What Do We Know?
Two Decades of Research on Research Integrity

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What do we know about research integrity?

- "Research fraud is historically a rare occurrence, especially at Caltech, where all members of the community are bound by a very effective code of honor."
  (http://www.its.caltech.edu/~ombuds/html/research_fraud.html)
- "Deliberate misconduct in research - a 'hot topic' worldwide - is rare at South African universities, while the occasional deviations from protocol that occur - most of them in clinical trials - are picked up and remedied quickly." (http://www.capetimes.co.za/index.php?fSectionId=271&fArticleId=2813316)
- ""Les cas qui sont clairement des manquements à l'intégrité scientifique sont très rares…." Rector, Laval University (http://www.scom.ulaval.ca/Au.fil.des.evenements/2006/03.16/ethique.html).

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What we know….?

- "Indeed, the best evidence we have shows that misconduct is a very rare occurrence in research. There have been 200 confirmed cases of misconduct in federally funded research in the last 200 years, which works out to a rate of 1 in 10,000 (or 0.01%)." (http://dir.niehs.nih.gov/ethics/whatisethics.htm)
- "Even on the rare occasions when scientists do falsify data, they almost never do so with the active intent to introduce false information into the body of scientific knowledge. Rather, they intend to introduce a fact that they believe is true, without going to the trouble and difficulty of actually performing the experiments required."
(http://en.wikipedia.org/wiki/Scientific_misconduct)

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Do we *in fact* know any of this?

- Yes - if "knowing" is believing what is said to be true
  - ✓ These and other "fact" are widely repeated and believed
- No - if "knowing" is based on empirical evidence
  - ✓ "Rare" has not been defined and therefore cannot be measured
    - Rare Disease, EU = .05%
    - Rare Disease, US = .07%
    - What % = "rare" in research
  - ✓ 20 years ago, no empirical information to test assumptions
- Solution: new field of research

Research on Research Integrity

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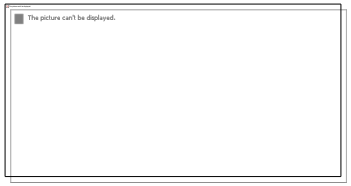
Driving force behind RRI

- Peer Review Congresses
  (http://www.ama-assn.org/public/peer/peerhome.htm)
  - ✓ Begun in 1989, held every four years
  - ✓ Aim: "to improve the quality and credibility of biomedical peer review and publication … throughout the world."
  - ✓ Result: growth of empirical research on publication practices



- ORI/NIH Research Program on Research Integrity
  (http://ori.hhs.gov/research/extra/index.shtml)
  - ✓ Planning started in 1999
  - ✓ First awards 2001
  - ✓ Funded 46 projects, $15,663,194 total funding, ~7 projects/year

- General scholarly interest in research behavior and misconduct

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Major focus of RRI = Misconduct (FFP)

- JM Ranstam, (2000, *Control Clin Trials* 21, 5:415-27)
  - ✓ Survey, 442 biostatisticians, 37% response
  - ✓ 51% knew about fraud in medical research
    - 26% involved FF
    - 31% directly involved in projects with misconduct
  - ✓ Estimates of rate, .69% –> .80% (.25% standard)
- Geggie, *(2001, J Med Ethics* 27, 5:344-6)
  - ✓ Survey, 305 new medical consultants, 64% response
    - 55.7% observed misconduct (FF lower)
    - 5.7% committed misconduct in the past
    - 18% would commit in future
    - 17% had research ethics training

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Studies continued…

- Gardner, *(2005, Contemp Clin Trials* 26, 2:244-51)
  - ✓ Authors pharmaceutical clinical trials (64% response)
  - ✓ 1% reported target article misrepresented the research
  - ✓ 5% reported fabrication in a study they had participated in over the last 10 years
  - ✓ 17% knew personally of fabrication in a study over the last 10 years
- Pryor, ~ 1645 trial coordinators (2007, *J Med Ethics* 33, 6:365-9)
  - ✓ 0.2% and 0.5% said plagiarism & falsification occurred "frequently"
  - ✓ 5.2% and 4.0% said plagiarism & falsification occurred "occasionally"
  - ✓ 18% reported first-hard experience with misconduct *over past year*
- Rossner, *Journal of Cell Biology* study, unpublished findings
  - ✓ 11 in 1,100 papers had serious improper digital image manipulation

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Conclusions?

- Findings:
  - ✓ Frequency range: ~ 0.1 –> 1.0%
  - ✓ over 10 years: ~.01 –> 0.1%
- Implications, cases/year:
  - ✓ US ~ 150 -> 1,500
  - ✓ EU ~ 100 -> 1,000
  - ✓ Japan ~ 60 -> 600
  - ✓ Other OECD ~ 40 -> 400
- Cases reported/year: US ~20/year; EU ~ 10/year
- Conclusions:
  - ✓ Evidence does not support view that misconduct is "rare"
  - ✓ Most research misconduct is not detected, reported and investigated

Science & Engineering Indicators 2006, Figure 3-36

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Is serious misconduct the only problem?

