# Reanalysis of the Care Management by Oncology Nurses to Address Supportive Care Needs cluster-randomized trials

## Contents

We applied our developed method (Wang et al. 2024) to estimate the survivor average causal effect (SACE) as an evaluation of the intervention effect in the clustered randomized clinical trial of the CONNECT (Care Management by Oncology Nurses to Address Supportive Care Needs) study (Schenker et al. 2021). The trial was conducted from July 25, 2016, to October 6, 2020 at 17 community general medical oncology practices within the University of Pittsburgh Medical Center Hillman Cancer Center Network in western Pennsylvania. Participants of the study were adult patients (aged $\geq$ 21 years) with metastatic solid tumors for whom the oncologist would agree with the statement "would not be surprised if the patient died in the next year." CONNECT used an oncology nurse led care management approach to improve the provision of primary palliative care within outpatient oncology practices. The clinical team's infusion room nurses were trained to address deficient care processes within their oncology practices. The intervention was designed to occur monthly over a 3-month period, with CONNECT visits taking place before and/or after regularly scheduled oncology clinic visits. Enrolled patients who were randomized to CONNECT met with the same nurse for all visits, and nurses had the option of conducting these visits by telephone. Enrolled patients who were randomized to standard care received oncology care according to best practices, including all supportive measures deemed appropriate by the oncology team.

Participants completed questionnaires at baseline and 3 months, either through a telephone interview or on paper. Demographic data were collected from baseline questionnaires. The primary outcome was quality of life. At baseline and 3 months, participants completed assessments of quality of life, FACIT (Functional Assessment of Chronic Illness Therapy-Palliative care) score. The score ranges from 0 to 184, with higher scores indicating better quality of life. Secondary outcomes include the Edmonton Symptom Assessment Scale (ESAS) score which ranges from 0 to 90, with higher scores indicating greater symptom burden. The hospital anxiety subscale score and the hospital depression subscale score were also used where each score ranges from 0 to 21 and scores $\geq$ 8 indicates substantial anxiety or depression symptoms. However, the outcome scores were not measured if participants died, withdrew from the study, or were lost to follow-up.

The data set in our analysis has 672 patients, 336 (50%) are in the intervention arm. During the study period, 80 (23.81%) patients died in the intervention arm and 60 (17.86%) patients died in the standard care arm. Table 1 shows the truncation frequency and the percentage for each of the outcome scores in each arm due to the reasons above. Similar truncation percentages are observed for all the outcomes.

Table 1: Truncation frequency and percentage for each outcome score by the arm.

| | CONNECT arm | Standard care arm |
|---|---|---|
| FACIT | 89, 26.49 | 120, 35.71 |
| ESAS | 90, 26.79 | 123, 36.61 |
| Depression | 90, 26.79 | 122, 36.31 |
| Anxiety | 90, 26.79 | 122, 36.31 |

Figure 1 further shows the truncation proportion of the primary outcome FACIT score by cluster size for

each arm. The plot suggests that the proportion is independent of the arm and also the cluster size. Similar patterns are observed for the other outcome scores and are thus not shown.

