

<https://go.nature.com/2Lz8Oce>

Europe's top science funder shows high-risk research pays off

The European Research Council publishes its third annual impact assessment of the projects it funds.

[Inga Vesper](#)

A popular and unusual self-review carried out by Europe's most prestigious science funder is back. The annual assessment, now in its third year, found that nearly one in five projects supported by the [European Research Council \(ERC\)](#) led to a scientific breakthrough.

The independent review, undertaken in 2017, assessed 223 completed ERC projects that had ended by mid-2015. It deemed that 79% of them achieved a major scientific advance, 19% of which were considered fundamental breakthroughs. That proportion rose to 27% for ERC Advanced Grants, which are awarded to experienced researchers. Only 1% of the total were judged to have made no appreciable scientific contribution. The review was [published on 31 May](#).

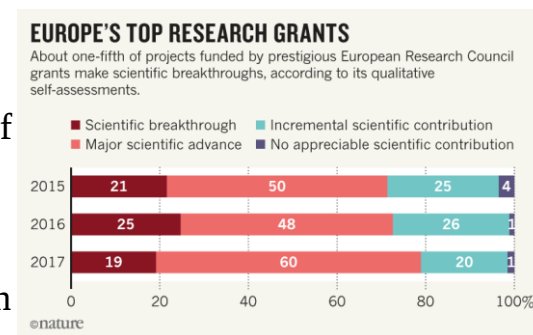
Established in 2007 [to improve the quality of Europe's science](#), the ERC is the European Union's premier funder of blue-skies research and is part of Horizon 2020, the EU's main science-funding programme. It awards generous, multiyear grants in any discipline and applications are judged solely on their quality. The council has undertaken annual reviews of the projects it funds since it ran a [popular pilot assessment in 2015](#). The strategy is pioneering among European funders, most of which evaluate success on a project-by-project basis, and it was praised for taking a qualitative approach rather than relying, for instance, on bibliometrics.

Risky business

The latest assessment was carried out by senior scientists convened by the ERC's Scientific Council. Each panel member was asked a series of questions about a randomly selected set of projects. This

year, evaluators were also asked to focus on a project's risk to a greater extent than in previous years. (A spokesperson for the ERC said that the council is still refining the assessment's methodology.)

The 19% figure of scientific breakthroughs in the latest assessment is lower than in previous years; 21% and 25% of ERC projects assessed in the [2015](#) and [2016](#) exercises, respectively, were classed as such (see 'Europe's top research grants').



Source: ERC

The reviewers deemed that most projects that made breakthroughs were high risk and high reward, and only 10% of projects were considered low risk. "The ERC has really pushed the expectation of raising the boundaries of science and taking more risks," says Jan Palmowski, secretary-general of the Guild of European Research-Intensive Universities, a lobby group in Brussels.

The assessment shows that risk-friendly funding is crucial for retaining talent in Europe, where research funders are generally risk-averse, says Martin Vechev, a computer scientist at the Swiss Federal Institute of Technology in Zurich who received an ERC grant aimed at early-career researchers in 2015, after spending time at computing firm IBM in the United States. The grant encouraged him to stay in Europe, and he says that the funding helped his team to develop a new sub-field of artificial intelligence that focuses on machines that automatically write computer code.

The reviewers also deemed that more than 50% of projects had already made an economic and societal impact. In a speech earlier this year, ERC president Jean-Pierre Bourguignon, said that council-

funded research generated 29% of patents approved from EU funding in 2007–13, despite receiving less than 17% of the money.

Funding incentive

The review comes at a crucial time for EU research funding, say observers. This week, the European Commission is expected to release a detailed budget plan for the next instalment of its main funding programme, which will include the ERC's next funding pot. The programme, called Horizon Europe, will run from 2021 to 2027 and has a [proposed budget of nearly €100 billion](#) (US\$117 billion). The latest review provides ammunition in the fight to raise the ERC's budget, says Palmowski. His organization advocates for a doubling of the annual budget, which in 2017 was €1.8 billion (it started with €300 million in 2007).

The findings should encourage policymakers around Europe to focus their national research funding on excellence, even if economic growth is their priority, says the League of European Research Universities (LERU). "The ERC clearly shows that focusing on excellence alone at application stage also leads to demonstrable impacts," says Laura Keustermans, senior policy officer at the LERU in Leuven, Belgium. Since its creation, ERC grantees have won six Nobel prizes and four Fields Medals, considered the most prestigious prize in mathematics.

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<http://bit.ly/2sFa5rk>

Collective gravity, not Planet Nine, may explain the orbits of 'detached objects'

Bumper car-like interactions at the edges of our solar system--and not a mysterious ninth planet--may explain the dynamics of strange bodies called "detached objects," according to a new study.

CU Boulder Assistant Professor Ann-Marie Madigan and a team of researchers have offered up a new theory for the existence of

planetary oddities like Sedna. This minor planet orbits Earth's sun at a distance of 8 billion miles but appears separated from the rest of the solar system.

One theory for its unusual dynamics is that an as-of-yet-unseen ninth planet beyond Neptune may have disturbed the orbits of Sedna and other detached objects. But Madigan and her colleagues calculated that the orbits of Sedna and its ilk may result from these bodies jostling against each other and space debris in the outer solar system. "There are so many of these bodies out there. What does their collective gravity do?" said Madigan of the Department of Astrophysical and Planetary Sciences (APS) and JILA. "We can solve a lot of these problems by just taking into account that question."

The researchers will present their findings on June 4 at a press briefing at the 232nd meeting of the American Astronomical Society, which runs from June 3-7 in Denver.

Detached objects like Sedna get their name because they complete humongous, circular orbits that bring them nowhere close to big planets like Jupiter or Neptune. How they got to the outer solar system on their own is an ongoing mystery.

Using computer simulations, Madigan's team came up with one possible answer. Jacob Fleisig, an undergraduate studying astrophysics at CU Boulder, calculated that these icy objects orbit the sun like the hands of a clock. The orbits of smaller objects, such as asteroids, however, move faster than the larger ones, such as Sedna. "You see a pileup of the orbits of smaller objects to one side of the sun," said Fleisig, who is the lead author of the new research. "These orbits crash into the bigger body, and what happens is those interactions will change its orbit from an oval shape to a more circular shape."

In other words, Sedna's orbit goes from normal to detached entirely because of those small-scale interactions. The team's observations

also fall in line with research from 2012, which observed that the bigger a detached object gets, the farther away its orbit becomes from the sun. Alexander Zderic, a graduate student in APS at CU Boulder, also co-authored the new research.

The findings may also provide clues around another phenomenon: the extinction of the dinosaurs. As space debris interacts in the outer solar system, the orbits of these objects tighten and widen in a repeating cycle. This cycle could wind up shooting comets toward the inner solar system--including in the direction of Earth--on a predictable timescale.

"While we're not able to say that this pattern killed the dinosaurs," Fleisig said, "it's tantalizing."

<http://bit.ly/2xWhMOQ>

Did extreme fluctuations in oxygen, not a gradual rise, spark the Cambrian explosion?

Five hundred and forty million years ago, during the Cambrian period, life suddenly went nuts.

Boulder, Colo., USA - "Blossomed" is far too mild a word: instead, geologists call this sudden diversification an "explosion." But what exactly sparked the Cambrian explosion?

Now, a new study suggests that wild swings in oxygen levels may have sent life scrambling to adapt, leading to a major burst of diversity. That, says lead author Guangyi Wei of Yale University, challenges the long-held explanation that gradually rising oxygen simply reached a life-fueling tipping point. The study was just published online ahead of print in *Geology*.

Wei explains that the goal was to reconstruct a continuous record of global marine oxygen levels from the late Ediacaran (latest pre-Cambrian) into the early Cambrian. To do that, the team, from Yale and Nanjing University in China, measured changes in uranium isotope ratios that reflect changing marine oxygen levels, as recorded in carbonates deposited during that interval, from China.

The results revealed huge global swings from anoxic-completely depleted in oxygen to oxygenated conditions over periods of two to ten million years. Such big ups and downs in oxygen, the scientists suggest, could have destabilized ecosystems, fragmented habitats, and triggered an explosion of changing life forms.

The study provides some of the first direct evidence that the Cambrian explosion came on the heels of major variations in oxygen, says Wei. "It would be great to get more data from other regions and time intervals," he adds.

Wei also poses the obvious next question: what caused such huge swings in oxygen in the first place? Some possibilities: Tectonics, biological processes, or climate shifts.

Marine redox fluctuation as a potential trigger for the Cambrian explosion

Guangyi Wei et al. Contact: wqynjues@gmail.com; guangyi.wei@yale.edu. *Geology*, <https://pubs.geoscienceworld.org/gsa/geology/article/531401/marine-redox-fluctuation-as-a-potential-trigger>.

<http://bit.ly/2JHRwN7>

Stanford study casts doubt on the predictive value of earthquake foreshocks

Foreshocks just like other small earthquakes

No one can predict when or where an earthquake will strike, but in 2011 scientists thought they had evidence that tiny underground tremors called foreshocks could provide important clues. If true, it suggested seismologists could one day warn people of impending temblors.

But a new study published in the online June 4 issue of *Nature Geoscience* by scientists at Stanford University and Boğaziçi University in Turkey has cast doubt on those earlier findings and on the predictive value of foreshocks.

The previous evidence came from a 7.6 magnitude earthquake in 1999 near Izmit, Turkey, that killed more than 17,000 people. A 2011 study in the journal *Science* found that the deadly quake was

preceded by a series of small foreshocks - potential warning signs that a big seismic event was imminent.

"We've gone back to the Izmit earthquake and applied new techniques looking at seismic data that weren't available in 2011," said lead author William Ellsworth, a professor (research) of geophysics at Stanford School of Earth, Energy & Environmental Sciences. "We found that the foreshocks were just like other small earthquakes. There was nothing diagnostic in their occurrence that would suggest that a major earthquake was about to happen."

"We'd all like to find a scientifically valid way to warn the public before an earthquake begins," said co-author Fatih Bulut, an assistant professor of geodesy at Boğaziçi University's Kandilli Observatory and Earthquake Research Institute. "Unfortunately, our study doesn't lead to new optimism about the science of earthquake prediction."

How do earthquakes begin?

Scientists including Ellsworth have proposed two ideas of how major earthquakes form, one of which - if scientists can detect them - could warn of a larger quake.

"About half of all major earthquakes are preceded by smaller foreshocks," Ellsworth said. "But foreshocks only have predictive value if they can be distinguished from ordinary earthquakes."

One idea, known as the cascade model, suggests that foreshocks are ordinary earthquakes that travel along a fault, one quake triggering another one nearby. A series of smaller cascading quakes could randomly trigger a major earthquake, but could just as easily peter out. In this model, a series of small earthquakes wouldn't necessarily predict a major quake.

"It's a bit like dominos," Bulut said. "If you put dominos on a table at random and knock one over, it might trigger a second or third one to fall down, but the chain may stop. Sometimes you hit that magic one that causes the whole row to fall."

Another theory suggests that foreshocks are not ordinary seismic events but distinct signals of a pending earthquake driven by slow slip of the fault. In this model, foreshocks repeatedly rupture the same part of the fault, causing it to slowly slip and eventually trigger a large earthquake.

In the slow-slip model, repeating foreshocks emanating from the same location could be early warnings that a big quake is coming. The question had been whether scientists could detect a slow slip when it is happening and distinguish it from any other series of small earthquakes.

Earlier studies

In 2011, a team argued in *Science* that the foreshocks preceding the 1999 quake in Izmit were driven by slow slip, and could have been detected with the right equipment - the first evidence that foreshocks would be useful for predicting a major earthquake.

"That result has had a large influence in thinking about the question of whether foreshocks can be predictive," Ellsworth said.

The city of Izmit is located on the North Anatolian Fault, which stretches about 900 miles (1,500 kilometers) across Turkey. For the 2011 study, a team analyzed data from a single seismic station several miles from the earthquake epicenter, which ultimately recorded seismograms of 18 foreshocks occurring about 9 miles (15 kilometers) below the surface - very close to the where the larger earthquake began - and each with similar waveforms.

Those similarities led the authors to conclude that all of the foreshocks repeatedly broke the same spot on the fault, driven by slow slip that ultimately triggered the major earthquake. They concluded that monitoring similar events could provide timely warning that a big quake is imminent. "The *Science* paper concluded that there was a lot of slow slip, and had we been there with the right instruments we might have seen it," Ellsworth said. "We decided to test that idea that the foreshocks were co-located."

Domino effect

Instead of relying on data from one seismic station, Ellsworth and Bulut analyzed seismograms recorded at nine additional stations during the 1999 earthquake.

With more stations, Ellsworth and Bulut identified a total of 26 foreshocks. None were identical, and the largest ones progressively moved from west to east along the fault. This finding is consistent with the cascade model, where an ordinary earthquake triggers another quake on a neighboring part of the fault, but doesn't necessarily predict a major quake.

Bulut and Ellsworth found no evidence that slow slip played a role in triggering the Izmit earthquake. "The authors of the Science paper were quite optimistic, but what they proposed had happened did not happen," Ellsworth said.

What the researchers don't know is why this series of cascading foreshocks triggered a massive earthquake when so many others don't. Ellsworth said that without better seismic instrumentation, important challenges like our ability to predict earthquakes will remain.

"We're not giving up on foreshocks just because we currently can't tell them apart from other earthquakes," Ellsworth said. "We want to understand if they have predictive value and if not, why not. To answer that question will require observations made close to the action, deep in the heart of the earthquake machine, not as we currently do from the surface where we're blind to changes deep underground."

<http://bit.ly/2JkKs9M>

New approach to immunotherapy leads to complete response in breast cancer patient

Novel approach to immunotherapy leads to the complete regression of breast cancer

A novel approach to immunotherapy developed by researchers at the National Cancer Institute (NCI) has led to the complete regression of breast cancer in a patient who was unresponsive to all other treatments.

This patient received the treatment in a clinical trial led by Steven A. Rosenberg, M.D., Ph.D., chief of the Surgery Branch at NCI's Center for Cancer Research (CCR), and the findings were [published June 4, 2018 in Nature Medicine](#). NCI is part of the National Institutes of Health.

"We've developed a high-throughput method to identify mutations present in a cancer that are recognized by the immune system," Dr. Rosenberg said. "This research is experimental right now. But because this new approach to immunotherapy is dependent on mutations, not on cancer type, it is in a sense a blueprint we can use for the treatment of many types of cancer."

The new immunotherapy approach is a modified form of adoptive cell transfer (ACT). ACT has been effective in treating melanoma, which has high levels of somatic, or acquired, mutations. However, it has been less effective with some common epithelial cancers, or cancers that start in the lining of organs, that have lower levels of mutations, such as stomach, esophageal, ovarian, and breast cancers. In an ongoing phase 2 clinical trial, the investigators are developing a form of ACT that uses tumor-infiltrating lymphocytes (TILs) that specifically target tumor cell mutations to see if they can shrink tumors in patients with these common epithelial cancers.

