Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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that will end this in a couple of weeks or a couple of months’. At this point, we can’t even guarantee that we’ll have a vaccine, so assuming that technology will save us is not something we should rely on.”

The good news is that we do have a recipe to avert disaster, built on knowledge and technologies that already exist. However, whether global preparedness will be prioritised in time for the next pandemic is a matter of political choice. President Donald Trump recently threatened to withdraw the US from the WHO and pull funding. What that would mean for the existing regulations and pandemic preparedness is unclear, but many fear it could undermine efforts to provide a coherent international response.

Regardless, it will cost money to boost preparedness, but as Timmis points out, nowhere near as much as it will cost – is costing – to deal with an actual pandemic. He argues that governments have a duty to their citizens to prepare for pandemics.

Governments may baulk at the idea of investing in resources that, by definition, are surplus to immediate requirements, says Timmis, but they spend vast sums on military capability that they hope to never have to use and should view pandemic preparedness in the same way. “It is simply one of several essential insurance premiums to which the state must commit,” he says.

Right now, pandemic preparedness may seem like the most pressing and obvious priority, but, warns Jacobsen, memories are short. “I think that by the end of this calendar year, it may be hard to get countries to invest in preparedness,” she says. “Panic-then-forget is how we operate. We’re already seeing the beginning of the ‘forget’ phase as we rush to reopen economies and shift our resources to economic recovery and away from prevention, detection and treatment.”

Back in 2011, the WHO concluded that the H1N1 flu pandemic could have been a lot worse. “We were lucky this time,” wrote Fineberg. Maybe when we look back at covid-19 we will conclude we were lucky this time, too. But third time lucky? Don’t bet on it.

IN MAY 1997, a 3-year-old boy with a fever arrived at Queen Elizabeth Hospital in Kowloon, Hong Kong. It was a few weeks before the handover of the territory to China by the UK, and it would turn out to be a new biological era as well as a political one. The boy’s disease was no usual illness: he was infected with H5N1, a strain of flu that had until then been a bird virus.

The realisation that H5N1 could infect people raised concerns that it might cause a pandemic. More than two decades later, that hasn’t yet happened, with only around 800 cases having been reported globally. In the meantime, however, humanity has experienced a range of other new diseases. They include SARS, caused by a coronavirus that infected 8000 people before it was contained in 2003, and the H1N1 “swine flu”, which circulated globally in 2009, probably killing more than 250,000 people. Now, covid-19 has led to more than 7 million confirmed cases, and counting.

Humanity has always experienced diseases that sweep the globe. But today, we are more exposed to them. Outbreaks spread rapidly because of widespread travel – of people, animals and animal products. And as we encroach on wilderness, viruses in animals have more opportunities to jump to humans.

When H5N1 appeared, it sparked renewed interest in the threat from pandemics. We have learned much since then. With the world in covid-19’s grip, it may not feel like it, but we know a lot more than we once did about emerging diseases. That knowledge is invaluable right now. It will also help us spot – and hopefully stop – the next pandemic.

Of the thousands of known viruses, at least 200 can infect people. Some researchers have suggested that we sequence the genomes of all unidentified viruses in mammals and birds that could be a threat to us and then use

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Containing a pandemic, step by step

We’ve controlled international outbreaks before – and we know how to do it again, says epidemiologist Adam Kucharski

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“We need to cut the transmission rate by at least 66 per cent to stop the outbreak growing”

machine-learning techniques to predict which ones could actually spread among people. But this would probably involve mapping millions of virus species, which could cost billions of dollars. Even then, it might not work. Machine learning can be very effective in situations where there is a lot of information to learn from. For example, Facebook’s facial recognition is so accurate because millions of people regularly upload and tag themselves in photos. But anticipating novel disease outbreaks using machine learning would be harder – you would be trying to predict rare events with very little data because new outbreaks are far less common than social media posts.

A more targeted approach may be preferable. For a new virus to emerge and spread globally, it must overcome biological, medical and social hurdles. To cope with pandemics, we must look at each of these and identify weak points we can target to improve our chance of controlling the infection.

