Corruption in Clinical Research

What is it? - and why it matters

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Corruption in Clinical Research

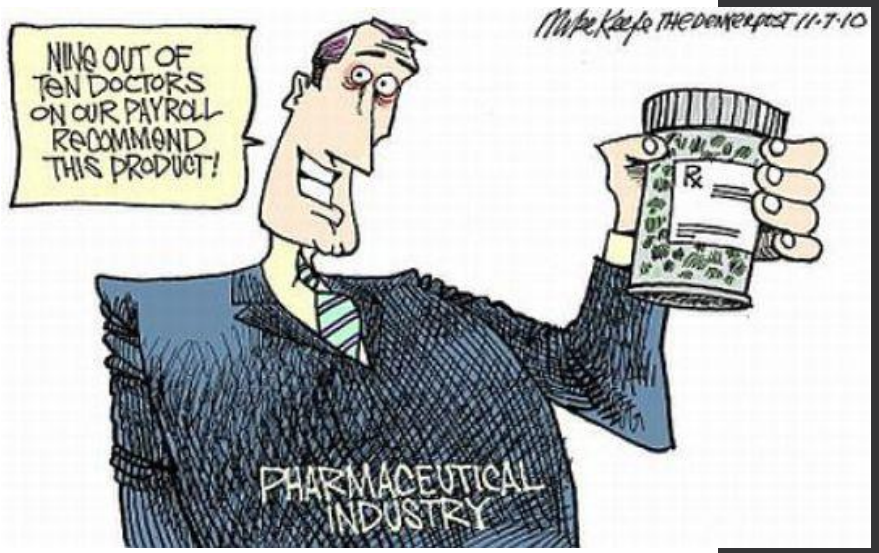
- Objectives
  - At the end of this lecture, participants should be able to:
    - Describe a working definition of corruption in science
    - Contrast research corruption from other kinds of undue influence in clinical research
    - Provide some examples of true research corruption and examples of ambiguous corruption
    - Describe the importance of research corruption for evidence based medicine, public policy, and ordinary medical practice

Corruption in Clinical Research

- Overview
  - What is corruption in science and clinical research?
  - Case examples of clinical research misconduct and how/if they count as ‘corruption’
  - The significance of corruption in clinical research for public policy, science, and clinical practice

Corruption in Clinical Research

- **What is corruption in clinical research?**
  - Corruption is a term that is often used in finger-pointing and in popular public discourse
  - As will be shown, it has also found its way into accusations against clinical investigators and their institutions.
  - Our ordinary sense is that 'corruption' is a serious moral charge -- which therefore requires us to be responsible in its use.
  - Hence this lecture.
  - Moreover, understanding corruption makes us more critically informed consumers of clinical research.



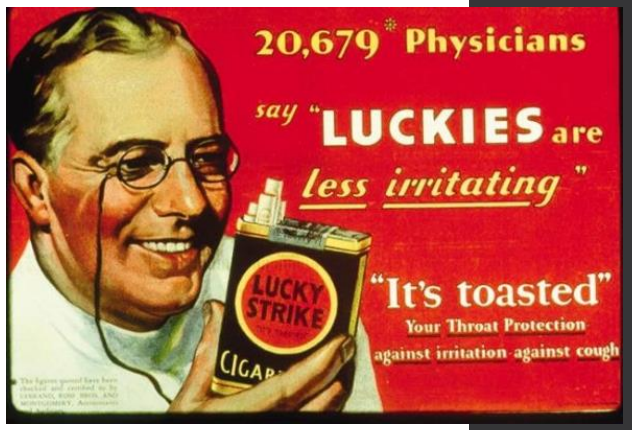
Corruption in Clinical Research

- **What is corruption in clinical research?**
  - Most of the social science literature about 'corruption' comes from economics, where there is keen interest about its function.
    - Interestingly, the scientific evidence from economics is mixed about whether corruption is 'bad' for economies.
  - Political science, law, and philosophy are interested in corruption; a key notion is that understanding corruption means one needs a standpoint about the ***proper functioning*** of the individual or institution in question.
    - What is it about democracies such that they can be corrupted?
  - Very little literature about what counts as corruption in science, and even less in clinical research.

