Commentaries

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Scientific Ethical Integrity and Human Research Subjects Protections Non-compliance Remediation: Commentary on Practical Considerations and Implications

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Remediation for Human Research Subjects Protections Non-Compliance: Practical Considerations and Implications

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Abstract

Medical science's advancements depend on preserving its credibility and the public trust, though as a human institution it is fallible and liable to ethical breaches that can void public confidence and support. There is no more egregious ethical departure than deviations / violations of Human Research Subjects Protections (i.e., non-compliance), which is remarkable given they are fairly widespread and often repeated. Once uncovered, this generally should result in the research's suspension or termination. Yet, there is a third option to preserve valuable and worthy research that went awry due to lapses in Human Research Subjects Protections, specifically, Remediation. Due to the sequestered nature of Remediation, little has been reported on its processes, and practically nothing, regarding practical considerations, recommendations, and implications for the remediation workers themselves—for this line of work is perilously risky. This commentary reports some of those best-practices, "first-hand grittier in-the-trenches" informed practical lessons learned. Implications are discussed in the interest of improving the reasonable, balanced, and competent

ethical conduct of research, addressing / avoiding Human Subjects Protections ethical non-compliance, and avenues for further inquiry regarding Remediation.

Introduction

Medical science is a vital and principal institution due to its promises of a far-reaching and alluring compendium of advancements through which there is greater predictability, control, and improvement in the human condition.[1-3] Nevertheless, it is a human institution—fallible, and prone to ethical breaches, misconduct and breaks from scientific integrity.[3-7] Thus, preservation of the scientific enterprise's credibility and the public trust vested in it is predicated on ensuring sound scientific integrity. In the post-modern era, with rapid dissemination of information and increased democratic processes, the risk of accusations of breaks in scientific integrity is magnified greatly.[9-10] The loss of public confidence in medical scientific research institutions may corrosively erode public support for medical scientists and their research programs everywhere.[3,9,11,12] Concern should be paramount and ubiquitous for preserving scientific integrity and to achieve reclamation, if possible, where there have been ethical breaches in otherwise valuable and meaningful research. [3,13-16]

Probably there is no more egregious ethical breach of scientific integrity in medical research than deviations or violations (i.e., non-compliance) of Human Research Subjects Protections, especially anything abrogating adequate informed consent to participate in research (e.g., no consent obtained, wrong consent, language not translated, improperly completed consent, consent P&P not followed, consent undocumented, etc.).[17-19, 20] The integrity of Human Research Subjects Protections is commonly considered inviolable and sacrosanct.[20] Unfortunately, violations are fairly common, even though there are a plethora of formally established safeguards, policies, procedures, regulations and agencies and agents, as well as punitive sanctions for such violations.[21-25] A large proportion of scientific research wrongdoing (approximately 50%) falls under the rubric of Human Research Subjects Protections non-compliance, with nearly 100% attributable to "Failure to Follow Procedures."[19] Conservatively, there are estimates over a two-year period of about 1,200 - 2,150 cases in the U.S. per year alone. No one can be exactly sure, because they are sensitive cases and therefore kept secret.[22, 27] Furthermore, most of the known offenders tend to be repeat offenders, even with multiple layers of prevention for recidivists. [26,28]

Background

Typically, after an audit finds substantial, continued, and patterned deviations, violations, and abuses, an Institutional Review Board (IRB) assigns a level of non-compliance; based on this level, there are two formal absolute options: suspension or termination.[29-32] However, there is a 3rd informal option of Remediation, depending on whether the research is valuable, worthy, and can be redeemed through restitution and reclamation, restoration of trust, significant risk management, remorse and contrition, and establishing preventive plans of actions to avoid recidivism.[22,33-36] Remediation offers scientific research institutions and agencies opportunities for reclaiming and salvaging otherwise worthwhile research studies that went astray due Human Research Subjects Protections non-compliance.[16,22, 35,36]

