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ORIGINAL REPORT

Reach Out to Enhance Wellness Home-Based Diet-Exercise Intervention Promotes Reproducible and Sustainable Long-Term Improvements in Health Behaviors, Body Weight, and Physical Functioning in Older, Overweight/Obese Cancer Survivors

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ABSTRACT

Purpose
Diet and exercise interventions have been tested in cancer survivors as a means to reduce late effects and comorbidity, but few have assessed adherence and health outcomes long term.

Methods
Between July 2005 and May 2007, the Reach Out to Enhance Wellness (RENEW) trial accrued 641 locoregionally staged, long-term (≥ 5 years from diagnosis) colorectal, breast, and prostate cancer survivors in the United States (21 states), Canada, and the United Kingdom. All participants were sedentary (< 150 minutes of physical activity [PA] a week), overweight or obese (body mass index, 25 to 40 kg/m^2), and over age 65 years. The trial tested a diet-exercise intervention delivered via mailed print materials and telephone counseling. RENEW used a wait-list control, cross-over design (ie, participants received the year-long intervention immediately or after a 1-year delay), which allowed the opportunity to assess program efficacy (previously reported primary outcome), durability, and reproducibility (reported herein). Measures included diet quality (DQ), PA, BMI, and physical function (PF).

Results
No significant relapse was observed in the immediate-intervention arm for DQ, PA, and BMI; however, rates of functional decline increased when the intervention ceased. From year 1 to year 2, significant improvements were observed in the delayed-intervention arm; mean change scores in behaviors and BMI and PF slopes were as follows: DQ score, 5.2 (95% CI, 3.4 to 7.0); PA, 45.8 min/wk (95% CI, 26.9 to 64.6 min/wk); BMI, −0.56 (95% CI, −0.75 to −0.36); and Short Form-36 PF, −1.02 versus −5.52 ($P < .001$ for all measures). Overall, both arms experienced significant improvements in DQ, PA, and BMI from baseline to 2-year follow-up ($P < .001$).

Conclusion
Older cancer survivors respond favorably to lifestyle interventions and make durable changes in DQ and PA that contribute to sustained weight loss. These changes positively reorient functional decline trajectories during intervention delivery.

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INTRODUCTION

Cancer survivors are a high-risk patient population at increased risk for second malignancies, cardiovascular disease, diabetes, osteoporosis, and functional decline.[1-4] A healthful diet and increased exercise may ameliorate these adverse events,[5] but changing lifestyle behaviors is difficult, and maintaining healthful behaviors long term is essential to ultimately impact health outcomes.[6] To date, few lifestyle interventions have addressed long-term adherence, and most show disappointing results.[7-14] Within cancer populations, only three studies (all dietary interventions in breast cancer) have reported long-term adherence (ie, periods exceeding 1 year).[15-18] Although adherence was good, all of these interventions were conducted continuously throughout the entire study period, and none assessed long-term durability after the intervention had ceased. This opportunity

presented itself in conducting the Reach Out to Enhance Wellness (RENEW) trial.

RENEW was a home-based diet-exercise intervention delivered to 641 older, overweight or obese survivors of breast, prostate, and colorectal cancer.[19] The 12-month intervention, delivered via tailored mailed-print materials and telephone counseling, significantly improved diet quality (DQ) and physical activity (PA) and also resulted in significant weight loss and higher levels of quality of life and physical functioning (PF). The latter outcome served as the primary end point, and these results were heralded as a significant breakthrough in geriatrics and gero-oncology because lifestyle change is difficult to accomplish in elders and because the intervention effectively and positively reoriented the trajectory of functional decline.[13] At 1-year follow-up, the delayed-intervention arm experienced a sharp decline in PF (−4.84; 95% CI, −3.04 to −6.63), which was significantly attenuated in the immediate-intervention arm (−2.15; 95% CI, −0.36 to −3.93; $P = .03$). Such differences equate to a 10% reduced risk of mortality if extrapolated to effects reported in the extant literature. Moreover, because declines in PF often signal the need for skilled nursing care, this intervention was credited as having the potential to reduce health care costs.[20]

RENEW used a cross-over design. At 1-year follow-up, the immediate-intervention arm was discontinued from treatment and observed (to assess durability), whereas the delayed-intervention arm was then provided with the identical home-based diet-exercise intervention (to assess reproducibility)[21]; both groups were reassessed at 2-year follow-up. These secondary aims of durability and reproducibility are reported herein.

