**Reproducibility Paper**

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**Assignment Acknowledgement**

This assignment uses generative AI, specifically Grammarly to check for grammatical correctness.

Part 1: What is the reproducibility crisis in biomedical research? What are the major consequences?

Reproducibility in science refers to the ability to achieve the findings of another study by employing the same methods within the same experimental conditions (National Academies of Sciences, Engineering, and Medicine, 2019). It serves as an integral aspect of scientific validity, affirming that the study’s results are reliable and not due to chance. Another critical premise of reproducibility is to gather consistent results that can be compiled for meta-analytical and statistical assessments, which heightens the impact of the findings. Such confirmation of results enhances reliability promoting the progression of the specific scientific area. This level of reliability further solidifies the basis upon which there is novel development of interventions or refinement of current therapies.

However, the recent scientific landscape has been suffering from a reproducibility crisis. Specifically in biomedical research, reportedly more than 70% of researchers failed when attempting to reproduce another scientist’s study results, with more than 50% unable to reproduce their results (Baker, 2016). This crisis has seeped into the roots of biomedical research to the extent that only 11-25% of cancer research experiments can be consistently replicated (Miyakawa, 2020).

The reproducibility crisis finds itself rooted in many different causes as outlined in Figure 1, however, a leading cause propelling this crisis is variation in methodology. In biomedical research, the slightest alterations in experimental design can lead to drastic changes in outcomes. Such variations are particularly emphasized in cancer research where upward of 70% of preclinical cancer studies could not be replicated due to inconsistencies in the methodologies. Such statistics reveal disparities in methodologies that lead to the irreproducibility of results, which undermines the scientific value of research findings and decreases the nature of applicability of these results to clinical practice. Another cause of this crisis is that when other research teams find incongruent findings during the replication of other studies, they often hold the assumption that their replication procedure must have been incorrect, as they fear questioning larger, more reputable labs (Franca & Monserra, 2018).

This crisis is one whose repercussions are far-reaching, specifically regarding its economic, societal and scientific influences. When considering scientific consequences, it is important to acknowledge that this crisis hinders the compilation of knowledge and disrupts the development of novel therapeutic interventions. Biomedical research provides a foundation for drug development and clinical trials, when such studies are found to be irreproducible, all knowledge obtained becomes unreliable and trust begins to waiver. Such unreliability not only delays scientific advancements but also runs the risk of propagating baseless conclusions through many disciplines (Loanndis, 2005). Furthermore, this crisis can lead to a dangerous cycle where the findings of irreproducible studies are cited and used as the groundwork for further research, which then exacerbates the inaccuracies and threatens the credibility of biomedical science.

The reproducibility crisis also translates to economic consequences. Funding agencies allocate dollars to research every year with the expectation of significant scientific revelations. This expectation is not met when studies fail to reproduce as the findings of the research are undermined due to an increased likelihood of chance behind the findings rather than a repetitive outcome, and thus billions of dollars are wasted that could have been invested into reproducible research. Irreproducible preclinical research costs the U.S. economy about $28 billion per year (Freedman et al., 2015). This financial loss limits funding availability for research projects that could have impactful findings and scientific advancements. This financial incongruency is concerning due to the competitive nature of research funding.

From a societal perspective, this crisis leads to a loss of public trust in scientific research. Society depends on scientific findings to inform evidence-based healthcare decisions, policies and personal beliefs regarding well-being. When high-profile biomedical studies are found to yield irreproducible findings, it can result in skepticism and decreased confidence in science as a discipline. Such erosion of trust can have catastrophic events for example the concerns with compliance regarding the COVID-19 vaccination regulations. A lack of faith in scientific findings can interrupt public compliance and acceptance of health directives which can weaken efforts to manage public health.

When considering the dire threats that the reproducibility crisis poses to the integrity of scientific research paired with its economic and societal impacts, such a predicament must be addressed through interdisciplinary approaches. It is through integrated mechanisms that the implementation of systemic changes sufficiently addresses the reproducibility crises..

A diagram of a problem

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**Figure 1.** Mind map that outlines the various technical and cultural causes of the reproducibility crisis in biomedical research (Begley & Ellis, 2012; Freedman et al., 2015; Munafò et al., 2017; Ioannidis, 2005; Baker, 2016).

Part 2A: What are six rules or guidelines that address reproducibility?

To ensure that research conducted at this academic institution is rooted in scientific validity and integrity, an interdisciplinary approach needs to be employed. To mitigate the consequences of the reproducibility crisis, the following six regulations are put in place to ensure a higher degree of reproducibility and scientific validity.

