

Paralysed by perfection

Some years ago, I had a great student working in my laboratory. He was extremely motivated, read widely, was skilled at the bench, and very critical of his work and any results that he produced. However, this critical attitude—although a highly beneficial skill for a researcher—ultimately undermined his career as a scientist; no result was good enough to allow for a detailed description of the molecular process he was studying. Because he emphasized the inevitable imperfections of his work and was not willing to address these with discussion rather than more data, no paper could be written nor any conclusions drawn and he eventually abandoned research. I hope that he realized with time that “perfection is the enemy of the good”; in real life, a 100% performance is a goal to which we aspire, but all too often we must choose to settle for less.

He is not the only person to have been paralysed by the quest for perfection. I know of other scientists, particularly those with exceptional intelligence, who are stuck in inaction with the results of a preliminary experiment as they design an impossible number of follow-up tests to explain all possible theoretical outcomes. They are not willing to tolerate any imperfection and, as they rarely get to do even the second experiment, their productivity suffers. It is difficult to argue with such purists that we must accept some inadequacies in order to move forward in research.

Although these examples might resonate with the research community, they are just a small part of a larger trend in society. Students with fantastic examination results, for example, are often more miserable about the few percentage points that they missed than they are happy about the 90 plus points they obtained through hard work and intelligence. The inability to accept that they are imperfect—as we all are—prevents many from being happy and content.

The effects of the foregoing examples are limited to individuals, but the increased push for perfection is causing problems on a broader scale. Pharmaceutical companies, for example, are well aware of the consequences of imperfection and the costs involved: any drug that is pulled from the market because of unanticipated side effects leads to extremely costly lawsuits and a sharp fall in share prices. Clearly, flaws in the design and analysis of clinical trials cause some of these failures and, in this regard, legal actions have improved trial design and led to safer drugs. However, some side effects cannot realistically be anticipated in clinical trials, no matter how good their design, and can only be detected once the drug is used by a sufficiently large and diverse group of patients.

The threatening spectre of punitive lawsuits is slowly affecting the whole system of pharmaceutical research and drug development. Companies carry out careful analyses to plot potential profits from a new product against potential losses through lawsuits because a new drug always has some risk of side effects. The decision to stop the development of a promising drug for fear of unanticipated side effects is prudent in many cases because it avoids potential human suffering in the future, but it also affects those patients who are in dire need of effective pharmaceuticals. A new drug that is shelved because of a statistical question mark might still have been beneficial for many people who are seriously ill without an alternative therapeutic; however, their hopes for a new treatment do not register in the bottom-line assessment.

Moreover, the number of new drugs in the research pipeline is decreasing. This might be because drug companies have already harvested the obvious and most promising compounds, but the trend might also reflect the increasingly strict standards of safety and efficacy that are applied to

new drug candidates and that drive up the cost of clinical trials.

Unfortunately, no compound can be perfect—that is, 100% effective with zero side effects in all patients given their diverse genetic, environmental and developmental backgrounds. This gives rise to new testing requirements—for example, including children in clinical trials, ensuring a proper gender distribution or a sufficiently wide genetic background in the trial. Testing on children is particularly fraught as parents would be understandably concerned if their child were a member of the control group and treated with a new therapeutic drug. Yet, the perfect pre-launch testing would include such a group even if it comes at a high price, emotionally and financially.

Just as it is hard to argue with a PhD student that he or she must move forward with what is possible and available, it is hard to argue for decreasing the size and scope of the tests and trials to which a new drug should be subjected. There is a fine line between taking short-cuts to increase profits and tolerating risks in the development of a new therapeutic. To ensure that we will have a range of efficient drugs in the future, we have to strike a balance between reality and perfection. More importantly, we have to start a dialogue about how to make rational choices between the two. Otherwise, we will slowly run out of new solutions to treat diseases and disorders, and we will have to rely on the drugs now available—many of which are known to cause side effects that would have stopped their development today.

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