As with other forms of ACT, the selected TILs are grown to large numbers in the laboratory and are then infused back into the patient (who has in the meantime undergone treatment to deplete remaining lymphocytes) to create a stronger immune response against the tumor. A patient with metastatic breast cancer came to the trial after receiving multiple treatments, including several chemotherapy and hormonal treatments, that had not stopped her cancer from

progressing. To treat her, the researchers sequenced DNA and RNA from one of her tumors, as well as normal tissue to see which mutations were unique to her cancer, and identified 62 different mutations in her tumor cells.

The researchers then tested different TILs from the patient to find those that recognized one or more of these mutated proteins. TILs recognized four of the mutant proteins, and the TILs then were expanded and infused back into the patient. She was also given the checkpoint inhibitor pembrolizumab to prevent the possible inactivation of the infused T cells by factors in the tumor microenvironment.

After the treatment, all of this patient's cancer disappeared and has not returned more than 22 months later.

"This is an illustrative case report that highlights, once again, the power of immunotherapy," said Tom Misteli, Ph.D., director of CCR at NCI. "If confirmed in a larger study, it promises to further extend the reach of this T-cell therapy to a broader spectrum of cancers."

Investigators have seen similar results using mutation-targeted TIL treatment for patients in the same trial with other epithelial cancers, including liver cancer and colorectal cancer.

Dr. Rosenberg explained that results like this in patients with solid epithelial tumors are important because ACT has not been as successful with these kinds of cancers as with other types that have more mutations.

He said the "big picture" here is this kind of treatment is not cancer-type specific. "All cancers have mutations, and that's what we're attacking with this immunotherapy," he said. "It is ironic that the very mutations that cause the cancer may prove to be the best targets to treat the cancer."

The research team includes Nikolaos Zacharakis, Ph.D.; Steven A. Feldman, Ph.D.; and Stephanie L. Goff, M.D.

For more on the clinical trial, see: <https://clinicaltrials.gov/ct2/show/NCT01174121>

<https://bbc.in/2JoLFbU>

'Remarkable' therapy beats terminal breast cancer *The life of a woman with terminal breast cancer has been saved by a pioneering new therapy, say US researchers.*

By James Gallagher Health and science correspondent, BBC News

It involved pumping 90 billion cancer-killing immune cells into her body. Judy Perkins had been given three months to live, but two years later there is no sign of cancer in her body. The team at the US National Cancer Institute says the therapy is still experimental, but could transform the treatment of all cancer.

Judy - who lives in Florida - had spreading, advanced breast cancer that could not be treated with conventional therapy. She had tennis ball-sized tumours in her liver and secondary cancers throughout her body.

She told the BBC: "About a week after [the therapy] I started to feel something, I had a tumour in my chest that I could feel shrinking. "It took another week or two for it to completely go away." She remembers her first scan after the procedure when the medical staff "were all very excited and jumping around".

It was then she was told that she was likely to be cured. Now she's filling her life with backpacking and sea kayaking and has just taken five weeks circumnavigating Florida.

Living therapy

The technology is a "living drug" made from a patient's own cells at one of the world's leading centres of cancer research.

Dr Steven Rosenberg, chief of surgery at the National Cancer Institute, told the BBC: "We're talking about the most highly personalised treatment imaginable."

It remains experimental and still requires considerably more testing before it can be used more widely, but this is how it works: it starts by getting to know the enemy.

A patient's tumour is genetically analysed to identify the rare changes that might make the cancer visible to the immune system.

Out of the 62 genetic abnormalities in this patient, only four were potential lines of attack. Next researchers go hunting. A patient's immune system will already be attacking the tumour, it's just losing the fight between white blood cells and cancer. The scientists screen the patient's white blood cells and extract those capable of attacking the cancer. These are then grown in huge quantities in the laboratory. Around 90 billion were injected back into the 49-year-old patient, alongside drugs to take the brakes off the immune system.

Dr Rosenberg told me: "The very mutations that cause cancer turn out to be its Achilles heel."

'Paradigm shift'

These are the results from a single patient and much larger trials will be needed to confirm the findings.

The challenge so far in cancer immunotherapy is it tends to work spectacularly for some patients, but the majority do not benefit.

Dr Rosenberg added: "This is highly experimental and we're just learning how to do this, but potentially it is applicable to any cancer. "At lot of works needs to be done, but the potential exists for a paradigm shift in cancer therapy - a unique drug for every cancer patient - it is very different to any other kind of treatment."

The details were [published in journal Nature Medicine](#).

Commenting on the findings, Dr Simon Vincent, director of research at Breast Cancer Now, said the research was "world class".

He told the BBC: "We think this is a remarkable result.

<http://bit.ly/2LytQaX>

'Carbon bubble' coming that could wipe trillions from the global economy

Demand for fossil fuels will decline in the near future with major macroeconomic and geopolitical consequences

This transition will result in clear winners, importers such as China and the EU, and losers, exporters such as Russia, the USA or Canada, which could see their fossil-fuel industries nearly shut down. If these countries keep up their investment and production levels despite declining demand, the global wealth loss could be huge: 1-4 trillion dollars, a loss comparable to that which triggered the financial crisis in 2007. Even the USA could not pull out from the transition, as it would only hurt itself even more. Global climate policy is therefore no longer a 'prisoner's dilemma' game. These findings by researchers from Radboud University, the University of Cambridge (C-EENRG), Cambridge Econometrics, The Open University (UK) and the University of Macau are published in *Nature Climate Change*.

A dangerous 'carbon bubble'

Several major economies rely heavily on fossil-fuel production and exports. The price of fossil-fuel companies' shares is calculated under the assumption that all fossil-fuel reserves will be consumed. But to do so would be inconsistent with the tight carbon budget set in the 2015 Paris Agreement, which limits the increase in global average temperature to 'well below 2°C above pre-industrial levels'. So far, this prospect has not deterred continuing investment in fossil fuels because many believe that climate policies will not be adopted, or at least not in the near future.

However, and crucially, researchers now show that ongoing technological change, by itself and even without new climate policies, is already reducing global demand growth for fossil fuels, which could peak in the near future. New climate policies would only aggravate the impact. Continuing investment in fossil fuels is therefore creating a dangerous 'carbon bubble' that could burst, with massive economic and geopolitical consequences.

Winners and losers

The scientists modelled the decline of demand for fossil fuels using novel modelling techniques that track the diffusion of low-carbon

technologies on the basis of empirical data. Examples are technologies in power generation, cars and households that become more efficient and therefore diminish the use of fossil fuels. They then tracked what this means for national economies, as some economies lose an important industry (mostly due to loss of competitiveness), while other economies get rid of high current fossil-fuel expenditures and imports. "This means that by 2035, Gross Domestic Product (GDP) growth is affected negatively in producer countries (e.g. USA, Russia), while it is affected positively in importing countries (e.g. EU, China)", Dr Jean-Francois Mercure of Radboud University/C-EENRG explains.

'Free-riding' climate change mitigation: good or bad idea?

With the USA's withdrawal from the Paris Agreement, the scientists also modelled what would happen if the USA did indeed continue to invest in fossil-fuel assets instead of diversifying and divesting from them. The analysis shows their GDP would be reduced even further. Dr Mercure clarifies this point: "With a declining global fossil-fuel demand, fossil-fuel production in the USA is becoming uncompetitive, and may shut down. If the USA remains in the Paris Agreement, it will promote new low-carbon technologies and reduce its consumption of fossil fuels, creating jobs and mitigating its loss of income, despite losing its fossil-fuel industry. If it pulls out, it will nevertheless lose its fossil-fuel industry, but by not promoting low-carbon technologies, will miss out on job creation opportunities, while increasing its fossil-fuel imports by not reducing its domestic fossil-fuel consumption. The outcome is therefore worse if the USA pulls out."

A new financial crisis?

The study findings support the existence of a carbon bubble which, if not deflated early, could lead to a discounted global wealth loss of between 1 to 4 trillion dollars, a loss comparable to what triggered the 2007 financial crisis. "If countries keep investing in equipment to

search for, extract, process and transport fossil fuels, even though their demand declines, they will end up losing money on these investments on top of their losses due to limited exports", Mercure explains. "Countries should instead carefully deflate the carbon bubble through investment in a variety of industries and steady divestment. The way in which this is done will determine the impact of the ongoing low-carbon transition on the financial sector."

Hector Pollitt, study co-author from Cambridge Econometrics and C-EENRG, adds: "This new research clearly shows the mismatch between the reductions in fossil fuel consumption required to meet carbon targets and the behaviour of investors. Governments have an important role to play in emphasising commitments to meet the Paris Agreement to ensure that the significant detrimental economic and geopolitical consequences we have identified are avoided."

Divestment and creative destruction

The process of transition towards a low-carbon economy is now becoming inevitable, as policies supporting this change have been developed and gradually implemented for some time. "New efficiency standards imply that we do more with the same amounts of energy, as older, less efficient technologies are gradually phased out. The transition is therefore irreversible; however its pace can vary according to whether and how new climate policies are implemented."

The scientists conclude that further economic damage from a potential bubble burst could be avoided by decarbonising early. "Divestment is a prudential thing to do. We should be carefully looking at where we are investing our money. For instance, much like companies, pension funds and other institutions currently invest in fossil-fuel assets. Following recommendations from central banks, commercial banks are increasingly looking at the financial risks of stranded fossil-fuel assets, even though their possible impacts have not yet been fully determined. Until now, observers mostly paid

attention to the likely effectiveness of climate policies, but not to the ongoing and effectively irreversible technological transition. This level of 'creative destruction' appears inevitable now and must be carefully managed", Mercure concludes.

Publication

J.-F. Mercure, H. Pollitt, J.E. Vinuales, N.R. Edwards, P.B. Holden, U. Chewpreecha, P. Salas, I. Sogannaes, A. Lam, F. Knobloch. Macroeconomic impact of stranded fossil-fuel assets. Nature Climate Change. DOI: 10.1038/s41558-018-0182-1

<http://bit.ly/2sOnFba>

Cancer fighting effects of aspirin revealed in bowel tumor study

University of Edinburgh

Researchers have shed light on how taking aspirin can help to stave off bowel cancer.

Experts found that the painkiller blocks a key process linked to tumour formation. Regular use of aspirin is known to reduce a person's risk of developing colon cancer but the drug's tumour fighting properties have not been well understood.

Researchers at the University of Edinburgh focused on a structure found inside cells called the nucleolus. Activation of the nucleolus is known to drive tumour formation and dysfunction has also been linked to Alzheimer's and Parkinson's.

The team at the University's Cancer Research UK Edinburgh Centre tested the effects of aspirin on cells grown in the lab and on tumour biopsies removed from colon cancer patients. They found that aspirin blocks a key molecule called TIF-IA, which is essential for the nucleolus to function.

Not all colon cancer patients respond to aspirin but the researchers say their findings could help pinpoint those most likely to benefit.

Aspirin has side effects that include internal bleeding and it can cause certain types of stroke. Long term use is not recommended. The researchers say the study paves the way for the development of new, safer therapies that mimic aspirin's effects.

The research, published in *Nucleic Acids Research*, was funded by the Medical Research Council and the Biotechnology and Biological Sciences Research Council. Worldwide Cancer Research, Bowel and Cancer Research and The Rosetrees Trust also supported the work. Dr Lesley Stark, of the Cancer Research UK Edinburgh Centre at the University of Edinburgh, said: "We are really excited by these findings as they suggest a mechanism by which aspirin may act to prevent multiple diseases.

A better understanding of how aspirin blocks TIF-IA and nucleolar activity provides great promise for the development of new treatments and targeted therapy."

<http://bit.ly/2sV1ccG>

On the origins of agriculture, researchers uncover new clues

Why did agriculture begin where it did, when it did?

The invention of agriculture changed humans and the environment forever, and over several thousand years, the practice originated independently in at least a dozen different places. But why did agriculture begin in those places, at those particular times in human history?

Using a new methodological approach, researchers at Colorado State University and Washington University in St. Louis have uncovered evidence that underscores one long-debated theory: that agriculture arose out of moments of surplus, when environmental conditions were improving, and populations lived in greater densities.

The first-of-its-kind study, "Hindcasting global [population](#) densities reveals forces enabling the origin of agriculture," published in *Nature Human Behaviour*, lends support to existing ideas about the origins of human agriculture.

In contrast, they found little support for two other, longstanding theories: One, that during desperate times, when environmental conditions worsened and populations lived at lower densities,

agriculture was born out of necessity, as people needed a new way of getting food. And two, that no general pattern exists, but instead the story of agriculture's origins is tied to unique social and environmental conditions in each place.

Senior author Michael Gavin, an associate professor in CSU's Department of Human Dimensions of Natural Resources, said the findings and the general methodological approach may help explain other watershed events in [human history](#).

"There have been several key threshold events in our history that changed the entire course of our species," Gavin said. "Agriculture is a link to so many other components for what the world is like today for billions of people. This begins to help us explain a key moment in human history."

Predicting into the past

Studying the depths of human history is challenging, as little data are available when looking back tens of thousands of years. Scientists typically rely on archeological evidence, but getting a broad picture is difficult, since archeological digs cover relatively small areas.

To overcome these limitations, the researchers modeled correlations between the environment, cultural traits and population densities of relatively recent foraging societies, which used hunting, fishing and gathering to obtain food.

Among the factors they considered as possible predictors of population density: environmental productivity; environmental stability; the average distance travelled when people in a community moved to a new location; whether people owned land or other resources; and distance to the nearest coast.

This model, the team found, did a remarkably good job at predicting recent population densities, which led the researchers to pair the model with data on past climate. In doing so, they could hindcast, or predict into the past, the potential population density of the entire globe dating back thousands of years.

Population maps

This study was the first to produce maps of potential population densities dating back as far as 21,000 years. The researchers used these maps to examine conditions that existed in each of the 12 centers of origin, at the point in time agricultural practices began.

Patrick Kavanagh, a CSU postdoctoral scientist and one of the study's lead authors, said the different centers of origin for agriculture all showed improving environmental conditions and increasing population densities. "All regions that developed agriculture showed the same pattern," he said.

Researchers believe that improving environmental conditions may have allowed people the luxury of tinkering with new ideas, and that having more people living in one place would allow ideas to be shared and honed, with sparks of innovation following.

While the researchers found commonalities in the surplus aspect of what was occurring in different locations, that doesn't mean the exact same conditions existed in each center of origin. Socially, the places and people studied were probably very different. In addition, the timing of when agriculture began in these major centers varied over thousands of years, and the species of plants they were working with was different.

