EDITORIALS

Editorials are usually commissioned. We are, however, happy to consider and peer review unsolicited editorials
See http://resources.bmj.com/bmj/authors/types-of-article/editorials for more details

Declaration of transparency for each research article

An antidote to inadequate reporting of research

Douglas G Altman director, Centre for Statistics in Medicine, University of Oxford, Botnar Research Centre, Oxford, UK doug.altman@csm.ox.ac.uk
David Moher senior scientist, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa Hospital - General Campus, Ottawa, ON, Canada K1H 8L6

"It is the responsibility of everyone involved to ensure that the published record is an unbiased, accurate representation of research."[1]

The research record is often manipulated for short term gain but at the risk of harm to patients. The medical research community needs to implement changes to ensure that readers obtain the truth about all research, especially reports of randomised trials, which hold a special place in answering what works best for patients.

Failure to publish the findings of all studies, especially randomised trials, seriously distorts the evidence base for clinical decision making. A recent systematic review of reboxetine for treating depression found that almost three quarters of included patients were in unpublished trials.[2] Of 904 completed trials of interventions for acute ischaemic stroke (1955-2008), a fifth were not properly published, "several of which may be large enough to influence clinical practice and the findings of systematic reviews and meta-analyses."[3]

Bad as non-publication is, incomplete or misleading publications cause greater problems. Results of clinical trials published in peer reviewed publications may differ from what was previously submitted to regulatory agencies,[4-6] with the published data being more positive. The primary outcome often differs from what the researchers had stated in the trial protocol[7 8] or clinical trial registry.[9 10] Selective non-publication favours statistically significant findings, biasing the literature.[11 12] Furthermore, authors often distort the presentation and interpretation of their findings. One study found that such "spin" was common in 72 reports of randomised controlled trials with statistically non-significant primary outcomes.[13] Similar findings have been reported recently for studies of the accuracy of diagnostic tests.[14]

Peer review is failing to ensure that journal articles contain the key clinical and methodological details that readers need. Reviews of published reports of randomised trials have found common deficiencies in the details of the interventions being evaluated,[15 16] participant eligibility criteria,[17] and outcomes.[18 19] Details of study methods are also often inadequate, especially in relation to allocation. A 2006 study found that only a third of trial reports described how the randomisation sequence was generated and only a quarter described an adequate method of allocation concealment.[20] A review of 357 phase III oncology trials concluded that "numerous items remained unreported for many trials."[21] Harms too are poorly reported.[22 23]

The problems associated with publishing and reporting other types of research may be worse than for randomised trials. Although less intensively studied, similar concerns have been expressed in relation to epidemiology,[24 25] pharmacoepidemiology,[26] diagnosis research,[27] prognosis research,[28] and preclinical research.[29 30] Of course, good reporting is not the same as high quality research. But a full and clear report allows readers to judge a study's reliability and relevance. There are concerns that commercially sponsored research may be more likely to remain unpublished,[2 31] but when published these trials are reported more fully.[32]

So what is needed? Published research articles should provide a clear description of how researchers conducted their study and what they found. Omission of important details of methods or study conduct should be deemed unacceptable, and journals should not publish them. Although detection of some deficiencies requires external information (for example, from a trials register or protocol), most deficiencies are inherent in a submitted manuscript and should be detected. Despite the availability of reporting guidelines such as CONSORT,[33] improvements are slow to materialise.[34]

By not making results of their research easily accessible, researchers are withholding knowledge, in contravention of the Declaration of Helsinki. Not only are current practices questionable on moral and scientific grounds, failure to publish all research findings is a massive waste of scarce resources and diminishes the social value of the research.[35] Researchers and funding organisations also fail the public when research findings are published in a misleading or inadequate way. Scientifically, this harms systematic reviewers who want to aggregate all of the evidence. Reviewing a partial picture provides biased and less precise estimates of effectiveness and safety than when the full information is used, and it may compromise the identification of what works best for patients.

