Proceedings of the 2017 Winter Simulation Conference
W. K. V. Chan, A. D'Ambrogio, G. Zacharewicz, N. Mustafee, G. Wainer, and E. Page, eds.

ESTIMATING MAIN AND INTERACTION EFFECTS OF A MULTI-COMPONENT RANDOMIZED CONTROLLED TRIAL VIA SIMULATION META-HEURISTICS

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ABSTRACT

Randomized controlled trials often are conducted on multi-component interventions in all-or-none manners for practical, logistic, or statistical purposes, typically allowing researchers the ability only to estimate the overall effect of the intervention en masse. In parallel, we propose a simulation-based approach to estimate main and interaction effect sizes of an intervention's sub-components based on conducting meta-heuristic parameter search on intra-trial longitudinal input, output, and context data. This approach is illustrated with a recent application to a healthcare intervention consisting of three information technology patient safety tools tested as a single intervention in a multi-unit staggered cluster crossover RCT design, with the overall objective being to reduce falls, infections, and other adverse events. (AEs) A high fidelity simulation of individual and combined use of these tools was developed and validated with retrospective data and then applied to prospective longitudinal data as clinical units varied in occupancy, staffing, patient risk, care team composition, and tool adherence, with parameter search estimating main and interaction effect sizes to maximally reproduce observed data. Computational results and implications are discussed.

1 INTRODUCTION

Despite many successes over the past two decades to improve patient safety, several challenges remain, which in turn has stimulated inquiry on additional approaches that might be effective, including advances in healthcare information technology (IT), stronger communication across care teams, and new ways to engage patients themselves in their safety. In parallel and given the urgency to improve patient safety, process interventions often are tested as a bundle or system of improvement without much focus on testing each element individually or in various combinations, and thus often producing learning at the aggregate level but less insight as to effect sizes of individual components nor their interactions. As one example, a set of three IT tools currently are being tested at a large academic medical center for their ability to engage patients, families, and care teams in improving real time awareness, communication, and mitigation of potential safety issues. These include a dashboard of each clinician's overall patient risks, an on-line tool to identify patients fall risks and recommend patient-specific prevention measures, and a patient portal that allows them or their families to notify staff in real time on any safety issues they perceive. While the tools are being tested in a randomized controlled trial as a combined intervention, it also is desirable to estimate the individual effect each tool has on AE rates individually and in various combinations.

2 METHODS

A computer simulation model was developed in the Julia open source programming language that mimics the overall process within which combined interventions are being tested while tracking outcomes, inputs,

978-1-5386-3428-8/17/$31.00 ©2017 IEEE

and various contextual data – here patients length of stay (LOS) within the daily operation of a clinical unit, their interaction with the patient portal, their care team's use of and response to the tools, compliance to tool use, response rates and delays, various system state measures (bed census, acuity levels, discharge rates, etc) and resulting improvement or worsening of safety risks, the occurrence of AEs, and the effect of these on increased LOS and additional risk exposures and realizations. This model then was used for two general purposes, (1) first to conduct what-if analysis based on input parameterizations developed from hospital data and the literature to estimate results under various conditions and scenarios, and (2) second to search for optimal parameterizations (individual tool and interaction effects sizes on each type of AE rate, impact of census on use rates, additional LOS, likelihood of additional AEs, etc) under different system state conditions that maximally reproduce observed longitudinal results. Metaheuristics used to maximize goodness-of-fit included a genetic algorithm, a tabu probabilistic method, and others, in each case seeking to minimize root mean squared error between the observed and simulated longitudinal vectors of inputs, system state, and outputs (adverse event rates, LOS, compliance rates).

3 RESULTS

In validation, the simulation produced good results including correlations between tool use compliance and AE rates, agreement with published literature, and general stakeholder face and directional validity. In scenario analysis, the model proved useful as a what-if method for examining several casual hypotheses and potential interventions (e.g. impact of clinical unit load, days with high discharge rates, and necessary compliance rates, the latter being non-linear with even modest usage increases producing significant safety improvements). In optimization, each search algorithm converged and produced relatively similar results for intervention main and interaction effect sizes, suggesting not-surprisingly a few dominant effects with several other being less significant; i.e. not all components of the intervention are equally important whereas a few interactions (simultaneous use) can produce greater results. In our case, and somewhat counter-intuitively, use of the patient portal had negligible effect on AEs, with the exception of moderate interaction effect between portal use and dashboard use, whereas the fall risk and dashboard tools had the largest effects, especially among high acuity patients and clinical unit conditions.

4 CONCLUSIONS

Secondary simulation analysis can effectively support clinical randomized controlled trials both to provide further insights as to effective interventions, interrelationships, and drivers of results and to estimate main and interaction effects sizes of multi-component interventions that are formally tested as a composite at the same time. The latter case essentially uses the simulation model, once sufficiently validated, to generate the same type of data that would be used in a prospective statistical study without randomization, and thus can serve as a third method for triangulating results for maximal insights without more costly, disruptive, and time consuming RCTs. The metaheuristics used converged rapidly and produced similar results, and with most results determined as reasonable and agreeing with experience when reviewed with process experts, all suggesting viability as a broader general approach in other contexts as well.

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