Fostering Integrity in Research: Definitions, Current Knowledge, and Future Directions

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ABSTRACT. *Over the last 25 years, a small but growing body of research on research behavior has slowly provided a more complete and critical understanding of research practices, particularly in the biomedical and behavioral sciences. The results of this research suggest that some earlier assumptions about irresponsible conduct are not reliable, leading to the conclusion that there is a need to change the way we think about and regulate research behavior. This paper begins with suggestions for more precise definitions of the terms "responsible conduct of research," "research ethics," and "research integrity." It then summarizes the findings presented in some of the more important studies of research behavior, looking first at levels of occurrence and then impact. Based on this summary, the paper concludes with general observations about priorities and recommendations for steps to improve the effectiveness of efforts to respond to misconduct and foster higher standards for integrity in research.*

Introduction: Fostering Integrity in Research

Researchers should practice research responsibly. Unfortunately, some do not. For the past 25 years, following public reports of major cases of irresponsible conduct, policy makers and the research community have been debating how to label, study, and respond to research behaviors that fall short of responsible conduct.

The consensus that emerged from these debates broadly separated research behaviors in to three categories: deliberate misconduct, commonly defined as fabrication, falsification, and plagiarism (FFP); questionable research practices (QRP);

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and responsible conduct of research (RCR). (Fig. 1) RCR represents the ideal standard institutions and individuals endeavor to meet. FFP encompasses practices everyone agrees should be avoided. QRP fall some place in between. Over time, some consensus has also emerged regarding the occurrence and significance of these behaviors. It is commonly assumed that the worst behaviors (FFP) are rare and that questionable practices (QRP), although troubling, are not serious enough to warrant government action. Finally, researchers and research institutions commonly assume that scientific research can for the most part effectively regulate its own behavior.

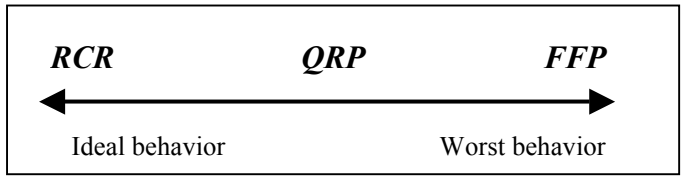

Fig. 1. Current framework for Defining Research Behaviors

When researchers and policy makers first confronted research misconduct in the 1980s and early 1990s, there was little empirical information about research behavior to test the assumptions that were made about research behavior. Informal surveys suggested that irresponsible conduct might be fairly common, leading to the conclusion that reported cases of misconduct might be the tip of a much larger iceberg.[1] Researchers countered these suggestions by arguing that misconduct could not be widespread since it was kept in check by peer review and self-regulation. In one optimistic early assessment of research behavior, the editor of *Science*, Daniel Koshland, claimed that "99.9999 percent of [scientific] reports are accurate and truthful, often in rapidly advancing frontiers where data are hard to collect." This assessment led him to conclude that "[t]here is no evidence that the small number of cases [of research misconduct] that have surfaced require a fundamental change in procedures that have produced so much good science."[2]

Over the last 25 years, a small but growing body of research on research behavior has slowly provided a more complete and critical understanding of research practices, particularly in the biomedical and behavioral sciences. Surveys have become more scientific and expanded their scope to include questions about motivations and attitudes as well as actual behaviors. Many studies of research behavior are now based on direct empirical observation. Researchers have directly measured whether resumes, abstracts, citations, and statistical analyses are accurate. The new evidence suggests that some earlier assumptions are not reliable, leading to the conclusion that there is a need to change the way we think about and regulate research behavior.

This paper begins with suggestions for more precise definitions of the terms "responsible conduct of research," "research ethics," and "research integrity." It then summarizes the findings presented in some of the more important studies of research behavior, looking first at occurrence and then impact. Based on this summary, the paper concludes with general observations about priorities and recommendations for

steps to improve the effectiveness of efforts to respond to misconduct and foster higher standards for integrity in research.

1. Basic terms and definitions

Researchers and policy makers use different terms to refer to the way researchers should and should not behave. Research institutions aspire to set high standards for *integrity in research*. The Federal government and many research institutions have policies to promote the *responsible conduct of research*. It is widely agreed that research should be undertaken ethically, which is usually discussed in terms of *research ethics*. As commonly as these and related terms are used, they are seldom formally defined. The lack of common definitions makes it difficult to establish a critical framework for assessing, responding to, and changing research behavior.

