Improving risk/benefit estimates in new drug trials

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It's all too familiar: researchers announce the discovery of a new drug that eradicates disease in animals. Then, a few years later, the drug bombs in human trials. In the latest issue of the journal *PLoS Medicine*, ethics experts Jonathan Kimmelman, associate professor at McGill's Biomedical Ethics Unit and Department of Social Studies of Medicine, and Alex John London, associate professor of philosophy at Carnegie Mellon University, argue that this pattern of boom and bust may be related to the way researchers predict outcomes of their work in early stages of drug development.

"We do a fairly good job of predicting the success of interventions that make it to later stages of clinical research," said London, who also directs CMU's Center for Ethics and Policy. "But when it comes to the leap from animal studies to the first trials in humans, there are serious problems."

Kimmelman and London suggest that the interpretation of pre-clinical results may suffer from a kind of myopia, in which a narrow focus on the data about the performance of a new drug in pre-clinical studies produces overly optimistic predictions.

"Clearly we need to look at the pre-clinical evidence about a new intervention when estimating its likely benefits and burdens in people," London said. "But we also need to look at how similar interventions have fared in the past. If drugs that work on the same principle have failed development, there may be good grounds for tempering our

expectations."

Kimmelman and London also question whether researchers are doing enough to minimize any factors that interfere with measuring a drug's true effects. They suggest that some of the techniques such as randomization and blind testing that are common in clinical tests involving human subjects should also be used at the pre-clinical stage. "Medical researchers do a lot to control bias in drug trials with humans. We think if these measures were taken up by researchers who test drugs in animals, we would have a better basis for designing human trials," says Kimmelman.

If researchers adopt Kimmelman and London's recommendations for improving the ways that they predict outcomes from preclinical trials they suggest that the research participants, drug developers and funding agencies will all be better equipped to make informed decisions about clinical drug testing, the study suggests.

"Pre-clinical studies provide a useful starting place for determining whether a new drug is clinically promising," Kimmelman said. "We think we can – and should – be doing more to ensure predictions about clinical activity rest on a more complete and sound evidence base."

More information: For an abstract of the paper: www.plosmedicine.org/home.action

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