MSR32

Instrumental Variables to Address Non-Compliance in Randomized Control Trials, a Scoping Review

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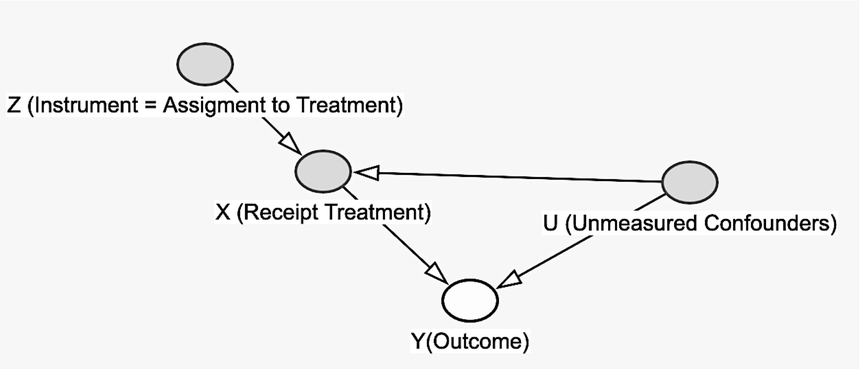
OBJECTIVE

Instrumental variable analysis offers an alternative approach, particularly in scenarios characterized by low compliance to treatment, as depicted in Directed Acyclic Graphs (DAG 1).
We aimed to explore how non-compliance have been recognized and analyzed with Instrumental Variable (IV) methods in Randomized Control Trials (RCTs).

METHODS

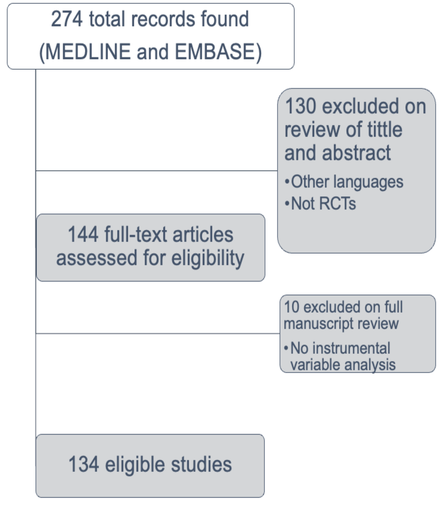
A scoping literature review was conducted. We searched articles that implemented IV method in RCTs in MEDLINE and EMBASE. The search strategy was “randomized control trial” AND “instrumental variable”. Articles were evaluated according to their methodological approach to causal inference in RCTs to identify the main methods for estimating causal effects in the presence of non-compliance. Specifically, the methods of Intent-to-Treat (ITT), Per-Protocol (PP), As-Treated (AT), and IV with and without bias correction were examined. Key concepts related to addressing non-compliance in randomized experiments was described. Also, estimates obtained from different methods were identified, and the results and conclusions were compared from their methodological approaches.

Graph 1. Directed Acyclic Graphs for IV in RCT

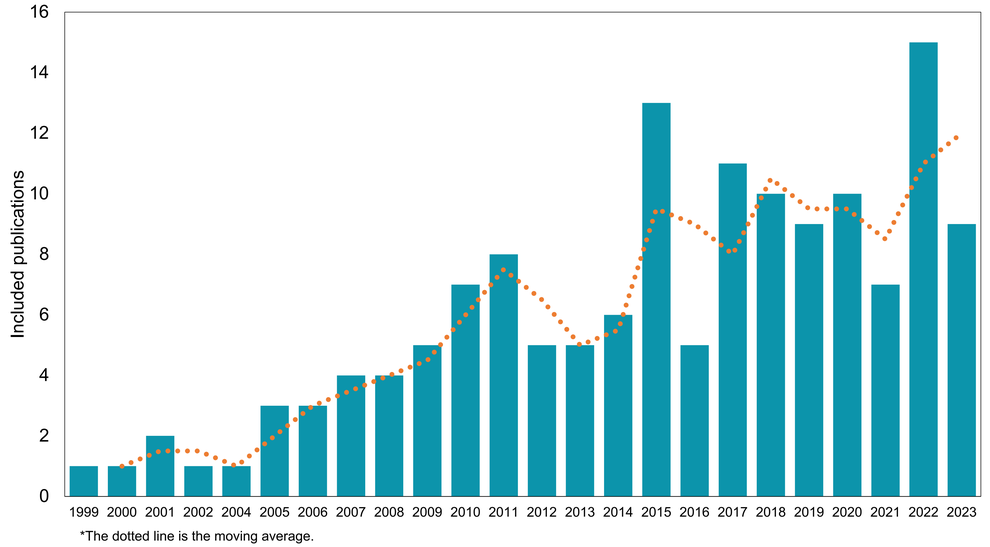


RESULTS

We found 274 articles from which 134 met the inclusion criteria. The greatest portion (51.9%) of evidence was published from 2015 to 2023; 9.6% just in 2015. Most researches (73.3%) were conducted either in the United States or the United Kingdom. Methodological approaches were focus mainly on ITT methods (95%), and just 12.5% estimated three methods for effect estimation (ITT, PP and AT) comparing with IV approach. 95% of the studies used RCTs data and 5% used simulated data. In 80% of the studies the conclusion based on the IV analysis was different compared to other methods: in 62% of these the change was that the measure of association increased, 17.5% due to changes from a significant association to non-significant association, 12.5% for changes due to a significant association and the rest owing to other types of modifications.



Graph 2. Trend of included publications of this scoping review*



*The dotted line is the moving average.

CONCLUSIONS

IV method is an emerging approach seen infrequently in the biomedical literature. Nevertheless, the IV analysis can bring qualitatively and quantitatively different results than that obtained with other methods, complementing the evaluation of health interventions.