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First genetically modified mosquitoes released in the United States

Biotech firm Oxitec launches controversial field test of its insects in Florida after years of push-back from residents and regulatory complications.

Emily Waltz

After a decade of fighting for regulatory approval and public acceptance, a biotechnology firm has released genetically engineered mosquitoes into the open air in the United States for the first time. The experiment, launched this week in the Florida Keys — over the objections of some local critics — tests a method for suppressing populations of wild *Aedes aegypti* mosquitoes, which can carry diseases such as Zika, dengue, chikungunya and yellow fever.

Oxitec, the firm based in Abingdon, UK, that developed the mosquitoes, has previously field-tested the insects in Brazil, Panama, the Cayman Islands and Malaysia.

But until now, owing to a circuitous series of regulatory decisions and pushback from Florida residents (see ‘A long road’), no genetically engineered mosquito had been trialled in the United States — even though the country previously allowed tests of a genetically engineered diamondback moth (*Plutella xylostella*) in New York and an engineered pink bollworm (*Pectinophora gossypiella*) in Arizona, both developed by Oxitec. “When something new and revolutionary comes along, the immediate reaction of a lot of people is to say: ‘Wait.’,” says Anthony James, a molecular biologist focused on bioengineered mosquitoes at the University of California, Irvine. “So the fact that [Oxitec] was able to get the trial on the ground in the United States is a big deal.”

Experiment launched

Aedes aegypti makes up about 4% of the mosquito population in the

Keys, a chain of tropical islands off the southern tip of Florida. But it is responsible for practically all mosquito-borne disease transmitted to humans in the region, according to the Florida Keys Mosquito Control District (FKMCD), which is working closely with Oxitec on the project. Researchers and technicians working on the project will release bioengineered male *Aedes aegypti* mosquitoes, which don’t bite, to mate with the wild female population, responsible for biting prey and transmitting disease. The genetically engineered males carry a gene that passes to their offspring and kills female progeny in early larval stages. Male offspring won’t die but instead will become carriers of the gene and pass it to future generations. As more females die, the *Aedes aegypti* population should dwindle.

FKMCD in 2010 approached Oxitec about testing its approach in the Keys, because Florida was — and still is — experiencing an increase in mosquito-borne disease. In 2009, the state began seeing cases of locally transmitted dengue, and, a few years later, locally transmitted Zika.

In late April of this year, project researchers placed boxes containing Oxitec’s mosquito eggs at six locations in three areas of the Keys. The first males are expected to emerge within the first two weeks of May. About 12,000 males will exit the boxes each week over the next 12 weeks. In a second phase later this year, intended to collect even more data, nearly 20 million mosquitoes will emerge over a period of about 16 weeks, according to Oxitec.

Genetically engineered mosquitoes are an alternative to insecticides, which are used heavily in the United States to control insect populations. This has resulted in the evolution of mosquitoes that are resistant to insecticides.

“Unfortunately, we’re seeing our toolbox shrinking due to resistance,” said Andrea Leal, executive director of FKMCD, at a press conference last week. “That’s one of the reasons why we’re

really looking at these new innovative tools and new ways to control this mosquito.”

To monitor the trial’s progress, researchers will use capture devices to trap mosquitoes for study. They will measure how far the male mosquitoes travel from the boxes, how long they live, how effectively they squelch the wild female mosquito population and whether all of the females with the gene are indeed dying. Oxitec mosquitoes carry a fluorescent marker gene that makes them glow when exposed to a specific colour of light, which makes identification easier.

The biotech firm plans to present the results to the US Environmental Protection Agency (EPA), which gave the green light for the trial. The data will help the EPA to determine whether Oxitec can release the mosquitoes more broadly in the United States. The company is still testing them in Brazil and other countries.

Residential pushback

Opposition to the Florida field trial has been fierce from some residents in the Keys. Worried about being bitten by the mosquitoes or that the insects will disrupt the Florida ecosystem — and generally unhappy about being chosen as a test site — some have threatened to derail the experiments by spraying insecticides near the release points. “As you can imagine, emotions run high, and there are people who feel really strongly either for or against it,” says molecular biologist Natalie Kofler, who lectures at Harvard Medical School in Cambridge, Massachusetts, and is the founder of Editing Nature, an organization that advocates for responsible development and oversight of gene-editing technologies. “And I can see how, if you didn’t agree to this, it could be really concerning to have mosquitoes released in your neighborhood.”

Many of the concerns stem from the uncertainty of a new technology, says Kofler, who has been following this project for

years. Oxitec has been engaging with the Florida Keys community to provide answers to queries. They explained, for instance, the very low likelihood that female mosquitoes with the lethal gene could reproduce. But many people don’t have confidence in what they’re hearing, because it’s coming from a company, says Kofler.

Kofler is hoping that enough data are gathered to assess the mosquitoes’ impact, including on other species in the Keys and local ecosystems, and that it’s done “in a way that’s transparent, and in a way that can make some community members feel better about the whole situation”.

Oxitec employees have taken precautions against vandalism by placing their mosquito boxes on private, fenced-in properties, and not disclosing their precise locations to the public.

A Long Road

Oxitec has faced regulatory assessments from three different US federal agencies and opposition from Florida residents over the past decade as it sought approval to release its experimental mosquitoes in the United States for the first time.

March 2010: Oxitec submits a request to the US Department of Agriculture (USDA) to run a field trial with its genetically modified mosquitoes.

October 2011: The USDA says it doesn’t have regulatory jurisdiction over Oxitec’s mosquitoes.

November 2011: The US Food and Drug Administration (FDA) claims jurisdiction over regulating the mosquitoes, so Oxitec submits an application to the agency for a trial in Key Haven, Florida.

August 2016: The FDA approves the trial. The start date depends on the Florida Keys Mosquito Control District (FKMCD) board’s approval of mosquito-release locations.

November 2016: Key Haven residents vote against the trial in a referendum, but elsewhere in Monroe Country, Florida, enough

residents vote in favour of it to keep the project afloat.

October 2017: The FDA transfers jurisdiction of Oxitec's mosquitoes to the US Environmental Protection Agency (EPA).

March 2019: Oxitec transitions to a second-generation mosquito because of advances in technology and requests from the EPA an experimental permit to conduct field trials in Monroe County.

April 2020: The EPA green-lights the project.

August 2020: The FKMCD board votes to proceed with the trial.

April 2021: The trial begins as boxes of genetically engineered mosquitoes are placed in Monroe County's Cudjoe Key, Ramrod Key and Vaca Key.

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<https://bit.ly/3vKbw5L>

The enzyme that could help 700 million people worldwide

University of South Australia researchers have identified an enzyme that may help to curb chronic kidney disease, which affects approximately 700 million people worldwide.

This enzyme, NEDD4-2, is critical for kidney health, says UniSA Centre for Cancer Biology scientist Dr Jantina Manning in a new paper published this month in *Cell Death & Disease*.

The early career researcher and her colleagues, including 2020 SA Scientist of the Year Professor Sharad Kumar, have shown in an animal study the correlation between a high salt diet, low levels of NEDD4-2 and advanced kidney disease.

While a high salt diet can exacerbate some forms of kidney disease, until now, researchers did not realise that NEDD4-2 plays a role in promoting this salt-induced kidney damage.

"We now know that both a high sodium diet and low NEDD4-2 levels promote renal disease progression, even in the absence of high blood pressure, which normally goes hand in hand with increased sodium," says Dr Manning.

NEDD4-2 regulates the pathway required for sodium reabsorption in the kidneys to ensure correct levels of salt are maintained. If the NEDD4-2 protein is reduced or inhibited, increased salt absorption can result in kidney damage. Even people on a low salt diet can get kidney damage if they have low levels of NEDD4-2 due to genetic variations or mutations in the gene.

Prof Kumar says the long-term goal is to develop a drug that can increase NEDD4-2 levels in people with chronic kidney disease (CKD). "We are now testing different strategies to make sure this protein is maintained at a normal level all the time for overall kidney health," Prof Kumar says.

"In diabetic nephropathy - a common cause of kidney disease - levels of NEDD4-2 are severely reduced. This is the case even when salt is not a factor."

The study also revealed a surprising finding: that the high salt diet induced kidney disease is not always due to high blood pressure.

"In a lot of cases, kidney disease is exacerbated by hypertension, so we wanted to investigate that link in our study. In fact, we found the complete opposite - that a high salt diet caused excessive water loss and low blood pressure. This is significant because it means that kidney disease can also happen in people who don't have high blood pressure," Dr Manning says.

A 2020 Lancet paper estimated that about 700 million people - or 10 per cent of the world's population - suffer from chronic kidney disease, which represents a 29 per cent increase in the past 30 years. The huge spike in CKD is mainly attributed to a global obesity epidemic in recent decades, leading to diabetes, one of the leading causes of chronic kidney disease along with high blood pressure.

World Health Organization statistics reveal a 300 per cent increase in diabetes between 1980 and 2014, making it one of the top 10 causes of death worldwide and showing the gravity of the problem facing scientists trying to tackle kidney disease.

"Obesity and lifestyle are two main factors driving chronic kidney disease but there are other things at play as well," says Dr Manning. "Acute kidney injuries, drugs taken for other conditions, high blood pressure and a genetic predisposition can also cause it."

The UniSA scientists are collaborating with clinicians from the Royal Adelaide Hospital and Flinders Medical Centre and hope to secure funding to take their research to the next stage - to find a way to regulate NEDD4-2 and protect against kidney disease.

<https://bit.ly/3b6WM98>

Low doses of radiation may improve quality of life for those with severe Alzheimer's

Remarkable improvements in behaviour and cognition days after receiving a new treatment that delivered low doses of radiation

Individuals living with severe Alzheimer's disease showed remarkable improvements in behaviour and cognition within days of receiving an innovative new treatment that delivered low doses of radiation, a recent Baycrest-Sunnybrook pilot study found.

"The primary goal of a therapy for Alzheimer's disease should be to improve the patient's quality of life. We want to optimize their well-being and restore communication with family and friends to avoid social isolation, loneliness and under-stimulation. Although the study was a small pilot and should be interpreted with caution, our results suggest that low-dose radiation therapy may successfully achieve this," says Dr. Morris Freedman, scientist at Baycrest's Rotman Research Institute, head of the division of neurology at Baycrest and senior author of the study.

The study was a clinical follow-up to a 2015 case report about a patient in hospice with Alzheimer's disease. After being treated several times with radiation to her brain, she showed such significant improvements in cognition, speech, movement and appetite that she was discharged from the hospice to a long-term care home for older adults.

High doses of radiation are known to have harmful effects on our

health. However, low doses, such as those used for diagnostic CT scans, can help the body protect and repair itself.

"Numerous neurological disorders, including Alzheimer's disease, are thought to be caused in part by oxidative stress that damages all cells, including those in the brain. We have natural protection systems to combat the damage, but they become less effective as we get older. Each dose of radiation stimulates our natural protection systems to work harder - to produce more antioxidants that prevent oxidative damage, to repair more DNA damage and to destroy more mutated cells," says Dr. Jerry Cuttler, a retired Atomic Energy of Canada scientist. He has been researching the effects of radiation on health for more than 25 years and is the lead author of the study.

In this study, published in the *Journal of Alzheimer's Disease*, four individuals living with severe Alzheimer's disease were given three treatments of low-dose radiation, each spaced two weeks apart. A CT scanner at Sunnybrook Health Sciences Centre was employed to provide the treatments, with the supervision and support of Dr. Sandra Black, senior scientist and neurologist, and Dr. Sean Symons, radiologist-in-chief, both at Sunnybrook. The researchers used standardized tests and observation to record changes in the patients' communication and behaviour after the treatment. Most importantly, they collected information (descriptions, photos and videos) from the patients' spouse, children and caregivers.

Remarkably, three of the four individuals showed improvements within one day of the first treatment, with their relatives reporting increased alertness and responsiveness, recognition of loved ones, mobility, social engagement, mood and more.

Two days after the first treatment, the son of one of the patients reported, "When I said hello, she looked at me and said, 'Hello dear.' She hadn't said this to me in years!"

The daughter of another patient noted: "I had an amazing visit with

my dad this evening. I'm speechless from last night. He was excited to see me - he spoke to me right away and gave me multiple kisses - real kisses like years ago. He was clapping his hands to the music. My mom agreed it's been years since he has done this. Everyone is amazed."

The results of this study offer hope for those with severe Alzheimer's disease and their loved ones. However, it is important to note that this was a small pilot study with some limitations, including missing a placebo group. Future research is needed to examine the effects of this novel therapy in larger clinical trials.

Dr. Freedman, senior author, was supported in part by the Saul A. Silverman Family Foundation as part of the Canada International Scientific Exchange Program (MF), and the Morris Kerzner Memorial Fund.

<https://bit.ly/3eoh8gf>

An animal able to regenerate all of its organs even when it is dissected into three parts

A surprising discovery in the Gulf of Eilat

An extraordinary discovery in the Gulf of Eilat: Researchers from Tel Aviv University have discovered a species of ascidian, a marine animal commonly found in the Gulf of Eilat, capable of regenerating all of its organs - even if it is dissected into three fragments.

The study was led by Prof. Noa Shenkar, Prof. Dorothee Huchon-Pupko, and Tal Gordon of Tel Aviv University's School of Zoology at the George S. Wise Faculty of Life Sciences and the Steinhardt Museum of Natural History. The findings of this surprising discovery were published in the leading journal *Frontiers in Cell and Developmental Biology*.