In general terms, research is a process that is variously defined in terms such as "critical search and investigation,"[3] "methodical investigation"[4] or "a course of critical or *scientific inquiry*."[3] Research is also today primarily a professional activity, meaning that it is carried out and in part guided by individuals who have been specially trained to do research. As professionals, researchers are expected to conduct their work in ways that conform to the norms, codes, and guidelines of their profession as well as to adhere to the guidelines, policies, rules and regulations of their employers (universities, industry, or research institutions) and of government (the public). These expectations in turn set standards that can be used to define **responsible conduct of research** (RCR). RCR is simply *conducting research in ways that fulfill the professional responsibilities of researchers, as defined by their professional organizations, the institutions for which they work and, when relevant, the government and public*.

The term "research integrity" refers to a characterization or presents an evaluation of research behavior. "Integrity" stems from the Latin word "integrita," which means *wholeness* or *completeness*. When applied to behavior, *integrity* describes a person who *wholly* or *completely* possesses "soundness of moral principle; the character of uncorrupted virtue, esp. in relation to truth and fair dealing; uprightness, honesty, sincerity."[3] If the context for discussing integrity is directed specifically to professional behavior, then professional integrity can be defined as "the quality of possessing and steadfastly adhering to high moral principles or professional standards."[4] Further applying the latter definition to research, research integrity becomes *the quality of possessing and steadfastly adhering to high moral principles* and *professional standards, as outlined by professional organizations, research institutions and, when relevant, the government and public*.[5]

Defining research integrity in terms of both moral principles *and* professional standards is problematic. Moral principles and professional standards play different roles in research. A moral obligation to "be truthful," even when backed by a professional code, does not function in professional life the same way as a professional responsibility or institutional requirement "to record and report data accurately in a bound, dated, and signed notebook." Moral principles bring moral reasoning and ethics into consideration, particularly when different moral principles apply to a situation or

when the moral principles themselves are the subject of debate. By implication, moral principles raise *questions about what researchers should do*. Professional standards, supplemented by institutional and government rules and regulations, provide more or less *clear guidance on what researchers should do*.

The different role moral principles and professional standards play in research is important enough to justify dividing the study of professional research behavior into two subfields: research behavior measured in terms of and guided by moral principles versus research behavior measured in terms of and guided by professional standards. The former reasonably falls under **research ethics** (RE) and can be defined as *the critical study of the moral problems associated with or that arise in the course of pursuing research*. The latter falls under what the Office of Research Integrity (ORI) has called "**research on research integrity**" (RRI), where **research integrity** (RI) is defined as *possessing and steadfastly adhering to professional standards, as outlined by professional organizations, research institutions and, when relevant, the government and public*[5] (see Fig. 2 below).

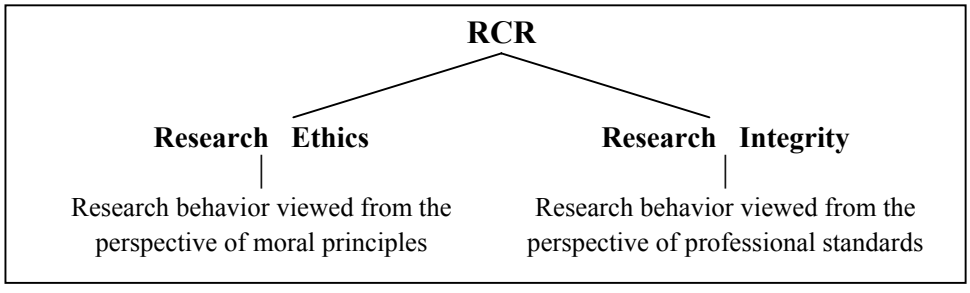

Fig. 2. Research ethics vs. research integrity

Dividing the study of RCR into two subfields, among other advantages, avoids the pitfalls encountered by the Institute of Medicine (IOM) Committee contracted in 2001 by ORI to define and recommend ways to measure research integrity.[6] The IOM Committee approached its task from an ethical (moral) perspective, specifically arguing that "…[j]udgments about a person's integrity are less about strict adherence to the rules of practice and are more about the disposition to be intellectually honest, accurate, and fair in the practice of science…."[6 (p.62)] The adoption of this position further prompted Committee members to resist "... defining integrity in terms of (1) adherence to … normative practices …, (2) the knowledge and awareness of the practices of responsible research, and (3) the attitudes and orientation toward the practices of responsible research …."[6 (p.62)] Having adopted this approach, when they endeavored to recommend ways to measure "disposition," as opposed to "adherence," they came up empty handed, concluding that "no established measures for assessing integrity in the research environment exist."[6 (p.3)]

While professional standards, supplemented by government regulations and institutional policies, are not necessarily the be-and-end-all for assessing responsible conduct, they in fact provide a very practical starting point for measuring whether the

funds the public invests in research are used responsibly. Intellectual disposition and ethical inclinations notwithstanding, failure to follow professional standards wastes professional time and public funds, potentially slows the course of research, undermines professional and public trust, and, at times, can result in public and/or personal harm. The failure to follow professional standards can also be measured and possibly corrected. The next two sections summarize the findings of scholarly investigations into research integrity, understood hereafter as adherence to professional standards and other rules. Section 2 summarizes what is known about behaviors that depart from professional standards; Section 3 discusses the impact of irresponsible behavior on research and the public that supports it.

