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**David Madigan\*** ([david.madigan@columbia.edu](mailto:david.madigan@columbia.edu)), 1255 Amsterdam Avenue, New York, NY 10027. *Towards systematic evidence generation from real-world healthcare data.*

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). 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. We demonstrate this new paradigm by generating evidence about all pairwise comparisons of treatments for hypertension for a relevant set of health outcomes using nine large electronic healthcare record databases from 3 continents. The result set consistently reflects current established knowledge where known, and its distribution shows no evidence of the faults of the current process. (Received August 18, 2019)