ONE TOO MANY: INVENTORY AND ALLOCATION POLICIES FOR EFFECTIVE MAINTENANCE OF CORD BLOOD BANKS

Background: Patients affected by hematological (blood-related) diseases such as leukemia, lymphoma, severe aplastic anemia etc. requires transplantation of genetically compatible hematopoietic stem cells (HSCs) extracted from the bone marrow (BM) of live donors or the umbilical cord blood (CB) of babies. Every year approximately 13,000 individuals require BM donations (outside of the family members) or compatible CB cells held in storage for treatment. For the transplant to take place successfully, the patient in need of the stem cell must be genetically compatible with the source and the compatibility is determined by similarity in the genetic codes. Put specifically, the compatibility often referred to as a "match", is the number of places the genetic codes are the same for a patient and the BM donor/CB cells in a string of genetic codes of length six (**called phenotype**). If all the six places in the phenotype matches between the BM donor/CBU cells and the recipient, this is referred to as a 6/6 match. If there is a mismatch in one place, it is a 5/6 match and so on. To facilitate the search for HSCs, BM registries (BMR) that collect the details of potential donors and public CB banks (CBB) that store units of CB (CBU) donated by the public are setup across the U.S. by National Marrow Donor Program (NMDP). NMDP through its flagship program called **"Be the match"** acts as interface between the patients (physicians) and the BMR/CBB. With over 10 million unique phenotypes in the US population and limited inventory relative to each variety, then the appropriate sizing, screening and allocation policy followed in the two institutions (BMR and CBB), is an important operations problem from a public policy viewpoint.

Problem Definition: The two sources of HSCs, BM, and CB cells, differ along different dimensions including sourcing, costs, availability, and, importantly, medical effectiveness (where BM donations performs slightly better than cord blood cells). Simply put, the BM donors are a cost-effective source with strict matching requirements (only 6/6 match) whereas the CB units are a cost-intensive source with flexible matching requirements (allows up to 4/6 match). Due to the medical effectiveness, a BM donor is always preferred for a transplant and only the unmet demand spills over to the CBBs. The fact the only a 6/6 match alone is possible in the case of BM transplant renders the capacity and allocation decision very straight forward despite both demand and supply uncertainty. However, with only spillover demand from the BM registry and the possibility of multiple choices to meet a demand (due to flexible 5/6 & 4/6 matches) it is unclear as to what the optimal inventory and allocation policy should be for the CBBs. The recent emergence of international BM donor networks further necessitates the efficient operations of the CB banks. In this work, we focus on designing evidence-based and cost-effective allocation rules and inventory policies for the CBBs that deliver high societal benefits. The allocation and inventory issues in the public CBBs haven't been studied in the relevant body of literature across operations, health economics and medical domains, and we are the first to address it to the best of our knowledge.

Methodology: Factors including the huge magnitude of unique population phenotypes (~10 million), partial substitutability among phenotypes (5/6 and 4/6 matches), spillover of demand from another source combined with both supply and demand uncertainty makes it extremely difficult to investigate the inventory/allocation policies for the CBBs through the standard

methods used in operations research. So, we develop a simulation-based optimization (SBO) framework that minimizes the immediate regret/estimated loss for the CBB during allocation of inventories to incoming demand. Similarly, the proposed approach screens incoming supplies of the CB units and admits them only if they increase the overall value of a CB bank. We compare the temporal variation in several performance measures related to the matching process for the proposed (SBO) framework against the current industry practice. Keeping in mind the complexity associated with practical implementation of the SBO framework, we also design several heuristics and benchmark them against the performance of the SBO framework.

Managerial Implications: The results showcase that our SBO approach along with some of the proposed heuristics perform substantially better than the current industry practice. Our research creates high societal value by providing simple and effective rules for CBB operation in addition to making lives easy for CBB managers bogged down by the complexity of the system.

Key words: Healthcare; Stem Cell transplant; Cord Blood; Optimization; Simulation; Inventory; Allocation.