Causes of clinical failures vary widely by therapeutic class, phase of study

Tufts CSDD study assessed compounds entering clinical testing in 2000-09

- Reasons for failure were identified for 41.4% of Phase I failures, 52.3% of Phase II failures, and 61.1% of Phase III failures.
- Commercial issues were the leading cause of Phase I failures.
- Efficacy issues outnumbered commercial considerations by 2:1 as the leading reason for Phase II failures.
- Efficacy and safety factors outranked commercial issues in Phase III failures.
- Efficacy issues dominated other reasons for failure for respiratory and systemic anti-infective drugs.
- Nearly half of cardiovascular failures were related to commercial issues.

Clinical testing, in which new medicinal compounds are studied in humans subjects, necessarily includes failures, as the point of such investigations is to determine which products can effectively and safely treat specific diseases. Drug candidates fail in clinical testing for a number of reasons, but primarily for issues relating to efficacy, safety, and commercial viability. In addition, these causes of clinical failure vary according to phase of study and among different therapeutic classes of drugs. Tufts CSDD sought to quantify these reasons for failure for products that entered clinical development in 2000-09. Highlights of that analysis are summarized in this Tufts CSDD Impact Report.

It is in the interest of drug developers to have new products fail earlier, rather than later, in development, as earlier terminations avoid the costs of larger, more complex studies while freeing resources for other product development programs. Commercial viability is particularly challenging to assess, as it depends in large part on an often-changing landscape of alternate treatment options. Safety and efficacy issues are also thorny, in that candidates that appear safe and effective in earlier studies may show a different profile when studied in larger populations. While there is natural resistance to give up on a compound too early, the need to reduce costs and boost productivity is leading developers to establish new approaches to R&D, including the increased use of biomarkers and novel clinical trial designs, with the goal of terminating candidates as early as possible.