Inside The BMJ:
highs, lows, & what editors are looking for

EQUATOR Network and Oxford Clinical Trials Unit

9 March 2015

Dr Trish Groves
Head of research, BMJ
& Editor-in-chief, BMJ Open
Competing interests

I’m editor in chief of BMJ Open and Head of Research at The BMJ, a wholly owned subsidiary of the BMA.

BMJ (the company) receives revenues from drug & device manufacturers through advertising, reprint sales, & sponsorship.

I receive a bonus based partly on the financial performance of The BMJ. Both The BMJ and BMJ Open publish all research with open access, supported by article publication fees.

The BMJ was a co-founder of the AllTrials campaign; I’m on the steering group. I’m also on the steering group of the EQUATOR Network.

The BMJ is campaigning for reproducible research.
What I’ll cover

- a few highs and lows from The BMJ
- what editors look for
- how to get your work published
  - choosing a journal
  - writing papers effectively
  - responding to reviewers
  - publication ethics
Is stockpiled oseltamivir a white elephant *?

*A possession that is useless or troublesome, especially one that is expensive to maintain or difficult to dispose of.

Oxford English Dictionary

April 2014
Oxeltravir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments

Tom Jefferson,1 Mark Jones,2 Peter Doshi,3 Elizabeth A Spencer,1 Igno Ons Urg,1 Carolyne Heneghan1

STUDY QUESTION
What is the regulatory evidence from randomised controlled trials of effectiveness and harms of oxeltravir for influenza in all age groups?

SUMMARY ANSWER
Oxeltravir shows a duration of influenza-like illness symptoms in treatment of adults and non-asthmatic children and prevents their appearance in prophylaxis, but also causes vomiting and nausea and increases the risk of headache and renal and psychiatric syndromes. It has no significant effect on hospitalisations, and its effects on pneumonia are unclear because of the lack of a verification outcome.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS
Neuraminidase inhibitors are used globally for treatment and prophylaxis of influenza, but the evidence for their effectiveness in preventing complications of influenza is sparse and significant regarding their adverse events is lacking. To address reporting bias in trials of oxeltravir, we included only full clinical study reports of randomised controlled trials and relevant regulatory comments (n = 150 000 papers), the first time that such methods have been used in a Cochrane review to our knowledge.

Selection criteria for studies
We examined clinical study reports of randomised controlled trials that tested the effects of oxeltravir for prophylaxis and treatment of influenza in healthy people or the chronically ill who have symptoms of influenza-like illness. These were among reports during drug testing.

Primary outcome(s)
We considered symptom reduction, compliance.

Main results and role of chance
In trials of treatment of influenza, oxeltravir had modest symptomatic effects. It reduced the time to first alleviation of symptoms in adults by 16.7 days (95% CI 9.4 to 25.1, P = 0.001). It had no effect in asthmatic children, but did in otherwise healthy children (mean difference 29 hours [1.2 to 67], P = 0.001). There was no difference in hospitalisation in adults, and sparse data in children. Secondary illness data (such as “pneumonia”) were captured by participant self-reporting to the investigator in 15/20 trials. Oxeltravir reduced investigator mediated, unverified “pneumonia” in treated adults, but the effect was not significant in the five trials that used a more detailed diagnostic process for pneumonia. The effect in children was not significant, and there was no significant reduction in risk of any other self-reported, investigator mediated, recognised complication of influenza. In treatment of adults oxeltravir increased the risk of nausea (risk difference 3.66% [0.9 to 7.19]), vomiting (4.56% [2.99 to 7.10]), and in treatment of children it induced vomiting (risk difference 3.59% [1.15 to 6.09]). In prophylaxis trials, oxeltravir reduced the proportion of symptomatic influenza in individuals by 55% (risk difference 3.05% [1.83 to 4.38]). However, it also increased the risk of psychiatric adverse events on and off treatment (risk difference 1.06% [0.07 to 2.16]), hospitalisation on treatment (5.15% [0.88 to 7.83]), renal events on treatment (3.67% [1.19 to 6.13]), and nausea on treatment (4.96% [1.95 to 8.15%]).