Polycarpa mytiligera Tal Zaquin

"It is an astounding discovery, as this is an animal that belongs to

the Phylum Chordata - animals with a dorsal cord - which also includes us humans," explains Prof. Noa Shenkar. "The ability to regenerate organs is common in the animal kingdom, and even among chordates you can find animals that regenerate organs, like the gecko who is able to grow a new tail. But not entire body systems. Here we found a chordate that can regenerate all of its organs even if it is separated into three pieces, with each piece knowing exactly how to regain functioning of all its missing body systems within a short period of time."

There are hundreds of species of ascidians, and they are found in all of the world's oceans and seas. Anyone who has ever opened their eyes underwater has seen ascidians without knowing it, as they often camouflage themselves as lumps on rocks and are therefore difficult to discern. The animal that is the subject of this new study is an ascidian from the species *Polycarpa mytiligera*, which is very common in the coral reefs of Eilat.

"By all accounts, the ascidian is a simple organism, with two openings in its body: an entry and an exit," says Tal Gordon, whose doctoral dissertation included this new research. "Inside the body there is a central organ that resembles a pasta strainer. The ascidian sucks in water through the body's entry point, the strainer filters the food particles that remain in the body, and the clean water exits through the exit point. Among invertebrates, they are considered to be the closest to humans from an evolutionary point of view."

Ascidians are famous for their regenerative ability, but until now these abilities have been identified mainly in asexual reproduction. Never before has such a high regenerative capacity been detected in a chordate animal that reproduces only by sexual reproduction.

"There are species of ascidians that perform simple regeneration in order to reproduce," Gordon says. "These are species with a colonial lifestyle, with many identical individuals connected to one another. They replicate themselves in order to grow. In contrast, the

ascidian from Eilat, *Polycarpa mytiligera*, is an organism with a solitary lifestyle, without the capacity for asexual reproduction, similar to humans. In previous studies we showed that this species is able to regenerate its digestive system and its points of entrance and exit within a few days. But then we wanted to see if it is capable of renewing all of its body systems. We took a few individual ascidians from Eilat and dissected them into two parts, which were able to replenish the removed sections without any problem. In a subsequent experiment, we dissected several dozen ascidians into three fragments, leaving a part of the body without a nerve center, heart, and part of the digestive system. And contrary to our expectations, not only did each part survive the dissection on its own, all of the organs were regenerated in each of the three sections. Instead of one ascidian, there were now three. This is very astonishing. Never before has such regenerative capacity been discovered among a solitary species that reproduces sexually, anywhere in the world."

Prof. Shenkar concludes: "Since the dawn of humanity, humans have been fascinated by the ability to regenerate damaged or missing organs. Regeneration is a wonderful ability that we have, to a very limited extent, and we would like to understand how it works in order to try and apply it within our own bodies. Anyone snorkeling in the Gulf of Eilat can find this intriguing ascidian, who may be able to help us comprehend processes of tissue renewal that can help the human race."

<https://bit.ly/3tqpmJd>

A Strange Effect of Aspirin May Help Protect Against Air Pollution, Scientists Say

A surprising new study has found older men taking anti-inflammatories, like aspirin, might be protected from some of the short-term effects of air pollution.

Carly Cassella

The research, which was conducted among nearly a thousand white males in the greater Boston area, found breathing even low levels of fine particulate matter and black carbon can result in poorer cognitive function in the short-term.

The authors couldn't find any direct relationship between aspirin and its effect on brain function, but those in the cohort who were taking non-steroidal anti-inflammatories (NSAIDs) scored significantly higher on tests that measure memory, concentration, and the ability to follow instructions.

"Our study indicates that short-term air pollution exposure may be related to short-term alterations in cognitive function and that NSAIDs may modify this relationship," the authors conclude.

The team thinks this might have something to do with how aspirin curbs inflammation in the brain, which can become chronic if air pollution is bad enough.

But that's just a hypothesis for now. We still don't really know what the short-term impacts of air pollution are on our brains, and scientists will need to conduct proper randomized clinical trials amongst larger cohorts to figure out whether non-steroidal anti-inflammatories, like aspirin, can actually moderate these effects.

Even if they do work, worldwide aspirin use is not a solution to our growing air pollution problem. Over the long-term, even low doses of this medicine come with increased risks of major hemorrhage.

"Our findings do not suggest yet that all older people should be on anti-inflammatory drugs, because these are medications with side-effects we cannot take lightly," environmental health scientist Andrea Baccarelli told *The Guardian*.

Figuring out why this medicine is doing what it's doing, however, could still be incredibly useful. The authors hope further research on this strange effect can help us narrow down exactly how air pollution might be impacting our brains and what can best be done about it.

Previous studies have found long-term air pollution can lead to reduced brain volume, causing damage similar to Alzheimer's disease, and the development of dementia – but this is one of the first studies to examine the more immediate effects of inhaling bad air.

The findings reveal higher levels of local air pollution in the month leading up to a cognitive test resulted in worse word memory, number recall, and verbal fluency scores. What's more, this was true even when fine particulate matter fell below health guidelines.

While aspirin shows no evidence of being able to help the effects of chronic diseases like Alzheimer's or dementia, the new research suggests it might have an impact on how our brain functions over shorter periods of time.

In tests following exposure to low levels of air pollution (relative to the rest of the study), those who were not taking any NSAIDs in the study were 128 percent more likely to get a low score on a widely used screening test for dementia. Those taking NSAIDs were only 44 percent more likely to get a low score during this same time period.

It definitely looks as though something significant is happening here, but we need more research among a much more diverse group of people, including women, to figure out what that relationship actually looks like and how we can use it to best protect the public from future air pollution.

"Thus, future analyses that investigate whether cognitive impairments are transient or persistent over the years would be of high scientific significance," the authors conclude.

"Our findings are also important for other locations around the world where air quality is poorer than in the United States and the impact of PM exposure on cognitive health is thus expected to be heavier."

The study was published in *Nature Aging*.

<https://bit.ly/3uoWLoT>

Citrus derivative makes transparent wood 100 percent renewable

Researchers have successfully tested an eco-friendly alternative to polymers: limonene acrylate, a monomer made from limonene

Since it was first introduced in 2016, transparent wood has been developed by researchers at KTH Royal Institute of Technology as an innovative structural material for building construction. It lets natural light through and can even store thermal energy.



A piece of the transparent wood is displayed. Céline Montanari

The key to making wood into a transparent composite material is to strip out its lignin, the major light-absorbing component in wood. But the empty pores left behind by the absence of lignin need to be filled with something that restores the wood's strength and allows light to permeate.

In earlier versions of the composite, researchers at KTH's Wallenberg Wood Science Centre used fossil-based polymers. Now, the researchers have successfully tested an eco-friendly alternative: limonene acrylate, a monomer made from limonene. They reported their results in *Advanced Science*.

"The new limonene acrylate it is made from renewable citrus, such as peel waste that can be recycled from the orange juice industry," says lead author, PhD student Céline Montanari.

An extract from orange juice production is used to create the polymer that restores delignified wood's strength and allows light to pass through.

The new composite offers optical transmittance of 90 percent at 1.2 mm thickness and remarkably low haze of 30 percent, the researchers report. Unlike other transparent wood composites

developed during the past five years, the material developed at KTH is intended for structural use. It shows heavy-duty mechanical performance: with a strength of 174 MPa (25.2 ksi) and elasticity of 17 GPa (or about 2.5 Mpsi).

Yet all along, sustainability has been a priority for the research group, says Professor Lars Berglund, the head of the KTH's Department of Fibre and Polymer Technology.

"Replacing the fossil-based polymers has been one of the challenges we have had in making sustainable transparent wood," Berglund says.

Environmental considerations and so-called green chemistry permeate the entire work, he says. The material is made with no solvents, and all chemicals are derived from bio-based raw materials.

The new advances could enable a yet unexplored range of applications, such as in wood nanotechnology, Berglund says. Possibilities include smart windows, wood for heat-storage, wood that has built-in lighting function - even a wooden laser.

"We have looked at where the light goes, and what happens when it hits the cellulose," Berglund says. "Some of the light goes straight through the wood, and makes the material transparent. Some of the light is refracted and scattered at different angles and gives pleasant effects in lighting applications."

The team is also working with Sergei Popov's photonics group at KTH to explore the nanotechnology possibilities even further.

<https://bit.ly/2Q13k23>

Humans weren't always agents of destruction when arriving on uninhabited islands

Influx of ancient humans to uninhabited islands doesn't always lead to widespread extinctions as is believed

An international team of researchers led by Griffith University discovered the arrival of ancient humans to uninhabited islands

doesn't always lead to widespread extinctions as is often thought.

Published in *Proceedings of the National Academy of Sciences*, the research team examined archaeological and paleontological records of all islands inhabited by humans over the last 2.6 million years, finding they weren't always destructive agents and their arrival often had minimal impacts on biodiversity loss.

"We have this picture that as soon as people arrive in a new ecosystem, they cause untold amounts of damage" said lead researcher Associate Professor Julien Louys, from the Australian Research Centre for Human Evolution, "but we found that this was only the case for the most recent human arrivals on islands."

Archaeologists and palaeontologists who work on islands with prehistoric records met in 2017 to compared records of human arrival and extinctions on islands spanning the past 2.6 million years, finding very little overlap between the two events.

"Based on classic cases of island extinction from the more recent past, we expected that mass extinction should shortly follow island colonisation. But, when we examined the data, there were very few cases where this could be demonstrated," Associate Professor Louys said.

"Even in cases where there was a close link between human arrival and island extinctions, these could not be disentangled from records of environmental change brought about by global climatic events and changing sea levels."

The team also recorded several examples of human ancestor extinctions and instances where humans had to abandon islands.

"The unique ecological conditions that drive island extinctions definitely didn't spare humans either," said Professor Sue O'Connor of the Australian National University, the senior researcher on the study.

"Island ecosystems are some of the most at risk in the world today and understanding the past impacts of people on these

environments is critical for safeguarding their future."

Associate Professor Louys said our results show that the successful colonisation of islands does not necessarily require wholesale destruction of ecosystems.

"It is only more recently, with advanced technologies, translocation of exotic species, and human population increases that we begin to see massive detrimental effects of humans on island ecosystems.

"By studying the cases where people lived on islands for thousands of years without tipping these fragile ecosystems off balance, we might gain valuable insights into how they can be better managed today."

More information: Julien Louys et al. No evidence for widespread island extinctions after Pleistocene hominin arrival, Proceedings of the National Academy of Sciences (2021). DOI: 10.1073/pnas.2023005118

<https://bit.ly/3hazJ17>

UCLA team discovers how to restrict growth, spread of head and neck cancers

Research on mouse models targets new 'checkpoint' that enables cancer stem cells to evade immune system

Researchers from the UCLA School of Dentistry have discovered a key molecule that allows cancer stem cells to bypass the body's natural immune defenses, spurring the growth and spread of head and neck squamous cell cancers.

Their study, conducted in mice, also demonstrates that inhibiting this molecule derails cancer progression and helps eliminate these stem cells.

Published in the journal *Cell Stem Cell*, the findings could help pave the way for more effective targeted treatments for this highly invasive type of cancer, which is characterized by frequent resistance to therapies, rapid metastasis and a high mortality rate.

Cancer stem cells, also known as tumor-initiating cells, are considered to be the original source of cancerous tissues -- the cells

that give rise to all other cancer cells.

Their ability to survive and proliferate in the early stages of cancer development, as well as during tumor growth and metastasis, suggests they have an intrinsic ability to evade detection by the body's immune surveillance system.

The researchers set out to better understand how and why this happens.

When the immune system is functioning properly, the body's natural infection-fighting T cells help to identify and ward off carcinogenic cells, foreign viruses and other invaders.

However, it is known that some cancer cells elude this immune response by means of protein molecules on their surface known as "checkpoints," which bind to similar molecules on the T cells, essentially nullifying the immune cells' cancer-killing capabilities.

To help rectify this, immunotherapy drugs called checkpoint inhibitors can be administered; these drugs turn off the cancer cells' checkpoint receptors, allowing T cells to perform their normal job.

In several types of cancer, including melanoma and non-small cell lung cancer, this approach has proven effective, decreasing the size of tumors and slowing their spread.

Yet results for head and neck squamous cell carcinomas have been mixed, indicating that something else may be occurring that mutes the immune system's response.

To begin the study, the researchers tested a common checkpoint inhibitor that uses anti-PD1 antibodies on a well-defined mouse model of head and neck squamous cell carcinoma.

The drug, they found, did very little to slow the spread of the cancer. At the same time, they discovered that cancer stem cells in head and neck tumors had a notably elevated expression of the gene CD276, which encodes a protein molecule on the cell surface.

They also found that CD276 expression was highest along the outer layers of tumors, suggesting that the CD276 molecule functions as

a checkpoint that shields both the stem cells and cells in the interior of the tumor from the body's T cell response to the cancer.

Similar to the use of checkpoint inhibitors, the researchers next administered anti-CD276 antibodies to a mouse model of the disease to see if this treatment could turn off the checkpoint and inhibit the growth and spread of the cancer.

After a month, they witnessed a significant decrease in the number of cancerous lesions and cancer stem cells.

