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What is the effect of area size when using local area practice style as an instrument?

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Abstract

Objectives: Discuss the tradeoffs inherent in choosing a local area size when using a measure of local area practice style as an instrument in instrumental variable estimation when assessing treatment effectiveness.

Study Design: Assess the effectiveness of angiotensin converting-enzyme inhibitors and angiotensin receptor blockers on survival after acute myocardial infarction for Medicare beneficiaries using practice style instruments based on different-sized local areas around patients. We contrasted treatment effect estimates using different local area sizes in terms of the strength of the relationship between local area practice styles and individual patient treatment choices; and indirect assessments of the assumption violations.

Results: Using smaller local areas to measure practice styles exploits more treatment variation and results in smaller standard errors. However, if treatment effects are heterogeneous, the use of smaller local areas may increase the risk that local practice style measures are dominated by differences in average treatment effectiveness across areas and bias results toward greater effectiveness.

Conclusion: Local area practice style measures can be useful instruments in instrumental variable analysis, but the use of smaller local area sizes to generate greater treatment variation may result in treatment effect estimates that are biased toward higher effectiveness. Assessment of whether ecological bias can be mitigated by changing local area size requires the use of outside data sources.

Keywords: Instrumental variables; Local area practice styles; Angiotensin converting enzyme inhibitors and angiotensin receptor blockers; Acute myocardial infarction; Survival; Local average treatment effects

1. Introduction

Instrumental variable (IV) estimators have been recognized as useful tools to assess the effectiveness of alternative treatments in health care using observational data [1,2]. The ''instruments'' required in IV studies must be measured factors that are strongly related to treatment choice but are unrelated to either study outcomes or other unmeasured factors related to study outcomes. Thus, instruments essentially provide an ex post randomization of treatment choice or exposure across patients [3−9]. IV methods yield estimates of the average treatment effect for the subset of patients whose treatment choices were mutable to changes in the instrument variable or ''instrument'' values [4,10−13]. IV estimates have been labeled a local average treatment effect (LATE) and are thought to be most suitable to assess the effect of treatment rate changes in a population [7,8,10−14]. Many researchers have used local area practice style measures as instruments in IV analysis [15−28], which conjectures that patients residing in areas where physicians have stronger preferences for a particular treatment are more apt to receive that treatment and unmeasured confounding variables are unrelated to the differential patient access to physicians with distinct treatment preferences.

Only two studies that used a local area practice style measure as instruments have reported whether their estimates were robust to adjustments in the size of the local area used to measure practice style [23,28], and there has been no discussion as to the potential effects of local area size on the properties of the resulting IV estimates. The size of the local area used to measure practice style may affect both the strength of the relationship between the instrument and treatment choice and whether the instrument is related

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What is new?

Key findings

- The use of smaller local areas to measure practice styles as instruments exploits more treatment variation and results in smaller standard errors. However, if treatment effects are heterogeneous, the use of smaller local areas may increase the risk that local practice style measures are dominated by idiosyncratic differences in average treatment effectiveness across areas resulting in treatment effect estimates that are biased toward greater effectiveness.

What this adds to what was known?

- Local area practice style measures can be useful instruments in instrumental variable analysis, but the use of smaller local area sizes to generate greater treatment variation may result in treatment effect estimates that are biased toward higher effectiveness. Assessment of whether ecological bias can be mitigated by changing local area size requires the use of outside data sources.

What is the implication and what should change now?

- Researchers should be aware that if treatment effects are heterogeneous across patients, the use of small-sized local areas as the basis to measure local practice style as an instrument may result in treatment effect estimates that are biased in favor of treatment.

to unmeasured confounding factors. One might expect that the larger the local area around a patient residence used to measure practice style the weaker the relationship will be between the instrument and the treatment choices for individual patients. Confounding emerges when local area practice style measures are correlated with differences in average unmeasured patient characteristics or ecological factors across areas that are related to patient outcomes. A priori relationships between local area size patient and ecological factors that may confound estimates do not generally exist. Ecological factors have been categorized as aggregate attributes (e.g., smoking rates, average health behaviors), contagion factors (e.g., flu prevalence), environmental factors (e.g., pollution, weather, sunlight hours); patterns of interaction among area individuals (e.g., social networks); and global factors (e.g., local regulations or market structures) [29]. One can envision that smaller local area sizes could introduce correlations between practice style and unmeasured neighborhood-level cultural and health behavior−related confounders. In contrast, use of larger local area sizes may introduce correlations with regional unmeasured confounders related to regulatory structures, regional health care systems, and climate. In addition, if the relationships between individual treatment choice and local area practice style measures weaken as local area size increases, this increases the *potential* for unmeasured patient and ecological factors to confound the treatment effect estimates. However, the only possible approach to validate assumptions of no correlation between local area practice style measures and confounding factors for specific area sizes and is to obtain secondary data sources describing these factors and directly estimate the correlations by area size.

If treatment effectiveness is heterogeneous across patients, another source of confounding related to local area size needs to be considered. ''Essential heterogeneity'' occurs when treatment effects are heterogeneous across patients and providers make treatment recommendations based on patient characteristics that are related to expected treatment effectiveness [19,21,30−32]. If the patient characteristics related to treatment effectiveness are unobserved by the researcher, we theorize that local area practice style *measures* will be positively correlated with average treatment effectiveness across areas causing LATE estimates to be biased toward positive treatment effectiveness. It will appear that higher treatment rates will yield better outcomes when in fact areas with higher treatment rates simply contained more patients apt to gain from treatment. However, as we discuss in Appendix A, as the number of patients used to define a local area increases, the favorable bias in LATE estimates from this effect will diminish.

The objective of this study is to discuss the tradeoffs involved in choosing a local area size when using local area practice style as an instrument. We used IV methods to estimate the LATE of renin−angiotensin system antagonists including angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) on 1-year patient survival among Medicare patients after acute myocardial infarction (AMI). ACE/ARB use post-AMI provides an interesting setting for this discussion because the benefits of ACE/ARBs are known to be heterogeneous across AMI patients with greater benefit for patients at higher risk of future cardiovascular events [33]. ACE/ARB survival benefit estimates from randomized controlled trials (RCTs) vary from 50 lives saved per 1,000 high-risk patients to 5 lives saved per 1,000 low-risk patients [34]. In addition, evidence shows substantial variation in ACE/ARB prescribing as only 50% of Medicare patients from two states received an ACE/ARB post-AMI in 2004 [35], and large geographic variation has been reported [36]. If providers believe ACE/ARB benefits are heterogeneous across patients and ACE/ARB treatments are sorted across AMI patients based on expected benefits—''essential heterogeneity'' [19,37]—we expect that local area ACE/ARB practice styles variation will reflect moderate-risk AMI patients whose ACE/ARB choices are more discretionary than either high- or low-risk patients. As a result, IV estimates of LATE for ACE/