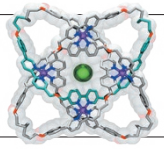
THIS WEEK



Stand up for vaccines

A presidential commission on a link between vaccines and autism would legitimize a dangerous and thoroughly debunked argument. Scientists must retaliate with the truth at once.

Critics call Donald Trump unpredictable. "Who knows what he will do next?" has become a popular rhetorical question in US politics. And yet, quite often his actions are entirely predictable. The difficulty comes in comprehending them.

A prime example is last week's revelation by environmental lawyer Robert F. Kennedy Jr that president-elect Trump may put together a commission to study "vaccine safety and scientific integrity". (Trump's team has countered that there are no definite plans to do so.) Kennedy says he would head the commission; he has in the past argued — unconvincingly — that a preservative in some childhood vaccines is linked to autism spectrum disorder, despite abundant evidence to the contrary.

Trump's embrace of the tiresome and discredited anti-vaccination movement is no secret. He has tweeted and publicly discussed his concerns that childhood vaccines may be linked to autism. He has previously met with like-minded activists, including Andrew Wakefield, a father of the 'anti-vaxxer' crusade who has been barred from practising medicine in the United Kingdom for professional misconduct.

Given the people Trump has chosen to listen to, his suggestion of a Kennedy-headed vaccine commission should be no surprise. But it remains difficult to grasp how someone in his position, with unlimited access to the world's best resources on vaccine safety, would selectively choose to overlook them all: the studies, the commissions, the scientists who have spent a lifetime studying vaccines. What good is another investigation of speculation already so thoroughly analysed and debunked — unless it is being set up to reach a different conclusion? It is a clear waste of money and effort. Much more frustratingly, it fuels an anti-vaccination movement that puts children and elderly people at risk.

Trump surely knows that there is already a federal commission to evaluate vaccine safety. The US Centers for Disease Control and Prevention (CDC) has an Advisory Committee on Immunization Practices that reports to the government on vaccine safety. Vaccines are also regulated by the US Food and Drug Administration — and often have particularly stringent safety requirements because they are used in healthy children.

There is already ample evidence that vaccines do not elevate the risk of autism. A 2015 study of more than 95,000 children found no association between the measles, mumps and rubella vaccine and an increased risk of autism — even among children with a family history of the disorder (A. Jain *et al. J. Am. Med. Assoc.* **313,** 1534–1540; 2015). As for Kennedy's argument about vaccine preservatives, the CDC has repeatedly tried — and failed — to find a link between that preservative, called thimerosal, and autism. In 2004, the US Institute of Medicine reported that a review of the literature had also found no such link (see go.nature.com/2jwe4ba). And in the United States, the argument is now moot: thimerosal was removed from most childhood vaccines administered in the country, as a precautionary measure, beginning in 2001. Autism diagnoses continued unabated.

All the evidence shows that it is actually misconceptions about vaccines — such as those promoted by Trump — that cause serious harm. The United States has already experienced a series of outbreaks of preventable diseases. In 2014, measles affected 667 people in the country, primarily those who were unvaccinated. The outbreaks are expensive, too: in 2011, it cost public-health institutions up to US$5.3 million to cope with 16 measles outbreaks that made 107 people ill.

If Trump moves ahead with his vaccine commission, he will give a sense of legitimacy to opponents of childhood vaccination. This could undercut efforts in some states, such as Texas and Michigan, to strengthen vaccination requirements for schoolchildren.

"The commission fuels an anti-vaccination movement that puts children and elderly people at risk."

In the wake of the news about the commission, the American Medical Association moved to reassert the safety of vaccines. The American Academy of Pediatrics said that it would welcome the chance to discuss vaccine safety with Trump.

Scientists, medics and commentators who have fought vaccine disinformation in the past must take a deep breath and return to the fray. There is no need to wait for this commission to be announced officially. There is no need to wait until it issues its findings. There is no cause to be surprised if it shows little regard for science — or even if it targets scientists who speak out in favour of vaccination. Those who claim a link between vaccines and autism can do so only by discrediting the scientific evidence and, often, the scientists who gathered it. Kennedy's reference to investigating vaccine safety "and scientific integrity" provides ample warning of what is to come. Scientists should get their retaliation in first. Lives are at stake. ■

The new normal

The 'ordinary' science of checking other people's work is essential to research.

Purists will tell you that science is about what scientists don't know, which is true but not much of a basis on which to develop new cancer drugs. Hence the importance of knowledge: how crucial this mutation or that cell-surface receptor really is to cancer growth. These are the findings that launch companies and clinical trials — provided, of course, that they have been published in research papers in peer-reviewed journals.

As we report in a News story this week (see page 269), a systematic effort to check some of these findings by repeating an initial five published cancer studies has reported that none could be completely reproduced. The significance of this divergence — how the specific

experiments were selected and what the results mean for the broader agenda of reproducibility in research — is already hotly contested.

Perhaps the most influential aspect of the exercise, called the Reproducibility Project: Cancer Biology, has nothing to do with those arguments. It lies beneath the surface, in the peer reviews of the project teams' replication plans, which were published before the studies began. These reviews can be read as part of the editorial decision letters linked to each replication plan, or 'registered report' (see go.nature.com/2jte08a).

What, one might ask, could be less interesting? What insights can emerge from technical feedback on plans to repeat what other groups of scientists have done? Plenty. The decision letters reveal the practice of science at its best: probing whether an experiment truly tests a particular idea; identifying shortcomings in the original set-ups; and proposing further, sounder tests. To those committed to improving science, reading these insights — the fruit of voluntary donations of time and effort — will prove a moving experience. Journal clubs would do well to read the original papers, and then compare their own analyses with those of the scholars who have reviewed the replication reports.