2. Levels of occurrence of irresponsible behavior in research

Early estimates of the occurrence of irresponsible conduct in research suffered from two shortcomings, which led to under- and over-estimations. Those supporting lower estimates of irresponsible behavior based their arguments on the number of confirmed cases, which has been, and remains to this day, low relative to the total number of researchers. In combination, the two agencies that confirm the most cases—the National Science Foundation (NSF) and the Department of Health and Human Service—report only 20-30 cases in a typical year.[7-9] Assuming there are about 2.5M researchers in the US, the rate of occurrence is seemingly less than .001% or 1 case of misconduct for every 100,000 researchers. However, as pointed out by Glick as early as 1989, confirmed cases of crimes and irresponsible behavior seldom provide reliable estimates of actual rates.[10 (pp. 78-79)] Moreover, studies have suggested that researchers do not report the misconduct they know about, thereby undermining the main mechanism for discovering misconduct.[11-15] Accordingly, the argument that misconduct in research is "rare" was not and to this day is not supported by hard evidence.

Earlier higher estimates of the occurrence of irresponsible behaviors came from surveys that did not control for duplicate reporting, that is, for two researchers knowing about and reporting the same case.[1,11,12,16,17] The early surveys also did not confirm whether those surveyed correctly understood what constituted irresponsible behavior or whether the cases they reported where in fact examples of irresponsible behavior. These weaknesses were understood at the time by some researchers. In the most ambitious early survey conducted by Swazey and colleagues in 1993, the authors clearly stated that they could not estimate "…what percentage of faculty or graduate students in a given department or in the four disciplines [studied] may be engaging in a particular type of misconduct or questionable research practice." This limited their findings to estimates of "… the exposure of graduate students and faculty to what they believe is ethically wrong or problematic conduct in their departments."[16 (p.544)] Consequently, early "tip-of-the-iceberg" arguments were in some ways as inconclusive about levels of occurrence as those suggesting that research misconduct is "rare."

2a. Serious misconduct

Although early misconduct surveys had their shortcoming, when combined with other evidence they should have raised suspicions that research misconduct is not as rare as argued by some. It was well known at the time that undergraduate academic misconduct rates, even in professional programs such as engineering or in honor-code schools, were commonly reported to be well above 50%.[18] Comparable studies of medical students turned up lower but still significant[a] rates of academic misconduct.[19-23] In 1992 Kalichman reported that over one third (36%) of a group of graduate students and postdoctoral students surveyed said they had observed some type of research misconduct. Kalichman also reported that 15% of his respondents said they would fabricate or falsify information if it would help get a grant funded or a paper published.[24] Similar levels of occurrence were reported by Brown in 1998 and Geggie in 2001, using the same instrument.[25,26] Over five percent (5.7%) of the respondents in Geggie's survey admitted that they themselves had committed misconduct in the past.[25(p.344)]

Over the last five years, more evidence has accumulated that appears to puts the level of occurrence for serious misconduct near 1%. Fifty one percent (51%) of 422 respondents in a survey sent to members of the International Society of Clinical Biostatistics had intimate knowledge of at least one case of serious misconduct over the last ten years; 31% had "…been engaged in a project in which fraud took place or was about to take place;" 13% had been asked to support fraud.[15] Broken down by field, this study also found that "…subjectively estimated prevalence of fraud in published reports was somewhat greater for epidemiological studies than for clinical trials (interpolated median values 0.80% and 0.69% respectively; $p = 0.047$)."[15 (p.419)] A second study of 330 authors responding to a survey about articles reporting the results of pharmaceutical clinical trials over the last 10 years arrived at similar numbers. Two authors (0.6%) reported serious misconduct in the target article and 15 (2.7%) reported serious misconduct in the study itself, including "fabricated or falsified data," "deleted data in an unjustified way," "deceptive or misleading report of design," "deceptive or misleading report of data," and "seriously misleading interpretation of results."[27 (p.248)] A third study summarized in an oral presentation at the 2004 Research Conference on Research Integrity reported that 8 of 800 (1%) submissions to *The Journal of Cell Biology* included digital images that had been improperly manipulated.[28]

