

Statistical Analysis Plan

Study Title: Advance Planning for Home Services for Seniors

Protocol Title: PLAN YOUR LIFESPAN Randomized Controlled Trial

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2 Abbreviations and Definitions

AE	Adverse Event
APHS	Advanced Planning for Home Services for Seniors
CRF	Case Report Form
IMP	Investigational Medical Product
POA	Power of Attorney
PYL	PLAN YOUR LIFESPAN
SAP	Statistical Analysis Plan
PCORI	Patient-Centered Outcomes Research Institute

3 Introduction

3.1 Preface

Seniors over the age of 65 years represent 13.1% of the United States population, with a projected 36% increase to 55 million by the year 2020.^{1,2} With advancing age, seniors experience an increased prevalence in memory loss, physical disability, and multiple chronic conditions (e.g., heart disease, emphysema, stroke, diabetes, cancers, hypertension, arthritis, osteoporosis, and macular degeneration).³⁻⁷ A large fear among seniors is loss of independence and removal from their homes to be placed in a nursing home.⁸⁻¹⁰

The Advanced Planning for Home Services for Seniors (APHS) study has three aims: (1) To develop, pilot test, and refine the PLAN YOUR LIFESPAN tool to assist seniors in making informed choices about issues in their health trajectory that influence their ability to remain in their own home, (2) to conduct a randomized, controlled trial of the PLAN YOUR LIFESPAN tool to determine the tool's influence on subject understanding of home care services, health trajectory, and other patient-centered outcomes compared with an attention control, and (3) to disseminate the PLAN YOUR LIFESPAN tool nationally through senior-focused organizations. After developing the PLAN YOUR LIFESPAN tool, we are now ready to pilot test the PLAN YOUR LIFESPAN tool as well as to conduct the proposed randomized, controlled trial.

3.2 Purpose of the analyses

These analyses will assess the efficacy of the PLAN YOUR LIFESPAN tool in influencing participant understanding of home care services, overall health trajectory, and other patient-centered outcomes.

4 Study Objectives and Endpoints

4.1 Study Objectives

Conduct a Randomized Controlled Trial of the PLAN YOUR LIFESPAN tool to determine subject understanding of home care services, advanced health planning, and other patient-centered outcomes.

4.2 Endpoints

The primary endpoint for this study is planning behavior score (ranging from 5-25 points) at the one-month follow-up time point as measured by the “Planning Implementation (Behavior)” assessment. Analyses will control for baseline planning behavior score.

Secondary endpoints include (analyses will control for relevant baseline assessment scores where appropriate):

- (a) Planning Implementation behavior score at three-month follow-up time point (to measure effect retention).
- (b) Planning perception score at all follow-up time points as measured by the “Planning Perception” assessment.
- (c) Change in individual planning intention item scores at all follow-up time points compared to baseline as measured by the “Planning Intention” assessment.
- (d) Confidence score at all follow-up time points as measured by the “Confidence in Accessing Home Services” assessment.
- (e) Knowledge of home services score at all follow-up time points as measured by “Understanding of Home Services” assessment.
- (f) Percentage showing increased communication with family/Power of Attorney (POA) and health providers at one- and three-month follow-up time points in comparison to baseline as measured by “Communication about Lifespan Planning Questionnaire” assessment.
- (g) Score of overall satisfaction with the intervention tool or attention control as measured by the “Satisfaction with Intervention Tool” assessment at all follow-up time points for the participants in the intervention arm.

4.3 Derived variables

Behavior score (PRIMARY ANALYSIS): This score will be calculated as the sum of the five behavior questions (each scored from 1-5 points) on the “Planning Implementation (Behavior)” assessment.

