



TITLE: Assurance-based sample size determination for replication studies under publication bias

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ABSTRACT: Replication crisis—the failure to replicate a substantial fraction of published research findings—has led to the emergence of metascience as a distinct scientific field, a shift in the direction of scientific funding priorities, and a decline in public trust in science. Several potential causes have been proposed including publication bias (the selective publication of positive or statistically significant results), hidden multiplicity (the use of many analytic methods to test multiple hypotheses, p-hacking), questionable research practices, and fraud. Understanding the relative contribution of these factors can help researchers design studies that appropriately test the efficacy and safety of experimental compounds using previously published evidence.

We developed an *in silico* generative model incorporating both publication bias and hidden multiplicity and conducted simulation studies to assess their impact on replication success rates and the magnitude of effect size exaggeration. Taken together with our previous work on statistical power assurance presented at NCS 2022, our results suggest that replication failures can be explained primarily by inadequate statistical power in replication studies that arises from unaccounted uncertainty in prior effect size estimates combined with their systematic inflation due to publication bias. Importantly, our findings provide little evidence for an additional substantial contribution from hidden multiplicity, fraud, or questionable research practices.

On the basis of these results, we argue that the so called “replication crisis” is largely a predictable consequence of statistical mechanisms, rather than evidence of fundamental unreliability of the scientific method or widespread scientific misconduct. Moreover, our results imply that replication studies can be prospectively designed to meet predefined operational characteristics by explicitly accounting for publication bias and effect size uncertainty. To this end, we propose a novel resampling based methodology for determining the sample size required for a replication study to achieve a target level of statistical power with assurance under conditions of publication bias, and we compare this approach with existing methodologies.

BRIEF SPEAKER BIO: Ondrej Libiger is a Director of Biostatistics at Johnson & Johnson Innovative Medicine, where he leads a team of biostatisticians providing statistical support to neuroscience drug discovery programs. Prior to joining Johnson & Johnson, he led a research team studying the effects of remote digital monitoring and behavioral interventions on the health outcomes of patients with chronic disease, and conducted research on the role of population genetics and genetic ancestry in susceptibility to chronic illness.