Good scientific practice (malpractice)
Why research misconduct matters

- It undermines public trust in medical research and health sciences
- It corrupts the scientific record and could lead to false conclusions later – papers are not always removed from journal websites
- Most countries do not have good systems of either treatment or prevention
Research misconduct is significant misbehaviour that improperly appropriates the intellectual property or contributions of others, that intentionally impedes the progress of research, or that risks corrupting the scientific record or compromising the integrity of scientific practices. Such behaviours are unethical and unacceptable in proposing, conducting, or reporting research, or in reviewing the proposals or research reports of others.
Definition of research misconduct proposed by a British consensus panel (1999)

- "Behaviour by a researcher, intentional or not, that falls short of good ethical and scientific standards."
Examples of research misconduct (ranked by seriousness)

- Fabrication: invention of data or cases
- Falsification: wilful distortion of data
- Plagiarism: copying of ideas, data or words without attribution
- Failing to get consent from an ethics committee for research
examples

This is mean ± sem. Imagine what the sd looks like!

Misrepresenting data or giving it a very favourable interpretation – if it doesn’t look significant it probably isn’t
If there is strange cutting and pasting and what looks like manipulation of the background you should suspect something
A preliminary taxonomy of research misconduct (ranked by seriousness)

- Not admitting that some data are missing
- Ignoring outliers without declaring it
- Not including data on side effects in a clinical trial
- Conducting research in humans without informed consent or without justifying why consent was not obtained from an ethics committee
A preliminary taxonomy of research misconduct (ranked by seriousness)

- Publication of post hoc analyses without declaration that they were post hoc
- Gift authorship or honorary authorship
- Not attributing other authors
- Redundant publication
- Not disclosing a conflict of interest
A preliminary taxonomy of research misconduct (ranked by seriousness) IV

- Not attempting to publish completed research
- Failure to do an adequate search of existing research before beginning new research
Examples: August 1996: a major breakthrough

- Worldwide media coverage of doctors in London re-implanting an ectopic pregnancy and a baby being born

- Doctors had been trying to do this for a century. It was a huge achievement
August 1996: a major breakthrough

- Achieved by Malcolm Pearce, a senior lecturer in at St George’s Hospital Medical School in London
- A world famous expert on ultrasonography in obstetrics
- From a paper in the *British Journal of Obstetrics and Gynaecology*. Pearce was an assistant editor.
August 1996: a major breakthrough

- A second author on the case report was Geoffrey Chamberlain, editor of the journal, president of the Royal College of Obstetricians and Gynaecologists, and professor and head of department at St George’s.
Autumn 1996: both papers are fraudulent

- A front page story in the Daily Mail exposed the two papers as fraudulent.
- Chamberlain said it was common within medicine for people to have their name on papers when they hadn’t done much.
What had happened?

● All the papers were retracted. Questions about ones before that.

● Pearce was fired and subsequently struck off by the General Medical Council.

● Chamberlain retired or resigned from all his positions, a terrible end to a distinguished career.

● His crime was gift authorship, which was normal at the beginning of his career, but scandalous by the end.
News

Nature 439, 122-123 (12 January 2006)
Published online 11 January 2006

Verdict: Hwang's human stem cells were all fakes
Korean scientist did not clone a human embryo but did clone a dog.
How common is fraud?

- Obviously depends on how fraud is defined

- How does serious fraud relate to minor fraud?
  - Are they quite separate?
  - Does minor progress to serious?
Study by Stephen Lock

- Asked 80 researchers who were friends, mostly British and mostly professors of medicine. Not a random sample.
- 100% response rate.
- Over half knew of cases:
- Over half the dubious results had been published - only 6 “retractions” - all vague and not using that term
How common is fraud?

- US congressional inquiry heard of over 700 cases
- The British General Medical Council has dealt with over 30 cases
- Committee on Publication Ethics has discussed over a 100 cases
How common is research misconduct?

- Redundant publication occurs in around a fifth of published papers.
- About a fifth of authors of studies in medical journals have done little or nothing.
- Many authors of studies in medical journals have conflicts of interest, yet they are declared in less than 5% of cases.
Conflict of interest: a case study
How common are competing interests?

- 75 articles
- 89 authors
- 69 (80%) responded
- 45 (63%) had financial conflicts of interest

**Only 2 of 70 articles disclosed the conflicts of interest**

Why don’t authors declare conflicts of interest?

- Some journals don’t require disclosure
- The culture is one of not disclosing
- Authors think it looks bad
- Authors are confident that they are not affected by conflicts of interest
Does conflict of interest matter?