We have a proposal that can be acted on almost immediately. We suggest that authors should sign a publication transparency declaration (box) as part of every journal submission. The same declaration could be appropriate for submissions in other contexts—for example, to regulatory agencies.

Editors and editorial groups can support this initiative by updating their instructions to authors so that a completed publication transparency pledge is required as part of the submission process. We see this action as a necessary scientific analogue of the current widespread practice of asking authors about conflicts of interest. Subsequent revelation of withheld or incorrect information would be evidence of scientific misconduct for which various actions could be taken. We hope that this step will encourage authors to reflect more carefully on how they write their article and encourage them to check that they have adhered to relevant reporting guidelines. The *BMJ*, for which one of us (DGA) is the senior statistics editor, and *BMJ Open* are leading the way by implementing this policy immediately. We invite other journals to do likewise and support the transparency declaration on the EQUATOR website (www.equator-network.org).

TRANSPARENCY DECLARATION

The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

*The manuscript's guarantor.

The scientific community and the public at large deserve an accurate and complete record of research; we need to make changes to ensure that we will get one. Widespread endorsement and implementation of a publication transparency declaration is one way to help to get the maximum value from medical research. It will, however, have no influence on the non-publication of studies, which is a continuing disgrace.

Competing interests: None declared.

Provenance and peer review: Not commissioned; externally peer reviewed.
References are in the version on bmj.com.

Cite this as: *BMJ* 2013;347:f4796

bmj.com

- News: H7N9 avian flu kills seven and infects 23 in China (*BMJ* 2013;346:f2222)
- News: H7N9 virus is more transmissible and harder to detect than H5N1, say experts (*BMJ* 2013;346:f2568)
- News: H7N9 avian flu infects humans for the first time (*BMJ* 2013;346:f2151)

Human to human transmission of H7N9

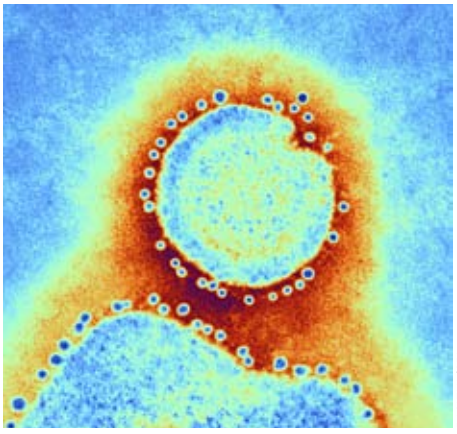
Limited transmission between humans is not surprising

James W Rudge lecturer, Communicable Diseases Policy Research Group, London School of Hygiene and Tropical Medicine, Mahidol University, Bangkok 10400, Thailand
james.rudge@lshtm.ac.uk
Richard Coker professor, Saw Swee Hock School of Public Health, National University of Singapore, Singapore

Since the new avian influenza virus, H7N9, first emerged in China, a primary concern has been whether it might spread between humans. The vast majority of the 133 confirmed cases reported so far seem to be epidemiologically unconnected, with many patients reporting a recent history of exposure to live poultry, which are suspected to be a main reservoir for the virus. Although an earlier study did report two family clusters of H7N9 cases, it was unclear whether these clusters resulted from person to person transmission or simply from exposure to a common animal source of infection.[1]

In the linked paper by Qi and colleagues, a detailed investigation into one of these clusters provides the strongest evidence yet of H7N9 transmission between humans.[2] The index case, a 60 year old man, was likely to have been infected at a nearby live poultry market, and subsequently developed a severe and ultimately fatal respiratory illness. His 32 year old daughter, who provided prolonged bedside care for her father before his admission to intensive care, later also became fatally infected. With no indication that the daughter was exposed to live poultry within the days before becoming sick, along with almost 100% genetic similarity between the viruses isolated from each patient, the evidence points to transmission from father to daughter.

