LETTER TO THE EDITOR

Expanding the evidence base of new cardiovascular treatments by systematic registry-based evaluation of their implementation in clinical practice

Health care resources are limited. It is therefore important to distinguish cost-effective and life-saving new treatments from costly but ineffective treatments, or costly treatments that are no more effective than less expensive alternatives. Unfortunately, few new treatments are systematically evaluated after they are implemented in clinical practice. We advocate for systematic large-scale evaluation of the efficacy and safety of new treatments when they are introduced in clinical practice; by pragmatic, cluster-randomized implementation strategies followed up through health care registries.

Randomized controlled trials (RCTs) represent robust and important tools for assuring that a new treatment is efficacious and safe prior to its implementation in clinical care, but even well-conducted RCTs rarely fully establish the efficacy and safety of treatment across different subsets of patients [1]. Furthermore, the RCTs that form the evidence base for the implementation of new treatments are often funded and conducted by profit-seeking organizations, a fact that arguably further justifies the continued evaluation of the performance of these treatments. Despite persisting uncertainties in their efficacy and safety at the time of their implementation in clinical practice, few treatments are systematically evaluated after their implementation [2]. Several treatments that were found to be inefficacious compared to less expensive alternatives many years after they were implemented could have been identified as ineffective earlier if they had been systematically evaluated when they were implemented [3].

Once a new treatment has been shown to be efficacious and safe in a traditional RCT, healthcare registries can be used as data capture systems to allow inexpensive further evaluation of the efficacy and safety of new treatments if the implementation of the treatment is done systematically using a cluster-randomized approach [4]. Cluster randomized designs represent flexible means of systematically implementing new treatments, by randomizing individual hospitals or health care regions (clusters of patients) to different treatments (parallel group design) or to the order in which they implement a new treatment (stepped wedge design) [5]. To reliably evaluate the implementation of a new treatment in a health care registry, the registry must be of sufficient detail and quality to allow for identification of the desired study population and reliable endpoint ascertainment. Some contemporary health care registries, such as the Nationwide Swedish Web-system for enhancement and development of evidence-based care in heart disease evaluated according to recommended therapies (SWEDEHEART), fulfill these criteria [4].

By systematically introducing new treatments using a cluster randomized approach and following up outcomes in already existing health registries, data can be acquired for a substantial number of patients at minimal cost. Cluster-randomized implementation of new treatments therefore represents an inexpensive means of validating (or refuting) the results of phase III multi-center RCTs, and for provides important high-quality data regarding the safety and efficacy of new treatments in the real-world setting for which the treatment is intended to be widely used (Figure 1). As such, cluster randomized implementation of new treatments represents an effective means of post-market surveillance (phase IV studies), a relatively neglected part of the evidence generating process for contemporary treatments [2].

![Diagram]

**Figure 1.** The role of pragmatic cluster randomized systematic implementation and evaluation of new treatments in the evidence generating process. Cluster-randomized systematic implementation of new treatments, with follow-up of key outcomes in pre-existing health registries represent an inexpensive means of considerably expanding the evidence base for contemporary cardiovascular treatments after their implementation in routine clinical care. RCT: Randomized clinical trial.
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