

News in focus

Nature Human Behaviour (D. Duke et al. *Nature Hum. Behav.* <https://doi.org/g2kw>; 2021).

The site lies alongside the now-dry channel of a prehistoric river called the Old River Bed, where people camped 13,000 to 9,500 years ago. While excavating a historical site located within the US Air Force's Utah Test and Training Range, the team found an ancient hearth containing four burnt tobacco-plant seeds.

The researchers used radiocarbon dating to determine how old the hearth and its contents were. The tobacco seeds themselves were too small and fragile to be dated, but the team determined that other burnt woody material in the hearth was around 12,300 years old. The charred seeds were presumed to be of a similar age.

Although the team cannot say for certain how the tobacco was used, the fact that only seeds remain implies that the leaves and stems of the tobacco plant – the parts with the intoxicant effect – were consumed. The seeds, which are small and easily caught in the sticky hairs of the plant, could have been picked up when the plants were harvested. “People in the Pleistocene likely smoked tobacco or chewed tobacco in a similar fashion to how it’s used today,” says Jaime Kennedy, an archaeologist at the University of Oregon in Eugene.

Duck bones

Artefacts found in and around the hearth provide context for the find. These include fragments of a Haskett, a spear tip commonly used by roaming hunter-gatherers in North America during the Pleistocene. In this case, the researchers say, it seems to have been used to hunt various species of duck: a large number of waterfowl bones were uncovered at the site.

Duke's team also found charred seeds from other plants traditionally eaten by Native American communities: goosefoot (*Chenopodium* spp.), red maids (*Calandrina* spp.) and hairgrass (*Deschampsia* spp.).

The tobacco seeds were unlikely to have been deposited into the hearth naturally, the researchers say, but they investigated this possibility. The seeds could have come from the hunted ducks' stomachs, or from plants growing in the vicinity of the hearth. But tobacco grows on higher ground – away from wetlands and typical waterfowl foods. “The birds would have to be away from their natural habitat and eating something that is basically toxic and not palatable,” says Duke. He and his team examined sediments from the area around the time of human occupation. “We found only common wetland plants, not tobacco,” he says.

It is especially interesting that tobacco was found along with seeds from edible plants such as goosefoot, says Kennedy. “This discovery highlights the ancient symbiotic relationship between people and plants like tobacco that flourish in anthropogenically disturbed soils,” she says.



A woman receives a dose of Sinovac's CoronaVac COVID-19 vaccine in Brazil.

CHINA'S COVID VACCINES HAVE BEEN CRUCIAL: NOW IMMUNITY IS WANING

Billions of shots have been given globally, but studies question the length of protection they offer.

By Smriti Mallapaty

China's CoronaVac and Sinopharm vaccines account for almost half of the 7.3 billion COVID-19 vaccine doses delivered globally, and have been enormously important in fighting the pandemic, particularly in less wealthy nations (see 'The race to vaccinate').

But as the doses have mounted, so have the data, with studies suggesting that the immunity from two doses of either vaccine wanes rapidly. Last week, the World Health Organization (WHO) announced advice from its Strategic Advisory Group of Experts on Immunization (SAGE) that people over 60 should receive a third dose to ensure sufficient protection. The recommendation is “sensible and necessary”, says Manoel Barral-Netto, an immunologist at the Oswaldo Cruz Foundation in Salvador, Brazil.

A number of countries are already offering third doses to all adults or are trying mix-and-match approaches. Some experts are even questioning whether China's jabs – based on inactivated virus – should continue to be used

at all when other options are available.

But others say that the vaccines are still important. “These are not bad vaccines. They're just vaccines that haven't been optimized yet,” says Gagandeep Kang, a virologist at the Christian Medical College in Vellore, India.

CoronaVac, produced by Beijing company Sinovac, is the world's most used COVID-19 vaccine. Not far behind is the vaccine developed in Beijing by state-owned Sinopharm.

In mid-2021, the WHO approved the shots for emergency use, on the basis of limited clinical-trial data suggesting that CoronaVac was 51% and Sinopharm 79% effective at preventing symptomatic disease. This was on a par with the 63% efficacy reported for the University of Oxford–AstraZeneca's viral-vector vaccine at the time of its WHO listing, but lower than the 90% and higher efficacies of the mRNA vaccines developed by Pfizer–BioNTech and Moderna.

Both the Chinese vaccines are ‘inactivated vaccines’, which use killed SARS-CoV-2 virus. Researchers say this type of vaccine seems to be less potent because it triggers an immune

response against many viral proteins. By contrast, mRNA and viral-vector vaccines target the response to the spike protein, which the virus uses to enter human cells.

About 2.4 billion doses of the Chinese vaccines have been administered in China, but almost one billion doses have gone to 110 other countries (see 'Biggest takers for China's vaccines'). Reports earlier this year of COVID-19 surges in several countries that had vaccinated many people with these vaccines – such as the Seychelles and Indonesia – prompted questions about the protection they offered.

Numerous studies have now been undertaken to understand waning immunity and protection in different groups.

Lower antibody responses

Some studies have found that compared with vaccines made using other technologies, China's inactivated vaccines initially generate lower levels of 'neutralizing' or virus-blocking antibodies – considered a proxy for protection – and that these levels drop quickly over time.

One study of 185 health-care workers in Thailand¹, not yet peer reviewed, found that 60% had high levels of neutralizing antibodies one month after a second dose of CoronaVac, compared with 86% of those who had received two shots of the Oxford–AstraZeneca vaccine.

Co-author Opass Putcharoen, an infectious-diseases specialist at the Thai Red Cross Emerging Infectious Diseases Clinical Center in Bangkok, says the team also found that three months after receiving the second CoronaVac shot, antibody prevalence dropped to just 12%.