Human Research Subjects Protections Deviation / Violation remediation projects may be widespread and fairly common—so much so that IRBs employ a common acronym: "HRSPD/V-CAPA" or "CAPA" for short (i.e., Corrective And Preventive Action plan) to describe them.[37,38,cf.39] Yet, little has been written and virtually no formal research has been done on how they are conducted, much less the practical implications for those burdened with conducting them.[22,39,40] Note: there are probably about as many Human Research Subjects Protections-related CAPAs as there are scientific

research-intensive institutions.[41,42] But any formal reports are usually vague summaries void of practical detail and limited to the extent IRBs require public dissemination and demonstrations of open contrition and penitence.[30,31] This is probably the consequence of their embarrassing and sensitive nature, so that only direct participants are truly privy to them.[17-20] Thus, the world of Human Research Subjects Protections non-compliance remediation is one that is a "known secret"—but dark, murky, nebulous and rarely discussed in public venues unless mandated, and then only to the extent mandated.[22]

Purpose

A substantial number of Human Research Subjects Protections CAPAs also are a testament to the notion that valuable scientific research studies can and do make related mistakes, but these can be redeemed through remediation. [3,13-16, 22] Yet, formal empirical studies on Human Research Subjects Protections violation remediation would be an admission that an egregious, non-condoned, profane violation occurred of something considered sanctified. "It is not supposed to happen, but it does, and how it is done and what does that mean for the one(s) who have to do it has been as-of-yet unspoken."[43,44] Nevertheless, given that these affairs and their repair are apparently widespread, and to fill the gap regarding this vital information, the purpose of this article is to provide some informed conceptual yet practical lessons learned on involvement with Human Research Subjects Protections non-compliance remediation projects—particularly from the perspective and best interests of those directly involved with them. The points derive from the author's first-hand experience with repairing, reclaiming, and resurrecting multiple errant research studies that were temporarily suspended due to Human Research Subjects Protections deviations and violations at multiple research-intensive institutions. Though the perspective is that of an outsider or distanced party brought-in and specifically tasked with fixing up, cleaning up and restoring a study or studies to ethical health, the advice, guidance, and recommendations are just as relevant to insiders involved with Human Research Subjects Protections Violation remediation.

Commentary

First, Human Research Subjects Protections Violation remediation projects can be extremely expensive and labor-intensive, as they probably will involve painstakingly re-conducting work that was done wrong or not at all for substantial numbers of human research subjects (e.g., hundreds, if not in the thousands).[45] "Remediation is a third option, but it is no free pass."[22] Also, remediation projects tend to be painful, ugly, and even dreadful affairs in that they involve an admission of extreme wrongdoing regarding a subject that should be sacrosanct— the defilement of which definitely is in the realm of professional discretization. So finger-pointing, "backbiting," and recriminations are not unusual—not to mention concerns about that 'the competitors in a highly competitive field might take the information and run with it should it leak out and become public.' The best possible course of action to counter all this is quickly: 'To get it out, you get it out, and you take control.'[46] Taking control involves transitioning quickly to acceptance of what happened, an accurate and visual needs assessment of the extent of wrongdoing, and the fast development of a course of action to correct it—and then implementing the plan as quickly and with as little fanfare as possible.[22,46] Also, it is better to propose a workable resolution developed from accurate data to the IRB and/or other regulatory agencies rather than have them propose an uniform one that is unworkable. Doing so also demonstrates control, competence, and subject-matter expertise regarding the situation, which can work wonders to restore trust and credibility.

Second, cleaning up and fixing up a mess often involves getting one's hands dirty. Specifically, there may be "guilt by association."[47] That is, the person or persons charged with remediation may become errantly typecast in the public eye—somewhere between ultimately responsible for the mess in the first place, or

associated with hard feelings surrounding the project itself (or both). Often, when Human Research Subjects Protections non-compliance is revealed—and especially where there was a substantial, longstanding pattern of behavior—the culprits responsible may attempt to run away, hide, and feign ignorance. Specifically, they turn tail and run knowing the true extent of the mess they created when faced with the unappealing and laborious prospect of cleaning-and-fixing-up a big mess with repercussions that may taint their reputations and careers. Moreover, anyone tasked with a remediation project should be cognizant that those involved in the non-compliance may use the self-serving and treacherous yet clever ruse of implying those involved in the remediation effort must have caused the non-compliance in the first place—or else they would not be involved in the remediation. This is not to mention that those privy to what resulted in the misconduct probably will be unavailable to those cleaning-up the resulting mess, so the Remediation Team will not have the benefit of their insight and knowledge to inform reclamation efforts.

