

A Randomized Controlled Trial of a Symptom Management Intervention for Post Treatment Cancer Survivors and Their Informal Caregivers Living in Rural or Urban Areas

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Abstract

Purpose. Survivors and informal caregivers often experience distressing symptoms after the end of cancer treatment. This study tested an adaptive symptom management intervention against attention control on symptom severity and health services use during 24 weeks after baseline assessment. The exploratory aim was to evaluate whether intervention effects differed according to rural or urban residence and sociodemographic factors.

Methods. In this parallel-arm randomized controlled trial, survivor-caregiver dyads (N = 229) were randomized 1:1 to an adaptive symptom management intervention or attention control. The adaptive intervention included 16 weekly telephone calls from a paraprofessional with suggestions to use a printed Symptom Management and Survivorship Handbook with symptom management strategies. If the survivor's psychological distress remained elevated during the first 8 weeks, an 8-week telephone interpersonal counseling (TIPC) intervention was added for the dyad. Symptom outcomes included severity index of 16 symptoms other than depression or anxiety during weeks 1–17 and 24, and depressive and anxiety symptoms at weeks 17 and 24. Scheduled and unscheduled health service use was self-reported by survivors and caregivers at weeks 17 and 24. Linear mixed effects models were used to assess differences between trial arms over time on symptoms and health services uses.

Results. Median time since survivor's cancer diagnosis was 20 months, with 9 months since treatment completed. Survivors and caregivers were over 60 years old on average; 67% of caregivers were spouses or partners. Out of 114 dyads randomized to the adaptive intervention, 28 (24.5%) needed the addition of TIPC. The symptom distress index was reduced in the intervention arm compared to attention control for survivors (mean difference – 6.42, 95% CI [-9.12, -3.72], $p < .01$) and caregivers (mean difference – 5.41, 95% CI [-8.09, -2.73], $p < .01$). Anxiety scores were reduced significantly for both survivors and caregivers, whereas depression reductions were statistically significant for caregivers but not survivors. There were no differences between trial arms on scheduled or unscheduled health services use. Exploratory moderator analyses indicated greater intervention effects on the symptoms for survivors living in rural as compared to urban areas and survivors of Hispanic ethnicity compared to non-Hispanic White (NHW) participants. Hispanic caregivers also benefited more than NHW caregivers in reduction of symptoms and depression.

Conclusions. The adaptive intervention can relieve symptoms for all survivors and caregivers, with larger improvements for rural residents and people of Hispanic ethnicity.

Background

After treatment ends, cancer survivors require management of persistent physical and psychological symptoms that, in some cases, intensify.[1] The post-treatment period presents new challenges for many survivors because many symptoms linger as survivors transition from oncology to primary care.[2] Caregivers also experience psychological distress and caregiving burden after the survivor's treatment.[3] The role of informal caregivers remains important during this post-treatment period, and symptom management interventions are needed for both survivors and caregivers. Unfortunately, social drivers of health (SDH) care use (e.g., distance to specialty care centers, available primary care providers, and public transportation) make access to care difficult, especially for survivors and caregivers who reside in rural areas.[4] The specific aims of this research were to (1) determine if a need-based adaptive intervention results in lower psychological distress (depression and anxiety) and severity of other symptoms (primary outcomes) and more appropriately scheduled and less unscheduled health services use (secondary outcomes) among survivors and caregivers compared to an attention control, and (2) to explore whether rural versus urban residence and associated (SDH) factors (e.g., ethnicity, socio-economic status [SES]) moderate the effects of the intervention among survivors and caregivers.

Physical and psychological symptoms present during survivors' treatment can persist for years post-treatment.[5] Clinically significant depressive symptoms were reported by 67% of survivors,[6] and one year after treatment, 45–50% of cancer survivors take psychiatric medications, which is a substantially higher rate than in the general population.[7] There is a strong association between depression and other symptoms commonly experienced in this population such as fatigue, pain, and sleep disruption.[8] Survivors with depressive or anxiety symptoms also have more patient care visits and higher rates of hospitalization.[9] Thus, depressive or anxiety symptoms are sentinel for elevated overall symptom burden.[10]

Caregivers experience psychological distress, exhaustion, financial burdens, and role changes following a cancer diagnosis.[11] Caring for the survivor often has negative consequences for caregiver health.[12] Between 30–50% of caregivers experience increased psychiatric morbidity, fatigue, and sleep impairment.[13, 14] Down-regulated well-being in caregivers can compromise their abilities to care for themselves and others, potentially worsening survivors' health outcomes.[15] Survivors whose caregivers have depressive symptoms report poorer quality of care.[16] Therefore, caregiver welfare is not only an important clinical endpoint in its own right, but is consequential to cancer survivor well-being. Psychosocial interventions directly improve caregivers' health, reduce psychological distress[17] and are potentially beneficial to both survivors and their caregivers.

Symptoms such as pain and psychological distress are prominent drivers of health services use.[18] Lower symptom severity is associated with lowered unscheduled health services use such as hospitalizations, urgent care, and emergency department (ED) visits.[19] In contrast, higher levels of depression and anxiety, for example, are associated with poorer health in survivors and caregivers and greater unscheduled health care usage.[19]

In this research, we tested the efficacy of an adaptive intervention consisting of an educational Symptom Management and Survivorship Handbook (SMSH) intervention with an available need-based step up to a psychosocial Telephone Interpersonal Counselling (TIPC) intervention for survivors or caregivers with persistent psychological distress. Both components of the intervention were delivered by telephone in English or Spanish to maximize accessibility.

The SMSH is an evidence-based printed self-management guide with symptom-specific chapters.[20] Each chapter contains information on what the symptom is, how people describe the symptom, the causes of the symptom, and a set of strategies presented for managing the symptom. The strategies include medication use, communication with healthcare providers, family members and friends, and lifestyle modifications such as diet and physical activity.[21] Trained health paraprofessionals call the participants and suggest using the SMSH chapters based on symptoms. The SMSH, and the Symptom Management Toolkit from which it was adapted, have been tested in multiple randomized clinical trials with demonstrated efficacy. [22, 23]

The 8-week TIPC intervention delivered by social workers using interpersonal communication techniques[24], targets psychological distress and its connection to social support and interpersonal communication with social network members. Like the SMSH, TIPC has also been shown to be efficacious for management of psychological distress in cancer survivors and their caregivers through multiple randomized controlled trials against attention control, telephone health education, and exercise.[25, 26]

Recent evidence supports the combination of SMSH + TIPC[23, 27] to build an adaptive intervention whereby all participants received the low intensity SMSH component first, with the availability of the higher intensity TIPC component for those with persistent distress. Our past research on SMSH and TIPC has addressed the questions of whether (1) it is necessary to start TIPC initially or add it only if there is no response to SMSH, and (2) the addition of TIPC to SMSH for non-responders results in improved outcomes compared to continued SMSH alone. Based on those findings we formulated the optimal decision rule of starting with SMSH alone and adding TIPC only if there is a demonstrated need. This study was a confirmatory trial of the adaptive intervention that was developed in previous phases of multiphase optimization strategy.[28]

Social drivers of health (SDH) are community level factors that influence health outcomes, in part, by facilitating or limiting access to health care services. We investigated rural versus urban residence, ethnicity, level of education, employment, and income as potential moderators of intervention effects. These factors could potentially moderate the effect of the adaptive intervention by providing services that may otherwise be lacking due to SDHs that may reduce symptom management and health service access.