But "waning of antibodies isn't necessarily the same as waning of immune protection", says Ben Cowling, an epidemiologist at the University of Hong Kong. He says that vaccines induce complex immune responses, including B cells and T cells, which might last longer than neutralizing antibodies.

One study from Hong Kong², which has not

been peer reviewed, showed that CoronaVac induces a significantly lower antibody response compared with Pfizer–BioNTech's mRNA jab one month after two doses, but that the T-cell response was comparable.

Another non-peer-reviewed study in China³, also found that B cells and T cells specific for SARS-CoV-2 could be detected five months after two doses of the Sinopharm vaccine.

So far, studies assessing protection over time are limited. But preliminary analysis of a mass-vaccination campaign with CoronaVac in Chile suggests a small but significant decline in efficacy against symptomatic disease, although protection against hospitalization remains high, says Eduardo Undurraga, a public-health researcher at the Pontifical Catholic University of Chile in Santiago.

Vaccines made using other technologies have seen a similar trend of waning protection against infection, but more-robust protection against severe disease and death. But researchers say that because the Chinese inactivated vaccines start at a lower base of neutralizing antibodies, the protection they offer could drop faster than that from vaccines with a head start.

The less-potent immune response from inactivated vaccines also has implications for the protection they offer to older people. The immune system weakens with age and vaccines are generally less effective in older people, says Kang, but the effect seems to be more pronounced with the inactivated vaccines.

A massive analysis of some one million people who were hospitalized with COVID-19 in Brazil⁴ found that CoronaVac offered up to 60% protection against severe disease up to the age of 79 – not far off the 76% protection offered by the Oxford–AstraZeneca vaccine.

But the picture changes drastically in people over 80, says co-author Daniel Villela, an epidemiologist at the Oswaldo Cruz Foundation in Rio de Janeiro, Brazil. In that group, CoronaVac was only 30% effective at preventing severe disease and 45% effective against death, compared with 67% and 85%, respectively, for the Oxford–AstraZeneca jab.

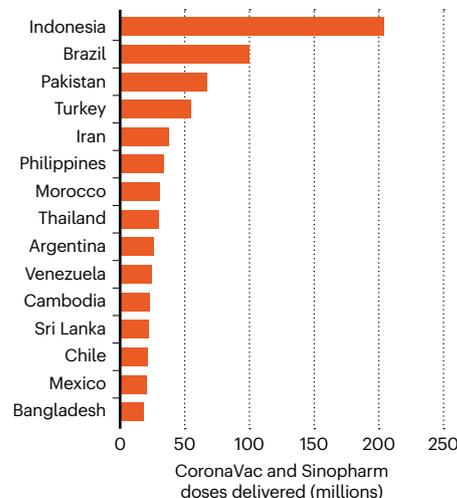
Research by Barral-Netto⁵ found that CoronaVac prevented only 33% of deaths in people 90 and older. Neither study has been peer reviewed, but Villela says they influenced Brazil's government to start giving people older than 70 a third shot of an mRNA or viral-vector vaccine in August – that decision has now been extended to people older than 60.

"It was better to receive CoronaVac than nothing," says Barral-Netto, but now that there are other vaccines in Brazil "it is probably not very wise to keep vaccinating people with this", he says, adding that the Brazilian government has said it will stop purchasing CoronaVac.

Other countries, including Chile, Abu Dhabi in the United Arab Emirates and China, are also giving booster jabs to those who received the CoronaVac or Sinopharm vaccines.

BIGGEST TAKERS FOR CHINA'S VACCINES

More than two billion doses of China's CoronaVac and Sinopharm vaccines have been administered in China, but nearly one billion doses have gone to 110 other nations.



SOURCE: DATA FROM AIRFINITY

Clinical-trial data from China⁶, not yet peer reviewed, suggest that a third dose of CoronaVac increases neutralizing-antibody levels, and a similar boost has been observed in studies of third doses of Sinopharm's vaccine.

And earlier this month, the Chilean government reported preliminary results on the effectiveness of booster shots, based on data from some two million people who had received two shots of CoronaVac, and a third shot of the CoronaVac, Pfizer–BioNTech or Oxford–AstraZeneca vaccines. Protection against COVID-19 jumped from 56% after two shots to 80% or higher after a third shot of any vaccine, with protection against hospitalization rising from 84% to 87%.

Mix and match

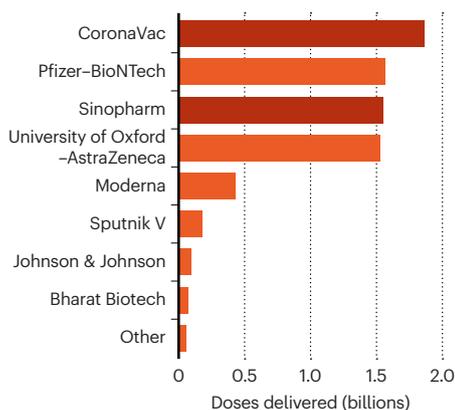
An alternative to a three-dose schedule might be to mix and match with just two doses.

Sompong Vongpunsawad, a virologist at Chulalongkorn University in Bangkok, led a team that studied antibody levels in people who received one dose of CoronaVac and one of Oxford–AstraZeneca. The results⁷, not yet peer reviewed, suggest that the response was similar to two doses of AstraZeneca, and higher than two doses of CoronaVac.

It is not yet clear how long that protection will last, but researchers say such mixing has merit.

THE RACE TO VACCINATE

Out of the eight vaccines that account for the vast majority of COVID-19 vaccine doses delivered globally, China's CoronaVac and Sinopharm jabs account for nearly half of all doses.



SOURCE: DATA FROM AIRFINITY

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