METHODS

Study Design

The RENEW methods have been published elsewhere.[19,21] The protocol was reviewed in accordance with the precepts established by the Helsinki Declaration and approved by the Duke University Health System Institutional Review Board and the North Carolina Central Cancer Registry. Written informed consent was obtained from all participants.

Study Participants

Figure 1 illustrates the study flow. Only individuals who were age ≥ 65 years, had body mass indices (BMI) of 25 to 40 kg/m^2, and a previous diagnosis of breast, prostate, or colorectal cancer ≥ 5 years previously with no evidence of progressive disease or second malignancies were considered eligible. Participants also had to be sedentary (< 150 minutes of moderate-to-vigorous PA a week),[5] community dwelling, and mentally and physically able to participate in telephone interviews and unsupervised PA. Between July 1, 2005, and May 17, 2007, 641 survivors were deemed eligible and block randomized on race, cancer type, and sex into immediate-intervention (n = 319) or delayed-intervention arms (n = 322). At 1-year follow-up, 87.1% of the sample was alive and actively engaged in the study. Cross over then occurred; the intervention was delivered to the 289 participants who had been wait-listed, whereas intervention contact was discontinued among the 269 participants who completed the program.

RENEW Intervention

The RENEW intervention consisted of a personally tailored workbook and quarterly newsletters and telephone counseling with automated prompts (15 sessions and eight prompts over 12 months).[19,21] The theoretically based intervention (Social Cognitive Theory and Transtheoretical Model)[22-24] endorsed 15 minutes of strength-training exercise every other day, 30 minutes of endurance exercise each day, daily consumption of ≥ seven servings (women) or ≥ nine servings (men) of fruits and vegetables, restriction of saturated fat to less than 10% of energy intake, and modest weight loss of less than 0.5 kg/wk—recommendations consonant with the American Cancer Society[5] and the US Dietary Guidelines for the prevention of commonly occurring diseases and promotion of overall health.[25] The intervention was tailored on current and previous diet and PA behaviors and body weight; self-efficacy and stage of readiness to exercise regularly and eat a diet low in saturated fat and high in fruits and vegetables; and sex and cancer type. Participants also received a pedometer, variable resistance exercise bands, an exercise poster depicting six lower extremity strength exercises, Portion Doctor tableware to guide food consumption (Portion Health Products, St Augustine Beach, FL), and personalized record logs to self-monitor daily exercise and dietary intake.

Outcomes

The primary outcome was change in PF, which was assessed quarterly using the PF subscale of the Medical Outcomes Study Short Form-36 (SF-36) questionnaire.[26,27] This subscale assesses the impact of health on performance of activities ranging from basic self-care to vigorous PA and has been widely used with good construct validity and sensitivity to change.[28-30] Moreover, because it has greater predictive value for independent living capability than clinically assessed physical performance batteries, it has been proposed as a primary outcome measure for clinical trial use—one that is inexpensive, easy to implement, and associated with minimal patient burden.[31] Because lower extremity function is central to the maintenance of independence,[32] the Basic and Advanced Lower Extremity Function subscales of the Late-Life Function and Disability Index were used.[33,34] Data on PA, diet, and weight loss were secondary outcomes and gathered annually. PA was assessed using the Community Health Activities Model Program for Seniors questionnaire.[35] This questionnaire was developed for use in older adults and is sensitive to change.[36] Dietary intake data were averaged from two unannounced 24-hour recalls at each time point using the Nutrition Data System for Research software (Version 2006; Nutrition Coordinating Center, Minneapolis, MN).[37,38] Global scores for DQ were generated using the Healthy Eating Index 2005 criteria[39] and methods used previously[40] (ie, using tallied weighted scores for consumption of total and saturated fat, added fats and sugars, dairy products, protein sources, fruits and vegetables, and whole grains). Self-reported height and weight were gathered for estimation of BMI and weight loss. All surveys were conducted by interviewers at Pennsylvania State University who were blinded to study condition.

All study participants were provided with a telephone number to report adverse health events. Health status also was assessed during each telephone contact. The investigative team (blinded to arm assignment) classified events as serious versus nonserious and as nonattributable, possibly attributable, or attributable to the intervention.