*Proper Record Keeping*

The first regulation involves the implementation of a standardized electronic lab notebook that is accessible by the designated data safety monitoring board, institutional review board, and other members of an overarching centralized regulatory body. An electronic lab notebook will limit the chances for misconduct, and tampering of raw data, and will also be a permanent record for the raw data allowing for a true reference for replication studies. The mandating of an electronic lab notebook allows for a level of standardization of record keeping for researchers regarding elements like observations, experimental details, data analyses, protocols, deviations and more (Munafò et al., 2017). This standardization increases the integrity of data by decreasing incongruencies that arise due to traditional lab notebooks. Moreover, the additional regulatory oversight of the lab notebook will allow for real-time monitoring proving to be a potent reference for future replication studies.

*Replication of Experiments*

To ensure pure scientific validity experiments need to be replicated to ensure that their findings are not a subject of chance, but due to a true scientific result that finds its roots in repetition and pattern. Ensuring more replicates of an experiment can enhance the robustness of the statistical analysis allowing for more concrete conclusions to be drawn.  Replication increases the reliability of results, ensuring that they can be achieved under similar conditions. Additionally, sufficiently conducted replications result in the effective use of funds as it mitigates the const of consequences like basing future research on inconsistent findings resulting in wasted funding (Randall & Welser, 2018). Replication of experiments can be done once the entire experiment in question is completed or for added verification, the experiment in question can be broken down into specific phases, with each phase being subjected to verification by replication studies and once verified can move forth to the next phase. Although the approach of independent phase verification can be time and resource-consuming, especially in biomedical research, it can provide added layers of verification. Additionally, this phase ensures that if there are any incongruencies, they are recognized and addressed early in the process of the study. Such replication procedures can be especially beneficial for studies that have direct applications in therapeutic settings where reliability is integral. Through embedding replication at various phases of an experiment, researchers can ensure that the future phases are based upon robust preliminary data and that there is mitigation of the risks affiliated with decisions based on unverified data.

*Standardization of Methods*

A primary reason behind the reproducibility crisis is the inconsistencies in the methodologies, slight alterations in small procedures like sample preparation, incubation times, and reagent concentration can all lead to changes in study outcomes resulting in potentially irreproducible findings (Freedman et al., 2015).  The implementation of SOPs ensures that general inconsistencies found in repeating methods are reduced. A consistent protocol allows for a step-by-step procedure for researchers to follow minimizing the variability. Incorporating such standardization will allow for mitigation of the discrepancies in methods that could impact experimental outcomes, hence making results more reliable and reproducible across different labs, research and disciplines. Additionally, with the implementation of standardized methods, academic institutions can enhance the training and onboarding of new faculty, allowing for consistent training across various levels of experience in a lab, which results in improved quality of data (Begley & Ioannidis, 2015).

*Study Blinding*

In research, scientists can remain unblinded and hence can manipulate the subject allocation in terms of intervention arm. To ensure increased reproducibility and outcome reliability it would be critical to blind the researcher to the intervention substance and allocation. This level of blindness in a study would ensure there is no bias (Begley & Ellis, 2012). Minimizing bias is critical for reproducibility as bias can compromise the reliability of the findings. Blinding decreases the chance of unconscious and conscious biases, as a researcher cannot subconsciously favour an intervention or selectively interpret data. Blinding research prevents any form of preferential treatment.

*Financial Transparency and Conflicts of Interest*

Bias is a prominent concern that feeds into the reproducibility crisis, as it can influence study design, how data is interpreted or other unethical conduct that translates to an altered outcome. Hence, requiring a level of transparency from researchers to disclose their conflicts of interest and transparency regarding funding is crucial to addressing this crisis. When funding comes from industry sponsors, they may invest with a desire for a specific outcome, which increases the bias of observations or data that supports those outcomes (Ioannidis, 2005). Disclosing these sources of bias has a positive impact on reproducibility as the study can be subjected to more objective scrutiny. This level of scrutiny influences researchers to strictly adhere to methodological guidelines, as they are aware of the perspective from which their research will be reviewed.

*Pre-Registration*

When considering the different biases involved in propelling the reproducibility crisis, it is important to acknowledge the publication bias. Studies have found that researchers face more challenges in publishing replication studies that produce negative results (Power, 2016). This challenge can be mitigated through a pre-registration of their study before commencement in a ‘registered report’. Researchers are only required to submit a detailed report outlining the study design and will need the approval of their choice of journal (Power, 2016). Implementing such a system will not only support replication studies but also result in an attitudinal shift increasing the validity and reliability of findings across all disciplines of study.

Part 2B: What are six suggestions for cultural changes that reduce problems with reproducibility?

Through the implementation of the guidelines outlined above, academic institutions can ensure that the research produced by their labs is of the utmost quality which can lead to scientific advancement. Although these guidelines serve as direct implementable measures, there must be regulations that can serve as measures to create attitudinal shifts. The following guidelines pertain to cultural changes that can lead to attitudinal shifts that can mitigate the reproducibility crisis.

