

Honest learning for the healthcare system: large-scale evidence from real-world data

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In practice, our learning healthcare system relies primarily on observational studies generating one effect estimate at a time using customized study designs with unknown operating characteristics and publishing – or not – one estimate at a time. When we investigate the distribution of estimates that this process has produced, we see clear evidence of its shortcomings, including an apparent over-abundance of estimates where the confidence interval does not include one (i.e. statistically significant effects) and indicators of publication bias. In essence, published observational research represents unabashed data fishing. We propose a standardized process for performing observational research that can be evaluated, calibrated and applied at scale to generate a more reliable and complete evidence base than previously possible, fostering a truly learning healthcare system. We demonstrate this new paradigm by generating evidence about all pairwise comparisons of treatments for depression for a relevant set of health outcomes using four large US insurance claims databases. In total, we estimate 17,718 hazard ratios, each using a comparative effectiveness study design and propensity score stratification on par with current state-of-the-art, albeit one-off, observational studies. Moreover, the process enables us to employ negative and positive controls to evaluate and calibrate estimates ensuring, for example, that the 95% confidence interval includes the true effect size approximately 95% of time. The result set consistently reflects current established knowledge where known, and its distribution shows no evidence of the faults of the current process. Doctors, regulators, and other medical decision makers can potentially improve patient-care by making well-informed decisions based on this evidence, and every treatment a patient receives becomes the basis for further evidence.

Joint work with Martijn J. Schuemie, Patrick B. Ryan, George Hripcsak, and Marc A. Suchard.

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