Statistical Analyses

The sample size calculation (n = 640) and power analyses (two-tailed $\alpha = .05$) were based on assumptions of 15% attrition and between-arm differences in PF change scores at the 1-year time point of 3.9 (standard deviation [SD], 16.2).[19,21,41] This secondary, exploratory analysis was conducted only on data from the 488 participants who completed the 2-year trial. Sensitivity analyses were performed according to White et al.[42] To evaluate sustainability of immediate-intervention effect, paired *t* tests were used to explore whether significant differences in health behaviors and BMI were detected after intervention (ie, from year 1 to year 2) in the immediate-intervention arm compared to the null hypothesis of no change. Because the trajectory of functional decline was of most interest, we tested whether the slopes of each PF measure from year 1 to year 2 were significantly different from those of baseline to year 1 in the immediate-intervention arm. To evaluate whether those in the delayed-intervention arm derived significant benefit from the intervention, paired *t* tests were used to explore whether the delayed-intervention arm experienced significant improvements in their health behaviors, weight status, and PF trajectory during exposure to the intervention during this same time period. Here, both unadjusted and adjusted analyses (which took into account baseline levels of the factor under study) were used. Means and 95% CIs were generated for changes between year 1 and year 2 values. Differences in health behaviors and BMI from baseline to year 2 completion also were assessed using paired *t* tests for both study arms to

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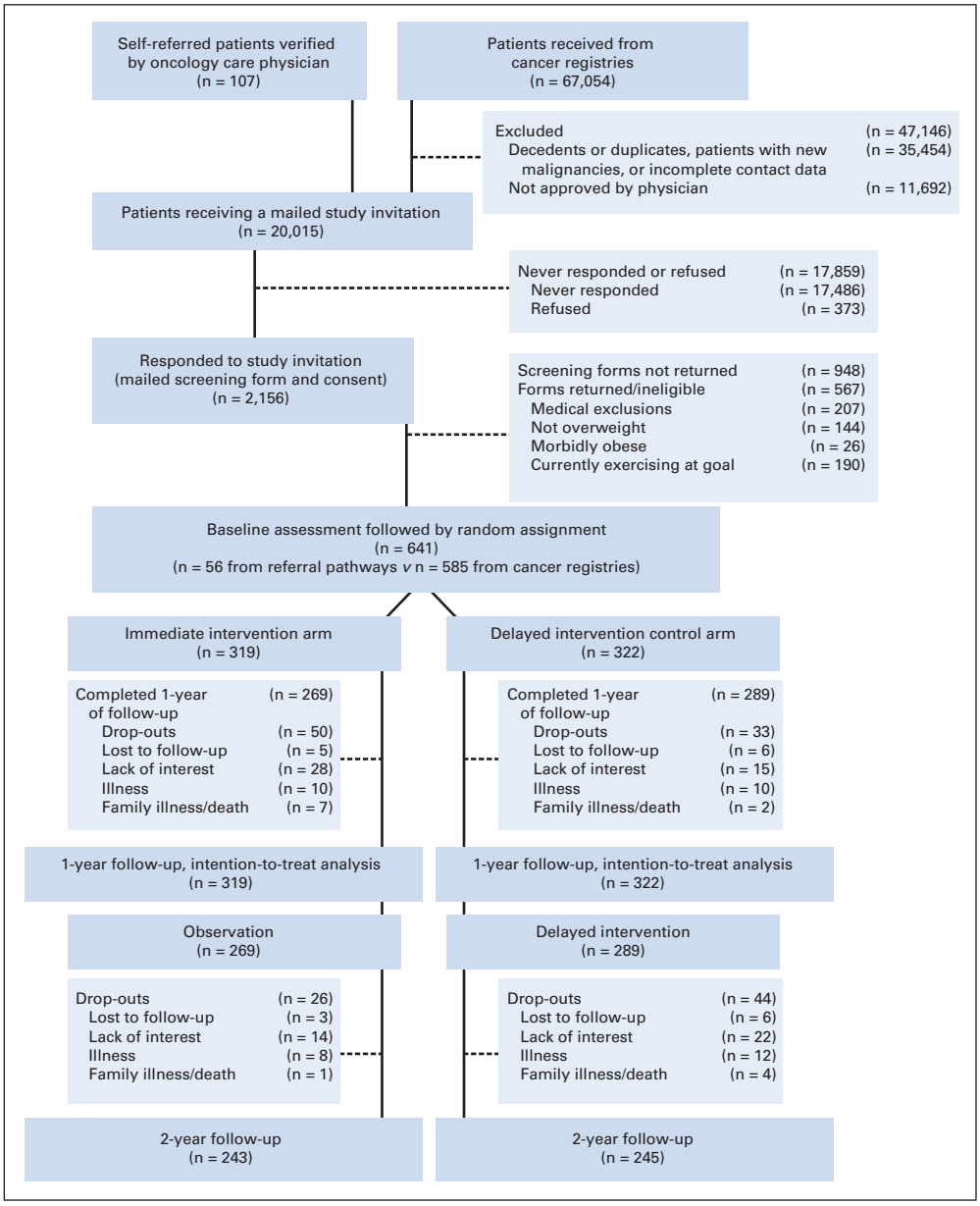