*Fostering Team Morale Through Consistent Communication*

When trying to mitigate the reproducibility crisis there must be open communication at the most essential level—within a research team. When a team faces a lack of communication discrepancies present within the methodologies can go unnoticed (Hensel, 2020). Irreproducibility finds itself rooted in these discrepancies, as small deviations in the protocol can lead to significantly drastic results (Hensel, 2020). Moreover, everyone in a team should be aware of the specific details even if they are not directly involved with that detail, knowledge of the small aspects allows for increased coordination (Hensel,2 020). Details involve knowledge regarding specific time points of data observation, concentrations of reagents used, and more. These details require a level of standardization that if not communicated can be deviated, and lead to results potentially subjected to chance and not valid repetition. Practicing good communication through consistent meetings and documentation will allow for a degree of standardization, and fewer deviations to ensure results that can be validated through replication studies.

*Appreciation for Negative Results*

Upon the discovery of negative results from a replication study, researchers often find it challenging to publish these findings due to the belief that there is no ‘true’ contribution to scientific advancement (Baker, 2016). This belief is what leads to fewer replication studies being conducted. There is a dire need to shift this attitude to be more accepting of negative results, as they have the power to change the course of many future directions and ensure that clinical interventions, or other aspects rooted in evidence-based decision-making, are not approved upon unreliable data (Mehta, 2019). Journals and the general scientific community need to award scientists who have dedicated their research towards replicating the work of others, as this research holds no incentive. Negative results need to be equally prioritized as positive results, as these findings direct decision-making, novel interventions and future direction in the correct path. By rewarding scientists who conduct replication studies and recognizing the importance of negative results, the reproducibility crisis can be tackled by attitudinal changes.

*Interdisciplinary Collaboration*

To increase the robustness and reproducibility of research fostering interdisciplinary collaboration from different perspectives is critical, especially when establishing a rigorous methodology. Researchers from various disciplines can collaborate to recognize and address different details of a multifaceted concern, leading to more reliable findings (Stawarczyk & Roos, 2023). A primary example of such collaboration is the use of statisticians and computer scientists to ensure that there is standardization in data analysis and the electronic data capture system.  Standardization of processes surrounding different aspects can be achieved through cross-collaborations which can create consistent protocols, allowing for replication studies to be more robust and detailed.

*Continuous Education*

When considering rectification methods for the reproducibility crisis it is critical to consider standardization of training to those involved with the research. Offering standardized professional development programs allows for those involved with studies to have a consistent level of training in experimental methods, statistical techniques and best practices (National Academies of Sciences, Engineering, and Medicine, 2019). Through the alignment of knowledge and skillset, such courses decrease potential variation found in experimental methods, managing and handling data and approaches for analysis. Providing standardized training results in unified foundational knowledge that translates to consistency in executing the approved protocol and methods. Additionally, it allows for those who have received the training to understand where discrepancies can arise and therefore allow for correction or correct reporting of deviations. Employing unified techniques for protocol execution contributes to a collective standard that enhances reproducibility.

*Prioritizing Peer Review*

To promote cultural changes that improve the reproducibility crisis, the establishment of a peer review committee is critical. Such a committee will be accountable for providing constructive feedback that addresses the discrepancies in the early study, and ongoing phases (Crow, 2024). Such discrepancies include recognizing potential biases, ensuring statistical robustness, verification of data handling methods, and more. When fostering a collaborative and supportive committee, that has open and ongoing communication with the researcher, it serves as encouragement for refinement of the methodologies to promote transparency. These refinements will lead to more reliable outcomes. When a researcher engages with a peer review committee, there will be an attitudinal change that will translate to the internalization of value to such a process. The cultural mindset will shift as constructive feedback will not be seen as criticism but as a mechanism to strengthen the rigour of their work and outcomes. The implementation of such feedback will allow for robust methodologies and mitigation of potential concerns like biases, to increase overall reproducibility.

*Recognizing and Rewarding*

When understanding how to mitigate this crisis it is important to recognize and reward methodological excellence rather than quantitative details, as such a thorough process will emphasize research integrity (Gärtner, Leising & Schönbrodt, 2024). By recognizing and rewarding researchers who conduct replication studies and upholding a high level of standards regarding data management, transparency and more, we can switch to an attitude that places more importance on methodology. Rewarding such rigour promotes a shift away from a culture that encourages a ‘publish-or-perish’ mindset to one that prioritizes the credibility and reliability of research findings. Such a shift will ensure that the research outcomes are rooted in verification, thus increasing reproducibility.

To mitigate the reproducibility crisis, it is critical to understand how different types of regulations lead to a sustainable solution that can correct the past while upholding certain reliability standards for the future. Guidelines that are rooted in cultural changes will ensure that there is a shift in attitudes that emphasize the practice of transparency and accountability. Through these values, embedding such guidelines will ensure that there is proper mitigation of the reproducibility crisis.

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