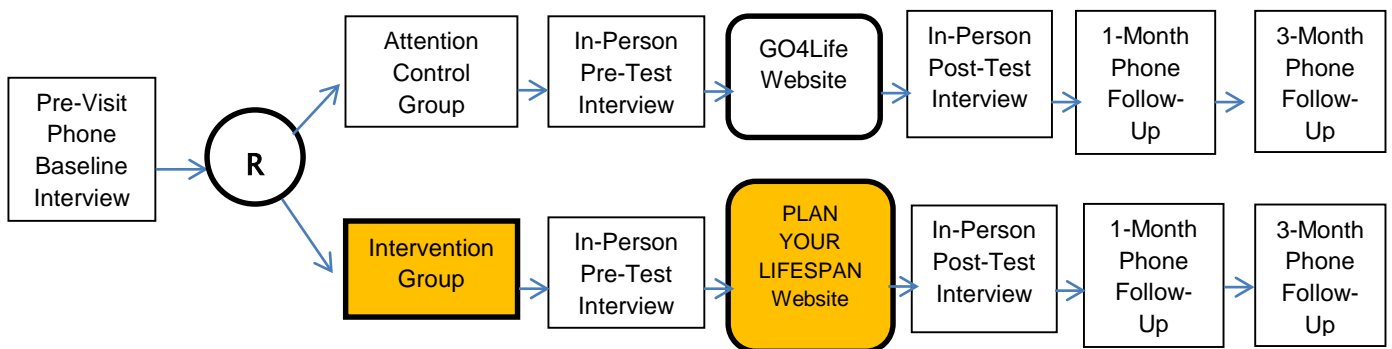
Confidence score (SECONDARY ANALYSIS): This score will be calculated as the sum of the five questions (each scored from 1-5 points) on the “Confidence in Accessing Home Services” assessment.

Perception score (SECONDARY ANALYSIS): This score will be calculated as the sum of the five perception questions (each scored from 1-5 points) on the “Planning Implementation (Behavior)” assessment.

5 Study Methods

5.1 General Study Design, Plan, and Randomization

We will conduct a two-armed (attention control and intervention), parallel, randomized controlled trial. Individuals will be randomly assigned to one of two interventions: attention control or PLAN YOUR LIFESPAN tool via a pre-generated central randomization list using equal (1:1) allocation and random permuted block design to ensure relatively equal allocation throughout the study. Our attention control group will control for the possibility that regular contact with the study team may improve outcomes in participants regardless of receipt of intervention. Participants randomized to the attention control group will go through an educational website on activities relevant to seniors, for 15-45 minutes. The educational website is sponsored by the National Institute on Aging and does not include information about advanced planning.



Please refer to the study protocol for specific inclusion/exclusion criteria.

Randomization codes will be created using SAS software, Version 9.3 of the SAS System for Windows. [Copyright © 2012, SAS Institute Inc., Cary, NC, USA.] The allocation order will be generated using a customization of the PROC PLAN procedure, modified to allow for a permuted block design.

6 Sample Size

Without prior knowledge of the distributional properties of the primary outcome (“Planning Implementation Behavior” score, ranging from 5-25), we can use Cohen’s d' to estimate the detectable effect size given the predicted accrual. With an overall recruitment goal of 600 participants and an 85% retention rate (i.e., 510 study completers with 255 in each arm), we anticipate being able to detect a small to moderate effect size (0.25) with 80% power, assuming a 5% type I error rate.

7 General Considerations

7.1 Timing of Analyses

The data set will be locked once 600 participants have completed the three-month call or have withdrawn or been lost to follow-up prior to the three-month visit. Data cleaning will take place during the month after the lock; upon identification of any anomalies, study coordinators will be granted access to the data set to make necessary corrections. The final analysis will be performed following data cleaning.

7.2 Analysis Population

Analyses will proceed according to the intention-to-treat principle. All randomized participants with available data will be included in the final analyses, with the exception of any participants that are found to be mis-randomized (i.e., those who should not have been enrolled based on inclusion/exclusion criteria).

Note: Planning intention questions will not be asked of all participants. Analyses of these individual items will be conducted only on the subset of participants with scores for both baseline and follow-up time points.

7.3 Missing Data

We are assuming data will be missing at random. If data for any endpoint variable is greater than 20% missing, we will employ a global sensitivity analysis² to determine level of robustness of overall trial results.

7.4 Interim Analyses and Data Monitoring

We will plan for a single interim analysis for primary outcome after enrollment and one-month follow-up of approximately half (300) of the target sample size. We will use an O’Brien-Fleming-type alpha spending function³, and if the calculated test statistic at the interim analysis surpasses the required threshold (associated with an approximate two-sided 0.5% level of significance) according to the O’Brien-Fleming criterion, we will consider early termination of the study for overwhelming efficacy or harm (i.e., if the intervention appears to influence planning behavior in an overall overwhelmingly positive *or* overwhelmingly negative direction).

The interim analysis will only be used to test for early stopping due to overwhelming efficacy or harm of the intervention. Aside from potential early study termination, there will not be adjustments to sample size as a result of the interim analysis. Since there will be no formal data and safety monitoring committee (DSMC), the results of the interim analysis will be communicated and presented to the study team and all relevant stakeholders. Should the stakeholders agree to stop the trial for overwhelming efficacy or harm due to interim analysis

results, the Sponsor (PCORI) will be notified. All parties will be in agreement to terminate the trial prior to commencement of termination procedures and study closeout.