Rural residents have less access to health care than urban residents due to cultural, financial, and transportation barriers, scarcity of services, lack of trained health care professionals, and poor internet access, and consequently have high risk for symptom burden.[29] Rural caregivers also report extensive challenges associated with geographic isolation, financial and emotional strain, inadequate access to transportation, and limited healthcare access.[30] Some of these obstacles are amenable to our intervention as telephone delivery of health information to rural residents has been associated with decreased feelings of social isolation and psychological distress.[31]

Hispanic survivors experience higher symptom occurrence[32], depression related treatment delays[33], and a higher cumulative symptom count during long-term survivorship[34] compared to their non-Hispanic White (NHW) counterparts. Hispanic cancer caregivers report higher caregiver burden[35] and often cite lack of language-appropriate services as an unmet need during

survivorship.[36] Other SDHs explored in this investigation include education, employment, and the relationship between survivor and partner (i.e., spouse/partner vs. other), as less formal education, lack of employment, and being a spousal caregiver have been linked to higher symptoms in survivors and caregivers.[37–39]

Methods

The trial was registered on ClinicalTrials.gov (NCT05360498, 4/27/22) and approved by the University of Arizona Institutional Review Board (STUDY00000923). After both members of the survivor-caregiver dyad completed the baseline telephone interview, dyads were randomized 1:1 to either the adaptive intervention or attention control. A computerized minimization procedure was run by the project coordinator to ensure allocation concealment. Balancing factors in minimization were the survivor's site of cancer, receipt of chemotherapy, rural or urban residence, and survivor-caregiver relationship (spouse/partner or other).

Participants

Inclusion criteria for the survivors were: 1) age 18 or older; 2) scheduled to complete curative intent cancer treatment within the next 4 weeks, or have completed it within 5 years; 3) able to perform basic activities of daily living; 4) cognitively oriented to time, place, and person (recruiter determined); 5) able to speak and understand English or Spanish; 6) access to a telephone and 7) has an informal caregiver who can be any relationship type (e.g., spouse, sibling, parent, friend) who was willing to participate with them. Exclusion criteria for survivors were: 1) diagnosis of psychotic disorder in the health record; 2) nursing home resident; 3) bedridden; and 4) currently receiving counseling and/or psychotherapy. Inclusion criteria for the caregivers were: 1) age 18 or older; 2) able to speak and understand English or Spanish; 3) telephone access; 4) not currently receiving counseling and/or psychotherapy; and 5) not currently treated for cancer.

In total, 230 dyads were included in the study. Of these, 179 (78%) were recruited at the oncology settings where survivors had their cancer surveillance visits; 159 of the 179 dyads were from Tucson, Arizona and the surrounding areas, and 20 were from other areas in Arizona. The other 51 dyads were identified through an online business that recruits research participants.

Procedure

Recruiters at oncology settings who held research roles explained the study either in person or by telephone. Survivors and caregivers individually signed paper or e-consent informed consent forms, in English or Spanish, based on their preference (88% English, 12% Spanish). Following consent, survivors and caregivers were contacted separately via the telephone for baseline interviews, and each interview lasted approximately 30 minutes with participants receiving a \$30 retail gift card after interview.

In the intervention arm, participants received a printed SMSH. The SMSH was mailed to dyads, after which they were called by a trained paraprofessional, to assess symptoms from the General Symptom Distress Scale (see Measures section) on a 0–10 scale. Participants who rated a symptom at ≥ 4 were directed to the appropriate SMSH chapter and interventionists also assessed enactment of SMSH strategies suggested in the prior week. For symptoms at 7 or higher, survivors and caregivers in both arms were asked to contact their health care provider. If psychological distress (depressive or anxiety symptoms) was 4 or higher for any two consecutive weeks during weeks 2–8, for either survivor or caregiver, TIPC was added for the dyad with 8 weekly calls. TIPC is delivered by social workers over the telephone to discuss psychological distress and its connection to social support, social roles, and interpersonal communication with social network members. Weekly calls average about 30 minutes. Counselors tailor the counseling intervention for the participant's specific needs as expressed during sessions while adhering to a structured protocol based on principles of interpersonal psychotherapy.[24] If neither member of the dyad reported elevated and persistent psychological distress in the first 8 weeks, the dyad continued through week 16 with the SMSH only.

In the attention control condition, weekly calls included assessment of symptoms only with no SMSH or TIPC. In this condition, the intervener asked survivors and caregivers to review the NCI brochure *Facing Forward: Life After Cancer Treatment*,[40] which represent the standard of care in survivorship, with no further discussion.

Measures

Participant demographics that were obtained included age, gender, education, employment, health insurance, ethnicity, race, marital status, relationship between the survivor and caregiver, and living arrangement.

Rural or urban residence – was determined based on the ZIP codes listed in Federal Office of Rural Health Policy data files available from the Health Resources and Services Administration. Although “rural” is defined by the US Census Bureau[41] as population not urban (urban with population $\geq 50,000$), there are some populations $\geq 50,000$ that share similar limitations with those $< 50,000$ in terms of access to care, which is reflected in this classification. Most survivors and caregivers lived in the same ZIP code, and when they did not, the survivor’s ZIP code was used for the dyad’s classification as rural or urban.

Comorbid health conditions – were assessed with the Bayliss Disease Burden Morbidity Assessment.[42] This self-report instrument assesses whether a participant was told by a doctor or nurse that they have one of 23 conditions; the count of conditions was derived.

