Zhang contacted China's Ministry of Health with details of the new virus but Eddie was sure that, in doing so, Zhang had merely confirmed

information that Beijing already knew. Eddie had screenshots of messages on WeChat, a social media platform in China, suggesting two private companies had already sequenced the virus in December 2019.

Eddie, disturbed at what was looking increasingly like a decision by China to hold back information on a new disease, saw my tweet about the two scientific papers about to come out. His name was on one of them. He rang me to tell me that he'd been trying to get the sequence released, with no luck.

After that call from Eddie, I realised that he and I were probably the only two people in the world outside China who knew there was this sequence in existence and what it was, with all the potential consequences. The information was stacking up: here was a mysterious new pneumonia and, with the sequence, we knew it was caused by a novel coronavirus closely related to SARS. Those are two big red flags.

But the really critical information, the kind that stops you sleeping at night, was still to come.



The news of a novel coronavirus outbreak in China at the start of 2020 chilled the blood of scientists, including me, who witnessed the appearance of severe acute respiratory syndrome (SARS) nearly two decades before. That disease, also associated with a fatal pneumonia, first emerged in the Guangdong province of southern China in 2002. It spread largely unchecked in southern China and then crossed borders. By August 2003, it had infected more than 8,000 people in 37 countries and killed 774. That was the virus that killed my friend Carlo in Vietnam.

Like so many of the viruses that feature in epidemiologists' anxiety dreams, SARS-CoV-1 is found naturally in bats – and the animals themselves seem untroubled by viruses that are so virulent in other species. The 2002/3 outbreak is thought to have been triggered by that virus passing from bats to humans via an intermediate species, with civet cats a probable culprit. These long-bodied, short-legged

animals, closer in appearance to a mongoose than to a cat, are commonly sold for food and have been found to harbour viruses closely resembling SARS-CoV-1.

SARS is a painful memory in the collective Chinese consciousness – and in the annals of global public health – because the government spent the early months of the epidemic covering it up. In fact, the parallels between that original SARS outbreak, caused by the virus SARS-CoV-1, and the Covid-19 pandemic, caused by the closely related virus SARS-CoV-2, go beyond virus names. Both are likely to have started in November and, while reported up the chain of public health command, failed to properly attract the attention of Beijing until January.

It is an auspicious time of arrival for any malevolent microbe, given the proximity of the Chinese New Year. The week-long holiday is the backdrop to the world's largest annual migration, as around 450 million people criss-cross the country to visit friends and relatives. That mass movement is the perfect spreading opportunity for a virus. The anticipation of a major public holiday is a distraction for otherwise diligent health officials on the lookout for new diseases.

The top-down, hierarchical way in which the Chinese Communist Party runs the country, with a compulsion to control the message, also seems set up to frustrate early disclosure. With the original SARS, three days were reportedly lost due to the lack of suitably senior staff to open a document about the new illness marked 'Top Secret'. When health alerts eventually came, they were sent out during the Chinese New Year, when many hospital staff were absent. It was February 2003 before the World Health Organization was officially notified, by which time more than 300 people had fallen ill. Insistence in Beijing that the SARS outbreak was being contained was followed by an effective news blackout in the run-up to the National Party Congress in March 2003.

In April 2003, a surgeon in Beijing finally blew the whistle, claiming many cases in the capital had been covered up. The authorities in Beijing were slow to consent to WHO requests to investigate. The epidemic, which seeded large, deadly outbreaks in Hong Kong,

Taiwan and Canada, was contained by August 2003 but the inglorious debut of SARS still serves as a benchmark for how not to handle a new disease. It took four months for China to report cases to the WHO, and another month before the coronavirus SARS-CoV-1 was unveiled as the pathogen responsible for the disease.

SARS was the costly catalyst for change in China: the country strengthened its disease surveillance network and put in place an online reporting system accessible by any hospital. It wasn't a half-hearted tweaking of the system but a radical rethink: the China CDC became a slick, professional, science-focused organisation, with fresh buildings, a new infrastructure and highly trained staff capable of gracing any world-class research institution – George Gao among them.

But the lessons from SARS still sting. Speed and openness are essential.

That is why Eddie contacted me. He needed to share the burden of the knowledge he had been building up in that first week in January: that the virus responsible for this mysterious pneumonia in Wuhan had been sequenced as far back as December 2019; that Zhang's consortium had a paper waiting to go; and that China knew the virus had been sequenced but had not yet released the information.

Eddie and I had a series of frantic calls between London and Sydney on the night of Thursday 9 January, which stretched into the early hours of Friday. We hatched a plan that Eddie would go back to his collaborators in China and I would go back to George Gao at China CDC. We would threaten to go public if they refused to disclose the information by Saturday morning GMT.

We decided to tell them, 'If you don't release the sequence in the next 24 hours we will release it the next day.' By 9.18pm London time, and 8.18am in Sydney, Eddie and I had committed to the high-stakes pact to force China's hand.

I felt terrible because I'd never done anything like that before – but issuing an ultimatum felt like the only way. News was filtering out about healthcare workers falling sick. Waiting for the wheels of China's bureaucracy to turn quickly enough to make a formal

declaration just before Chinese New Year, which lay two weeks away, was too dangerous. It would have taken days and, frankly, we didn't have days. Once it was clear this was a SARS-related coronavirus spread by the respiratory route and that healthcare workers were succumbing, it was clear that things were going to deteriorate quickly.

The world had to have access to that sequence because the world needed to be able to diagnose it. It was going to appear in Beijing, in Hong Kong and Singapore in the hours or days that followed. It was going to spread everywhere.

Eddie remembers the pressure-cooker atmosphere of those days too. Zhang deserved public credit for leading the consortium's sequencing breakthrough – but Eddie also knew his colleague would also be at the sharp end of Beijing's displeasure for shattering the government's code of silence. 'My big concern was not getting Zhang in trouble,' Eddie says now. 'I called him and said, "There's a lot of pressure to release the sequence. I think we have to do it". Zhang was on a plane going from Shanghai to Beijing, on the runway literally waiting to take off.'

Zhang asked his collaborator for a moment to think. It didn't take long. Perhaps Zhang had already decided the world had waited long enough. Before the plane took to the skies, Zhang rang Eddie back with a simple message: 'OK, let's release it.' Eddie phoned me immediately.

By the time Zhang's plane touched down just over two hours later, the information was out.



The drama that preceded publication was followed by first comedy and then tragedy.

Comedy, because almost as soon as Eddie had promised to Zhang he would release the sequence, he realised he didn't have it. Eddie had no need of the sequence itself in order to carry out his virological analysis for the *Nature* paper; his contribution just entailed sending suggestions of further work to colleagues in China. A colleague of Zhang's in Shanghai quickly emailed the sequence over.

Without a moment to lose, Eddie rang Andrew Rambaut, an evolutionary biologist at the University of Edinburgh and a trusted contact. The clock was approaching midnight for Andrew but, as Eddie knew, his friend always worked late into the night. Andrew runs an open-source website, virological.org, collating information, including genome sequences, on viruses that might be of interest to other scientists – and agreed during the phone call from Eddie to publish the sequence.

Andrew had no qualms about being an accomplice to the release: ‘I’ve known Eddie for years,’ Andrew says. ‘I trusted that he and Zhang knew it was the right thing to do. Once it had been quality controlled and we were sure it was the right genome, there was no justification for delay.’

Eddie and Andrew set about compiling all the information that would go public. They wrote a little blurb about what the sequence was, who it came from (Zhang’s consortium) and who to ask permission from if anyone wanted to use the data. That blurb went back and forth a few times between Sydney and Edinburgh to make sure it had all the correct information. Andrew immediately uploaded it to virological.org and Eddie posted news of the data release on Twitter.

Eddie is rightly proud of how quickly things happened: ‘I’ve timed it: I had that sequence in my possession for 52 minutes before it was published.’ Speed matters perhaps more than anything else in disease outbreaks.

But Eddie had also been so consumed with the cloak-and-dagger intrigue of publishing the sequence that it dawned on him he hadn’t stopped to check it before pressing ‘upload’. ‘It could have been any old shit,’ he smiles now, wincing at the memory. ‘After I’d posted it, I thought I’d better check it was actually a coronavirus. Luckily it was!’

It was done. At 1.05am GMT on Saturday 11 January 2020, under a week after the virus was sequenced by his colleagues in China, a post entitled simply ‘Novel 2019 coronavirus genome’ appeared on virological.org, under Eddie’s name. A short note underneath explained he was acting on behalf of a consortium led by Professor

Yong-Zhen Zhang of Fudan University. The consortium included hospitals and health authorities in Wuhan, plus the Chinese CDC and Sydney University.

I had been on high alert for this moment, and immediately praised the release on Twitter:

Potentially really important moment in global public health must be celebrated, everyone involved in Wuhan, in China & beyond acknowledged, thanked & get all the credit. Sharing of data good for public health, great for those who did the work. Just needs those incentives & trust.'

I wanted to send out the message that fast data-sharing in a global public health emergency is absolutely the right way to go. It opened the floodgates in the way we hoped it would: other researchers jumped on the newly released data and immediately started analysing it. Unsurprisingly, Andrew was one of the first: he concluded there was 89 per cent overlap with a coronavirus found in bats.

The publication, in defiance of the gagging order, seemed to wake China up. Later, on 11 January, China CDC sent the genetic sequence privately to the WHO; the agency responded by saying it hoped China would make the sequence public. This China did, on Sunday 12 January, confirming the sequence that Eddie and Zhang had posted.

As time has passed, Eddie has come to believe the silence from the Chinese government and CDC in the earliest days of January 2020 was down to panic management, control of the message, and, remarkably, the prestige of publishing first. As Eddie puts it: 'They [the Chinese government] didn't want panic, because the word SARS is toxic to them. They wanted to control the message, because that's what China does, and they wanted the big paper themselves. So much of science is about ego, for me as well. Who doesn't want the first paper?'

That the information wasn't shared earlier, Eddie thinks, may also have been down to a miscalculation: that this new virus was sufficiently like the original SARS virus that it would only transmit when people had symptoms. Eddie says: 'I think in early January

2020 people in China thought it would just cause an outbreak in Wuhan. It might get a bit further, but it won't spread that far and they'll control it. I honestly think that's what they thought would happen.'

That delay would turn out to be a misjudgement for both China and the world. Asymptomatic and pre-symptomatic transmission allowed the virus to spread widely: at the beginning of an epidemic, people cannot contain what they cannot see.

If that January weekend opened with a mixture of drama and comedy, it ended on a note of tragedy. On Saturday 11 January came the first reported death from the new coronavirus, a 61-year-old man who regularly visited the seafood market. The day after, Zhang's laboratory at Fudan University in Shanghai was shut down temporarily by the authorities for 'rectification'. It was the price that Zhang, who had set up his own lab partly to cut loose of CDC shackles, would pay for defying the Chinese government.



On the day that Zhang's laboratory was shuttered, the WHO released a news update stating it was 'highly suggestive' that the outbreak was related to exposure at the seafood market. The statement noted that no cases had been seen outside Wuhan, downplaying fears that it might be contagious: 'there is no infection among healthcare workers, and no clear evidence of human-to-human transmission'.

By the time this statement was posted, several people inside China must have known this to either be untrue or contrary to emerging evidence. The intelligence came via an email from someone I had worked with before, a researcher at Erasmus University in the Netherlands.