The 1% figure emerged most recently in an innovative study of NIH-funded researchers conducted by Martinson and others. Two key features set this study apart from earlier work. First, it specifically asked researchers about their own behavior over a relatively short period of time—the last three years. Second, the behaviors singled out for study are ones that researchers themselves identified in focus groups as worthy of concern. While the final results from this study have yet to be published, the initial findings published in *Nature* again place the level of occurrence of the most serious misbehaviors at around 1% or higher. Of the roughly 3,300 researchers responding, 0.5% admitted to "falsifying or 'cooking' research data," 1% to using "another's ideas

a. Throughout this paper, the term "significant" implies roughly 10% or greater.

without obtaining permission or giving due credit," 5.3% to failing "to present data that contradict one's own previous research," and 12.8% to overlooking "others' use of flawed data or questionable interpretation of data."[29 (p.737)] Since self-reporting in this case serves no obvious purpose and there seems to be no incentive for those who engaged in these behaviors to report in higher numbers, there is no obvious reason to view these numbers as inflated.

While many of the practices reported in the Martinson study might not fall within the narrow definition of research misconduct adopted by the Federal government (see Section 4 below), the fact remains that practices researchers themselves classify as problematic seem to occur at much higher rates than previously assumed. More work needs to be done to clarify the significance of the higher levels of occurrence, their relative presence in different fields, and their causes. But at the very least, it seems time to shift the burden of proof from those who feel serious misconduct may be fairly common to those who continue to argue that it is rare and therefore not a major concern.

2b. Questionable Research Practices (QRP)

In its 1992 report, a National Academies of Science committee defined QRP as "…actions that violate traditional values of the research enterprise and that may be detrimental to the research process."[30 (p.28)] It separated these practices from FFP because they do not "directly damage the integrity of the research process" [30 (p.28)] and are therefore presumably less serious. The pool of NIH respondents mentioned above,[29] reported in engaging in these practices at higher rates than FFP, as might be expected; 4.7% said they had published the same data or results in two or more publications, 10.0% had inappropriately assigned authorship credit, and 27.5% admitted to inadequate record keeping. These percentages are comparable to those reported in other empirical studies of a wide range of questionable practices (QRP) that violate traditional values or commonly accepted practices, from initial project design through to publication and peer review. Some of the more important findings about the occurrence of QRP include the following:

Misrepresentation. Researchers should honestly and accurately represent their contributions to research publications. Studies have shown that significant numbers do not. Resume checks have found that on average more than one in ten medical students applying for research fellowships inflates his or her role in research by changing the order of authors, listing unaccepted papers as "in press," or inventing bogus publications.[b,32-41] Similar rates (15.6% single discrepancy; 4.4% multiple discrepancies) were reported in one study of faculty resumes.[35]

Significant numbers of researchers do not appropriately represent their contributions to research publications, based on commonly accepted authorship rules, such as the *Uniform Requirements for Manuscripts Submitted to Biomedical Journals*

b. One study has questioned the accuracy of these findings, based on a more complete effort to track down suspected publications in one field. The more complete effort to track down sources reduced the suspected rate of misrepresentation to 1.8%.[31]

published by the International Committee of Medical Journal Editors.[42] Estimations of the occurrence of honorary authorship (insufficient contribution to a publication to justify author status) range from a low of 9% to a high of 60%.[43-50] Ghost authorship (authors who contributed to but are not listed on publications) estimates range from 9% to 11%.[44, 47] One study of the changing characteristics of authors on multiple-author papers found the greatest increases in professors and department chairs, pointing to these positions as one possible source of misrepresented contributions.[51]

Researchers also misrepresent the originality of publications by publishing the same information more than once without informing readers (duplicate publication).[52-61] The estimated rate of duplicate publication varies from a few percent to more than 20%, depending on field of study and criteria used to define duplicate publications. So-called "salami slicing" publication (publishing the results of one experiment into several partial publications primarily for the purpose of increasing the number of publications) is probably more common but is not as well studied.

Inaccuracy. Research misconduct policies commonly exclude honest errors and careless mistakes.[62 (p.76,262)] Errors and mistakes are not uncommon in research and can have significant impacts (see discussion in Section 3). Whether they are truly innocent (i.e. not intentional) in some cases is questionable.