Bias, confounding and other reasons for caution

When using this data, please cite the original publication:

Additionally, please cite the Dryad data package:
Tamiflu data: Who saw what when

See all correspondence with the following organisations:

- Roche
- The World Health Organization (WHO)
- Centers for Disease Control and Prevention
- The European Medicines Agency
- The European Ombudsman
- National Institute for Health and Clinical Excellence

New! - Tamiflu timeline
The AllTrials petition has been signed by 532 organisations.
AllTrials campaign

THE PROBLEM

Thousands of clinical trials have not reported results. Information on what was done and what was found in these trials could be lost forever to doctors and researchers, leading to bad treatment decisions, missed opportunities for good medicine, and trials needlessly repeated.

WHAT ARE PEOPLE DOING?

• since January 2013 >80,000 individuals have signed the petition
• the campaign has directly influenced policies on clinical trial transparency in the UK, EU, US and Canada
• AllTrials now auditing pharma transparency and working with investors’ groups
Smoking and tobacco

Systematic review and meta-analysis of opioid antagonists for smoking cessation

Sean P David1,2, Isabella M Chu2, Tim Lancaster3, Lindsay F Stead4, A Eden Evins6, Judith J Prochaska5

Author Affiliations

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Research

Trajectories of risk after hospitalization for heart failure, acute myocardial infarction, or pneumonia: retrospective cohort study

BMJ 2015;350 doi: http://dx.doi.org/10.1136/bmj.h411 (Published 06 February 2015)

Cite this as: BMJ 2015;350:h411

Open review
Financial incentives for smoking cessation in pregnancy: randomised controlled trial

BMJ 2015; 350 doi: http://dx.doi.org/10.1136/bmj.h134 (Published 27 January 2015)
Cite this as: BMJ 2015;350:h134

A larger context for considering the Tappin et al. report on financial incentives for smoking cessation in pregnant and newly postpartum women

We commend Dr. Tappin and colleagues on an important study and report. As is carefully reviewed in their report, smoking during pregnancy and postpartum is associated with many serious adverse maternal and infant health outcomes. Yet after almost 30 years of treatment development research in this area, there remains a tremendous need for more effective interventions. The Tappin et al.
Patient peer review: making research more relevant to shared decision making

Guidance for BMJ patient reviewers

Patient peer review at *The BMJ*

If you’re a patient living with disease, a carer of a patient, a patient advocate acting on behalf of a patient group, or you play a leading part in advocating for patient participation and partnership in healthcare we’d like to invite you to take part in a unique initiative. The BMJ has committed to improving the relevance and patient centredness of its research, education, analysis, and editorial articles by asking patients to comment on them. We need your help to make these changes.

If you already review for The BMJ as a researcher or clinician, but you are also interested in reviewing as a patient or patient advocate, you can do this too. We will, however, need you to register a new additional account with a different personal email address, using the guidance below so that we can distinguish your role as a patient reviewer versus a traditional peer reviewer.
Data sharing: 100 linked datasets
**The Facts in the Case of Dr. Andrew Wakefield**

And we're a long way from the pre-Enlightenment middle ages.

The world has been transformed by scientific knowledge.

Yet suspicion of science seems never to have been higher.

Fear and anger have obliterated rational discourse.

Facts and evidence are seen as just a matter of opinion, rather than a proven truth.

A British former surgeon, best known for his work regarding the measles, mumps, and rubella vaccine.

Wakefield was the lead author in a paper published in the Lancet.

The paper reported a study of twelve children all diagnosed with autism.

The Lancet

To which the authors suggested a link with the MMR vaccine.

During a press conference, Wakefield stated that giving children the vaccine in three separate doses...

Wold be safer than a single vaccination.