Hellman D. 2013. Defining corruption and constitutionalizing democracy. Michigan Law Rev 111(8):1396-85.

Corruption in Clinical Research

- **What is corruption in clinical research?**
  - Many terms are related to 'corruption' in CR
    - Conflict of interest and conflict of duty
    - Research 'bias' of various kinds – selection, confirmation, etc.
    - Scientific fraud – intentional fabrication or falsification of data, analysis, or conclusions
    - Even sloppy, careless research practices could be 'corruption'
  - A clear understanding of 'corruption' should clarify the relationship of these ideas to corruption proper
    - Dennis Thompson: ". . . corruption is a disease of the body politic" – so, what makes the health of the body politic?
  - What is it about science that can be corrupted?



Thompson DF. 1995. Ethics in Congress. Washington, DC: The Brookings Institution.

Corruption in Clinical Research

- **What is corruption in clinical research?**
  - What is it about science that can be corrupted?
    - Science is a social enterprise that aims to develop genuine, or more accurately, ***credible*** knowledge about the world.
    - Science has a particular set of methods, but for the purposes of understanding corruption, I focus more on the ***social aspects of science***, as corruption is a more social than methodological phenomenon.
    - Hellman: "Most theories agree that corruption requires the violation of a normative standard, some benefit (personal or political), and some connection between the two" (p. 1393)
    - What is the social organization of science that facilitates its goal of genuine, credible knowledge of the world?

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Longino, H. E. (1990). *Science as Social Knowledge: Values and Objectivity in Scientific Inquiry*. Princeton, NJ: Princeton University Press.

Corruption in Clinical Research

- **What is corruption in clinical research?**
  - Social features of science – social values of science
    - We tend to think of science as defined by methods or procedures – hypothesis-testing, experimentation, etc.
    - But science has many and diverse methods – compare
      - Clinical trials
      - Ethnography in cultural anthropology
      - Evolutionary biology
      - Quantum physics
    - Few would dispute these as legitimate science, but their methodologies are barely comparable.
  - So what are the common features of 'science' broadly speaking?

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Corruption in Clinical Research

- Social features of science – social values of science
  - Science can be characterized as a particular social enterprise which respects particular values in meeting its goals.
  - The ***social structure*** centers around the task of generating credible knowledge. To this end, the structures include:
    - ***Peer review*** – grants, journal editorial considerations
    - ***Meetings*** – scientists associate to compare findings
    - ***Criticism*** – knowledge claims are tested by peer critical comments
    - ***Continuity*** – prior knowledge is crucial in building new knowledge
    - ***Observation, evidence, explanation*** – methodological core

Sadler JZ. 2005. Values and Psychiatric Diagnosis. Oxford/New York: Oxford University Press.

Corruption in Clinical Research

- Social features of science – social values of science
  - Science can be characterized as a particular social enterprise which respects particular values in meeting its goals.
  - The ***values of science*** complement the task of generating credible knowledge. To this end, the values include:
    - ***Openness*** – scientists exchange evidence, reasoning, methodologies
    - ***Equality of opportunity*** – in principle, anyone willing and able can participate in the scientific community
    - ***Peer review*** – judgments of scientific worth are made consensually, with protections against abuse/power
    - ***Epistemic freedom*** – scientists freely organize and discuss foci of interest, methods, styles of thinking, and procedures.
    - ***Criticism***: All aspects of scientific interest are subject to criticism: methods, procedure, evidence, interpretation, background assumptions

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Corruption in Clinical Research

- **What is 'corruption' in science?**
  - With these background considerations of science, we can now be more clear about 'corruption'.
  - Hellman's frame: Corruption involves the purposeful violation of a ***normative*** standard for personal or political gain, and a connection between the two.
  - "Normative" is key – what's normal?
  - Here is where the social and value structures of science come in:
    - **Corruption violates the normative (social/value) standards of science as previously described.**
      - Particular incidents can be considered against this definitional framework.
      - It's likely some aspects of science structure and values can be corrupted, while other aspects are not . . . .