Symptom outcomes

Eighteen symptoms were assessed weekly using the adapted General Symptom Distress Scale (GSDS)[43]: depression, anxiety, and 16 other symptoms: fatigue, sleep difficulties, pain, headache, difficulty concentrating or remembering things, lack of appetite, nausea, vomiting, constipation, diarrhea, numbness or tingling, skin rashes or sores, swelling in arms, legs, hands or feet, weakness, shortness of breath, and cough. Respondents indicated the presence of each symptom (yes/no) and rated their distress on the scale from 1 to 10. The 0–10 ratings of 16 symptoms other than depression and anxiety were summed into an index at baseline interview, each weekly contact (weeks 1–16), weeks 17 and 24 interviews. Internal consistency reliability is not applicable to an index.

Psychological Distress

In addition to brief GSDS ratings of depression and anxiety used for determination of the need for TIPC, detailed measures of depression and anxiety were the Patient Reported Outcomes Measurement Information System (PROMIS)[44] 8-item Depression short form, and PROMIS 8-item Anxiety short form during interviews at baseline, weeks 17 and 24. The PROMIS scores were on the t-metric with a mean of 50 and a standard deviation of 10 for the general US population. Higher scores reflect greater depression or anxiety.

Health services use

Unscheduled (e.g., hospitalizations, urgent care, ED visits) and scheduled health services use (primary care, specialty care other than oncology, and oncology for survivors) – were measured at baseline, week 17, and week 24 over the telephone. Each dyad member was asked to recall unscheduled and scheduled visits and for each service.

Statistical Analysis

Survivor and caregiver baseline characteristics were summarized. Attrition was examined in terms of counts and baseline characteristics. The primary analyses followed the intent to treat approach analyzing data regardless of adherence to interventions. For the analysis of the GSDS symptom distress index, linear mixed effects (LME) models related repeated measures of the index over weeks 1–17 and 24 to baseline version of the outcome, trial arm, time (week), and factors used in randomization. Two random effects were specified: for dyad (with survivor and caregiver nested within the same dyad), and time (repeated measures nested within individual). A similar approach was followed for the analysis of two repeated measures (weeks 17 and 24) of PROMIS depression and anxiety.

The analyses of the secondary outcomes of health services use were performed separately for survivors and caregivers using logistic regression for each service use over 24 weeks since baseline using interview data, adjusting for baseline service use and factors used in randomization. If service use was reported in either the weeks 17 or 24 interview, it was defined as “yes” over 24 weeks (6 months). For survivors and caregivers who completed only one of the 17- or 24-week interviews and did not endorse

services use, sensitivity analyses were conducted for two scenarios of treating missing values as using or not using health service over 24 weeks under a Missing at Random assumption.

Exploratory moderation analyses for symptom outcomes were performed for the following potential moderators: rural versus urban residence, Hispanic ethnicity versus non-Hispanic White, employment (full or part time versus other), level of education (4-year college or graduate degree versus other), and survivor-caregiver relationship (spouse/partner versus other) by adding the trial arm by the potential moderator interaction to the mixed models.

All statistical tests were two-sided at .05 level of significance and conducted in SAS 9.4. In exploration of moderating effects, we noted p-values < .10 for the trial arm by potential moderator interaction term for survivors or caregivers, and effect sizes exceeding $d = 0.5$ for differences in intervention effects according to the levels of the potential moderator.

Sample size and power considerations

The trial was powered to detect the between-arm differences in symptom outcomes corresponding to effect size of Cohen's $d = 0.63$ with power of .80 in two-sided tests at .05 level of significance. The resulting sample size requirement was $n = 41$ dyads per arm (82 total to randomize). With a projected 23% attrition, we planned to recruit to $n = 106$ dyads total. This planned sample size was exceeded as we enrolled $N = 230$ dyads and analyzed $N = 229$. Given the achieved sample size, the effect size of Cohen's $d = 0.37$ or higher for between-arm comparisons (main intervention effect) was detectable as statistically significant. The analyses of moderating effects were exploratory and hypothesis-generating, thus formal power analysis was not applicable.

Results

Sample demographics and descriptive statistics appear in Table 1. Median time since the survivor's cancer diagnosis was 20 months and median time since completion of the survivor's cancer treatment was 9 months. At baseline, mean scores of PROMIS depression for survivors and caregivers were approximately $\frac{1}{2}$ standard deviation better (lower) than the mean of the general US population. Few participants dropped out after baseline (Fig. 1). Out of 114 dyads randomized to the adaptive intervention, 28 (24.5%) needed the addition of TIPC.

Table 1
Characteristics of survivors and caregivers

Age	Survivors, Mean (SD) or N (%)	Caregivers, Mean (SD) or N (%)
	N = 230	N = 230
	63.90 (12.97)	61.03 (14.01)
Number of comorbid conditions	5.84 (2.84)	4.21 (2.90)
Gender		
Female	135 (59%)	146 (63%)
Male	95 (41%)	84 (37%)
Race/ethnicity		
Hispanic	67 (29%)	65 (28%)
Non-Hispanic white	150 (67%)	149 (65%)
Other or missing	12 (5%)	16 (7%)
Relationship: caregiver is survivor's		
Child	26 (11%)	
Parent	10 (4%)	
Friend	18 (8%)	
Other	9 (4%)	
Sibling	14 (6%)	
Spouse	153 (67%)	
Location of residence		
Rural	84 (37%)	
Urban	146 (63%)	
Living arrangement		
Separately	67 (29%)	
Together	162 (70%)	
Missing	1 (< 1%)	
Marital status		
Divorced	22 (10%)	18 (8%)
Married/Living with a partner	177 (77%)	181 (79%)
Single/never married	16 (7%)	23 (10%)
Widowed	15 (6%)	8 (3%)
Level of education		
High school or less	70 (30%)	57 (25%)
Vocational school/some college	42 (18%)	55 (24%)
* PROMIS=Patient-Reported Outcomes Measurement Information System; SD=standard deviation		