The suggestion was not supported by the paper, and subsequent peer review studies...

This began a global health scare.

Fear spread among parents who were unsure what immunisation choices to make.

And parents of autistic children began to question the MMR vaccination.

He was fine before that first jab.

By 1998, health bodies in the United Kingdom, the United States, Canada, Australia, and many other countries were reporting outbreaks of measles.

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Darryl Cunningham

http://student.bmj.com/student/view-article.html?id=smj.d355&locale=en_US
HOW THE LINK WAS FIXED
The *Lancet* paper was a case series of 12 child patients; it reported a proposed “new syndrome” of enterocolitis and regressive autism and associated this with MMR as an “apparent precipitating event.” But in fact:

- Three of nine children reported with regressive autism did not have autism diagnoses at all. Only one child clearly had regressive autism.
- Despite the paper claiming that all 12 children were “previously normal,” five had documented pre-existing developmental concerns.
- Some children were reported to have experienced first behavioural symptoms within days of MMR, but the records documented these as starting some months after vaccination.
- In nine cases, unremarkable colonic histopathology results—note no or minimal fluctuations in inflammatory cell populations—were changed after a medical school “research review” to “non-specific colitis.”
- The parents of eight children were reported as blaming MMR, but 11 families made this allegation at the hospital. The exclusion of three allegations—all giving times to onset of problems in months—helped to create the appearance of a 14 day temporal link.
- Patients were recruited through anti-MMR campaigners, and the study was commissioned and funded for planned litigation.
A lighter note

Published 27 January 2009. doi:10.1136/bmj.b288
Cite this as: BMJ 2009;338:b288

Letters

Cello scrotum confession

Murphy's lore

Perhaps after 34 years it's time for us to confess that we invented cello scrotum.¹

Reading Curtis's 1974 letter to the BMJ on guitar nipple,² we thought it highly likely to be a spoof and decided to go further by submitting a letter pretending to have noted a similar phenomenon in cellists, signed by the non-doctor one of us (JMM). Anyone who has ever watched a cello being played would realise the physical impossibility of our claim.

Somewhat to our astonishment, the letter was published.³ The following Christmas we sent a card to Dr Curtis of guitar nipple fame, only to discover that he knew nothing about it—another joke we suspect.

We have been dining out on this story ever since. We were thrilled once more to be quoted in "A symphony of maladies."¹

Cite this as: BMJ 2009;338:b288

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References

What do editors look for?

Importance and relevance
Potential to improve decisions
And...
How to choose a journal: factors to consider

- journal scope, reach, & readers
- indexed, peer reviewed
- Impact Factor **
- open access or not?
- and...
  - rejection rate
  - time to decision; time to publication
  - article length restrictions
  - charges: OA publication fees, pages, colour

** Impact factor is used as a measure of the academic usefulness of a journal

IF = recorded number of citations in a year (e.g., 2010) to scholarly articles in the journal in preceding two years (e.g., 2008 and 2009)

BMJ 2012 IF 17.2
Always consider inquiring when you’re:

- unsure about suitability for the journal
- seeking rapid review/publication
- wanting to explain special circumstances

Provide sufficient study information:

- article abstract
- perceived value to journal audience
- relationship of study to existing body of work
What does The BMJ prioritise?

Original, robust research studies that can improve doctors’ decision making in medical practice, policy, education, or future research and will be important to general medical readers internationally.

The BMJ’s purpose: “Answering questions; questioning answers”
Writing research papers

What is a research question?

The researcher asks a very specific question and tests a specific hypothesis. Broad questions are usually broken into smaller, testable hypotheses or questions.

Often called an objective or aim, though calling it a question help to focus the hypothesis and think about how to find an answer.
Introduction: why ask this research question?

Methods: what did I do?

Results: what did I find?