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Corruption in Clinical Research

- **What is 'corruption' in science?**
  - I propose that corruption in science is, therefore:
  - **The purposeful violation of, or interference with, one or more of the social structures and values of science, toward some personal or institutional gain. These science structures are peer review, meetings, criticism, continuity, observation/evidence/explanation. The science values are openness, equality of opportunity, peer review, epistemic freedom, and criticism.**
- Implications:
  - Purposefulness is difficult to assess.
  - Corruption, not surprisingly, is not either/or, but a continuum.
  - Corruption can be personal and/or institutional.

Corruption in Clinical Research

- **Case examples of corruption in clinical research science**
- First, some obvious, generic examples of corruption:
  - **Case 1**: An investigator alters the data collected to favor a hypothesis (e.g., scientific fraud)
    - The behavior is intentional, and personal benefit clear
    - Disrespects the central role of evidence in science
    - Secret nature of altering data undermines openness and peer review
    - Compromises the conduct and value of criticism.

Corruption in science

Purposeful violation of/interference with social structures & values of science for personal and/or institutional gain

These structures include:

- Peer review
- Meetings
- Criticism
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These values include:

- Openness
- Equality of opportunity
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- Criticism

Corruption in Clinical Research

- **Case examples of corruption in clinical research science**
- First, some obvious, generic examples of corruption:
  - **Case 2**: A pharmaceutical firm fails to register a clinical trial in *clinicaltrials.gov* and then hides the study data when the study drug is found to be ineffective/inferior.
    - Tanking a study has a transparent financial motive
    - Interferes with peer-review, meeting presentations, criticism, continuity, and explanation (for the negative findings) – as structural violations
    - Undermines the scientific values of openness, equality of opportunity, peer review, epistemic freedom, and criticism.

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Chalmers I. 1990. Underreporting research is scientific misconduct. JAMA 263:1405-1408; Prayle et al. 2011. Compliance with mandatory reporting of clinical trial results in ClinicalTrials.gov: cross sectional study. BMJ doi: 10.1136/bmj.d7373

Corruption in Clinical Research

- **Case examples of corruption in clinical research science**
- First, some obvious, generic examples of corruption:
  - **Case 3**: In preparing a review article, a beginning investigator copies large portions of text verbatim from a prior review article in a relatively obscure journal.
    - Potential personal gain is clear
    - Interferes with the continuity of science; the appropriation of previous work without credit dispenses with the value of critically appraising past work
    - Thus criticism is compromised, as is peer review
    - Secretive quotation disrespects openness as well.

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Cameron C, Zhao H, McHugh MK. 2012. Perspective: Publication and the emerging scientific workforce. Understanding "plagiarism" in a global context. Acad Med 87 (1): 51-54

Corruption in Clinical Research

- **Case examples of corruption in clinical research science**
- Second, some more questionable or ambiguous, but generic examples of 'corruption':
  - **Case 4**: A prominent child psychiatrist and clinical investigator receives $1.6 million in pharma money over 7 years. Angell (2009) claims he is corrupt.
    - Without more information about his conduct, simply having a financial interest from pharma does not constitute corruption, under my rubric
    - Having a conflict of interest, as we all do in our spheres of practice and research, does not in itself constitute corruption
    - It does, however, raise questions about bias; an important but different concept.

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Angell M. 2009. Drug Companies & Doctors: A Story of Corruption- The New York Review of Books May 20.

Corruption in Clinical Research

- **Case examples of corruption in clinical research science**
- Second, some more questionable, but generic examples of 'corruption':
  - **Case 5**: A clinical investigator with a $5000 consultant contract with Extra Pharmaceuticals is designing a comparative effectiveness trial. A junior colleague on his team is puzzled why several Extra products are in the trial, while some familiar standard drugs are not. The senior investigator realizes with embarrassment that he unintentionally is biased toward Extra products.
    - Not corruption, as any violation is not purposeful/intentional
    - Indeed, the investigator's response indicates he is open to peer review and criticism, self observation, and evidence, all positive scientific values.