Fig 1. CONSORT diagram.

determine whether participants ended the study with marked improvements over baseline. χ^2 tests were conducted to determine whether adverse events differed by study arm or intervention delivery status. All analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC). Because the durability and reproducibility aims of the RENEW trial were considered secondary (and therefore exploratory), no correction for multiple testing was performed.

RESULTS

Study participants largely resided in 21 US states, although a small number were from Canada and the United Kingdom. See Table 1 for characteristics of the study sample who completed the entire trial and whose data are included in this analysis. Similar to our original report,[19] the sample was comprised primarily of white breast and prostate cancer survivors who had some college education. At 2-year follow-up, the sample was obviously 2 years older and more distal from diagnosis.

As depicted in Figure 1, of the 641 individuals initially randomly assigned, 87.1% (n = 558) completed 1-year follow-up, and 76.1% (n = 488) completed 2-year follow-up. Attrition was driven largely by lack of interest and was greater during intervention delivery. As in the original sample, the current sample was evenly divided between study arms, with no between-arm differences noted in any sociodemographic or health parameters tested. No significant differences were observed between study dropouts versus completers on any of these factors.

Change in Targeted Behaviors and BMI

Changes in DQ, PA, and BMI from baseline to 2-year follow-up are plotted in the uppermost graphs in Figure 2 and reported in Table

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Table 1. Demographics and Clinical Characteristics of the Study Sample Who Completed the RENEW Trial (n = 488)

Demographic or Clinical Characteristic	Immediate-Intervention Arm (n = 243)		Delayed-Intervention Arm (n = 245)	
	No.	%	No.	%
Age at baseline, years				
Mean	73.0		72.9	
SD	5.2		5.0	
Range	65-87		65-86	
Non-Hispanic white	221	91.0	218	89.0
Male	111	45.7	107	43.7
Any college education	153	63.0	149	60.8
Cancer type				
Breast	111	45.7	110	44.9
Prostate	99	40.7	94	38.4
Colorectal	33	13.6	41	16.7
Years since diagnosis at baseline				
Mean	8.7		8.6	
SD	2.8		2.6	

Abbreviations: RENEW, Reach Out to Enhance Wellness; SD, standard deviation.

2. The immediate-intervention arm experienced improvements from baseline to year 1, and then these values stabilized with no significant differences observed between year 1 and year 2 levels, with the exception of fruits and vegetables, which decreased significantly. In contrast, those in the delayed-intervention arm experienced no significant improvements in all of these measures from baseline to year 1, but did so from year 1 to year 2 (period of intervention exposure). Both arms experienced significant behavioral and weight status improvements ($P < .05$) from baseline to 2-year follow-up.

Change in PF

Figure 2 shows trajectories of PF as measured by the SF-36 PF subscale, and data on all PF measures are provided in Table 3. Rates of decline slowed significantly in each arm during intervention delivery but increased in the year after intervention completion in the immediate-intervention arm.

Adverse Events

Over the entire study period, a total of 441 events were reported, reviewed, and classified. Because any cardiac, musculoskeletal, or digestive concerns were considered possibly attributable to the diet-exercise intervention, 179 of the 441 events were classified as such. Of these, 61 involved hospitalization and considered serious. Only six events were considered directly attributable to the intervention, with one deemed as serious (hospitalization for posthiking dehydration). Other attributable, nonserious events included increased blood pressure, hip pain, and calf pain with exercise and pulled hamstring and a fall while walking/hiking. No between-arm differences during periods of observation or intervention were found for the total number of events or events in subcategories.