And

Discussion: what might it mean?
IMRaD format

- Introduction
- Methods
- Results
- Discussion

Scientific method

1. Ask question, do background research, develop hypothesis
2. Test hypothesis
3. Analyse your data
4. Interpret your findings
Introduction

Brief background for this audience
  • 3-4 paragraphs only: mind the word limit
  • what’s known/not known on research question
  • don’t bore readers, editors, reviewers
  • don’t boast about how much you have read

The research question
  • state it clearly in last paragraph of introduction
  • say why the question matters
Novelty and originality: why the literature search matters

“To be perfectly original one should think much and read little, and this is impossible, for one must have read before one has learnt to think.”

But cite only the most relevant studies in the introduction – those that explain why the question adds to knowledge, and why it matters now.
Does the research question fill an evidence gap?

"Research funders should make information available about how they decide what research to support, and fund investigations of the effects of initiatives to engage potential users of research in research prioritisation."

How to increase value and reduce waste when research priorities are set. Chalmers I, Bracken MB, Djulbegovic B, Garattini S, Grant J, Gülmezoglu AM et al. The Lancet Volume 383, Issue 9912, Pages 156-165 (January 2014) DOI: 10.1016/S0140-6736(13)62229-1
• descriptive studies answer “what’s happening?”
• analytic observational studies answer “why or how is it happening?”
• analytic experimental studies answer “can it work?”
Where do other study designs fit in?

- Experimental non-randomised studies e.g. lab studies, phase I trials
- Before and after studies
- Modelling studies
- Genetic association and risk prediction studies
Methods

Like a recipe; should be reproducible
Most important section for informed readers

Describe:

• PICO/PECO
• all methods – with references where appropriate
• statistical methods – follow SAMPL guidelines
• sample size calculation

Follow reporting guidelines at EQUATOR Network
http://equator-network.org
Describe measures to ensure ethical conduct
Reporting guidelines for many types of study
• use the reporting guideline to help you write or edit your manuscript: remember, it’s a minimum set
• if guideline includes a flowchart, make it figure 1
• complete the checklist, with page numbers to show where items appear in your manuscript
• if items are irrelevant or weren’t done, explain why
• submit your completed checklist with your paper, if the journal requests it
Nature checklist to improve design and reporting of life sciences studies

Statistics and general methods
1. Sample size
2. Inclusion/exclusion for samples
3. Method of randomization if used to determine how samples/animals were allocated to experimental groups
4. Blinding/masking if used
5. Are statistical tests justified and appropriate?

http://www.nature.com/authors/policies/checklist.pdf
• report results fully & honestly, as prespecified
• text (story), tables (evidence), figs (highlights)
• report primary outcomes first
• give confidence intervals for main results
• report essential summary statistics
• leave out non-essential tables and figures
• don’t start discussion here
Primary analyses
• describe purpose of analysis
• identify variables
• identify smallest clinically relevant difference
• describe fully each method to analyse main objectives of study
• verify that data conformed to test assumptions eg skewed data were analysed with non-parametric tests
• indicate how any allowance was made for multiple comparisons
• indicate how any outlying data were treated in the analysis
• state whether tests were one-tailed or two-tailed and justify this
• report the alpha level eg 0.05 that denoted statistical significance
• name the statistical software used
• The guidelines also cover preliminary and supplementary analyses
Structured discussion

Don’t simply repeat the introduction. Include:

• statement of principal findings
• strengths & weaknesses of the study
• strengths & weaknesses in relation to other studies (especially systematic reviews), & key differences
• possible mechanisms & explanations for findings
• potential implications for clinicians or policymakers
• unanswered questions and future research
Abstract: general rules

very important

often only part of study that will be read

must be accurate & not hyped

all authors must approve it

editors may screen papers by reading only the abstracts

for The BMJ abstracts need:

• 300-400 words
• structured format
• active voice
• results plus p values
• %s with denominators
• no references
• trial registration details
“Spin,” defined as specific reporting strategies (intentional or unintentional) emphasizing the beneficial effect of the experimental treatment, was identified in about half of press releases and media coverage.