But, amazingly, although the centers of origin varied in time by thousands of years and ranged from the New Guinea Highlands to Central America and the Middle East, they all had one thing in common: improving [environmental conditions](#), and the potential for higher [population densities](#).

"In all of these major origin centers of [agriculture](#), there were some critical environmental changes that needed to occur," Kavanagh added. "Environmental [conditions](#) needed to improve—which we saw in all 12 centers of origin—despite variation in the timing and the diverse geographic locations in which they occurred."

The research team is now exploring other applications for the maps they produced.

"It is amazing to examine these maps of the potential population [density](#) of the world dating back tens of thousands of years," said Gavin. "We could potentially create them going back to the dawn of our species. This provides a new tool to explore many unanswered questions about human history."

More information: Patrick H. Kavanagh et al, *Hindcasting global population densities reveals forces enabling the origin of agriculture*, *Nature Human Behaviour* (2018). [DOI: 10.1038/s41562-018-0358-8](#)

<http://bit.ly/2HymOAx>

Research shows dogs prefer to eat fat, and cats surprisingly tend toward carbs

Dogs gravitate toward high-fat food, but cats pounce on carbohydrates with even greater enthusiasm, according to research into the dietary habits of America's two most popular pets.

CORVALLIS, Ore. - The study sheds new light on optimal nutrition for the animals and refutes a common notion that cats want and need a protein-heavy regimen. Findings were [published this month in the *Journal of Experimental Biology*](#).

"The numbers were much different than what traditional thinking would have expected," said the study's corresponding author, Jean Hall, a professor in the Carlson College of Veterinary Medicine at Oregon State University.

"Some experts have thought cats need diets that are 40 or 50 percent protein. Our findings are quite different than the numbers used in marketing and are going to really challenge the pet food industry."

Dietary proteins contribute to a number of important physiological functions such as blood clotting, production of hormones and enzymes, vision and cell repair.

Protein also has the most power to make the eater feel satiated; carbohydrates are No. 2 in that regard, followed by fat.

Hall's research involved monitoring 17 healthy adult dogs and 27 cats over 28 days and used four types of food that were designed to taste equally good; with flavor out of the equation, the animals could make macronutrient choices based only on what their bodies were telling them they needed.

"Previous studies have shown that if you don't balance palatability between foods, cats do in fact prefer to eat very high levels of protein and dogs want to eat a lot of fat," Hall said.

"When you balance palatability, both dogs and cats prefer significantly different macronutrient content than what they would choose based on taste."

The animals studied by Hall and her collaborators could choose among high-fat, high-carbohydrate, high-protein and balanced foods. Each day, dogs had an hour to eat all they wanted up to a predetermined caloric intake - that is, they could get all the calories they needed for metabolic requirements and to maintain weight, but no more.

The cats in the study were likewise not allowed to overeat, though even if given unlimited access to food that tastes how they like it, cats tend to eat in a weight-maintenance way by adjusting their intake based on the food's energy density. In the study, cats had 24-hour food access up to the point of hitting their caloric threshold.

Food container placement for both dogs and cats was changed daily to guard against "bowl position bias" affecting the results, which showed the cats on average chose to get 43 percent of their calories from carbs and 30 percent from protein.

Dogs on the other hand went for 41 percent fat and 36 percent carbs. Not a single dog or cat chose to get the highest percentage of its calories from protein.

Within the aggregate cat findings were trends correlating with age and lean body mass - how much muscle an animal has.

Younger cats with less lean body mass tended more strongly toward protein consumption than younger cats with more lean body mass; younger cats in general wanted protein more than older cats.

On the dog side of the study, high-protein foods were the least popular among younger animals with less fat body mass; dogs with greater fat body mass had the strongest preference for getting calories from protein.

"Because the choice of macronutrients was influenced in both dogs and cats by age and either lean body mass or fat body mass, that suggests a physiological basis for what they chose to eat," Hall said. The research also involved determining the diets' effect on selected metabolites of each macronutrient class - what they break down into in the body.

Hall found the older cats' blood had much lower levels of DHA, a long-chain omega-3 fatty acid that's important for the brain, heart and eyes, than the younger cats.

"None of the foods had ingredient sources of DHA or EPA, another long-chain omega-3, but cats are able to synthesize DHA by elongating and desaturating fatty acids," Hall said. "The older cats, though, are a lot less efficient at that."

More potential bad news for the older cats: Their concentrations of sulfated microbial catabolic products - protein-breakdown leftovers that in humans are connected to cardiovascular and kidney disease - were significantly higher.

"Just like with older people, older cats may have a different gut microbiome than younger cats, which would mean different microbial metabolic activities," Hall said. Basically, if a younger cat gets more protein than it can use, it can safely deal with and dispose of the excess a lot better than an older cat can.

The Pet Nutrition Center of Hill's Pet Nutrition, Inc., supported this research.

<http://bit.ly/2HvUU8y>

Coffee helps teams work together, study suggests

Caffeine makes people more positive by making them more alert

Columbus, Ohio - Good teamwork begins with a cup of coffee for everyone, a new study suggests.

Researchers found that people gave more positive reviews for their group's performance on a task - and their own contribution - if they drank caffeinated coffee beforehand.

A second study showed that people talked more in a group setting under the influence of caffeinated coffee - but they also were more on-topic than those who drank decaf.

Coffee seems to work its magic in teams by making people more alert, said Amit Singh, co-author of the study and a doctoral student in marketing at The Ohio State University's Fisher College of Business.

"We found that increased alertness was what led to the positive results for team performance," Singh said. "Not surprisingly, people who drank caffeinated coffee tended to be more alert."

Singh conducted the study with Vasu Unnava and H. Rao Unnava, both formerly at Ohio State and now with the Graduate School of Management at the University of California, Davis. The study appears online in the *Journal of Psychopharmacology*.

While many studies have looked at how caffeine affects individual performance, this is the first to examine the impact it has on teams, Singh said.

The first study involved 72 undergraduate students who said they were coffee drinkers. They were instructed not to drink coffee before the experiment.

Half of them first participated in what they were told was a coffee-tasting task. They were split into groups of five. After drinking a cup of coffee and rating its flavor, they were given 30 minutes of filler tasks to give the caffeine a chance to kick in. The other half of the participants did the coffee tasting at the end of the experiment.

Each group then read about and were asked to discuss a controversial topic - the Occupy movement, a liberal movement that highlighted social and economic inequality. After a 15-minute discussion, group members evaluated themselves and the other group members.

Results showed that those who drank the coffee before the discussion rated themselves and their fellow team members more positively than did those who drank coffee after the discussion, Singh said.

The second study was similar, except that 61 students all drank coffee at the beginning of the study. However, half drank decaf and the others drank caffeinated brew.

Those who drank caffeinated coffee rated themselves and their fellow group members more positively than those who drank decaf. It had to do with alertness. All participants rated how alert they felt at the end of the study, and those who drank the caffeinated coffee rated themselves as more alert than the others.

A key finding was that people who rated themselves as more alert - whether they drank caffeinated coffee or not - also tended to give higher marks to themselves and their fellow group members.

This suggests that any intervention that increases alertness (such as exercise) may also produce similar results, which the authors propose in the paper as a future research topic. "We suspect that when people are more alert they see themselves and the other group members contributing more, and that gives them a more positive attitude," Singh said.

But the caffeine does more than just increase good feelings. The researchers did an analysis of the group discussion in the second study, rating how much each group member talked and stayed on topic. Results showed that people tended to talk more after drinking caffeine, but they also tended to stay more on topic.

"They're talking about more relevant things after drinking caffeinated coffee," he said.

One might think that if people are talking more about a controversial topic like the Occupy movement, that may cause friction in the group. But that's not what the study suggests. People who drank caffeinated coffee were more likely than those who drank decaf to say they would be willing to work with their group again.

"Even though they are talking more, agreeing and disagreeing, they still want to work with them again," Singh said. "Coffee didn't seem to make group discussions too uncomfortable and disagreeable."

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Dogs can be a potential risk for future influenza pandemic

Dogs are a potential reservoir for a future influenza pandemic, according to a study published in the journal mBio.

Washington - The study demonstrated that influenza virus can jump from pigs into canines and that influenza is becoming increasingly diverse in canines.

"The majority of pandemics have been associated with pigs as an intermediate host between avian viruses and human hosts. In this study, we identified influenza viruses jumping from pigs into dogs," said study investigator Adolfo García-Sastre, PhD, director of the Global Health and Emerging Pathogens Institute and principal investigator, Center for Research on Influenza Pathogenesis (CRIP), Icahn School of Medicine at Mt. Sinai, New York City.

Influenza can jump among animal reservoirs where many different strains are located; these reservoirs serve as mixing bowls for the genetic diversity of strains. Pandemic influenza occurs when viruses jump from animal reservoirs to humans; with no prior exposure to the virus, most people do not have immunity to these viruses. The main animal hosts for influenza are wild birds, poultry and other domestic birds in a species pack; swine; and horses. Some of the viral genes from the 2009 pandemic H1N1 virus originated in birds, from an avian virus that jumped to pigs, exchanged some of its genes with

previously circulating swine viruses and then jumped from pigs into humans. Birds and swine are major reservoirs of viral genetic diversity, whereas equines and canines have historically been restricted to one or two stable influenza A viruses lineages with no or very limited transmission to humans.

Fifteen years ago, researchers documented an influenza virus in a horse jumping into a dog, and this created the first circulating canine influenza viruses. Five years ago, researchers identified an avian-origin H3N2 canine influenza virus circulating in farmed dogs in Guangdong, China.

"In our study, what we have found is another set of viruses that come from swine that are originally avian in origin, and now they are jumping into dogs and have been reassorted with other viruses in dogs. We now have H1N1, H3N2, and H3N8 in dogs. They are starting to interact with each other. This is very reminiscent of what happened in swine ten years before the H1N1 pandemic."

Specifically, in the new study, the researchers sequenced the complete genomes of 16 influenza viruses obtained from canines in Southern China (Guangxi autonomous region) during 2013-2015. Other key study collaborators included Martha Nelson, PhD, a specialist in phylogenetic analysis and transmission reconstruction at CRIP, and Ying Chen, PhD, an influenza surveillance specialist who brought the samples from China. The researchers found that the genomes contained segments from three lineages that circulate in swine in China: North American triple reassortant H3N2, Eurasian avian-like H1N1, and pandemic H1N1. In addition, the swine-origin H1N1 viruses were transmitted onward in canines and reassorted with the CIV-H3N2 viruses that circulate endemically in Asian dogs, producing three novel reassortant CIV genotypes (H1N1r, /H1N2r, and H3N2r).

The viruses in the study were collected primarily from pet dogs presenting with respiratory symptoms at veterinary clinics. Dogs in

certain regions of China, including Guangxi, are also raised for meat and street dogs roam freely, creating a more complex ecosystem for canine influenza virus transmission. "The new virus we have identified in our study is H1N1, but it comes from swine and is of avian origin, so it is different antigenically from the new H1N1s that were seen in the pandemic and a different origin as the previous H1N1 seen in humans," said Dr. García-Sastre.

Future studies will focus on characterizing the virus further and assessing, using human sera, whether humans have existing immunity against canine H1N1 or not. "If there is a lot of immunity against these viruses, they will represent less of a risk, but we now have one more host in which influenza virus is starting to have a diverse genotypic and phenotypic characteristics, creating diversity in a host which is in very close contact to humans," said Dr. García-Sastre. "The diversity in dogs has increased so much now that the type of combinations of viruses that can be created in dogs represent potential risk for a virus to jump to a dog into a human."

The researchers say it is time to think about ways to restrict the circulation of the influenza virus in dogs. The United States is free of avian influenza because every time avian influenza has been detected in poultry in this country, the chickens or turkeys are culled and eliminated from circulation," said Dr. García-Sastre. "There are attempts to restrict influenza virus in pigs through vaccination and one could consider vaccination for dogs."

CRIP is one of five Centers of Excellence for Influenza Research and Surveillance funded by the National Institute of Allergy and Infectious Diseases.

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**Companies to Help People Sell or Rent Out Their Health Data
Luna DNA, Nebula Genomics, and other "bio-brokers" will allow
customers to make money by granting access to their genetic and
personal information for research purposes.**

By Catherine Offord | June 5, 2018

A growing number of companies are developing business models that center on consumers selling their genetic or health data, according to a report published yesterday (June 3) in *The San Diego Union-Tribune*. California-based startups [Luna DNA](#) and [Nebula Genomics](#) have built platforms to offer pay-to-access information to researchers from universities, medical institutes, and pharmaceutical companies—and turn a profit for the customer.

“There is currently little incentive for consumers to contribute their DNA and health information to a third party database,” Luna DNA explains on its [website](#). The company’s solution, it continues, is a “community owned database that rewards individuals shares in the database for contributing their DNA and other medical information. . . . The proceeds flow back to the community like dividends as researchers pay to access the data for discovery.”

Both companies, along with similar efforts by Hong Kong-based [Longenesis](#) and Russian project [Zenome](#), aim to meet the rising demand for biological data for everything from basic medical research to the development of drugs and diagnostics. Most incorporate the highly secure technology blockchain and will pay their customers in a cryptocurrency such as bitcoin.

Nebula Genomics, which was founded by a group of Harvard University researchers including George Church and recently partnered with Longenesis, plans for customers to undergo whole-genome sequencing, and then sell or rent those data to pharmaceutical or biotech companies at the same time as they learn more about their own DNA.

“The pitch to the average person is that you’re not just monetizing your genetic data,” Nebula cofounder Kamal Obbad told *MIT Technology Review* in February. “We’re also going to provide you with insights, similar to what 23andMe and Ancestry.com do.”

Luna DNA, meanwhile, is planning to create a database of information that people have already received from direct-to-

consumer sequencing companies such as 23andMe and Ancestry.com. Customers of Luna DNA would receive compensation for allowing access to that information, explains the company’s president, Dawn Barry.

“Individuals will be rewarded when proceeds are generated through the sale of access to the data,” she tells the *Union-Tribune*. “Think of it like a co-op where the value comes from the data set as a whole and dividends are paid out to the individuals that contribute their genomic and health information. The more data you share, the more shares in the database you own, the greater your percentage of the proceeds.”

For now, it remains to be seen how many customers will want to take part. Blockchain technology offers better data privacy than what consumers currently have access to now, Polina Mamoshina, a researcher at biotech Insilico Medicine, which helped develop Longenesis, told *Medium* in February. “There is a hidden data market right now, and a lot of companies are selling our data, which is super valuable, without us knowing about it,” she says. Nevertheless, she acknowledges, “it’s hard to say whether people are going to do this.”

