INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Programme of Study	:	Ph.D.
Thesis Title	:	Adaptive Sequential Multiple Assignment Randomized Trial Designs
Name of Thesis Supervisor(s)	:	Dr. Palash Ghosh
Thesis Submitted to the Academic Division	:	Mathematics
Date of completion of Thesis Viva-Voce Exam	:	17 November 2025
Key words for description of Thesis Work	:	Adaptive Intervention, SMART, Adaptive Randomization, Dynamic Treatment Regime, M-bridge Data, SMART Weight Loss Management, Optimal Design, Binary Outcomes, Continuous Outcomes, Covariate Adjusted

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Sequential Multiple Assignment Randomized Trial (SMART) is an experimental trial framework for evaluating multiple adaptive interventions that tailor treatment sequences to individual responses over time. Traditional SMART designs rely on fixed (non-adaptive) randomization probabilities at each stage and fail to leverage information accumulated during the trial. This may raise ethical concerns by continuing to allocate participants to inferior treatment options. This thesis presents a comprehensive methodology for developing optimal adaptive randomization in SMART designs to enhance both ethical and statistical efficiency. The primary contribution of this work is the derivation of optimal adaptive allocation ratios and procedures for two-stage SMART designs, applicable to both binary and continuous primary outcomes. Building on optimal adaptive randomization theory for two-arm randomized controlled trials, we formulate constrained optimization problems that minimize the total expected number of treatment failures for a binary outcome, subject to fixed asymptotic-variance constraints for prespecified objective functions. For continuous outcomes, the objective function differs. Optimal second-stage allocation ratios are first obtained and are then recursively propagated backward to derive the optimal first-stage allocation.

Theoretical properties of the proposed estimators are established, and extensive simulation studies demonstrate convergence of the estimated allocation ratios to their theoretical optima and improved efficiency. We also demonstrate substantial reductions in the expected number of failures for binary outcomes and in the total expected outcome for continuous outcomes, compared with non-adaptive and existing adaptive SMART designs. The proposed methods also maintain desirable inferential properties, including valid hypothesis testing and competitive power. Applications to real-world studies, including the M-bridge study and a SMART weight-loss management study, illustrate the practical feasibility and advantages of the proposed designs. The thesis further extends the methodology of optimal adaptive allocation ratio in binary outcome SMART to covariate-adjusted adaptive SMART designs, incorporating baseline covariates into the allocation mechanism to further enhance efficiency and ethical performance. Overall, this work provides a comprehensive framework for optimal adaptive randomization in SMART designs, advancing the methodological foundation for the development of data-driven, ethical, and efficient adaptive interventions in all clinical research.