Age	Survivors, Mean (SD) or N (%)	Caregivers, Mean (SD) or N (%)
	N = 230	N = 230
	63.90 (12.97)	61.03 (14.01)
4-year college	55 (24%)	49 (21%)
Graduate/professional degree	63 (27%)	68 (30%)
Missing	0 (0%)	1 (< 1%)
Income		
Under \$40,000	71 (31%)	55 (24%)
\$40,000-\$69,999	39 (17%)	51 (22%)
\$70,000-\$99,999	46 (20%)	47 (20%)
\$100,000 or more	64 (28%)	67 (29%)
Missing	10 (4%)	10 (4%)
Income meets needs		
Not at all	10 (4%)	6 (3%)
Barely	79 (34%)	65 (28%)
Meets needs	136 (59%)	153 (67%)
Missing	5 (2%)	6 (3%)
Employment		
Full time	46 (20%)	72 (31%)
Part time/ Unemployed but seeking employment	42 (18%)	29 (13%)
Other (retired, disabled, homemaker)	142 (62%)	128 (56%)
Missing	0 (0%)	1 (< 1%)
Survivor's site of cancer		
Breast	96 (42%)	
Colon	12 (5%)	
Lung	7 (3%)	
Prostate	13 (6%)	
Other	102 (44%)	
Survivor's cancer recurrent		
No	196 (85%)	
Yes	28 (12%)	
Missing	6 (3%)	
Symptom severity index	25.80 (21.33)	17.42 (17.71)
PROMIS Depression score	45.49 (8.49)	44.06 (7.19)
PROMIS anxiety score	47.82 (9.59)	46.89 (9.24)
* PROMIS=Patient-Reported Outcomes Measurement Information System; SD=standard deviation		

Age	Survivors, Mean (SD) or N (%)	Caregivers, Mean (SD) or N (%)
	N = 230	N = 230
	63.90 (12.97)	61.03 (14.01)
Hospitalizations in the past 6 months		
Yes	41 (18%)	9 (4%)
No	188 (82%)	220 (96%)
Missing	1 (< 1%)	1 (< 1%)
Urgent care or ED use in the past 6 months		
Yes	73 (32%)	61 (27%)
No	157 (68%)	168 (73%)
Missing	0 (0%)	1 (< 1%)
Number of primary care visits in the past 6 months		
0	61 (27%)	75 (33%)
1	82 (36%)	96 (42%)
2–4	78 (34%)	52 (23%)
5 or more	9 (4%)	5 (2%)
Missing	0 (0%)	2 (1%)
Number of specialty care (other than oncology) visits in the past 6 months		
0	72 (31%)	105 (46%)
1	53 (23%)	60 (26%)
2–4	69 (30%)	52 (23%)
5 or more	35 (15%)	12 (5%)
Missing	1 (< 1%)	1 (< 1%)
Number of oncology visits in the past 6 months		
0	14 (6%)	
1–4	158 (69%)	
5 or more	57 (25%)	
Missing	1 (< 1%)	
* PROMIS=Patient-Reported Outcomes Measurement Information System; SD=standard deviation		

The GSDS symptom distress score was reduced in the intervention arm compared to attention control for survivors (mean difference – 6.42, 95% CI [-9.12, -3.72], $p < .01$) and caregivers (mean difference – 5.41, 95% CI [-8.09, -2.73], $p < .01$). PROMIS anxiety scores were reduced significantly for both survivors and caregivers, whereas PROMIS depression reductions were statistically significant for caregivers but not survivors (Table 2). There were no differences between trial arms on scheduled or unscheduled health services use (Table 3). This finding did not change appreciably in two sensitivity analyses treating missing data on health services use as a “yes” or a “no”.

Table 2

Differences between trial arms on symptom outcomes over time (main intervention effect) for survivors and caregivers

Outcome	Survivors				Caregivers			
	Intervention arm, LS Mean (SE)	Attention control arm, LS Mean (SE)	Trial arm difference (SE), (95% CI)	P	Intervention arm, LS Mean (SE)	Attention control arm, LS Mean (SE)	Trial arm difference (95% CI)	P
Symptom distress index (GSDS, weeks 1–17 and 24)	15.06 (0.99)	21.48 (1.02)	-6.42 (1.38), (-9.12, -3.72)	< .01	11.82 (1.00)	17.23 (0.99)	-5.41 (1.37), (-8.09, -2.73)	< .01
PROMIS depression (weeks 17 and 24)	43.75 (0.49)	44.79 (0.49)	-1.04 (0.68), (-2.38, 0.30)	.13	41.94 (0.50)	44.21 (0.50)	-2.26 (0.68), (-3.61, -0.92)	< .01
PROMIS anxiety (weeks 17 and 24)	45.91 (0.62)	48.05 (0.62)	-2.14 (0.86), (-3.83, -0.45)	.01	44.23 (0.63)	46.99 (0.62)	-2.75 (0.86), (-4.44, -1.06)	< .01
*GSDS=General Symptom Distress Scale; PROMIS= Patient-Reported Outcomes Measurement Information System; LS=Least square; SE=standard error; CI=confidence interval. Models adjusted for adjusted for baseline version of the outcome, survivor-caregiver relationship (spouse/partner or not), residence (rural or urban), and type of survivor's last systemic cancer treatment (chemotherapy/targeted therapy or hormonal therapy only)								

Table 3
Comparison of trial arms on health services uses during 24 weeks after baseline for survivors and caregivers

Outcome	Survivors				Caregivers			
	Intervention arm, N (%)	Attention control arm, N (%)	Adjusted OR for trial arm comparison, (95% CI)	P	Intervention arm, N (%)	Attention control arm, N (%)	Adjusted OR for trial arm comparison, (95% CI)	P
Hospitalizations			1.27 (0.58, 2.83)	0.55			Not tested due to low counts	
Yes	16 (14%)	14 (12.2%)			6 (5.7%)	4 (3.6%)		
No	92 (80.7%)	96 (83.5%)			97 (92.4%)	104 (93.7%)		
ED or urgent care visits			1.17 (0.65, 2.14)	0.60			1.32 (0.66, 2.66)	0.43
Yes	34 (29.8%)	32 (27.8%)			25 (23.8%)	22 (19.8%)		
No	73 (64%)	79 (68.7%)			78 (74.3%)	86 (77.5%)		
Primary care visits			0.62 (0.33, 1.17)	0.15			0.75 (0.41, 1.36)	0.34
Yes	77 (67.5%)	88 (76.5%)			67 (63.8%)	75 (67.6%)		
No	31 (27.2%)	22 (19.1%)			37 (35.2%)	33 (29.7%)		
Specialty care visits other than oncology			0.83 (0.40, 1.73)	0.62			1.20 (0.62, 2.34)	0.59
Yes	84 (73.7%)	92 (80%)			68 (64.8%)	69 (62.2%)		
No	23 (20.2%)	19 (16.5%)			35 (33.3%)	39 (35.1%)		
Oncology visits			0.50 (0.19, 1.25)	0.15	N/A	N/A	N/A	N/A
Yes	94 (82.5%)	102 (88.7%)						
No	14 (12.3%)	8 (7%)						
*OR=odds ratio; CI=confidence interval; models adjusted for baseline version of the outcome, survivor-caregiver relationship (spouse/partner or not), residence (rural or urban), and type of survivor's last systemic cancer treatment (chemotherapy/targeted therapy or hormonal therapy only)								

Exploratory moderator analyses indicated greater intervention effects on the GSDS symptoms for survivors living in rural areas and survivors of Hispanic ethnicity (Table 4). Hispanic caregivers also benefited more from the adaptive intervention than NHW on the GSDS symptoms; Hispanic survivors also had greater reductions in PROMIS depression compared to NHW survivors. There was no evidence of moderating effects by survivor-caregiver relationship, level of education, income, or employment.

