Subagging for Inference of the Mean Outcome Under Optimal Treatment Regimes

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Abstract: Precision medicine is an emerging medical approach that allows physicians to select the treatment options based on individual patient information. The goal of precision medicine is to identify the optimal treatment regime (OTR) that yields the most favorable clinical outcome. Although considerable research has been devoted to estimating the optimal treatment regime (OTR) in the literature, less attention has been paid to statistical inference of the OTR. In this paper, we develop a novel inference method for the mean outcome under an OTR (the optimal value function) based on subsample aggregating (subagging) and refitted cross-validation. The proposed method can be applied to multi-stage studies where treatments are sequentially assigned over time.

Bootstrap aggregating (bagging) and subagging have been recognized as effective variance reduction techniques to improve unstable estimators or classifiers (Buhlmann and Yu, 2002). However, it re-mains unknown whether these approaches can yield valid inference results. We show the proposed confidence interval (CI) for the optimal value function achieves nominal coverage even in the nonregular cases where the OTR is not uniquely defined. In addition, due to the variance reduction effect of subagging, our method enjoys certain statistical optimality. Specifically, we prove the length of the proposed CI is on average shorter than the CI constructed based on the online one-step method (Luedtke and van der Laan, 2016). Moreover, under certain conditions on the propensity score function, we show the proposed CI is asymptotically narrower than the CI of the "oracle" method which works as well as if an OTR were known. Numerical studies are conducted to back up our theoretical findings.