"Not only did we see a reduction in cancer stem cells and tumors in our model when we introduced the CD276 antibodies, but we also noticed that the total number of tumors that metastasized to the lymph nodes was significantly reduced," said Dr. Cun-Yu Wang, the study's corresponding author and a professor of oral biology and medicine.

"We were able to show that by blocking the gene CD276, we could effectively stop the growth of tumors derived from cancer stem cells."

Dr. Paul Krebsbach, dean of the UCLA School of Dentistry and a study co-author said, "These findings suggest that by focusing our attention on the CD276 gene and the immune response process, there is the potential for promising preventive therapeutic approaches against head and neck squamous cell carcinoma."

The work was supported by grants from the National Institute of Dental and Craniofacial Research, part of the National Institutes of Health.

Dr. Wang is the Dr. No-Hee Park Professor of Dentistry, a professor at the UCLA Samueli School of Engineering and a member of the UCLA Jonsson Comprehensive Cancer Center and the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA.

Additional authors included Cheng Wang, Yang Li, Lingfei Jia, Jiong Li, Peng Deng and Wuchang Zhang, all of whom are part of the Laboratory of Molecular Signaling at the dentistry school and members of the Jonsson Comprehensive Cancer Center and the Broad Stem Cell Research Center. Dr. Paul Krebsbach and Jin koo Kim are both from the UCLA School of Dentistry.

<https://bit.ly/3be4sqt>

One bone fracture increases risk for subsequent breaks in postmenopausal women

Hip or spine fractures for increasing the risk for subsequent bone breaks. A new study suggests fractures in the arm, wrist, leg and other parts of the body should also set off alarm bells

Current guidelines for managing osteoporosis specifically call out hip or spine fractures for increasing the risk for subsequent bone breaks. But a new UCLA-led study suggests that fractures in the arm, wrist, leg and other parts of the body should also set off alarm bells.

A fracture, no matter the location, indicates a general tendency to break a bone in the future at a different location, said Dr. Carolyn Crandall, the study's lead author and a professor of medicine at the David Geffen School of Medicine at UCLA.

"Current clinical guidelines have only been emphasizing hip and spine fractures, but our findings challenge that viewpoint," Crandall said. "By not paying attention to which types of fractures increase the risk of future fractures, we are missing the opportunity to identify people at increased risk of future fracture and counsel them regarding risk reduction.

"Postmenopausal women and their physicians may not have been aware that even a knee fracture, for example, is associated with increased risk of future fractures at other locations of the body."

The study will be published May 5 in the peer-reviewed journal *EClinicalMedicine*.

The researchers examined records from 1993 through 2018 for more than 157,000 women aged 50 through 79. Data was sourced from the Women's Health Initiative, a national study funded by the National Heart, Lung, and Blood Institute.

The researchers found that among postmenopausal women, initial fractures of the lower arm or wrist, upper arm or shoulder, upper

leg, knee, lower leg or ankle, and hip or pelvis were associated with an approximately three- to six-fold increase in risk for subsequent fractures. That finding held for all of the age groups studied, with higher risks being more pronounced among non-Hispanic Black, Hispanic or Latina, and Asian Pacific Islander women than among non-Hispanic White women.

The authors noted some limitations to the study, including the fact that the fractures were self-reported by participants. However, earlier research has demonstrated that statistics for self-reported fractures is fairly accurate compared with statistics from medical records.

Also, the researchers did not have information about broken ribs, which may have led them to underestimate the risk for other fractures -- it's possible that the true effect could be even more pronounced than the results show -- and bone mineral density was measured for only a subset of participants, so the researchers could not investigate whether the risk for future fractures was associated with bone density.

Although there is a need for more studies to understand why women of some ethnicities have a greater risk for a subsequent fracture following an initial bone break, the researchers write that their findings "indicate that aggressive follow-up of postmenopausal women who experience initial fracture is indicated. Our results will inform counseling, future guidelines, and the design of intervention trials regarding the selection of appropriate candidates for pharmacotherapy."

The study's co-authors are Rebecca Hunt of the Fred Hutchinson Cancer Research Center, Andrea LaCroix of UC San Diego, Dr. John Robbins of UC Davis, Jean Wactawski-Wende of State University of New York, Buffalo, Dr. Karen Johnson of University of Tennessee, Dr. Maryam Sattari of University of Florida, Katie Stone of California Pacific Medical Center Research Institute and San Francisco Coordinating Center, Julie Weitlauf of the Veterans Affairs Palo Alto Health Care System and Stanford University, Dr. Tanya Gure of Ohio State University and Jane Cauley of University of Pittsburgh. The study was funded by the National Institutes of Health.

<https://go.nature.com/2R3yMNx>

A child's grave is the earliest known burial site in Africa

The discovery of the burial of a young child in a cave in Kenya around 78,000 years ago sheds new light on the role of symbolism in the treatment of the dead during the Middle Stone Age.

Louise Humphrey

Much of the current debate surrounding the location and timing of the emergence of modern human behaviour focuses on Africa during the Middle Stone Age (MSA), which lasted from about 320,000 to 30,000 years ago. The first known appearances of a suite of modern human innovations relating to technology, social organization, symbolism and exploitation of the landscape and resources occurred in Africa during this period¹. This time frame is also associated with the earliest known hominin fossils placed in the modern human lineage^{2,3}. The emergence of more-complex behaviours surrounding the treatment of the dead is often framed in the broader context of an increase in symbolic capabilities⁴. Writing in *Nature*, Martín-Torres *et al.*⁵ present a convincing case for the intentional burial of a young child in eastern Africa, at Panga ya Saidi, a cave in Kenya (Fig. 1). The authors' meticulous recording of this archaeological evidence has revealed the earliest known human burial in Africa.

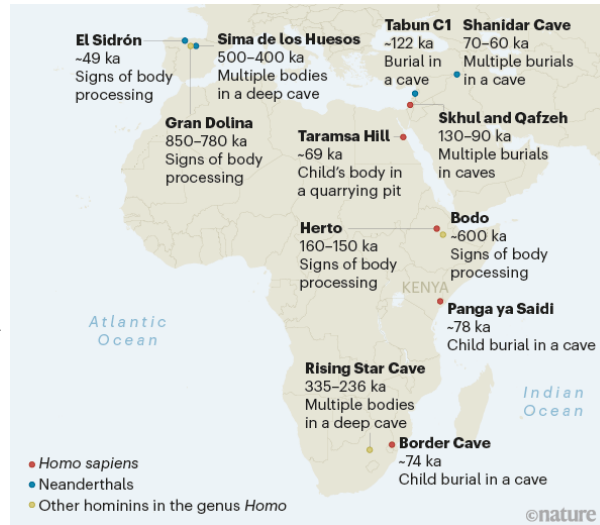
The child, estimated to have been around three years old, seems to have been carefully arranged in a deliberately excavated pit and then covered by sediment scooped up from the cave floor. Microscopic features of the bone structure and the chemical composition of the sediment surrounding the bones reveal that the body was fresh when it was buried, and decomposed in the grave. The arrangement of the surviving bone fragments reveals that the child was placed lying gently inclined on their right side, with their legs folded and drawn up towards their chest.

Figure 1 | Archaeological sites where treatments of the dead have been found.

*A range of behaviours are associated with ancient handling of the dead, which include body processing (sometimes associated with cannibalism), placement of a body in a relatively inaccessible location (such as a deep cave) or signs of a deliberate burial. Some sites at which such behaviours have been identified are linked to *Homo sapiens*^{5,10–14} and to other closely related species^{7–9,15–18} (other hominins belonging to the genus *Homo*).*

*Martinón-Torres et al.⁵ report the excavation of a child's grave at Panga ya Saidi in Kenya dated to around 78,000 years ago (78 ka), which is the earliest known human burial in Africa. The fossils at El Sidrón, Sima de los Huesos, Tabun C1 and Shanidar Cave are those of Neanderthals (*Homo neanderthalensis*); those at Gran Dolina are *Homo antecessor*; the cranium at Bodo is *Homo heidelbergensis* or *Homo rhodesiensis*; and the fossils at Rising Star Cave are *Homo naledi*.*

Several anatomical connections between adjacent bones have survived, which suggests that the body was covered quickly after burial. A gradual trickle of sediment from above the corpse presumably prevented the bones from collapsing into the empty spaces that would have otherwise formed during the putrefaction of the soft tissues. An exception to this was the cranium and three neck bones, which collapsed into a void thought to have been created by the decay of a perishable head support. The right clavicle (one of the bones of the shoulder girdle) and two ribs had rotated in the grave, which might imply that part of the upper body was



originally tightly wrapped in a perishable material.

The burial pit and the archaeological layers surrounding it and directly above it are associated with MSA stone tools, securely anchoring the burial in the MSA. Martinón-Torres *et al.* date the burial itself to $78,300 \pm 4,100$ years ago. The date was obtained using probabilistic modelling and a technique called optically stimulated luminescence to determine the age of the entire sequence of the assessed archaeological layers. This finding demonstrates that humans in East Africa were deliberately burying their dead at least 78,000 years ago.

Archaeological and fossil records reveal a wide spectrum of mortuary treatments carried out by early humans (species in the genus *Homo*) spanning at least 800,000 years or so (Fig. 1). The first step towards understanding the nature of these mortuary behaviours — the actions and beliefs surrounding the treatment of the dead — is to reconstruct the series of human actions associated with the deposition of a body.

Not all mortuary behaviours leave traces that are archaeologically visible. The importance of a burial is that it documents a sequence of planned and deliberate actions involving: the creation of an artificial space to contain the body; the placement of a body or body parts into that space; and the covering of the body, often using the sediment that was removed during preparation of the grave⁶. Each of these stages can, but might not always, leave visible archaeological traces, so not all burials will be recognized as such. Other actions that leave enduring traces in the archaeological record relate to processing of the corpse, and might involve the removal of soft tissues, separation of body parts, or signs of cooking or chewing indicative of cannibalism. Examples have been found in the archaeological record of human bones that have been shaped into tools and used as decorative objects.

The second step towards understanding these mortuary behaviours

is to infer whether there was any meaning associated with the treatment of the dead beyond the practical measures required to avoid attracting animal scavengers to spaces used by the living and to prevent contamination of those spaces during decay of the body. Strictly functional interventions might also include disarticulation of the body to facilitate transportation, nutritional cannibalism, or the opportunistic use of bones or teeth as tools or as a raw material for manufacturing an object. Inferring signs of symbolic behaviour in burials is one of the more contentious areas of archaeology.

Behaviours that might point towards a departure from purely practical motivations and towards a more meaningful treatment of the dead are those that involve an investment of time and resources beyond what is strictly required to dispose of or make use of the corpse. Such actions include careful placement of the corpse in the grave to achieve a desired body position or orientation, the wrapping or binding of the body for reasons other than to aid transportation, or the deliberate incorporation of items of value in the grave. Such items include objects that could reasonably be considered to have a personal or decorative significance, and those linked to the social role of the deceased. The interred objects might also encompass articles thought to be needed by the deceased in another existence, such as food or medicine. Repeated depositions of corpses over a prolonged period at a single location might signify the recognition of a place for the dead⁶, particularly if that location is difficult to access and other causes for the accumulation of the remains can be ruled out. The fossil assemblages at Sima de los Huesos in Spain⁷ and Rising Star Cave in South Africa⁸ can be interpreted as early examples of placement of the dead in a designated space (Fig. 1).

The presence of symbolic aspects elevates treatment of the dead from mortuary behaviour to funerary behaviour⁹. The burial reported by Martínón-Torres and colleagues reveals the care and

effort taken to achieve a desired body position by supporting the child's head and wrapping the upper body. This burial, together with a previous report of the burial of a child around 74,000 years ago, associated with a shell ornament in South Africa at Border Cave¹⁰, suggests that a tradition of symbolically significant burials, at least for the very young, might have been culturally embedded in parts of Africa in the later part of the MSA.

Understanding the treatment of the dead intersects with our understanding of social organization, symbolic behaviours and the use of landscape, resources and technology. The act of burial restricts dispersal of the body and the other contents of the grave, increasing the likelihood of archaeological recovery, and provides an unambiguous association between the deceased — and hence the species they represent — and a certain set of behaviours at a specific time and place. Future discoveries in Africa and beyond could shed even more light on the evolution of modern traits and behaviour during the emergence of our species.

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<https://bit.ly/3xP82km>

Breathing problems are the second most common symptom of heart attacks

One in four heart attack patients have atypical symptoms such as breathing difficulties, extreme exhaustion, and abdominal pain

Sophia Antipolis - One in four heart attack patients have atypical symptoms such as breathing difficulties, extreme exhaustion, and abdominal pain, according to a study published today in *European Heart Journal - Acute Cardiovascular Care*, a journal of the European Society of Cardiology (ESC).¹ Patients with atypical symptoms were less likely to receive emergency help and more likely to die within 30 days compared to those with chest pain.

"We found that atypical symptoms were most common among older people, especially women, who called a non-emergency helpline for assistance," said study author Ms. Amalie Lykkemark Møller, PhD student, Nordsjællands Hospital, Hillerød, Denmark. "This suggests that patients were unaware that their symptoms required urgent attention."

Heart attacks require fast treatment to restore blood flow and reduce mortality. Symptom recognition by patients and health staff is crucial to reduce delays. Ms. Møller said: "Little is known about how symptoms influence the actions of patients and medical services and impact survival."