From: T. Kuiken

Date: Saturday, 18 January 2020 at 16:08

To: Jeremy Farrar

Subject: Wuhan coronavirus

Dear Jeremy,

Sorry to bother you on the weekend, but I have a dilemma about not disclosing info about the Wuhan coronavirus that I think should be made public. Do you mind to phone me about this at your earliest convenience at +31 ...

Best wishes, Thijs.

Thijs Kuiken, a veterinary pathologist by training who advises the Dutch government on the threat posed by zoonotic diseases (diseases that are transmitted between species, usually from animals to humans), is one of the unsung scientific heroes of the pandemic. He was sent a research paper on 16 January 2020 by the *Lancet* medical journal, to review for publication. This was one of the standout moments in the whole epidemic, the reddest in a constellation of red flags.

The *Lancet* paper set out how, in early January, a team led by scientists at the University of Hong Kong studied a family of six from Shenzhen, a southeastern city in China, who had travelled to Wuhan over the New Year to stay with relatives. None of them had gone to the seafood market, though two had visited a Wuhan hospital. Five caught the novel corona-virus. On their return to Shenzhen, another family member who had not travelled to Wuhan fell ill.

Here was the critical information that suggested the virus could jump from one person to another, and that it was spreading outside Wuhan. The paper concluded: 'Our findings are consistent with person-to-person transmission of this novel coronavirus in hospital and family settings, and the reports of infected travellers in other geographical regions.'

Even more alarmingly, the paper contained two other vital pieces of information about the new disease: one infected family member was excreting virus without showing any clinical symptoms, suggesting the frightening possibility of asymptomatic spread; and some of the other infected relatives had diarrhoea as their chief or only symptom, which did not feature among the signs that medics had been urged to look out for.

Scientists who review research papers – to check before publication for errors, and that the methods, analysis and conclusion seem reasonable – are sent those papers in confidence. Secrecy is a

golden rule for most journals during this well-established checking process, known as peer review. Not only is it a courtesy to peers to judge each other's work in confidence but original research is also harder to get published if it is already in the public domain.

The confidentiality requirement put Thijs in a dilemma: his role as reviewer officially precluded him from sharing the findings – but it meant he was sitting on information that was obviously vital to an unfolding health emergency in which every passing day mattered. And it was information that, for whatever reason, China had not yet disclosed to the WHO.

'I was asked to review the paper within 48 hours so I sent in the review the next day, on the Friday morning,' says Thijs. 'Separately, I immediately contacted the *Lancet* to say the information should be made public because it was the first scientific proof that the virus was spreading human to human. They either would not or could not do it. I also strongly recommended to the authors that they should make the findings public. That did not happen either.'

Thijs spent Friday and Saturday morning monitoring emails, Twitter, ProMED and WHO updates to see if the information had trickled through the system and out into public channels, but there was still no word of human-to-human transmission. That prompted Thijs's email to me on 18 January.

I called him straight back and agreed wholeheartedly that the information should be shared as soon as possible in the interests of public health. If there was a novel contagious disease that could spread asymptotically between people, and a relative of SARS at that, the world needed to know immediately. I emailed and called the *Lancet's* editor-in-chief, Richard Horton, left him a message, and took our dog Coco for a walk to clear my head. I emailed Thijs when I got back:

Date: Saturday, 18 January 2020 at 18:11

To: T. Kuiken

Subject: Re: Wuhan coronavirus

Thijs

Thinking aloud whilst trying to get through to Richard.

Option A – Do nothing and wait for it to go through the system

Option B – Leave until Monday and speak with Richard then

Option C – release a summary online such as

Aware of a manuscript submitted which shows

H-2-H transmission within a family cluster in a city away from Wuhan.

That people are viral +ve and may be infectious when asymptomatic/very mild symptoms and afebrile.

That transmission may be by more than respiratory ie diarrhoea.

That this is present in cities in China beyond Wuhan.

That there is ongoing transmission.

Viral sequence available.

Releasing this information for public health benefit.

Encourage those with this (investigators and editors) to release immediately and publish at a later date

Thoughts?

I would be happy to do Option C if you felt appropriate and if you think the summary accurate reflection of the important public health message.

To be honest I was angry that Thijs had found himself in this impossible position. With Thijs's permission, I rang Maria Van Kerkhove, from the WHO's Health Emergencies Programme, to alert her, without revealing Thijs's identity. Maria, who I trust completely, immediately saw the seriousness of the situation, and asked for the anonymous reviewer to contact her in confidence.

By Saturday evening, Thijs had had enough. He emailed his contact at the *Lancet* to say that if the information had not been made public by the morning of Sunday 19 January, he would inform the WHO.

In his willingness to go rogue, Thijs made a selfless calculation. He could understand why the *Lancet* was unlikely to break cover: it would be damaging for a prestigious journal to rip up its covenant of confidentiality to scientists submitting manuscripts. He also grasped

that the scientists were frightened of going public because the Chinese government was threatening to jail anyone revealing sensitive information about the epidemic. Evidence of human-to-human transmission was about as sensitive as it could get. The shutdown of Zhang's lab after releasing the coronavirus sequence against the will of Beijing, and the arrest of those in Wuhan spreading information on social media, was having the desired chilling effect.

The only thing Thijs had to lose was his reputation – and the trust of his colleagues. Yet he was prepared to make that sacrifice, an enormous one for a leading scientist. He reflects now: 'I knew I would be breaking a very strong rule for a scientist [by going public], and that I might not get sent any more manuscripts for review because journals and scientists might not trust me. But it would just be me who was burnt and I thought it was for the public good.

'I had been involved with SARS and I knew that it was only stopped from being a worldwide outbreak because of good public health measures, plus the fact that the virus was just a little bit too slow. I worried that this new coronavirus was going to be a big pandemic because it was spreading so fast out of Wuhan. There were too many cases to be explained just by direct transmission from animals. There was only a small chance of stopping it, and this information was one of the things that could make a difference.'

In one way Thijs handled it perfectly and correctly: he did not send either me or Maria the paper, only a two-page summary and the conclusion (he did initially think of sending the entire paper to the WHO but could not bring himself to do it). Given the sensitivities, Maria concluded the journal should publish as soon as possible; and meanwhile she began quietly incorporating the possibility of asymptomatic human-to-human transmission into WHO discussions on guidance and actions to be taken by countries.

Thijs could so easily have taken the easy option: reviewed the paper, stayed silent and waited for the news to come out on publication, which could have added weeks of delay. The world should be grateful that he did not.

The next day, on 20 January, China confirmed human-to-human transmission. The paper was published online by the *Lancet* on 24 January 2020. So, it was official: the new decade had recorded its first new highly transmissible viral respiratory disease, which could kill some and yet leave others untouched. Carriers could be both asymptomatic and infectious. The world had no natural immunity to this novel virus, and no diagnostic tests, vaccines or treatments.

The virus had all the makings of a nightmare.



Eddie has screenshots taken from social media in China about the coronavirus sequence. They suggest the full genome was known by a genomics company in China by 27 December 2019. It was reported to both China CDC and the hospital who provided the patient sample, on 27 and 28 December. Samples appear to have been sent to a second sequencing company, who provided the sequence by 30 December.

That would fit in with Eddie thinking that Zhang was merely confirming what Beijing already knew.

Something has bothered me since: how could George Gao confidently rule out SARS as the cause of the mystery pneumonia cases, as he asserted to me at the beginning of January, without either evidence or a strong suspicion that it was something else? Good scientists like George don't pluck facts from thin air, nor indulge in random guesswork. George has not replied to requests for an interview but he has assured me he did as much as he could to push information into the public domain, including through international journals, as quickly as possible. I believe he did as much as humanly possible within a system.

Frankly, we don't know for sure how long China sat on any of this information in December 2019. All the elements that Eddie mentioned – about China seeking to control the message and avoid panic, and coveting the first scientific paper – are probably relevant, but it was also nearly Chinese New Year and the middle of the flu season. Sifting out a novel pathogen from lab samples will always be

challenging: respiratory samples are filled with microbial bystanders, a cocktail of benign viruses, fungi and bacteria that can obscure a rare interloper. I tend to believe in cock-up as much as conspiracy.

There is, however, one message that must cut through: we have got to be quicker and do better when it comes to novel disease outbreaks. Diagnosis is difficult and must improve: having people come in with a respiratory infection that remains undiagnosed is not acceptable anymore. We must be nimble at spotting clusters of illness, such as among family members, and, especially, taking notice when health workers start falling sick. We should be on high alert for unusual symptoms, particularly in critical care; every epidemic of the past two decades has been spotted by critical care clinicians first. The science needs to be shared more speedily, too. Not immediately releasing the sequence is unacceptable. The lag in reporting the human-to-human transmission that had been discovered weeks before it was revealed in the *Lancet*, hindered the early outbreak response.

If each of these elements builds in a delay of half a week, and you've got five different elements, that adds up to a nearly three-week delay. A hierarchical, bureaucratic reporting line system, from a hospital to a provincial arm of the China CDC to the Beijing CDC and back again, doesn't help, especially around Chinese New Year. That could easily build in another two-week delay. That equates to five lost weeks in which spread could have been contained. Even though sectors like online retail and finance live in an age of real-time digital data flows, public health data flows remain stubbornly analogue.

I often wonder whether London, with its nine million people and many hospitals, could have done any better than Wuhan. We could have had one patient in King's College Hospital in south London, two in University College Hospital in central London, one with relatively mild pneumonia and one in intensive care, and two in the Royal Free Hospital, to the north of the city; perhaps another two who'd commuted north out of London to different towns, and another two who had travelled south. Would we have picked up a handful of unusual pneumonias in such a big city in a month, in the middle of flu

season? I doubt it. In 2019, the American Thoracic Society noted that, for most pneumonia patients, the microbe causing the infection is never identified.*

In most parts of the world, people with a respiratory infection will not undergo a diagnostic test. Others might get a blood culture; in a few places around the world they might get a swab sent off to check for flu or respiratory syncytial virus, another common respiratory virus. If those came back negative, most doctors would shrug their shoulders and say, 'There's something wrong with this patient but I haven't got a clue what it is. Let's start antibiotics and hope for the best.'

Look what happened with the SARS-CoV-2 variant B.1.1.7, which created havoc in the UK at the end of December 2020 and was the dominant variant of coronavirus around the globe within three months. The UK reported it to the WHO in December, but it first appeared and was sequenced three months previously, in September. Its prevalence only became an issue once genomic surveillance revealed the variant was linked to a surge of infections in Kent in south-east England.

Knowledge must be shared in hours and days, not weeks, and knowledge must lead to action. China may have delayed releasing the information for two or three weeks in December 2019, but the world had all the information it needed by 24 January: a potentially fatal novel respiratory disease that could spread between people without symptoms, with no vaccines or treatments, that had already ravaged a huge, highly connected Chinese city. Early scientific papers from China were spelling out its grim clinical consequences in patients: early symptoms of fever, dry cough, body aches, headaches, progressing to difficulties with breathing, blood clots, pneumonia and, in the worst cases, wider organ failure and death.

Many countries failed to act for many weeks after, or took too long to convert decisions into action. As the virus stirred, much of the world slumbered.

Instead, the new coronavirus kindled a different kind of interest. That is how I came to possess a burner phone.

* Pneumonia is an inflammation of the lungs, and specifically the small air sacs, called alveoli, that make up the lungs. The inflammation can be caused by a bacterium, virus or fungus. The infection causes the air sacs to fill with fluid or pus. Symptoms can run from mild to severe and include coughing, fever, chills and trouble breathing. Infants and the over-65s are most vulnerable.