Since we anticipate a single interim analysis, we will adjust final primary outcome analysis significance level to an approximate two-sided 4.5% (note that the final adjustment will depend on the actual calculated type I error “spent” at the interim analysis such that the overall type I error rate remains at 5%).

The interim analysis of the primary outcome will be conducted by a second statistician so the statistician handling the final analysis of the primary outcome is not biased by the interim results.

7.5 Multiple Testing

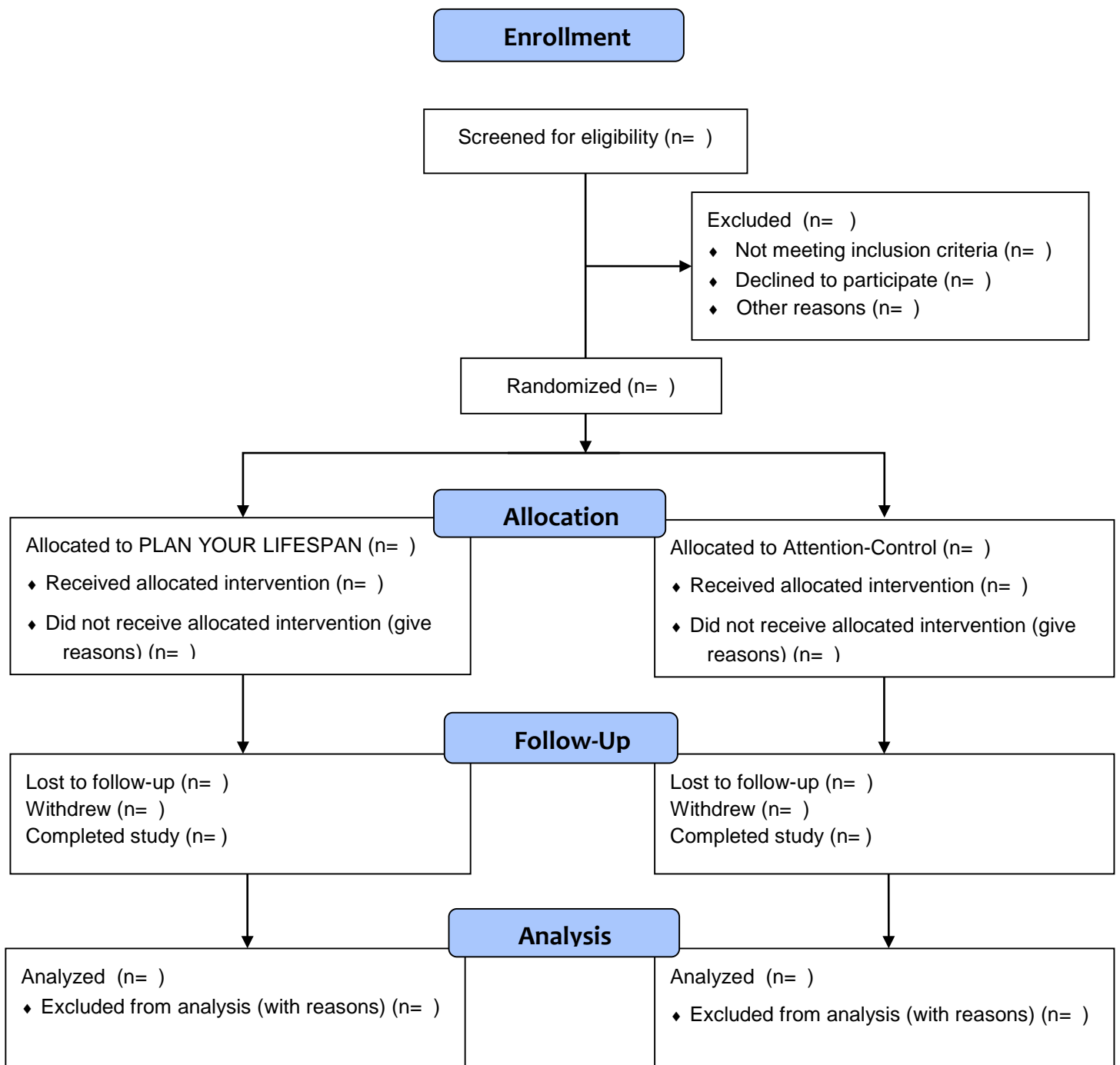
Aside from the adjustment for the interim analysis, we will not adjust type I error rate for multiple testing during the final analyses primary and secondary analyses.