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  - Evidence/
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Corruption in Clinical Research

- **Case examples of corruption in clinical research science**
- Third, analysis of other, more subtle cases:
  - **Case 6**: Dr. Distinguished is the chairman of a prominent clinical department in a prominent academic medical center. Now 62 and at the top of his game, he has a longstanding relationship with Extra Pharmaceuticals though speakers fees and advisory committee contracts to the tune of $100k/year. For these fees he is involved in research design of Extra's products, assisting in ghostwriting the papers from the company's contract research organization, and serving as a nominal author in their industry-sponsored publications. His presentations are listed as "promotional" not CME.
  - Are any aspects of this research arrangement corrupt?

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- **Case examples of corruption in clinical research science**
- Third, analysis of other, more subtle cases:
  - **Case 6**: Analysis
    - Lessig, Light, and others have considered ***institutional corruption*** as 'bending' policy, or in this case, research, in directions favorable to industry. Industry doesn't pay for results, but pays for the direction research takes, how it is promulgated, and how it is promoted. Dr. D is a "key opinion leader"(KOL) for Extra Pharmaceuticals.
    - Is this a 'purposeful violation' of structure/values of science? No, not purposeful. Indeed, KOLs and industry take special care to prevent the KOL from looking like a sellout.
    - As a KOL, Dr. D is in a position to distort and direct research and practice interest in directions favorable to Extra. He may influence treatment guidelines policies, influence federal grant reviews, initiate topics friendly to Extra and professional meetings, etc.

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Sismondo S. 2013. Key opinion leaders and the corruption of medical knowledge: what the Sunshine Act will and won't cast light on. Journal of Law, Medicine, & Bioethics, 635-643.

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- **Case examples of corruption in clinical research science**
- Third, analysis of other, more subtle cases:
  - **Case 6**: Analysis
    - Judgements of such bending of research practices & policy require extraordinary scrutiny, often requiring peeking behind closed doors at "proprietary" practices, and then, only in the context of a lawsuit or public demand.
    - Re: observation/evidence/explanation, KOLs may shape what observations, evidence, and explanations count.
    - As influential leaders in their field, junior colleagues may be conflicted about criticizing the KOL's science, worrying about recommendations, mentoring, placement on study sections, etc.

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- **Case examples of corruption in clinical research science**
- Third, analysis of other, more subtle cases:
  - **Case 6**: Analysis
    - Regarding the values of science, industry data, procedures, and use of KOLs are proprietary, undermining the value of openness, peer review, and criticism.
    - Most powerfully, I think the use of KOLs interferes with epistemic freedom – the idea that scientists can choose freely what to study. This bending of epistemic freedom occurs by the use of financial influence; what is funded is bent to pharma interest or other medical industries.
      - 2015: Industry sponsorship of clinical trials is 6x NIH funded trials. http://www.jhsph.edu/news/news-releases/2015/industry-financed-clinical-trials-on-the-rise-as-number-of-nih-funded-trials-falls.html

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- **Case examples of corruption in clinical research science**
- Third, analysis of other, more subtle cases:
  - **Case 6**: Analysis
    - Conclusion: by my criteria, Dr. D is **complicit** in **institutional corruption** of clinical research, the latter on a grand scale, as will be seen in other ways, later in the lecture.
      - Dr. D's bending of science may not be purposeful, but accidental; an 'unintended consequence'.
      - However, industry's bending of science is quite purposeful, as Sismondo's paper below, among others, attests.

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Corruption in Clinical Research

- **Case examples of corruption in clinical research science**
- Third, analysis of other, more subtle cases:
  - **Case 7**: Van Spall et al (2007) published a systematic review of use of ***exclusionary criteria*** in selecting RCT participants. In 12% of the studies sampled (n=283) exclusion criteria were **not reported**. Unreported exclusion criteria were more likely to be in industry-sponsored trials (p<.001). Reasons for exclusion included gender, age (children, aged), socioeconomic, medical comorbidities, use of other medications. Rationales for exclusion criteria in publications were absent in 37% of the studies.
    - Do unreported exclusionary criteria represent corruption in science?