2

What do the Chinese know that we don't?

20 JANUARY 2020

Known cases: 282.

(China: 278; Thailand: 2; South Korea: 1; Japan: 1)

6 deaths in Wuhan.

ON 20 JANUARY 2020, Tedros Adhanom Ghebreyesus, the WHO director general, texted me. He was due in Davos, Switzerland, next day, for the three-day annual gathering of the World Economic Forum but things were moving too quickly for him to leave Geneva. Could I take on some of his commitments, he asked, while I was at Davos? He was anxious for the world's decision-makers to understand the significance of the new transmissible respiratory virus emerging in China.

He had changed his plans because the WHO was due to hold an emergency meeting on 22 and 23 January. The meeting would establish whether the Wuhan outbreak constituted a Public Health Emergency of International Concern (PHEIC).

A PHEIC is defined, under the International Health Regulations that frame the WHO's mandate, as 'an extraordinary event that may constitute a public health risk to other countries through international spread of disease and may require an international coordinated response'. The 'Wuhan coronavirus' (by then named 2019-nCoV,

meaning 2019-novel coronavirus) had spread beyond China, with cases detected in South Korea, Japan, Thailand and Singapore. Now the WHO, and Tedros specifically, had to decide whether it posed a threat to the world. Given this was a SARS-like coronavirus known to be passing from person to person, a declaration seemed likely.

The groundwork for these judgement calls is laid by a WHO Emergency Committee, a select band of around 20 unpaid specialists from such diverse fields as virology, infection control, vaccine development and infectious disease epidemiology. One member of the Covid-19 Emergency Committee is Marion Koopmans, a virologist in the Netherlands who would later play a key role in researching the origins of the virus. Members draw on evidence and advice from many others.*

The framework is frustratingly binary: an outbreak either is, or is not, a public health emergency. Both conclusions come with double-edged consequences. A declaration can, usefully, spur countries to act, to prepare for a possible surge in illness, but can also disrupt trade and travel if borders close. Shuttering countries can also stop medical supplies getting to where they are needed.

Shying away from a declaration, on the other hand, might prevent panic but if the globe's top health agency doesn't deem an outbreak a global emergency, the world tends to shrug its shoulders.

The last PHEIC came in 2019, when Ebola broke out in the Democratic Republic of Congo (distinct from the biggest recorded Ebola outbreak in West Africa, a 2014 PHEIC). Before that, a declaration was made in 2016 for the Zika virus epidemic in Brazil (the epidemic came to light after doctors noted a rise in the number of babies born with microencephaly, or unusually small heads).

These high-stakes calls can burnish or tarnish a WHO director general's legacy. Margaret Chan, Tedros's predecessor, is believed by many to have taken too long to call a PHEIC in 2014 over Ebola in West Africa. The Ebola PHEIC in 2019 was called at the fourth time of asking: it could, and should, have been called the year before. Tedros accepts that.

A declaration gets things moving, unlocks funds, galvanises leaders – ultimately, it saves lives.



The International Health Regulations Emergency Committee teleconference meeting on the novel coronavirus opened in Geneva at midday on 22 January 2020, with a briefing by WHO lawyers. Committee members were reminded of the gravity of their responsibility and urged to act ethically and with a duty of confidentiality. More than four hours later, after hearing about the situation in Wuhan, and China’s response, the committee declared itself divided on whether to issue a declaration. By this time, remember, the WHO was privy to information contained in the *Lancet* paper that Thijs Kuiken in the Netherlands was sent in confidence; namely, that there was evidence of human-to-human transmission, including without symptoms.

And then came a dramatic update: word arrived from China that the government was going to take the unprecedented step of locking down its citizens to contain the virus. From 10am on Thursday 23 January 2020, reported China’s *People’s Daily* newspaper, nobody would be allowed to leave Wuhan apart from under exceptional circumstances. The airport and train stations would be shut; bus, subway, ferry and other transport services, suspended. Citizens would be ordered to stay at home or risk arrest.

Eleven million inhabitants would be trapped inside the city, just two days before the start of Chinese New Year. This would be the biggest recorded quarantine in history. The news sent shockwaves through the WHO and around the world. Tedros had not been informed in advance of China’s drastic plan. He asked the Emergency Committee to take this extreme measure into account during their deliberations the following day, when a final decision would be arrived at.



As the tension was ratcheting up in Geneva, I was co-hosting a lunch in Davos, listening to the head of a global bank telling an audience at the World Economic Forum about his struggle with work-related stress. António Horta-Osório, who ran Lloyds Banking Group until July 2020, revealed how he had sought help from the Priory Clinic, a mental health retreat usually associated with celebrities undergoing rehabilitation for drug and alcohol problems. Most people don't talk frankly about their personal troubles but that's the bizarre thing about Davos: here was a top executive discussing his mental breakdown in front of some of the most powerful people in the world. I can't think of anywhere else that brings people together quite like that – from the worlds of business, money, politics, health, academia, plus global agencies and the world's media.

That is why I have been attending for the past five years. You can reach so many audiences – and, whether we like it or not, capitalists can and mostly do make the world a better place. They certainly have a responsibility to do so. Davos hosted the launches of both GAVI, the Vaccine Alliance, in 2000, and the Coalition for Epidemic Preparedness Innovations (CEPI) in 2017. Both have brought about incredibly positive change: GAVI, by vaccinating more than 800 million children in the poorest countries; CEPI, by financing and developing vaccines for diseases including Nipah fever, Lassa fever, Ebola, MERS and Covid-19 (CEPI gave early financing to the Moderna Covid-19 vaccine). During the past two decades, GAVI has prevented an estimated 14 million deaths.

The lunch at which António spoke was co-hosted by Wellcome and Lloyds and boasted a starry list of guests, including the British model Lily Cole. It was intended to lay the groundwork for the 2021 World Economic Forum, on the theme of mental health, particularly in the workplace.

Instead, rumours of China's mystery pneumonia were swirling everywhere and everyone wanted to know more. When the CNN anchor Fareed Zakaria interviewed the then chief executive of Hong Kong, Carrie Lam, on stage at Davos, he opened not with the pro-

democracy protests in the former British colony but with the new disease.

‘Let me start by asking you something that’s on people’s minds right now,’ Zakaria said smoothly. ‘What can you tell us about the Wuhan virus, or what some people are calling the China virus? How rapidly does it seem to spread? How worried should we be?’

Lam gently reminded Zakaria that it was now being referred to as the novel coronavirus pneumonia and Hong Kong was well prepared: holiday camps were being turned into isolation facilities.

Then she added: ‘A couple of hours ago, Hong Kong health authorities have just announced we have the first case of highly suspicious infection in Hong Kong from a passenger from Wuhan ...’



For the well-connected delegates at the World Economic Forum, this unknown pneumonia was still happening a long way away. There were no travel restrictions, no social distancing, no masks. The world looked just as it always had.

I appeared at a press conference at Davos on 23 January 2020 with Richard Hatchett, the head of CEPI and a White House adviser during the H1N1 outbreak of 2009; and Stéphane Bancel, the now superstar head of biotech company Moderna. Stéphane was already working with CEPI on other vaccines and only that week had inked an agreement with Richard to start work on a coronavirus vaccine.

The sombre meeting, in a darkened Issue Briefing Room, was briskly chaired by Juliana Chan, a science communicator from Singapore (where I was born). Just before the press conference, Singapore announced its first case of the ‘Wuhan virus’. There were one or two Western journalists present but it was mostly Chinese media in attendance.

I was asked to speak first. I was in the spotlight. The truth could not be sugar-coated.

‘We are about six weeks into this outbreak and this virus can now clearly spread between humans,’ I told the audience, explaining it

could be passed on like influenza, through coughing and sneezing. 'It is not SARS. The virus is in a similar family as SARS but this looks different ... and the difference is probably it is easier to pass between human beings. I think we can expect many more cases in China and many more cases in other parts of the world.'

Richard then emphasised how much was unknown, such as how infectious the virus was; the pattern of transmission; the range of symptoms and whether they ran from mild to severe; the exact number of cases; how far it had spread geographically.

It is strange to watch the press conference now, to see how little attention anyone paid to Stéphane. Nobody in the audience asked him a single question. His company had quietly picked up the genetic sequence more than a week earlier, on 13 January 2020, and had already begun prepping to produce a prototype messenger RNA (mRNA) vaccine. This is completely new technology: it injects mRNA, a set of genetic instructions for building a bit of the target virus, so that the body's own cells can make the viral protein in-house, to stimulate an immune response. This technology platform, as we have since learned, has the potential to go much faster than conventional vaccine production.

Stéphane urgently needed cash, he had told Richard a few days before Davos, to turn Moderna's baby steps on this new coronavirus into phase 1 trials. In the end, there were just three days between Stéphane's pitch and Richard's sign-off. The tie-up was being announced at the press conference, along with two other CEPI partnerships (with Inovio, for a DNA vaccine, and the University of Queensland in Australia).

As we sat lined up behind the desk and the microphones, Stéphane could see Richard's and my phones buzzing constantly with new updates from Wuhan. The three of us had been meeting up and pooling information, some of it coming from Wuhan and the rest from contacts in the infectious disease community.



In the Q&A session at the press conference, a journalist asked if there was any precedent for China's strict lockdown of Wuhan. Richard pointed out that 'when you don't have treatments and you don't have vaccines, non-pharmaceutical interventions are literally the only thing that you have ... isolation, containment, infection prevention and control, and these social distancing interventions'.

And yes, Richard nodded, there was indeed a precedent: how US cities shielded themselves during the Spanish flu pandemic of 1918. 'We found that cities that introduced multiple interventions early in an epidemic had much better outcomes,' he said.

He was referring to a 2007 study of how 43 US cities responded to the arrival of Spanish flu in 1918: those that closed schools and banned large gatherings for long periods earliest in the pandemic fared best. A comparison of excess deaths per 100,000 of population between September 1918 and February 1919 is instructive: Philadelphia, which had 51 days of closures, but belatedly and with not every measure applied at the same time, saw about 250 excess deaths per 100,000 at the peak; St Louis, which acted early and shut down hard for 143 days, saw 30.

But such measures, Richard added, come with drawbacks: they are hard to sustain and create mass anxiety, making the search for vaccines and treatments even more urgent. That's why CEPI had signed three deals; researchers could start working on vaccines straightaway.

Juliana, the moderator, noted that Chinese New Year lay just two days away, when an estimated 450 million Chinese would normally be on the move. Some had already left. 'In many ways, this outbreak could not be happening at a worse time,' I agreed, unthinkingly clicking a ballpoint pen on and off.

I admitted I'm not a huge fan of travel restrictions because people can get round them by using other routes, though they do usefully signal to the public that the situation is serious. They also buy time to put tried and tested health measures in place: testing, contact tracing and quarantine. It might only be a day, a week or a month, but that is better than nothing. Still, there was a catch: border controls must be

put in place early, comprehensively and for a long time, as New Zealand did.

Meanwhile, China's sudden lockdown was adding uncertainty and complexity to the second day of emergency deliberations in Geneva. The WHO Emergency Committee advised Tedros that not much had changed from the day before; they still could not decide whether to declare a global emergency.

It was clear that, at that time, there was more to worry about than the week before. There were mass lockdowns in China; rising concerns in the region and beyond about an entirely new transmissible, untreatable respiratory virus of unknown origin; cases were climbing in China and appearing in other countries. People were beginning to draw parallels with 1918.

