Medicinal Chemistry & Drug Discovery
Section 1.4.1 – Fail Fast, Fail Cheap

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Learning goals

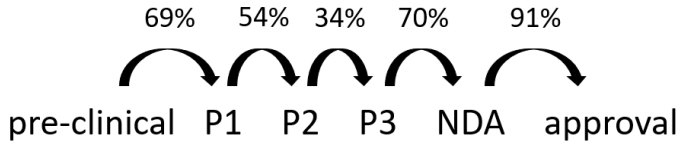
- contrast failure rates of molecules in different development stages
- identify approximate costs of each development phase
- infer opportunities for reducing clinical trial failures

Vocabulary

- none

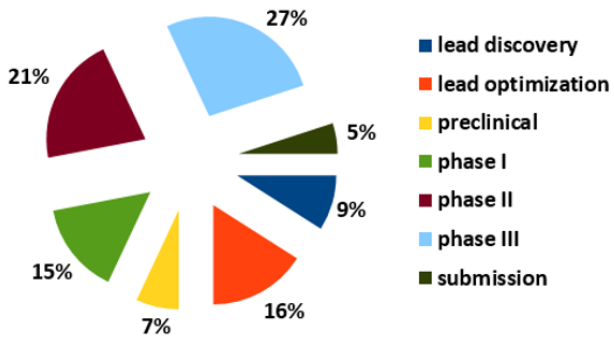
The data in this video are from drug development programs at Eli Lilly: Paul, S. M. *Nat. Rev. Drug Discov.* **2010,** *9,* 203-214.

The probability of a lead being advanced from the preclinical stage (animal testing) and into Phase 1 trials is 69%. The most challenging step is the transition from Phase 2 to Phase 3 trials with a probability of success of only 34%. This is why Phase 2 trials, especially Phase 2b, are called "pivotal trials". These are the first trials in which the efficacy of the drug is established in humans, and many assumptions from previous research (all the way back to target selection) are tested. If you work through these probabilities from Phase 1 through approval, the overall success from an IND, which is the start of Phase 1, to approval is 11.7% or about 1 in 8.5 molecules. These data are somewhat dated and only from one company, but the trend is still valid. People often cite a clinical trial success rate of 10 to 15%.



What is the cost of bringing one drug to market? In 2016 the cost was estimated as US$2.6 billion by Joseph DiMasi of Tufts University. That figure includes not just the cost of the successful drug but also the approximately 7.5 other molecules that failed in clinical trials.

What are some lessons from these numbers? Well, many molecules advance into Phase 2, only to fail because of lack of efficacy. Such a failed molecule will have accumulated over 2/3 of the total development cost. The lesson is clear: improve efficacy confirmation earlier so that fewer doomed, costly molecules are lost during Phase 2 trials.



This idea of minimizing expensive, long-term failures has been called “fail fast, fail cheap”. Identify bad leads earlier so resources may be spent on more promising molecules. If successful, such an effort would reduce the cost of developing drugs and also likely reduce the cost of drugs in the marketplace. The drug industry is aware of this opportunity, and researchers actively work to improve predictions of human efficacy in early discovery stages.