Not surprisingly, in environments where the pressure to secure funding and publish can be intense, researchers make careless mistakes in notes and bibliographies. Typically, checks of the accuracy of citations (citational errors) turn up error rates in the range of 30%-50% or higher.[63-79] Less commonly, but still in the 10%-30% range, researchers make substantive errors when quoting other publications—errors commonly labeled "quotational errors."[65-79]

Citational errors presumably just waste time; quotational errors can be more serious since they can lead to improper conclusions. One study of references to an AIDS intervention trial reported that 8% of the citations improperly characterized the findings. The trial showed that greater access to primary care physicians could lower mortality rates whereas the citations said mortality was reduced with greater access to specialty or expert care.[78] The impact of these and other inaccuracies is compounded by the fact that researchers also fail to confirm the authenticity of the publications they are using, as evidenced by the fact that articles with flawed information continue to be cited long after they are retracted.[80-84]

Inaccuracies also make their way into research through the summaries researchers present of their work in abstracts, descriptions of methods, and summaries or discussions. Studies have shown that significant numbers of researchers improperly or inadequately summarize findings and conclusions in abstracts.[85-88] Researchers also sometimes fail to provide enough information about methods to allow other researchers to evaluate or replicate their findings.[89] In some cases, poor reporting of methods could lead researchers to discount or ignore valid findings. One extensive study of reported versus actual protocols in 56 randomized controlled radiation therapy trials reported that proper methods were used in most trials (75% or greater) but described in 20% or less of the publications from these trials.[90, see also 91] The accuracy of research is also

compromised by the use of improper statistics and data analysis. Whether due to carelessness or lack of proper training, some researchers simply fail to use appropriate statistical methods to analyze their findings.[92, 93]

Bias. Research strives to bring objectivity to investigations. This implies that researchers should make reasonable efforts to separate personal, subjective views from experimentally based factual information. The extent to which this is possible or even desirable has been the subject of considerable debate. Nonetheless, it is today widely agreed that some bias, particularly bias resulting from financial considerations, is inappropriate and at the very least should be reported or perhaps altogether avoided. Such agreement notwithstanding, various forms of bias are fairly common in research and may adversely impact the research process.

Researchers have studied the influence of bias—making decisions or presenting evidence for other than scientific or scholarly reasons—in many aspects of research. Studies have documented the presence of bias in the publication process.[94] The sources of the bias in publication have been linked to country of origin,[95] institutional affiliation,[96] research orientation,[97] and author vs. reader status.[98] Bias can also be introduced in the design of studies, the way data are interpreted and/or the way data are reported.[99-104] Rates of bias are difficult to quantify. The main measure used in most studies is "statistical significance," meaning that the suspected bias has been identified using appropriate statistical tests.

Many studies have documented the increased complexity of the financial basis of research, with particular attention to the growing influence of industry funding.[105-114] Three recent studies report significant correlations between published findings and source of funding. Briefly summarized, researchers are more likely to report a drug or treatment effective if they are funded by the entity that has a financial interest in the drug or treatment than researchers who have other sources of funding. The reported odds ratio for bias in the three studies ranged from roughly 2.5 to 4.0.[115-117] That this bias reflects irresponsible behavior has been argued for specific cases[118, 119] and in general studies of financial conflict of interest.[120, 121] There are, however, factors that may account for some of this bias, making it difficult to estimate the level of occurrence of improper financial conflicts of interest.

3. The Impact of Irresponsible Behavior

Measuring the size of the irresponsible research conduct iceberg (levels of occurrence) does not provide information about its density or, as termed here, its "impact." Irresponsible behavior can adversely impact research in at least four ways. It can: 1) undermine the reliability of the research record, 2) weaken the trust colleagues have in one another and the trust the public has in researchers, 3) waste research funds, and 4) lead to decisions that cause public and/or personal harm. As obvious as these impacts may appear, ironically, little is known about the extent to which they occur in practice or their relative importance.

3a. Fabrication, Falsification and Plagiarism

Although it might seem counter-intuitive to suggest, there are good reasons for questioning how much the three presumed most serious research misbehaviors—FFP—adversely impact the research record or society. Plagiarism has no necessary impact on the reliability of the research record. Results are results, whether or not the person reporting them deserves credit for their discovery. Plagiarism may waste some funds—the funds used to review and publish a plagiarized article or to pay a person who may not deserve a particular position or promotion. It can also undermine trust between colleagues, if they become fearful of having their ideas improperly used by others, and potentially cause some public harm, if a plagiarist is not truly an expert in some field of study and is called upon to give advice in that area. Therefore, for a number of reasons plagiarism cannot be ignored, but the extent of its impact on research is probably small in comparison to other irresponsible behaviors.