For all that, the Emergency Committee still could not make up their minds. Tedros had to come down one way or another. On 23 January 2020, the WHO issued a statement concluding that the pneumonia spreading from Wuhan was not a Public Health Emergency of International Concern.

The committee would meet again in a week, sooner if necessary.



Moderna started working on the Wuhan coronavirus in early January as a test run for when a real pandemic hit – never expecting this would be it.

Stéphane recalls: 'Our mindset was, let's do this vaccine to see how quickly we can go, because one day there's going to be a flu pandemic and we'll know what we can do. I was worried it might be a distraction. We already had 20 products [in development] in clinic and it was really busy – there was nobody sitting idle to do the project.' Stéphane made a pact with Anthony Fauci, the director of the National Institute of Allergy and Infectious Diseases (NIAID) in the US: Moderna would make up an experimental vaccine and Tony's labs would do the clinical testing.

Davos changed everything, Stéphane told me later. The three of us – Richard, Stéphane and I – were texting each other and grabbing quick coffees between sessions so we could share the real-time updates coming directly from contacts on the ground in Wuhan, which were ahead of the officially reported figures. We were scribbling back-of-the-envelope calculations of how the new coronavirus was spreading, and sketching out scenarios on paper napkins (I wish I had kept the napkins). We were getting case descriptions of patients' symptoms from ground zero, which was exactly the kind of intel that Stéphane wanted to know; Richard and I were laying out everything we knew about coronaviruses.

During one of our meetings, Stéphane realised how little he knew about Wuhan. He recalls: 'I was a bit slow. I knew it was in China but I didn't know how big it was. So, I get my iPad out during one of the coffee chats and find it's this big industrial city. And then I look at the flights out of Wuhan and realise they go to all the Asian capitals, all the European capitals, and all the big cities on the West Coast of the US. I remember looking up and saying, "Oh shit, it's everywhere".'

It was while we were in Davos that China locked down Wuhan. Stéphane ran into us the next morning, saying 'Jeez, I don't remember any government shutting down a city of that size – ever. What does the Chinese government know that we don't know?'

That was when he knew Moderna had to get serious about its hastily convened side-project. He was meant to be in Germany the weekend after Davos for a business meeting but woke up in a sweat one night, convinced he had to change plans. Stéphane cancelled, sent his apologies and asked his assistant to book him a one-way ticket to Washington DC.

He arranged back-to-back meetings in DC with: Tony Fauci; John Mascola, head of the Vaccine Research Centre at the National Institutes of Health (NIAID comes under the NIH umbrella); and John's deputy Barney Graham, who would fix up the vaccine trials. He also trudded round an alphabet soup of organisations involved in epidemic response: DARPA, BARDA and the FDA.*

‘I have never done a thing like this in my life – gone somewhere not knowing when I’m going to come back,’ Stéphane says now. ‘But that week, and those days at Davos, really changed my mind from, “This is an outbreak” to “Shit, this is a pandemic like 1918 and it’s going to affect the entire planet for a long time”. I have worked in infectious diseases for 25 years and knew every day mattered, because of exponential spread. I knew we had to start running for our lives with the vaccine.’

There followed a heartbreaking struggle during the spring of 2020 to raise money to build manufacturing lines, which saw him touring the world pleading for cash: ‘I begged the entire planet: foundations, governments, heads of state. In May I hit my lowest point. I was so depressed and upset because I felt I’d failed the world.’

But on 18 May 2020, within five months of the novel disease coming on to the world’s radar, the first promising results landed from the phase 1 clinical trials. The vaccine, code-named mRNA-1273, was safe, well-tolerated and, crucially, producing the right kind of antibodies in participants.

Moderna was about to tout for more investment when a call came through from James Gorman, CEO of Morgan Stanley. It was the lifeline that Stéphane had been hoping for: ‘He was like, “I don’t want you to waste time, you need to focus on the vaccine. The bank will buy the stock and take the risk to sell it back to investors.”’

When the markets closed that day, Gorman made good on his promise to the tune of \$1.3 billion. For Moderna, at least, the race to a vaccine was back on.



By the last week in January 2020, many of us feared the number of cases in China was the tip of an iceberg, because of mild or asymptomatic cases accumulating unseen beneath the surface, as that early *Lancet* paper had suggested. I was baffled by the WHO’s decision not to declare a health emergency, as was Tony Fauci in the US.

At Davos, Richard Hatchett from CEPI began looping me into emails with people in the US who were trying to parse the size of the threat and how to get ahead of it. The group included figures in Homeland Security, healthcare companies, the army and public health; they would each bring one or two other voices into the loop to crowdsource information. It was driven by a fascinating left-field thinker called Carter Mecher, who Richard had met during his time advising the White House. Carter is a doctor and former public health adviser in the US Department of Veteran Affairs. He had also worked on pandemic preparedness under George W. Bush, and his emails brought some of the old team together (they had called themselves the Wolverines, after the fictional Marvel Comics character with superhuman senses). By 22 January, Carter had pulled together a quick comparison of SARS, MERS and the new coronavirus and wrote: ‘This is taking off faster than SARS...’ Early on, he was advising we assume some asymptomatic transmission.

Carter brought incredible insight into those nascent discussions, translating information from China and pointing out that, as had happened with disasters such as the *Deepwater Horizon* oil spill and the Fukushima nuclear accident, public blogs would be a valuable source of inside information and scattered with the technical detail we needed to make forecasts (among those he recommended was flutrackers.com). By 23 January, Carter had pulled together an Excel spreadsheet with case numbers pulled from ProMED-mail and various blogs, coupled with dates of when people had fallen ill and died. His verdict? ‘[We are] not going to be able to outrun it.’ Back then, he was already mooted TLC, or ‘targeted layered containment’, the kind of measures that many countries would eventually adopt.

That was the day that Wuhan was locked down. It was also the day that he asked us all a question that would stay with me: ‘Two weeks from now, are there things that we wished we could have done to reshape the challenge we will likely face? ... We have a very narrow window to act.’

The aim, Carter said, was to ‘shape the battlefield’.



After Davos, I was sure this was turning into a global pandemic. I discussed with Patrick Vallance and Chris Whitty, the UK government's chief scientific and medical advisers, how the country should prepare and that we should try to start vaccine clinical trials as soon as possible in case US President Donald Trump refused to share future American-made vaccines. I harboured reservations about the lacklustre reaction in the UK. There was a notable lack of public communication on what was unfolding abroad and intensive care units across the UK were already running at full capacity, which has, unfortunately, become the norm.

At my own organisation, Wellcome, a contingencies team was already contemplating the possibility of home working, travel disruption and school closures. As I wrote in an email sent (apologetically) on Saturday 25 January 2020 to a handful of colleagues:

This cannot be contained in China. and will become a global pandemic over the next few days/weeks of uncertain severity. Since Influenza 1918 things have never turned out quite as bad as they appear early on ... but this is the first time since SARS I have been worried ... I worry they [the UK government] are underestimating the potential impact.

On Monday 27 January, I joined a teleconference that brought together, among others, chief scientific adviser Patrick Vallance (he organised the meeting); chief medical adviser Chris Whitty; Mark Walport, who then led the government funding body UK Research and Innovation (and my predecessor as Wellcome Trust director); Jonathan Van-Tam and Jenny Harries, England's deputy chief medical officers.

That crucial call listed the first steps the UK needed to take to get on top of vaccines, treatments and diagnostics, such as scouting out experts on coronaviruses, issuing a call to vaccine research groups (we expected Imperial College in London and Oxford University to apply, and both duly did), and asking the national drug regulator to streamline its approval process. One suggestion aired at that

conference was for Porton Down, the government's top biohazards laboratory, to work on developing a diagnostic test for asymptomatics, the hidden spreaders who carry the virus without showing symptoms.

But at the time a new and even deeper crisis was brewing. After the genetic sequence of the virus was published, people began noticing something peculiar about its molecular structure. In the last week of January 2020, I saw email chatter from scientists in the US suggesting the virus looked almost engineered to infect human cells. These were credible scientists proposing an incredible, and terrifying, possibility of either an accidental leak from a laboratory or a deliberate release.

That got my mind racing. This was a brand-new virus that seemingly sprang from nowhere. Except that this pathogen had surfaced in Wuhan, a city with a BSL-4 virology lab which is home to an almost unrivalled collection of bat viruses. 'BSL' stands for 'Biosafety Level' and 4 is the highest designation, indicating authorisation to handle the nastiest pathogens known to humankind, such as the Ebola and Marburg viruses.

These kinds of labs are, unsurprisingly, rigorously controlled environments: the air is filtered; the water and waste is treated before it leaves the lab; workers change into hazmat suits and shower before and after stepping inside the containment facility. The BSL-4 at the Wuhan Institute of Virology (WIV) is built above a flood plain to withstand a magnitude-7 earthquake. The security in these labs around the world is remarkable.

It seemed a huge coincidence for a coronavirus to crop up in Wuhan, a city with a superlab. Could the novel corona-virus be anything to do with 'gain of function' (GOF) studies? These are studies in which viruses are deliberately genetically engineered to become more contagious and then used to infect mammals like ferrets, to track how the modified virus spreads. They are carried out in top-grade containment labs like the one in Wuhan. Viruses that infect ferrets can also infect humans, precisely the reason ferrets are a good model for studying human infection in the first place. But GOF

studies always carry a tiny risk of something going wrong: the virus leaking out of the lab, or a virus infecting a lab researcher who then goes home and spreads it.

GOF studies polarise opinion among specialists and the public. The studies tend to focus on worrisome flu strains like H5N1, which I tackled in Vietnam, and H1N1, which caused a pandemic in 2009 (it came to be known as swine flu because parts of the virus matched flu viruses that commonly circulate in pigs). Many scientists believe such studies are a necessary evil to prepare against future pandemics and to get ahead on vaccines. Others disagree, instead believing that public health goals are more meaningfully served by improving vaccine production or honing our ability to predict pandemics. I believe, broadly, that GOF research can furnish scientific findings that are ultimately useful. Bans are often unworkable in practice; it is better to be transparent and regulate – and such studies are heavily regulated.

The novel coronavirus might not even be that novel at all. It might have been engineered years ago, put in a freezer, and then taken out more recently by someone who decided to work on it again. And then, maybe, there was ... an accident? Labs can function for decades and often store samples for just as long. In 2014, six old vials of freeze-dried variola virus, which causes smallpox, were uncovered in a lab in Maryland, US; though the samples dated back to the 1950s, they still tested positive for variola DNA. Some viruses and microbes are disturbingly resilient.

It sounded crazy but once you get into a mindset it becomes easy to connect things that are unrelated. You begin to see a pattern that is only there because of your own starting bias. And my starting bias was that it was odd for a spillover event, from animals to humans, to take off in people so immediately and spectacularly – in a city with a biolab. One standout molecular feature of the virus was a region in the genome sequence called a furin cleavage site, which enhances infectivity. This novel virus, spreading like wildfire, seemed almost designed to infect human cells.

To say that all this worried me would be an understatement. US–China politics were in a bad place in January 2020; a trade war that started in 2018 with import tariffs was escalating, with high-profile Chinese companies being put on export blacklists. It was obvious that people would soon begin hunting for a scapegoat for what was rapidly turning into a global health disaster. Trump was seeking to blame the virus on China and was calling it the ‘China virus’ and ‘kung flu’. The security services in the US were on high alert for any hint that would prop up the accusations.