The study examined the associations between initial heart attack symptoms, the medical service response and 30-day mortality. The researchers collected data on all calls to a 24-hour medical helpline

and an emergency number in the Capital Region of Denmark from 2014 to 2018. At the two services the primary symptom is registered along with the response. The researchers identified adults aged 30 and over who received a heart attack diagnosis within 72 hours of the call. Patients were divided into groups according to their primary symptom.

During the five-year period, a specific primary symptom was recorded for 7,222 of 8,336 heart attacks - chest pain was the most common (72%) while 24% of patients had atypical symptoms, the most frequent being breathing problems. The prevalence of chest pain was highest among men aged 30-59 calling the emergency number and lowest among women older than 79 calling the medical helpline. Atypical symptoms were mainly found among older patients, especially women, who called the helpline.

Among heart attack patients with chest pain, 95% and 76% received an emergency dispatch from the emergency number and medical helpline, respectively. In comparison, just 62% and 17% of heart attack patients with atypical symptoms received an emergency dispatch from the emergency number and medical helpline, respectively.

The 30-day mortality rate for heart attack patients with chest pain was 5% among those who called the emergency number and 3% among those who called the helpline. Rates were higher among heart attack patients with atypical symptoms: 23% and 15% died within 30 days after calling the emergency number and helpline, respectively.

To make a more like-for-like comparison of mortality between patients with chest pain versus atypical symptoms, the researchers standardised for age, sex, education level, diabetes, previous heart attack, heart failure, and chronic obstructive pulmonary disease. The standardised 30-day mortality was 4.3% for patients with chest pain and 15.6% for those with atypical symptoms.

Ms. Møller said: "Taken together, our results show that heart attack patients with chest pain were three times more likely to receive an emergency ambulance than those with other symptoms. People with atypical symptoms more often called the helpline, which could indicate that their symptoms were milder, or they were not aware of the severity. Vague symptoms may contribute to health staff misinterpreting them as benign."

While breathing difficulties, extreme exhaustion, impaired consciousness, and abdominal pain were the most common heart attack symptoms after chest pain, Ms. Møller noted that in most cases these problems are not caused by a heart attack. "Unfortunately, people in this situation will not know the cause, but we hope our study improves awareness - particularly among older patients and health professionals - that it could be a heart attack," she said.

"Death within 30 days was more than three-fold higher in those with atypical symptoms compared to chest pain," she added. "This could be due to treatment delays caused by not receiving the appropriate emergency dispatch. However, it is unknown whether an increase in emergency dispatches alone would improve survival among heart attack patients with atypical symptoms - we aim to investigate this in future research projects."

Møller AL, Mills EHA, Gnesin F, et al. Impact of myocardial infarction symptom presentation on emergency response and survival. Eur Heart J Acute Cardiovasc Care. 2021. doi:10.1093/ehjacc/zuab023. Link will go live on publication:

<https://academic.oup.com/ehjacc/article-lookup/doi/10.1093/ehjacc/zuab023>

<https://bit.ly/3b6VIIV>

Prediabetes may not be as benign as once thought

Study shows greater risk of serious cardiac events; suggests need for more aggressive treatment

People with prediabetes were significantly more likely to suffer a heart attack, stroke or other major cardiovascular event when compared with those who had normal blood sugar levels, according

to research being presented at the American College of Cardiology's 70th Annual Scientific Session. Researchers said the findings should serve as a wake-up call for clinicians and patients alike to try to prevent prediabetes in the first place.

"In general, we tend to treat prediabetes as no big deal. But we found that prediabetes itself can significantly boost someone's chance of having a major cardiovascular event, even if they never progress to having diabetes," said Adrian Michel, MD, internal medicine resident at Beaumont Hospital-Royal Oak, MI, and lead author of the study, which he said is one of the largest to date. "Instead of preventing diabetes, we need to shift focus and prevent prediabetes."

Prediabetes is a condition in which the average amount of sugar in the blood is high but not high enough to be diagnosed as Type 2 diabetes. While Type 2 diabetes is a well-known, leading risk factor for heart attack, stroke and blockages in the heart's arteries, the role of prediabetes has been less clear. Yet prediabetes is fairly common. The U.S. Centers for Disease Control and Prevention estimates that 34 million Americans--just over 1 in 10--have diabetes, and another 88 million--approximately 1 in 3--have prediabetes.

This study revealed that serious cardiovascular events occurred in 18% of people with prediabetes compared with 11% of people with normal blood sugar levels over a median of five years follow-up. The relationship between higher blood sugar levels and cardiovascular events remained significant even after taking into account other factors that could play a role, such as age, gender, body mass index, blood pressure, cholesterol, sleep apnea, smoking and peripheral artery disease.

"Based on our data, having prediabetes nearly doubled the chance of a major adverse cardiovascular event, which accounts for 1 out of 4 deaths in the U.S.," Michel said. "As clinicians, we need to spend more time educating our patients about the risk of elevated

blood sugar levels and what it means for their heart health and consider starting medication much earlier or more aggressively, and advising on risk factor modification, including advice on exercise and adopting a healthy diet."

Of particular concern was the finding that even when patients in the prediabetes group were able to bring their blood sugar level back to normal, the risk of having a cardiovascular event was still fairly high. Events occurred in just over 10.5% of these patients compared with 6% of those with no diabetes or prediabetes.

"Even if blood sugar levels went back to normal range, it didn't really change their higher risk of having an event, so preventing prediabetes from the start may be the best approach," Michel said.

This single-center, retrospective study included data from 25,829 patients treated within the Beaumont Health System in Michigan between 2006 and 2020. Patients were then split into either the prediabetes or control group based on at least two A1C levels five years apart; the control group included patients who maintained a normal hemoglobin A1C during the study. A total of 12,691 patients and 13,138 were included in the prediabetes and control groups, respectively. Participants ranged in age from 18 to 104 years. All patients were followed for the 14-year study period and researchers used international classification of disease codes or diagnostic codes to determine whether a major adverse cardiovascular event occurred.

The relationship between prediabetes and events were strongest among males, Blacks and people with a family history of cardiovascular disease or personal risk factors for heart disease. People who were overweight had the highest rates of cardiovascular events among all patients, even more than those who were obese, which is something Michel said needs to be studied further.

Prediabetes is thought to play a role in heart health because elevated glucose levels in the blood can damage and cause inflammation

within the vessels. This causes injury to the vessels in the body and can lead to narrowing of the vessels and ultimately cardiovascular injury, Michel said.

The study findings are an important reminder for adults to know their blood sugar numbers, especially as prediabetes usually has no symptoms. As with diabetes, prediabetes is diagnosed based on results from blood sugar tests, including an A1C, which reflects someone's average blood sugar for the past two to three months; a fasting plasma glucose test, which measures your blood sugar after not eating or drinking for at least eight hours beforehand; and/or an oral glucose tolerance test, which checks how well the body processes sugar after drinking a sweet drink given by the clinician. Prediabetes is suspected with an A1C between 5.7-6.4%, fasting blood sugar of 100-125 mg/dl, or an oral glucose tolerance test of 140-199 mg/dl, according to the American Diabetes Association.

More research is needed to validate these findings.

<https://bit.ly/3tsq6gH>

'It's like the embers in a barbecue pit.' Nuclear reactions are smoldering again at Chernobyl

35 years later fission reactions are smoldering again deep inside a mangled reactor hall

By [Richard Stone](#)

Thirty-five years after the Chernobyl Nuclear Power Plant in Ukraine exploded in the world's worst nuclear accident, fission reactions are smoldering again in uranium fuel masses buried deep inside a mangled reactor hall. "It's like the embers in a barbecue pit," says Neil Hyatt, a nuclear materials chemist at the University of Sheffield. Now, Ukrainian scientists are scrambling to determine whether the reactions will wink out on their own—or require extraordinary interventions to avert another accident.

Sensors are tracking a rising number of neutrons, a signal of fission, streaming from one inaccessible room, Anatolii Doroshenko of the

Institute for Safety Problems of Nuclear Power Plants (ISPNNP) in Kyiv, Ukraine, reported last week during discussions about dismantling the reactor. “There are many uncertainties,” says ISPNNP’s Maxim Saveliev. “But we can’t rule out the possibility of [an] accident.” The neutron counts are rising slowly, Saveliev says, suggesting managers still have a few years to figure out how to stifle the threat. Any remedy he and his colleagues come up with will be of keen interest to Japan, which is [coping with the aftermath of its own nuclear disaster](#) 10 years ago at Fukushima, Hyatt notes. “It’s a similar magnitude of hazard.”

The specter of self-sustaining fission, or criticality, in the nuclear ruins has long haunted Chernobyl. When part of the Unit Four reactor’s core melted down on 26 April 1986, uranium fuel rods, their zirconium cladding, graphite control rods, and sand dumped on the core to try to extinguish the fire melted together into a lava. It flowed into the reactor hall’s basement rooms and hardened into formations called fuel-containing materials (FCMs), which are laden with about 170 tons of irradiated uranium—95% of the original fuel.

The concrete-and-steel sarcophagus called the Shelter, erected 1 year after the accident to house Unit Four’s remains, allowed rainwater to seep in. Because water slows, or moderates, neutrons and thus enhances their odds of striking and splitting uranium nuclei, heavy rains would sometimes send neutron counts soaring. After a downpour in June 1990, a “stalker”—a scientist at Chernobyl who risks radiation exposure to venture into the damaged reactor hall—dashed in and sprayed gadolinium nitrate solution, which absorbs neutrons, on an FCM that he and his colleagues feared might go critical. Several years later, the plant installed gadolinium nitrate sprinklers in the Shelter’s roof. But the spray can’t effectively penetrate some basement rooms.

Chernobyl officials presumed any criticality risk would fade when

the massive New Safe Confinement (NSC) was slid over the Shelter in November 2016. The €1.5 billion structure was meant to seal off the Shelter so it could be stabilized and eventually dismantled. The NSC also keeps out the rain, and ever since its emplacement, neutron counts in most areas in the Shelter have been stable or are declining.

But they began to edge up in a few spots, nearly doubling over 4 years in room 305/2, which contains tons of FCMs buried under debris. ISPNNP modeling suggests the drying of the fuel is somehow making neutrons ricocheting through it more, rather than less, effective at splitting uranium nuclei. “It’s believable and plausible data,” Hyatt says. “It’s just not clear what the mechanism might be.”

The threat can’t be ignored. As water continues to recede, the fear is that “the fission reaction accelerates exponentially,” Hyatt says, leading to “an uncontrolled release of nuclear energy.” There’s no chance of a repeat of 1986, when the explosion and fire sent a radioactive cloud over Europe. A runaway fission reaction in an FCM could sputter out after heat from fission boils off the remaining water. Still, Saveliev notes, although any explosive reaction would be contained, it could threaten to bring down unstable parts of the rickety Shelter, filling the NSC with radioactive dust.

Addressing the newly unmasked threat is a daunting challenge. Radiation levels in 305/2 preclude getting close enough to install sensors. And spraying gadolinium nitrate on the nuclear debris there is not an option, as it’s entombed under concrete. One idea is to develop a robot that can withstand the intense radiation for long enough to drill holes in the FCMs and insert boron cylinders, which would function like control rods and sop up neutrons. In the meantime, ISPNNP intends to step up monitoring of two other areas where FCMs have the potential to go critical.

The resurgent fission reactions are not the only challenge facing Chernobyl's keepers. Besieged by intense radiation and high humidity, the FCMs are disintegrating—spawning even more radioactive dust that complicates plans to dismantle the Shelter. Early on, an FCM formation called the Elephant's Foot was so hard scientists had to use a Kalashnikov rifle to shear off a chunk for analysis. "Now it more or less has the consistency of sand," Saveliev says.

Ukraine has long intended to remove the FCMs and store them in a geological repository. By September, with help from European Bank for Reconstruction and Development, it aims to have a comprehensive plan for doing so. But with life still flickering within the Shelter, it may be harder than ever to bury the reactor's restless remains.

<https://bit.ly/3uzlG9s>

Blocking viruses' exit strategy

Tests of a new antiviral that aims to prevent the deadly Marburg virus from spreading in the body show promise, according to a study led by University of Pennsylvania researchers

The Marburg virus, a relative of the Ebola virus, causes a serious, often-fatal hemorrhagic fever. Transmitted by the African fruit bat and by direct human-to-human contact, Marburg virus disease currently has no approved vaccine or antivirals to prevent or treat it. A team of researchers is working to change that. In a [new paper in the journal *Antimicrobial Agents and Chemotherapy*](#), investigators from Penn's School of Veterinary Medicine, working together with scientists from the Fox Chase Chemical Diversity Center and the Texas Biomedical Research Institute, report encouraging results from tests of an experimental antiviral targeting Marburg virus. The compound blocks the virus from departing infected cells, thus putting the brakes on the spread of infection. Their findings are the first to show that this novel class of inhibitors can be effective

against the infection in an animal model.

In addition, due to possible similarities in virus-host interactions between Marburg and SARS-CoV-2, the team has conducted experiments on the culprit behind the coronavirus pandemic. While preliminary and thus-far-unpublished, their initial tests show signs of promise.