In multivariable analysis, the main factor associated with “spin” in press releases was the presence of “spin” in the article abstract conclusion.

Abstracts as haikus

Use of caffeinated substances and risk of crashes in long distance drivers of commercial vehicles (BMJ 2013;346:f1140).

Long and winding road, caffeinated trucker: No happy ending —Francis Toolis

Unhealthy behaviours and disability in older adults (BMJ 2013;347:f4240).

Fit, fruit-fed, no cigs: Old able. Autumn leaves fall Slowly, gracefully —Jeremy Holmes
Never use a metaphor, simile or other figure of speech which you are used to seeing in print [a cliché]

Never use a long word where a short one will do

If it is possible to cut out a word, always cut it out

Never use the passive where you can use the active

Never use a foreign phrase, a scientific word or a jargon word if you can think of an everyday [English] equivalent

Orwell G. Politics and the English language. 1946
Marginalized
Notes in manuscripts and colophons
made by medieval scribes and copyists

~ New parchment, bad ink;
   I say nothing more.

~ I am very cold.

~ That's a hard page and a
   weary work to read it.

~ Let the reader's voice
   honor the writer's pen.

~ This page has not been
   written very slowly.

~ The parchment is hairy.

~ The ink is thin.

~ Thank God, it will
   soon be dark.

~ Oh, my hand.

~ Now I've written
   the whole thing: for
   Christ's sake give me
   a drink.

~ Writing is excessive
   drudgery. It crooks your
   back, it dims your sight,
   it twists your stomach
   and your sides.

~ St. Patrick of Armagh,
   deliver me from writing.

Sentences you will probably never
read in a published paper:

"We were totally surprised it worked!"

"We just thought it'd be a neat thing to do."

"I'm only doing this to get tenure."

"Oops."

"Previous work by XXX et al. is actually pretty good!"

"To be honest, we came up with the hypothesis
after doing the experiment."

"The results are just 'OK'."

"Future work will... ah, who are we kidding?
We won't get more funding to do this."
Publication ethics
“No, it’s my wife’s turn to be the first author on your paper.”
ICMJE authorship rules

Authorship credit must be based on substantial contributions to:

- conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- drafting the work or revising it critically for important intellectual content; AND
- final approval of the version to be published; AND
- agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Authors
- should be able to identify which co-authors are responsible for specific other parts of the work
- should have confidence in the integrity of the contributions of their co-authors
- must fulfil the criteria; no one who fulfils the criteria should be excluded
- should have participated sufficiently to take public responsibility for appropriate portions of the content.

Acquisition of funding, collection of data, or general supervision of the research group alone does not constitute authorship.
A person has a **competing interest** when he or she has an attribute that is **invisible** to the reader or editor but which **may** affect his or her judgment.

Always declare a competing interest, particularly one that would embarrass you if it came out afterwards.

http://www.icmje.org/coi_disclosure.pdf
Fabrication: making up data or results and recording or reporting them

Falsification: manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record

Plagiarism: the appropriation of another person's ideas, processes, results, or words without giving appropriate credit
<table>
<thead>
<tr>
<th>Type of reporting bias (in reporting results of research)</th>
<th>Definition – all depending on nature and direction of results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Publication bias</td>
<td>Publication or non-publication</td>
</tr>
<tr>
<td>Time lag bias</td>
<td>Rapid or delayed publication</td>
</tr>
<tr>
<td>Multiple/duplicate publication bias</td>
<td>Multiple or singular republication, depending</td>
</tr>
<tr>
<td>Location bias</td>
<td>Publication in journals with different ease of access or levels of indexing in standard bibliographic databases, depending on nature and direction</td>
</tr>
<tr>
<td>Citation bias</td>
<td>Citation or non-citation</td>
</tr>
<tr>
<td>Language bias</td>
<td>Publication in a particular language</td>
</tr>
<tr>
<td>Outcome reporting bias</td>
<td>Selective reporting of some outcomes</td>
</tr>
</tbody>
</table>

Cochrane handbook for systematic reviews of interventions, 2008. Chapter 10
Incomplete reporting of results = misconduct

"...If one assesses the sins they have ranked in terms of their potential for doing harm to patients, biased reporting of research surely has far more serious practical consequences than undeserved authorship and plagiarism."

