We propose a new method for reducing the impact of unobserved confounding in large pharmacoepidemiological studies [1]. The method relies on discrepancies between a) treatment actually received by individual patients versus b) treatment expected based on their observed characteristics and their physicians’ prescribing preferences. In simulations, for risk difference analyses of the association of a binary exposure on a binary outcome, our estimates largely reduce bias, have much smaller variance than Instrumental Variable estimates, and have best overall accuracy of all methods considered. We apply the method to re-assess gastrointestinal safety of COX-2 inhibitors vs. traditional NSAIDs.


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