Table 4

Moderating effects of residence type and Hispanic ethnicity for symptom outcomes of survivors and caregivers. P-values<.10 and effect sizes Cohen's d > 0.5 are bolded

Outcome	Rural residents				Urban residents				
	P-value and effect size for the moderating effect	Intervention arm, LS Mean (SE)	Attention control arm, LS Mean (SE)	Trial arm difference (SE), (95% CI)	P	Intervention arm, LS Mean (SE)	Attention control arm, LS Mean (SE)	Trial arm difference (95% CI)	P
Survivors' GSDS symptom severity index (weeks 1–17 and week 24)	P = 0.04, d = 0.72	14.33 (1.60)	24.45 (1.61)	-10.12 (2.25), (-14.54, -5.71)	< .01	15.10 (1.22)	19.33 (1.25)	-4.23 (1.72), (-7.61, -0.85)	.01
Caregivers' GSDS symptom severity index (weeks 1–17 and week 24)	P=.37 d = 0.31	11.51 (1.62)	18.53 (1.61)	-7.02 (2.27), (-11.47, 2.56)	< .01	11.62 (1.24)	16.09 (1.23)	-4.47 (1.72), (-7.84, -1.11)	< .01
Survivors' PROMIS depression (weeks 17 and 24)	P=.55, d = 0.22	43.56 (0.81)	45.13 (0.78)	-1.57 (1.12), (-3.77, 0.63)	.15	43.84 (0.61)	44.57 (0.61)	-0.73 (0.86), (-2.41, 0.95)	.40
Caregivers' PROMIS depression (weeks 17 and 24)	P=.99, d = 0.00	41.89 (0.81)	44.15 (0.80)	-2.26 (1.14), (-4.50, -0.03)	.047	41.97 (0.62)	44.23 (0.62)	-2.26 (0.86), (-3.96, -0.56)	< .01
Survivors' PROMIS anxiety (weeks 17 and 24)	P=.28, d = 0.40	45.53 (0.99)	48.86 (0.98)	-3.32 (1.40), (-6.07, -0.58)	.02	46.09 (0.77)	47.51 (0.78)	1.42 (1.08), (-3.56, 0.72)	.19
Caregivers' PROMIS anxiety (weeks 17 and 24)	P=.85, d = 0.07	44.18 (1.03)	46.71 (1.00)	-2.54 (1.43), (-5.35, 0.27)	.08	44.22 (0.78)	47.11 (0.77)	-2.89 (1.08), (	.16
Hispanic participants					Non-Hispanic White participants				
	P-value and effect size for the moderating effect	Intervention arm, LS Mean (SE)	Attention control arm, LS Mean (SE)	Trial arm difference (SE), (95% CI)	P	Intervention arm, LS Mean (SE)	Attention control arm, LS Mean (SE)	Trial arm difference (95% CI)	P
Survivors' GSDS symptom severity index (weeks 1–	P=.099, d = 0.61	12.61 (1.87)	23.08 (1.76)	-10.47 (2.58), (-15.54, -5.40)	< .01	15.43 (1.19)	20.85 (1.29)	-5.42 (1.70), (-8.76, -2.08)	< .01
*GSDS=General Symptom Distress Scale; PROMIS= Patient-Reported Outcomes Measurement Information System; LS=Least square; SE=standard error; CI=confidence interval.									

Outcome	Rural residents				Urban residents				
	P-value and effect size for the moderating effect	Intervention arm, LS Mean (SE)	Attention control arm, LS Mean (SE)	Trial arm difference (SE), (95% CI)	P	Intervention arm, LS Mean (SE)	Attention control arm, LS Mean (SE)	Trial arm difference (95% CI)	P
17 and week 24)									
Caregivers' GSDS symptom severity index (weeks 1–17 and week 24)	P=.07, d = 0.70	9.35 (2.07)	18.65 (1.68)	-9.30 (2.66), (-14.52, -4.08)	< .01	12.54 (1.19)	16.10 (1.29)	-3.56 (1.70), (-6.90, -0.22)	.04
Survivors' PROMIS depression (weeks 17 and 24)	P=.095, d = 0.65	42.08 (0.93)	45.09 (0.85)	-3.01 (1.27), (-5.50, -0.51)	.02	44.55 (0.59)	45.05 (0.62)	-0.50 (0.83), (2.12, 1.13)	.55
Caregivers' PROMIS depression (weeks 17 and 24)	P=.31, d = 0.43	40.33 (1.03)	43.63 (0.83)	-3.30 (1.30), (-5.90, -0.70)	.01	42.64 (0.58)	44.35 (0.65)	1.71 (0.84), (-3.37, -0.06)	.04
Survivors' PROMIS anxiety (weeks 17 and 24)	P=.32, d = 0.40	43.93 (1.19)	47.43 (1.11)	-3.50 (1.64), (-6.72, -0.28)	.03	46.73 (0.75)	48.30 (0.79)	1.57 (1.07), (-3.65, 0.52)	.14
Caregivers' PROMIS anxiety (weeks 17 and 24)	P=.64, d = 0.19	43.96 (1.33)	47.14 (1.07)	-3.17 (1.70), (-6.51, 0.17)	.06	44.56 (0.75)	46.80 (0.81)	-2.25 (1.07), (-4.35, -0.14)	.04
*GSDS=General Symptom Distress Scale; PROMIS= Patient-Reported Outcomes Measurement Information System; LS=Least square; SE=standard error; CI=confidence interval.									

Discussion

This study was designed to test an adaptive need-based intervention for management of symptoms and reduction of unscheduled health service use among post-treatment cancer survivors and their informal caregivers. Both components of the intervention (SMISH, TIPIC) have been proven to be individually effective for symptom management in past research, and their potentially optimal sequencing was formulated.[23, 27] The present study tested this sequencing against the attention control condition. Results showed that both survivors and caregivers benefitted from the intervention over the 24-week duration of the study with reduced symptoms, compared to attention control. However, there were no differences in health service use between the two arms. There was also a more beneficial effect of the intervention on symptoms for rural participants and Hispanic participants.

