

## Letter to the Editor

Word Count: 400 words

Reference Limit: 5 references (including the article itself)

Mirza S. Khan, MD (mirza.khan2@va.gov)

U.S. Department of Veterans Affairs, Nashville, TN

Chaiyachati et al. conducted a valuable study on providing rideshare-based transportation to those at high-risk for missed appointments.<sup>1</sup> The study faced a significant degree of non-adherence stemming from participant non-response and disinterest; 56.3% of responders in the intervention arm were uninterested in the rideshare offer. This suggests that ridesharing may be unpalatable to this population. Information on rideshare use in the control arm and general patient population may be more revealing.

In studies with poor adherence, the results of intent-to-treat (ITT) analyses, such as was used in this study, may provide unreliable clinical information and exhibit bias towards the null effect.<sup>2,3</sup> The authors attempt to remedy some of these shortcomings by treating the intervention as a rideshare offer (rather than rideshare utilization) and conducting secondary analysis using an 'as-treated' (AT) approach. Another study that also suffered from low adherence found twice the effect size when using a 'per-protocol' (PP) analysis as compared to their ITT analysis.<sup>2-4</sup> The authors may find PP analysis provides a better estimate of the effect of full adherence.

Furthermore, the baseline missed appointment rate of 49% decreased to 36% in both study arms. The authors found no other changes in appointment reminder practice to explain this decline. Per their study design, both groups received a manual phone call from research staff beyond the "usual care" automated reminder.<sup>1</sup> Given the decrease in both arms, I question if the manual phone calls contributed to the reduction in missed appointments. I compared study participants who answered the phone (responders) to those who did not (non-responders) using naïve AT and PP methods and  $\chi^2$  analysis. Among non-responders, the missed appointment rate was 40.1% and 52.8% in the control and intervention arms, respectively ( $p = 0.07$ ). The AT method compares non-responders to responders irrespective of the randomized assignment. Of the 228 non-responders and 558 responders in both arms, 106 and 182 missed appointments, respectively (46.5% vs. 32.6%;  $p = 2.5 \times 10^{-4}$ ). PP analysis compares non-responders assigned to the control arm with intervention arm responders. The 122 control arm non-responders accounted for 50 missed appointments, whereas the 288 intervention arm responders had 88 missed appointments (40.1% vs. 30.6%;  $p = 0.04$ ).

Consistent with previous work,<sup>5</sup> these findings suggest that the reduction in missed appointment rates in both study arms may be attributed to answering manual phone calls. This confounding may contaminate the published results and provide invalid estimates of the effect of the rideshare offering intervention.

## References

1. Chaityachati KH, Hubbard RA, Yeager A, et al. Association of Rideshare-Based Transportation Services and Missed Primary Care Appointments: A Clinical Trial. *JAMA Intern Med*. 2018;178(3):383-389. doi:10.1001/jamainternmed.2017.8336
2. Hernán MA, Robins JM. Per-Protocol Analyses of Pragmatic Trials. *N Engl J Med*. 2017;377(14):1391-1398. doi:10.1056/NEJMsm1605385
3. Murray EJ, Hernán MA. Adherence adjustment in the Coronary Drug Project: A call for better per-protocol effect estimates in randomized trials. *Clinical Trials*. 2016;13(4):372-378. doi:10.1177/1740774516634335
4. Holme Ø, Løberg M, Kalager M, et al. Effect of Flexible Sigmoidoscopy Screening on Colorectal Cancer Incidence and Mortality: A Randomized Clinical Trial. *JAMA*. 2014;312(6):606. doi:10.1001/jama.2014.8266
5. Hasvold PE, Wootton R. Use of telephone and SMS reminders to improve attendance at hospital appointments: a systematic review. *J Telemed Telecare*. 2011;17(7):358-364. doi:10.1258/jtt.2011.110707