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Van Spall HCC et al 2007. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: A systematic sampling review. JAMA 297 (11): 1233- 1240.

Corruption in Clinical Research

- **Case examples of corruption in clinical research science**
- Third, analysis of other, more subtle cases:
  - **Case 7**: Analysis
    - RCTs use exclusionary criteria for variety of reasons, some legit, even essential, others not. Most common include:
      - Specified populations more likely to show treatment signal compared to populations with multiple confounding variables
      - Fewer confounding variables, smaller n, less expensive and often easier to conduct study
      - Excluding some subjects on the basis of clinical interest/importance of core subjects.

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- Third, analysis of other, more subtle cases:
  - **Case 7**: Analysis
    - Exclusionary criteria can also have adverse effects:
      - Excluding children, women, elderly, people with comorbidities and other meds – compromises generalizability
      - In clinical practice, may place patients who fall outside of study criteria at risk, in that no one knows the adverse effects and interactions of the study drug in the excluded population.
      - Social justice issues: not everyone is an adult male, but adult males are the primary participants & beneficiaries of clinical research

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- **Case examples of corruption in clinical research science**
- Third, analysis of other, more subtle cases:
  - **Case 7**: Analysis
    - Use of exclusionary criteria, in themselves, do not undermine the social structures and values of science.
    - What about the ***non-disclosure*** of exclusionary criteria? Is that corrupt?
      - The rationales for withholding disclosure of exclusion criteria are many and seldom discussed. Could include:
        - Space-saving of journal editorial space
        - They were described in another, related, paper
        - Were withheld to increase sales (false generalizability)

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- **Case examples of corruption in clinical research science**
- Third, analysis of other, more subtle cases:
  - **Case 7**: Analysis
    - Is non-disclosure of exclusionary criteria corrupt?
      - The rationales for withholding exclusion criteria are obscure. Could include:
        - Space-saving of journal editorial space
        - Were described in another, related, paper
        - Were withheld to increase sales (false generalizability)
      - If the latter (for sales) were true, then that would meet the "purposeful violation" and violate multiple structures and values of science, and therefore, be a corrupt practice

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- Third, analysis of other, more subtle cases:
  - **Case 7**: Analysis
    - Is non-disclosure of exclusionary criteria corrupt?
      - But this would be very difficult to demonstrate.
      - Regardless, withholding disclosure of exclusionary criteria for any reason erodes some scientific values – openness, peer review, and constrains criticism, for example.
      - So while withholding the publication of exclusionary criteria may not be frankly corrupt by my criteria, it probably does not represent the best science either!

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- Third, analysis of other, more subtle cases:
  - **Case 8**: In an analysis of publicly-available documents from 1998-2013, Charles Seife's team looked for evidence of impact of FDA citations of ethics violations in clinical research. They looked for publications resulting from the offending research, and of ones connected to one or more publications. 57 projects were found which were censured by the FDA. Of those 73 pubs linked to the 57, only 3 acknowledged the FDA censure in any way. The other papers were published without acknowledgement of research misconduct by authors, or journal editors.
  - Does the failure, by authors and editors, to acknowledge FDA-identified research misconduct constitute corruption?

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Seife C. 2015. Research Misconduct Identified by the US Food and Drug Administration: Out of Sight, Out of Mind, Out of the Peer-Reviewed Literature. *JAMA Intern Med*. doi:10.1001/jamainternmed.2014.7774

Corruption in Clinical Research

- **Case examples of corruption in clinical research science**
- Third, analysis of other, more subtle cases:
  - **Case 8**: Analysis
    - But perhaps a prior question should be addressed: Is disclosure of research misconduct important to the scientific enterprise?
      - Yes. Misconduct undermines the potential for ***peer review*** and ***criticism***. It provides for potentially false knowledge for later investigators to build upon (undermining ***continuity***). It also undermines ***equality of opportunity***, in that investigators who play by the rules are disadvantaged compared to those who do not.
    - Is the violation purposeful? Impossible to tell. Seife and FDA staff have little insight into the reasons for these omissions. Corruption?!?