In contrast, fabrication and falsification obviously can have significant impacts on research. A researcher who intentionally publishes fabricated or falsified research results clearly undermines the reliability of the research record and of all decisions and/or relationships based on that research. However, many of the confirmed cases of misconduct revolve around actions undertaken before the work in question is published or, in some cases, circulated outside the laboratory. Over the past three years, only 2 of 25 cases closed by ORI involved five or more publications; 15 were limited to raw data, in-house reports, grant applications or unpublished manuscripts. (Table 1)

# Publications	Cases
5+	2
3	1
2	1
1	6
0	15
Total cases	25

Table 1. Frequency of tainted publications
ORI misconduct cases, 2003-2005

A majority of cases focused on staff, graduate students or postdocs, whose misbehavior was detected before the results made their way into print, thus reducing (not eliminating) the overall impact of the irresponsible behavior.

Even in major cases of misconduct that have included publications, the full impact on the course of research is difficult to assess. Bell Labs researcher Eric Schön did mislead colleagues and wasted the time it took to try to duplicate his fabricated and falsified experiments, but he also may have stimulated critical inquiry in an emerging research field.[122-125] Victor Ninov's falsified reports on the alleged discovery of new elements at Lawrence Berkeley National Laboratory wasted the time of colleagues and might have undermined public support for physics research, but the research record

was quickly corrected without any apparent long-lasting effect.[126, 127] The two best-known cases from the late 1980s, the Imanishi-Kari and Gallo cases, were eventually dismissed and therefore are not officially cases of misconduct, although there are certainly those who feel they represent serious misbehavior and had significant public costs.[128] In sum, *impact*, even in major cases that attract national attention, is neither obvious nor easily measured.

One major case recently closed by ORI provides a good example of how little is known about the actual impact of FFP. For nearly a decade, University of Vermont researcher Eric Poehlman fabricated and falsified research results that appeared in at least 10 publications and several grant applications. His work was and still is cited and presumably used by colleagues. Just what impact his misconduct had on his field of research, however, is still far from certain. To date, no evidence has been gathered to show that his work seriously misled other researchers. His work has not been linked directly to improper policy decisions, although it potentially had important direct applications to decisions about women's health and hormone replacement therapy. That it took 10 years to uncover his misconduct could undermine trust in research, but the fact that the University of Vermont took decisive action once allegations were made could actually bolster public confidence. In other words, apart from wasted research funds, which in this case amount to at least several million dollars, and adverse impacts on the careers of some of those who worked with Poehlman, the overall impact of his serious misconduct is at best uncertain and perhaps not particularly significant for his field of research.[129-131]

3b. Questionable Research Practices

The same cannot be said for QRP. If for no other reason, simply based on higher levels of occurrence, QRP should have proportionally greater impacts on research than FFP. For example, two questionable practices—duplicate publication and 'salami slicing' publication—result in more research articles appearing each year than is presumably necessary to record the normal course of research. As noted above, duplicate publication rates have been calculated to be 10-20% in some fields. There have been no studies of the level of occurrence of 'salami slicing' publication. Assuming the rates are comparable to the more serious offense of duplicate publication and taking the lower estimate of 10%, these two irresponsible practices are probably resulting in 1,000s if not 10,000s of unnecessary publications each year. NLM adds over 500,000 citations to its article database each year.[132] If roughly half of the citations are to research articles and one in ten of the research articles is unnecessary, 25,000 publications could presumably be eliminated without seriously hampering the course of research. The savings (waste), in terms of editorial, review, and journal subscription costs, from 25,000 fewer publications each year could easily run into the millions of dollars.

Unfortunately, the impact of QRP can be much more serious than wasted publication dollars. In two recent cases that involved the death of research subjects, Jessie Gelsinger at the University of Pennsylvania[133-137] and Ellen Roche at Johns

Hopkins University School of Medicine,[138-140] it has been suggested that more careful attention to prior research findings could have prevented the deaths. The Gelsinger case also raised concerns about conflict of interest.[141] Neither of these offenses—failure to conduct a proper literature review or failure to disclose conflicts of interest—would qualify as misconduct under the Federal definition of misconduct and most institutional policies. Their impact, measured in terms of public and personal harm, is nonetheless much greater than, for example, a field worker falsifying a few interviews in survey research.[142, 143]

As tragic as the death of individual human subjects may be, QRP probably has its greatest impact in the area of research-based, health-care decisions—new drugs, new medical devices and procedures, new treatment protocols and the like. Critics of the pharmaceutical industry, such as Marcia Angell, argue that bias and unprofessional conduct in research wastes $100s of million of US health-care dollars and adversely impacts public health. Angell specifically singles out two areas of questionable practice, biased reporting and improper study design, as major contributors to the unwarranted growth in health-care costs in the US. The improper practices she singles out include: the use of inappropriate controls and treatment periods, the improper choice of subjects, the improper administration of competing treatments, and the selective publication of data to support desired conclusions.[120 (pp.106-111)] In the end, these practices lead to what Angell characterizes as "bias and hype" rather than the objective research that is needed to make responsible health-care decisions.[120 (p.114)]

While not as pointed in expressing their concerns, other researchers seem to be as troubled by QRP as Angell. Besides "falsifying or 'cooking' research data," the serious misbehaviors identified by the research community in the Martinson study recently published in *Nature* include:[29]

- Not properly disclosing involvement in firms whose products are based on one's own research.
- Failing to present data that contradict one's previous research.
- Changing the design, methodology or results of a study in response to pressure from a funding source.
- Withholding details of methodology or results in papers or proposals.
- Using inadequate or inappropriate research designs.

