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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Several weeks before the novel coronavirus became a serious issue in the UK, I attended a friend’s birthday party. Already, much of the conversation centred on the virus and the illness it causes, COVID-19. While most people were talking about how to avoid catching it, one guest suggested that everybody “get infected to boost their immune system.”

As a student of evolutionary biology, the idea alarmed me. I became even more concerned when, in early March, the UK’s chief scientific adviser recommended that 60 per cent of the population be infected with the coronavirus to build up herd immunity. Of course, the government rapidly ditched the policy and put the UK into lockdown. However, now that infection rates seem to have plateaued in several countries and governments around the world are looking for “exit strategies” from lockdown, talk of exposing people to the virus to build up herd immunity has returned. It remains a dangerous idea.

To understand why, it is crucial to think about how the virus is changing as it jumps from host to host and circulates in the human population. As biologist Theodosius Dobzhansky said almost half a century ago: “Nothing in biology makes sense, except in the light of evolution.” It may not seem obvious, but evolutionary processes have profound implications for pandemics. As well as helping us think clearly about herd immunity, they can explain where new diseases come from and help predict where they are going. Yet, an evolutionary perspective has been lacking in the current...
Pinning down the deadliness of SARS-CoV-2, the virus that causes Covid-19, hasn’t been easy. Undoubtedly, it is far more serious than a common cold – a quarter of which are caused by four other coronaviruses. But it is far less lethal than its sister disease, SARS, which struck in the early 2000s killing one in 10 of those who contracted it.

However, estimates of the Covid-19 mortality rate have ranged from below 1 up to 6 per cent, with the World Health Organization publishing a rate of between 3 and 4 per cent in March. By early May, there had been more than 3.2 million confirmed cases worldwide, and some 230,000 deaths, corresponding to a mortality rate of around 7.2 per cent. How many cases haven’t been confirmed, and how consistently countries are deciding what counts as a Covid-19-related death, is unknown.

However, there are two data sets that offer a fuller picture. On the Diamond Princess cruise ship, all 3711 passengers and crew were tested for SARS-CoV-2 and 1.2 per cent of those infected subsequently died. In Iceland, which is the first country to attempt to screen the whole population, the mortality rate is even lower. By early May, more than 52,000 people had been tested, revealing 1800 cases and 10 deaths, indicating a mortality rate of less than 0.6 per cent. The difference between rates might reflect the fact that the cruise ship passengers were older on average than the population of Iceland, with age a known risk factor for dying from Covid-19. But there may be something else going on.

What’s especially significant about these two results is the time between them, says Paul Ewald, an evolutionary biologist at the University of Louisville in Kentucky. The Diamond Princess infections began in late January or early February, whereas the outbreak in Iceland didn’t begin until later. If there is a true difference in mortality between these samples, it could indicate that the virus is evolving to become less deadly as it spreads.

How lethal is Covid-19?
to adapt and survive. This rapid pace of evolution helps explain why viruses are the most abundant type of organism we know of. It also explains how a virus specialising in infecting one host species can quickly adapt to a new host – as long as the context is right for significant evolutionary change.

Deadly conditions

The importance of context for viral evolution can be seen clearly with the H1N1 swine flu pandemic of 2009. The disease, which probably killed more than 250,000 people globally, started when the influenza virus evolved within a densely packed pig farm in Mexico. The virus was able to become extremely deadly, very quickly, because each new host was right next to the last one. In such conditions, survival of the fittest allowed the most aggressive, virulent strains to run rampant through the population, outcompeting the less deadly ones. Pigs are biologically similar enough to humans to pass on the newly evolved strain, so there was then an explosion of cases among people.

SARS-CoV-2 seems to have emerged under similar conditions. It probably originated in bats, which are reservoirs for many viruses because their unusual metabolism makes them capable of hosting them without becoming ill. However, genetic comparisons indicate that by the time the covid-19 pandemic began there were intermediate forms of the virus circulating in the Huanan wet market in Wuhan, where live animals and people crowd together. “High selective pressure allows one viral strain to become more successful in a particular species,” says Stanley Perlman at the University of Iowa in Iowa City. “The more times it infects a single host, the better it will do.”

In other words, Wuhan’s bustling market provided the conditions in which a virulent strain of coronavirus could successfully adapt to a variety of host species, including humans. As with the swine flu outbreak, the current pandemic arose in conditions that humanity created. This is the first lesson evolution can teach us: pandemics tend to emerge when we put people and animals in close proximity – be they factory farms or live animal markets. We can’t stop viruses evolving, but we can reduce the risk of future pandemics by changing these conditions.

An evolutionary perspective on swine flu also offers insights into what might happen next with SARS-CoV-2. As H1N1 moved geographically from the epicentre of the pandemic, the disease became less deadly. This is a general trend for viruses and is seen in four other coronaviruses that have made the leap to humans in recent centuries and now cause a quarter of all common colds. To work out whether covid-19 will follow a similar evolutionary trajectory, we need to understand why the virulence of a virus changes as it spreads. The key here is that there is generally a trade-off between how lethal a virus is and how successfully it can spread. A pathogen that kills each host before it has had time to infect other susceptible
individuals will rapidly die out. So, while a highly virulent strain can thrive in conditions where hosts are crowded together, once the virus jumps into the wider population, natural selection will tend to favour strains that are less deadly. Put bluntly, dead hosts don’t travel, and so don’t spread the virus to new susceptible hosts.