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- **Case examples of corruption in clinical research science**

Corruption in Clinical Research - relation to other concepts & practices		
Likely to be corruption	**Likely not corruption**	**Unclear - examine case**
research fraud/falsifying data	sloppy, careless data collection, naive mistakes	
failure to register clinical trial in clinicaltrials.gov; hides trial data		excessive delays or failure to publish negative results of a clinical trial
use of Key Opinion Leaders to bend treatment guidelines, and prioritize program funding	simple conflict of interest	conflict of interest with consistent industry-favorable outcomes
significant plagiarism	investigator-initiated oversight journal publication retraction	failure to disclose exclusion criteria

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- **The significance of corruption in clinical research for, science, clinical practice, and public policy**
  - How common is corruption under my definition?
    - Short answer: Unknown – my framework is new.
    - The cases have identified a variety of ways science can be corrupted; no taxonomy exists to lump them together and count them.
    - However, there is some research on the commonality of two kinds of research corruption:
      - Fraud – deliberately altering study data, outcomes, results
      - Nondisclosure of (negative) clinical trial results
  - Will consider these two examples very briefly

Corruption in Clinical Research

- **The significance of corruption in clinical research for, science, clinical practice, and public policy**
  - How common is corruption under my definition?
    - **Fraud – deliberately altering study data, outcomes, results**
      - Fanelli 2009 meta-analysis of all scientific citation databases, scientific journals, grey literature, and internet search engines → 18 studies.
      - Specific to 'falsification' and "fabrication' research misconduct, other kinds excluded
      - About 2% of scientists self-admitted to at least one instance of fabrication/falsification of data.
      - About 14% of scientists reported colleagues' fabrication/falsification.
      - Trend toward biomedical/pharmacological researchers to report more misconduct than in other areas of science

Fanelli D. 2009. How many scientists fabricate and falsify research? A systematic review and meta analysis of survey data. PLoS One 4 (5): e5738, 1-11.

Corruption in Clinical Research

- **The significance of corruption in clinical research for, science, clinical practice, and public policy**
  - How common is corruption under my definition?
    - **Fraud – deliberately altering study data, outcomes, results**
      - Fanelli 2009 meta-analysis of all scientific citation databases, scientific journals, grey literature, and internet search engines → 18 studies.
        - Self reports likely to underestimate
        - However, the threshold was 'at least one' – no requirement for a pattern
        - Self-admissions have decreased over the years – unclear why
        - Up to 34% admitted to other kinds of questionable research practices

Fanelli D. 2009. How many scientists fabricate and falsify research? A systematic review and meta analysis of survey data. PLoS One 4 (5): e5738, 1-11.

Corruption in Clinical Research

- **The significance of corruption in clinical research for, science, clinical practice, and public policy**
  - How common is corruption under my definition?
    - **Nondisclosure of negative clinical trial results**
      - Beginning in the late 1990's, clinical investigators and clinicians became increasingly aware of pharma's withholding of clinical trial results, resulting in a number of studies to examine how common this practice was. Knowledge of withholding emerged from public lawsuit disclosures and investigator complaints of "gag rules".

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      - In 1999, NIH established www.clinicaltrials.gov , a website intended to serve as a registry for (ideally) all US clinical trials. It was established in response to concerns about unavailable clinical trial information. Clinicaltrials.gov went public in 2000.
      - 2005 – the International Committee of Medical Journal Editors mandated drug trials be registered by jurisdiction. www.icmje.org
      - 2007 – Food & Drug Administration Amendments Act (FDAAA) mandated sponsor/investigator registration with clinicaltrials.gov, and that investigators post basic results of trials within 1 year of the completion of data collection.
    - This set the stage of assessing compliance with FDAAA.