<http://bit.ly/2HzzvLr>

80 years since the first calculations showed that the Earth was warming due to rising greenhouse gas emissions

Research into greenhouse gases and their influence on our climate is not a new craze. It has roots that extend back to the discoveries of quantum mechanics and the structure of the atom.

by Marit-Solveig Seidenkrantz, Aarhus University, [ScienceNordic](#)

Some people argue that concern for global warming is a modern phenomenon. And that scientists and environmental activists invented these worries to raise awareness of rising greenhouse gases from burning fossil fuels.

Why are we suddenly so worried about [carbon dioxide](#) (CO₂) when just a few decades ago there was talk of a new ice age?

In the same breath, they might also question how changes in the amount of CO₂ in the atmosphere can really change the Earth's [climate](#).

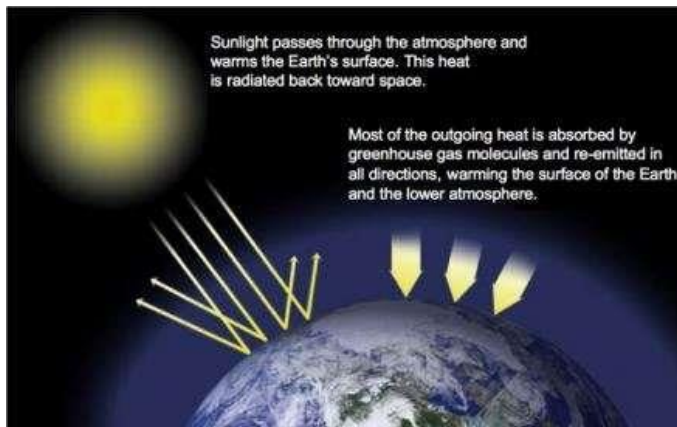
The atmosphere after all contains relatively little CO₂ compared with other gases. For example, there's much more water vapour, which is also an important greenhouse gas. So, how can a tiny amount of CO₂ be so important?

Let's take a look at these questions.

The greenhouse effect was discovered more than 100 years ago

In 1896, the world renowned Swedish scientist and Nobel Prize Winner Svante Arrhenius (1859-1927), described how CO₂ influences the climate. He suggested that increasing emissions of CO₂ from burning [fossil fuels](#) could lead to a global warming—the so-called [greenhouse effect](#).

In the subsequent decades, research into [greenhouse gasses](#) continued. But it was not until 1938 that Guy Callendar first showed how the Earth's temperature was already increasing.



Greenhouse gases trap energy from the sun in the lower atmosphere.

Without these gases, the Earth would be a chilly minus 18 degrees Centigrade. In contrast, the atmosphere on Mars is almost entirely made of carbon dioxide, but it has a very thin atmosphere and little to no methane or water vapour, producing a weaker greenhouse effect. NASA

Callendar was born in 1898, just two years after Arrhenius first published his work on CO₂. He was an engineer by trade but he was

also fascinated by the atmosphere, and he devoted his spare time to studying it. He measured the concentration of gases, the atmosphere's structure, how atmospheric currents moved around the planet, and the influence of the sun's rays at various latitudes.

And it was this work that led to the world's first climate model.

His model was very primitive in comparison with the well established models used to predict the weather and climate by meteorologists and climate scientists today. But it formed the basis upon which all modern studies of climate science have since developed.

His work culminated in this 1938 study, which showed that humans had already emitted enough CO₂ into the atmosphere to increase the average temperature on Earth and that the Earth was responding: Over the previous 50 years, the average temperature had indeed increased as per Arrhenius's proposed greenhouse effect.

Callendar's hypothesis becomes accepted theory

Callendar's hypothesis was not taken particularly seriously by some other scientists at first: He wasn't a meteorologist and at this time there simply wasn't enough data to test this hypothesis. But he continued, undeterred.

He collected masses of new data, and by the time he died in 1964 his work had gained widespread scientific acceptance.

After a congressional hearing in the American Senate in 1988, the role of [greenhouse gases](#), and in particular that of CO₂, in driving global temperature was broadly acknowledged, and the number of opponents to the theory was shrinking.

Why is CO₂ such an important greenhouse gas?

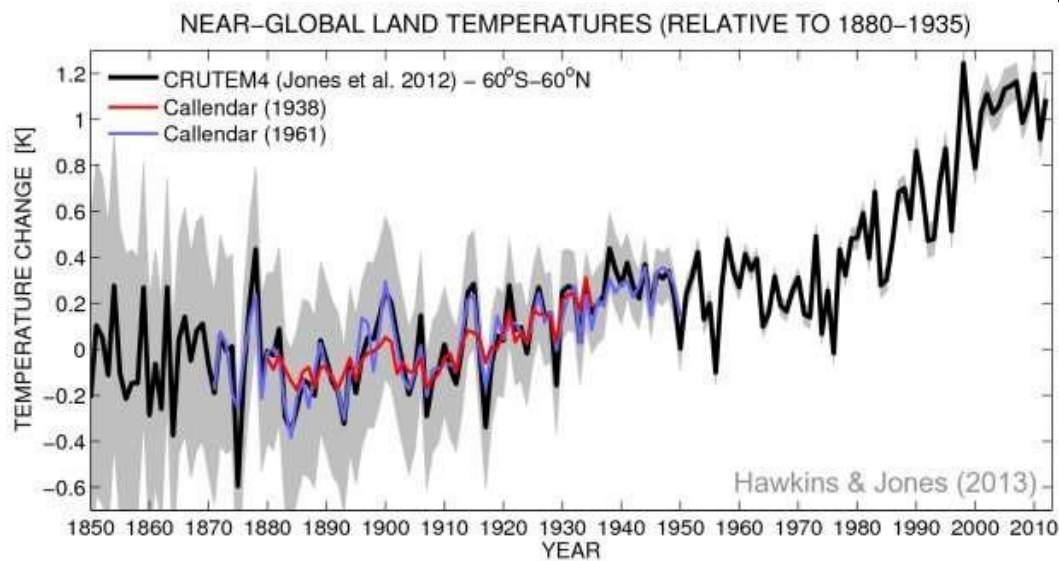
In between ice ages, the Earth's atmosphere typically contains around 0.03 per cent CO₂. Today, it's around 0.04 per cent, or 410 parts per million as it's often referred to. But this is still an infinitesimally small number.

So how can CO₂ have such a big impact on the climate?

The light emitted by the Sun contains a broad spectrum of light: Ultraviolet, infrared, microwaves, radio waves, visible light, and so on. About half of the light that reaches Earth is either reflected by clouds or absorbed by the atmosphere.

The rest reaches the Earth's surface and is absorbed by the land, sea, and plants, warming the surface. When the Earth warms, it emits infrared light (heat), which is reflected back to Earth, trapped in the atmosphere. This is the greenhouse effect in a nutshell.

The greenhouse effect occurs because the Earth's atmosphere retains some of the heat that would otherwise be lost into space. Without greenhouse gases like CO₂, the atmosphere couldn't hold onto this, and the Earth would quickly turn into a frozen sphere.



Climate scientists have since compared Callendar's original temperature data from his 1938 study (red) with modern climate data (black line). Callendar published a new dataset in 1961, shown in blue. Grey shading shows the 5-95% uncertainty ranges for the modern data. Climate Lab Book / Hawkins & Jones, 2013

Carbon dioxide: A greenhouse gas in a league of its own

The current composition of greenhouse gases (CO₂, but also methane, water vapour, and some others) keeps the Earth's [average temperature](#) at a comfortable 15 degrees centigrade. Without them it would be a very chilly ca. -18 degrees.

The greenhouse effect acts as a thermostat, but today it is on a knife edge, keeping the world warm but not too warm.

Over 95 per cent of the Earth's atmosphere is made up of nitrogen and oxygen, neither of which can absorb infrared light and are very poor greenhouse gases. Another important component of the atmosphere is water vapour, which is a very effective [greenhouse gas](#) and absorbs most of the infrared light reflected off the Earth's surface. Water vapour plays a huge role in keeping the Earth warm enough for us to live here. But luckily, it doesn't soak up all of the infrared radiation and some of it slips through and out into space.

If this wasn't the case, and it absorbed all of the infrared radiation, the Earth would quickly become too warm to support life. But Callendar discovered that CO₂ closes these "holes" and captures a large proportion of the [infrared radiation](#) that [water vapour](#) lets escape.

So, the more CO₂ there is in the atmosphere, the more of these gaps are closed. And even though CO₂ forms such a small part of the entire atmosphere, it has an incredibly significant role on how it regulates heat and, therefore, the climate. In addition, CO₂ lasts a long time in the [atmosphere](#) compared to many other greenhouse gases, making it even more potent.

Is global warming a new craze?

Research into [greenhouse](#) gases and their influence on our climate is not a new craze. It has roots that extend back to the discoveries of quantum mechanics and the structure of the atom.

Just like all the other branches of science, hypotheses have gradually developed and been refined as new data and knowledge becomes

available. And a more detailed understanding of how the climate works and what impacts it, has emerged.

The most [recent research](#) indicates that man-made global warming was already occurring in the first half of the 19th century, which is much earlier than Callendar had thought.

This doesn't mean that Callendar was wrong, just that he didn't have access to so many types of data that we do today.

More information: G. S. Callendar. *The artificial production of carbon dioxide and its influence on temperature*, *Quarterly Journal of the Royal Meteorological Society* (2010).

[DOI: 10.1002/qj.49706427503](https://doi.org/10.1002/qj.49706427503)

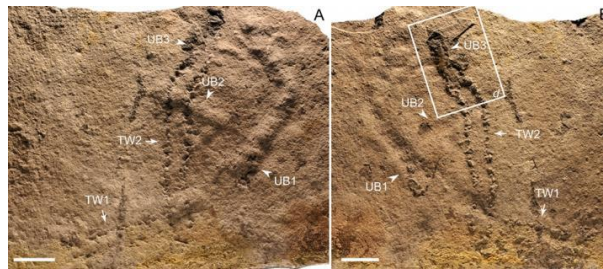
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When did animals leave their first footprint on Earth?

On July 20, 1969, Neil Armstrong put the first footprint on the moon. But when did animals leave the first footprint on Earth?

Recently, an international research team reported discovering fossil footprints for animal appendages in the Ediacaran Period (about 635-541 million years ago)

in China. This is considered the earliest animal fossil footprint record. The research was published in *Science Advances* on June 6, 2018.



Trackways and burrows excavated in situ from the Ediacaran Dengying Formation. Credit: NIGP

Bilaterian animals such as arthropods and annelids have paired appendages and are among the most diverse animals today and in the geological past. They are often assumed to have appeared and radiated suddenly during the "Cambrian Explosion" about 541-510 million years ago, although it has long been suspected that their evolutionary ancestry was rooted in the Ediacaran Period. Until the current discovery, however, no fossil record of animal appendages had been found in the Ediacaran Period.

Researchers from the Nanjing Institute of Geology and Palaeontology of the Chinese Academy of Sciences and Virginia Tech in the United States studied trackways and burrows discovered in the Ediacaran Shibantan Member of the Dengying Formation (551-541 million years ago) in the Yangtze Gorges area of South China. The trackways are somewhat irregular, consisting of two rows of imprints that are arranged in series or repeated groups.

The characteristics of the trackways indicate that they were produced by bilaterian animals with paired appendages that raised the animal body above the water-sediment interface. The trackways appear to be connected to burrows, suggesting that the animals may have periodically dug into sediments and microbial mats, perhaps to mine oxygen and food.

These trace fossils represent some of the earliest known evidence for animal appendages and extend the earliest trace fossil record of animals with appendages from the early Cambrian to the late Ediacaran Period. The body fossils of the animals that made these traces, however, have not yet been found. Maybe they were never preserved.

The study was supported by the Chinese Academy of Sciences, the National Natural Science Foundation of China, the U.S. National Science Foundation, and the National Geographic Society.

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Is a stress shot on the horizon?

Immunization with beneficial bacteria makes brain more stress resilient, study shows

Immunization with beneficial bacteria can have long-lasting anti-inflammatory effects on the brain, making it more resilient to the physical and behavioral effects of stress, according to new research by University of Colorado Boulder scientists.

The findings, if replicated in clinical trials could ultimately lead to new probiotic-based immunizations to protect against posttraumatic

stress disorder (PTSD) and anxiety or new treatments for depression, the authors say.

"We found that in rodents this particular bacterium, *Mycobacterium vaccae*, actually shifts the environment in the brain toward an anti-inflammatory state," said lead author Matthew Frank, a senior research associate in the Department of Psychology and Neuroscience. "If you could do that in people, it could have broad implications for a number of neuroinflammatory diseases."

Anxiety, PTSD and other stress-related mental disorders impact as many as one in four people in their lifetime. Mounting research suggests that stress-induced brain inflammation can boost risk of such disorders, in part by impacting mood-influencing neurotransmitters like norepinephrine or dopamine.

"There is a robust literature that shows if you induce an inflammatory immune response in people, they quickly show signs of depression and anxiety," said Frank. "Just think about how you feel when you get the flu."

Research also suggests that trauma, illness or surgery can sensitize certain regions of the brain, setting up a hair-trigger inflammatory response to subsequent stressors which can lead to mood disorders and cognitive decline. "We found that *Mycobacterium vaccae* blocked those sensitizing effects of stress too, creating a lasting stress-resilient phenotype in the brain," Frank said.

A previous CU Boulder study, published in the *Proceedings of the National Academy of Sciences (PNAS)*, found that mice injected with a heat-killed preparation of *M. vaccae* and then placed with a larger aggressive male for 19 days exhibited less anxiety-like behavior and were less likely to suffer colitis or inflammation in their peripheral tissues.

For the new study, [published this week in the journal *Brain, Behavior and Immunity*](#), Frank and senior author Christopher Lowry, an

associate professor in integrative physiology, set out to find out what exactly *M. vaccae* does in the brain.

Male rats injected with the bacterium three times, one week apart, had significantly higher levels of the anti-inflammatory protein interleukin-4 in the hippocampus -- a brain region responsible for modulating cognitive function, anxiety and fear -- eight days after the final injection.

After exposure to a stressor, the immunized animals also showed lower levels of a stress-induced protein, or alarmin, called HMGB1, believed to play a role in sensitizing the brain to inflammation, and higher expression of CD200R1, a receptor key for keeping glial cells (the brain's immune cells) in an anti-inflammatory state.

The immunized rats, as in the first study, exhibited less anxious behavior after stress.

"If you look at the field of probiotics generally, they have been shown to have strong effects in the domains of cognitive function, anxiety and fear," said Lowry. "This paper helps make sense of that by suggesting that these beneficial microbes, or signals derived from these microbes, somehow make their way to the hippocampus, inducing an anti-inflammatory state."

Lowry envisions a day when *M. vaccae* (which was first isolated from the mud on the shores of Lake Kyoga in Uganda) could be administered to people at high risk of PTSD - such as soldiers preparing to be deployed or emergency room workers - to buffer the effects of stress on the brain and body. It could also possibly be used to prevent sepsis-induced cognitive impairment.

