Moral and philosophical underpinnings in drug development

Key Themes from the Webinar

The webinar discussion presented by Dr Jonathan Kimmelman (McGill University) focused on the foundational role of mentorship, philosophical clarity, and community engagement in the shift toward reproducibility in biomedical research and drug development.

Please find attached the summary report, which outlines the key themes and discussions. You can find the recording of the event here and the slides here.

1. The Reproducibility Crisis in Biomedical Research

The talk began by revisiting one of the discussions in the reproducibility crisis: a report suggesting that only about 11% of preclinical cancer studies could be successfully reproduced by industry researchers attempting to validate findings before drug development.

This finding raised major concerns about the reliability of academic preclinical research. However, the original publication itself illustrated a paradox:

- The article did not clearly define how reproducibility was measured.
- It lacked methodological transparency, including the absence of a detailed methods section.

This irony highlights a broader challenge within meta-research, where even studies about reproducibility must themselves adhere to reproducible standards.

2. Large-Scale Replication Efforts in Preclinical Science

The presentation discussed efforts by the Center for Open Science to systematically examine reproducibility through structured replication initiatives such as the Reproducibility Project: Cancer Biology (RPCB).

These projects aimed to provide a clearer and more rigorous understanding of how reproducible influential biomedical findings actually are.

However, replication efforts often encountered practical challenges such as incomplete reporting, unavailable materials, or methodological ambiguity in the original studies.

3. Ethical Implications for Clinical Research

A central theme of the presentation was that reproducibility is not only a methodological issue but also an ethical one.

Preclinical studies often form the evidentiary basis for human clinical trials. When these foundational studies are unreliable, several ethical concerns arise:

- Patients may be exposed to risks based on weak scientific evidence
- Research resources may be wasted on poorly supported hypotheses
- Clinical trial participants may contribute time and effort to studies unlikely to produce valid knowledge

From an ethical perspective, unreliable preclinical evidence challenges the justification for conducting human trials.

4. Limited Oversight and Regulatory Constraints

Another major issue discussed was the limited ability of oversight bodies to detect or address reproducibility problems.

Institutional Review Boards (IRBs) and other regulators typically review participant protections, consent procedures, eligibility criteria and statistical analysis plans.

However, they rarely evaluate the strength or reproducibility of the preclinical evidence supporting a trial.

Even when concerns arise, oversight bodies may face significant institutional and political pressures to approve studies rather than challenge the underlying scientific rationale.

As a result, many replication problems remain invisible to regulatory systems.

5. Improving Transparency and Accountability

The presentation emphasized several practices that could strengthen reproducibility and ethical oversight:

- Pre-registration of preclinical studies in publicly accessible databases
- Improved documentation of experimental methods and materials
- Greater emphasis on replication before clinical translation
- Stronger cultural recognition of reproducibility as an ethical responsibility

These measures could help ensure that clinical research is built on more reliable and transparent scientific foundations.

Conclusions

The webinar highlighted that the reproducibility crisis extends beyond methodological concerns and has significant ethical implications for biomedical research. When unreliable preclinical evidence informs clinical trials, it risks exposing participants to unnecessary harm and undermining public trust in science.

Addressing these challenges will require systemic changes, including improved research transparency, stronger incentives for replication, and greater consideration of evidentiary quality in ethical oversight processes.

Acknowledgements

Special thanks to Dr **Jonathan Kimmelman** for his insights on the philosophical and practical challenges of Reproducibility in drug development.