Corruption in Clinical Research

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  - How common is corruption under my definition?
    - **Nondisclosure of negative clinical trial results**
    - No meta-analyses as yet but several studies document poor compliance with FDAAA & outcomes disclosures on clinicaltrials.gov.
    - Key studies include:
      - Lexchin J et al. 2003. Pharmaceutical industry sponsorship and research outcome and quality: Systematic Review. BMJ 326: 1167, 1-10.
      - Law MR et al 2011. Despite law, fewer than one in eight completed studies of drugs and biologics are reported on time on clinicaltrials.gov. Health Affairs 30 (12): 2338-2345.
      - Wieseler et al. 2011. Impact of document type on reporting quality of clinical drug trials: A comparison of registry reports, clinical study reports, and journal publications. BMJ 344:d8141 doi: 10.1136/bmj.d8141 (Published 3 January 2012)
      - Prayle et al. 2012. Compliance with mandatory reporting of clinical trial results on clinicaltrials.gov: Cross sectional study. BMJ 344:d7373 doi: 10.1136/bmj.d7373
      - Ross JR et al 2009. Trial publication after registration in clinicaltrials.gov: A cross-sectional analysis. PLoS Medicine 6(9): e1000144. doi:10.1371/journal.pmed.1000144
      - Zarin DA et al. The clinicaltrials.gov results database – Update and key issues. NEJM 364: 852-60.
      - Riveros C et al. 2013. Timing and completeness of trial results posted at clinicaltrials.gov and published in journals. PLoS Medicine 10 (12): e1001566

Corruption in Clinical Research

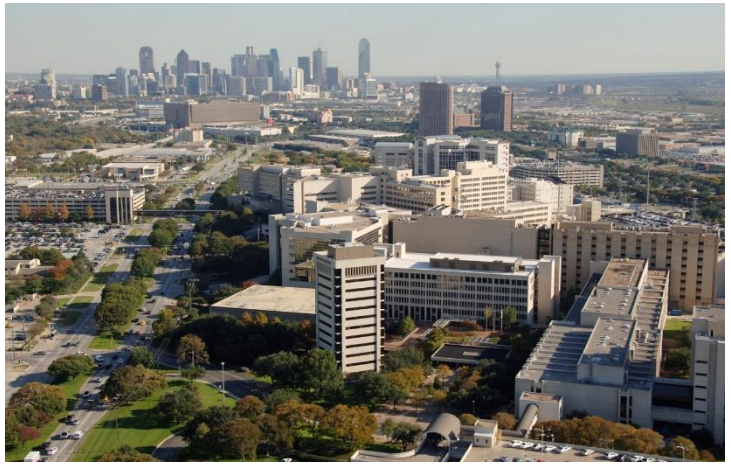
- **The significance of corruption in clinical research for, science, clinical practice, and public policy**
  - Conclusions
    - Corruption under my definition (or any definition) is difficult to study, with complex variables and need for big data.
    - Nevertheless, the studies I reviewed indicated that while under-reporting of clinical research data is still too common, modest progress has been made in improving matters.
    - The practicing clinician still faces enormous barriers to access of current clinical trial, safety, and related data.
    - Outright fraud, while seemingly large in absolute numbers, when considered in the context of millions of scientific studies published, is a very small phenomenon.
    - But what about the significance of clinical research corruption?

Corruption in Clinical Research

- **The significance of corruption in clinical research for, science, clinical practice, and public policy**
  - Significance
    - The literature discusses, and I agree, that the withholding of negative results seriously ***undermines the clinical evidence*** base and the ***viability of evidence-based medicine***.
    - Moreover, I think this undermining of the past & present validity of our evidence base is ***underappreciated*** by most everyone, including practitioners.
    - The ***harm to patients*** of false, biased, or incomplete clinical knowledge is unknown, but hard to imagine that these factors do not make substantial contributions to adverse clinical events and poor outcomes.
    - Moreover, the public perception of corrupt science could easily ***undermine confidence*** in medicine, political support, and funding support for clinical research.