Conspiracy theories that were circulating about the origins of the virus were bound to add fuel to an already raging fire. The rumours centred on the virus being man-made and then either accidentally leaked from a laboratory or, worse, deliberately released. In effect, one idea that was spreading was that the novel coronavirus might be a bioweapon. I remember sitting in the kitchen with my wife Christiane and saying, ‘This could be an engineered virus. It could be a lab accident – or worse.’ Saying it out loud felt like a bombshell.

It’s sobering to look back on it now but there we were, sitting in our home in leafy Oxford, potentially caught up in one of the most polarised moments in history since the Cold War. And sitting on a suspicion that was terrifying – and explosive, if true. This period was much more frightening and uncertain than discussions around the release of the genome a fortnight earlier. With extremely tense US relations and an unpredictable American president determined to see a biological threat through the distorting lens of nationalism, it didn’t feel too melodramatic to wonder if an engineered virus, either accidentally leaked or intentionally released, might be the sort of thing countries could go to war over.

Christiane, who is Austrian, is a very calm, pragmatic and logical person. She’s also a professor in tropical diseases at Oxford University and knows her immunology. She told me, correctly, that I couldn’t get stuck on this idea that the virus was man-made: ‘Jeremy, you have to go through the science, you have to look at far more sequences and you’re going to have to bring people together. Oh, and you’re not an evolutionary biologist.’



The idea that an unnatural, highly contagious pathogen could have been unleashed, either by accident or design, catapulted me into a world that I had barely navigated before. This issue needed urgent attention from scientists – but it was also the territory of the security and intelligence services.

I had overlapped with the security services once before, when I was trying to drum up interest in the record Ebola outbreak in West Africa, which started in 2013. Epidemics are as politically destabilising as wars: they spread chaos along with disease. Back then I had trudged to Whitehall to try to convince the security services that the outbreak mattered, because it was threatening to creep into conflict zones. They really do keep a low profile – I remember being sent to an unmarked office down a nondescript corridor.

There is mutual gain to be had from scientists sharing insights with spooks. Just as Wellcome could offer wisdom on how to tackle disease outbreaks, civil servants offered a valuable perspective on the ethnic and political rivalries in North Kivu, the contested border region between the Democratic Republic of Congo and Rwanda. That knowledge greatly helped my Wellcome colleagues working on the Ebola frontline. Andrew Parker was the head of the UK intelligence service MI5 at that time; he has since moved on, but we also spoke about the coronavirus outbreak in early 2020, when he was visiting Wellcome chair Eliza Manningham-Buller, his predecessor at MI5.

When I told Eliza about the suspicions over the origins of the new coronavirus, she advised that everyone involved in the delicate conversations should raise our guard, security-wise. We should use different phones; avoid putting things in emails; and ditch our normal email addresses and phone contacts.

Use different phones? These are not things that normal people do and I had no idea where to start. I contacted the communications tech manager at Wellcome:

27 Jan 2020, at 11:59:

Special request!

Can I get a second phone today? Separate number, need to have one separate to my existing Wellcome one, I hope just for 3–6 months – can explain when we meet

He found me a blank phone in the Wellcome cupboard and left it charging on my desk while I was in a meeting. I didn't know the term then but I now had a burner phone, which I would use only for this purpose and then get rid of.

When I got home, Christiane insisted I rang people close to us, so they would understand what was going on in case anything happened to me.

First, I dialled my older brother Jules, a designer and landscape architect in Edinburgh. I told him that a few scientists, including me, were beginning to suspect this might be a lab accident because it looked, at first glance, as if the virus might not be a natural thing – and, if that turned out to be the case, it would have massive implications for everyone and everything. I told him the British and American intelligence services were involved.

I don't recall him saying very much. What can anyone say? Jules phoned me back about an hour later, to make sure he'd understood it all correctly. And, of course, to run through the usual things you'd expect anyone in his situation to say. Like, if Christiane or the children needed anything, they should let him know.

I had a much longer conversation with Tim.



Tim Cook is a consultant and professor in anaesthesia and intensive care medicine at the Royal United Hospitals in Bath, in south-west England. He is one of my closest friends, ever since we were thrown together 35 years ago during our clinical training at the now-vanished Westminster and Charing Cross Hospital.

I came from University College London; Tim, from Cambridge University. We both loved rugby and cricket and we ended up in the same social group. We also shared an intellectual interest in our chosen profession. As Tim says, you would expect everyone who is

studying medicine to be really interested in it, but that is not always so.

Tim has been a sounding board, particularly on matters of intensive care, ever since. He was one of the first people I contacted when I began worrying, as coronavirus crept closer, about how health systems would cope with a surge. In late January, after getting off the phone to Wuhan, I emailed him to tell him the situation was worsening fast and doctors were dying. I wanted him and his colleagues to know what might be coming and I wanted to know if the NHS was prepared (his answer was no).

When I worked in Vietnam, he and his colleague Jerry Nolan, who wrote the go-to textbook on emergency care anaesthesia, used to fly out every couple of years to give lectures and train local doctors. In turn, they were tutored by my local colleagues about less familiar tropical diseases such as dengue and malaria.

When I moved back to the UK, Tim smoothed my passage into an amateur cricket club near Oxford. He and I now meet at least once a year for an annual friendly. The pandemic, incidentally, cost me my chance at the rotating captaincy; I'm a batsman and I had been looking forward to becoming the Joe Root of Steeple Aston during the 2020 season. I love cricket; it's pure escapism on a Sunday afternoon in beautiful surroundings, where you can stop thinking about work for a few hours. No matter what you do for a living, there are always irritations, tensions and stresses. On the pitch, nobody gives a toss about who you are or what you do. We all need places like that, whether it's playing a sport or being in an orchestra – a box where the rest of the world becomes irrelevant.

When I dialled Tim, he was on call in intensive care. He told me afterwards that he would not have answered had it been my usual number. On-call doctors never turn down mystery numbers in case it's an emergency admission, such as a patient with sepsis (a potentially fatal immune overreaction to an infection).

He could hear the fear in my voice and, in turn, it made him nervous. I told him that there were concerns that the virus might be

man-made – and that I was letting him know what was going on in case anything happened to me.

‘It was a pretty scary call to get from a mate,’ Tim says now, recalling it only lasted two or three minutes. He retreated into a sideroom, with nurses and doctors coming in and out. ‘I was lost for words and my head was spinning. Your mind races when you hear something like that. If this is an experimental virus that’s fallen out of a lab somehow, or been intentionally released, the implications are absolutely massive. So, I’m immediately thinking, this goes from being an absolutely horrendous epidemic to potentially a global disaster with implications for a war.’

Tim didn’t tell anyone, not even his wife, for months. Information like this feels like a burden. The last thing you want to do is weigh down anyone else.

The only other time he can remember being as shocked was three years before, again doing a ward round in intensive care. A paramedic rang him from the back of an ambulance: ‘Tim, I’ve got your dad. He’s just had a heart attack and I’m bringing him to your department.’



Days after I returned from Davos, Eddie Holmes was on his way home to Sydney from another Swiss ski resort. He had travelled to Grindelwald to attend the 30th Challenge in Virology, an annual conference held by the Swiss Academic Foundation for Education in Infectious Diseases.

His scheduled talk was on the emergence and evolution of infectious diseases, and how RNA viruses move from one species to another. When he got there, he and another delegate, Isabelle Eckerle, a virologist at the University of Geneva, delivered an impromptu session on the new corona-virus that everyone was talking about.

The conference was also a chance to take his family skiing – and to take his mind off the constant worry of what was happening to

Zhang in China, after the release of the coronavirus sequence without the approval of the Chinese government.

Eddie was in a hotel in Bern when my email landed on 28 January, requesting a chat about the possibility that the virus might have escaped from a lab, given the presence of a BSL-4 facility in Wuhan. I gave him the number of the burner phone to call.

He was tired from travelling and my message was the last thing he wanted to deal with. Still, he pulled out his laptop and began searching for scientific papers that might offer a comparison between the new respiratory virus and its closest known relatives in the animal kingdom. Among a bunch of preprints on BioRxiv,^{*} he found a spot-the-difference paper showing how closely this new human virus, then called 2019-nCoV (short for ‘2019 novel coronavirus’) resembled a bat coronavirus.

Despite scanning the pictures and graphs, he could not easily discern any discrepancies between the bat virus and the human one – at least, none that spooked him. After all, if an animal virus has simply crossed over into humans, then the genetic sequences in the virus samples taken from the two species should, genetically speaking, line up pretty well.

And they did seem to marry up, Eddie recalls: ‘The virus in humans seemed to have the same variability as the closest related bat virus. If it had been engineered, you’d expect its evolution to look a bit different. I didn’t think much of it, if I’m honest. I was busy travelling and trying to write a scientific paper.’

The indifference soon evaporated. The day after arriving back in Sydney, Eddie opened an email from Kristian Andersen at Scripps Research Institute in California, asking for a Zoom call. Kristian has conducted major international collaborations investigating how deadly pathogens, such as Ebola, Zika and Lassa viruses, emerge, spread and evolve. It was only a matter of time before the Wuhan coronavirus, as it was still being called, fell under his lab’s scrutiny.

During the call, Kristian confessed to Eddie that three things bothered him about the new virus. The first was that the receptor binding domain, the bit of the spike protein in the virus that attaches

to the host cell to infect it, looked too good to be true – like a perfect ‘key’ for entering human cells.

The second klaxon was that this ‘key’ was accompanied by a short genome sequence known as a furin cleavage site, seen in highly contagious flu viruses. ‘It kind of gives flu superpowers, by making it more transmissible and more pathogenic’, Kristian explains, ‘and we had never seen it before in these coronaviruses’. If someone had set out to adapt an animal coronavirus to humans by taking a specific bit of genetic material from somewhere else and inserting it, this was what it might end up looking like.

And then Kristian delivered his denouement: he’d found a scientific paper where exactly this technique had been used to modify the spike protein of the original SARS-CoV-1 virus, the one that had caused the SARS outbreak of 2002/3. At first glance, the paper Kristian had unearthed looked like a how-to manual for building the Wuhan coronavirus in a laboratory. The pair knew of a laboratory where researchers had been experimenting on coronaviruses for years: the Wuhan Institute of Virology, in the city at the heart of the outbreak.

‘Fuck, this is bad,’ was Eddie’s first reaction to Kristian’s observations. His second instinct was to call me on the burner phone.

* ‘What does the Chinese government know that we don’t know?’
Stéphane Bancel, CEO Moderna

* One such adviser is Anders Tegnell, the epidemiologist at Sweden’s Public Health Agency who advocated against strict lockdowns in his country during most of 2020.

* DARPA (Defense Advanced Research Projects Agency) is a research and development agency of the US Department of Defense. BARDA (Biomedical Advanced Research and Development Authority) is a US Department of Health and Human Services office responsible for the procurement and development of medical countermeasures, principally against bioterrorism, as well as pandemic influenza and emerging diseases. The FDA (Food and

Drug Administration) is a US federal agency responsible for protecting and promoting public health.

- * Preprint servers are online repositories of draft manuscripts that have not yet been published in an academic journal. The drafts can be checked and commented on by others before formal submission to a journal. Preprint servers such as medRxiv (pronounced med-archive) have allowed pandemic-related research to be disseminated rapidly in the interests of public health, though the lack of peer review means that poor-quality studies can also slip through.