8 Summary of Study Data

8.1 Subject Disposition

The table below includes specific fields that will be summarized regarding subject disposition at relevant study time points. Study data will be collected and managed using REDCap electronic data capture tools hosted at Northwestern University⁴. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. Relevant fields from the study database are listed below, followed by the planned CONSORT⁵ schematic of participant flow through the study.

Item	Form	Variable	Values
Passed pre-screen	Phone recruitment	Eligible	0, No; 1, Yes
Reason for failing pre-screen	Phone recruitment	exclusion	1, Less than 65 years old 2, Non-English speaker 3, Not interested 4, Participated in pilot or focus group 5, Not comfortable using computer 6, Not comfortable using the Internet 7, Did not score at least 4 on the Brief Cognitive Screen
Consented	Informed consent	consentedyn	0, No; 1, Yes
Group assignment	Informed consent	study_group	0, Attention Control 1, PLAN YOUR LIFESPAN
Missed visit reason	Missed visit	missed_q1	1, Unable to be reached by phone within study window (e.g., disconnected phone, number changed) 2, Cognitively impaired at time of phone call 3, Hospitalized or at rehabilitation facility 4, Technical problems (e.g., did not have hearing aid in place) 5, Other
Study termination / completion visit	Termination	term_q2	1, Baseline 2, Immediately post-tool 3, Month 1 4, Month 3
Study termination / completion reason	Termination	term_q3	1, Completed Study 2, Lost to follow-up 3, Withdrew consent 4, Death 5, Misrandomization



8.2 Protocol Deviations

We will not be monitoring protocol deviations during the course of this study.

8.3 Demographic and Baseline Variables

See data dictionary file that may be exported from REDCap. Demographics and baseline variables in general will be summarized via descriptive statistics (mean±standard deviation for continuous data and count along with percentages for categorical data) overall and by arm.

8.4 Intervention Usage

Subjects will use the website for their assigned treatment arm for a brief period during the baseline visit. Subsequent interaction time with that website will be measured via self-report (Use of Website form) during the one- and three-month follow-up phone interviews. These data will also be summarized via descriptive statistics overall and by arm.

9 Analyses

The main hypotheses to be addressed in analyses are as follows:

H₁: Compared to participants in the attention control group and controlling for baseline assessments, participants receiving the PLAN YOUR LIFESPAN tool will show increased planning with regard to implementation/behavior, perception, and intention (measured via the Planning Assessment tool) one (efficacy) and three (effect retention) months after intervention.

H₂: Compared to participants in the attention control group and controlling for baseline assessments, participants receiving the PLAN YOUR LIFESPAN tool will show increased confidence in accessing home services (measured via the Confidence in Accessing Home Services tool) one (efficacy) and three (effect retention) months after intervention.

H₃: Compared to participants in the attention control group and controlling for baseline assessments, participants receiving the PLAN YOUR LIFESPAN tool will show increased understanding of home services (measured via the Understanding of Home Services tool) one (efficacy) and three (effect retention) months after intervention.

H₄: Compared to participants in the attention control group and controlling for baseline assessments, participants receiving the PLAN YOUR LIFESPAN tool will be more likely to report communicating their preferences about issues related to lifespan planning to people who may need to make decisions for them (measured via the Communication about Lifespan Planning Questionnaire) one (efficacy) and three (effect retention) months after study intervention.

H₅: Compared to participants in the attention control group, participants randomized to the intervention arm will report overall satisfaction with the intervention/attention control (measured via the Satisfaction with Intervention tool).

Tests will be performed at a two-sided 5% significance level. Assumptions associated with linear regression models will be examined via residual diagnostics. In cases of violations of

relevant assumptions, we will consider transformations of variables with appropriate accompanying analyses (e.g., if dichotomization is required, we will perform logistic regression analyses) and/or nonparametric methods. Primary analyses will not adjust for potential confounders, but additional analyses may employ backward stepwise selection in which covariates of interest (e.g., baseline demographics) will only be included in an initial model if they are found to have a significant one-on-one association with the outcome variable.

9.1 Descriptive summary statistics

In general, data will be summarized by treatment group. Non-missing sample size (n), mean, standard deviation, median, minimum and maximum will be used to summarize continuous variables, while non-missing sample size (n) and percent will be used for categorical variables. Confidence intervals will be presented where appropriate.

