STUDY TITLE: HOME BASED CHRONIC KIDNEY DISEASE CARE IN NATIVE AMERICANS OF NEW MEXICO – A DISRUPTIVE INNOVATION

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Statistical Analysis Extract From Final PCORI Report

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Statistical Analysis

The primary analyses that addressed the questions of principal interest in this study focused on comparisons between groups defined by random allocation to the treatments under investigation, upon screening eligible and agreeing to participate. The primary outcome for this intervention was the total activation score derived from the 13-item PAM survey. To compare the measured primary outcome between the two treatment groups, we utilized linear mixed model approaches. In these models, we included a random intercept term for household membership to account for within-household clustering, and per-visit (baseline, 6 months, and 12 months) repeated measures to account for the longitudinal nature of the study design. The primary analysis for the outcome of PAM total activation score was an intention to treat analysis, which incorporated a last observation carried forward (LOCF) imputation approach to accommodate loss to follow-up under the assumption that loss to follow-up equated to the result of no change in patient activation over time. In this primary comparison, longitudinal changes in the PAM Total score were compared between study arms while accounting for the random effects and repeated measures terms outlined above. In this model, adjustments were also made for Native community membership to account for the blocked nature of the randomization strategy. Subsequent analyses were conducted after adjustment for demographic measures (age, gender, and educational attainment), and measures of body mass index (BMI) and systolic blood pressure obtained at screening.

Additional analyses were applied to address other research questions of interest for this study. We compared participation rates between those randomized to the two treatment arms using Fisher's exact tests, and estimated odds ratios (ORs) and 95% Confidence Intervals (CIs) to summarize the magnitude of the participation differences between groups. We applied the analytic models described for the primary outcome to compare differences between those randomized to the treatment arms for factors associated with clinical outcomes (secondary outcomes for Aim 2 are shown in Tables 7 and 8), and for measures capturing aspects of health-related quality of life (outcomes for Aim 3 are shown in Tables 9 and 10). These analyses differed from the analysis of the primary analysis of PAM total scores in one respect: rather than using an intention-to-treat analyses, we compared these outcomes between treatment groups using all observed data points without imputation. We made this decision as the observed-data results of the PAM total score primary outcome did not differ substantially from those obtained using the intention-to-treat analyses with LOCF imputation.

Our planned analyses were structured such that a number of key considerations were considered and assessed prior to reporting the results from the analyses, as outlined in the list below.

a. Assessment of assumptions: Linear models require that the distribution of the residuals from the model, as applied to the outcome variable, be normally distributed and of constant variance across the predicted values of the response variable. We verified that these two key assumptions were met. When they were not, we applied transformations, either logarithmic or inverse normal, and performed analyses on the alternative data scale in order to ensure that statistical conclusions were drawn from models that were appropriate for the distribution of the measured data values.
b. Accounting for missing data: Due to the circumstances arising from the time when this study was active, in particular relating to the COVID-19 pandemic, there was a considerable amount of data missingness. We used an intention to treat analysis that incorporated LOCF approaches to

accommodate missed follow-up time points for our primary outcome in Aim 1. We also performed a number of sensitivity analyses for this outcome. These included an analysis of observed data measurements only, where observations (not participants) with missing data were dropped from the longitudinal analyses, and an analysis using only data from individuals who provided data at all three time points (baseline, 6 months, and 12 months). These extreme-case analyses made it possible to determine how sensitive the between-groups comparisons were to the presence of missing data. We had planned to repeat our analyses using pattern-mixture models.[73,74] However, given the limited amount of data available to us, and the fact that major differences in interpretation were not required for the results from the various sensitivity analyses, we deemed it to not be necessary to carry out such analyses. Because of the lack of evidence suggesting a need to accommodate informative missingness in our analyses, for all but the primary outcome of PAM total scores we report as primary the results obtained based on all observed data. This enabled the use of data from all individuals in the linear mixed effects models as long as they had provided data in at least one observation period.

c. Heterogeneity of treatment effect: In this randomized trial, the primary potential for heterogeneity of treatment effect was among the four native communities in the Southwest from which participants were recruited. To determine whether there are differences in treatment effect among these four communities, we had planned to conduct a secondary series of analyses, where we would have directly modeled potential treatment effect differences among the communities using interactions between the longitudinal effect terms and the four native communities. Given the substantial loss to follow-up due to the COVID pandemic, we did not have sufficient data to provide an adequate basis for these analyses. We there chose to forgo these analyses. Future work will be required to not only evaluate the possibility of treatment effect heterogeneity but also the possibility of any treatment effect overall.