DESIGN AND IMPLEMENTATION OF A FULLY AUTOMATED PROSPECTIVE RANDOMIZED EFFECTIVENESS TRIAL

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Introduction: Performing prospective trials with uncommon endpoints such as mortality historically requires a significant investment in research infrastructure and manpower to individually recruit, enroll, and track the thousands of patients required. We demonstrate a system for automating enrollment, randomization, and followup for a large prospective study.

Investigators at the Cleveland Clinic found in a retrospective study that a "triple low" of low Bispectral Index (BIS less than 45), low mean arterial pressure (MAP less than 75 mmHg), and low end-tidal minimum alveolar concentration (MAC) was associated with higher mortality and length of stay. These investigators also found that a "double low" of low BIS and low MAP, regardless of MAC, led to higher mortality and length of stay. We wished to test if an automated "double low" alert encouraging anesthesiologists to address the MAP or BIS would reduce mortality.

Methods: Our institution’s IRB granted permission to inform patients of the study by letter and allow them to opt out of the study if they chose not to participate. We designed a real-time data capture layer to gather data from our AIMS for study purposes. All operating rooms in our institution are watched by the trial administration software, and patients are enrolled as soon as they meet inclusion criteria. Once enrolled, patients are randomized to the treatment (alerts) or control (no alerts) arm of the study. During the case, the decision support software watches for "double low" vital signs. Upon a double low in the treatment group, the workstation is alerted (Figure 1) and the attending is paged.

To assess the success of this automated trial system, we examined the number of patients enrolled, number randomized, reasons for exclusion, and significant issues identified.

Results: From May 2011 through December 2012, 48,636 patients were considered for enrollment in the study. 37,323 were excluded for various reasons, including not meeting inclusion criteria (36,024), opting out of the study (305), previously enrollment in the trial (980), and other reasons (14). 11,313 patients were randomized to the control or treatment arm.

Issues identified included a need for manual health checks to identify software failure. Another issue is that BIS monitors would fail or be removed from certain ORs, reducing
room enrollment to zero. Both issues were addressed with daily and monthly reports on trial progress, both overall and per room. In some cases, patients felt they were not adequately informed of the trial. This was addressed with periodic refresher training of the surgical registration staff to ensure that the study letter was seen by patients.

**Conclusion:** We found that large-scale automation of a prospective trial is possible. To ensure trial success, diligent followup and monitoring are required.

**References:**

1. Sessler DI, Sigl JC, Kelley SD, Chamoun NG, Manberg PJ, Saager L, Kurz A, Greenwald S: Hospital stay and mortality are increased in patients having a “triple low” of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anesthesia. Anesthesiology 2012; 116:1195-203