As the authors acknowledge, there are some limitations to the study but, on balance, human to human transmission looks probable. So does this imply that H7N9 has come one step closer towards adapting fully to humans? Probably not. Crucially, there is still no evidence of sustained transmission among humans—all 43 close contacts of these two patients, including a son in law who also helped care for the father, tested negative for infection. In addition, the receptor binding sites of the viruses from the two patients are no more adapted towards humans than those of other available H7N9 isolates. In many ways, the evidence corroborates, rather than challenges, previous assertions that the transmissibility of H7N9 between humans is currently low.



PASIEKA/SPL

In many ways, the evidence corroborates, rather than challenges, previous assertions that the transmissibility of H7N9 between humans is currently low

Indeed, the occasional transmission event from human to human appears to be the norm rather than the exception for influenza viruses that sporadically cross the species barrier into humans. Limited human to human transmission has been reported for highly pathogenic avian influenza H5N1,[3 4] which continues to cause (usually fatal) infections in humans, as well as another bird flu subtype, H7N7, which caused an outbreak of mostly mild infections in the Netherlands in 2003.[5] To observe some transmission of H7N9 from human to human is therefore not surprising, and does not necessarily indicate that the virus is on course to develop sustained transmission among humans.

Nevertheless, several traits of H7N9 are of particular concern. The linked paper[2] comes close on the heels of studies showing airborne transmissibility of H7N9 between ferrets in the laboratory, a mammalian model.[6 7] Also, it is now well documented that owing to its non-lethality in birds, H7N9 can spread undetected through avian populations. In addition, Chinese surveillance data suggest that the number of confirmed human cases is just the tip of the iceberg—many mild cases are likely to have passed undetected.[8] The upside of this is that the actual fatality rate among H7N9 cases is likely to be substantially lower than that observed among confirmed cases.[9] The flipside is that the incidence of human infections, and therefore opportunities for H7N9 to adapt to humans or to re-assort through mixed influenza infections, could be much greater than for other bird flu viruses such as H5N1.

Although the number of H7N9 cases has fallen abruptly since April 2013, with no new cases reported for several weeks, we have been warned to expect a resurgence later in the year owing to seasonal effects on transmission.[10] Thus, while the paper by Qi and colleagues[2] might not suggest that H7N9 is any closer to delivering the next pandemic, it does provide a timely reminder of the need to remain extremely vigilant: the threat posed by H7N9 has by no means passed.

Competing interests: RC has received funding via research grants from Roche to the London School of Hygiene and Tropical Medicine of $1.8m over five years, to conduct surveillance on flu in Indonesia (on which JWR has also been involved), and $1m over four years to support a clinical registry of human cases of H5N1 in South East Asia. No other conflicts of interest are declared.

Provenance and peer review: Commissioned; not externally peer reviewed.

