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Non-Fiction

Rigor Mortis by Richard Harris – sloppy science

In-depth investigation of the dysfunctional \$30bn biomedical research industry



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We live in a world with an awful lot of corners, the science writer Richard Harris wryly observes. We are told that cures for diseases such as cancer and Alzheimer's lurk just around them. Mostly, it turns out that the wall is endless – or that the corner is not a corner at all but a spiral of wasted dreams coiled around shoddy science.

His thesis, set out starkly in *Rigor Mortis*, is that there is something seriously wrong with the way biomedical scientists go about their business. I started this book bristling at the schlocky subtitle: "How sloppy science creates worthless cures, crushes hope, and wastes billions". By the time I had finished, I felt it was somewhat justified.

He estimates that maybe half of the \$30bn spent by US taxpayers on biomedical science – research that underpins treatments and cures – goes on work that turns out to be wrong. It takes an extreme optimist to wave away such wastage as the normal run of scientific trial and error.

Harris, an award-winning reporter for National Public Radio, captures an angst that is rife in biomedicine: if the goal of research is to deepen knowledge, then it is structured in exactly the wrong way. Grants and publications are awarded on the basis of novelty, with academics plunged into a "publish or perish" culture. This fosters an ultra-competitive "publish first, correct later" spirit, which militates against the collaborative milieu in which truly great insights are so often born. And since everyone is busy moving on to the next big thing – and anxious not to be embarrassed in front of their peers – errors tend to languish and pervert the record indefinitely. As Harris notes, "it's important to distinguish between speed and haste".

This sense of competitiveness also disadvantages academics who share methods and data with rivals. Data-sharing is essential for ensuring studies are reproducible but it is equivalent to assisting the enemy. Many studies cannot, in fact, be replicated, a phenomenon known as the "reproducibility crisis".

Mistakes are sometimes only uncovered when drug companies sieve the literature for possible therapeutic leads. A scientist at Amgen tried to repeat 53 promising studies he had come across; he managed to reproduce just six. This can sometimes be blamed on carelessness: academics can buy, say, brain cancer cells to study a cure for glioblastoma (tumour) but those cells might later become contaminated in the lab. That renders subsequent work with the same cell line invalid.

But the reproducibility crisis also attests to the many ways in which scientists can sway or manipulate their results. These techniques include, but are not confined to, HARKing (hypothesising after the results are known), creative statistical analyses, choosing particular patient subsets, having too few people in a study, and over-extrapolating from animal studies.

The manipulation can be unwitting or deliberate, and, for academics, is ultimately geared towards publishing in high-impact, one-name journals such as Science, Nature or Cell. A researcher's publication list is her CV, basically her ticket to future funding and a secure faculty position. In the marketplace of ideas, it is the radical breakthroughs that tend to get noticed. The temptation to hype becomes almost irresistible – and I am sorry to admit that journalists can end up colluding in the distortion.

The stakes are higher in drug development, where marketing approval for a medicine can reap dizzying rewards and the temptation to design trials for success immense. A number of drugs fail after licensing because trial results do not pan out in the real world. A standout example is Vioxx, touted as Merck's blockbuster anti-

arthritis drug but withdrawn after being linked to heart attacks.

Now that researchers have begun airing science's dirty little secret, there is hope for a cleaner future. Social media and online publication makes it harder for researchers to ignore credible challenges to their work. The AllTrials campaign has encouraged the disclosure of even the dullest clinical trials, meaning that avenues of therapeutic futility need not be travelled twice. Harris's lament is a rewarding read for anyone who wants to know the unvarnished truth about how science really gets done.

The writer is a science commentator

RIGOR

HOW SLOPPY SCIENCE
CREATES WORTHLESS
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AND WASTES BILLIONS

RICHARD HARRIS

Rigor Mortis, by Richard Harris Basic Books, £25/\$28