Tales of Deception
Falsification and Fabrication of Clinical Research Data

Kristen Grace, M.D., Ph.D.
Division of Investigative Oversight (DIO)
Office of Research Integrity (ORI)
NIH Clinical Center Grand Rounds
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• Is this decision really in the best interest of the potential research subject?
• What are the consequences:
  • To the research subject?
  • To the researcher?
  • To the institution?
  • To science?
  • To society?
Data and Safety Monitoring Plans
Andrew Wakefield
Former gastroenterologist
Graduate of the Imperial College School of Medicine, 1981
Fellow of the Royal College of Surgeons, 1995

- Early work linking measles virus and Crohn’s disease
- 1998 - "Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children". _Lancet_ 351
RETRACTED: Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

Dr AJ Wakefield FRCS a, SH Murch MB b, A Anthony MB a, J Linnell PhD a, DM Casson MRCP b, M Malik MRCP b, M Berelowitz FRCPsych c, AP Dhillon MRCPath a, MA Thomson FRCP b, P Harvey FRCP d, A Valentine FRCR e, SE Davies MRCPath a, JA Walker-Smith FRCP a

Summary

Background
We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods
12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.
Parag Patel, DO
Interventional Cardiologist, Cardiology Fellowship Director
Advocate Health Care, Park Ridge IL

- Vest Prevention of Early Sudden Death Trial (VEST).
- Multi-center randomized, controlled trial to test the hypothesis that a non-invasive wearable automatic defibrillator vest will reduce sudden death mortality on the first 60 days following a myocardial infarction in participants with a LVEF equal or less that 35%.
Parag Patel, DO
Interventional Cardiologist, Cardiology Fellowship Director
Advocate Health Care, Park Ridge IL

• Initially funded with an NIH grant and co-funded by Medtronic, GE Healthcare and Zoll-LifeCor.
• NIH eventually pulled funding due to low and difficult enrollment.
• Advocate was continually one of the highest enrolling centers.
Parag Patel, DO
Interventional Cardiologist, Cardiology Fellowship Director
Advocate Health Care, Park Ridge IL

- Corporate sponsors provided iPads, honorariums and travel to highest enrollers.
- Patel’s cardiac fellowship program was provided with a corporate sponsored cardiac anatomy lab.
During the course of a Cardiac Fellowship program review fellows complained that Patel was directing the fellows and attending's to change LVEF scores in order for patients to qualify for inclusion into the study. The fellows reported that some people felt threatened and felt uncomfortable being asked to do this and that both the fellows and some of the attendings felt intimidated.
“ORI and Advocate Health Care found that the Respondent engaged in research misconduct by directing or intimidating fellows and others to influence left ventricular ejection fraction (LVEF) scores of ≤ 35% and requesting attending physicians to reassess scores of LVEF to be reported as ≤ 35% for research subjects after being diagnosed with acute myocardial infarction, thereby causing and being responsible for falsification of research records. These falsifications made subjects eligible for enrollment into the “Vest Prevention of Early Sudden Death Trial” (VEST) when they otherwise may not have been eligible.”

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Dr. Patel continued to assert, through his attorney, that he has only ever had the best interests of his patients in mind. Five years of collected data from Dr. Patel’s arm of the study was thrown out.
Research misconduct means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

- **Fabrication** is making up data or results and recording or reporting them.

- **Falsification** is 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.

> Research misconduct does not include honest error or differences of opinion.
Research Misconduct In Clinical Research

• **Falsifications:**
  • Substitutions of one subject’s record or samples for another’s.
  • Altering eligibility dates, test results etc.
  • Falsifying dates on Pt. screening logs.
  • Selectively eliminating data.
Research Misconduct In Clinical Research

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Research Misconduct In Clinical Research

• Fabrications:
  • Not conducting interviews with subjects and creating records of the interview.
  • Making up Pt. visits and inserting that record into the medical chart.
  • Filling in missing vitals.
Research Misconduct In Clinical Research

Asking or intimidating someone to falsify or fabricate.
By policy, in clinical trials, certain types of issues are not handled by ORI as allegations of research misconduct. These can include:

Administering a trial drug to non-study participant.
By policy, in clinical trials, certain types of issues are **not** handled by ORI as allegations of research misconduct. These *can* include:

Forging a physician’s signature on orders.
By policy, in clinical trials, certain types of issues are *not* handled by ORI as allegations of research misconduct. These *can* include:

Failure to obtain informed consent.
By policy, in clinical trials, certain types of issues are not handled by ORI as allegations of research misconduct. These can include:

Improper consent.

