

The Impact of Protocol Amendments on Clinical Trial Performance and Cost

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Abstract

Background: Tufts Center for the Study of Drug Development (Tufts CSDD), in collaboration with 15 pharmaceutical companies and contract research organizations, gathered data on substantial global protocol amendments to better understand how to manage and to reduce the significant unplanned expense and delays associated with major changes to finalized protocol designs. *Methods:* Data from 836 phase I-II/IV protocols were analyzed to understand amendment prevalence. Impact assessments were based on data from 136 randomly selected amendments. Data from 52 protocols were analyzed to derive estimates of the direct cost to implement amendments. *Results:* Tufts CSDD found that 57% of protocols had at least one substantial amendment, and nearly half (45%) of these amendments were deemed “avoidable.” Phase II and III protocols had a mean number of 2.2 and 2.3 global amendments, respectively. Protocols with one or more global amendments tended to be larger in scope, with longer patient recruitment durations and overall study durations compared with those without a global amendment. Protocols with at least one substantial amendment had fewer actual screened and enrolled patients relative to the original baseline plan than did those protocols without an amendment. The median direct cost to implement a substantial amendment was US\$141,000 for a phase II protocol and \$535,000 for a phase III protocol. *Conclusions:* The study findings provide insights into optimizing development planning, protocol design, and clinical trial management practices.

Keywords

protocol amendments, protocol design, protocol complexity, protocol design changes

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