The percentage of researchers who said they had engaged in these practices over the last three years ranged from 0.3% (not properly disclosing involvement in firms …) to 13.5% (using inadequate … designs). Researchers therefore both understand that practices generally classed as QRP are improper and still engage in these practices at what are presumably unacceptably high levels.

Similar results emerged from a study of clinical research practices using a three-round Delphi Survey approach. Based on this survey, Al-Marzouki and colleagues developed a list of 60 practices that a group of 40 prominent clinical researchers agreed (50% or more) could adversely impact research results. Only three of the 60 practices—data falsification, data fabrication and altering results in knowledge of allocation—fell under the Federal definition of misconduct (FFP) and all three dropped

off the list of practices that most concerned researchers when "likelihood to occur" was factored in. The final list of irresponsible practices that researchers felt were both likely to occur and likely to adversely impact results falls outside the Federal definition of research, overlaps significantly with practices generally listed under FFP, and mirrors in many cases the practices that Angell and others claim are wasting health-care dollars and adversely impacting health-care decision making. (Table 2)

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

Table 2. Percent agreement on likelihood of irresponsible behaviors to affect clinical trials

4. Conclusions and recommendations

In a recent "Word from the President" of the Association of American Medical Colleges (AAMC), Jordan Cohen wrote concerning the irresponsible research behaviors reported in *Nature*:[29]

> How can we ensure that all investigators conduct their research responsibly? Inviting federal oversight by expanding the definition of scientific misconduct to encompass these behaviors is most assuredly **not** the answer. Fabrication, falsification, and plagiarism are well-understood words. They describe actions that are unambiguous, easily documented, and deserving of stern sanctions. The kinds of behaviors more frequently cited by respondents to the survey reported in *Nature* are much less definitive and far better handled at the institutional level. This is a matter that calls urgently for self-discipline by the profession, not more regulation by government.[144]

A committee of the National Academy of Sciences voiced a similar position in 1992 when it coined the term "questionable research practices."[30 (pp.28-29)] Unfortunately, in the intervening thirteen years, the research community has not taken the steps needed to assess where weaknesses lie, design strategies to address these weaknesses, and

move forward in an effort to assure the public that its investment and trust in research are well placed. The lack of action suggests that it is time to refocus efforts to study and respond to irresponsible conduct in research.

When the first major cases of misconduct broke in the late 1970s, government was intent on eliminating all misconduct from publicly funded research. The first Congressional hearings were called to investigate *Fraud in biomedical research*.[145] The earliest enabling legislation, the 1985 Health Research Extension Act, couched its discussion of "scientific misconduct" in terms of "public trust," concluding: "Biomedical research—particularly that supported with public funds—must be conducted with the highest ethical and intellectual standards."[146 (p.710)] Over time, however, and at the urging of a few key players in the research community, this broad effort, based heavily on *public interest*, was slowly replaced by one overriding *scientific/research interest*: protecting researchers from perceived burdensome and unnecessary regulation.

The shift from public interest to the interests of the research community took place over a number of years. By 1989, the initial discussion of "fraud" in research,[2,11,80,81] which carried implications of criminal conduct, was recast in the legally less binding term "misconduct." The first definitions of misconduct, however, contained one crucial clause, the so-called "other practices" clause, that allowed government to investigate behaviors that "seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research."[147] This clause, which was seldom if ever used, was strongly opposed by some members of the research community[148] and criticized in the 1992 NAS report. The latter recommended that "federal agencies should review their definitions of misconduct in science to remove ambiguous categories such as 'other serious deviations from accepted research practices'."[30 (p.14)] After more pressure to restrict government authority to FFP, the "other practices" clause was dropped in 2000, when a Committee under the Office of Science and Technology Policy proposed a new common Federal definition for research misconduct. The new and current definition not only dropped the "other practices" clause but further narrowed the government's authority by limiting misconduct to behaviors that "deviate from the common practice of science."[62 (p.76,262)] As a result, the clause that had initially been designed to broaden government authority *in the public's interest* is now used to restrict that authority to protect the perceived *interests of the research community*.[149]

The growing body of research on research integrity discussed above clearly shows that the public's investment in research is not adequately protected from irresponsible practice. Research is not uniformly "conducted with the highest ethical and intellectual standards."[146] The most recent research findings also strongly suggest that the greatest public harm in terms of wasted dollars and questionable health-care decisions stems from QRP, not FFP. Jordan and others have recognized the potential seriousness of this situation. Researchers, research institutions, and professional societies are making efforts to improve training and to foster greater responsibility in research. However, it is questionable whether these efforts will succeed without a fundamental change in the way irresponsible conduct in research is studied, taught, and regulated.

