Pragmatic clinical trials in cardiovascular medicine: trends over time in major medical journals

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Topic(s):
Trial Design

Citation:
Dr. Sepehrvand receives scholarship from Alberta Innovates Health Solutions.

Background: Pragmatic trials provide results that may be more applicable to the population in which the intervention will be eventually applied and are discussed extensively in the current healthcare environment. The aim of this study was to investigate how pragmatic or explanatory cardiovascular (CV) randomized controlled trials (RCT) are, if this was changing over time, and if they were more or less likely to meet their primary endpoint.

Methods: Using the six top-ranked (based on impact factors) medical and CV journals, all CV-related RCTs that were published during the years of 2000, 2005, 2010 and 2015 were identified, data extracted and reviewed by 2 adjudicators. The PRECIS-2 tool was used to evaluate the level of pragmatism. PRECIS-2 uses a 5-point ordinal scale (ranging from very pragmatic to very explanatory) across 9 domains of trial design, including eligibility, recruitment, setting, organization, intervention delivery, intervention adherence, follow-up, primary outcome, and analysis. A higher score indicates a more pragmatic score on an individual domain, and aggregated scores are a simplified formula across all domains. Cohen’s D was used to quantify the mean difference relative to the variation.

Results: There were 616 RCTs, distributed evenly over the 2 decades, and 64% achieved their primary endpoint. The mean (±SD) PRECIS-2 score was 3.26 ± 0.70 among 616 included RCTs. The level of pragmatism increased over time from a score of 3.07 ± 0.74 in 2000 to 3.47 ± 0.67 in 2015 (p <0.0001 for trend; Cohen’s D relative effect size 0.57). The increase in pragmatism occurred mainly in the domains of eligibility, setting, intervention delivery, and primary endpoint (Figure). PRECIS-2 score was higher for neutral trials than those with positive results (p=.0015) and in phase III/IV trials as compared to phase I/II trials (p<.0001) (Figure). Furthermore, trials that involve more sites, with larger sample sizes, longer follow-ups, and those with mortality as the primary endpoint were found to be more pragmatic. There was no difference in the level of pragmatism between different sources of funding (public, industry, or both; p=0.52). Conclusion: The PRECIS-2 tool can be used for appraising trials to assess their placement in the pragmatic-explanatory continuum. The level of pragmatism increased over time in CV trials. Greater focus on the design and delivery of CV trials will be required for the broad application.
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