News in focus

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Social dynamics are back to pre-pandemic norms in many parts of the world.

WILL THERE BE A COVID WINTER WAVE? WHAT SCIENTISTS SAY

Emerging variants and waning immunity are likely to push infection rates higher in the Northern Hemisphere, with influenza also expected to make a comeback.

By Ewen Callaway

Evidence is building that the Northern Hemisphere is on course for a surge of COVID-19 cases this autumn and winter. New immune-evading strains of the Omicron variant of SARS-CoV-2, changes in people's behaviour and waning immunity mean that many countries could soon see large numbers of COVID-19 infections — and potentially of hospitalizations — say scientists.

Nature explores the factors that might drive a COVID-19 wave — and what countries can do to blunt the effects with the new generation of vaccines that target Omicron.

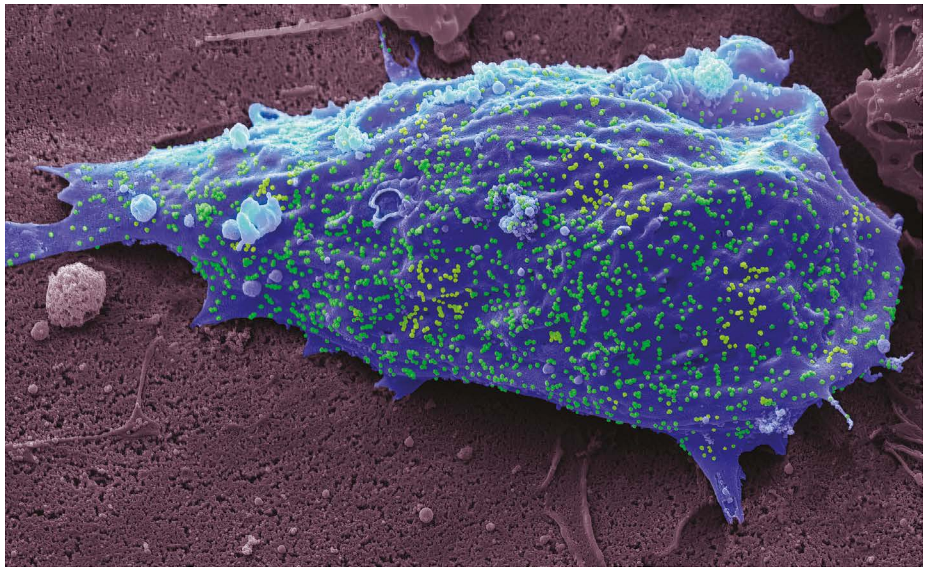
Will there be a COVID-19 wave this autumn and winter?

In mid-August, an effort called the COVID-19 Scenario Modeling Hub laid out several scenarios for the United States over the coming months. After surges caused by the BA.5 Omicron variant — resulting in high levels of immunity in the population — the United States could be in for a relatively quiet COVID-19 season, the models suggested, as long as vaccine-booster campaigns began quickly and new variants didn't emerge. Even with a new variant, a big surge in cases wasn't certain.

More than a month on, hospitalizations are declining in line with projections, says Justin Lessler, an infectious-disease epidemiologist at the University of North Carolina at Chapel Hill, who leads the modelling effort. But other factors on the horizon could spell trouble. The roll-out of 'bivalent' boosters that target both the original SARS-CoV-2 strain and Omicron "has been a little bit slow", says Lessler. And there are now subtle signs that Omicron is evolving and spawning a new generation of immunity-dodging variants. "It could lead to some upswings as we go into the fall and winter months," Lessler adds. Some US states are already beginning to see an uptick in cases, notes epidemiologist Jennifer Nuzzo at Brown University in Providence, Rhode Island.

The United Kingdom's weekly population survey of SARS-CoV-2 infections, a gold standard in COVID-19 data, has documented an increase in COVID-19 prevalence in England and Wales in its past two reports. The number of people hospitalized after testing positive for SARS-CoV-2 is rising quickly – although from low levels – in Britain and other European countries.

In the background, a slew of immunity-dodging variants are emerging globally, and researchers think these will fuel an autumn–winter wave.



STEVE GSCHMEISSNER/SPL

Viral particles (green) on a cell. Descendants of the Omicron lineage are gaining mutations.

Are new variants behind rising case numbers?

Probably not yet, says Tom Wenseleers, an evolutionary biologist at the Catholic University of Leuven in Belgium. The current rise in SARS-CoV-2 infections is probably occurring mainly because, in most people, immunity generated by vaccines or previous infections is waning. People are also mixing more than they did earlier in the pandemic. In many countries, including the United Kingdom, social dynamics are nearly back to pre-pandemic levels, say health officials. Factors that cause other respiratory viruses to thrive in cooler months – including extra time spent indoors – could also be at play.

Will we see a new Omicron strain this autumn?