"It really is exciting," says Ronald Harty, a co-corresponding author of the research and a professor at Penn Vet. "These viruses are quite different but may be interacting with the same host proteins to control efficient egress and spread, so our inhibitors may be able to block them both."

While many antivirals target the virus itself, the drug candidates that Harty and colleagues have been developing for years are known as "host-oriented." They prevent virus-host interactions by blocking the proteins in host cells that viruses hijack during late stages of infection.

Not only does this approach help avoid the likelihood that a virus would evolve to resist such a therapy, but it also increases the chance that a drug could be used against multiple viruses, as many rely on the same host cell machinery to reproduce and spread.

The Marburg and Ebola viruses use the VP40 protein to interact with a host protein called Nedd4 to complete the process of "budding" off a host cell. This stage of infection, which is key to viral spread, is the one the research team has targeted.

In previous studies, they had tested a variety of small molecule inhibitors of this process using laboratory tests that relied on non-infectious and more-benign viral models. Those assays helped them land on a leading candidate, FC-10696, for further study.

In the current work, they zeroed in on this candidate with rigorous evaluations. First, they tested the inhibitor to ensure it would be safe and retained long enough in the body to have an effect. Next, because the live Marburg virus is too dangerous to study safely in

anything but a Biosafety Level 4 (BSL-4) laboratory, they used an assay to look at what are known as virus-like particles, or VLPs, which can bud off of a host cell like the live virus but are not infectious. Using the Biosafety Level 2 laboratory at Penn, "it's a very quick way we can test these inhibitors," Harty says.

After seeing a dose-dependent response to FC-10696 on VLP budding in cells in a cell-culture dish, the researchers tested the compound using the real Marburg virus. These studies were done in a BSL-4 lab at Texas Biomedical Research Institute and found the compound inhibited the budding and spread of live Marburg virus in two human cell types, including in macrophages, an immune cell type commonly infected by the virus.

Finally, they evaluated the compound in mice that had been exposed to Marburg virus. Those mice treated with FC-10696 took longer to display disease symptoms and had a reduced viral load.

"These are the first promising in vivo data for our compounds," Harty says. "Whereas the control group all became sick very quickly and died, with the treated animals there was one survivor and others showed delayed onset of clinical symptoms. It's showing that our inhibitors are having an effect."

A portion of the VP40 protein in Marburg and Ebola viruses that enables budding is known as a PPxY motif. SARS-CoV-2 also happens to have this motif on its Spike (S) protein, which it uses to infect human cells. In a follow-up experiment that is not yet published, the researchers found evidence that FC-10696 was able to inhibit budding of the SARS-CoV-2 coronavirus in human lung epithelial cells. "The SARS-CoV-2 studies are ongoing, and they're very exciting," Harty says.

Ronald N. Harty is a professor of pathobiology and microbiology in the University of Pennsylvania School of Veterinary Medicine.

Harty's coauthors were Ziyang Han, Jingjing Liang, Ariel Shepley-McTaggart, and Bruce D. Freedman of Penn Vet; Hong Ye, Jay E. Wrobel, and Allen B. Reitz of the Fox Chase Chemical Diversity Center; Michael S. Saporito of Intervi, LLC; and Alison Whigham,

Katrina Kavelish, and Olena Shtanko of the Texas Biomedical Research Institute. Han was first author and Harty and Shtanko were co-corresponding authors. Harty and Freedman are co-founders of Intervi, LLC.

The study was supported in part by the National Institutes of Health (grants A1138052, A1138630, A1129890, and AI070077) and an Innovator Award from The Wellcome Trust.

<https://bit.ly/3ux2l8z>

Archaeologists have discovered the earliest anthropogenic landscape on Earth

Archaeologists can now prove that we altered the ecology and landscape to our benefit almost 100,000 years ago

by Mari Lilleslåtten

As far as we know, humans as a species have been around for at least 300 000 years. Recently, we have come to realize that our impact on the climate and earth's ecology is unsustainable. Landscape change driven by humans is nothing new, however.

In a new study, archaeologists suggest that we have always altered the ecology and [landscape](#) to our benefit. At least they can now prove that we did so, almost 100,000 years ago.

"This is essentially what we call the earliest anthropogenic landscape on Earth," says David Wright, Professor of Archaeology at the University of Oslo.

Together with his colleagues Jessica Thompson from Yale University, Sarah Ivory from Penn State University and an international, interdisciplinary team, he is now presenting new findings about human-driven climate change in the current issue of *Science Advances*.

"We can see that [early humans](#) significantly altered ecology and landscapes using fire," Wright says.

The earliest evidence that humans burned the landscape and changed the environment so far was found in Australia. But whereas that appears to have happened 40,000 years ago, this study proves that the technology goes back more than double the time, to 92 000 years ago.

92,000 years ago: humans arrive at Lake Malawi

Let us travel with Wright to the Karonga district in Malawi. This area, northeast of Lake Malawi, has an ancient history and a long archaeological tradition. One of the methods archaeologists use to figure out what humans have been doing in earlier times is to take lake cores from deep in the earth's surface and use those to interpret how the climate has changed.

"The lake core we are using was drilled in 2005, and extends 636,000 years into the past," Wright explains.

What they found in the lake core was charcoal that they interpreted to stem from humans burning forests around 100 000 years ago. Over time, the charcoal tapered off, but the forests never grew back as before during similar wet periods.

The researchers analyzed the geological data from this lake core together with long archaeological records from the area and the evolution of climate, to understand the relationship between climate and landscape formation before and after humans showed up in the area. They made two important discoveries about what happened when humans came around.

"Hunter-gatherers who go after hooved mammals can find it hard to hunt prey when it's in a closed tree environment. So we suspect the humans who arrived in the Karonga district started burning down the forest to open the landscape for hunting. It may also have provided new foods like starchy tubers that like to grow in open areas."

The Stone Age in Africa

In Europe and North-Africa, the earlier phases of the Stone Ages are divided into the Lower-, Middle- and Upper Palaeolithic.

As for Sub-Saharan Africa, it is common to divide the Palaeolithic into:

Early Stone Age (2,6 million – 230 000 years ago)

Hominins including Homo habilis and Homo erectus, the predecessors

to Homo sapiens, developed and used simple tools to open nuts and process starchy tubers.

Middle Stone Age (315 000 – 20 000 years ago)

Homo sapiens, modern humans, appear. They develop projectile weapons, like spears, to use for hunting. They traded ostrich egg shell beads and other items over hundreds of kilometres with each other.

Late Stone Age (50 000 – 2000 years ago)

Tools are made of small rocks (microliths), trade networks are vast and people left Africa to explore new continents.

The findings by Wright and his colleagues are from the Middle Stone Age.

Rain and alluvial fan formation

As a consequence of the burning, the landscape started to erode.

"The Rift Valley along Lake Malawi is bordered by really steep mountains, and so you get big alluvial fans, essentially big sediment packages. We interpret these as human artifacts—because they weren't there before humans came around," says David Wright.

The other important discovery was that human activity changed the overall ecology in northern Malawi. "The period after humans arrived is actually one of the wettest in the last 636,000 years."

The lake level has been steadily increasing over the last 100,000 years, and the area has been quite wet compared to the long record. However, the researchers saw a disconnection from the plant communities to the natural climate signal. According to the archaeologist, it is natural to have big forests of trees that are not tolerant of fire when lake levels are high, because there is not a lot of natural burning.

"But after humans came into the area, you see a totally different species complexion, with very fire tolerant trees and lots of grass. That is totally anomalous compared to the previous 515,000 years," says Wright.

Simple tools—sophisticated people

Archaeologists have been confused by the fact that Stone Age

people used the same methods over long stretches of time. Archaeologist J. Desmond Clark, for instance, mistakenly interpreted an elephant butchery site in Karonga to be 200,000 years old. Wright and his colleagues, primarily Dr. Jeong-Heon Choi at the Korea Basic Science Institute, were able to correct this using modern dating techniques, concluding that the excavation site was from 30 000 years ago, in the later part of the Middle Stone Age (*see fact box*). "For a very long time there is no obvious technological change," Wright points out.

"Stone Age people may have seemed fairly simple in terms of their tools and technology and their ways of communicating with each other. But in fact, they were using the landscape in really novel ways. They burned and managed the landscape in ways that are really sophisticated and that benefited them."

Wright believes that the methods people used in this part of Malawi allowed them to survive there for 70 000 years, even as there were obvious technological changes going on in other parts of Africa.

"For several thousand years, the rest of the continent experienced an extremely dry period, and in many places the lakes completely dried up. This did not happen in Malawi. We believe the people who lived in this area, defended it by managing the landscape the way they did."

Humans learned how to modify the environment to our benefit

Today, humans are masters of the universe and inhabit almost every corner of the earth. However, 92 000 years ago, our relatives shared the earth with other hominin species such as Neanderthals and Denisovans, who lived in Europe and Asia, even though current science believes that our species had not yet left Africa.

A first step toward inhabiting the rest of the world was learning how to modify the landscapes in Malawi to our benefit.

"We learned the tools of how to populate the planet in Africa. With a set of tools developed under challenging environments in Africa,

we could later go to more inhospitable climates like northern Europe, northeastern Asia and eventually North America, South America, Australia."

Today, human-forced [climate change](#) has accelerated to an unsustainable level, and the climate crisis threatens to make parts of the world inhabitable for humans. However, changing landscapes and adapting to them is a hallmark of our species, according to the archaeologist.

"We are pretty defenseless in the natural world, but we use our tools, technologies and ability to cooperate with each other, to plant, to manage landscapes and to cooperate in hunting and trading. We learn from our ancestors and evolve continuously."

Adding nuance to the Anthropocene

In the humanities and social sciences, the geological term "Anthropocene" is used to describe how [human](#) beings are the major geological force of our epoch. Wright and his colleagues' study adds nuance to the understanding of the Anthropocene.

"Wherever humans are, we transform landscapes because of our natural vulnerabilities as a species. We cannot manage landscapes without changing them." Therefore, it is difficult to decide on a beginning of the Anthropocene, which he argues goes back tens of thousands of years on local levels. "I also feel like we are going to find earlier instances, the more we look for it."

He thinks learning from the ancient past can help us take a broader view of the relationship between culture and nature. "Ninety-nine percent of our history has been as hunter-gatherers. The ecology of this planet has evolved with us as hunter-gatherers, and we have co-evolved with it." With our historical records we can also project where we are going in the future and make decisions as a species.

"The Earth has no agenda, it is just going to do what it does. It does not care if we are here or not. So it is on us to decide what we want to do with our society in relation to the environment."

More information: Jessica C. Thompson et al. Early human impacts and ecosystem reorganization in southern-central Africa, *Science Advances* (2021). DOI: [10.1126/sciadv.abf9776](https://doi.org/10.1126/sciadv.abf9776)

<https://wb.md/3f75PIE>

Prioritize Goals of Older Patients With Multimorbidities

Prioritizing patient goals is more effective and efficient than trying to address each condition in isolation

Will Pass

When caring for older adults with multiple chronic conditions, prioritizing patient goals is more effective and efficient than trying to address each condition in isolation, said [Mary Tinetti, MD](#), Gladys Phillips Crofoot Professor of Medicine and Public Health and chief of geriatrics at Yale University, New Haven, Conn.

During a virtual presentation at the American College of Physicians annual Internal Medicine meeting, the gerontologist noted that primary care providers face a number of challenges when managing elderly patients with multimorbidity. These challenges include a lack of representative data in clinical trials, conflicting guideline recommendations, patient nonadherence, and decreased benefit from therapies due to competing conditions, she said.

"Trying to follow multiple guidelines can result in unintentional harms to these people with multiple conditions," Tinetti said. She gave examples of the wide-ranging goals patients can have.

"Some [patients] will maximize the focus on function, regardless of how long they are likely to live," Tinetti said. "Others will say symptom burden management is most important to them. And others will say they want to live as long as possible, and survival is most important, even if that means a reduction in their function. These individuals also vary in the care they are willing and able to receive to achieve the outcomes that matter most to them."

For these reasons, Tinetti recommended patient priorities care,

which she and her colleagues have been developing and implementing over the past 5-6 years.

"If the benefits and harms of addressing each condition in isolation is of uncertain benefit and potentially burdensome to both clinician and patient, and we know that patients vary in their health priorities ... then what else would you want to focus on in your 20-minute visit ... except each patient's priorities?" Tinetti asked. "This is one solution to the challenge."

What Is Patient Priorities Care?

Patient priorities care is a multidisciplinary, cyclical approach to clinical decision-making composed of three steps, Tinetti explained. First, a clinician identifies the patient's health priorities. Second, this information is transmitted to comanaging providers, who decide which of their respective treatments are consistent with the patient's priorities. And third, those decisions are disseminated to everyone involved in the patient's care, both within and outside of the health care system, allowing all care providers to align with the patient's priorities, she noted.

"Each person does that from their own expertise," Tinetti said. "The social worker will do something different than the cardiologist, the physical therapist, the endocrinologist – but everybody is aiming at the same outcome – the patient's priorities."

In 2019, Tinetti led a [nonrandomized clinical trial](#) to test the feasibility of patient priorities care. The study involved 366 older adults with multimorbidity, among whom 203 received usual care, while 163 received this type of care. Patients in the latter group were twice as likely to have medications stopped, and significantly less likely to have self-management tasks added and diagnostic tests ordered.

