9.3: Science in a Filing Cabinet

Earlier we saw the impact of multiple comparisons and truth inflation on study results. These problems arise when studies make numerous comparisons with low statistical power, giving a high rate of false positives and inflated estimates of effect sizes, and they appear everywhere in published research.

But not every study is published. We only ever see a fraction of medical research, for instance, because few scientists bother publishing "We tried this medicine and it didn't seem to work."

Consider an example: studies of the tumor suppressor protein TP53 and its effect on head and neck cancer. A number of studies suggested that measurements of TP53 could be used to predict cancer mortality rates, since it serves to regulate cell growth and development and hence must function correctly to prevent cancer. When all 18 published studies on TP53 and cancer were analyzed together, the result was a highly statistically significant correlation: TP53 could clearly be measured to tell how likely a tumor is to kill you.

But then suppose we dig up *unpublished* results on TP53: data that had been mentioned in other studies but not published or analyzed. Add this data to the mix and the statistically significant effect vanishes.[36] After all, few authors bothered to publish data showing no correlation, so the meta-analysis could only use a biased sample.

A similar study looked at reboxetine, an antidepressant sold by Pfizer. Several published studies have suggested that it is effective compared to placebo, leading several European countries to approve it for prescription to depressed patients. The German Institute for Quality and Efficiency in Health Care, responsible for assessing medical treatments, managed to get unpublished trial data from Pfizer – three times more data than had ever been published – and carefully analyzed it. The result: reboxetine is not effective. Pfizer had only convinced the public that it's effective by neglecting to mention the studies proving it isn't.[18]

This problem is commonly known as publication bias or the file-drawer problem: many studies sit in a file drawer for years, never published, despite the valuable data they could contribute.

The problem isn't simply the bias on published results. Unpublished studies lead to a duplication of effort – if other scientists don't know you've done a study, they may well do it again, wasting money and effort.

Regulators and scientific journals have attempted to halt this problem. The Food and Drug Administration requires certain kinds of clinical trials to be registered through their website ClinicalTrials.gov before the trials begin, and requires the publication of results within a year of the end of the trial. Similarly, the International Committee of Medical Journal Editors announced in 2005 that they would not publish studies which had not been pre-registered.

Unfortunately, a review of 738 registered clinical trials found that only 22% met the legal requirement to publish.[47] The FDA has not fined any drug companies for noncompliance, and journals have not consistently enforced the requirement to register trials. Most studies simply vanish.