Again, these situations have the potential to become rife with finger-pointing and blame-laying, especially at the innocent feet of the remediation workers. A viable recommended strategy for the remediation crew to counter the implications of "guilt by association" is to emphatically and publicly insist they were not the parties causing the original non-compliance with Human Research Subjects Protections; they are charged with helping to formulate and implement a viable solution. Vigorous support from research institutions' regulators and administrators of these public relations efforts should be obtained in advance of a remediation assignment.

Third, given the seriousness of allegations by the IRB or regulatory agencies, it is always a good idea to conduct a parallel internal investigation of the breadth and depth of external probes and findings (i.e., a needs assessment).[22] In other words, auditor / regulator reports should not be relied on exclusively. Typically, they only represent a sampling of detectable, significant Human Research Subjects Protections non-compliance, which might merely scratch the surface and fail to delve extensively into the problems.[22,32,37,38,43] Naturally, once detected in substantial and patterned amounts, formulations of systematic remediation plans should be predicated on a comprehensive needs assessment survey.[22] This survey should be conducted to visually depict any patterns and connections and to keep all parties focused and honest. This survey should be reported to the IRB.[22] This will facilitate a more hands-on, practical apprehension of what happened, how it happened, and how it can be fixed and improved or prevented going forward.[39,46,48] Also, it will help prevent the remediation team from cutting corners in the interest of expediency.

Most likely, one reason significant problems occurred in the first place was that no routine internal audit mechanism was established—or, if there was one, it was not comprehensive or involved enough. An internal needs assessment is the opportunity to establish a routine audit mechanism. A comprehensive survey entails a replete inventory and description of particular types and amounts of non-compliance. These are the "what happened" factors related to the unmet Human Research Subjects Protections regulatory standards; these types of problems can be ranked in terms of amounts and severity and the aggravating circumstances of whether they were unintentional or willful.[22] Addressing each issue then can become a collaboration between the IRB, regulatory agencies and study investigators. Doing so comprehensively and systematically can be a great confidence restorer by showing that the remediation workers are ethically "true to their word."

Fourth, remediation workers should be keenly aware that they are involved in the airing and cleaning of dirty laundry. In an industry that emphasizes image and professional reputation and prides itself on adherence and compliance with best-practices standards, there may

be fears that the workers might talk.[7,40] Remediation projects necessarily have deadlines for completion imposed by IRBs. When the work is over, there is an intrinsic risk—rather than gratitude for the Herculean tasks and egregious conditions under which they were accomplished—that the remediation workers may be disposed of over contrived reasons, much like sweeping yesterday's dirt under the rug with prejudice.[49] Any protests they register will be met with counter-protests of "sour grapes."[49] Likewise, public awards and tokens of appreciation for their hard work and a job well done will probably not be forthcoming, because this would be a formal acknowledgement that something sordid and scandalous occurred, which would rather be buried and forgotten.[49] Also, study administrators and investigators may want to be rid of constant haunting reminders of past transgressions. The remediation work may just be over with anyway.[49] One way to allay these fears would be for remediation workers to sign self-imposed non-disclosure agreements to secure their employment and ensure their discretion.

In sum, the interest of furthering the discourse on scientific integrity, this article attempted to provide some practical cautionary considerations and recommendations regarding involvement in Human Research Subjects Protections Violation remediation and reclamation projects for those "in the trenches." In terms of the consequences of considerations and aspects of Human Research Subjects Protections Violation remediation, this article proposes a practical, gritty real-world in-the-trenches depiction of scientific research ethics that can be synthesized and summarized as the following: "In the end, doing the right thing because it is the right thing to do will probably hurt," or, "No good deed has ever gone unpunished." But one still does the right thing anyway so as to look oneself in the mirror in the morning.

