Clinic-based vs home-based support to improve care and outcomes for older asthmatics Statistical Analysis Plan
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**DATA ANALYSIS (Months 10-36)**

**a Analysis Plan** A HIPAA waiver will be obtained to use de-identified data to compare non-participants (available from recruitment lists) to participants on age, gender, and ethnicity. Assessment of Measurement Invariance: We will examine whether measures are invariant across language and racial/ethnic groups. Measurement invariance will be assessed with MIMIC models or with a method adopted from Rasch analysis for small group sizes.[232] The baseline characteristics of enrolled patients will be compared across the 3 study arms using a chi-square test or ANOVA, as appropriate. We will assess the distribution of the dependent variables as well as other statistical assumptions and apply transformations as necessary.

**b Aim 1 Primary Analyses.** *Compare the effectiveness of clinic and home-based asthma care coordination and self-management support to improve care and asthma-related outcomes*. All effectiveness analyses will be conducted using an intent-to-treat approach. The goal of the analyses is to evaluate if the ACC and CHW interventions are superior to UC and test the non-inferiority of the ACC vs. CHW arms. Change from baseline to 14 weeks and 9 months in ACQ and AQLQ scores, resource utilization, and self-management behaviors will be the primary study outcomes. To test our hypothesis about the impact of the intervention on asthma control, we will fit a mixed linear model with change in ACQ or AQLQ scores as the outcome, random patient and provider effects (to model clustering within providers and repeated measures on each patient), and fixed effect components for study site, baseline control status, treatment group, and time. The mean difference in ACQ and AQLQ scores from baseline to post-intervention between the ACC and CHW arms with UC will be estimated with a contrast with the associated 95% confidence intervals. To assess the equivalence of the ACC and CHW intervention, we will compare the upper bound of the confidence interval of the difference in ACQ scores. We will use a Bonferoni correction to maintain the overall alpha level (i.e., 0.05) of the experiment. The impact of the intervention on resource utilization will be evaluated using a negative binomial mixed model; dichotomous outcomes (adherence [MARS score >4.5], trigger avoidance, and use of action plans we will assessed using generalized mixed linear models (logit link and binomial variance). The primary analysis will be based on the test of the main effect for treatment (i.e., the overall effect of the intervention at 14 weeks and 9 months). Then, we will add interactions between treatment arms and time to assess the intervention's sustainability at 9 months (i.e., a significant interaction term with a negative point estimate will suggest lack of sustainability). We will compare the ACC and CHW arms with UC separately at each time point using appropriate contrasts. We will analyze residuals of the fitted models to identify outliers and influential observations. We will conduct secondary analyses adjusting for baseline covariates if distributional imbalances exist across arms.

**Table 5. Sample Size Calculation for Aim 1**

| Contrast | Outcome | Difference Between Arms | SD[1] | Adjusted[2] Total Sample Size |
|---|---|---|---|---|
| ACC and CHW vs UC[3] | ACQ[4] scores | 0.7 | 0.4 | 30 |
| | Resource utilization | 25% | - | 242 |
| | AQLQ[5] scores | 0.5 | 0.3 | 42 |
| | $FEV_1$ % predicted[6] | 5 | 5 | 72 |
| Equivalence of CHW vs UC | Adherence | 25% | - | 242 |
| | ACQ scores | 0.175 | 0.4 | 360 |
| | Resource utilization | 15% | - | 510 |
| | AQLQ[5] scores | 0.125 | 0.3 | 393 |
| | $FEV_1$ % predicted[6] | 1.25 | 5 | 372 |
| | Adherence | 15% | - | 510 |

[1]SD: standard deviation, [2]Adjusted for clustering between providers. Total N for 80% power. [3]ACC: asthma care coordinator, CHW: community health worker, UC: usual care, [4]ACQ: asthma control questionnaire, [5]AQLQ: Asthma Quality of Life Questionnaire, [6]FEV1: forced vital capacity in 1 second.

Sample Size Calculation for Aim 1. (Table 5) We powered the study to identify a clinically meaningful difference in ACQ scores of 0.7 units, 0.5 AQLQ units, and a 25% change in acute asthma-related resource utilization and adherence.[138] Assumptions about the distribution of outcomes are based on published literature and our prior studies.[130,138,209-211] Sample size was adjusted for the expected correlation of outcomes due to clustering of patients within physicians using the method described by Friedman et al.[233] Given the multifactorial determinants of asthma control and the relatively random distribution of patients between providers, we expect low correlation of outcomes among patients cared by the same provider (from our prior data, intraclass correlation <0.15). We will have multiple observations per patient but performed conservative sample size calculations assuming a single measure per participant. Calculations were performed using two-sided p-values and an overall alpha level of 0.05. For equivalence comparisons, we estimated the sample size to be able to identify a minimal difference between the ACC and CHW arms >0.175 units (i.e., no larger than 25% of the minimal clinically significant difference in ACQ scores); for

resource utilization we used a difference of 15%, a usually accepted standard.[234] Our study will be powered to assess primary and key secondary outcomes assuming a dropout rate ~15%. Twelve-month retention in our current asthma cohort study is >90%.

Aim 1 Secondary analyses will examine the impact of the interventions on daily activities, $FEV_{1,}$ patient's perspective of services, and caregiver satisfaction. These analyses will be conducted as specified above.

**c Aim 2 Analyses**. These analyses will assess whether the CHW intervention may be more suited for a subset of elderly asthma patients. Specifically, we hypothesize that minority patients with psychosocial issues, functional or cognitive impairment will benefit more from a CHW compared to an ACC-based intervention. Functional impairment will be defined as 1 or more dependency with instrumental activities of daily living, in other words, whether the individual requires assistance with housework, food preparation, shopping for groceries or clothing, using a telephone, managing medications, and or managing money.[227] Cognitive impairment will be defined as a mini-mental status exam score of ≤27;[235] depression as a PHQ-9 score of ≥15 (moderately severe);[198] serious and persistent mental illness as having a current or past diagnosis of schizophrenia, schizoaffective disorder, or bipolar disorder; problematic alcohol use as 4 or 5 at one time in the past year for women and men, respectively;[236] and, substance abuse as any current use of an illegal drug or prescription drug used for non-medical purposes.[230] Later exploratory analyses will involve testing other thresholds for these measures. We will limit the analyses to the primary outcomes and compare them between the ACC vs. CHW arms. Hypothesis testing will be based on the final model for ACQ and AQLQ scores, resource utilization and adherence rates described above. We will add an interaction term between treatment arm (ACC vs. CHW) and the factor of interest (i.e., psychological issues, functional or cognitive impairment). The significance of the beta coefficient for the interaction term will be used to assess if the CHW intervention may be more beneficial for these subgroups.

Sample Size Calculation for Aim 2. The expected number of individuals with psychological issues, functional or cognitive impairment was estimated based on data from our cohort study of asthma in the elderly.[14,49,67,235] We calculated the power of the study to identify whether the regression coefficients for the association between intervention arm and ACQ/AQLQ scores will be different for patients with vs. without substance abuse or functional or cognitive impairment (equivalent to testing the interaction between treatment arm and presence or absence of these conditions). These analyses showed that with 150 subjects per arm, the study will have an >80% power to detect a difference ≥0.5 units between the slopes of patients with and without these conditions.