To make substantive progress in the drive to foster integrity and deter irresponsible conduct in research, we propose four steps for discussion and serious consideration:

First, irresponsible conduct in research should be approached from the perspective of professional standards, not professional ideals. To be sure, one would hope that some broader sense of ethical responsibility exists, some deeper "disposition to be intellectually honest, accurate, and fair in the practice of science."[144] It is also important to discuss moral issues raised by research as part of the study of *research ethics*. Nonetheless, in the final analysis what matters most, when measured in terms of public investment and public safety, are the behaviors researchers adopt when they design, undertake, and publish research. This is where efforts to improve integrity in research need to begin, with the careful study of deviations from professional standards, their causes, and measures that might reasonably be expected to change behavior.

Second, research institutions and professional societies, working with government, should increase their efforts to make sure that professional standards for responsible research are clear, easily accessed, taught, and monitored. Important steps have been taken over the past two decades to improve professional standards, some as a result of government mandates (e.g. IRB regulations and misconduct policies), some at the initiative of researchers (e.g. publication rules and standards for reporting clinical trials). There remain, however, major gaps in coverage and the need to assure better education and monitoring. Moreover, it is important to recognize that guidance on responsible conduct will have no impact if the recommended conduct is not openly embraced by the research community, passed on to future generations of researchers, and effectively self-monitored.

The call for more attention to clear guidance on and to self-enforcing the rules for responsible practice is not new. The 1992 NAS Report firmly concluded that:

- Research mentors, laboratory directors, department heads, and senior faculty are responsible for defining, explaining, exemplifying, and requiring adherence to the value systems of their institutions.
- Administrative officials within the research institution also bear responsibility for ensuring that good scientific practices are observed in units of appropriate jurisdiction and that balanced reward systems appropriately recognize research quality, integrity, teaching and mentorship.[30, pp. 7-8]

AAMC has recently partnered with ORI to provide support for professional societies to develop RCR guidelines, codes and programs.[150] However, even though the situation "calls urgently for self-discipline by the profession,"[144] progress is still slow.

Third, more attention needs to be directed to the "institutional" dimensions of research integrity, so clearly identified in the 2002 IOM report, appropriately subtitled: "Creating an environment that promotes responsible conduct."[6] Although support for research continues to grow generally, shifting patterns of support (e.g. less government and more industry funding or less emphasis on basic and more on applied research) place demands on researchers that could influence (positively or negatively) research behavior.[151] To date, little has been done to implement two key IOM recommendations:

- Research institutions should evaluate and enhance the integrity of their research environments using a process of self-assessment and external peer review in an ongoing process that provides input for continuous quality improvement.
- Institutional self-assessment of integrity in research should be part of existing accreditation processes whenever possible.[151 (pp.13-14)]

The slow progress in this and other areas suggests, notwithstanding likely strong objections from some elements of the research community, one final and crucial step.

Fourth, government authority for studying and responding to irresponsible conduct in research should be expanded to include behaviors that seriously compromise the public's investment in research or lead to decisions that adversely impact the general health and welfare of the Nation and of individual citizens. Any expansion of government authority needs to be undertaken with caution. It is unrealistic to expect research to be error free. Even after checking and rechecking sources and the subsequent proofing by the journal editor, I assume there are still errors in this paper. It is not in the public interest for research institutions to set standards for research integrity too high or for government to venture into areas where significant public impact is not evident. However, when evidence suggests that irresponsible research practices occur at unacceptably high levels and have significant impacts, which research on research integrity suggests it does, it makes no sense to deny government the authority it needs to look into those practices simply because they do not fall under FFP.

Most of the steps taken over the past two decades to foster greater integrity in research and to confront irresponsible behavior have been in response to government action, including the definition of misconduct, the adoption of research misconduct policies, and the establishment of RCR education programs. Others, of course, have made significant efforts to call attention to the importance of integrity in research and made important contributions to program development. But more often than not, urging from government made the difference in determining whether the next important step was taken. To assure that the next steps are taken in the continuing challenge to improve integrity in research, it is essential for government to have the authority it needs to work with the research community to improve integrity in research.

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