

Signal, Safety, and Success: An Analysis of Risk, Benefit, and Translation after Detection of Clinical Activity in Drug Development

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Lay Abstract

The vast majority of new drugs entering clinical development never show adequate safety and efficacy. As a result, many patients are harmed and resources wasted. This grant is aimed at discovering whether there are ways to better protect patients, learn from failure, and save resources during drug development. Our preliminary research shows that drug developers often run trials that are based on guesswork or biased evidence; when this occurs, studies can fail and patients are harmed. We want to determine how frequently drug developers run drug trials based on solid clinical evidence, and measure the impact of solid evidence on patient outcomes in trials and drug licensing.

Description:

This project will investigate how risk, benefit, and translational outcomes in drug trials vary depending on the way earlier phase studies are designed and implemented. When new drugs are developed, drug developers typically test the drug against a disease for which the drug was originally intended (“lead indications”), as well as related diseases that might also respond (“non-lead indications”). As well, some early phase trials use methodologies that better protect causal inferences from validity threats. Our goal is to determine whether risk, benefit, and translational outcomes relate to whether 1) a trial is run in a lead indication, and 2) a trial is run on the basis of earlier trials that have minimized validity threats. In addition, we will examine the way researchers and drug developers incorporate findings- both “positive” and “negative” ones- into the design and implementation of subsequent trials of new drugs.

We are entering this study with three hypotheses: 1) studies that test against lead indications have better outcomes; 2) studies that are run on the basis of well designed and implemented earlier phase studies have better outcomes; 3) trials of new agents should demonstrate a learning curve, whereby later trials show better outcomes as compared with earlier trials of a given phase.

The grant will proceed in a stepwise fashion.

- 1- identify 2 cohorts of new drugs: a) recently licensed by FDA, and b) reached late phase testing but were not licensed.
- 2- obtain all trials testing efficacy of the new drug, including prior phase 2 studies.
- 3- extract trials for design parameters, outcomes, adverse events, etc.
- 4- perform a descriptive analysis of our data, and test hypotheses.