How Electronic Health Records Can Help

In an interview, Tinetti suggested that comanaging physicians communicate through electronic health records (EHRs), first to

ensure that all care providers understand a patient's goals, then to determine if recommended therapies align with those goals.

"It would be a little bit of a culture change to do that," Tinetti said, "but the technology is there and it isn't too terribly time consuming." She went on to suggest that primary care providers are typically best suited to coordinate this process; however, if a patient receives the majority of their care from a particular specialist, then that clinician may be the most suitable coordinator.

Systemic Obstacles and Solutions

According to [Cynthia Boyd, MD](#), interim director of the division of geriatric medicine and gerontology, Johns Hopkins University, Baltimore, clinicians may encounter obstacles when implementing patient priorities care.

"Our health care system doesn't always make it easy to do this," Boyd said. "It's important to acknowledge this because it can be hard to do. There's no question," Boyd said in an interview.

Among the headwinds that clinicians may face are clinical practice guidelines, the structure of electronic health records, and quality metrics focused on specific conditions, she explained.

"There's a lot of things that push us – in primary care and other parts of medicine – away from the approach that's best for people with multiple chronic conditions," Boyd said.

Tinetti said a challenge to providing this care that she expects is for clinicians, regardless of specialty, "to feel uneasy" about transitioning away from a conventional approach.

Among Tinetti's arguments in favor of providing patient priorities care is that "it's going to bring more joy in practice because you're really addressing what matters to that individual while also providing good care." To get the most out of patient priorities care, Boyd recommended that clinicians focus on 'the 4 M's': what matters most, mentation, mobility, and medications.

In an effort to address the last of these on a broad scale, Boyd is co-

leading the [US Deprescribing Research Network](#) (USDeN), which aims to "improve medication use among older adults and the outcomes that are important to them," according to the USDeN website. To encourage deprescribing on a day-to-day level, Boyd called for strong communication between co-managing providers.

In an ideal world, there would be a better way to communicate than largely via electronic health records, she said.

"We need more than the EHR to connect us. That's why it's really important for primary care providers and specialists to be able to have time to actually talk to each other. This gets into how we reimburse and organize the communication and cognitive aspects of care," Boyd noted.

Tinetti disclosed support from the John A. Hartford Foundation, the Donaghue Foundation, the National Institute on Aging, and the Institute for Healthcare Improvement. Boyd disclosed a relationship with UpToDate, for which she coauthored a chapter on multimorbidity.

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<https://bit.ly/3uwArtq>

China's carbon pollution now surpasses all developed countries combined

As China's coal-reliant economy has boomed, so, too, have its emissions.

Tim De Chant

Carbon pollution from China's bustling, coal-intensive economy last year outstripped the carbon pollution of the US, the EU, and other developed nations combined, making up a whopping 27 percent of all greenhouse gas emissions worldwide.

As China's economy has grown in the last 30 years, so too have its emissions. While pollution from developed countries has largely been flat since 1990, it has more than tripled in China. The

country's soaring emissions and stable population mean that its per capita emissions have grown quickly, too. At 10.1 tons per person, emissions are just below the 10.5 ton average of the 37-nation Organization for Economic Cooperation and Development, or OECD.

The US still leads the world in per capita emissions, at 17.6 tons per person, according to Rhodium Group's numbers, though President Joe Biden has pledged that the US will [halve emissions by 2030](#). The other developed countries in the report include all 27 current EU member states: the UK, Australia, Canada, Chile, Iceland, Israel, Japan, Korea, Mexico, New Zealand, Norway, Switzerland, and Turkey.

China's draconian lockdowns early in the COVID-19 pandemic allowed the country's economy to bounce back relatively quickly, and as a result, Rhodium expects that China's emissions per capita in 2020 will surpass the average of the OECD nations.

Over the last few years, China's growing carbon emissions have drawn the attention of leaders from around the world. In 2018, the Communist Party lifted a ban on the construction of new coal plants, and its policies have become more generous in years since. Though China has installed a large number of solar panels and wind turbines, fossil fuels still power the vast majority of its industries and transportation modes. Its electrical grid is particularly carbon-intensive—[half of the world's coal](#) is burned inside China's borders. China counters that it's within its rights to burn such vast quantities of fossil fuels since developed countries did the same over the past few centuries. The country is not entirely wrong: developed economies have produced the most cumulative emissions since 1750, around 1,000 gigatons. But China's rise means it has swiftly become the largest contributor in recent years. The country emitted 52 megatons of carbon dioxide and equivalent greenhouse gases in 2019, according to a [report](#) by the Rhodium Group, and has emitted

a cumulative 200 gigatons since 1750.

China's argument has merit, but it also elides the fact that renewable sources like wind and solar were not available on the same scale as fossil fuels for much of the last 300 years. Half the OECD's cumulative carbon emissions were produced before 1980, when wind and solar were expensive compared with fossil fuels. Today, though, those numbers have largely flipped. In the US, it's now [more expensive](#) to run 80 percent of the nation's coal power plants than it would be to shut them down and install new wind farms and solar plants.

Wind and solar prices are dropping in China, too. They're expected to [undercut new coal plants](#) this year, according to consultancy Wood Mackenzie, which could make the [247 GW of coal power](#) the country has under development look not just archaic but unnecessarily expensive. It could imperil China's investments elsewhere. The country is the world's largest financier and developer of coal plants abroad, with over 100 GW funded by Chinese companies.

China's pledge for the Paris Agreement states that it will hit its carbon pollution peak in 2030 and reach net zero 30 years later. Those targets appear achievable, according to the [Climate Action Tracker](#), an independent analyst, but the group says the goals are "highly insufficient" to reach the 2° C warming target set forth in the agreement.

<https://bit.ly/3tFTws9>

The legume family tree

Massive molecular study uncovers clues to the evolution and diversification of essential plant family

The most comprehensive study of the family tree for legumes, the plant family that includes beans, soybeans, peanuts, and many other economically important crop plants, reveals a history of whole-genome duplications. The study also helps to uncover the evolution

of genes involved in nitrogen fixation--a key trait likely important in the evolutionary spread and diversification of legumes and vital for their use as "green manure" in agriculture. To reconstruct the family tree, researchers compared the DNA sequence of more than 1500 genes from 463 different legume species, including 391 newly sequenced species, that span the diversity of this large plant family. A paper describing the study, led by Penn State Professor of Biology Hong Ma, appears in the [May 2021 issue of the journal *Molecular Plant*](#).

"Legumes make up the third largest family of flowering plants and are incredibly diverse--ranging from tiny herbs to giant trees," said Ma, who is the Huck Distinguished Research Professor of Plant Molecular Biology at Penn State. "They are essential food crops for both humans and livestock, can be used as lumber, and have many other uses. Maybe most importantly, they can 'fix' nitrogen--extracting the vital nutrient from the atmosphere and storing it in nodules on their roots in a symbiotic relationship with soil bacteria--making them important as green manure to improve soil health."

There are over 19,000 species in the legume family divided into six subfamilies and then further divided into narrower and narrower groupings based on their evolutionary relationships. There are 765 genera--the grouping one level above species--of which the team sampled members of 333. To build the family tree, the team analyzed gene sequences from the transcriptomes--the portion of the genome that is expressed as genes--of most of the 463 species and a small number of shallowly sequenced whole genomes from across legume diversity.

"This is the largest study of this kind for a single plant family," said Ma. "We went to great lengths to sample as many species as we could to get a broad representation of the legume family, but it is often difficult to get well-preserved specimens that we can extract DNA or RNA from, especially for species found in remote

locations. Having this broad representation of species allowed us to build the most detailed nuclear-gene family tree for legumes to date."

In addition to helping researchers understand the evolution and diversification of legumes, the new legume family tree helps to clarify the relationship between crop plants and their wild relatives. Although the close relatives of important agricultural crops are often known, studying more distant wild cousins could reveal traits that could be exploited to help plants thrive in changing environments and resist diseases or insect pests.



[Illustration of a tree representing the legume family tree with branches representing the six subfamilies. On each branch are flowers or pods of species belonging to the subfamilies. The lines extending from the nutrient bag on the upper left corner indicate the positions of some of the proposed whole-genome duplications.](#) Yiyong Zhao, Chien-Hsun Huang, and Hong Ma

Across the legume family tree, the research team identified strong evidence for 28 separate whole-genome duplication events. Whole-genome duplications, evolutionary events that result in complete duplication of the entire genome, are fairly common among flowering plants and are thought to allow for functional innovation and evolutionary diversification. One of the duplication events that the team identified appears to have occurred in the ancestor of all

members of the legume family.

"Because for most of the species in our study we used transcriptomes and do not have entire genome sequences, we consider these as 'proposed' genome duplication events," said Ma. "These kinds of studies are kind of like solving a mystery. If you only have one or a few witnesses it might be difficult to convince a jury of your evidence, but if you have a hundred witnesses who have different perspectives and they all point to the same thing it becomes difficult to dismiss that evidence. In our case, the different species are like our witnesses. The size of our study allowed us to identify events that we might otherwise have dismissed."

The two largest subfamilies account for over 17,000 legume species and include all of the species with the ability to fix nitrogen. Nitrogen is an important plant nutrient--most commercial fertilizers contain a mix of nitrogen, phosphorus and potassium--so the symbiotic relationship between some legumes and the microorganisms that allow them to assimilate nitrogen from the atmosphere using root nodules has spurred their success by allowing them to colonize areas with less fertile soil. The research team also identified clues to the evolution of the genes responsible for this important trait.

"Our data support the idea that nodulation and nitrogen fixation originated a single time early in the history of legumes and other related nitrogen-fixing plants and the whole-genome duplication event at the origin of legumes might have been crucial for the evolution of this process," said Ma. "In addition to this duplication event, we are also able to see gene loss in plants that do not have the ability to nodulate, and evolutionary changes in genes that contributed to their role in nodulation."

In addition to Ma, the research team includes Yiyong Zhao, Rong Zhang, Kaiwen Jiang, Ji Qi, Yi Hu, Jing Guo, Renbin Zhu, Taikui Zhang, Ashley N. Egan, Ting-Shuang Yi, and Chien-Hsun Huang. This research was funded by the National Natural Science Foundation of China, the Strategic Priority Research Program of Chinese Academy of the

Sciences, the State Key Laboratory of Genetic Engineering, the Ministry of Education Key Laboratory of Biodiversity Science and Ecological Engineering at Fudan University, and Penn State.

<https://bit.ly/2SxPODL>

There's Evidence Volcanoes Are Active on Mars, Raising Chances of Recent Habitability *Evidence seems to be mounting for a geologically and volcanically active [Mars](#).*

[Michelle Starr](#)

A new, close study of volcanic features on the surface of the red planet has found that a lava deposit on the Elysium Planitia appears to be very recent indeed - as in, within the last 50,000 years.

On geological timescales, that's shockingly short. And it could mean that Mars was potentially habitable just as recently, with parts of it similar to regions of volcanic activity in glacial areas such as Iceland, where various forms of extremophile bacteria thrive.

"This may be the youngest volcanic deposit yet documented on

Mars. If we were to compress Mars geologic history into a single day, this would have occurred in the very last second," [said astronomer David Horvath](#) of the Planetary Science Institute and the University of Arizona.



*Volcanic deposit seen around a fissure in the Cerberus Fossae.
(NASA/JPL/MSSS/The Murray Lab)*

Mars has been full of surprises recently, for such an apparently dry, dusty ball of rock, with several lines of evidence suggesting volcanic activity.

One is the presence of liquid water under the surface. Mars, for all its warm coloring, is a very cold place; [a 2019 paper](#) found that internal heating might be necessary to keep subsurface water from freezing. Then last year, another paper described how a Martian

meteorite contained [evidence of volcanic convection](#) in the Martian mantle.

Now, using satellite data, a team of astronomers led by Horvath has found another clue - a volcanic deposit on the Elysium Planitia, a broad, smooth plain just north of Mars' equator.

"This feature is a mysterious dark deposit, covering an area slightly larger than Washington DC. It has a high thermal inertia, includes high-calcium pyroxene-rich material, and is distributed symmetrically around a segment of the Cerberus Fossae fissure system in Elysium Planitia, atypical of aeolian, or wind-driven, deposits in the region," [Horvath said](#).

"This feature is similar to dark spots on [the Moon](#) and Mercury suggested to be explosive volcanic eruptions."

Most volcanic features on the Martian surface are from surface lava flows, not volcanic explosions, although explosive volcanic features are certainly not unknown. What makes the team's discovery so interesting is that it is on top of other, surrounding lava flows - meaning it occurred more recently.

It also appears to be relatively fresh, containing lava and ash.

"This eruption could have spewed ash as high as 10 kilometers (6.2 miles) into the Martian atmosphere but likely represents a last gasp of erupted material," [Horvath explained](#).

"Elysium Planitia hosts some of the youngest volcanism on Mars, dating around 3 million years ago, so it is not entirely unexpected. It is possible that these sorts of deposits were more common but have been eroded or buried."

Interestingly, other hints of activity have been detected in the same region. The Mars InSight lander is just 1,600 kilometers (1,000 miles) or so from the feature, and has [detected earthquake activity in the Cerberus Fossae](#).

Put together, the two pieces of evidence suggest that activity inside Mars may be ongoing. It's important not to over-interpret the

detections, since near-surface lava so late in Mars' life is unlikely without the presence of surface lava flows, and therefore deeper magma is required to explain the eruption.