Meanwhile, Lowry is working with researchers at University of Colorado Denver on a study exploring whether veterans with PTSD can benefit from an oral probiotic consisting of a different bacterial strain, *Lactobacillus reuteri*. "More research is necessary, but it's possible that other strains of beneficial bacteria or probiotics may have a similar effect on the brain," he said.

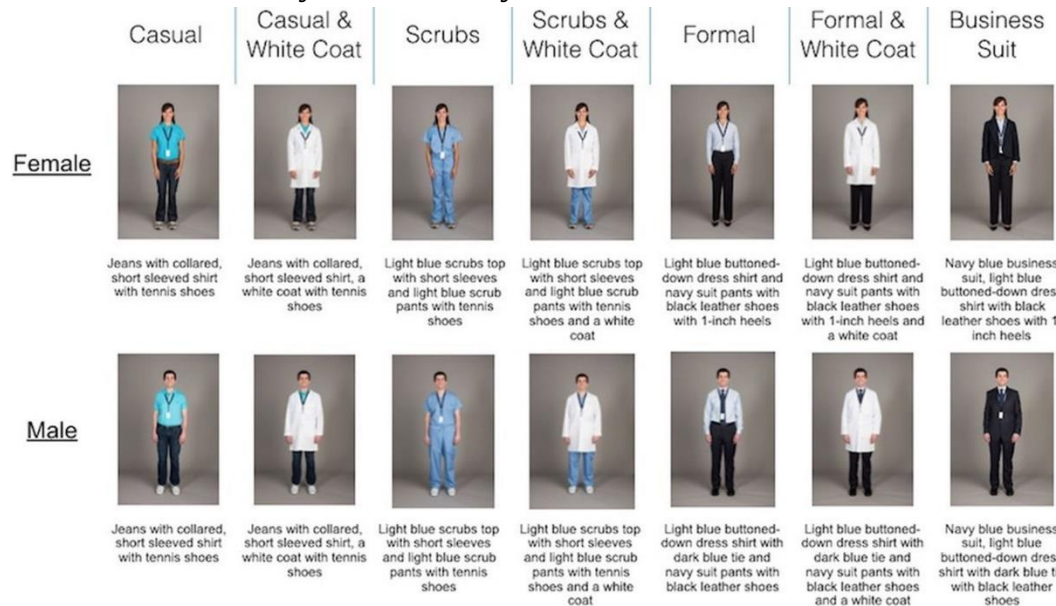
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What doctors wear really does matter, study finds

Survey of more than 4,000 patients isn't just about fashion -- patient satisfaction may be affected

Physicians may want to dig a little deeper into their closets, or grab their white coats on the way out of the operating room, if they want patients to view them favorably, according to the largest-ever study of patient preferences for doctors' attire. In fact, what medical doctors wear may matter more than most doctors - or even patients - might think, say the researchers behind the new paper in [BMJ Open](#).

Based on their findings, they call for more hospitals, health systems and practice groups to look at their dress standards for physicians, or create them if they don't already have one.



The study asked 4,000 patients to choose from among seven options for both male and female physicians, ranging from casual to business suits. University of Michigan/BMJ Open

Just over half of the 4,062 patients surveyed in the clinics and hospitals of ten major medical centers said that what physicians wear

is important to them - and more than one-third said that what a doctor wears influences their satisfaction with their care.

"Professional dress on Wall Street, law and nearly every other industry is relatively clear - and it typically mirrors what applicants would wear to their job interview," says Christopher Petrilli, M.D., lead author of the study and an assistant professor of hospital medicine at the University of Michigan Medical School, who worked in the finance industry before entering medicine. "In medicine, the dress code is quite heterogeneous, but as physicians we should make sure that our attire reflects a certain level of professionalism that is also mindful of patients' preferences."

Patients' views on physician attire

The study also asked patients to look at pictures of male and female physicians in seven different forms of attire, and to think of them in both inpatient and outpatient clinical settings. For each photo, they rated the providers on how knowledgeable, trustworthy, caring and approachable the physician appeared, and how comfortable the attire made the patient feel.

The options were:

- **Casual:** Short-sleeved collared shirt and jeans with tennis shoes, with or without white coat
- **Scrubs:** Blue short-sleeved scrub top and pants, with or without white coat
- **Formal:** Light blue long-sleeved dress shirt and navy blue suit pants, with or without white coat, with black leather shoes with one-inch heels for women and black leather shoes for men, and a dark blue tie for men
- **Business suit:** Navy blue jacket and pants with the same dress shirt, tie and shoes as in the "formal" option, no white coat

Formal attire with a white coat got the highest score on the composite of five measures, and was especially popular with people over age 65. It was followed by scrubs with a white coat, and formal attire without a white coat.

Variation by specialty, setting and region

When asked directly what they thought their own doctors should wear, 44 percent said the formal attire with white coat, and 26 percent said scrubs with a white coat. When asked what they would prefer surgeons and emergency physicians wear, scrubs alone got 34 percent of the vote, followed by scrubs with a white coat with 23 percent.

The results were largely the same for physicians of either gender except for male surgeons. Patients tended to prefer that they go with formal wear, without a white coat.

The setting of care mattered, too. Sixty-two percent agreed or strongly agreed that when seeing patients in the hospital, doctors should wear a white coat, and 55 percent said the same for doctors seeing patients in an office setting. The percentage preferring a white coat fell to 44 percent for emergency physicians.

Though the surveys were conducted during business hours on weekdays, the researchers asked patients what they thought doctors should wear when seeing patients on weekends. In this case, 44 percent said the short-sleeved outfit with jeans was appropriate, though 56 percent were neutral or disapproved of such a look even on weekends.

Interestingly, patients in the northeast and midwest parts of the country were less insistent on white coats and formal attire - 38 percent and 40 percent preferred it in these regions, compared with 50 percent in the west and 51 percent in the south. Northeasterners were more than twice as likely as southerners to prefer scrubs alone for surgeons.

Importance for patient satisfaction

Tying physician attire to patient satisfaction isn't just an exercise - hospitals are paid by the Centers for Medicare and Medicaid based in part on scores on patient satisfaction surveys.

Before launching the study that led to the new paper, the researchers reviewed the medical literature for other studies on this topic, and [published their findings three years ago](#). They also contacted top hospitals across the country and found that only a few at the time had formal guidance for physicians on their attire.

"This is by far the largest study to date in this area. We used the expertise gained from our previous systematic review along with a panel of psychometricians, research scientists, choice architects, survey experts, and bioethicists to develop our study instrument. Given the size, methodological rigor and representativeness of these data, local, nuanced policies addressing physician attire should be considered to improve the patient experience," says Petrilli, who treats patients in the hospitals of Michigan Medicine, U-M's academic medical center, and holds a position at the VA Ann Arbor Healthcare System. He is a member of the U-M Institute for Healthcare Policy and Innovation.

The researchers note that while studies have shown that while physicians' white coats, neckties and sleeves have been shown to harbor infectious organisms, leading some countries to require physicians' arms to be "bare below the elbow," no studies have shown actual transmission of infection to patients through contact with physician attire.

However, other research has suggested that physicians may be more attentive to tasks when wearing their white coats, perhaps increasing patient safety.

"Patients appear to care about attire and may expect to see their doctor in certain ways. Which may explain why even white lab coats received a high rating for 'approachability' - patients may see a white coat similar to a physician's 'uniform' and may similarly also expect formal attire in most settings," notes Petrilli, who is a member of the U-M/VA Patient Safety Enhancement Program. "Patients don't always have the opportunity to choose their doctor. In this era of

appropriately increased focus on patient centeredness and satisfaction, physician attire may be an important, easily modifiable component of the patient care experience."

For consistency, and to keep other factors from influencing ratings, all the physicians shown were young, slender and Caucasian. Patients were approached in the outpatient waiting rooms of general medicine and specialty clinics, and non-surgical inpatient units. About two-thirds of the surveys were completed by inpatients, and the sample was 71 percent white and 65 percent male, with 70 percent having attended some college or having a college degree.

In addition to Petrilli, the study's authors were senior author Vineet Chopra, M.D., M.Sc., an associate professor at U-M, IHPI and PSEP member, and chief of the Division of Hospital Medicine, PSEP director and IHPI member Sanjay Saint, M.D., M.P.H., PSEP staff Latoya Kuhn and Ashley Snyder, and Joseph Jennings, M.D., of Georgetown University and Andrew Caruso, M.D., of Baylor College of Medicine.

<http://bit.ly/2JHnPL>

Why Do Genes Suggest Most Men Died Off 7,000 Years Ago?

By Yasemin Saplakoglu, Staff Writer | June 6, 2018 02:00pm ET

Modern men's genes suggest that something peculiar happened 5,000 to 7,000 years ago: Most of the male population across Asia, Europe and Africa seems to have died off, leaving behind just one man for every 17 women.

This so-called population "bottleneck" was first [proposed in 2015](#), and since then, researchers have been trying to figure out what could've caused it. One hypothesis held that the drop-off in the male population occurred due to ecological or climatic factors that mainly affected male offspring, while another idea suggested that the die-off happened because some males had more power in society, and thus produced more children.

Now, a new paper, published May 25 in the journal [Nature Communications](#), offers yet another explanation: People living in

patrilineal clans (consisting of males from the same descent) might have fought with each other, wiping out entire male lineages at a time. That ratio of 17 females for every one male "struck us as being very extreme, and there must be another explanation," said senior study author Marcus Feldman, a population geneticist at Stanford University in California. According to their new explanation, the male population didn't take a nosedive, but rather the diversity of the Y chromosome decreased due to the way people lived and fought with each other. In other words, there weren't actually fewer males, just less diversity among the males.

Humans have [23 pairs of chromosomes](#) that carry most of our genes. Of these, the 23rd pair is what determines our sex: Whereas females have two X chromosomes, males have one X chromosome and one Y chromosome.

Because offspring inherit one chromosome from each parent, genes usually get shuffled around, increasing the diversity across species. But the Y chromosome, having no female counterpart, doesn't get shuffled, so it [stays pretty much the same](#) from grandfather to father to son (save for any mutations that occur, which explains why the Y chromosome does differ among males).

War might've caused the Y chromosome bottleneck

To test their theory, the researchers conducted 18 simulations in which they created different scenarios for the bottleneck that included factors such as Y chromosome mutations, competition between groups, and death. Their simulations showed that warfare between patrilineal clans could have caused this so-called "Y chromosome bottleneck," because the members of each patrilineal clan would have very similar Y chromosomes to each other. So, if one clan killed off another, it would also slash the chance of that family's Y chromosome moving on to offspring.

In the researchers' simulations in which patrilineal clans didn't exist, however, the bottleneck didn't occur.

What's more, there was no such bottleneck in the women of the time, as is shown by mitochondrial DNA — a type of DNA that's [passed down only from mother to child](#).

"In that same group, the women could have come from anywhere," Feldman told Live Science. "They would've been brought into the group from either the victories that they had over other groups, or they could've been females who were residing in that area before."

As an example, he added, if you look at colonization throughout history, people generally "killed all the men and kept the women for themselves."

Monika Karmin, a population geneticist at the University of Tartu in Estonia who was not part of the new study, told Live Science that the "beauty of their study" is the way the researchers framed their hypothesis and demonstrated that "fighting clans are indeed likely to cause a drastic drop in male genetic diversity.

"However, we do have to keep in mind that there is very little information on the actual societal organization from that time," said Karmin, who was the lead author of the 2015 study that first proposed the bottleneck. So, there could have been other "sociocultural" forces at play, she said.

The researchers did "careful computer simulations, whereas the previous papers had not," said Chris Tyler-Smith, an evolutionary geneticist at the Sanger Institute in the United Kingdom who was not involved with the study. "The assumption that [the cause of the bottleneck] was warfare is a reasonable one," especially given the time period, he added.

People were still living in [small clans](#) doing small-scale farming 5,000 to 7,000 years ago, a time right before people moved into larger societies and built large cities. It was a "transition between early farming using stone tools and later farming in societies using metal tools," Tyler-Smith told Live Science.

But after this bottleneck, "you see the start of societal organizations and the shift from small-scale societies to having cities and organizations of people into groups that are not so intent on maintaining the Y chromosome lineage," Feldman said. During this time, the male population bounced back, he added.

Normally, researchers focus on [behavior that may have a genetic basis](#) but not on behavior that influences genes, Feldman said. The new finding is "an example of what a cultural preference can do in changing the level of genetic variation."

<http://bit.ly/2JxYX5S>

How to suck carbon dioxide from the sky for fuels and more

Someday, the gasoline you buy might trace its heritage to carbon dioxide pulled straight out of the sky rather than from oil pumped out of the ground.

By removing emitted carbon dioxide from the atmosphere and turning it into fresh fuels, engineers at a Canadian firm have demonstrated a scalable and cost-effective way to make deep cuts in the carbon footprint of transportation with minimal disruption to existing vehicles. Their work appears June 7 in the journal *Joule*.

"The carbon dioxide generated via direct air capture can be combined with sequestration for carbon removal, or it can enable the production of carbon-neutral hydrocarbons, which is a way to take low-cost carbon-free power sources like solar or wind and channel them into fuels that can be used to decarbonize the transportation sector," says lead author David Keith, founder and chief scientist of Carbon Engineering, a Canadian CO₂-capture and clean fuels enterprise, and a professor of applied physics and public policy at Harvard University.

Direct air capture technology works almost exactly like it sounds. Giant fans draw ambient air into contact with an aqueous solution that picks out and traps carbon dioxide. Through heating and a

handful of familiar chemical reactions, that same carbon dioxide is re-extracted and ready for further use--as a carbon source for making valuable chemicals like fuels, or for storage via a sequestration strategy of choice. It's not just theory--Carbon Engineering's facility in British Columbia is already achieving both CO₂ capture and fuel generation.

The idea of direct air capture is hardly new, but the successful implementation of a scalable and cost-effective working pilot plant is. After conducting a full process analysis and crunching the numbers, Keith and his colleagues claim that realizing direct air capture on an impactful scale will cost roughly \$94-\$232 per ton of carbon dioxide captured, which is on the low end of estimates that have ranged up to \$1,000 per ton in theoretical analyses.

That price-point is low enough to use direct air capture to start tackling the roughly 20% of global carbon emissions that result from driving, flying, trucking, and other ways of getting people and goods around. "Electricity from solar and wind is intermittent; we can take this energy straight from big solar or wind installations at great sites where it's cheap and apply it to reclaim and recycle carbon dioxide into new fuel," Keith says, adding that "Making fuels that are easy to store and transport eases the challenge of integrating renewables into the energy system."