Rather than just a guidebook for side-stepping potential landmines, this article also tacitly highlighted that the pristine, ideal environment in which Human Subjects Protections are expected to be kept, the substantial efforts, personnel and resources expended to do so, and the absolutist sanctions for failing to do so, have seemingly established a Zero-Defect culture around an enterprise in which human error is the norm rather than the exception.[26,50] A Zero-Defect culture[51] dictates that such standards are so sacrosanct and inviolable that the research intensive institution and its personnel could not possibly engage in their violation or even deviation—whether this is actually true or not. A Zero-Defect culture, which is commonly considered ineffective, exists where the administration is intolerant of any errors, deviations or violations; it may choose to ignore evidence of any kind. As such, workers are not held accountable or empowered by failures and become complacent and unmotivated.[51] As such, in this culture workers who identify and report and fix mistakes (i.e., "stop-the-line") tend to be held in contempt and public opprobrium, even if they were not the source of the mistakes.[49]

This can be synergistically compounded by a scientific research culture of Paternalism.[50,51,61-71] Specifically, this is where renowned and funded medical researchers maintain a notion that they hold high authority due to their subject matter expertise in a particularly complicated and technical discipline; this tempts them to involuntarily or volitionally conduct research for their own interests and/or the greater good of science rather than in their patients' interests—because their patients "could never understand." The two cultures together and unchecked can synergistically result in a perfect storm that spawns substantial hidden Human Research Subject non-compliance, until some unexpected event causes them to surface.[49, 26]

This destructive pattern can be countered by a commitment to a: (1) Participatory Study approach to engaging patients where they are treated less as research subjects and more as participants in a collaborative effort [52-55, 26]; and (2) a Culture of Safety that acknowledges, though mistakes and errors should be avoided, that mistakes and errors do happen as we are all human.[56-58] Both (1) and (2) together mean that (1) actively engaged Study Participants have much to teach

researchers and (2) admission and study of ethical mistakes can be learning experiences from which to enhance adherence to policy and procedures and foster innovation from lessons learned. This combined approach has the additional benefit of workers and administrators taking responsibility and accountability for their actions, thus anyone can "stop-the-line," if they realize things have gone awry.

Conclusion

At heart this article is a stark admission that there is an unavoidable professional commitment to ensure that scientific research is conducted both ethically and competently; but failing that, remediation cannot entirely fix and make it like new again. Remediation can resurrect studies but cannot turn back the clock as if any wrongdoing or errors never happened. Nevertheless, remediation may be the one saving grace to reclaim valuable and important research despite Human Research Subjects Protections non-compliance. To fill a gap in the scientific integrity and ethics literature regarding information about the personal risks and hazards of those in the "remediation trenches," this article provided pointers with practical implications along with recommendations of best practices.

At minimum, this article acknowledges a known problem that has been kept in the shadows due to its sensitive, controversial, and taboo nature. At best, this article serves as the impetus for more definitive and perhaps empirical works and discourses on the subject matter. Then the hushed whispers and disquietude surrounding a heretofore forbidden and censured subject will be brought to light and transformed into acceptable and credible peer-reviewed scientific articles. After all, prevention is far less costly than cure, and the focus should be on preventing scientific misconduct and ethical breaches, especially Human Subjects Protections non-compliance, rather than fixing and cleaning up the damage afterward. Yet, without a common body of knowledge about Human Subjects Protection Violations / Deviations and their corrective remediation, this less costly prevention is improbable.

Declarations

Ethical Approval and Consent to Participate

Non-applicable, this was a commentary supported by a review of supporting open-source documents and analyses of anonymous publically available data.

Consent for Publication

Yes.

Availability of Data and Materials

Yes, publications and sources are available on-line or provided by author upon request.

Competing Interests

None declared.

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Authors' Contribution

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