1 Li Q, Zhou L, Zhou M, Chen Z, Li F, Wu H, et al. Preliminary report: epidemiology of the avian influenza A (H7N9) outbreak in China. *N Engl J Med* 2013, doi:10.1056/NEJMoa1304617.
2 Qi X, Qian Y-H, Bao C-J, Guo X-L, Cui L-B, Tang F-Y, et al. Probable person to person transmission of novel avian influenza A (H7N9) virus in Eastern China, 2013: epidemiological investigation. *BMJ* 2013;347:f4752.
3 Wang H, Feng Z, Shu Y, Yu H, Zhou L, Zu R, et al. Probable limited person-to-person transmission of highly pathogenic avian influenza A (H5N1) virus in China. *Lancet* 2008;371:1427-34.
4 Ungchusak K, Auewarakul P, Dowell SF, Kitphati R, Auwanit W, Puthavathana P, et al. Probable person-to-person transmission of avian influenza A (H5N1). *N Engl J Med* 2005;352:333-40.
5 Du Ry van Beest Holle M, Meijer A, Koopmans M, de Jager CM. Human-to-human transmission of avian influenza A/H7N7, The Netherlands, 2003. *Euro Surveill* 2005;10:264-8.
6 Zhang Q, Shi J, Deng G, Guo J, Zeng X, He X, et al. H7N9 influenza viruses are transmissible in ferrets by respiratory droplet. *Science* 2013, doi:10.1126/science.1240532.
7 Belser JA, Gustin KM, Pearce MB, Maines TR, Zeng H, Pappas C, et al. Pathogenesis and transmission of avian influenza A (H7N9) virus in ferrets and mice. *Nature* 2013, doi:10.1038/nature12391.
8 Ip DK, Liao Q, Wu P, Gao Z, Cao B, Feng L, et al. Detection of mild to moderate influenza A/H7N9 infection by China's national sentinel surveillance system for influenza-like illness: case series. *BMJ* 2013;346:f3693.
9 Yu H, Cowling BJ, Feng L, Lau EH, Liao Q, Tsang TK, et al. Human infection with avian influenza A H7N9 virus: an assessment of clinical severity. *Lancet* 2013;382:138-45.
10 Centers for Disease Control and Prevention. Avian influenza A (H7N9) virus. 2013. www.cdc.gov/flu/avianflu/h7n9-virus.htm.

Cite this as: *BMJ* 2013;347:f4730

RESEARCH, p 9

bmj.com/blogs
- Krishna Chinthapalli: The birth and death of the Liverpool care pathway
- Readers' editor: The Liverpool care pathway—anyone care outside the UK?

bmj.com/poll
- Is the UK government right to scrap the Liverpool care pathway?

The Liverpool care pathway: a cautionary tale

Warns us of the dangers of implementing tools that are not properly evidence based

Katherine E Sleeman clinical lecturer in palliative medicine, King's College London, Department of Palliative Care, Policy and Rehabilitation, Cicely Saunders Institute, London SE5 9PJ, UK
katherine.sleeman@kcl.ac.uk
Emily Collis consultant in palliative medicine, Pembridge Palliative Care Centre, Central London Community Healthcare Trust, St Charles' Centre for Health and Wellbeing, London, UK

After a six month independent review commissioned by the minister of state for care support, Norman Lamb, a series of recommendations has been made to improve end of life care in England.[1] The review, led by Julia Neuberger, was prompted by press reports of poor end of life care associated with the Liverpool care pathway for the dying patient (LCP). The review panel concluded that in the light of numerous accounts from bereaved family members of poor care associated with the LCP, and without strong evidence of the pathway's potential benefits or harms, use of the LCP could no longer be justified. The panel recommended that the pathway should be phased out, and replaced within six to 12 months by individualised care plans and condition specific guidance.[2]

If used appropriately, the LCP can provide a model of good practice for the care of dying patients. However, undoubtedly some patients have received poor care in association with the pathway. The review panel was told of many experiences where communication was inadequate and patients seemed to have been over-sedated or denied food and drink.

Was this a failure of the paperwork or of its implementation? If implementation and training are key, would investment in these areas—rather than developing guidelines from scratch—be a more efficient use of resources? The lack of strong evidence of the LCP's benefits undermines this argument. However, the converse is also true: the absence of prospective evidence of harm should caution us against the assumption that simply withdrawing the LCP will improve end of life care.

How anecdote ruled

Ultimately, the decision to phase out the LCP was made on the basis of little more than an accumulation of anecdotal evidence. Without independent prospective evidence from controlled trials, the LCP became unusable. This should serve to warn us of the dangers of the national implementation of tools that are not properly evidence based. The recommendation by the panel to phase in condition specific guidance over the next six to 12 months should therefore be approached with caution. It is imperative that we do not repeat the same mistakes, and introduce new guidance without first testing it properly.

