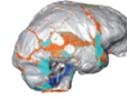


THIS WEEK

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The fight against bird flu

China's well-handled response to outbreaks of H7N9 avian influenza belies the country's bad reputation from its past dealings with disease. But there are still improvements to be made.

China deserves credit for its rapid response to the outbreaks of H7N9 avian influenza, and its early openness in the reporting and sharing of data.

A bad reputation is difficult to shake. A decade ago, China failed to report early cases of severe acute respiratory syndrome (SARS) and fumbled its initial response to the threat. Today, some commentators view its reaction to H7N9 with mistrust. But from all the evidence so far, China's response to the virus, which had caused 104 confirmed human cases and 21 deaths as *Nature* went to press, is next to exemplary.

China reported the H7N9 outbreak to the World Health Organization (WHO) on 31 March, just six weeks after the first known person fell ill. On the same day, it published the genomic sequences of viruses from the three human cases then identified on the database of the Global Initiative on Sharing Avian Influenza Data (GISAID). It has also shared all the sequences with the WHO, and live virus with the WHO and other laboratories. This has allowed scientists to identify the virus's mutations, trace its origins and develop crucial diagnostic tests. China continues to report new cases daily, and its media discusses H7N9 fairly openly. Chinese and other researchers have quickly published detailed analyses of the virus in journals (R. Gao *N. Engl. J. Med.* <http://doi.org/k7r>; 2013). Chinese President Xi Jinping added political clout last week when he called for an effective response, and said that the government must ensure the release of accurate information about the outbreaks.

China's response to the epidemic has also been brisk. Diagnostic tests have been distributed to hospitals and research labs across the country. The response, spearheaded by the Chinese Center for Disease Control and Prevention in Beijing, has united clinicians, virologists, and epidemiologists. Live-bird markets at which H7N9 has been found have been shut down, and birds culled. The agriculture ministry has tested tens of thousands of birds and other animals for the virus, to try to pin down the sources of human infections and explain their occurrence in cities hundreds of kilometres apart — no mean task given that China has some 6 billion domestic fowl and half a billion pigs, which can also carry the virus. So far, however, apart from birds at the live markets, the sources of infection remain elusive. To help track them down, and to collaborate in efforts to control H7N9, China has invited a team of WHO scientists and international flu experts to the country. They arrived last week, and are expected to report their preliminary conclusions this week.

Yet suspicions linger. Some critics have questioned, for example, the time between the first person falling ill on 19 February and China's first announcement about the virus, and have asked whether the announcement was deliberately delayed. This is unfair. With just a handful of severe pneumonia cases caused by the virus by mid-March, it is impressive that China realized as quickly as it did that something was amiss. It took the United States, which has one of the world's most advanced disease-surveillance systems, an almost identical amount of time to identify a novel H3N2 swine virus that caused serious illness in a child in 2011.

China has made a good start, but it is crucial for the country to

continue its openness over the H7N9 outbreaks. In particular, it must promptly report any evidence of human-to-human spread. There are also areas for improvement: data made public on human cases are often limited to basic facts such as age, sex, date of onset of illness and location. Epidemiologists also need more detailed data, including possible exposures to infection and underlying medical conditions. Case reports should be published in full in journals or online as quickly as possible.

It is also important that sequences from as many cases as possible are submitted to publicly accessible databases, because sequence data are important in tracking evolutionary changes such as new mutations that could allow the virus to spread between humans more easily. They can also provide clues to the source of infection (see page 399).

Even as the Chinese authorities are being open and transparent on H7N9, some scientists are hoarding epidemiological and other data, because of intense competition to be the first to publish. Competition can be healthy, but in the face of a virus that has the potential to cause a pandemic, researchers have a duty above all else to share important data. Journals must be ready and willing, as in any public-health emergency, to fast-track peer review of H7N9 papers, and not let rapid publication of preprints stand in the way of considering papers for publication. Meanwhile, observers should continue to scrutinize China's response to H7N9, but they should also give credit where credit is due. It is time to recognize that China has changed. ■

“China has made a good start, but it is crucial for the country to continue its openness over the H7N9 outbreaks.”

Across the divide

Diagnostic boundaries separating mental disorders hamper effective treatments.

Scientists who attended the 2009 Winter Workshop in Psychoses in Barcelona, Spain, may not have realized it at the time, but they were part of a revolution. In previous years, organizers named the event the Winter Workshop on Schizophrenia and Bipolar Disorders. It was one of the few conferences at which those who studied schizophrenia and those who worked on bipolar illnesses would meet.

As Nick Craddock, a psychiatrist who studies both conditions at Cardiff University, UK, says in a News Feature on page 416, a merger of these two distinct groups — even in semantic terms — would have been unthinkable until very recently. Psychiatrists diagnose

schizophrenia and bipolar disorder as two separate conditions. This separation is respected by drug companies, regulators, research funders, journals and bench researchers. Add that lot up, and you get a fundamental problem with psychiatry.