- NAS Report (1992) distinguished FFP and QRP
  - ✓ QRP (questionable research practices) are actions that violate traditional values of the research enterprise and that may be detrimental to the research process. …
  - ✓ QRP do not directly damage the integrity of the research process
  - ✓ …they can
    - erode confidence in the integrity of the research process,
    - violate traditions associated with science,
    - affect scientific conclusions,
    - waste time and resources and
    - weaken the education of new scientists.
- What do we know about QRP?

*National Academy of Science, *Ensuring the Integrity of the Research Process*, Washington DC, National Academy Press, 1992.

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Detrimental to more than research process

- Can have devastating consequences
  - ✓ Improper and unreported conflicts
  - ✓ Improper literature review
  - ✓ Poor design and/or review
- At a minimum, costly and wasteful
  - ✓ Geoffrey Chang retraction
    - Lab did not check work carefully
    - Editors & funders ignored reviewers
    - Who more important than what
- Cases provide anecdotal information
- What are the overall significant and impact of QRP?

Gelsinger

Roche

Abdelhady

Chang

Areas of concern:

Plan
- ✓ Bias design ~ select methods/control that favor results
- ✓ Failure to disclose conflicts of interest
- ✓ Less than honest information to review committees

Conduct
- ✓ Failure to follow protocols, particularly human subject
- ✓ Improper or inadequate procedures for recording data
- ✓ Inadequate supervision

Interpret
- ✓ Inappropriate statistical methods
- ✓ Improper selection of data and controls
- ✓ Unjustified or unsupported conclusions

Publish
- ✓ Honorary and Ghost authorship
- ✓ Misleading and inaccurate notes and abstracts
- ✓ Withhold crucial information

Review
- ✓ Failure to maintain confidentiality
- ✓ Cursory review
- ✓ Bias toward or against particular colleagues or fields

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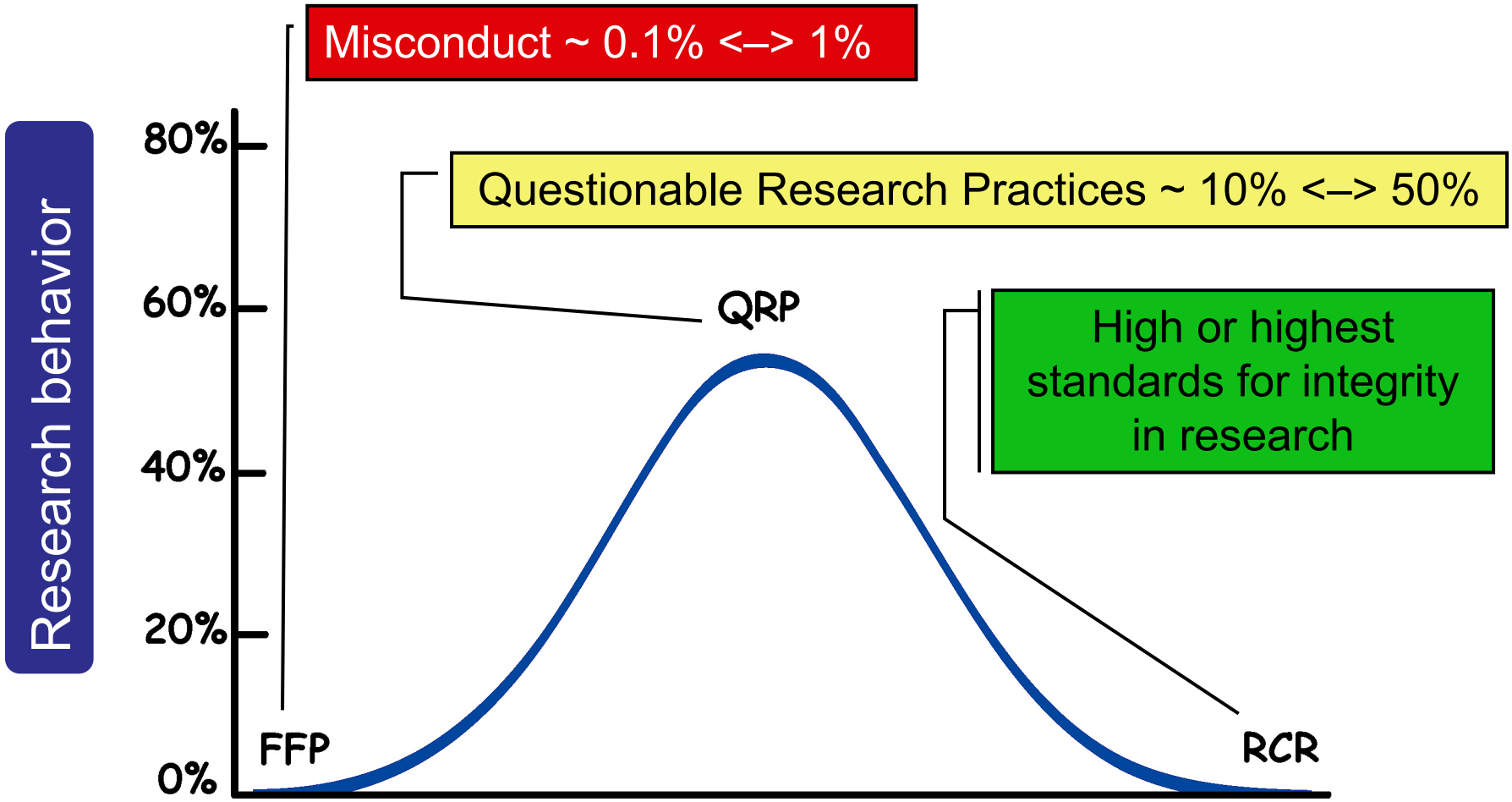
General findings