Correspondingly, the panel strongly recommended the need for investment in research, into both the biology and the experience of dying. Recent data from the National Cancer Research Institute show that in 2012, of £507m (€588m; $781m) spent on cancer research, just 0.31% went to end of life care.[3] In non-cancer conditions, spending on end of life research is likely to be even less. A stronger evidence base is needed to guide both policy and practice in end of life care. For such research, evaluation of patients' and families' outcomes, including their experience of care and quality of death, is essential; analysis of process is not an adequate proxy.

Retrospective national surveys of the bereaved consistently report that the quality of end of life care is poorer in hospitals than in hospices.[4] The well intentioned aim of the LCP was to bridge this gap by distilling the key elements of end of life care from the hospice setting, and transforming them into a series of prompts to guide care in hospitals and across community settings. But dying can be a complex process, and requires individual treatment decisions, with skilled staff, frequent senior review, and a supportive environment. By reducing end of life care to a series of prompts, did the LCP over-simplify the care of dying patients? Did the pathway's paperwork become a substitute for thought and care? Certainly, it seems possible in some cases. The LCP was rolled out rapidly across England as a key part of the National End of Life Care Programme and the End of Life Care Strategy. During this process, what was intended as a guide may have become interpreted by some as a protocol.

The hospice movement has shown us that it is possible to provide good care to people who are dying. The failure of the LCP has demonstrated that translating this care to other settings is far from straightforward. Publication of the review should be used as a catalyst to improve end of life care, through research, education, and investment in infrastructure. Healthcare professionals need to be provided with the knowledge, skills, and attitudes required to care for dying patients. In addition, they need a system that allows them time, continuity, and sufficient resources to support this care 24 hours a day, including access to senior support and specialist palliative care advice. The ability to communicate uncertainty and share decision making with patients and families is essential.

This is a cautionary tale. The LCP, once suggested as a model of good practice by the Department of Health, General Medical Council, and National Institute for Health and Clinical Excellence in the United Kingdom, is being phased out. It improved the deaths of some patients, but has been the focus of profound grief and regret for others. The independent review has made wide ranging and valuable recommendations to improve end of life care, with implications for healthcare practitioners, commissioners, and policy makers. As Neuberger and other members of the review panel identify, for end of life care to improve, we need to shift the focus away from process, and towards outcomes and experiences of care—as reported by patients, their loved ones, and carers.

Competing interests: None declared.

Provenance and peer review: Not commissioned; not externally peer reviewed.

1 Department of Health. More care, less pathway: a review of the Liverpool Care Pathway. July 2013. https://www.gov.uk/government/publications/review-of-liverpool-care-pathway-for-dying-patients.
2 Chinthapalli K. The birth and death of the Liverpool care pathway. *BMJ* 2013;347:f4669.
3 National Cancer Research Institute. CaRD 2012. 2013. www.ncri.org.uk/default.asp?s=1&p=3&ss=6.
4 Office for National Statistics. National bereavement survey (VOICES). 2012.

Cite this as: *BMJ* 2013;347:f4779

bmj.com

- Views and review: Tear gas is a chemical weapon, and Turkey should not use it to torture civilians (*BMJ* 2013;346:f3801)
- Views and reviews: Protests in Turkey, state violence, and how doctors are helping: it's about much more than a park (*BMJ* 2013;346:f3789)
- Analysis: Healthcare in Turkey: from laggard to leader (*BMJ* 2011;342:c745)

Attacks on medical personnel in Turkey

A call to honour medical ethics and end violations of medical neutrality

Vincent Iacopino senior medical adviser, Physicians for Human Rights (PHR), New York, NY, USA
Vivienne Nathanson director of professional activities, BMA, London WC1H 9JP, UK vnathanson@bma.org.uk
Otmar Kloiber secretary general, World Medical Association (WMA), Ferney-Voltaire, France
On behalf of nine other authors; full details available online

Doctors and other healthcare workers in Turkey, and the facilities in which they work, are facing sustained and intense attacks for treating patients injured during the current civil unrest in the country.[1]

By providing emergency assistance to the injured, medical workers in Turkey are fulfilling their duty under the International Code of Medical Ethics.[2] Had they not done so, they would have risked international condemnation, faced professional disciplinary proceedings, and violated the Turkish penal code.[3] Equally, as ethical practitioners, failing to provide such care would have breached the principles by which health workers practise and would have undermined their sense of responsibility to the society they serve. In the current circumstances, rendering treatment should be regarded as an ethical response to a need, not a political response to the unrest.