Emerging infections

The first step in a pandemic typically occurs before a virus gets into humans. New viral infections often start in animals. So we can try to identify viruses that are a threat to us in the kind of animals that usually harbour them before they cause us harm. We know, for instance, that emerging human diseases often originate in bats and spread to us via a range of intermediate hosts, often involving mammals and birds in overcrowded live animal markets and factory farms.

We can also target places where growing human populations have expanded into wild animal habitats. Tracking viruses in animals can certainly help us understand how and why certain infections make the leap to people. However, we still run into the problem of predicting which will cause an outbreak (see “Where could the next pandemic come from?”, page 35).

Targeting the next step in the emergence of a pandemic, we can try stopping known threats from infecting us. This has worked in the past. In 2013, the H7N9 bird flu virus infected 147 people in China, of whom 47 died. In response, China closed numerous live bird markets, reducing the risk to humans by an estimated 95 per cent in
**Vaccine hesitancy**
The spread of misinformation has caused falls in measles–mumps–rubella (MMR) vaccination in countries including the US and UK, contributing to an uptick in measles cases worldwide. The collapse of HPV vaccination in Japan in 2013 due to fears about adverse events is expected to cause some 5000 extra cervical cancer deaths. Vaccine hesitancy featured on a World Health Organization list of 10 major health threats in 2019.

Yet even among people who desperately want vaccines, diminished access may be a knock-on effect of the current pandemic. In some places in Africa, people queue for 5 hours to get the yellow fever vaccine, says Sylvie Briand, director of the WHO’s Pandemic and Epidemic Diseases Department. “But in other countries, where people have not experienced those kinds of diseases, we need to better communicate the benefits of vaccines.”

**Antifungal resistance**
Fungal infections are estimated to kill more people than malaria and breast cancer combined. A 2018 review described the recent rate of emergence of treatment-resistant pathogenic fungi as “unprecedented” and their effects on human health as “spiralling.” Growing levels of resistance to antifungal drugs have been recorded in *Candida auris*, which has caused deadly outbreaks worldwide, and *Aspergillus fumigatus*, which triggers serious complications for people with conditions including asthma, cancer, HIV and cystic fibrosis. The Global Action Fund for Fungal Infections is calling for increased surveillance, better diagnostics and more research.

**Disease X**
In 2018, the WHO included “disease X” on its list of the most serious potential public health threats. It stands for any unknown epidemic disease for which preventive and curative treatments don’t exist. Covid–19 fits the bill. The WHO has highlighted the value of preparing surveillance, personnel, communication and interventions for as-yet unknown risks. “For all-hazard preparedness, we need to develop generic capacity that can be applied to a variety of threats,” says Briand. “Countries need actionable plans, which are exercised and questioned regularly, with a menu of interventions they can choose from depending on the type of disease.”

**Long-term, we also need systems changes, such as clean water being available to patients, and healthcare workers adopting appropriate hygiene practices everywhere.”**

**Things could have been very different.**
Take SARS. It had an R of between 2 and 3 in the early stages of the outbreak, which began in late 2002. However, because most transmission involved people who were clearly ill, contact tracing was able to bring the outbreak under control. Swine flu had a lower R of around 2 but, crucially, transmission often occurred when people weren’t very ill. As a result, contact tracing was far less effective at containing the infection when it arrived in new countries. Based on current evidence, covid-19 has a similar initial R to SARS, but transmission tends to occur earlier, when people are less ill or asymptomatic. This means intensive contact tracing can slow the infection – as it has in Singapore and South Korea – but unless a very high proportion of new infections and at-risk contacts are traced, the outbreak is eventually likely to grow and additional control measures will be needed.

There is yet more we can do to reduce the spread of infection. To explain these next many locations. One reason this measure was so successful is that almost all H7N9 infections were the result of bird-to-human rather than human-to-human transmission. Things could have been very different. “Detecting and tracking a partially human-adapted H7N9 virus in a city as vast as Shanghai or Beijing would be difficult; tracking a fully adapted virus would be impossible,” wrote emerging disease specialist Peter Horby at the University of Oxford shortly after the outbreak.