By this logic, SARS-CoV-2 should be losing virulence. One way to find out is to track mortality rates and see whether, over time, fewer people with covid-19 are dying. That requires accurate universal testing to find out how many people have been infected and hence what proportion of them has died. We don’t yet have that information, except for a couple of small data sets, which is why our current estimates of death rates from covid-19 vary so widely (see “How lethal is covid-19?”, page 42).

There is another approach, although it is even more challenging: real-time tracking of pathogen evolution. In 2018, a group of researchers set up an open-source project called Nextstrain to do just that, looking at a range of diseases from seasonal flu and measles to West Nile virus and Zika. Now they have turned their attention to SARS-CoV-2, analysing all publicly available genomic sequences of the virus, and using analytic and visual tools to discover how it is changing as it spreads across the planet.

“We look at the genetic material of the virus, evaluating the small changes over time as the virus copies itself over and over,” says Emma Hodcroft at the University of Basel, Switzerland, who is a co-developer of Nextstrain. By comparing the random mutations in different samples, the team can start to see how strains are related. This lets them make what is called a phylogeny, an evolutionary history of the pathogen, “which helps us track how the virus is spreading through time and space,” she says.

Working out whether strains of SARS-CoV-2 are becoming less deadly is another matter, however. After decades of research on the flu virus, geneticists still struggle to make predictions about which strains are more or less virulent. Coronavirus are larger than typical RNA viruses—they have about 30,000 bases of genetic information compared with just 13,000 in flu—and it is unclear exactly what different genetic mutations represent in terms of evolutionary adaptations. What is clear is that SARS-CoV-2 isn’t changing much genetically. “The amount of diversity we’re seeing is basically nothing. The maximum difference is 40 differences in 29,000 bases,” says Hodcroft. “There just hasn’t been time for [natural] selection to act.” That said, we don’t know how much genetic change will be necessary to reduce the virulence of SARS-CoV-2. Just one mutation, if it is the right one, can fundamentally alter how a virus affects human populations, says Susanna Manrubia at the Spanish National Centre for Biotechnology.

On the other hand, there is a possibility that this particular virus won’t become milder. “Evolutionary predictions are much like weather forecasting,” says Manrubia.
Quarantining people with virulent strains of a virus can help promote less deadly ones

Jonathan R. Goodman is at the Leverhulme Centre for Human Evolutionary Studies, University of Cambridge, UK

“If we can catch SARS-CoV-2 evolving, we might even be able to give it a helping hand.”

There are just too many variables.” And when it comes to predicting the evolutionary trajectory of SARS-CoV-2, two confounding factors stand out. First, there is the fact that people tend to transmit the virus to others very soon after they are infected, with some evidence suggesting that between a quarter and half of infections are asymptomatic. Then there is the huge variability in people’s responses, with a strain that causes minor or even asymptomatic disease in one individual able to kill another. “SARS-CoV-2 is spreading successfully, so short-term evolutionary changes aren’t necessary,” says Hodcroft.

Losing virulence

Others are more optimistic that SARS-CoV-2 will become milder, although it is unknown how long this might take. After all, crowded conditions in Wuhan led to the evolution of a virus that was both highly transmissible and highly virulent, and conditions are changing again as it circulates further from its source. That makes adaptation likely, even if the virus can be transmitted by people who lack symptoms, according to evolutionary biologist Paul Ewald at the University of Louisville, Kentucky.

If SARS-CoV-2 is becoming less deadly, then we will have less to fear from it as time passes. What’s more, if we can catch it evolving we might even be able to give it a helping hand. “If mortality is declining, then the molecular make-up of the viruses associated with low mortality can be compared with that of viruses associated with high mortality to determine any evolutionary changes,” says Ewald. In theory, we could artificially select more benign strains by strictly quarantining people infected with the most virulent strains – and anyone who has been in contact with them. In practice, this might not work, however. “Quarantining people with severe disease may lower the infection rate, but not necessarily the overall severity of the illness,” says Perlman. Until we understand why the same strain can be benign in one person and deadly in another, exposing people even to milder strains of the virus is risky, which is why the idea of herd immunity is problematic.

Of course, there is another way to gain herd immunity: vaccination. But until we have a vaccine, most experts say the best policy is to limit the virus’s spread. Evolutionary thinking can help us cope, especially if we can integrate it into our predictive models to forecast how SARS-CoV-2 is likely to change through time and space. It will take unprecedented collaboration, but projects like Nextstrain illustrate that this is already happening. Dobzhansky was right. Evolution can help us make sense of covid-19. It can also reduce the risk of another pandemic like this happening in the future.