Corruption in Clinical Research

- **Thanks for your attention and comments.**



UT Southwestern
Program in Ethics in Science & Medicine

http://www.utsouthwestern.edu/education/programs/ethics_program/index.html

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      - Lexchin et al (2003) published a review of studies (n = 30) addressing the question of publication of results favoring the industry sponsor. The results indicated that pharma sponsorship was 4x more likely to result in publication favoring the sponsor's products.

Lexchin J et al. 2003. Pharmaceutical industry sponsorship and research outcome and quality: Systematic Review. BMJ 326: 1167, 1-10.

Corruption in Clinical Research

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  - How common is corruption under my definition?
    - **Nondisclosure of negative clinical trial results**
    - No metaanalyses as yet but several studies document poor compliance with FDAAA & outcomes disclosures on clinicaltrials.gov.
    - Very difficult to assess non-registration of studies on clinicaltrials.gov
    - Nevertheless, Wieseler et al in Germany compared reporting quality on three types of publications over 2006-11: registry reports, clinical study reports, journal publications
      - Of 268 studies over this period, report availability was 72% for journal publications, 38% for company reports, and 29% for registry reports.

Wieseler et al. 2011. Impact of document type on reporting quality of clinical drug trials: A comparison of registry reports, clinical study reports, and journal publications. BMJ 344:d8141 doi: 10.1136/bmj.d8141 (Published 3 January 2012)

Corruption in Clinical Research

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  - How common is corruption under my definition?
    - **Nondisclosure of negative clinical trial results**
    - Joseph Ross & colleagues have published a few studies examining publication after registration in clinicaltrials.gov
      - 2009: A sample of trials registered between 1999 and 2007, with *two* year followup re: publication in journals
      - Only 66% reported trial outcomes in clinicaltrials.gov
      - Industry-sponsored trials were less likely to be published (40%) as were gov't sponsored trials (47%), than nonindustry/nongov't sponsored trials (56%)

Ross JR et al 2009. Trial publication after registration in clinicaltrials.gov: A cross-sectional analysis. PLoS Medicine 6(9): e1000144. doi:10.1371/journal.pmed.1000144

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    - **Nondisclosure of negative clinical trial results**
    - Carolina Riveros' French team examined a random sample of clinicaltrials.gov phase III & IV RCTs with posted results for publication any time afterward.
      - 50% had no journal publication after results posting
      - Of the 202/600 with registry postings and publications, 66% of the journal publications reported serious adverse events (SAEs) against 99% posted in the registry. Adverse events were reported 73% /45% respectively. Results were reported 69%/79% respectively.
      - Conclusion: efficacy and safety data are more complete at clinicaltrials.gov. Why withhold publication of SAEs 1/3 of time?

Riveros C et al. 2013. Timing and completeness of trial results posted at clinicaltrials.gov and published in journals. PLoS Medicine 10 (12): e1001566

Corruption in Clinical Research

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  - How common is corruption under my definition?
    - **Nondisclosure of negative clinical trial results**
    - Prayle and colleagues (2012) examined compliance with mandatory reporting of summary clinical trial results within one year of completion, comparing trials w/mandatory FDAAA reporting with ones without mandatory reporting. Selected phase II or later stage.
      - 22% of mandatory-reported trials reported on time
      - 10% of nonmandatory-reported trials reported 'on time'
      - Industry sponsored trials significantly more likely to report than nonindustry sponsored trials
      - Conclusions: registries are positive, but reporting is poor

Prayle et al. 2012. Compliance with mandatory reporting of clinical trial results on clinicaltrials.gov: Cross sectional study. BMJ 344:d7373 doi: 10.1136/bmj.d7373

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  - How common is corruption under my definition?
    - **Nondisclosure of negative clinical trial results**
    - Deborah Zarin, Joseph Ross and colleagues at NIH report on outcomes with clinicaltrials.gov
      - 2011: a random sample of 150 (of 2078) completed records, 78 (52%) had associated publications within 2 years after posting in the registry.

Zarin DA et al. The clinicaltrials.gov results database – Update and key issues. NEJM 364: 852-60.