We might see three or more. The Omicron subvariants that drove past waves – BA.2, BA.4 and BA.5 – are subsiding, but their descendants are gaining mutations that seem to be helping them to spread.

SARS-CoV-2-watchers are tracking an unprecedented menagerie of variants from a number of branches of the Omicron family tree, says Tom Peacock, a virologist at Imperial College London. Despite these variants' distinct ancestries, they share many mutations in the SARS-CoV-2 spike protein (the part of the virus that immune systems target). "Clearly, there's an optimal way for a variant to look going into this season," says Peacock.

Researchers are keeping a close eye on certain sublineages. The United Kingdom and some other European countries, for instance, are seeing the swift ascent of BQ.1 (a descendant of BA.5 with several key changes). In India, spawn of the BA.2.75 variant that drove an infection wave several months ago are now outcompeting all others, says microbiologist Rajesh Karyakarte, based in Pune, who coordinates SARS-CoV-2 genetic sequencing in the state of Maharashtra. In samples his team sequenced in late September, a subvariant called BA.2.75.2 was the most common, followed by a close relative. Another BA.2 offshoot, BA.2.3.20, is growing quickly in Singapore, and has turned up in Denmark and Australia.

"I'm fairly confident that at least one of these variants or a combination of them will lead to a new infection wave," says Wenseleers. And, because they all seem to be behaving similarly, "at the end of the day, it's not that important which of these becomes the next big thing".

Why are these variants on the rise?

Two words: immune evasion. All the variants that researchers are tracking contain multiple overlapping changes to a portion of the spike protein called the receptor binding domain, which is targeted by potent infection-blocking, or neutralizing, antibodies. That numerous viruses are independently developing the same spike mutations suggests that these changes provide a big advantage to the viruses' ability to spread, says Yunlong Richard Cao, an immunologist at Peking University in Beijing.

"The degree of immune escape and evasion is amazing right now, crazy."

In a September preprint[1], Cao and his colleagues evaluated the capacity of the new crop of variants to evade neutralizing antibodies from vaccination and previous infection with other variants. They found that BQ.1.1 (a member of the BQ.1 family with one extra spike change) and BA.2.75.2 were the most immune evasive, even able to dodge most neutralizing antibodies elicited by infection with BA.5. Two antibody drugs were still effective against BA.2 and BA.5, but they are likely to lose much of their potency against many of the emerging Omicron subvariants, the study suggests. Another team[2], including Peacock, came to similar conclusions about BA.2.75.2. "The degree of immune escape and evasion is amazing right now, crazy," says Cao.

How big will the waves be?

On the basis of initial estimates, Wenseleers thinks that autumn–winter waves will be similar in size to BA.5 surges, at least as far as infections go. What's harder to predict is hospitalizations. The build-up of population immunity from vaccination and previous infection is likely to keep admissions lower than during past COVID-19 waves, say researchers, but how much lower is unclear. "While a completely different game than it would have been in 2020 or 2021, a surge still would probably be associated with an increase in deaths and an increase in hospitalizations," says Lessler.

But even a relatively muted COVID-19 wave could put strain on hospitals, which are facing backlogs and other conditions that put a heavy burden on health systems in the winter. Influenza, which has barely registered over the past two winters, is likely to come back with a vengeance in the Northern Hemisphere this season, stoking fears of a 'twindemic' of influenza and COVID-19. "In a bad flu year, hospital systems get pretty stressed," says Lessler.

What about the new vaccines?

Boosters, including bivalent vaccines, are likely to offer some protection against infection with emerging variants. But this might not last long, say scientists. One part of the bivalent vaccines is based on an Omicron subvariant – BA.1 in UK-approved vaccines and BA.5

in the United States. But there are signs[3] that the vaccines tend to stimulate the production of neutralizing antibodies that best recognize not Omicron, but the ancestral virus on which the first vaccines were based. A second dose of the boosters might be needed to generate high levels of Omicron-specific neutralizing antibodies, says Cao.

Fortunately, all evidence suggests that COVID-19 vaccines old and new remain highly effective at preventing severe disease, which Nuzzo argues should be the main goal of booster programmes. This means concentrating booster campaigns on those at the highest risk of severe disease, including older people and people with underlying health conditions, who will benefit the most from the added protection. "We need a laser focus on protection against severe illness," she says.

1. Cao, Y. *et al*. Preprint at bioRxiv https://doi.org/10.1101/2022.09.15.507787 (2022).
2. Sheward, D. J. *et al*. Preprint at bioRxiv https://doi.org/10.1101/2022.09.16.508299 (2022).
3. Alsoussi, W. B. *et al*. Preprint at bioRxiv https://doi.org/10.1101/2022.09.22.509040 (2022).

PHYSICS NOBEL FOR 'SPOOKY' QUANTUM ENTANGLEMENT

Award goes to three physicists whose research laid the groundwork for quantum information science.