That's possible, though. Earthquakes can cause eruptions of magma here on Earth, and earthquakes have been detected in the Cerberus Fosse; that suggests one potential mechanism. The feature is also not far from a contemporaneous impact crater, called Zunil. That impact could also have triggered volcanic activity.

However the eruption was triggered, the detection raises the intriguing prospect - albeit still a slim prospect - of relatively recent life on Mars, similar to those found at hydrothermal vents on Earth, where extremely cold conditions meet boiling hot temperatures. Microbial life thrives at these locations, relying not on photosynthesis but chemical reactions for survival.

"The interaction of ascending magma and the icy substrate of this region could have provided favorable conditions for microbial life fairly recently and raises the possibility of extant life in this region," [Horvath said](#).

This could help plan out future Mars missions by providing a location where evidence of life might be found.

The research has been published in [Icarus](#).

<https://go.nature.com/3nXUpLi>

The error-prone step at the heart of making an embryo
High-resolution imaging shows why the union between two sets of chromosomes goes awry as least as often as not.

After a sperm fertilizes an egg, the chromosomes of both unite into a single genome, if all goes according to plan. Now, observations of developing embryos show that this all-important process often goes awry — a finding that helps to explain why at least half of newly formed human embryos have the wrong number of chromosomes.

Some 50–70% of embryos have aneuploidy, an abnormal number of chromosomes. Such embryos are often miscarried.

To find out why aneuploidy is so common, Melina Schuh at the Max Planck Institute for Biophysical Chemistry in Göttingen, Germany, and her collaborators used high-resolution microscopes to observe the early stages of human and cow development. They discovered a crucial step: maternal and paternal genomes, which start off enclosed in their own structures, cluster around the location where they will fuse.

This clustering enables rapid and error-free unification of the two genomes. But this complex process has many steps that can go wrong. Failures lead to aneuploidy and fragments of nuclei containing subsets of chromosomes — both of which impair the development of healthy embryos. *Cell (2021)*

<https://bit.ly/3ba1kf6>

Deep sub-surface “microbial dark matter” hasn’t evolved since Pangea

The ancient microbes have survived brutal conditions for millions of years and hit pause on evolution

Kristen Witte

At two miles below ground, the sun last touched the buried rock when carbon dioxide filled the sky, before the days of Earth’s oxygen.

Drops of water formed time capsules for early microbial life to survive the deep sub-surface, their methods and madness hidden from Earth’s surface for millions of years.

Despite accounting for about 10 percent of the planet’s total biomass, we know little of these organisms, which scientists have called “[microbial dark matter](#).” Until recently, our understanding of microbes was limited to those that could [grow in a lab](#).

Advancements in genome sequencing and culture techniques have now brought light to the darkness, and from the shadows, microbial secrets emerged.

Some survived on the buried remnants of photosynthesis, while

others house tools [unlike any life on the surface](#).

One species was *Candidatus Desulforudis audaxviator*, or CDA, a sulfur-breathing microbe that has spent the last several hundred million years in total isolation, its only companion the radioactivity spilling from its rocky confines.

Now, researchers from the Bigelow Laboratory for Ocean Sciences have found that 165 million years ago, CDA abandoned the very engine of life on Earth: evolution.

Scientists originally discovered CDA in [a South African gold mine](#), and later in both North America and Eurasia. This geographic separation let researchers study how CDA evolved after millions of years.

The team used DNA sequencing tools to read the genomes from individual cells. Strikingly, the CDA genomes from all three continents were nearly identical.

While cross-contamination was obvious initial explanation, the team found no evidence of CDA spreading by air, land, or sea. Nor did the microbes stall as spores. All were actively respiring and replicating.

After ruling out all of these possible reasons for their results, the [researchers concluded](#) that as the supercontinent Pangea split, between 55-165 million years ago, these microbes hit pause on evolution.

CDA is a living fossil, subverting evolutionary change yet surviving millions of years of changes to our planet, including a mass extinction.

How CDA managed an evolutionary standstill — perhaps through a meticulous replication process — may have immense application in biotechnology. It may also upend our understanding of microbial evolution. What other secrets to survival might microbial dark matter be hiding?

<https://bit.ly/3be83on>

Remains of nine Neanderthals found in cave south of Rome

Italian archaeologists believe most of Neanderthals were killed by hyenas then dragged back to den

Lorenzo Tondo in Palermo

Italian archaeologists have unearthed the bones of nine [Neanderthals](#) who were allegedly hunted and mauled by hyenas in their den about 100km south-east of Rome.



Fossilised remains of nine Neanderthals in the Guattari Cave in San Felice Circeo, south of Rome, Italy. Photograph: Italian culture ministry/AFP/Getty

Scientists from the Archaeological Superintendency of Latina and the University of Tor Vergata in Rome said the remains belong to seven adult males and one female, while another are those of a young boy.

Experts believe the individuals lived in different time periods. Some bones could be as old as 50,000 to 68,000 years, whereas the most ancient remains are believed to be 100,000 years old.

The Neanderthal remains, which include skullcaps and broken jawbones, were found in the Guattari cave, which had already gained notoriety for the presence of fossils of these distant human cousins, which were found by chance in 1939. Since then, no further human remains had been uncovered in Guattari.

“It is a spectacular find,” said Mario Rolfo, professor of archaeology at Tor Vergata University. “A collapse, perhaps caused by an earthquake, sealed this cave for more than 60,000 years, thereby preserving the remains left inside for tens of thousands of years.”

Researchers found traces of vegetables alongside human remains

and those of rhinoceroses, giant deer, wild horses and, of course, ferocious hyenas.

According to the researchers, most of the Neanderthals had been killed by hyenas and then dragged back to the cave they had transformed into their den. Once inside, the animals consumed their prey.

“Neanderthals were prey for these animals,” said Rolfo. “Hyenas hunted them, especially the most vulnerable, like sick or elderly individuals.”

Even before these ferocious predators took possession of the cave, experts do not exclude the possibility that Neanderthals had at one time made it their home. Rolfo has announced that his team of researchers intended to analyse the DNA of these individuals to understand their ways of life and history.

A preliminary analysis of dental tartar has revealed that their diet was varied. They primarily consumed cereals, which contributed to the growth of their brains. “It is an extraordinary discovery that the whole world will talk about,” said Italy’s culture minister, Dario Franceschini. “These findings will help to enrich studies on Neanderthals.”

Neanderthals inhabited Eurasia, from the Atlantic coast to the Ural mountains, from about 400,000 years ago until a little after 40,000 years ago, disappearing after our species established itself in the region. Last year, remains and tools found in Bulgaria, revealed that modern humans and Neanderthals were present at the same time in [Europe](#) for several thousand years, giving them ample time for biological and cultural interaction.

Often portrayed as the simple, stocky relatives of modern humans, Neanderthals had, in fact, similar brains and [developed a rich culture](#). Beyond their complex stone tools and painted jewellery, [the Neanderthals used to adorn](#) caves in art, leaving [hand stencils behind](#) for modern humans to ponder long after they died out.

<https://bit.ly/3vTV9UA>

Hospital Food Is Never Great, But For Some Patients It Means Death

People who are hospitalized with chronic heart failure should be fed fresh and balanced meals to keep their ticker in tip-top shape.

[Carly Cassella](#)

The typical tray of hospital food is not the medicine these patients need. In Switzerland, among 645 people hospitalized with chronic heart failure, a randomized trial found those who were given regular hospital food – as opposed to a personal nutrition plan – had an almost doubled risk of mortality within 30 days.

The findings suggest the lack of nutrition found in most hospital food could be putting the health and well-being of vulnerable patients at serious risk.

"Our trial thus does not provide evidence for effects of single nutritional components," the authors [explain](#), "but rather suggests that the overall strategy of providing nutritional support to reach different nutritional goals during a hospital stay for an acute illness is beneficial for patients with chronic heart failure."

Within two days of being hospitalized, half the patients in the trial received nutritional support from a trained registered dietician, who helped them identify and achieve their energy, protein, and micronutrient goals with individualized meals and check-ups every one or two days. Before they were discharged, these patients also received dietary counseling and nutritional supplements if needed.

The other half of the trial group had their diet largely ignored. They received standard hospital food during their stay "[according to their ability and desire to eat, with no nutritional consultation and no recommendation for additional nutritional support](#)".

As it turns out, the two different diets were associated with significant differences in quality and quantity of life.

After 180 days, roughly a quarter of the patients who received

nutritional counseling and support in hospital had died, which goes to show how serious chronic heart failure is. In comparison, however, about a third of those who had no dietary support ended up passing away in the same timeframe – a big increase.

Hospital food has a reputation for being pre-packaged and heavily processed, so this may not be a huge surprise. Instead of having a menu based on the best nutritional science, these meals are often sculpted by [a desire to save money](#).

While this corner-cutting might prove harmless to most patients, for patients with particularly serious conditions like chronic heart failure, such a food plan could ultimately be deadly.

Eating processed and fatty foods can cause additional plaque to build up in the arteries, which puts someone at even greater risk of heart failure in the future. Evidence suggests these patients should instead be [focusing on fruits and vegetables](#), while limiting their intake of sodium and fluids. But while previous research has shown a lack of nutrition is especially dangerous for those with chronic heart failure, there hasn't been much research on how direct nutritional support can benefit patients.

The trial in Switzerland was conducted among a relatively small cohort and was not [double-blind](#), but the findings nonetheless suggest nutritional advice and support within the hospital can improve a person's quality of life – and possibly even save their life, especially among those who are deemed at high risk of malnutrition. Compared to those at moderate risk of malnutrition, the authors found patients at high risk were 65 percent more likely to die 180 days after being admitted to hospital. This was also the group that showed the most benefit from nutritional support during their hospital stay.

It's unclear how these patients kept eating once they left the hospital, but given all the patients had an average length of stay of about 10 days, the results seem to suggest that many in the nutritional

support group took at least some of the advice on board.

To know for sure, though – among other things – will require more research.

"Clearly," the authors [write](#), "there is need for additional trials validating our findings in the population of patients with chronic heart failure including also continued outpatient treatment."

The study was published in [Journal of the American College of Cardiology](#).

<https://bit.ly/3nZLpoO>

Do other animals get heart attacks?

They could, in theory. So, why don't they?

By [Ashley P. Taylor - Live Science Contributor](#)

Every 40 seconds, someone in the U.S. has a heart attack, which amounts to about [805,000 heart attacks every year](#). Of course, this statistic applies only to humans. But what about other animals — do they also experience this debilitating and potentially deadly condition?

For the most part, other animals don't get heart attacks — not even one of our closest living relatives, [chimpanzees](#) (*Pan troglodytes*). Nonhuman animals experience other cardiac problems, but as far as scientists know, heart attacks are rare in other creatures.

"In general, animals don't naturally die from the typical heart attack that you see where you clog up the coronary arteries in humans," Philip Gordts, an assistant professor who studies [heart disease](#) at the University of California, San Diego (UCSD), told Live Science.

What is a heart attack?

A heart attack occurs when a [blood vessel](#) distributing oxygenated blood to the [heart](#) gets blocked and a piece of heart tissue dies from [oxygen](#) deprivation, according to Flavio Fenton, a professor of physics at the Georgia Institute of Technology who studies the electrical aspects of both human and other animal species' hearts. When a piece of the heart dies, it can't contract and also fails to propagate the electrical wave that moves through the rest of the

heart telling it to contract. That can cause the heart to stop, leading to death unless an intervention, such as CPR, is performed.

"All mammalian hearts are very similar," Fenton said. "So, most mammalian hearts, in principle, could have heart attacks."

Although they could theoretically happen, for the most part, they don't. For instance, heart attacks occur very rarely in dogs, according to [Oakland Veterinary Referral Service](#), in Bloomfield Hills, Michigan. Not even chimpanzees in captivity, which are not only closely related to humans but also share similar risk factors for heart disease, such as physical inactivity and high [cholesterol](#) levels, have heart attacks, as UCSD husband and wife duo Dr. Nissi Varki and Dr. Ajit Varki pointed out in a 2009 paper in the journal [Evolutionary Applications](#). Nor are rodents and [rabbits](#) prone to atherosclerosis, the buildup of fats, cholesterol and other substances on artery walls, according to the same paper. Even in rodents and rabbits that are genetically modified to have high cholesterol and blood lipids for the purpose of inducing atherosclerosis and other human diseases, actual heart attacks rarely occur, according to the 2009 paper.

Rather than asking why other animals don't get heart attacks, it might make more sense to ask why humans do. You might think it has to do with our sedentary behavior and poor diet, and those factors certainly do play roles. Atherosclerosis is a leading cause of heart disease, and an unhealthy diet high in red meat and full-fat dairy products and a lack of exercise are risk factors for atherosclerosis, [according to the Mayo Clinic](#).

Yet [15% of first-time heart attacks](#) occur in people without any cardiac risk factors. Rather, humans may be particularly heart-attack-prone because of a mutation that's unique to humans. This mutation prevents us from making a particular sugar molecule called Neu5Gc, as Gordts, the Varkis and colleagues reported in a 2019 study published in the journal [Proceedings of the National](#)

[Academy of Sciences](#) (PNAS).