Results from this investigation show that symptom management can be successfully accomplished by providing an accessible informational intervention that helps dyads to understand and address the symptoms that are bothering them. This was primarily accomplished with the printed SMISH and weekly assessments that reviewed symptoms with direction to the relevant parts of the SMISH for self-management, with available step-up to telephone interpersonal counseling. Because both components of the intervention were delivered by telephone, at times that were convenient to participants, this effectively eliminated access barriers. Health information that is organized, understandable, and easily accessible can help reduce uncertainty about symptoms with

salubrious effects on cancer survivors' adjustment.[45] Results suggest that the higher intensity counseling component may be delivered to survivors and caregivers on an as-needed basis.

Cancer survivors who reside in rural medically underserved areas are at particularly high risk for symptom burden.[29] By removing access barriers, but still involving regular contact from another person, the rural dwelling survivors appeared to experience an even greater benefit from the intervention in terms of reduced symptoms, compared to those in urban areas. Rural caregivers did not evidence the same enhanced reduction in symptoms, although their symptom burden was not as high as survivors'.

Hispanic survivors and caregivers evidenced enhanced response to the intervention in terms of reduced symptoms, and reduced depression for survivors only. Hispanic survivors generally have more symptoms than non-Hispanic White survivors.[32] Although the reasons for this are undoubtedly manifold, access to appropriate services is one obvious reason. The telephone delivered intervention, that was selected in Spanish by 12% of the participants, may have put more Hispanic participants in contact with helpful services than NHW participants who may have already had such access.

Results of this study revealed no significant effect of the intervention on health service usage. Across the intervention and control arms, certain types of health care usage were common with over 2/3 of survivors and caregivers using primary and specialty care during the 24-week investigation. These results may reflect declining health issues associated with the older age of this sample and presence of 4–5 comorbid conditions on average.

There are important scope conditions around these findings that must be considered as part of their interpretation. First, the sample was predominantly female, married, and surviving breast cancer. Second, this sample scored below the national average for depression and anxiety at baseline. This undoubtedly explains the relatively low level of need for the step-up TIPC component.

In conclusion, this study shows that an accessible informational intervention, that can be referred to repeatedly and at will, along with weekly check ins and guidance to appropriate handbook chapters, can result in reduction of symptoms in post treatment cancer survivors and their informal caregivers. These reductions were especially pronounced in the participants who resided in a rural area or were of Hispanic ethnicity.

Declarations

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Institutional Review Board of the University of Arizona, STUDY00000923.

Consent to Participate

Informed consent was obtained from all participants of the study.

Consent to Publish

The manuscript does not contain any individual personal data. All data are presented on aggregate so that no individual can be identified.

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Author Contribution

Conceptualization: A.S., T.B., C.S. Data curation: all authors. Formal Analysis: A.S., N.C. Methodology: A.S., C.S., T.B. Supervision: T.B., C.S., A.S. Writing - original draft: C.S., A.S., T.B., C.S. Writing - review & editing: all authors. All authors read and approved the final manuscript.

Data Availability

We will share the data upon request made to Terry Badger and Chris Segrin. Data from this study will be available to other researchers and key stakeholders under the following conditions: 1) appropriate human subjects protection is in place; 2) data have been de-identified; and 3) study investigators have publicly presented and published key findings.

Availability of Code

SAS code used to produce the results is available upon request made to Alla Sikorskii.

References

1. Kjaer, T.K., et al., *Prevalence of concurrent severe self-reported late symptoms and functional limitations in cancer survivors: a cross-sectional study of sociodemographic, clinical, and lifestyle associations*. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer, 2026. 34(3).
2. Lo-Fo-Wong, D.N.N., et al., *Risk factors of unmet needs among women with breast cancer in the post-treatment phase*. Psycho-oncology, 2020. 29(3): p. 539–549.
3. Xie, H., et al., *Caregiver burden, anxiety, and quality-of-life among informal caregivers of patient with head and neck cancer: a systematic review*. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer, 2026. 34(9).
4. Zhang, M., et al., *Public health determinants of screening accessibility, diagnostic and treatment timeliness, care adherence, and survival outcomes in breast cancer patients*. Frontiers in public health, 2026. 14: p. 1808014.
5. Mitchell, A.J., et al., *Depression and anxiety in long-term cancer survivors compared with spouses and healthy controls: a systematic review and meta-analysis*. Lancet Oncol, 2013. 14(8): p. 721–32.
6. Owen JE, O.C.B.E., Pagano IS, Stanton A, *Randomized Trial of a Social Networking Intervention for Cancer-Related Distress*. Ann Behav Medicine 2017.
7. Lee, M.J., et al., *Investigation of anxiety and depressive disorders and psychiatric medication use before and after cancer diagnosis*. Psychooncology, 2021. 30(6): p. 919–927.
8. Yildirim, D., et al., *The Mediating Role of Depressive Symptoms in the Association Between Pain and Self-Reported Cognitive Failures Among Gynecological Cancer Patients Undergoing Brachytherapy*. Seminars in oncology nursing, 2026. 42(4): p. 152248.
9. Vaughn, D.M., et al., *Factors Associated with Health Care Utilization at the End of Life for Patients with Acute Myeloid Leukemia*. Journal of palliative medicine, 2022. 25(5): p. 749–756.
10. Miaskowski C, B.A., Berger A, Casagrande R, Grady PA, Jacobsen P, Kutner J, Patrick D, Zimmerman L, Xiao C, Matocha M, Marden S, *Advancing Symptom Science Through Symptom Cluster Research: Expert Panel Proceedings and Recommendations*. J Natl Cancer Inst., 2017. 109(109): p. pii: djw253.
11. Rezaei, M., et al., *Caregiving consequences in cancer family caregivers: a narrative review of qualitative studies*. Front Public Health, 2024. 12: p. 1334842.
12. de Moor, J.S., et al., *Employment implications of informal cancer caregiving*. J Cancer Surviv, 2016.
13. Kotronoulas, G., Y. Wengstrom, and N. Kearney, *Sleep patterns and sleep-impairing factors of persons providing informal care for people with cancer: a critical review of the literature*. Cancer Nurs, 2013. 36(1): p. E1-15.