3

Am I supposed to call the FBI?

30 JANUARY 2020

Known cases: 7,834
China: 7,736 (plus 12,167 suspected)
98 cases in 18 other countries
170 deaths

I GOT EDDIE'S CALL on the day that the WHO's Emergency Committee met for a second time, on 30 January 2020. By now the disease had reached Europe: Germany's Patient Zero, confirmed on 27 January, was a worker at a Munich car factory infected by a colleague visiting from Shanghai, a spark that led to four generations of infection. The virus was on a relentlessly upward trajectory.

At last, the Emergency Committee was unanimous. On 30 January, after a five-hour teleconference, Tedros, on behalf of the WHO, declared the novel coronavirus 2019 a Public Health Emergency of International Concern. It was belated acknowledgment of what many of us already feared: everything was going the wrong way, and the epidemic was spinning out of control. But at least the declaration would put countries on notice that they had to act under the International Health Regulations, such as to notify the WHO of cases.

The next day, I contacted Tony Fauci about the rumours over the origins of the virus and asked him to speak with Kristian Andersen at Scripps. We agreed that a bunch of specialists needed to urgently look into it. We needed to know if this virus came from nature or was

a product of deliberate nurture, followed by either accidental or intentional release from the BSL-4 lab based at the Wuhan Institute of Virology. Depending on what the experts thought, Tony added, the FBI and MI5 would need to be told.

I remember becoming a little nervous about my own personal safety around this time. I don't really know what I was scared of. But extreme stress is not conducive to thinking rationally or behaving logically. I was exhausted from living in two parallel universes – my day-to-day life at Wellcome in London, and then going back home to Oxford and having these clandestine conversations at night with people on opposite sides of the world. Eddie in Sydney would be working when Kristian in California was asleep, and vice versa. I didn't just feel as if I was working a 24-hour day – I really was. On top of that, we were getting phonecalls through the night from all over the world. Christiane was loosely keeping a diary and recorded 17 calls in one night.

It's hard to come off nocturnal calls about the possibility of a lab leak and go back to bed. I'd never had trouble sleeping before, something that comes from spending a career working as a doctor in critical care and medicine. But the situation with this new virus and the dark question marks over its origins felt emotionally overwhelming. None of us knew what was going to happen but things had already escalated into an international emergency.

On top of that, just a few of us – Eddie, Kristian, Tony and I – were now privy to sensitive information that, if proved to be true, might set off a whole series of events that would be far bigger than any of us. It felt as if a storm was gathering, of forces beyond anything I had experienced and over which none of us had any control.



Kristian remembers that anxious time at the end of January 2020. 'I drank about three beers after that early call with Eddie,' he says. My overriding concern was to get to the bottom of the origins of the virus as quickly, calmly and scientifically as possible. The first task was to

discreetly gather a panel of top-class scientists to ponder aloud about what we were dealing with. I set up a conference call.

We already had Eddie and Kristian. They had been having conversations in the background with Andrew Rambaut and Bob Garry, an expert on viruses at Tulane University in Louisiana and one of Kristian's regular collaborators. Bob had independently clocked what looked like peculiarities in the virus. Kristian had also sought the opinion of his Scripps colleague Michael Farzan, who had made important discoveries about how SARS-CoV-1 binds to human cells.

Michael confessed he was struggling to figure out how the new coronavirus could have acquired its features in a natural way. My wife Christiane recommended Marion Koopmans and Ronald Fouchier, both at Erasmus University in the Netherlands, plus Christian Drosten, who directs the Institute of Virology at the Charité Hospital in Berlin. Christiane pointed out that a truly international group would scotch any rumbling that this was a conspiratorial Anglo-American stitch-up against China.

The panel made a dream team: all globally respected, opinionated scientists who would challenge each other without fear or favour. Marion serves as a science adviser to the WHO – we work together on the science advisory committee for the WHO R&D Blueprint, which focuses on the research strategy for new diseases – and was a member of the Emergency Committee that declared the public health emergency. Later, she would also form part of the WHO delegation that went into Wuhan to investigate the origins of SARS-CoV-2. Ron is a renowned virologist who is a longtime advocate, and practitioner, of gain of function studies. He would be able to give us an insider's view of how likely this kind of research might be at the heart of the mystery.

There was derision down the phone line.

Eddie recalls: 'The general feeling from the biologists was that they just didn't believe a word of it. They could not countenance the fact it might be a lab escape, for good reason: if someone was engineering a coronavirus, they wouldn't use some random bat virus in their own lab. They'd use a familiar strain that they knew could

infect cells.’ Marion, who did her PhD on coronaviruses, took this view, as did Ron and Christian Drosten. She says: ‘There was just no close genetic backbone in the literature, despite there being hundreds and hundreds of genomes of SARS-like viruses in the databases. If you are going to make something, why wouldn’t you use one of those to play with?’

This novel coronavirus did, at first sight, seem to be a random bat virus – one not specifically documented before either in nature or in the lab. Its closest relative, RaTG13, a 96 per cent match, had just been sequenced but not yet published; I had got hold of a preliminary analysis. It had come from a horseshoe bat and it seemed reasonable to assume this novel coronavirus had come from a bat too. RaTG13 was a closer fit than the two viruses, ZXC21 and ZC45, that Kristian and Andrew had previously been looking at, which were a 86 to 87 per cent fit.

There was a difference of opinion on whether the molecular features were a cause for alarm: nature is a fearsome conjuror, and strange characteristics, like the furin cleavage site in the genome sequence that was catching everyone’s eye, can crop up and then vanish through natural evolution. ‘You get insertions like that in viruses all the time,’ Marion says. ‘It happens in nature.’ Kristian cautioned that just because it happened in nature did not rule out unnatural origins, especially as closely related coronaviruses lacked some of the same structural features. Ron, meanwhile, worried that focusing on what seemed like an outlandish question would end up distracting busy researchers.

We needed to solicit further opinions, especially as Eddie and Kristian were still nursing concerns. ‘At that point,’ confesses Eddie, ‘I was about 80 per cent sure this thing had come out of a lab.’ Kristian was about 60 to 70 per cent convinced in the same direction. Andrew and Bob were not far behind. I, too, was going to have to be persuaded that things were not as sinister as they seemed.

Patrick Vallance informed the intelligence agencies of the suspicions; Eddie did the same in Australia. Tony Fauci copied in Francis Collins, who heads the US National Institutes of Health (the

National Institute of Allergy and Infectious Disease, which Tony heads, is part of the NIH). Tony and Francis understood the extreme sensitivity of what was being suggested, given the anti-China rhetoric coming from both President Trump and US Secretary of State Mike Pompeo. Christiane's advice kept running through my head: 'Stick to the science'.



The next challenge was to find an appointment for a secure conference call that could bring in extra voices. We settled on Saturday 1 February 2020 at 7pm GMT, which was 2pm for Tony in Washington and 6am Sunday for Eddie in Sydney. Kristian and Eddie asked Andrew Rambaut and Bob Garry to dial in. The others on the call were: Francis Collins; Ron Fouchier, Marion Koopmans, Christian Drosten; Stefan Pohlmann, a virologist at the German Primate Centre in Gottingen; Mike Ferguson, Wellcome's deputy chair and a biochemist; Paul Schreier, also from Wellcome; and Patrick Vallance.

Ron, Marion and Christian again argued there was no need to invoke an unseen hand to cook up this particular coronavirus. The ingredients were probably out there in the wild, given that animal viruses are known to cross over into humans all the time or cross over into other species and then into people, where again they mostly hit a wall. The new virus was more convincingly explained, scientifically, as a natural spillover than a laboratory event. The call lasted around an hour; I remember Francis having to step out of his granddaughter's swimming gala because he couldn't hear us properly.

Afterwards, participants swapped emails on what they thought was going on. Andrew explained that, while the furin cleavage site was arresting, his hunch was that the virus acquired it in an intermediate host species before jumping into humans.

The next day I gathered everyone's thoughts, including people like Michael Farzan, and emailed Tony and Francis:

On a spectrum if 0 is nature and 100 is release – I am honestly at 50! My guess is that this will remain grey, unless there is access to the Wuhan lab – and I suspect

that is unlikely!

We agreed it had to be looked at quickly and forensically, ideally under a WHO umbrella, but that did not materialise (the agency was taken up with the emergency response). So, after those initial conversations, five scientists came together to take an investigation forward: Kristian; Eddie; Andrew; Bob; and W. Ian Lipkin, a Columbia University virologist who, in addition to being a well known virus hunter and SARS veteran, was scientific adviser to the film *Contagion*. They resolved to undertake a fingertip search of the literature, rake through accumulating research on the virus, study the epidemiological data and scrutinise samples of the virus, all to detect the trace of an unseen hand

Despite his experience with Ebola and Zika, Kristian had never fronted such a pressured and sensitive investigation: ‘I was battling with the idea that, having raised the alarm, I might end up being the person who proved this new virus came from a lab,’ he says. ‘And I didn’t necessarily want to be that person, well-known across the world ... And I was thinking, how do we even do this? Am I supposed to call the FBI? What burden of proof were we looking for?’

‘This couldn’t just be me fiddling around with my analyses and then saying, “Yeah, it came from a lab” or “No, this virus is probably natural.” When you make big claims like that, you had better be sure that you can conclude something based on evidence and not on speculation.’ The matter was so sensitive that, apart from a handful of senior colleagues, his lab companions did not know what he was working on.

I included a reference to the conversations in a circular to select Wellcome colleagues afterwards:

You may have read in social media and others asking what the origins of this virus were. Very difficult to work out and exquisitely sensitive. We are engaged with China, with scientists in Australia, EU, UK, USA and with the WHO on this.



It was indeed imperative to engage with China. In that first weekend of February, as it became clear from everyone that the origins of the virus deserved closer inspection, I got in touch, via an impeccably connected American friend, with an old contact in China. Chen Zhu was China's minister of health between 2007 and 2013. Originally trained as a 'barefoot doctor'* in rural China, he studied in Paris, learned to speak several languages and become a celebrated haematologist, specialising in leukaemia treatments. He is, without doubt, one of the most remarkable people I have ever met. Zhu is respected globally for his work in ensuring China is plugged in scientifically to the rest of the world, regardless of what is happening politically.

The phone call to Zhu took place on a secure line around midnight, which seemed appropriate for what I wanted to talk to him about. We discussed the outbreak and how it would cause disruption on a global scale. I mentioned the rumours that the novel coronavirus could be the result of a lab accident, though it was too early to say much more. I just wanted to let him know that, of course, people would be asking questions. If a man-made virus became the narrative, I told him, we would be in for some turbulence and I wanted to make sure there were links into China whatever the outcome. I wanted him to know that scientists were working to establish the truth – but with a resolutely open mind. As ever, he took the news calmly.

My American friend Marty Murphy also joined the conversation but on an urgent practical matter: he had collected donations from US companies to send to Wuhan, then at the terrible peak of its epidemic. The Chinese city was running out of personal protective equipment and the local airports were shut. Marty managed to pull together a miracle of global generosity and solidarity: 154 pallets of PPE donated by US companies, including the pharmaceutical giant Amgen, sent on a UPS MD-11 cargo jet to Shanghai. From there, the PPE was loaded on to two Chinese domestic carriers and flown into Wuhan. That the UPS plane was allowed in Chinese airspace at all is down to Zhu.

Together, Marty and Zhu made impossible things happen.