In humans, this mutation inactivates a gene (CMAH) that's responsible for making the Neu5Gc sugar, according to the PNAS study. When the researchers inactivated that same gene in [mice](#) that were genetically modified to have high cholesterol and develop atherosclerosis, the mice developed atherosclerosis at twice the severity of mice with a functioning version of the gene. (However, the mice did not actually have heart attacks, Gordts said.) More broadly, this mutation could explain why humans are prone to atherosclerosis and heart attacks while other mammals are not, the authors suggested in their paper.

Heart attacks in vertebrates

Despite reports that other animals mostly don't have heart attacks, the truth is that there haven't been a lot of experiments investigating this question.

"There's very little [in the scientific literature] about heart attacks in anything that's not mammalian," Tomasz Owerkowicz, a comparative vertebrate physiologist at California State University, San Bernardino, told Live Science. "You can observe [that] an animal has suddenly died. But very rarely would you actually perform the autopsy and look for blockages in the coronary arteries. We just don't know whether other animals suffer heart attacks."

But based on heart structure, researchers can make predictions about which vertebrates (animals with backbones) are most likely to have heart attacks. Mammalian and bird hearts have just one source of oxygen, the coronary arteries, according to Owerkowicz. These [branch](#) into smaller arterioles and capillaries, where heart muscle cells pick up oxygen and discard carbon dioxide. In the mammalian heart, "the only way you can get the blood and the oxygen everywhere inside the heart is through the vessels," Fenton said. This is also thought to be true for birds, Owerkowicz noted. For that reason, if a coronary artery is blocked in a bird or mammal,

the heart loses its oxygen supply and the creature is likely to have a heart attack, Owerkowicz said.

The hearts of some nonmammalian vertebrates have a slightly different system that may protect them from heart attacks, according to Owerkowicz; in addition to blood vessels and capillaries supplying oxygen, they have spongy heart tissue, which allows oxygenated blood within the heart's chambers to travel deep into the walls of the heart, like water moving into the air pockets of a sponge. Because the blood penetrates so deep within the heart tissue, oxygen can diffuse straight from the blood into heart cells. This doesn't happen in birds and mammals because the walls of their hearts are more compact, Owerkowicz said.

Even if a coronary artery is blocked, a spongy-hearted vertebrate may avoid a heart attack thanks to this back-up system of oxygen diffusion, Owerkowicz said. Because spongy-hearted vertebrates have a back-up source of oxygen and birds and mammals don't, researchers believe that the former are much less likely to get heart attacks, Owerkowicz said.

Owerkowicz and Fenton are collaborating on experiments on heart attacks on one such spongy-hearted critter, the [alligator](#).

"In an alligator heart, you have the vessels; but also, because it's spongy, there's a lot of blood around it, not necessarily coming from the vessels. There's some perfusion of the tissue from the blood surrounding the structure," Fenton said.

According to the researchers' experiments so far, alligators don't have heart attacks. Owerkowicz said he tied off a coronary artery in an alligator, but doing so didn't result in any health problems for the animal. "Even when the animal was exercised, its heart worked just fine. I assume it's because alligator ventricles [the lower two chambers of the heart] are very spongy," Owerkowicz said. An autopsy showed the alligator heart tissue had no signs of cell death, he added.

<https://lat.ms/3be80sP>

Single shot of two-dose COVID-19 vaccine can prevent serious illness and death

In a pinch, a single shot certainly helps.

By [Melissa Healy](#) Staff Writer

A first look at the potential [effect of stretching limited COVID-19 vaccine supplies](#) has found that just one dose of the Pfizer-BioNTech vaccine was 60% to 70% effective at preventing symptomatic disease in people age 70 and older.

That protection started 10 to 13 days after receiving the shot and lasted for more than six weeks, according to a preliminary report released Tuesday by [Public Health England](#).

The study allowed the health service to gauge the effects of the country's unorthodox vaccination strategy. Faced with limited doses, surging infection rates and a [new strain that was spreading about 56% more readily](#) than its predecessors, British officials opted to immunize larger numbers of people with a first dose rather than maintain strict adherence to the set schedule of giving first and second doses three weeks apart.

Researchers from Public Health England, which advises the United Kingdom's National Health Service, tracked roughly 157,000 Britons 70 and over who were tested for COVID-19 between Dec. 9 and February 19. Their vaccination status and health outcomes were compared at different intervals to determine how protective vaccine was and when those effects became apparent.

The study authors found that a month after Brits 80 and over got a first dose of the Pfizer-BioNTech vaccine, they were 43% less likely to be admitted to the hospital with COVID-19 than their unvaccinated peers. They were also 51% less likely to die of the disease.

In cases where people over 70 received a second dose of the vaccine, the risk of developing any type of COVID-19 symptoms

was reduced by 85% to 90% — a level of protection in line with that seen in clinical trials. That benefit was apparent even if the time between the first dose and second was more than the three weeks originally planned.

“During my time at Redlands, my communication skills have absolutely grown. I used to be so shy—I didn’t speak up in class or join any clubs. But now I want to be a part of everything; I feel so confident,” says transfer student Jenny Solis '21.

There was more good news. The study found that these effects were undiminished by the widespread presence of the United Kingdom’s more transmissible coronavirus strain, dubbed B.1.1.7 by scientists. Finally, the encouraging results were all seen in Britons over the age of 80. This group — which got first dibs on vaccine in the U.K. and was there therefore first to be studied — has been particularly vulnerable over the course of the pandemic. Their robust response to inoculation was also heartening because people of this age do not always mount an effective response to vaccines, experts noted.

The new research gives the British government greater confidence that there were few risks, and potentially many benefits, to [allowing more than three weeks](#) to elapse between the administration of first and second doses of the Pfizer vaccine.

“The fact that the vaccine appears to be preventing symptomatic disease, including with the new variant of concern, is encouraging,” the study authors wrote. “This is likely to have a significant impact on case detections and severe outcomes at a population level.”

In early December, just as the first vaccine was going into Britons’ arms, the discovery of the B.1.1.7 variant set off alarm bells and prompted British Prime Minister Boris Johnson to announce a shake-up in the country’s vaccination strategy.

That change prompted skepticism from experts in the United States, [including Dr. Anthony Fauci](#), President Joe Biden’s top advisor on infectious diseases. And as recently as this weekend, the CDC’s

vaccine advisory panel reiterated its preference to keep to the schedules tested in clinical trials.

“We don’t have sufficient data to delay second doses beyond what’s currently recommended,” said [Dr. Grace Lee](#) of Stanford University, a member of the CDC’s Advisory Committee on Immunization Practices.

The findings may prompt American experts to shift their views, especially since the CDC expects [the U.K. strain to become dominant here](#) sometime this month. The [Pfizer-BioNTech vaccine](#) and a similar one [made by Moderna](#) are two of the three COVID-19 shots now authorized for emergency use in the U.S.

The British study also provides a glimpse of Britons’ early response to a two-dose COVID-19 vaccine not yet available in the United States, but due to be considered for emergency use soon.

In people 70 and older, the [vaccine produced by AstraZeneca](#) began to reduce the risk of COVID-19 two to three weeks after a first dose was administered. After 35 days, a single shot was 73% effective, on average, at protecting them from developing any symptoms of COVID-19.

In keeping people out of the hospital with COVID-19, a single shot’s efficacy was estimated to be 80%.

The AstraZeneca vaccine’s single-dose protection thus appears to be on a par with that of the Pfizer-BioNTech vaccine. But because Pfizer’s vaccine rolled out in Britain several weeks earlier than AstraZeneca’s, the British researchers were able to track the effectiveness of Pfizer’s vaccine for longer — and to consider outcomes that take longer to occur, such as death.

But early evidence suggests the AstraZeneca results could be good. The researchers said the vaccine’s efficacy was still rising when they cut off their data analysis. But they also cautioned that they had less data available to make a judgment about how long a single shot’s protection would last.

“This study provides early evidence that the vaccine is having a significant effect on COVID-19 cases in England,” the authors wrote. “We see a clear effect of the first dose of vaccine, supporting the decision to maximize the number of individuals vaccinated with a single dose.”

<https://bit.ly/3o2DuXW>

'Dracula's Castle' Swaps Fangs For Jabs in Pivot to COVID Vaccination Hub

Visitors to Romania's forbidding Bran Castle, known as the inspiration for the lair of Dracula, are being jabbed with needles rather than vampiric fangs this weekend

AFP

Visitors to Romania's forbidding [Bran Castle](#), widely known as the inspiration for the lair of Dracula, are being jabbed with needles rather than vampiric fangs this weekend in a [coronavirus](#) vaccination drive.

"I came to visit the castle with my family and when I saw the poster I gathered up my courage and agreed to get the injection," said 39-year-old engineer Liviu Necula



(Laszlo Baranyai/500px/Getty Images)

Those who take the jab are handed a certificate hailing their "boldness and responsibility" promising they will be welcome at the castle "for the coming 100 years" - as well as offered a free tour of the "torture chamber".

Nestled in a misty valley in the Carpathian mountains, Bran Castle is associated with the 15th-century Romanian prince Vlad Tepes, known as "the Impaler", although he never stayed there.

Dracula author Bram Stoker is believed to have been inspired by Vlad and descriptions of Bran Castle when writing his 1897 novel that helped found the modern vampire genre.

Romania's government has turned to local vaccination drives and [24-hour "marathons"](#) at major venues like the National Library in Bucharest to get as many citizens as possible immunized.

"These centers are for everyone who wants to get vaccinated but doesn't feel like making an appointment online," Marius Nasta hospital director Beatrice Mahler told AFP.

But she added that it would still be difficult to reach people living in the many areas without local doctors.

Almost 3.6 million Romanians of the country's 19 million people have received at least one vaccine dose, with authorities aiming for five million by June.

<https://bit.ly/3txsKBZ>

'Living Fossil' Thought Extinct For 273 Million Years Found Thriving on Ocean Floor

A symbiotic relationship between two marine lifeforms has just been discovered thriving at the bottom of the ocean, after disappearing from the fossil record for hundreds of millions of years.

[Michelle Starr](#)

Scientists have found non-skeletal corals growing from the stalks of marine animals known as [crinoids](#), or sea lilies, on the floor of the Pacific Ocean, off the coasts of Honshu and Shikoku in Japan.

"These specimens represent the first detailed records and examinations of a recent *syn vivo* association of a crinoid (host) and a hexacoral (epibiont)," [the researchers wrote in their paper](#), "and therefore analyses of these associations can shed new light on our understanding of these common Paleozoic associations."

During the Paleozoic era, crinoids and corals seem to have gotten along very well indeed. The seafloor fossil record is full of it, yielding countless examples of corals overgrowing crinoid stems to climb above the seafloor into the water column, to stronger ocean currents for filter-feeding.

Yet these benthic besties disappeared from the fossil record around 273 million years ago, after the specific crinoids and corals in question went extinct. Other species of crinoids and corals emerged in the Mesozoic, following the [Permian-Triassic extinction](#) - but never again have we seen them together in a symbiotic relationship.



(Zapalski et al., *Palaeogeogr. Palaeoclimatol. Palaeoecol.*, 2021)

Well, until now. At depths exceeding 100 meters (330 feet) below the ocean's surface, scientists have found two different species of coral - hexacorals of the genera *Abyssoanthus*, which is very rare, and Metridioidea, a type of sea anemone - growing from the stems of living Japanese sea lilies ([Metacrinus rotundus](#)).

The joint Polish-Japanese research team, led by paleontologist Mikołaj Zapalski of the University of Warsaw in Poland, first used stereoscopic microscopy to observe and photograph the specimens. Then, they used non-destructive microtomography to scan the specimens to reveal their interior structures, and DNA barcoding to identify the species.

They found that the corals, which attached below the feeding fans of the crinoids, likely didn't compete with their hosts for food; and, being non-skeletal, likely didn't affect the flexibility of the crinoid stalks, although the anemone may have hindered movement of the host's cirri - thin strands that line the stalk.

It's also unclear what benefit the crinoids gain from a relationship with coral, but one interesting thing did emerge: unlike the Paleozoic corals, the new specimens did not modify the structure of the crinoids' skeleton.

This, the researchers said, can help explain the gap in the fossil record. The Paleozoic fossils of symbiotic corals and crinoids

involve corals that have a calcite skeleton, such as Rugosa and Tabulata.

Fossils of soft-bodied organisms - such as non-skeletal corals - are rare. Zoantharia such as *Abyssoanthus* have no confirmed fossil record, and actiniaria such as Metridioidea (seen as a dry specimen in the image below) also are extremely limited.

If these corals don't modify the host, and leave no fossil record, perhaps they have had a long relationship with crinoids that has simply not been recorded.

This means the modern relationship between coral and crinoid could contain some clues as to Paleozoic interactions between coral and crinoid. There's evidence to suggest that zoantharians and rugose corals share a common ancestor, for instance.

The number of specimens recovered to date is small, but now that we know they are there, perhaps more work can be done to discover the history of this fascinating friendship.

"As both Actiniaria and Zoantharia have their phylogenetic roots deep in the Palaeozoic, and coral-crinoid associations were common among Palaeozoic Tabulate and Rugose corals, we can speculate that also Palaeozoic non-skeletal corals might have developed this strategy of settling on crinoids," [the researchers wrote in their paper](#).

"The coral-crinoid associations, characteristic of Palaeozoic benthic communities, disappeared by the end of Permian, and this current work represents the first detailed examination of their rediscovery in modern seas."