The Turkish government's response to the protests has included using tear gas as a weapon (firing directly at protestors at close range and in closed spaces), firing rubber bullets and live ammunition directly at protestors at close range, using water cannons spiked with tear gas, and beating and detaining hundreds of protestors.[1] Many people have been injured and needed medical help. At the same time, the Turkish Medical Association,[4] the Human Rights Foundation of Turkey,[5] and Physicians for Human Rights[1] have gathered evidence of law enforcement officials deliberately attacking identifiable medical personnel and facilities with tear gas, water cannons, and rubber bullets. Police have detained dozens of doctors and other medical personnel for providing emergency care to those injured by the police.

According to Physicians for Human Rights,[1] the Ministry of Health has not only failed to provide adequate medical care to injured demonstrators—as it routinely does in other medical emergencies—but has also required medical personnel to report the names of injured demonstrators. This is in clear breach of the ethical obligation to respect patient confidentiality.

AHMET SIK/EPA/CORBIS

How to fall foul of the Turkish authorities

The Turkish government's response shows a lack of any understanding of medical neutrality and its central position in the practice of medicine. States need to understand the importance of medical neutrality, not only in everyday practice but also during unusual and extreme events. Medical neutrality ensures that healthcare workers treat patients according to need rather than according to any judgment of worthiness.

Given that health workers make decisions about treatment priorities every day, it is essential that patients and populations trust that those decisions are based on need. Triaging treatments is one example of such decision making, but it exists less overtly when decisions to order tests, or refer for further treatment, are made. If patients and their relatives believe that such decisions are based on judgments of worthiness, rather than need, they will stop cooperating in the medical triage systems that allow every healthcare system to function effectively.

It is alarming that a health bill, recently submitted by the Ministry of Health to the Turkish parliament, will—if passed—criminalise the provision of unlicensed or unauthorised emergency medical care, not only to demonstrators, but to anyone in need of emergency medical assistance in Turkey. The requirements of this law would put doctors in direct conflict with their ethical and professional obligations to provide care to those in need. Civil unrest inevitably puts health workers in a difficult position. By responding to medical need—their ethical duty—they may find themselves in danger.

The role of governments is clear. They are required to do their best to protect healthcare facilities, the workers offering care, and the patients to whom care is being offered. Failing to do so shows a disregard for human life and dignity that may exacerbate the conflict that led to the medical need in the first place.

International standards in human rights and medical ethics make it clear that doctors, nurses, paramedics, and other health workers must be able to carry out their professional responsibilities to provide emergency medical care to those in need without interference or fear of reprisal. The Turkish government has a duty to support and protect health workers who are discharging their moral, ethical, and professional responsibilities to provide care for the sick and injured.

The international medical community must respond strongly to this attack on medical neutrality. We urge doctors to join Physicians for Human Rights, the World Medical Association, the BMA, the Standing Committee of European Doctors, and the German Medical Association (Bundesärztekammer) in signing a letter to Prime Minister Recep Tayyip Erdoğan and the Turkish government, urging them to halt attacks on independent medical personnel who provide care to the injured (http://physiciansforhumanrights.org/turkey-action).

Competing interests: None declared.

Provenance and peer review: Not commissioned; not externally peer reviewed.

References are in the version on bmj.com.

Cite this as: *BMJ* 2013;347:f4933