Improper consenting.
By policy, in clinical trials, certain types of issues are **not** handled by ORI as allegations of research misconduct. These *can* include:

Under or over enrolling.
By policy, in clinical trials, certain types of issues are **not** handled by ORI as allegations of research misconduct. These *can* include:

- Breach of patient confidentiality.
By policy, in clinical trials, certain types of issues are **not** handled by ORI as allegations of research misconduct. These *can* include:

Mis-diagnosing (non-intentionally).
By policy, in clinical trials, certain types of issues are not handled by ORI as allegations of research misconduct. These can include:

Not adhering to protocol scheduling. (Unless reported as data in the RR).
By policy, in clinical trials, certain types of issues are **not** handled by ORI as allegations of research misconduct. These *can* include:

Unauthorized protocol deviation such as entering ineligible subjects, administering an off-protocol drug etc. (Unless reported as data in the RR).
Roger Poisson, MD  
St. Luc’s Hospital, Montreal  
National Surgical Adjuvant Breast and Bowel Project (NSABP)  

CASE STUDY

- Poisson fabricated or falsified data related to laboratory tests and dates of procedures in 115 separate instances in 14 projects, involving 99 patients from 1977-1990.
- All falsifications/fabrications lead to the enrollment of ineligible.
- There were cases in which women who previously had cancer were reported as cancer-free, cases of breast cancer that were deliberately downgraded or misclassified, dates of treatment that were falsified, and cases in which proper informed consent was never obtained.
CASE STUDY

Doctor Says He Falsified Cancer Data to Help Patients

MONTREAL, MARCH 31—Dr. Roger Poisson, a prominent Montreal surgeon who has admitted falsifying data in a major North American breast cancer study, said today that he might have broken some rules but did so out of devotion to patients whose inclusion in the research qualified them for state-of-the-art treatment.
Roger Poisson, MD
St. Luc’s Hospital, Montreal
National Surgical Adjuvant Breast and Bowel Project
(NSABP)

CASE STUDY

New York Times, April 1, 1994

Doctor Says He Falsified Cancer Data to Help Patients

Dr. Poisson said that in 30 years of treating breast cancer patients, his goal had been to provide "the best treatment available with the least amount of mutilation possible."

He asked not to be judged on the discrepancies in his research data but on his larger contributions to patient well-being.
Post Mastectomy treatment (tamoxifen vs. placebo)

Pt. enrolled despite skin findings that would have made patient ineligible

Physical exam record from Pt. Chart

Falsified NSABP enrollment form
Data and Safety Monitoring Plans

POUMONS: PA & LATERAL

Cardiomégalie importante avec index cardio-thoracique de 18.5/27 cm.
Plaque athéromateuse calcifiée au niveau de la crosse de l'aorte.
Vascularisation pulmonaire normale.
Pas d'infiltration parenchymateuse actée.

CONCLUSION: Fibrillation auriculaire avec fréquence ventriculaire moyenne à 80/min.
Signes d'ischémie latérale compatible avec insuffisance coronarienne.
PATIENT HISTORY

Has the patient had:

1. A myocardial infarction?

2. Congestive heart failure?

Does the patient have:

1. Angina pectoris which requires anti-anginal medication?

2. Cardiac valvular disease with documented cardiac function compromise?

Has the patient had a radiological oophorectomy?

Has the patient had any other malignancies?

- If yes, specify:
  [The only acceptable cancers are: squamous or basal cell carcinoma of the skin which has been effectively treated; carcinoma in situ of the cervix treated operatively only]
Protocol requires WBC $\geq 4000$

Lab results from Pt. Chart

Falsified NSABP enrollment form
Eric Poehlman, Ph.D.
University of Vermont

- Internationally recognized gerontologist who studied menopause and metabolism.
- Published > 200 papers over the course of two decades.
- His findings were incorporated into medical school curriculum.
• TEE measurements using deuterium H2O (heavy water)
• World-wide shortage of dH2O in the 1990’s
• Many of his 100 volunteers did not have all of their TEEs measured.
• Poehman was anxious to obtain NIH grant to continue the study and to publish a series of papers on the progress to date.
Eric Poehlman, Ph.D.
University of Vermont

• In 2001 was alleged of falsifying and fabricating spreadsheets.

• In 2005 he finally admitted to 54 findings of research misconduct, including 17 grant applications and 10 papers.

• Lifetime Federal Government debarment.

• He was sentenced to one year and one day in prison and $180,000 in restitution.
• Public outraged ensued from the hundreds of female clinical trial volunteers from the Burlington community, who willingly underwent time-consuming, tedious uncomfortable and occasionally painful testing, and had to return periodically to go through it again - - -

All for naught.
Paul Kornak
Research coordinator
Stratton VA Medical Center, Albany, NY

- Responsible for organizing, coordinating, implementing and directing all research elements in the Stratton VA Medical Center oncology research program.
- Iron (Fe) and Atherosclerosis Study (FeAST), Tax 325 and Tax 327 study, bladder cancer study.
- Mr. Kornak posed as a physician, although he had never completed medical school.
• From May 1999 through July 2002 Kornak falsified eligibility criteria for 27 ineligible patients causing allowing them to be entered as subjects in the research studies.
• In 2005 Kornak was sentenced to 6 years in prison for criminally negligent homicide.
Paul Kornak  
Research coordinator  
Stratton VA Medical Center, Albany, NY

“Mr. Kornak caused the death of a study subject when he failed to perceive a substantial and unjustifiable risk that death would occur when he knowingly and willfully made and used documents falsely stating and representing the results of blood chemistry analysis... which net the inclusion and exclusion criteria for participation on the Tax 325 study, when the actual results did not meet the criteria and showed impaired kidney and liver function, and the study subject thus was administered chemotherapeutic drugs and died as a result.”

(Federal Register Vol. 71, No. 37, 2006)
Questions?