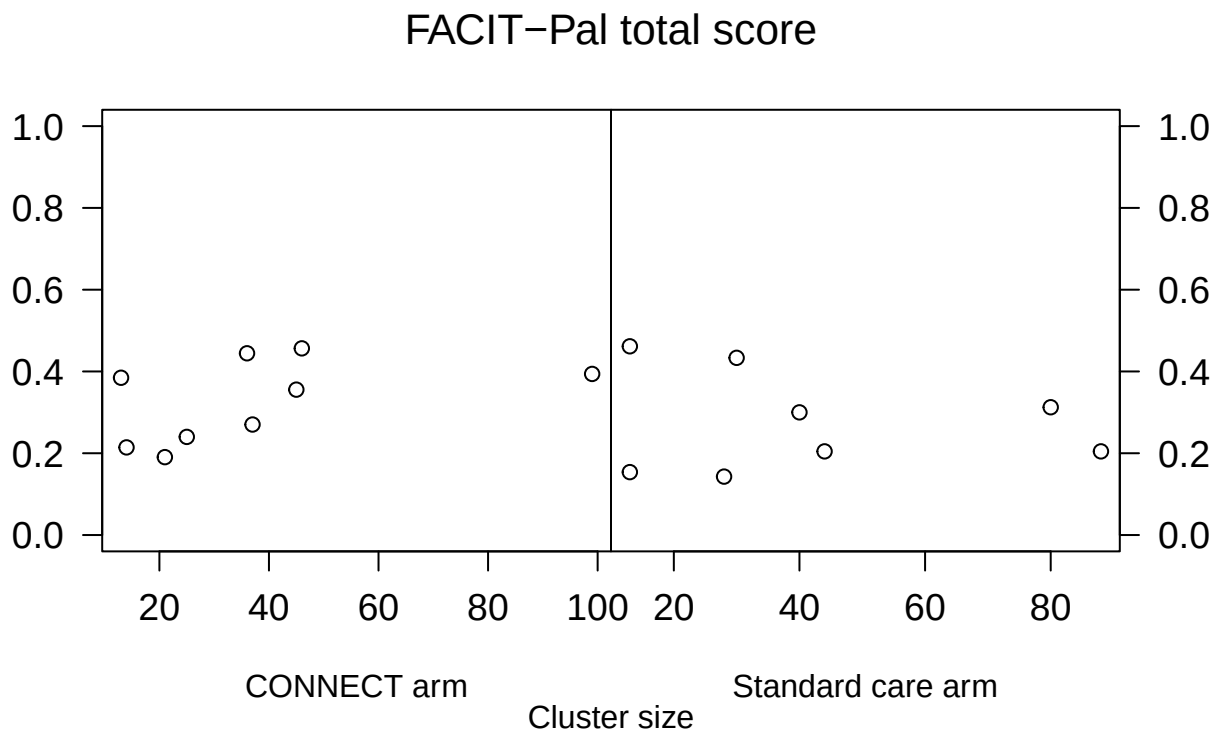


Figure 1: The proportion of truncation for the outcome FACIT score in each cluster vs. the cluster size by arm

We apply the proposed approaches in (Wang et al. 2024) to analyze each score at 3 months adjusting for the corresponding baseline score, age, chemotherapy treatment, and the Eastern Cooperative Oncology Group Performance Status score (0, 1 or 2). For ease of reference, we abbreviate the fixed-effects only approach there as the FE approach, the approach with clustering in the outcome model only as the ME approach, and the approach with clustering in the outcome model and the membership model as the ME2 approach. R functions to implement the methods (FE, ME and ME2) are available online at https://github.com/harhay-lab/SACE/_PS/_LMM.

Table 2: The estimated outcome ICC from the ME and ME2 approaches, and the estimated ICC of the strata membership by the ME2 approach.

| | Outcome model (ME) | Outcome model (ME2) | Membership model (ME2) |
|---|---|---|---|
| FACIT | 0.02 | 0.02 | 0.03 |
| ESAS | 0.02 | 0.02 | 0.04 |
| Depression | 0.01 | 0.02 | 0.03 |
| Anxiety | 0.01 | 0.01 | 0.03 |

The estimated outcome model intracluster correlation coefficients (ICC's) are in Table 2 from the ME and

ME2 approaches, and the estimated ICC of the strata membership by the ME2 approach. The outcome model ICC's are similar by the two approaches.

Table 3 shows the SACE estimates together with their 95% confidence intervals based on 10 bootstrap replicates. We obtain the confidence interval of the estimate using the bootstrap method of sampling the clusters with replacement. We randomly sample the treated clusters and the control clusters separately. For each bootstrap sample, we fit the model and obtain the SACE estimate. The 95% confidence intervals are obtained from the 2.5% and the 97.5% quantiles of the bootstrap estimates.

Table 3: The estimated SACE by the FE, ME and ME2 approaches.

| | FE | ME | ME2 |
|---|---|---|---|
| FACIT | -4.08 (-8.4, -3.38) | -4.13 (-8.46, -0.19) | -4.03 (-8.19, -0.49) |
| ESAS | -1.41 (-4.82, 1.89) | -1.34 (-4.11, 0.39) | -1.43 (-3.9, 2.02) |
| Depression | 0.09 (-0.03, 0.78) | 0.08 (-0.41, 0.97) | 0.08 (-0.75, 0.94) |
| Anxiety | 0.27 (-0.19, 0.65) | 0.27 (-0.5, 0.71) | 0.28 (-0.6, 1.18) |

Schenker, Yael, Andrew D. Althouse, Margaret Rosenzweig, Douglas B. White, Edward Chu, Kenneth J. Smith, Judith M. Resick, et al. 2021. "Effect of an Oncology Nurse–Led Primary Palliative Care Intervention on Patients with Advanced Cancer: The CONNECT Cluster Randomized Clinical Trial." *JAMA Internal Medicine* 181 (11): 1451–60.

Wang, W., G. Tong, S. P. Hirani, S. P. Newman, S. D. Halpern, D. S. Small, F. Li, and M. O. Harhay. 2024. "A Mixed Model Approach to Estimate the Survivor Average Causal Effect in Cluster-Randomized Trials." *Statistics in Medicine* 43 (1): 16–33.