The resulting fuels, including gasoline, diesel, and jet fuel, are compatible with existing fuel distribution and transportation infrastructure. Thanks to ultra-low life cycle carbon intensities, they are a promising route for reducing carbon emissions in heavy transportation and other sectors of the energy system that are demanding and difficult to electrify.

Centuries of unchecked human carbon emissions also mean that atmospheric carbon dioxide is a virtually unlimited feedstock for transformation into new fuels. "We are not going to run out of air anytime soon," adds Steve Oldham, CEO of Carbon Engineering.

"We can keep collecting carbon dioxide with direct air capture, keep adding hydrogen generation and fuel synthesis, and keep reducing emissions through this AIR TO FUELSTM pathway."

Keith and Oldham are optimistic that they have reduced scale-up risks by implementing direct air capture at reasonable costs using standard industrial equipment. That means that all the pieces are in place to move on to full-size plants capable of manufacturing 2,000 barrels of fuels per day-- totaling over 30 million gallons per year across plants. Commercialization of such plants would allow direct air capture to make a dent in transportation emissions by connecting low-cost renewable energy to low-carbon transportation fuels using Carbon Engineering's AIR TO FUELSTM pathway.

"After 100 person-years of practical engineering and cost analysis, we can confidently say that while air capture is not some magical cheap solution, it is a viable and buildable technology for producing carbon-neutral fuels in the immediate future and for removing carbon in the long run," says Keith.

In addition to funds raised by Carbon Engineering, this work was supported by the British Columbia Innovative Clean Energy Fund, Sustainable Development Technologies Canada, the Industrial Research Assistanceship Program, and the U.S. Department of Energy.

Joule, Keith et al.: "A process for capturing CO₂ from the atmosphere"

[https://www.cell.com/joule/fulltext/S2542-4351\(18\)30225-3](https://www.cell.com/joule/fulltext/S2542-4351(18)30225-3)

<http://bit.ly/2JzLYpk>

Researchers discover multiple alkali metals in unique exoplanet

Researchers have observed a rare gaseous planet, with partly clear skies, and strong signatures of alkali metals in its atmosphere

The extrasolar planet WASP-127b is one of the least dense exoplanets ever found. It has a radius 1.4 times greater than Jupiter, but only 20% of its mass. Such a planet has no analogue in the solar system and is rare even within the exoplanet diversity. It takes just

over four days to complete an orbit around its parent star and its surface temperature is around 1400 K (1127 ° C).

The observations of WASP-127b reveal the presence of a large concentration of alkali metals in its atmosphere, allowing [simultaneous detections of Sodium, Potassium and Lithium, for the first time in an exoplanet](#). The Sodium and Potassium absorptions are very broad, which is a characteristic shape in relatively clear atmospheres, and model fits indicate that the skies of WASP-127b are approximately 50% clear.

Guo Chen, a postdoctoral researcher at the IAC and first author of the article, explains "the particular characteristics of this planet allowed us to perform a detailed study of its rich atmospheric composition". And adds that "The presence of Li is very valuable to understand the evolutionary history of the planetary system and could shed light on the mechanisms of planet formation". In fact, the planet's host star, WASP-127, is also Li rich, which could point to an AGB star or supernovae having enriched the cloud of material from which this system originated.

Enric Pallé, a researcher at the IAC and co-author of the study, points out that they also found possible signs of water. "While this detection is not statistically significant, as water features are weak in the visible," he says, "our data indicates that additional observations in the near-infrared should detect it with high significance."

The results obtained indicate the great potential of ground-based telescopes for the study of planetary atmospheres. "In particular, the detection of a trace element such as Li in a planetary atmosphere is a major breakthrough and motivates new follow-up observations and detailed theoretical modelling to corroborate the findings", says Nikku Madhusudhan, from the University of Cambridge.

We are just starting to probe the atmospheres of these planets with ground-based telescopes, but Chen believes that this "will also be a reference exoplanet for future studies with space telescopes such as

the James Webb." These future studies will reveal the detailed nature of WASP-127b as a benchmark for this new class of very low density exoplanets.

The WASP-127b observations were conducted using the OSIRIS instrument of the GTC, from the Roque de los Muchachos Observatory, in Garafía (La Palma). The Observatories of the Instituto de Astrofísica de Canarias (IAC) and the Gran Telescopio CANARIAS (GTC) are part of the Spanish Unique Scientific and Technical Infrastructures (ICTS) network.

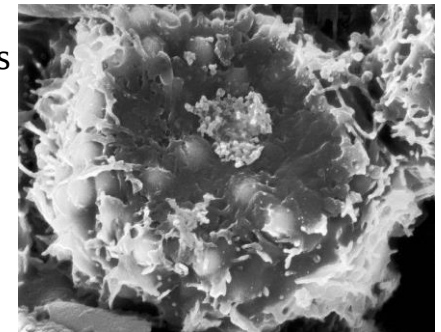
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A Promising Cancer Treatment Made Patients Worse, Not Better

Drugs that activate the immune system to fight cancer have brought remarkable recoveries to many people in recent years.

By [Denise Grady](#)

But one of those drugs seems to have had the opposite effect on three patients with an uncommon blood cancer who were taking part in a study. After a single treatment, their disease quickly became much worse, doctors reported in a [letter to The New England Journal of Medicine](#).



A white blood cell infected with the virus that causes adult T-cell leukemia-lymphoma, a rare blood cancer. An immunotherapy drug, nivolumab, seemed to make patients sicker, not better. Dennis Kunkel Microscopy/Science

Source

The cases are a sobering reminder that immunotherapy is still in its early days, and can unleash powerful forces that are not fully understood. Patients and doctors are eager to try the treatments when other options have run out, even for cancers in which they haven't yet been tested. Sometimes those hail-Mary efforts work. But they can backfire.

The patients, treated last year at different hospitals, had adult T-cell leukemia-lymphoma, which is caused by a virus. The drug was

nivolumab, or Opdivo, which belongs to a class called checkpoint inhibitors. The drugs cost more than \$100,000 a year. Nivolumab, made by Bristol-Myers Squibb, has been approved to treat eight types of cancer, but not this type of lymphoma.

The virus linked to the lymphoma — HTLV-1 — infects millions of people around the world, with the highest known prevalence in Japan, Africa, South America, the Caribbean and parts of Australia. But only 5 percent or fewer of those infected develop adult T-cell leukemia lymphoma; the reason is not known. The virus can be transmitted through sex, breast-feeding, needle-sharing, transfusions and transplants.

In the United States, lymphoma from the virus is seen most commonly in immigrants from affected regions.

The patients described in the journal were the first three in a nationwide clinical trial meant to test the drug in 20 people with the lymphoma. But after the third got worse instead of better, researchers shut down the study, which was funded by the National Cancer Institute. They wrote to the journal to alert other doctors to the potential risk of giving the drug, a form of immunotherapy, to patients with that type of lymphoma.

“I don’t think we should use nivolumab in this disease at all, considering our experience,” said Dr. Murali Janakiram, an author of the letter, who treated a patient at Montefiore Medical Center in the Bronx, N.Y. “That’s why we wanted to get this publication out. With other T-cell lymphomas, we should be cautious that this could potentially happen, but continue with the clinical trials.”

“We really were quite shocked by the results with all three of these patients,” said Dr. Lee Ratner, of Washington University School of Medicine in St. Louis, who designed and organized the trial.

This type of lymphoma has four subtypes, including two that are often fatal less than a year after being diagnosed. People with the other two can survive longer.

The first patient, who joined the study in February 2017 and was treated at the National Institutes of Health, had an indolent form called “smoldering,” and had survived, with various treatments, for more than 20 years, according to Dr. Thomas A. Waldmann, a physician and scientist there.

“She lived through the time from where she had infants to where she had kids in college,” Dr. Waldmann said.

But she had painful skin lesions and other signs that the disease was worsening. The doctors had run out of treatment options.

Trying a checkpoint inhibitor seemed to make sense. The cancerous cells in this type of lymphoma have a lot of mutations, and the drugs had been found to work best in that situation.

“We thought this approach in this patient would be beneficial,” Dr. Waldmann said. “What we observed was just the opposite. All the aspects of smoldering were replaced by the characteristics of the very aggressive, acute T-cell malignancy.”

Less than a week after one nivolumab infusion, the patient’s skin lesions turned swollen and warm. Her spleen became massively enlarged and painful, and there was a 63-fold increase in her levels of DNA from the cancer-causing virus.

“If one has been studying and working with a patient for 20 years, one develops a relationship,” Dr. Waldmann said. “It was very disconcerting to see this.”

Doctors used radiation treatments to shrink the patient’s spleen and skin lesions. They did not know if the nivolumab was to blame, but they gave her no more of it. She seemed to return to the condition she’d been in before receiving the drug, with worsening disease. She died a few months later.

At the time, Dr. Waldmann suspected that the drug might have made the disease progress. Checkpoint inhibitors work by activating white blood cells called T-cells, a part of the immune system that should

attack tumors. But in patients with this type of lymphoma, the drugs might mobilize diseased T-cells as well as healthy ones.

Still, the researchers could not be sure if the patient's decline had just been an unfortunate coincidence.

Then, a few months later, something similar happened at Ohio State University. Just days after being treated, a patient with smoldering disease developed flulike symptoms, and within a few weeks, "the leukemia had just massively progressed into the bones and bone marrow and everywhere," said Dr. Jonathan E. Brammer, an oncologist there.

She had to be taken off the study and treated with chemotherapy. Dr. Brammer said he did not know how she is now, because she had traveled to Ohio State for the study, and then went back home and continued treatment with local doctors.

"In science, when you administer a drug, you expect one outcome, but until you actually do it you don't know what the outcome is going to be," Dr. Brammer said.

The third patient, treated at Montefiore last November, had an acute form of the disease and had already been through several types of chemotherapy. The disease becomes very resistant to chemo, so the nivolumab study seemed like a better option than more chemo, Dr. Janakiram said.

"We gave him the first dose, and within 15 days, by the time he was ready to receive the next dose, his disease was just taking off," Dr. Janakiram said. "It was even more aggressive."

The patient was switched back to chemo, and stabilized. He had gone to Montefiore to join the study, and then went back to his original doctors. Dr. Janakiram said he did not know how the patient ultimately fared.

Researchers at the three centers, along with Dr. Ratner, compared notes and decided to call off the study.

"This is a disease that can worsen at any point of time," Dr. Janakiram said. "But then it's just so soon after the drug that we cannot rule out that it's the drug causing the problem."

Dr. Jedd D. Wolchok, an immunotherapy expert at Memorial Sloan Kettering Cancer Center who was not involved in the study, said the information was important, and he agreed that patients with any type of T-cell lymphoma — and there are many — should be carefully monitored if given a checkpoint inhibitor.

"This is a time of very rapid learning," he said.

<https://nyti.ms/2xZoe7N>

Life on Mars? Rover's Latest Discovery Puts It 'On the Table'

The identification of organic molecules in rocks on the red planet does not necessarily point to life there, past or present, but does indicate that some of the building blocks were present.

By [Kenneth Chang](#)

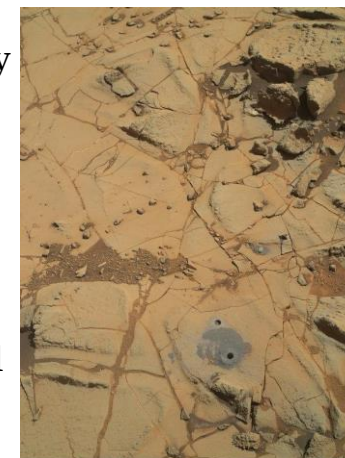
Scientists for the first time have confidently identified on Mars a collection of carbon molecules used and produced by living organisms.

That does not prove that life has ever existed on Mars. The same carbon molecules, broadly classified as organic matter, also exist within meteorites that fall from space. They can also be produced in chemical reactions that do not involve biology.

In 2015, the Curiosity rover drilled into a mudstone called "Mojave." Analysis of those drill cuttings yielded organic molecules.

NASA/JPL-Caltech/MSSS

But [the discovery, published on Thursday by the journal Science](#), is a piece of the Mars puzzle that scientists have long been seeking. In



1976, NASA's two Viking landers conducted the first experiments searching for organic matter on Mars and appeared to come up empty. "Now things are starting to make more sense," said Jennifer L. Eigenbrode, a biogeochemist at NASA's Goddard Space Flight Center in Greenbelt, Md., and lead author of the Science paper. "We still don't know the source of them, but they're there. They're not missing any more."

The data comes from NASA's Curiosity rover, which has been exploring a former lake bed within the 96-mile Gale Crater where it landed in 2012. The discovery shows that organic molecules can be preserved near the Martian surface, surviving the bombardment of radiation from the sun.



A self-portrait of Curiosity from 2013. NASA

"It's very exciting for Mars geology and for the search for life," said Sanjeev Gupta, a professor of earth sciences at Imperial College London in England, who was a co-author on the paper.

A second paper in Science adds wrinkles in the Martian puzzle of methane — a simple molecule of one carbon and four hydrogen atoms — that could also play an important part in figuring out whether life ever arose there and might even persist underground today.

The organic matter was found in pieces of solidified mud that Curiosity drilled into in 2015. The rocks formed about 3.5 billion years ago when Mars was drying out, although Gale Crater was still filled with water for stretches of thousands to millions of years.

The rock fragments were heated to more than 900 degrees Fahrenheit, and the rover's instruments looked at the molecules that wafted away

at the high temperatures. Then the scientists sifted through the results to figure out what might be genuine Martian organics.

The analysis was complicated in part because a cup of solvent [within the rover's mobile laboratory](#) had leaked, contributing misleading signals. In addition, some of the readings could have come from contamination that had tagged along from Earth; others could have been produced in combustion as the sample was heated, [which may have been the case in an earlier detection of organics by Curiosity](#).

"If we weren't sure, we removed it," Dr. Eigenbrode said.

In the end, a few smidgens of organics remained, including benzene and propane molecules.

"The detective work they did is worthy of Sherlock Holmes," said Katherine Freeman, a professor of geosciences at Pennsylvania State University who was not involved with the research. "What they show is that organics were present early on in Mars."

Intriguingly, the organics Dr. Eigenbrode and her colleagues detected looked like they were pieces that came from more complex material. The molecules could have come from something like kerogen, a component of fossil fuel that is found in coal and oil shale. But the scientists cannot say what the larger molecules were or how they formed.

"We've considered three possible sources for the organics: geology, meteorites and biology," she said. When they did experiments in their laboratory on Earth to bake samples containing those three types of organic carbon, the readings were all consistent with what was detected on Mars.

That means they do not have compelling evidence for a biological origin of the carbon, but the possibility is not ruled out, either. "It's on the table with all the other ones," Dr. Eigenbrode said.