By Davide Castelvecchi & Elizabeth Gibney

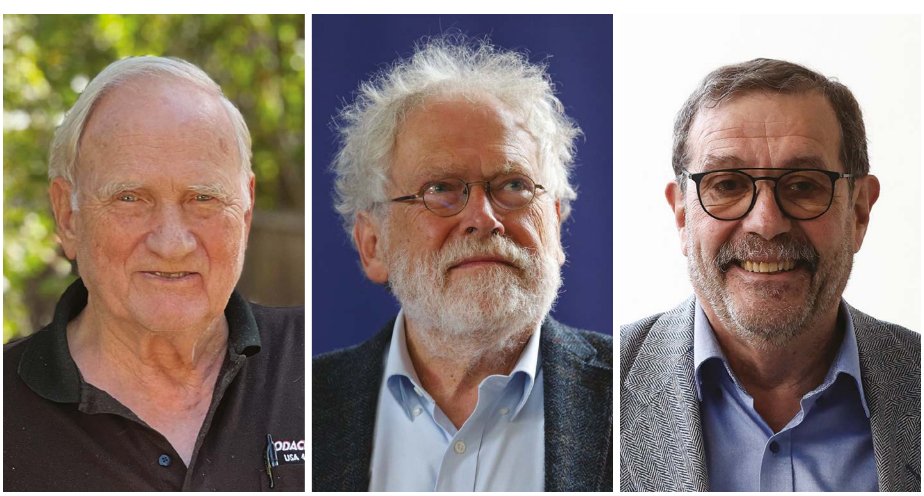
Three quantum physicists have won the 2022 Nobel Prize in Physics for their experiments with entangled photons, in which particles of light become inextricably linked. Such experiments have laid the foundations for an abundance of quantum technologies, including quantum computers and communications.

Alain Aspect, John Clauser and Anton Zeilinger will each share one-third of the 10-million-Swedish-kronor (US$915,000) prize.

"I was actually very surprised to get the call," said Zeilinger, a physicist at the University of Vienna, at the press conference announcing the award. "This prize would not be possible without the work of more than 100 young people over the years."

Aspect, a physicist at the University of Paris-Saclay, received the call during a committee meeting. "I happened to be sitting near Aspect this morning when he got the call," says Serge Haroche, an experimental physicist at the Collège de France in Paris who won a share of the 2012 Nobel Prize in Physics for work in quantum physics. When he left the room, Haroche added, Aspect's colleagues guessed correctly that it was the Royal Swedish Academy of Sciences in Stockholm calling.

The trio's experiments proved that connections between quantum particles were not down to local 'hidden variables', unknown factors that invisibly tie the particles' outcomes together. Instead, the phenomenon comes from a genuine association in which manipulating one quantum object affects another far away. German physicist Albert Einstein famously called the phenomenon 'spooky action at a distance' — it is now known as quantum entanglement.



REMI VORANO/AFP/GETTY; HEINZ-PETER BADER/GETTY; BENOIT TESSIER/REUTERS

From left: John Clauser, Anton Zeilinger and Alain Aspect won this year's physics Nobel prize.

All three winners are pioneers in the fields of quantum information and quantum communications, says Pan Jianwei, a physicist at the University of Science and Technology of China in Hefei who participated in some of Zeilinger's landmark experiments as a graduate student in the 1990s. The recognition was long overdue, Pan says. "We have been waiting for this for a very, very long time."

The win is "beautiful news" agrees Chiara Marletto, a theoretical physicist at the University of Oxford, UK. The modern versions of the experiments pioneered by the three winners, she says, could be central to one of the great open questions of physics today — how to reconcile quantum mechanics with Albert Einstein's general theory of relativity.

Particle pairs

Because of the effects of quantum entanglement, measuring the property of one particle in an entangled pair immediately affects the results of measurements on the other. This is what enables quantum computers to function. The machines, which seek to harness quantum particles' ability to exist in more than one state at once, carry out calculations that would be impossible on a conventional computer. Today, physicists are using entanglement to develop quantum encryption and a quantum internet that would allow for ultrasecure communications and new kinds of sensors and telescopes.

But whether particles could be fundamentally linked in this way — such that measuring one determines the properties of another, rather than just revealing a predetermined state — had been a topic of debate since physicists laid the foundations of quantum mechanics in the 1920s.

In the 1960s, physicist John Bell proposed a mathematical test known as Bell's inequality. This said that experimental results that seemed to be correlated beyond a particular value would be possible only through quantum entanglement, rather than being due to certain kinds of hidden variable. Quantum mechanics predicts a higher degree of correlation than would be possible in classical, or pre-quantum, physics.

In 1972, Clauser — now a physicist at J.F. Clauser & Associates in Walnut Creek, California — and his colleagues developed these ideas into a practical experiment that violated the Bell inequality, supporting the theories of quantum mechanics.

David Kaiser, a quantum physicist and historian of science at the Massachusetts Institute of Technology in Cambridge, says