Clinical Trial Data and the Risk of Bias

In 2018, HAI co-funded a study investigating the risk of bias in cancer drug trials submitted to the European Medicines Agency (EMA) to inform the approval of the drugs for public use (Naci et al: 2019). The study found that half of cancer drug approvals between 2014 and 2016 were based on potentially biased clinical trial data.

In an effort to make the findings of this research more accessible and to walk the talk when it comes to data accessibility, we worked with Aero Data Lab to create a living database that allows medical professionals, policy makers, and importantly, patients and their families, to search through its findings and understand how each trial included performed.

In September 2019, shortly after the paper was published in the BMJ, HAI wrote a blog to unpack the findings of the study. The blog concluded:

> *'Although significant, this study shouldn't be of undue concern to patients and families, and we certainly aren't implying that the EMA is at fault for authorising these drugs. But it's clear that increased scrutiny is required to ensure drugs entering the market are robustly evidenced as increasing therapeutic value and have met EU regulations around transparency. As its authors conclude, these findings should lead to improvements in the design, conduct and reporting of cancer drugs trials, and regulatory action to ensure pharmaceutical companies are evaluating products meaningfully, so that patients, clinicians and healthcare systems have the information they need.'*

The Need for Scrutiny

The study served as a reminder of the need for high-quality scrutiny of new drugs entering the market, and for high levels of transparency and it pointed out that processes must be improved to meet these needs.

In some ways, the opposite has happened. The advent of the COVID-19 pandemic has brought about a significant shift in regulatory approvals, with processes being expedited within authorities and subject to unprecedented press attention. Suddenly the world, and crucially the world's media, was scrutinising clinical trial data as never before. Indeed, there was regular examination of trial data in government offices and on the front page of the world's media, even before study reports were peer reviewed or analysed by medicines regulators. Pharmaceutical companies made the most of the press attention and issued press releases with favourable data; a practice that risks biasing both medical professionals, and the public. Never has transparency of clinical trial data been so critical, but under so much pressure.

Meeting Legal Obligations

While Naci et al.'s study only considered cancer drug trials, the findings can be applied more broadly. We must acknowledge the risk of bias in trials and do everything we can to ensure peer review processes in the medical journals and regulatory scientific analysis and scrutiny continue to be prioritised and protected irrespective of whether there is a global pandemic. In fact, the expedited clinical trials we've seen during the pandemic, make it even clearer that we need a better understanding of the use of indicators that do not necessarily correspond to therapeutic outcomes (surrogate endpoints) and better scrutiny to ensure time-saving decisions are being made with patient-safety, rather than speed, as their primary motivation.

Finally, we need to urgently act on the issue of missing post-marketing authorisation trial data across the board: far too many pharmaceutical companies do not meet their legally required reporting obligations. Indeed, we can use the COVID-19 technology assessments to our advantage here: perhaps we can harness this unprecedented attention on vaccine trial outcomes to push pharmaceutical companies to deliver on their broken promises.

We hope the living database will set a precedent for truly transparent clinical trial data, and for the increased use of interactive tools to support medical professionals and regulators to engage with the risk of bias. And we hope that the COVID-19 pandemic hasn't done permanent damage to clinical trial transparency and public confidence in trial data.

If you have any data or research that would add to the database, please get in touch.