14. Butow, P.N., et al., *Caring for women with ovarian cancer in the last year of life: a longitudinal study of caregiver quality of life, distress and unmet needs*. Gynecol Oncol, 2014. 132(3): p. 690–7.
15. Segrin, C. and T. Badger, *Interdependence in family systems adjusting to breast and prostate cancer*, in *Going through this together: Family communication and health transitions*, M.M. Day, Editor. 2012, Hampton Press: Cresskill, NJ.
16. Litzelman K, K.E., Mollica M, Rowland JH, *How does caregiver well-being relate to perceived quality of care in patients with cancer? Exploring associations and pathways*. Journal of Clinical Oncology, 2016. 34: p. 1–8.
17. Waldron, E.A., et al., *A systematic review of psychosocial interventions to improve cancer caregiver quality of life*. Psychooncology, 2013. 22(6): p. 1200–7.
18. Van Beek, F.E., et al., *Psychological problems among cancer patients in relation to healthcare and societal costs: A systematic review*. Psycho-oncology, 2021.
19. Yan, K., et al., *Anxiety trajectories in cancer patients during active treatments: Clusters, influencing factors, and impact on quality of life and health service utilization*. Journal of affective disorders, 2026. 408: p. 121900.
20. Badger TA, S.A., Segrin C, Crane TE, Hadeed M., *Symptom Management and Survivorship Handbook*. 2nd ed, ed. H.M. Badger TA. 2020, Tucson, AZ: University of Arizona College of Nursing. 220.
21. Mishra SI, S.R., Snyder C, Geigle, P, Gotay C, *The effectiveness of exercise interventions for improving health-related quality of life from diagnosis through active cancer treatment*. Oncol Nurs Forum, 2015. 42(1): p. E33-53.
22. Sikorskii, A., et al., *An Automated Intervention Did Not Improve Adherence to Oral Oncolytic Agents While Managing Symptoms: Results From a Two-Arm Randomized Controlled Trial*. J Pain Symptom Manage, 2018. 56(5): p. 727–735.
23. Badger, T., Segrin, C., Crane, T.E., Chalasani, P., Arslan, W., Hadeed, M., Given, C.W., & Sikorskii, A., *A sequential multiple assignment randomized trial of symptom management for cancer survivors during treatment and their informal caregivers* Supportive Care in Cancer, 2024. 32(8): p. 523.
24. Weissman MM, M.J., Klerman GL, *The Guide to Interpersonal Psychotherapy: Updated and expanded edition*. 2018, New York: Oxford University Press.
25. Badger, T.A., et al., *Telephone-delivered health education and interpersonal counseling improve quality of life for Latinas with breast cancer and their supportive partners*. Psychooncology, 2013. 22(5): p. 1035–42.
26. Segrin, C., T. Badger, and A. Pasvogel, *Loneliness and emotional support predict physical and psychological distress in Latinas with breast cancer and their supportive partners*. The Open Psychology Journal, 2015. 8.
27. Sikorskii, A., et al., *A Sequential Multiple Assignment Randomized Trial of Symptom Management After Chemotherapy*. J Pain Symptom Manage, 2023. 65(6): p. 541–552 e2.
28. Collins, L.M., J.C. Strayhorn, and D.J. Vanness, *One view of the next decade of research on behavioral and biobehavioral approaches to cancer prevention and control: intervention optimization*. Translational behavioral medicine, 2021. 11(11): p. 1998–2008.
29. Schmitz, K.H., et al., *Worse Function and Symptoms Among the Most Rural Patients With Advanced Cancer: A Cross-Sectional Analysis*. Cancer medicine, 2026. 15(6): p. e72033.
30. Park, S., et al., *"The aspect of caregiving becomes incredibly complex": lived experiences of rural cancer caregiving identified through community advisory board engagement*. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer, 2026. 34(5).
31. Fennell, K.M., et al., *The consumer-driven development and acceptability testing of a website designed to connect rural cancer patients and their families, carers and health professionals with appropriate information and psychosocial support*. Eur J Cancer Care (Engl), 2017. 26(5).
32. Lee, Y., et al., *Distinct Symptom Occurrence Subgroups Among Patients With Colorectal Cancer: Differences in Social Determinants of Health and Diet Quality*. Research in nursing & health, 2026.
33. Gbogbo, D., et al., *Impact of Pre-Diagnosed Depressive Symptoms on Treatment Choice, Delay in Initiating Treatment, and Mortality Among Women Aged ≥ 65 Years with Breast Cancer*. International journal of environmental research and public health, 2026. 23(3).
34. Freyer, D.R., et al., *Symptom burden among long-term survivors of young adult cancer: a report from the Project Milestones cohort*. Journal of cancer survivorship: research and practice, 2026.

35. Badger, T.A., et al., *Social Determinants of Health and Symptom Burden During Cancer Treatment*. Nursing research, 2023. 72(2): p. 103–113.
36. Ratnapradipa, K.L., et al., *African American and Hispanic Cancer Survivors' and Caregivers' Experiences in Nebraska*. Journal of immigrant and minority health, 2024. 26(3): p. 554–568.
37. Liu, L., et al., *A marginal structural model analysis for the effect modification by education on the association between cancer diagnosis history and major depressive symptoms: Findings from Midlife Development in the U.S. (MIDUS)*. Journal of affective disorders, 2023. 341: p. 202–210.
38. Tan, C.J., et al., *Investigating how cancer-related symptoms influence work outcomes among cancer survivors: a systematic review*. Journal of cancer survivorship: research and practice, 2022. 16(5): p. 1065–1078.
39. Hasson-Ohayon, I., et al., *Women with advanced breast cancer and their spouses: diversity of support and psychological distress*. Psycho-oncology, 2010. 19(11): p. 1195–1204.
40. Institute, N.C. *Facing Forward: Life After Cancer Treatment* 2018; Available from: <https://www.cancer.gov/publications/patient-education/facing-forward>.
41. Ratcliffe, M., et al., *Defining Rural at the U.S. Census Bureau*. 2016. ACSGEO-1: p. 1–8.
42. Bayliss, E.A., J.L. Ellis, and J.F. Steiner, *Seniors' self-reported multimorbidity captured biopsychosocial factors not incorporated into two other data-based morbidity measures*. Journal of Clinical Epidemiology, 2009. 62(5): p. 550–557.
43. Badger, T.A., C. Segrin, and P. Meek, *Development and validation of an instrument for rapidly assessing symptoms: the general symptom distress scale*. J Pain Symptom Manage, 2011. 41(3): p. 535–48.
44. Cella, D., et al., *Initial item banks and first wave testing of the Patient-Reported Outcomes Measurement Information System (PROMIS) network: 2005–2008*. Journal of Clinical Epidemiology, 2010. 63: p. 1179–1194.
45. Broadbridge, E., et al., *Facilitating psychological adjustment for breast cancer patients through empathic communication and uncertainty reduction*. Patient education and counseling, 2023. 114: p. 107791.

