Amendments reduce number of patients, but at high cost, longer study times

Nearly half of all substantial amendments are deemed avoidable

- 57% of all protocols, across all phases, have at least one substantial global amendment (defined on page 4 in “About this study”).
- Phase II protocols have the highest incidence of substantial amendments (77%), averaging 2.2 amendments per protocol.
- The most frequent changes stemming from amendments are associated with modifications and revisions to study volunteer demographics and eligibility criteria.
- Protocols with even one amendment experience a substantially lower actual number of patients screened and enrolled relative to plan, compared to protocols without any amendments.
- Study conduct durations for protocols with at least one substantial amendment take, on average, three months longer.
- The total median direct cost to implement a substantial amendment for Phase II and Phase III protocols is $141,000 and $535,000, respectively.

Unplanned delays, disruptions, and costs associated with protocol amendments have spurred the research-based biopharmaceutical industry to identify new approaches to simplify protocol design, reduce the frequency of amendments, and better inform decision-making. A new Tufts CSDD analysis, results of which are summarized here, builds on an analysis conducted in 2010 and explores the impact of substantial protocol amendments on study conduct performance and cost. The results provide new insights into protocol design decision-making and how to anticipate and better manage amendments.

The incidence and frequency of substantial amendments remain high and their impact on study cycle time and budgets are substantial. Drug sponsors are responding through piloted and broad use of feasibility review committees, common protocol templates, and investigative site and patient feedback panels.