- Financial benefit makes doctors more likely to refer patients for tests, operations, or hospital admission, or to ask that drugs be stocked by a hospital pharmacy.
- Original papers published in journal supplements sponsored by pharmaceutical companies are inferior to those published in the parent journal.
- Reviews that acknowledge sponsorship by the pharmaceutical or tobacco industry are more likely to draw conclusions that are favourable to the industry.
Does conflict of interest matter?

- 106 reviews, with 37% concluding that passive smoking was not harmful and the rest that it was.
- Multiple regression analysis controlling for article quality, peer review status, article topic, and year of publication found that the only factor associated with the review's conclusion was whether the author was affiliated with the tobacco industry.
- Only 23% of reviews disclosed the sources of funding for research.

- Barnes DE, Bero LA. Why review articles on the health effects of passive smoking reach different conclusions. JAMA 1998; 279: 1566-1570
Why does scientific fraud happen?

- Why wouldn’t it happen? It happens in all other human activities.
- Pressure to publish.
- Inadequate training. Not taught good practice. Indeed, sometimes taught the opposite.
- Does sloppy behaviour spill over to fraud?
- You can get away with it. The system works on trust.
What does a country need to respond to research misconduct?

- A recognition of the problem by the medical community and its leaders
- An independent body to lead with investigations, prevention, teaching and research
- An agreement on what fraud is
- Protection for whistleblowers
- A body to investigate allegations
- A fair system for reaching judgements
- A code of good practice
- Systems for teaching good practice
MMR Vaccine and Autism: a recent example
Background

- A paper published by a medical doctor in Lancet reported that a small cohort of patients – 12 children – had bowel and brain problems stemming from vaccination with the combined measles mumps rubella MMR vaccine.
Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

Paper published in February, 1998
‘findings’

- The paper claimed that the 12 patients had not only an inflammatory bowel disease but a loss of language function – basically an acquired autism.

- A single study with 12 patients caused a worldwide scare – lasting 10 years.
Interestingly, Wakefield who became the champion of the anti-vaccine lobby – was not pushing for no vaccine – he was pushing for single vaccines.

In both UK and US vaccination rates dropped – 60 minutes ran an episode entitled ‘An epidemic of autism’ etc. etc.
Conflict of interest

- 2 years before the Lancet paper – Wakefield had been hired by a lawyer to help attack the MMR vaccine – the lawyer was hoping to start a class action against the companies that manufacture the vaccine
- Wakefield earned £435,000 plus expenses and £55,000 up front – never declared to Lancet
Conflict of interest

- In total £18 million was shared among a group of doctors and lawyers trying to prove a link.

- Wakefield predicted a link and predicted the existence of a syndrome ‘autistic enterocolitis’ before he started doing any research.
Conflict of interest

- To make matters worse, he filed a patent on a supposedly safer single measles vaccine – which would wipe the MMR vaccine off the market
The patients

- 12 children supposedly routine series with developmental and digestive disorders who presented at a London hospital

- In fact, the 12 were recruited via MMR anti-vaccine campaign groups – none lived in London, one was flown in from the US
Clinicians and hospital pathology had found no data supporting a link with vaccination.

Delving into patient records showed in most cases that Wakefield had changed and misreported diagnoses.

When re-interviewed, families admitted that autism symptoms, seizures etc. were apparent in children **before** vaccination.
Data

- In reality, none of the 12 cases stood up to scrutiny, either showing symptoms before vaccination, showing no signs of autism after vaccination or never showing signs of autism.
Consent and ethics

- Wakefield reported that the patients – who were from 2 – 9 years old, had been subjected to a battery of procedures including anaesthesia, colonoscopy, lumbar puncture, brain scans, EEG, radioactive drinks and x-rays – this was done without ethics approval.
Sophisticated molecular techniques showed no evidence of measles virus in the children’s gut or blood – even Wakefield’s own experimental data.

No other labs were able to show similar findings – yet vaccination levels dropped and there were the first reported deaths from measles in Britain in 14 years.
outcome

- Wakefield eventually was struck off in the UK
- In the US took a $280,000 a year job with an anti-vaccination institute
- Took a 2 year libel suit against the newspaper and journalist
outcome

- 28 January, 2010 – found guilty of 36 charges of dishonest and unethical behaviour, 12 involving the abuse of developmentally-challenged children

- 5 days later Lancet finally retracted the paper
First part on fraud is largely based on a lecture by Professor Richard Smith, Editor of the British Medical Journal on publication ethics and the committee on publication ethics (COPE) http://www.publicationethics.org/resources

- Brian Deer, investigative journalist who published MMR investigation in the Sunday Times and British Medical Journal

http://briandeer.com/

http://www.bmj.com/content/342/bmj.c5347