Figures

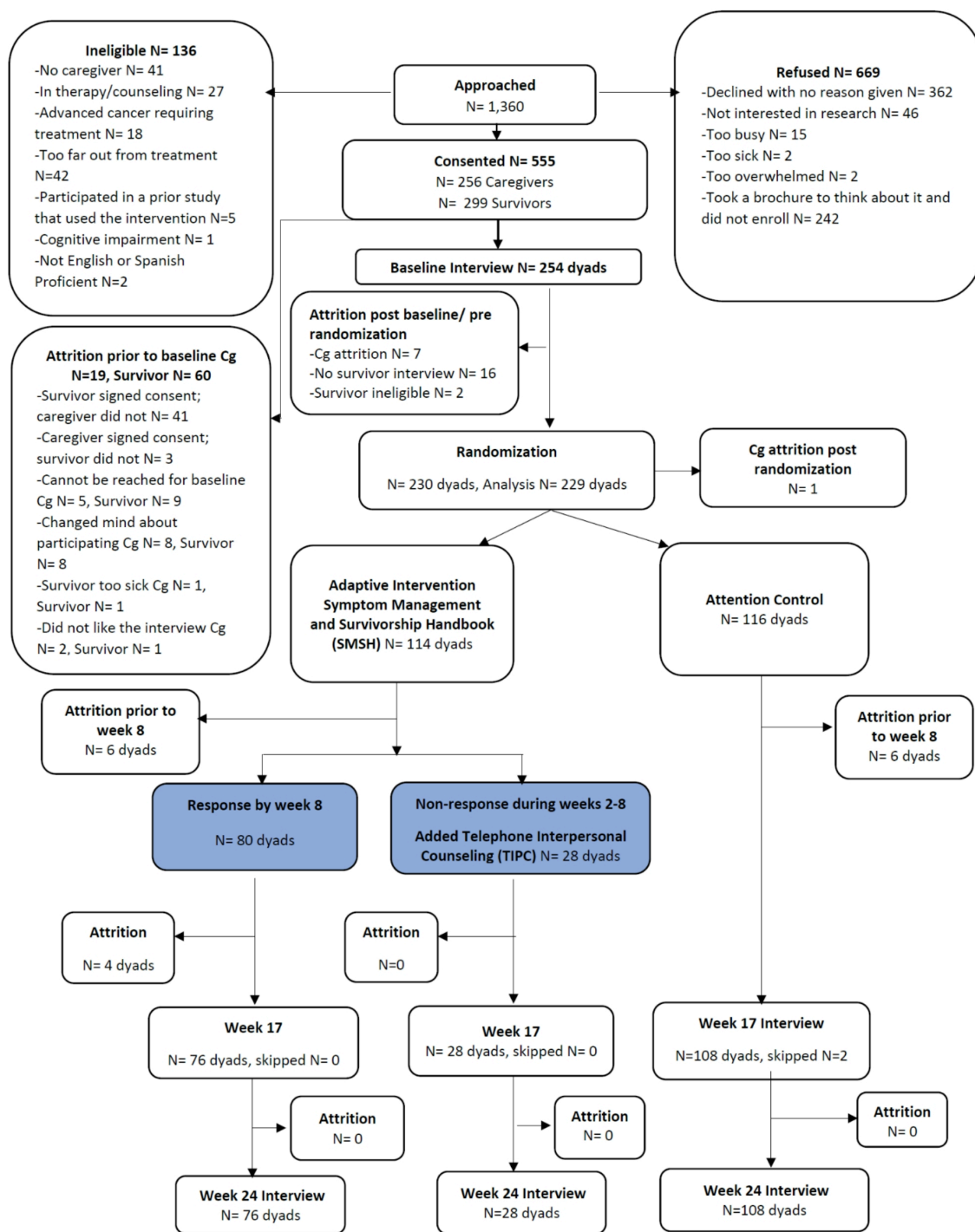


Figure 1

CONSORT Flow Chart

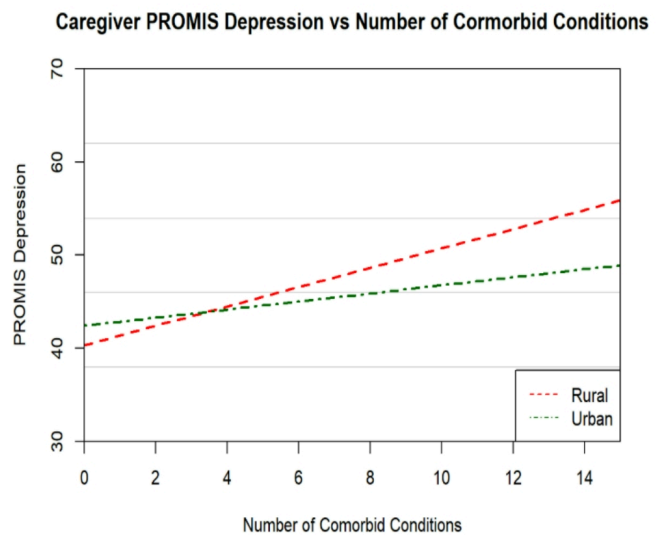
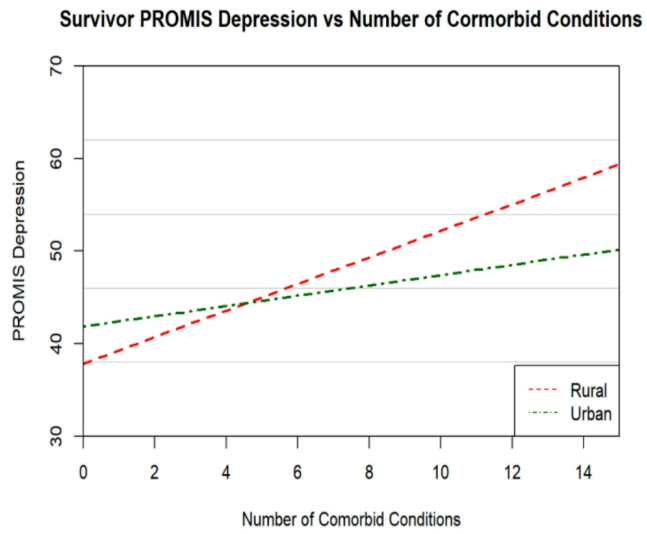


Figure 2

Moderating effects of the rural or urban residence on the association between the number of comorbid conditions and depression for survivors and caregivers