

## **Clinical Trial Design and Small Studies: A Coordinating Center Perspective**

In 1996, the Surgical Treatments Outcomes Study for Dysfunctional Uterine Bleeding (STOP-DUB) was funded by the Agency for Health Care Policy and Research (now AHRQ). STOP-DUB is a multicenter randomized controlled trial (RCT) designed to assess the efficacy and effectiveness of hysterectomy compared to endometrial ablation for the treatment of dysfunctional uterine bleeding in women unresponsive to medical interventions. The primary outcome was “major problem solved”, and this was later modified by the data and safety monitoring board to include bleeding, fatigue, and pain, as well. STOP-DUB was originally designed as an “equivalence” trial because hysterectomy and endometrial ablation were thought to be likely to be equally effective. Subsequently, a new RCT indicated that the two interventions were not likely to be equally effective in terms of bleeding outcomes, which was the major problem STOP-DUB women named, and a new sample size was estimated assuming one intervention would be beneficial over the other for the three other primary outcomes. Like all RCTs, STOP-DUB had its share of excitement, with the tribulations exacerbated by the fact that recruitment, computer programming, and data collection, management, and interim analyses had to keep up the fast pace that trials must maintain to finish on schedule. Challenges not already mentioned included a move of institutions for the Coordinating Center, slow recruitment, the Agency’s request to translate study materials into Spanish, extending patient followup and reconsenting enrolled patients, and a decision by the agency not to extend funding for followup. Although each trial is unique, there are also common challenges that must be recognized and addressed: slower than expected recruitment, difficulties of hiring experienced staff, short time spans allowed for trials by NIH (5 years), and under-funding of clinical sites.