Iain Chalmers
James Lind Initiative, Oxford

Lancet 2006;368:450

*Magnh Nylenæ, Sigmund Simonsen
Department of Public Health and General Practice, Norwegian University of Science and Technology, N-7489 Trondheim, Norway
Lancet 2006;367:1882-4
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 Twitter website combines social networking and microblogging, wherein members are asked a question and they respond with a maximum of 140 characters.

Some people think Twitter is trivial, but you'd really be surprised at how much information people can pack into those 140 characters.

It is used many ways.

Using a two-alternative forced-choice oddity task, we measured the ability of human listeners to detect local time reversals in a marmoset twitter call.

From Asian disasters to SoCal wildfires, Twitter has often been the first source for vital updates.
These apparently duplicated images have been used as evidence for the presence of different proteins produced in different experiments.

1. First, an image of three bands on a gel is used to represent a control for an experiment in which stem cells are made to differentiate into bone cells (*Blood*, vol 98, p 2620).

2. On the same page of the *Blood* paper, a reversed version of the same image, with some small modifications, is used to show the production of collagen II in stem cells made to differentiate into cartilage cells.

3. The same reversed image is used in US patent 7015037 to show the production of a bone-specific protein in stem cells made to differentiate into bone cells.
Committee on Publication Ethics: advises editors of >5000 journals

COPE is a forum for editors and publishers of peer reviewed journals to discuss all aspects of publication ethics. It also advises editors on how to handle cases of research and publication misconduct. Read more about COPE.

FEATURED
COPE Digest: Publication Ethics in Practice. May 2014

The May issue of COPE Digest has now been published, and contains a round up of what has been happening in publication ethics as well as news from COPE. Do click on the link below to view.

Learn more

NEWS & OPINION view all

News / COPE North American seminar 13 August 2014
13/5/2014 4.49pm
Register for COPE’s 5th North American seminar, which will be held in collaboration with ISMTE (International Society of Managing & Technical Editors), on Wednesday 13 August 2014 at the Hyatt Regency Philadelphia at Penn’s Landing, Philadelphia, Pennsylvania, USA. For more details and to register, see here.

News / COPE Australian Seminar 23 June 2014
13/5/2014 2.37pm
COPE is delighted to announce its 3rd Australian Seminar, which will take place at the Karstens Melbourne Conference Rooms, 123 Queen Street, Melbourne, Australia, on Monday 23 June 2014. The theme of the seminar is “Publication ethics from student to professional”. For more information and to register, click here.

Cases

All the cases COPE has discussed since its inception in 1997 have been entered into a searchable database. This database now contains over 400 cases together with the advice given by COPE.

http://publicationethics.org/
Surviving peer review
The BMJ’s peer review process

- **Research submitted**
  - Up to 4000 annually

- **Screen**
  - 3000 rejected

- **External review**
  - Approx 1000 for open review
  - 500 then rejected

- **Editorial meeting**
  - 500 with Editor and adviser, statistician, BMJ team

- **Accept**
  - 4-7% with Open access
  - No word limits
  - BMJ pico Editorials
Peer reviewers’ signed comments and authors’ responses available for all published papers.
Be confident at resubmission

Most reviewers & editors want to be helpful

Follow journal instructions

Address all comments; but need not agree with all

Avoid easy fixes/shortcuts

If rejected; tell next journal how you addressed reviewers’ comments
Thank you

tgroves@bmj.com

@trished

THINGS GOT REALLY INTERESTING WHEN THE STATISTICIAN STARTED DOING WARD ROUNDS