Statistical Power Considerations in Building Better Caregiver Study

Study: R01 AG057855-01
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> This document is a response to the DSMB recommendation: "*The study team should provide a written explanation and revision to account for the changes in power calculations, particularly regarding drop-out rates.*"

Summary from study team. The statistical power consideration was revised based upon updated information on the challenges in the recruitment and retention provided by the study team. The study team, which includes the study biostatistician, has selected the randomization approach "*Varying (flexible) randomization ratio (1:1, 2:1, 3:1)*" described below based on changes in expected retention and power calculations also described below.

The original statistical power consideration was based on 1:1 randomization to treatment and control. Assuming 70% retention rate, 448 caregivers at the end of the study will allow us to detect an effect size of 0.265 in the primary outcome PHQ-8 depression symptoms score with a power of 0.80 at a significance level of 0.05 (two-sided). The effect size of 0.265 corresponds to about 1.5 difference in PHQ-8 score (range 0-24) between groups assuming a common standard deviation of 5.6 (Lorig K, Thompson-Gallagher D, Traylor L, et al. Building Better Caregivers: a pilot online support workshop for family caregivers of cognitively impaired adults. *Journal of Applied Gerontology.* 2012;31:423-437.)

The recruitment and retention challenge came to light based on new information from the accumulated experience with the VA BBC workshop, which has enrolled over 5,000 Veteran caregivers. Unpublished data made available to the study team demonstrates that if caregivers' respective assigned workshops do not start within 2 weeks, they quickly lose interest and do *not* attend the workshops. This new data prompted the current study team to reconsider the recruitment, randomization, and retention plan. The study team recognized that if study enrollment could not accrue fast enough to fill both a workshop group and attention control group within a 2-week period (i.e., total of 54 participants per 2-week period) at 1:1 randomization, then retention would drop precipitously similar to what has been documented for some VA caregivers. The new data suggest that the original 1:1 randomization plan may lead to a retention rate of 50%, and 320 caregivers at the end of study will provide a power of 0.66 to detect the same effect size of 0.265.

The revised statistical power consideration was based on randomization with ratios of 1:1, 2:1 or 3:1 to treatment and control, depending on the actual recruitment process of participants within each 2-week period of recruitment. The 2:1 and 3:1 randomizations are expected to help with the recruitment and retention.

Fixed randomization ratio (2:1, 3:1)

Assuming that a fixed ratio of 2:1 will be used in randomization and the retention rate will increase from 50% to 75%, then the sample size of 480 caregivers (320 in treatment and 160 in control) at the end of the study will provide us a power of 0.78 to detect the same effect size of 0.265.

Assuming that a fixed ratio of 3:1 will be used in randomization and the retention rate will increase from 50% to 75%, then the sample size of 480 caregivers (360 in treatment and 120 in control) at the end of the study will provide us a power of 0.71 to detect the same effect size of 0.265.

Varying (flexible) randomization ratio (1:1, 2:1, 3:1)

If enough caregivers are enrolled in a 2-week period (e.g., 54) to use a 1:1 randomization, that will be used; if there are somewhat fewer (e.g., 41), 2:1 randomization will be used; if fewer (e.g., 36), 3:1 randomization will be used. Use of this flexible approach has achieved high retention rates in the prior trials (e.g., Lorig KR, Sobel DS, Stewart AL, et al. Evidence suggesting that a chronic disease self-management program can improve health status while reducing hospitalization: a randomized trial. *Medical care* 1999;37:5-14). Assuming that the

randomization with varied ratios will increase the retention rate from 50% to 75% and the randomization ratio will be controlled for as a categorical variable in the analysis model, 480 caregivers at the end of the study will allow us to detect a partial correlation of 0.13 between the treatment and outcome with a power of 0.82 at a significance level of 0.05 (two-sided).

Randomization plan	Total sample size	Retention rate	# participants at the end of the study	Power	Effect size
Original 1:1	640	70%	448	0.80	0.265 (a treatment group difference of 1.5 in PHQ-8 score)
Original 1:1 but with revised downward estimate of retention based on new information from VA	640	50%	320	0.63	0.265
Fixed 2:1	640	75%	480	0.78	0.265
Fixed 3:1	640	75%	480	0.71	0.265
Varying 1:1, 2:1, 3:1	640	75%	480	0.82	A partial correlation of 0.13 between treatment and PHQ-8 score.