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ORI/NIH RRI Findings?

- Data sharing (*Acad Med* 81, 2: 128-36):
  - ✓ ~1 in 4 life science trainees in the US reported problems gaining access to information related to published research
  - ✓ ~1 in 2 reported that withholding slowed or stopped their research
  - ✓ ~ 8% denied other researchers access to information
- Clinical trials (J Med Ethics 33, 6: 365-9):
  - ✓ Clinical trial coordinators experienced "frequently" or "occasionally"
    - Intentional protocol violations 1.2% 7.5%
    - Coercion of potential subjects 1.2% 9.1%
    - Selective dropping of data 0.7% 3.7%

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Research on Publication

- Citation errors (2007, *Cochrane Database Syst Rev* 2:MR000002)
  - ✓ Summary of 35 studies of citational accuracy
  - ✓ 39% citation error rate
  - ✓ 20% quotation error rate
- Authorship
  - ✓ 75% ghost authorship in industry-initiated randomized trials
    - *2007, PLoS Med* 4 (1):e19.
  - ✓ 59% clinical researchers accepted honorary authorship, ignored ICMJE
    - 2005, *J Med Ethics* 31 (10):578-81. (French researchers)
  - ✓ 60% of authors in Croatian Medical Journal did not meet ICMJE criteria
    - 2004, *Sci Eng Ethics* 10 (3):493-502
- Abstracts (2004, *Ann Pharmacother* 38 (7-8):1173-7)
  - ✓ Six pharmacy-specific journals; accuracy of abstracts
  - ✓ ~25% omissions; 33% omission or inaccuracy; ~60% classified as deficient

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Other Findings

- **Al-Marsouki, Practices felt likely to occur *and* adversely impact research** (2005, *Contemp Clin Trials* 26 (3):331-7)

83%	Over-interpretation of “significant" findings in small trials
80%	Selective reporting based on p-values
76%	Selective reporting of outcomes in the abstract
75%	Subgroup analyses done without interaction tests
68%	Negative or detrimental studies not published
68%	Putting undue stress on results from subgroup analysis
64%	Inappropriate subgroup analyses
64%	Selective reporting of (i) subgroups (ii) outcomes (iii) time points
60%	Selective reporting of positive results/omission of adverse events data
60%	Failure to report results or long delay in reporting
59%	Post-hoc analysis not admitted
56%	Giving incomplete information about analyses with non significant results
54%	Analysis conducted by the sponsor of the trial

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Conflict of Interest Studies

- Bekelman (2003, *JAMA* 289, 4:454-65)
  - ✓ Meta-analysis of 37 COI studies (1,000s of trials)
  - ✓ Positive correlation (3.60 OR) , industry sponsorship & positive outcomes
- Lexchin (2003, *BMJ* 326, 7400:1167-70)
  - ✓ Meta-analysis of 30 COI studies
  - ✓ Positive correlation (4.05 OR), industry sponsorship & positive outcomes
- Friedman (2004, *J Gen Intern Med* 19, 1:51-6)
  - ✓ 398 publications, *NEJM* and *JAMA*
  - ✓ Correlation (2.35-2.64 OR), industry/positive outcomes

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Why fund and conduct RRI?

- Essential for policy making:
  - ✓ Are FFP the major problems?
  - ✓ Do questionable practices present (greater) problems?
  - ✓ Currently developing solutions without fully understanding of problems
- Essential for developing measures to improve integrity:
  - ✓ Why do researchers fail to follow sound professional practices?
  - ✓ Is integrity influenced by institutional climate?
  - ✓ Current emphasis on training individuals may not be effective
- Essential for maintaining public confidence and support:
  - ✓ Research integrity policy has been driven by crises and public pressure
  - ✓ Responsible self-study and self-regulation are essential for maintaining (restoring) public support.

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