9.2 Primary Analysis

The primary endpoint for this study is planning behavior score (ranging from 5-25 points) at one month post-intervention/attention control. This score will be calculated as the sum of the five behavior questions (each scored from 1-5 points) on the “Planning Implementation (Behavior)” assessment. Primary endpoint analyses will consist of an analysis of covariance (ANCOVA) comparing mean planning behavior score at one month post-intervention/attention control while controlling for baseline planning behavior score. The significance level on the final primary analysis will be adjusted appropriately to account for type I error spent at the interim analysis. We will assume the following underlying theoretical relationship between outcome (Y) at one month and intervention arm (0=control, 1=arm), controlling for baseline outcome value (Y₀). We will test for efficacy using model Wald output at the appropriate type I error rate.

$$E(Y) = \beta_0 + \beta_1(\text{arm}) + \beta_2(Y_0)$$

9.3 Secondary Analyses

Secondary analyses will compare baseline variables (current utilization of services, physical function assessment, co-morbidities, social support, health literacy, self-efficacy, and sociodemographics) with outcome (one-at-a-time). Those found to have a significant association with outcome will be included in a linear mixed model for primary outcome, with random effects for intercept and slope (time). A backward stepwise model building process will be used to determine an overall parsimonious model for planning behavior score.

The following general model will be used to analyse secondary endpoints of interest:

$$Y_{ij} = \beta_0 + \beta_1(\text{arm}_i) + \beta_2(Y_{0i}) + \beta_3(\text{variable}_{1i}) + \dots < \text{add'l fixed effect} > \dots + b_i + \epsilon_{ij}$$

Here $i=1, \dots, N$ and indicates the participant, and $j=1, 2$ and indicates follow-up time points at one and three months, respectively. Thus, Y_{0i} signifies participant i 's baseline outcome value; and we assume $b_i \sim N(0, \sigma_b^2)$, signifying the random participant effect; and we further assume that $\epsilon_{ij} \sim N(0, \sigma^2)$, signifying random error.

Additional outcomes are listed below:

1. Planning Implementation behavior score at three-month follow-up time point (to measure effect retention).
2. Change in individual planning intention item scores at all follow-up time points compared to baseline as measured by the “Planning Intention” assessment.
3. Planning perception score at all follow-up time points as measured by the “Planning Perception” assessment.
4. Confidence score at all follow-up time points as measured by the “Confidence in Accessing Home Services” assessment.
5. Knowledge of home services score at all follow-up time points as measured by “Understanding of Home Services” assessment.
6. Overall satisfaction with the intervention or attention control as measured by the “Satisfaction with Intervention Tool.”

Individual items on the “Planning Intention” assessment tool will only be asked of participants who express lack of behavioral planning (i.e., a score of 1-3 or “Prefer not to answer” on the corresponding item on the “Planning Behavior” assessment tool). Thus, a subset of the study data will be analyzed with respect to these items. Changes in scores between baseline and all follow-up time points for individual items on “Planning Intention” assessment will be analyzed via a series of Wilcoxon Rank-Sum tests.

We will use a two-sample test for binomial proportions to compare the percentage of participants showing an increase in communication with family/Power of Attorney (POA) and health providers (as measured by “Communication about Lifespan Planning Questionnaire” assessment) across arms at the one- and three-month follow-up time points.

9.4 Pilot and Exploratory Analyses

Pilot data will be collected separately for all time points from 15 individuals not participating in the main trial. Prior to the interim analysis, we will look at changes in the descriptive statistics across the time points in the pilot data set to get a sense of the variability of the primary and secondary outcome variables.

At the time of the development of this version of the SAP, no exploratory analyses of the main trial data set are planned. Any additional, unplanned analyses will be labelled as exploratory for reporting purposes.

10 Reporting Conventions

P-values ≥ 0.001 will be reported to three decimal places; p-values less than 0.001 will be reported as “<0.001”. Calculated statistics other than quantiles will be reported to one decimal place greater than the original data. Quantiles, such as median, or minimum and maximum will use the same number of decimal places as the original data. Estimated parameters will be reported to three significant figures.

11 Technical Details

All analyses will be performed using SAS software, Version 9.4 of the SAS System for Windows. [Copyright © 2014, SAS Institute Inc., Cary, NC, USA.] Plots, figures, and analysis verification may be done in the most recent version of R.

A review statistician will examine the code and output for accuracy. Any discrepancies will be documented, the primary statistician will make corrections, and the review statistician will sign off on all finalized code and results.

12 Listing of Tables, Listings and Figures

Tables and figure shells are omitted in this version of the SAP as the final figures and summarizations will depend upon the nature of the data. We plan to follow CONSORT guidelines⁵ in reporting trial results, and tables and figures for dissemination will depend on conventions of relevant journals and/or scientific meeting constraints.

13 References

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