Next month, the American Psychiatric Association will release the long-awaited fifth version of its *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*, which lists mental illnesses and their symptoms. Work on preparing the *DSM-5* has been clouded in controversy, and the arguments over which conditions should have been included and which left out will rumble on for some time.

The more fundamental problem, as the News Feature explores, is growing doubt about the way the *DSM-5* classifies mental disorders. Psychiatrists have long known that the illnesses of patients they see in the clinic cannot be broken down into discrete groups in the way that is taught at medical school. Symptoms overlap and flow across diagnostic boundaries. Patients can show the signs of two or three disorders at the same time. Treatments are inconsistent. Outcomes are unpredictable.

Science was supposed to come to the rescue. Genetics and neuro-imaging studies would, all involved hoped, reveal biological signatures unique to each disorder, which could be used to provide consistent

and reliable diagnoses. Instead, it seems the opposite is true. The more scientists look for biomarkers for specific mental disorders, the harder the task becomes. Scans of the DNA and brain function of patients show the same stubborn refusal to group by disease type. Genetic risk factors and dysfunction in brain regions are shared across disorders.

“Patients’ illnesses cannot be broken down into discrete groups in the way that is taught at medical school.”

Psychiatrists joke that their patients have not read the textbooks. The reality is serious and more troubling — the textbook is wrong.

The American Psychiatric Association routinely points out that its *DSM* disease categories are intended only as diagnostic tools. It does not claim that they mark genuine biological boundaries. But the system is set up as if they do. That might explain why biomarkers and new drugs for mental illness remain elusive. The system should change. Funders and journals must encourage work that cuts across the boundaries. Researchers should be encouraged to investigate the causes of mental illness from the bottom up, as the US National Institute of Mental Health is doing. The brain is complicated enough. Why investigate its problems with one hand tied behind our backs? ■

ANNOUNCEMENT

Reducing our irreproducibility

Over the past year, *Nature* has published a string of articles that highlight failures in the reliability and reproducibility of published research (collected and freely available at go.nature.com/hubbyr). The problems arise in laboratories, but journals such as this one compound them when they fail to exert sufficient scrutiny over the results that they publish, and when they do not publish enough information for other researchers to assess results properly.

From next month, *Nature* and the Nature research journals will introduce editorial measures to address the problem by improving the consistency and quality of reporting in life-sciences articles. To ease the interpretation and improve the reliability of published results we will more systematically ensure that key methodological details are reported, and we will give more space to methods sections. We will examine statistics more closely and encourage authors to be transparent, for example by including their raw data.

Central to this initiative is a checklist intended to prompt authors to disclose technical and statistical information in their submissions, and to encourage referees to consider aspects important for research reproducibility (go.nature.com/oloeip). It was developed after discussions with researchers on the problems that lead to irreproducibility, including workshops organized last year by US National Institutes of Health (NIH) institutes. It also draws on published concerns about reporting standards (or the lack of them) and the collective experience of editors at Nature journals.

The checklist is not exhaustive. It focuses on a few experimental and analytical design elements that are crucial for the interpretation of research results but are often reported incompletely. For example, authors will need to describe methodological parameters that can introduce bias or influence robustness, and provide precise characterization of key reagents that may be subject to biological variability, such as cell lines and antibodies. The checklist also consolidates existing policies about data deposition and presentation.

We will also demand more precise descriptions of statistics, and

we will commission statisticians as consultants on certain papers, at the editor's discretion and at the referees' suggestion.

We recognize that there is no single way to conduct an experimental study. Exploratory investigations cannot be done with the same level of statistical rigour as hypothesis-testing studies. Few academic laboratories have the means to perform the level of validation required, for example, to translate a finding from the laboratory to the clinic. However, that should not stand in the way of a full report of how a study was designed, conducted and analysed that will allow reviewers and readers to adequately interpret and build on the results.

To allow authors to describe their experimental design and methods in as much detail as necessary, the participating journals, including *Nature*, will abolish space restrictions on the methods section.

To further increase transparency, we will encourage authors to provide tables of the data behind graphs and figures. This builds on our established data-deposition policy for specific experiments and large data sets. The source data will be made available directly from the figure legend, for easy access. We continue to encourage authors to share detailed methods and reagent descriptions by depositing protocols in Protocol Exchange (www.nature.com/protocolexchange), an open resource linked from the primary paper.

Renewed attention to reporting and transparency is a small step. Much bigger underlying issues contribute to the problem, and are beyond the reach of journals alone. Too few biologists receive adequate training in statistics and other quantitative aspects of their subject. Mentoring of young scientists on matters of rigour and transparency is inconsistent at best. In academia, the ever increasing pressures to publish and chase funds provide little incentive to pursue studies and publish results that contradict or confirm previous papers. Those who document the validity or irreproducibility of a published piece of work seldom get a welcome from journals and funders, even as money and effort are wasted on false assumptions.

Tackling these issues is a long-term endeavour that will require the commitment of funders, institutions, researchers and publishers. It is encouraging that NIH institutes have led community discussions on this topic and are considering their own recommendations. We urge others to take note of these and of our initiatives, and do whatever they can to improve research reproducibility. ■