The following month, after the addition of important new information, endless analyses, intense discussions and many sleepless nights, Kristian Andersen, Andrew Rambaut, Ian Lipkin, Eddie Holmes and Bob Garry were ready to pronounce on the origins of the novel coronavirus. On 17 March 2020, in a clear, short paper entitled ‘The Proximal Origin of SARS-CoV-2’, the researchers stated: ‘Our analyses clearly show that SARS-CoV-2 is not a laboratory construct or a purposefully manipulated virus.’

To begin with, the paper, published in the journal *Nature Medicine*, noted the two features of the coronavirus that had sparked concern. First, the virus glues itself with suspicious enthusiasm to human cells – or, in the language of the paper, ‘appears to be optimised for binding to the human cell receptor ACE2’.* The receptor binding domain (RBD) of the virus fits the ACE2 receptor like a hand in a glove.

Second, the virus is then able to gain entry to cells almost as if it had a key. That is because the spike protein, the piece of the virus that enables infection, features a distinctive furin cleavage site. That was the specific bit of the genome that had caused so much consternation. It allows the spike protein to be cleaved, or split, to start the infection process – like removing a key from a bunch in order to unlock a door. Similar sites are seen in virulent pathogens like the viruses that cause bird flu and Ebola.

But many things, the authors explained, did not make sense if this was an engineered virus. The new coronavirus attached itself to cells quite differently from SARS-CoV-1 – and was also unlike any of the known viruses used in gain of function research in labs. That rendered deliberate manipulation an implausible scenario. Why? A malevolent scientist is still a scientist – and the most methodical way of conjuring up a nightmare virus would be to take a virus that is already a known quantity, such as SARS-CoV-1, and crank up its infectivity using known methods.

Or, as Kristian puts it, somewhat bluntly: ‘Scientists are lazy. If we want to make viruses in the lab, we follow recipes we’ve used for decades because we know they work. This virus bore no lab signature whatsoever.’ That spoke to Marion’s early observation: why would a scheming scientist not use a known virus?

Rather, SARS-CoV-2 looked like a malign gift from nature. The paper offered two pieces of circumstantial evidence: first, that a bat coronavirus called RaTG13 was 96 per cent genetically similar to SARSCoV-2 but differed in the receptor binding domain; and second, that coronaviruses featuring identical receptor binding domains had just been found in Malayan pangolins, known to be imported illegally into parts of China. In short, the paper showed that the ingredients for SARS-CoV-2 were out in the wild. They did not need to have escaped, or been unleashed, from a containment lab.

That tallied with Andrew’s idea that he circulated after the conference call with Tony Fauci and Francis Collins: that the receptor binding domain, a crucial portion of the virus, might have originated in an as-yet-unidentified intermediate species between bats and humans.

The paper then offered two scenarios. In the first, a bat coronavirus crossed into an intermediate species – perhaps a pangolin – and underwent further mutations. This new virus, having gained the genetic capability to survive in a broader range of hosts than just bats, then jumped into humans.

The second scenario is that a precursor to the new coronavirus crossed the species barrier undetected into humans many times, potentially over months or even years. Each transmission shuffled the genetic deck slightly, mostly resulting in viruses that didn’t go anywhere. Eventually, a combination of random biological changes and natural selection hit a sweet spot, conjuring up a form of the virus able to clinch a foothold in a human host and, critically, acquire the capacity to pass from one person to another.

It is a respectable guess that SARS-CoV-2 could have appeared in this way, as HIV did in the 1930s from chimpanzees. With its newly minted ability to infect and transmit between people, SARS-CoV-2

took off sufficiently to cause an observable outbreak in December 2019 (strange though it sounds, it can be really hard to spot an outbreak: it means first looking for a signal among the noise, such as a slew of unexplained pneumonias, and recognising it as sufficiently anomalous to dig further).

Just because the natural world provides all the ingredients for SARS-CoV-2 does not prove the virus did not come from a lab; it is impossible to prove a negative without access to lab documents. But the simplest explanation remains the likeliest: nature plus bad luck. 'We know how powerful biology can be,' Marion says.

When the paper by Kristian and co was published, Bill Gallaher, a microbiologist at Louisiana State University, commented on virological.org that the lack of a matching RNA sequence in the literature rendered a lab origin highly unlikely:

No known viral RNA sequence is the daddy of SARS-CoV-2. No match. If it doesn't fit, you must acquit. It is all bat guano.



The paper has been accessed online more than 5 million times and, Kristian accepts, might end up being the defining paper of his career: 'We never set out to write a historic paper that would be one of the best-read ever. We thought that when it was published it would be mostly ignored, because, well, there's a pandemic. We wrote it because scientists wanted to know whether this virus came from a lab. Today, researchers can cite our paper and say, "This lot looked at it and they're the kind of people who know what they're doing." I'm really happy that we managed to do that.'

Unlike Kristian, I expected the paper to whip up attention. As the virus spread, I could see the blame game was shaping up into an explosive political issue. Without a serious scientific investigation, published at speed, the rumours were going to fuel ongoing trouble.

Other theories still circulate. The Wuhan Institute of Virology housed a sample of the closest virus, RaTG13. Given that one of the institute's aims is to sample bat-borne viruses, the coincidence is not surprising. However, there has been intense focus on the work of Shi

Zhengli, a Chinese virologist known as the 'Bat Woman' because of her work on bat viruses at the WIV. In 2012, she visited a copper mine in Yunnan where six miners were sickened by a mystery respiratory disease with similar symptoms to Covid-19. Three of the miners later died. She and her team collected a host of viruses, including RaTG13, from that mine and others afterwards, but her conclusion was that the miners' illness had been caused by a fungus. She had been studying coronaviruses at the lab and there had been security concerns raised about the WIV by US diplomats.

Is it possible that an infected bat researcher at the institute unwittingly spread the disease in Wuhan? Andrew believes that the probability of accidental escape from a lab, through someone becoming infected and then going on to infect others, is 'vanishingly small. It would mean someone going out into the wild, collecting the one-in-a-million virus capable of infecting humans, bringing it back to the lab and then making a whole series of mistakes.'

Andrew explains: 'That's just one very specific way of going from bat viruses in nature to a human epidemic, whereas there are tens of thousands or even millions of exposures to bat viruses in the wild potentially over long periods of time in large geographical areas. If a human-infectious virus was out there, it is infinitely more likely that one of these very large numbers of contacts could have acquired it.'

Could RaTG13, a sample of which is known to have been at WIV, have been worked up into something capable of infecting humans and then leaked or released? Any scientist wanting to turn RaTG13, or similar, into SARS-CoV-2 would have needed to conduct 'serial passage' of the starting virus, repeatedly growing the virus in different conditions to mimic the process of evolution. It is almost impossible, Kristian says, to put bat viruses through this process in the lab. He has tried to culture bat viruses many times and failed. Unsurprisingly, bat viruses prefer bats to Petri dishes.

The chain of infection into humans does not need to be directly bat-to-human; it could have happened via another species. Pangolins are not the only species in the frame. SARS-CoV-2 infects animals like ferrets and mink (known as mustelids) as efficiently as it infects

humans, raising the possibility of a wild or farmed animal being the stepping stone between bats and people.

A joint WHO/China report published in March 2021 on the origins of SARS-CoV-2 concluded that a laboratory accident or deliberate release was very unlikely. It suggested the two most probable scenarios are: a jump from the host species, likely bats, to humans via an intermediate species; or direct infection from the host species.

Marion Koopmans was part of the WHO team that went into China, looked at the (possibly incomplete) evidence that the Chinese government made available and co-authored the March 2021 report. A virus journeying from bats into people via pangolins, Marion says, is a 'credible hypothesis, in terms of what we see in emerging diseases. [Pangolins] are endangered but also a delicacy for locals and tourists, so there is a big market. They are being collected from a wider and wider geographical area along smuggling routes. It's really a textbook way of getting problems with viruses.'

Another scenario favoured by authorities in China is that SARS-CoV-2 virus was imported into China via frozen food supply chains. A handful of outbreaks with apparent links to food markets led China to screen 1.4 million samples of frozen food; around 30 had traces of the virus (though Marion says this could be surface contamination). The WHO then commissioned its own studies to see whether the virus could withstand the subzero temperatures.

Marion explains: 'It's typical to get viruses in food but with freezing you would expect to lose a lot of infectivity. The WHO studies showed *Bingo!* If you put virus on a fish and freeze it for three weeks, you can just grow the virus back. It's stable. Based on all those kinds of findings, we said, "OK, we cannot rule it out."'

A smoking gun, like the unambiguous link that Marion helped to discover between camels and Middle East respiratory virus, would help to settle the matter. It would mean finding an extremely close match to SARS-CoV-2 in either nature or a lab. Andrew Rambaut speculates there may be a bat virus somewhere out there that is a closer match to SARS-CoV-2 than RaTG13. That might fill the gap in understanding the origins of this pandemic virus.

One reason why rumours persist is that the WHO delegation to China, which Marion joined, included Peter Daszak from the EcoHealth Alliance. The non-profit research organisation has funded research at the Wuhan Institute of Virology and Daszak had previously dismissed the idea of a lab origin for SARS-CoV-2. Even though he is an accomplished scientist, it would have been better for him to have recused himself and for the WHO to have appointed someone who would have been perceived as more impartial.

In May 2021, several scientists including Ralph Baric, one of the world's leading coronavirus researchers at the University of North Carolina, and Jesse Bloom, whose Seattle lab has been at the forefront of studying mutations, wrote a letter to the journal *Science* asking for a fresh investigation and demanding that labs, including the Wuhan Institute of Virology, open their books and documentation to outsiders. Soon after, President Biden also requested a fresh look at the evidence.

We need to know where this virus came from, especially if we want to prevent something similar happening in the future. So we should continue looking for answers – and hope that new evidence comes to light. There is, though, no guarantee that we will find the evidence we seek, nor any certainty that we will understand how the outbreak started. As things currently stand, the evidence strongly suggests that Covid-19 arose after a natural spillover event, but nobody is yet in a position to rule out an alternative. In the meantime, we should be reducing the chances of future spillovers and making sure labs are safe and transparent in their work.



The intense drama around the origins question made me stop and think about the biases we all bring to the table, the kind of biases that feed conspiracy theories. Mine was seeing a peculiar feature in the virus and wondering why it had started in Wuhan, a city known for its lab. I had put two and two together and made five.

Kristian admits to having his own biases too, which took a proper scientific analysis to overturn: 'I look back now and think, man, there

was a lot of stuff we didn't know. Like just how prevalent the features that worried us were; how they come and go all the time in coronaviruses and there's nothing mysterious about them. One huge bias was only comparing the new virus to SARS-CoV-1. Because SARS-CoV-1 didn't share these odd features, we assumed something mysterious was going on. That's not how evolution works.'

The tragedy is that this entire controversy over the origins of the pandemic coronavirus turned out to be a distraction. The Trump administration, which demanded that the US National Academy of Medicine investigate, threw so much energy and effort into finger-pointing that it failed to adequately prepare for the pandemic. The conspiracist blame game was a fig leaf to disguise the failure of American governance.

By early February, the new virus was causing havoc and geopolitical tensions everywhere, including in international waters. On 5 February 2020, the *Diamond Princess*, a luxury cruise ship built for more than two thousand passengers and a crew of a thousand-plus, was quarantined in the Japanese port of Yokohama. The Japanese government instigated the drastic measure because an 80-year-old passenger from Hong Kong had disembarked on 25 January and subsequently tested positive. By 21 February, 634 people on board had tested positive.