In the second Science paper, scientists led by Christopher R. Webster of the NASA Jet Propulsion Laboratory in Pasadena, Calif., find that levels of methane in the thin Martian atmosphere are usually very

low, less than 0.5 parts per billion by volume. But with data now extending over five years, the scientists reported that methane levels go up and down by a factor of three, and the variations appear to follow Martian seasons.

“It’s very, very fascinating and puzzling,” Dr. Webster said.

Planetary scientists originally expected little methane in the Martian atmosphere, because that molecule is readily destroyed by sunlight and chemical reactions. But in 2003, observations from Earth indicated plumes of methane over parts of Mars. Those readings vanished two years later.

Because methane does not last in the atmosphere, any significant amounts there today must have been released recently. Methane can be created by geological interactions between rock, water and heat, or it could be a product of microbes that release methane as a waste product.



A view of Mount Sharp on Mars. A second paper revealed that methane levels in Mars’s atmosphere vary, and appear to follow the seasons of the planet. NASA/JPL-CALTECH/MSSS

Curiosity added to the mystery when it looked for methane and initially didn’t find any at all. A refined technique was able to measure lower levels, below 1 part per billion. Then in 2013 it recorded a burst of methane that lasted at least two months.

The rover has measured a few more methane spikes, but the new wrinkle is the undulations in the low background levels — higher in

summer than winter. With the seasonal patterns, scientists can now begin to test ideas on the source of the methane, Dr. Webster said.

Michael J. Mumma, a scientist at the Goddard Space Flight Center who led earlier Earth-based measurements and who is not involved with the Curiosity research, said the work was carefully done and confirms the low background levels, but that he was not yet convinced of the seasonality of the variations.

He said his team has conducted another round of ground-based measurements earlier this year but they have not yet analyzed the data.

Additional information will come from the European Space Agency’s Trace Gas Orbiter, which began its scientific data gathering a couple of months ago. Eventually, it will produce a global map of methane, but no results have been released yet.

[Future missions](#) could also provide additional clues to help scientists solve both the methane and organics puzzles. [NASA’s InSight spacecraft, currently en route](#), will measure marsquakes. It is possible that the impacts of meteors, which InSight might be able to record, rupture the surface and allow underground pockets of methane to rise into the atmosphere.

Two rovers launching in 2020, [one from NASA](#) and one from the European Space Agency, will also gather better rock samples to study organics. The European one will be able to drill a couple of yards into Martian rock, much deeper than the couple of inches that Curiosity was able to delve into.

The next NASA rover plans to collect rocks that will be brought back to Earth on a later mission where scientists will be able to examine them with a much wider array of instruments.

“Imagine what we can do on Earth in Earth laboratories in 10 years’ time,” Dr. Gupta said.

<http://bit.ly/2l0vqjd>

At what size does a minority group become influential?

What size does a minority need to reach to hit a tipping point?

When a viewpoint is held by a minority, what size does that minority need to reach to hit a tipping point, where their view becomes widely accepted in the rest of the population?

Why a population would first converge on a common norm or belief, and then suddenly shift to another one - an event that could hold great social importance - has remained a question.

To date, theoretical studies have estimated a minority population need only be 10% of the population, to create a tipping point that can shift broader views, while observational studies have reported the minority representation needs to be as high as 40%.

To better explore this phenomenon, Centola and colleagues [performed a series of controlled experiments](#) in which they recruited nearly 200 online volunteers and partitioned them into groups. Within each group, members were randomly paired up, and were tasked to simultaneously assign names to a pictured object (i.e., a face). If they coordinated and both assigned the same name to the object, they were rewarded. These interactions quickly resulted in group-wide coordination.

Once a convention was established among all experimental participants, the researchers introduced a small number of members, a "committed minority," into each group, who attempted to overturn the established convention by advancing a novel alternative. They then varied the sizes of the committed minorities.

Across all groups, the minority sizes necessary to bring about change ranged from 15 to 35%, with a median threshold of 25%. In a series of additional trials, the authors found that minority groups smaller than 25% could only sway, on average, 6% of the remaining population; however, when minority groups were larger than this

threshold size, they could persuade 72 to 100% of the rest of the population to adopt the new alternative.

<https://wb.md/2HABWNO>

HPV Vaccine's 'Extraordinary Benefits' Seen in Cochrane Review

Extremely important report just published by the Cochrane Library

Maurie Markman, MD

Hello. I'm Dr Maurie Markman from Cancer Treatment Centers of America in Philadelphia. I wanted to briefly discuss an extremely [important report just published by the Cochrane Library](#), a group responsible for high-quality meta-analyses on health-related issues. This article, "Prophylactic Vaccination Against Human Papillomaviruses to Prevent Cervical Cancer and Its Precursors,"^[1] demonstrates once again the extraordinary benefits and safety associated with human papillomavirus (HPV) vaccination.

The analysis looked at results of 26 phase 3 trials involving more than 73,000 participants. These were randomized, blinded trials that looked at placebo controls, with follow-ups as long as 8 years. The study demonstrated the extraordinary effectiveness—almost to the point of 100%—in preventing high-grade cervical intraepithelial neoplasia (CIN) grade 3 cervical lesions in young women who had not previously had evidence of HPV persistent infections—basically, before these young women had the opportunity to be exposed to HPV through sexual transmission.

In addition, in this very large database there was no difference in the incidence of side effects observed and no evidence for increased risk for miscarriage.

Of course, we've had these data for a long time. This compilation of large high-quality studies with long-term follow-up once again emphasizes the very major benefits associated with HPV vaccination and the potential substantial reduction in cervix cancer.

I encourage all individuals involved in public health matters, oncologists, gynecologists, pediatricians, and parents of young girls to see, review, and understand this report. Obviously, HPV vaccination is relevant for boys, but in this case we're talking about cervix cancer. This is an extremely important public health measure. I thank you for your attention.

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New hope from the 'seven year switch' in Type 1 diabetes

New research has shown that the rapid decline in insulin production that causes type 1 diabetes continues to fall over 7 years and then stabilizes

New research has shown that the rapid decline in insulin production that causes type 1 diabetes continues to fall over seven years and then stabilises.

A team at the [University of Exeter Medical School](#) found evidence that the amount of insulin produced declines by almost 50% each year for seven years. At that point, the insulin levels stabilise.

The finding is a major step forward in understanding Type 1 diabetes and contradicts previous beliefs that the insulin produced by people with the condition drops relentlessly with time. It offers the hope that by understanding what changes after seven years, new strategies could be developed to preserve insulin secreting beta-cells in patients. The study, published in *Diabetes Care*, measured C-peptide, which is produced at the same time and in the same quantities as the insulin that regulates our blood sugar. By measuring C-peptide levels in blood or in urine, scientists can tell how much insulin a person is producing themselves, even if they are taking insulin injections as

treatment. The team studied 1,549 people with Type 1 diabetes from Exeter, England and Tayside, Scotland in the UNITED study.

Dr Beverley Shields, at the University of Exeter Medical School, who led the research, said: "This finding is really exciting. It suggests that a person with Type 1 diabetes will keep any working beta-cells they still have seven years after diagnosis. We are not sure why this is; it may well be that there is a small group of "resilient" beta-cells resistant to immune attack and these are left after all the "susceptible" beta-cells are destroyed. Understanding what is special about these "resilient" beta-cells may open new pathways to treatment for Type 1 diabetes."

Type 1 diabetes affects around 400,000 people in the UK. The disease commonly starts in childhood but can develop at any age, and causes the body's own immune system to attack and destroy the insulin-producing cells in the pancreas, leaving the patient dependent on life-long insulin injections.

Professor Andrew Hattersley, a Consultant in Diabetes at the Royal Devon and Exeter Hospital and Research Professor at the University of Exeter Medical School, looked forward. "Now we know there is a "seven year switch", the next question is why? Has the immune attack stopped or are we left with "super beta-cells" that can resist the immune onslaught. Any insights into halting the relentless destruction of the precious insulin-producing cells are valuable. We could not have made this progress without the help of over 1,500 patients. We owe it to them to try to find answers that might help patient care quickly."

Karen Addington, UK Chief Executive of the type 1 diabetes charity JDRF, said: "These results provide further evidence that the immune system's assault on insulin-producing beta cells is not as complete as we once believed - and may change over time. This further opens the door to identifying ways to preserve insulin production in people diagnosed with or living with type 1 diabetes."

The study was supported by the JDRF, the Department of Health and Social Care and Wellcome Trust through the Health Innovation Challenge Fund and the NIHR.

The full paper, 'C-peptide decline in type 1 diabetes has two phases: an initial exponential fall and a subsequent stable phase', is published in Diabetes Care. Authors are Beverley M Shields, Timothy J McDonald, Richard Oram, Anita Hill, Michelle Hudson, Pia Leete, Ewan R Pearson, Sarah J Richardson, Noel G Morgan, Andrew T Hattersley on behalf of the TIGI I would not expand it does not help understanding (Type 1 diabetes Immunology and Genetic predictors of endogenous Insulin secretion) consortium.

<https://go.nature.com/2JpoJx7>

A simple test helps pinpoint a baby's arrival date

RNA released from the placenta holds clues.

A blood test can predict how far along a woman is in her pregnancy and also identifies women at risk of delivering their babies early.

Obstetricians determine when a pregnant woman is likely to give birth using either costly ultrasound scans or menstrual-cycle dates, which are often unreliable. In search of an alternative, Mads Melbye and Stephen Quake at Stanford University in California and their colleagues analysed cell-free RNA in the blood of 38 pregnant women. The team found that measurements of RNA from nine genes expressed in the placenta estimated gestational age with an accuracy comparable to that of an ultrasound scan. A similar blood test flagged women who would go into labour early.

The authors caution that a larger trial, including a more diverse cohort of women, is needed before the tests can be used in clinics.

[Science \(2018\)](#)

<http://bit.ly/2sWnFWz>

Holes in the head

A UM neurorehabilitation expert chronicles the remarkable skill of ancient Peru's cranial surgeons

Even with a highly skilled neurosurgeon, the most effective anesthesia, and all the other advances of modern medicine, most of us would cringe at the thought of undergoing cranial surgery today. After all, who needs a hole in the head? Yet for thousands of years, trepanation--the act of scraping, cutting, or drilling an opening into

the cranium--was practiced around the world, primarily to treat head trauma, but possibly to quell headaches, seizures and mental illnesses, or even to expel perceived demons.

But, according to a new study led by the University of Miami Miller School of Medicine's David S. Kushner, M.D., clinical professor of physical medicine and rehabilitation, trepanation was so expertly practiced in ancient Peru that the survival rate for the procedure during the Incan Empire was about twice that of the American Civil War--when, more three centuries later, soldiers were trepanned presumably by better trained, educated and equipped surgeons.



More ancient skulls bearing evidence of trepanation -- a telltale hole surgically cut into the cranium -- have been found in Peru than the combined number found in the rest of the world. University of Miami

"There are still many unknowns about the procedure and the individuals on whom trepanation was performed, but the outcomes during the Civil War were dismal compared to Incan times," said Kushner, a neurologist who has helped scores of patients recover from modern-day traumatic brain injuries and cranial surgeries. "In Incan times, the mortality rate was between 17 and 25 percent, and during the Civil War, it was between 46 and 56 percent. That's a big difference. The question is how did the ancient Peruvian surgeons have outcomes that far surpassed those of surgeons during the American Civil War?"

In their study published in the June issue of *World Neurosurgery*, "Trepanation Procedures/Outcomes: Comparison of Prehistoric Peru with Other Ancient, Medieval, and American Civil War Cranial Surgery," Kushner and his co-authors--biological anthropologists

John W. Verano, a world authority on Peruvian trepanation at Tulane University, and his former graduate student, Anne R. Titelbaum, now of the University of Arizona College of Medicine--can only speculate on the answer.

But hygiene, or more accurately the lack of it during the Civil War, may have contributed to the higher mortality rates in the later time period. According to the study, which relied on Verano's extensive field research on trepanation over a nearly 2,000-year period in Peru and a review of the scientific literature about trepanation around the world, Civil War surgeons often used unsterilized medical tools and their bare fingers to probe open cranial wounds or break up blood clots.

"If there was an opening in the skull they would poke a finger into the wound and feel around, exploring for clots and bone fragments," Kushner said, adding that nearly every Civil War soldier with a gunshot wound subsequently suffered from infection. "We do not know how the ancient Peruvians prevented infection, but it seems that they did a good job of it. Neither do we know what they used as anesthesia, but since there were so many (cranial surgeries) they must have used something--possibly coca leaves. Maybe there was something else, maybe a fermented beverage. There are no written records, so we just don't know."

Whatever their methods, ancient Peruvians had plenty of practice. More than 800 prehistoric skulls with evidence of trepanation--at least one but as many as seven telltale holes--have been found in the coastal regions and the Andean highlands of Peru, the earliest dating back to about 400 B.C. That's more than the combined total number of prehistoric trepanned skulls found in the rest of the world. Which is why Verano devoted an entire book, *Holes in the Head--The Art and Archeology of Trepanation in Ancient Peru*, to the 800-plus skulls, most of which were collected from burial caves and

archaeological digs in the late 1800s and early 1900s and reside in museums and private collections today.

It's also why Kushner, a medical history buff and Tulane alumnus, jumped at the chance to join Titelbaum in co-authoring one of the book's chapters, "Trepanation from the Perspective of Modern Neurosurgery," and continues to research the subject.

Published in 2016, the book analyzes the techniques and survival rates of trepanation in Peru through the demise of the Incan Empire in the early 1500s. The researchers gauged survival by classifying the extent of bone remodeling around the trepanned holes, which indicates healing. If there was no evidence of healing the researchers assumed the patient died during or within days of the surgery. If the margins of the trepanation openings showed extensive remodeling, they considered the operation successful and the patient long-lived.

Those classifications, Kushner, Verano and Titelbaum reported in the *World Neurosurgery* paper, show how ancient Peruvians significantly refined their trepanation techniques over the centuries. They learned, for example, not to perforate the protective membrane surrounding the brain--a guideline Hippocrates codified in ancient Greece at about the same time, 5th century, B.C., that trepanning is thought to have begun in ancient Peru.

The long-term survival rates from such "shallow surgeries" in Peru during those early years, from about 400 to 200 B.C., proved to be worse than those in the Civil War, when about half the patients died. But, from 1000 to 1400 A.D., survival rates improved dramatically, to as high as 91 percent in some samples, to an average of 75 to 83 percent during the Incan period, the study showed.

"Over time, from the earliest to the latest, they learned which techniques were better, and less likely to perforate the dura," said Kushner, who has written extensively about modern-day neurosurgical outcomes. "They seemed to understand head anatomy and purposefully avoided the areas where there would be more

bleeding. They also realized that larger-sized trepanations were less likely to be as successful as smaller ones. Physical evidence definitely shows that these ancient surgeons refined the procedure over time. Their success is truly remarkable."