Again and again, the peer reviewers and the replicators clash. The reviewers are eager to produce the best experiment to test a publication's conclusions; they want to correct deficiencies in the design of the original high-impact studies. The replicators do, on several occasions, agree to add an extra measurement, particularly of positive and negative controls that had originally been neglected. Often, however, they resist calls for more definitive studies. Testing "the experiment's underlying hypothesis," they insist, "is not an aim of the project."

This is a frustrating, if understandable, response. It is easier to compare the results of highly similar experiments than to assess a conclusion. Thus, the replication efforts are not especially interested in, say, the big question of whether public gene-expression data can point to surprising uses for new drugs. They focus instead on narrower points — such as whether a specific finding that an ulcer drug stalls the growth of lung cancer in mice holds up (it did, more or less; see I. Kandela *et al.* *eLife* **6,** e17044; 2017). Even so, the results are not definitive. One set of dissimilar results can't establish that the original result was a false positive; nor do similar results show that the original conclusion is correct.

Yet a project that sticks to direct replication and eschews broader 'truth' can still raise bigger issues. After all, grand conclusions are built on myriad laboratory experiments. How well (or not) such experiments work outside the original lab is too often communicated through gossip rather than open discourse. For just US$2 million in private funding — less than a typical 5-year grant from the US National Institutes of Health to a single investigator — this replication project shines a very public light on the sticking points of experiments.

"Grand conclusions are built on myriad laboratory experiments."

One aspect that merits increased focus is how markedly the results of control experiments varied between the original work and replications. In one case, mice in the control group of an original study survived for nine weeks after being engrafted with tumours, whereas those in the replication survived for just one. In another, a bioluminescent signal used to track tumour burden differed markedly between the original and replication studies. Such situations occur frequently in biology, but are often overlooked because researchers focus only on results in their own laboratories. There is great value in highlighting variability in 'established' experimental systems.

Such results deserve more attention, both technically and philosophically. Researchers routinely optimize experimental conditions to see the signals that they are looking for. But how far can this proceed until confirmation bias makes results uninterpretable? How does one do pilot studies without overly encouraging favourable results?

More than 50 years ago, the philosopher Thomas Kuhn defined 'normal science' as the kind of work that faithfully supports or chisels away at current hypotheses. It is easy to dismiss this as workmanlike and uninteresting. But only by doing such normal science — and doing it well — can we recognize when revolutions are necessary. ■

Pricing the planet

The social cost of carbon must be based on science, not politics.

Take a step back. Earth is an orb reeling through the emptiness of space, warmed from the inside by molten rock and from the outside by the Sun. Thanks to the wonders of physics, a magnetic shield protects us from the most damaging cosmic radiation, and our exceedingly thin atmosphere forms a protective blanket that keeps the surface temperature at more or less acceptable levels for a wild variety of life. Humans have no control over the former, but it's now crystal clear that maintenance of the latter is on us.

One of the many innovations that enabled humanity's rise to global dominance is the development of money, which is a measure of relative value. Humans put a price on almost everything, from tomatoes and houses to entertainment and information. Scientists and economists have even sought to put a value on services rendered by the global climate. More specifically, the 'social cost of carbon' (SCC) represents the hidden costs from climate impacts such as extreme weather, declining crop yields and rising sea levels. At present, the US government's central estimate of this is US$36 per tonne of carbon dioxide.

It might seem arcane, but the administration of US President Barack Obama has used this metric to estimate the costs and the benefits of a wide variety of government decisions that affect greenhouse-gas emissions, including climate regulations targeted at the fossil-fuel industry. Despite obvious challenges in settling on a single number, this figure is a way of accounting for the far-reaching impacts of decisions. The social cost of carbon is also a target for the incoming administration of president-elect Donald Trump, and his operatives have hardly hidden their animosity towards the idea. In its notorious, and eventually disavowed, memorandum to the US Department of Energy, the Trump transition team sought the names of employees who attended meetings related to the social cost of carbon. And in a memo last November, issued before former industry lobbyist Thomas Pyle was selected to lead Trump's transition team for the same department, Pyle said that Trump could seek to limit the use of the social cost of carbon in federal rule-making.

That could be difficult given that US courts have both ordered and upheld the metric's use in the past, but Pyle also said that the Trump administration will push for a review of the underlying science. "If the SCC were subjected to the latest science, it would certainly be much lower than what the Obama administration has been using," Pyle wrote.

This is simply not true. Some have indeed argued that it is too high, but numerous studies have concluded that the price tag for damages is too low — perhaps much too low. Indeed, a 2014 meta-analysis suggested a floor of $125 (J. C. J. M. van den Bergh and W. J. W. Botzen *Nature Clim. Change* **4,** 253–258; 2014).

Last week, the US National Academies of Science, Engineering, and Medicine weighed in with a lengthy report. It did not name a specific price, but it did outline a series of technical recommendations intended to tap the latest research to bolster the underlying science and to increase transparency. The panel also recommended establishing a process for updating the carbon price every five years.

The recommendations are timely. Most important of all, given the disregard for science that Trump and his political appointees have shown so far, is the call for transparency. There is, of course, plenty of room for debate. But any useful assessment of the carbon price must take into account the full range of scientific and economic research, and not bend to the political proclivities of those in charge. ■