Once a virus can spread rapidly between humans, our response becomes less about transmission from animals and more about ongoing transmission among people. In the early stages of this scenario, public health measures are usually three-pronged: isolate people who are ill, trace anyone they have had contact with and quarantine those contacts so they can’t spread infection. Two factors influence the success of this approach. One is how easily the virus spreads. We measure this using the reproduction number, R, which tells us how many people an infected person spreads the virus to, on average. The second factor is how that transmission happens: is the virus spread mostly by people with obvious symptoms or can it spread when infected people still feel reasonably well? If the latter, infected people are less likely to be identified and their contacts less likely to be traced.

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There is yet more we can do to reduce the spread of infection. To explain these next
steps, it helps to break down R into four main components. I call these the DOTS – Duration, Opportunities, Transmission probability and Susceptibility. R depends on duration: how long a person is infectious for. It also depends on opportunities: how many interactions they have each day they are infectious. But not all opportunities will necessarily spread infection, so we also need to consider the probability of transmission during an interaction. Finally, how susceptible is the other person and could they themselves become infectious? Multiplying these four components together indicates how readily a disease can spread: \( R = D \times O \times T \times S \).

**Connect the dots**

The DOTS show how different control measures might reduce R. If we isolate people who are infected, it shortens the duration they are spreading infection. But if isolation and contact tracing alone can’t contain the outbreak, we need to consider targeting other aspects of transmission. Social distancing reduces the opportunities for transmission. People who are ill with covid-19 can also reduce the likelihood of transmission by wearing a face mask. But it is important that other aspects of behaviour remain the same. If, for example, infected people lower the transmission probability by wearing a mask, but go out more and so increase the opportunities of spreading a virus, then R might remain the same – or even rise. Because R for the covid-19 virus can be around 3 without any control measures, we need to cut transmission by at least 66 per cent to get R below 1, the level required to stop the outbreak growing. Lockdowns do this by limiting interactions. Preliminary analysis my colleagues and I did at the London School of Hygiene and Tropical Medicine found that social contacts fell by 70 per cent after the UK lockdown started. But lockdown is a blunt instrument that severely disrupts our lives.

A successful exit strategy will need to be more targeted to produce a similar reduction in transmission with less disruption. That will entail identifying situations where transmission is particularly high, which is easier in retrospect. During the SARS outbreak, transmission was high in hospitals, while funerals were “superspreading events” during the 2014 to 2016 Ebola epidemic. There have been reports of covid-19 superspreading in workplaces and at large meals and family gatherings. Curbing such risky events could disproportionately help reduce transmission, but it isn’t clear how large the effect would be if other aspects of life resume.

With any infectious disease, the ultimate goal is to target the last element of the DOTS formula, by using a vaccine to reduce susceptibility. If enough people are immune, we don’t have to worry so much about contact tracing or social distancing, because the virus will struggle to spread even if we behave normally. But the challenge in any pandemic is producing a vaccine that is safe, effective and widely available. Although swine flu was identified in April 2009, vaccination didn’t begin until October – and this is for a strain of influenza, a well-studied disease that we routinely vaccinate against.

Vaccine timelines are improving, yet they are still much slower than the outbreaks they aim to stop. As the Ebola epidemic spread through West Africa in mid-2014, researchers hurried to generate a vaccine. Just a year later, initial results revealed one, called rVSV-ZEBOV, to be highly effective. It was a remarkable achievement – but they had an advantage. In the late 2000s, Canadian and US government scientists had shown that rVSV-ZEBOV could produce a protective immune response to Ebola in animals. So the vaccine was waiting “on the shelf”, ready to be tested in people when the Ebola outbreak started.

In the past few decades, we have witnessed a surge in new viruses jumping from animals to humans. Some, like H5N1 and H7N9, caused severe disease, but stuttering transmission in humans. Other severe infections, including SARS, have been more transmissible, but we managed to contain them relatively early on through isolation and contact tracing. Our efforts to stop the spread of swine flu were less successful, but luckily it turned out to be milder than other pandemic strains. The new coronavirus combines the troublesome features of all these viruses to give a disease that is both easily transmissible and can overwhelm health systems. As for vaccines, the shelves were pretty bare.

For now, we are firefighting. We have the knowledge to bring this pandemic under control, but it has exposed countries’ lack of preparedness. In the future, we need to invest in research when times are quiet. That will ensure we can respond effectively when another disease threatens, because there is no reason to assume that covid-19 will be the last – or the worst – pandemic we face.