Almost as remarkable is how, by the end of World War I, cranial surgery evolved into the distinct profession of neurosurgery, which continues to improve our understanding of brain anatomy, physiology and pathology. As Kushner notes, today's neurosurgeons regularly cut into the brain to remove tumors and blood clots, reduce intracranial pressure from massive strokes and trauma, repair vascular and structural anomalies and treat a myriad of other complex problems--with great success.

"Today, neurosurgical mortality rates are very, very low; there is always a risk but the likelihood of a good outcome is very high," he said. "And just like in ancient Peru, we continue to advance our neurosurgical techniques, our skills, our tools, and our knowledge."

<http://bit.ly/2HAWcz8>

A 'super' receptor that helps kill HIV infected cells
Unique set of "super" receptors on immune cells is capable of killing HIV across genetically diverse populations

While treatments for HIV mean that the disease is no longer largely fatal, the world still lacks a true therapy that can eradicate the virus across a globally - and genetically different - population.

Monash researchers, together with colleagues from the Pasteur Institute in Paris, have discovered a unique set of "super" receptors on immune cells capable of killing HIV across genetically diverse populations, making them a potential candidate for immunotherapy treatments. The work was published today in [Science Immunology](#).

Associate Professor Stephanie Gras and her team from Monash University's Biomedicine Discovery Institute (BDI) and ARC Centre of Advanced Molecular Imaging, and her colleagues from the Pasteur Institute in Paris, studied fifteen unique individuals who all

had been infected with HIV (ANRS CO21 CODEX cohort), but have immune systems that protect them from AIDs progression. These rare individuals, called HIV controllers, could hold clues to the cure for the disease.

Upon HIV infection, CD4 T cells, which are an important part of our protective immune system, can be depleted and drop dramatically in numbers, leading to a weak immune system with the progression of the disease to AIDs. These CD4 T cells can remain low even when the disease is kept in check with anti-retroviral therapy (ART), which is currently provided to more than half of people living with HIV globally. ART lowers the risk of mortality but does not eradicate the virus.

Associate Professor Gras and her colleagues found that HIV controllers are able to retain CD4 T cells of a higher quality, and are able to detect and react to minute amounts of virus, therefore representing a great opportunity to study their potential role in HIV infection.

"We discovered that those CD4 T cells, usually viewed as helper cells for the killer CD8 T cells that destroy infected cells, could be turned into killer cells themselves in HIV controllers. These killer CD4+ T cells could recognise very low amounts of HIV thanks to the expression of "super" T cell receptors on their surface. Importantly when they studied these receptors - they found identical receptors across multiple HIV controllers," Associate Professor Gras said.

"The likelihood of finding the exact same T cell receptor in different individuals is extremely low, like winning the lottery, and is likely playing a role in the control of HIV" Monash BDI's Dr Carine Farenc, a co-lead author of the study said.

T cell receptors recognise virus or bacteria fragments bound to specialised molecule called Human Leukocyte Antigen (HLA). HLA molecules are like fingerprints: every person has a specific

combination of HLA molecules, which help the immune system recognise foreign invaders like bacteria or viruses.

Monash University researchers used the Australian Synchrotron, effectively a giant microscope the size of a football field, to study the binding of this super T cell receptor in complex with the HIV antigen. This revealed another remarkable feature of those killer CD4 T cells: their ability to recognise HIV fragment in genetically diverse individuals (with different HLA molecules).

The Gras team and their colleagues found that these killer CD4 T cells can bind with HLA molecules shared by a quarter of world population, a figure that is likely to increase as studies progress, according to Associate Professor Gras.

Statistics (from the World Health Organization):

In 2016:

- *there were 36.7 million people living with HIV*
- *1 million died from the disease*
- *19.5 million people living with HIV were receiving antiretroviral treatment (ART)*

Read the full paper in [Science Immunology](#) titled *CD4+ T cell mediated HLA class II cross-restriction in HIV controllers*.

<http://bit.ly/2M8OqQx>

New life sciences institute wants to make drug discovery 10 times more efficient

High-throughput facility aims to make drug discovery up to 10 times more productive

By [Katrina Krämer](#) 8 June 2018

Drug discovery will receive a £103 million boost at the [UK's new national life sciences institute](#) the Rosalind Franklin Institute. Robotics, synthesis and biophysics will be brought together in a high-throughput facility that aims to make drug discovery [up to 10 times more productive](#). A fully automated workflow will make drugs for clinical testing within weeks rather than months.

'The way we do drug discovery currently is based around a design–make–purify test cycle,' explains synthetic chemist [Adam Nelson](#) from the University of Leeds, who will be leading the Rosalind Franklin Institute's chemistry for medicine programme. Although medicinal chemistry already uses automated processes, they tend to focus on individual stages in this cycle. 'We want to increase the throughput of each stage and integrate them better.'

However, the Rosalind Franklin Institute, which will be based at the Harwell science campus in Oxfordshire, won't be doing drug discovery in a traditional sense. 'It's all about developing underpinning technologies to facilitate discovery,' Nelson tells *Chemistry World*. The University of Oxford's [Ian Walmsley](#), chair of the interim board, [said](#) that the institute will 'embrace high-risk, adventurous research that will transform the way we develop new medicines'. In collaboration with 10 UK universities, researchers will also work on imaging technology, structural biology methods, biological mass spectrometry and protein synthesis.

One of the topics Nelson's team will work on is adding to the medicinal chemist's toolkit. Currently, just a handful of reactions dominate most drug discovery labs. 'They are largely focused around reactions that allow you to functionalise nitrogen or oxygen. There is only one carbon–carbon bond forming reaction that's widely used – the Suzuki reaction,' Nelson says, emphasising the need for more C–H functionalisation methods.

'Exploring chemical space only with a narrow toolkit is a bit like exploring the UK using only local bus routes,' says Nelson. Being able to use different modes of transport – different reactions – should allow chemists to explore new corners of chemical space, he adds. The facility, which was announced by the government in 2017, will open its doors in 2020. Until then, projects will run in temporary facilities near in Harwell.

<https://wb.md/2JuRGrB>

How Hubris Impairs the Care of the Elderly

Inspired by a [case presented by Dr Anish Koka on Twitter](#), Dr John Mandrola ponders the issues involved in care of the very old patient.

John M. Mandrola, MD

A very elderly man with atrial fibrillation asks whether to continue taking a clot-blocking drug to prevent stroke. For the sake of argument, this patient could be male or female, 90 years old or 100 years old.

The pro-side of using preventive therapy in the elderly is that the older the patient, the higher the risk for stroke, particularly a devastating one. Use of an anticoagulant in an elder, therefore, provides a robust degree of probability benefit in the future, albeit with the downside of a higher risk for bleeding.

The scenario here is similar to the quandaries faced in treating a number of chronic conditions in the elderly patient. One of the main debates surrounding the [2017 American College of Cardiology/American Heart Association hypertension guideline](#) is how aggressively to lower blood pressure in older patients. Similar concerns have been raised about aggressive blood glucose control in older patients with diabetes, resulting in the [American College of Physicians issuing a guideline](#) contradicting recommendations in the [American Diabetes Association's 2018 Standards for Diabetes Care](#).

When There Is No Evidence

Evidence cannot help us here. Randomized controlled trials only rarely include patients in their ninth or tenth decade. The word for using evidence acquired in 60-year-olds to determine care in the very elderly is...*foolish*.

Also foolish is the idea of letting the patient decide. How in the world is the patient supposed to know the right answer? The way we frame the decision to treat or not will surely sway the patient. Yes, it is right

to share the decision with the patient, but the advisor must be clear about the decision at hand. Giving patients a menu of choices is akin to abandonment. This decision, like so many in medicine, requires judgment. It also means resisting hubris.

The typical hubristic reasoning considers two potential errors. An error of omission occurs here if we choose not to use the anticoagulant or extra blood pressure medicine and the patient has an adverse event, such as a stroke from emboli or hypertensive disease. An error of commission occurs if we choose to use the anticoagulant and the patient suffers serious bleeding. Or perhaps we add the extra blood pressure or antidiabetes medication and the patient suffers a catastrophic fall. We committed the patient to preventive therapy and that commission played a role in his demise.

Many doctors struggle with this choice.

The struggle exposes our hubris. We falsely think that we control outcomes in a person who has lived for many decades. To be sure, we do *not* control outcomes in this group.

One need not consult actuarial tables to determine the chance of a 90- or 100-year-old person dying in the next year. It is high—whether we recommend preventive therapy or not.

That being said, I would not take the nihilistic view that there is not a correct answer. I believe there is a best answer.

It is: Do not treat.

Let me explain.

When Not Treating Is the Best Treatment

During a recent trip to the University of Calgary, my electrophysiology colleague [Dr George \(Yorgo\) Veenhuizen](#) taught me an important lesson about decision making under uncertainty. It goes like this: When there is true equipoise of a treatment (a complete counterbalance), and that treatment has potential harm and added cost, the right answer is not to treat.

Of course it is. The doctor's golden rule is: First, do no harm.

In the very elderly, there is no proven benefit of preventive therapies—such as anticoagulants or aggressive blood pressure control. This would require studies of very elderly people. There are none, nor will there ever be. There is, however, a well-known increased risk for harm (and added cost) from these therapies.

I would also add to my Canadian friend's logic that people who have been lucky enough to live to old age deserve the right to avoid iatrogenesis—or harm brought by us. Preventive therapies may work in younger people, but that does not apply to older people who have much less organ reserve.

The Fallacy of Doing Nothing

Some may make the decision to treat an older person a choice between "do nothing" or "do an intervention." I dislike this framing. "Do nothing" is not the alternative. One of the greatest errors of our time, one that frustrates me immensely, is the idea that not doing an invasive procedure or prescribing yet another drug equates to doing nothing. How many times have I heard a nurse or doctor say, "We have nothing to offer?"

We have plenty to offer people at the end of life. We can offer caring. And nowhere in the definition of caring is pharmacotherapy or invasive procedures. We can care for our elderly patients by attending to their needs and trying to relieve suffering. We can provide palliative care.

Clinicians can also help the elderly by reframing our thinking about life and death. Rather than bemoan the end-of-life event in an elder who was previously vigorous, we could celebrate the fact that he or she lived a long life, one that was lived with a short period of illness before death. Stanford University rheumatologist Dr James Fries called this ideal situation the compression of morbidity.^[1] Most people aim for an outcome described in the poem "[The Deacon's Masterpiece](#)" by Oliver Wendell Holmes, which memorialized a one-horse shay that worked perfectly for 100 years, then fell apart all at

once. When we intervene at the end of life, we too often merely extend the period of illness before death.

In this era of death denial and increasingly invasive medical technology, it would be wise to heed the words of the late Ivan Illich, a critic-philosopher, and once Catholic priest.

Presciently, in 1975, Illich wrote of three forms of iatrogenesis wrought by the medical establishment.^[2] Clinical iatrogenesis is harm from medical error. Social iatrogenesis is the medicalization of normal life. But the most insidious form of harm from the medical guild is a cultural iatrogenesis—or medicalization that corrupts the essence of what it is to be human.

Illich wrote that "the medicalization of society has brought the epoch of natural death to an end. Western man has lost the right to preside at his act of dying."

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<https://bbc.in/2MeCVH6>

Could an emoji save your life?

Emoji might not be your first line of communication in a disaster...

By Mary Halton Science reporter, BBC News

But researchers feel they could make a difference during emergencies like earthquakes, where every second counts. Now, an international group of scientists are lobbying for an earthquake emoji to be added to the Unicode set - the standard group of icons available on digital devices worldwide. But can one emoji really make a difference in a crisis?

Emoji-quake

"Maybe up to one third of the world's population might be exposed to some [seismological] hazard," explains University of

Southampton seismologist Dr Stephen Hicks, a founder of the [Emoji-quake campaign](#).

"So we really want to be able to communicate to all of those regions, all of those different languages, and an emoji is an amazing way of doing that."

The campaign aims to find an earthquake-appropriate design to be submitted to Unicode.

Dr Sara McBride, a communications specialist with the United States Geological Survey, is also part of the

effort. "Emoji can cross the boundaries of written language, helping communicate valuable information to people who may struggle to read a certain language... [they] help us communicate this complex threat faster to more people," she told BBC News.

Why earthquakes?

"The problem with an earthquake," says Dr Hicks, "is it's a very complex process; it's sort of hidden. It's not as tangible as a volcano or a tornado."

Unlike many other weather and climate related events, where longer warning times or visible signs are available, earthquakes move incredibly quickly and are difficult to measure while they are still occurring.

Populations in areas like Japan and Mexico are reliant on earthquake early warning technology, which issues an alert on digital devices and broadcast media.

"You may have seconds to get under a table or to protect yourself," explains Dr Hicks. "That can be life saving in many cases. If you send a text message as part of that alert you don't want too much wording in there."

A catfish icon appears with Japan's alerts, echoing the country's earthquake mythology



Being (relatively) young as a language, there aren't any conclusive studies on emoji and response times in emergency situations.

However, pictographs and other visuals have a track record of being faster and easier to understand than written information - which is why the safety card on the back of your aeroplane seat looks the way it does.

"A few studies do suggest that the use of emoji decreases the time it takes to mentally digest information," says Dr McBride. "But... we always want more data."

However, the emoji wouldn't just play a role in warning systems - it might actually help seismologists to work out where and when earthquakes are happening.

Currently, people are most likely to tweet a version of "did I just feel an earthquake?" in their own language.

But with one earthquake emoji being used around the world, it would be the equivalent of having a vast population of seismometers.

"Tweets can be geotagged... we can often then detect the earthquake using social media faster than we can through seismic waves travelling through the Earth. So if we know that an earthquake's happened sooner, then we know how to respond to it and send aid teams in there," Dr Hicks told the BBC.

Could emerji be a thing?

The potential usefulness of emoji in emergencies could extend well beyond earthquakes. "They're the closest thing we have to a universal language," says Sara Dean, a designer and architect in San Francisco. "One of the big bottlenecks in using social media as an emergency response tool is language... bridging that gap and reducing that bottleneck is especially important during the first couple of days after an emergency."

Ms Dean and a team of other designers came up with [emerji](#) - an entire set of emoji dedicated to climate and environmental events.

Unicode are currently considering Emerji's flood and earthquake designs. "People are already using emoji to talk about emergencies all the time. But because we don't have climate disaster emoji they're piecing them together from other emoji," commented Ms Dean.



Sara Dean/Beth Ferguson

Twitter users have combined the fire and tree emoji to share information about California wildfires. But Ms Dean points out that this is problematic as it's difficult to predict what emoji combinations people will choose to use.

For her, it feels essential that people have a means to share resources across language barriers on social media in a crisis situation.

"These are global issues and we need to be able to have global conversations about them," she told BBC News.