Slipped deadlines and sample size shortfalls in clinical trials: a proposed remedy using a Bayesian model with an informative prior distribution

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Background: The most common reason why clinical trials fail is that they fall well below their goals for patient accrual. Researchers will frequently overpromise and underdeliver on the number of patients that they can recruit during the proposed time frame. The result is studies that take far longer than planned and/or that end with fewer patients than planned. This raises serious economic and ethical issues. Our research efforts have focused on (1) getting reliable data on the scope and magnitude of problems with slow patient accrual in clinical trials, and (2) developing a Bayesian model for accrual that will encourage careful planning of accrual rates as well as allow regular monitoring of accrual patterns during the conduct of the clinical trial. **Methods**: A random sample of 130 prospective studies approved by the Children's Mercy Hospital (CMH) IRB from 2001 through 2005 were retrospectively reviewed for the proposed and actual accrual rates. At the same time, a Bayesian model for accrual was developed and applied to a clinical trial at Kansas University Medical Center to produce monthly reports projecting estimated final sample sizes with uncertainty limits given the initial projection and currently available enrolment data. **Results**: 117 (90%) of the studies submitted to the IRB did not specify a start date, a completion date, or both, making it impossible to assess the accrual rate. Of the remaining studies, two failed to list actual start or end dates. Of the remaining 11 studies, 8 took more time than proposed and the average increase in duration in these 8 studies was 100%. Among the 109 studies that included both a target and an actual sample size, 59 (54%) fell short of the proposed sample size. The average shortfall across these 59 studies was 55%. The informative prior used in the Bayesian model was reasonable and produced early estimates of total sample size that were an accurate reflection of the end result. **Conclusions**: A large number of studies failed to meet the specified sample sizes and the average shortfall among these studies was considerable. The Bayesian model for accrual produced useful reports for a particular study and provided reassurance to the researchers that their accrual rates were on target. The Bayesian model, however, also has the capability of correcting an inaccurate prior distribution as the accumulated accrual patterns provide contradictory results. Future research should focus on collaborations with organizations that conduct large numbers of clinical trials to get more data on existing problems with slipped deadlines and sample size shortfalls and to test the Bayesian accrual model on a wide range of clinical trials