The docked vessel became a hotbed of transmission and a staple of international news bulletins. It focused minds on the still-complex issue of how to balance public health with global justice. Passengers, running short of medicines and patience, were pleading to be allowed to leave. Countries sent charter planes to rescue nationals from the plague ship and protested at their incarceration. There was confusion over who was supposed to manage the crisis: Japanese officials, the ship's captain or the company that owned the ship.

It was a tragic situation not just for passengers but for the crew: four to a bathroom, lacking the facilities to isolate if they fell ill, and working across the whole vessel to keep it functioning. At the lowest point of the crisis, the *Diamond Princess* accounted for the largest cluster of cases outside mainland China.

The ship was also a contained environment that allowed some of the disease's characteristics to be teased out. One of its key contributions was to confirm the role of asymptomatic people in spreading the virus: at first, people without symptoms were not tested. When the policy was changed to universal testing, it revealed that, by 20 February according to the medical journal *Eurosurveillance*, around 18 per cent of those infected showed no symptoms. Cruises attract an older clientele; it was reasonable to assume an even higher proportion of people showing no symptoms in the general population.

In mid-February, a contact in the US sent me a back-of-the-envelope calculation of how the epidemic might play out in the US, based in part on the epidemiological information emerging from the *Diamond Princess*. Assuming a population of 325 million and an attack rate of 30 per cent, the guesstimates were horrifying: 98 million people falling sick, 12 million hospitalised, two million in intensive care and between 300,000 and 1,000,000 deaths over the course of a year.

These figures, sadly, were closer to the ballpark than President Trump's analysis in March 2020 that the virus 'will disappear'. By 22 February 2021, a year after the *Diamond Princess* episode, there had been 28 million confirmed cases in the US and more than 500,000 deaths.



In 2016, following the record Ebola epidemic in West Africa, the World Health Organization decided it needed a strategy and preparedness plan, to guide research activities in the event of future shocks. Four of us – WHO assistant director general Marie-Paule Kieny; Ana-Maria Henao-Restrepo, a WHO specialist in vaccines; Mike Ryan, director of the WHO's Health Emergencies Programme; and me – set up something called the WHO R&D Blueprint, that would bring together scientists, public health specialists and regulators in an emergency to fast-track research into diagnostics, treatments and vaccines. Its first achievement was the Merck vaccine against Ebola, which came out of trials in Guinea during the epidemic. It was an incredible validation

of what a mix of strategy and speed could pull off: a first-ever vaccine for a disease delivered in the middle of a catastrophic epidemic.

In the perpetual tussle between people and pathogens, the Blueprint would become part of the battle plan. Other critical legacies from the previous outbreak, and now part of that battle plan, include CEPI (Coalition for Epidemic Preparedness Innovations), set up to finance and coordinate vaccine efforts; and ISARIC (International Severe Acute Respiratory and emerging Infection Consortium), which allows standardised clinical data to be collected and shared in public health emergencies. Both have revolutionised the speed at which things can happen. By the third week of January 2020, when scientists were still discussing whether this new virus could pass between people, CEPI was signing agreements with vaccine companies like Moderna; and ISARIC had swung into action in Wuhan. These three additions to the global health armamentarium – the WHO R&D Blueprint, CEPI and ISARIC – are particular achievements that I am proud to be associated with.

On 11 and 12 February 2020, the WHO held its first R&D Blueprint meeting on the novel coronavirus, bringing together at least 500 people in Geneva, in person and remotely, to set the scientific agenda for what would need to be done, both for understanding the disease itself and developing countermeasures, such as diagnostic tests, drugs and vaccines.

I ended up arriving late. I had committed, for environmental reasons, not to fly if travelling in Europe and, after leaving Lyon, my train got stuck just outside Geneva. It was a little embarrassing: I was co-chairing the meeting with Marie-Paule and joined after a coffee break.

It seems remarkable now, but it seemed as if the world was there in the grand main hall at the WHO HQ. Tedros was there. George Gao, head of China CDC, joined by video. Doctors from Wuhan and elsewhere in China turned up in person or remotely. People from all over the world, and in social sciences, ethics, virology and immunology, were represented. Countries sent diplomats from their missions in Geneva. There was a poignant absence: Peter Salama,

until 2019 a key figure in the WHO's Health Emergencies Programme. Peter, who I spent a lot of time with during the Ebola crisis, died suddenly in late January, aged just 51.

By the time of that first Blueprint meeting, approaching mid-February, people were just starting to grasp the scale of the epidemic in China and surrounding countries. I had compiled a bullet-point list on this unknown disease and circulated it to a few Wellcome colleagues before leaving for Geneva:

Estimates on

Incubation period (time from being infected to symptoms) – 3–10 days

Infectious period (time you can pass it on to someone else) – 1–10 days

Infectious with very mild symptoms – sore throat, mild cough, headache (possibly asymptomatic) through to very severe.

R0 estimates – 2.5–3.0

These are extraordinary characteristics for a novel pathogen for which we have no immunity

In China, Case Fatality Rate (CFR) is likely >10% ...

Estimate now that there are perhaps 200,000–300,000 people who have been or are infected in Hubei Province ...

To give you an idea of the pressure hospitals in Wuhan are under – the number of patients with severe disease is increasing by an order of magnitude every 7 days.

A 1000 bed hospital has been built in a week and gymnasiums have been turned into additional hospitals...

Few reports yet in children not clear why ...

Increasing number of healthcare workers becoming ill.

These estimates obviously have serious consequences – they are closer to UK reasonable worst case scenario for planning of a pandemic.

The case fatality rate (CFR) is the proportion of confirmed cases that end in death within a certain time period. R0 (or R-nought), refers to the basic reproduction number, which represents how quickly a disease spreads without any interventions (such as social distancing or masks). An R0 of 3 meant each infected person was passing it to

three others on average. In turn, those three would spread it to another nine in total; those nine to another 27. That is the nature of exponential spread.

That WHO R&D Blueprint Meeting put the agency at the centre of the global response and served as the catalyst that got the world moving: the sharing of samples; more companies starting vaccine work; the kick-starting of networked clinical trials across the world that would allow us to pool findings on potential treatments. That meeting, plus the sense of urgency that many of us had radiated at Davos, was why we got Covid-19 diagnostics, treatments, vaccines in less than a year.



‘Are you a spy?’ asked the taxi driver, as I jumped into his cab at Munich airport on Friday 14 February 2020. I was on my way to the Munich Security Conference, which takes place in one of the city’s hotels every year and, with its focus on global security, seems to draw an even more exclusive crowd than Davos. Panellists that year included Nancy Pelosi, Justin Trudeau, Emmanuel Macron and Jens Stoltenberg, NATO’s secretary general. For the past five years, I have attended it every February, and my first-hand experience of the controversy over the origins of the new coronavirus made my 2020 trip to Munich feel especially relevant.

Outside the hotel, there are always a lot of big men walking round in uniform wearing earpieces, and black cars lining up to deliver important-looking people. Inside, it is how I imagine the Silk Road to have been, a melting pot with people of all nationalities rubbing shoulders. I just wander around amused by the fact that the Iranian spies and the American spies are meeting for coffee (at least, I assume they are spies). It’s almost exclusively male.

It is not the sort of conference to which you can blag an invitation. Mine came through Sam Nunn, the Democratic senator who set up the Nuclear Threat Initiative, which has since broadened its remit to look at other security threats, including biosecurity. I got in touch with Sam a few years ago because I felt that the world was highly

vulnerable to emerging risks and threats from nature, and that we scientists could learn something from the spies. In 2014, for example, we jointly ran a tabletop exercise at Munich simulating the deliberate release of a pathogen. Wellcome has teamed up on projects with organisations like the NTI ever since.

A nuclear or terrorist threat is very much like the challenge we face in public health and epidemiology: seeing the signal for the noise. How do we sift through millions of events to identify the ones that matter? How do we respond immediately to a biological threat to potentially prevent a pandemic? It is not that easy, in practice, to spot early outbreaks of a new disease.

That difficulty is compounded by the inability to go into countries and look for biological threats in the way that agencies can demand access to countries to search for chemical or nuclear weapons. I am not sure any country would allow such an investigation. Another parallel between terrorism and biosecurity is the variety of actors who can stir up trouble: technological advances mean that big states and rich institutions no longer have a monopoly on building either bombs or bioweapons. The counterpart of the lone gunman could be a hobbyist genetically modifying viruses in her garage.

Maintaining a scientific presence in the security world also achieves another end: making sure that decisions on dual-use technology, such as the gain of function research that scientists like Ron Fouchier practise, are not monopolised or controlled by the security community. Dual-use technology, like the techniques to make viruses more contagious or deadly, can seem very scary. But shutting them down would mean critical science, needed for threat surveillance and safety, not being done or being carried out under the radar. We need to be more nuanced and pragmatic about it.

At Munich, I met with Sam, as well as Ernest Moniz, who served as Obama's Energy Secretary. We talked a lot about the new coronavirus. I was rattling on at length about how worrying it was and laying out where I thought the epidemic was heading. The virus itself was not news to them but the depth of concern in the global health community was.

By then, in mid-February, very few people in the US had grasped how fast things were moving. Even at Munich, among the very community tasked with spotting black swans, the crises that spring from nowhere, the coronavirus outbreak was gliding towards them relatively unchecked. Certainly, the White House was nowhere near assigning it the seriousness it merited. It is fair to say it was in denial.



Straight after the conference, I caught the train from Munich to Salzburg. This is part of the Farrar family's annual routine: I travel from Munich, which is usually just before the February half-term, to meet Christiane and the children, who fly in from the UK. We then head to a little village called Hinterstoder in the mountains.

We have been going there to ski for about 20 years, and started taking the kids as toddlers. This time it was four of us rather than five, as our eldest son, Sam, was at college. We always head to the same farm: on top of a mountain with just ten simple rooms and no through road. It is unbelievably beautiful. The owners have become family friends, a link that deepened after a skiing accident there in 2015 put me in hospital for two nights.

It was supposed to be a week off, but of course that was never going to happen. This was a very intense time. There were so many phone calls: with Eddie and Kristian about the origins paper (then yet to be published), conversations with Peter Horby and Bin Cao, a doctor in China, on the clinical studies they had set up in Wuhan, an important piece of the WHO Blueprint plan. It wasn't much of a holiday and I barely hit the slopes.

By this time, the new virus was spreading quietly across Europe. Researchers would later count more than 1,300 separate occasions when the virus was seeded into the UK, mostly in February and March. The kindling for the UK's epidemic was not flying in from China but from elsewhere in Europe. It was being innocently imported by families like ours, fresh from half-term skiing trips in snowy northern Italy; others brought it back weeks later from sunshine breaks in Spain and France.

Spring was in the air and thousands of chains of transmission were being sparked across Europe.

-
- * 'How do we even do this? Am i supposed to call the FBI?' Kristian Andersen, Scripps Research Institute, California
 - * In the late 1960s, Chairman Mao promoted the idea of 'barefoot doctors', villagers who underwent a short period of training and returned to their rural communities as village doctors, promoting prevention and offering basic treatment based on a mix of western and traditional medicines.
 - * ACE2 (Angiotensin-converting enzyme 2) is present in many organs, including the lungs, heart, blood vessels, kidneys and liver. Among other functions, it helps to regulate blood pressure and inflammation.