DISCUSSION

To date, there have been few long-term multibehavior interventions that combine both diet and exercise to promote weight loss in any

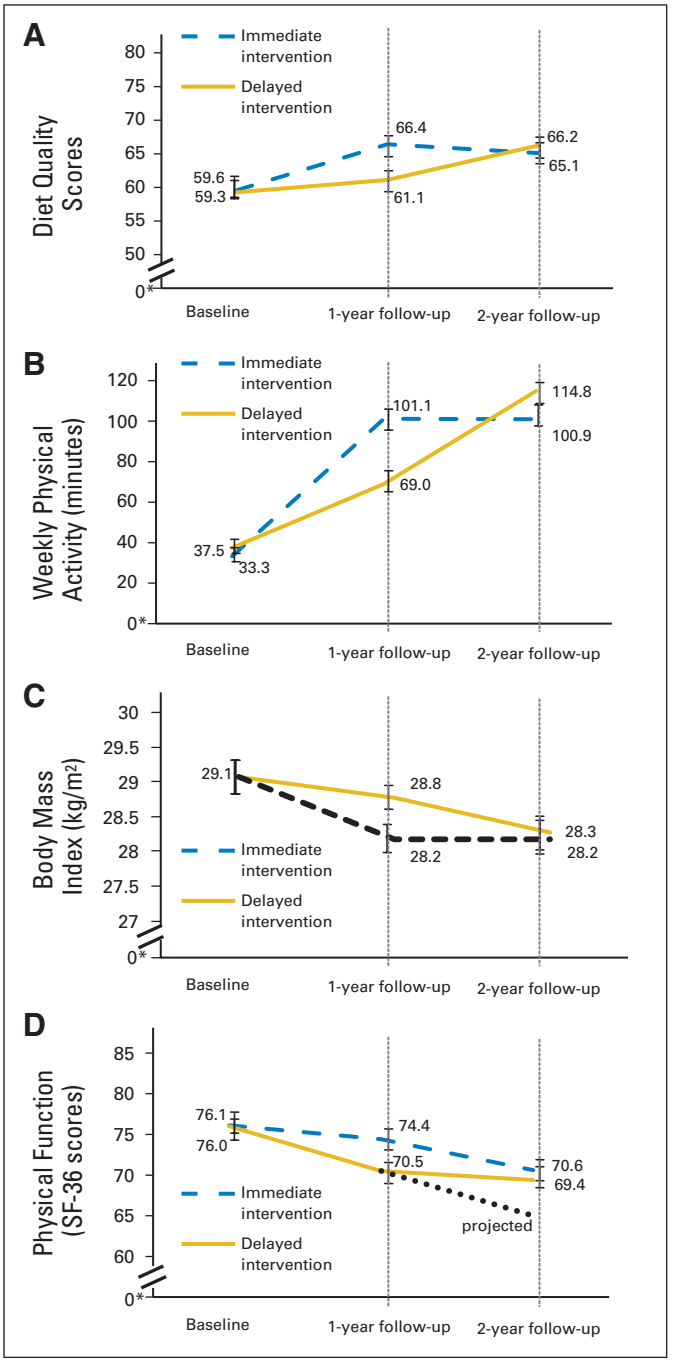

Fig 2. Change in (A) dietary intake and quality, (B) physical activity, (C) body mass index (BMI), and (D) physical functioning in response to the Reach Out to Enhance Wellness intervention in the immediate- versus delayed-intervention arms over 2 years. (*) Scales are truncated to show typical ranges or, in the case of BMI, a range characteristic of borderline overweight/obese populations. SF-36, Short Form-36.

population, and virtually none in cancer survivors.[9,13,41] RENEW contributes to our understanding in all of these arenas.

Although there are some success stories in promoting weight loss, systematic reviews suggest that most programs have high rates of attrition (often > 50% during the intervention period alone) and significant weight regain in the year after completion.[43] In contrast, attrition in RENEW was only 12.9% in the first year and 23.9% overall.

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Table 2. Diet Quality, Physical Activity, and Weight Status Over Time of Participants Who Completed the RENEW Trial Focusing on Year 1 to Year 2 Data

Measure	Baseline	1-Year Follow-Up	2-Year Follow-Up	Year 1 to Year 2 Change		*P**† 1 Year to 2 Years)	*P**‡ Baseline to 2 Years
				Mean	95% CI		
Immediate intervention							
Diet quality score				−1.19	−2.89 to 0.51	NS	< .001
Mean	59.6	66.4	65.2				
SE	0.9	0.8	0.9				
Daily servings of fruits and vegetables, No.				−0.76	−1.05 to −0.47	< .001	< .001
Mean	3.9	5.2	4.5				
SE	0.1	0.2	0.2				
Participants meeting goal (women ≥ 7; men ≥ 9)				—		.016	.028
No.	20	44	31				
%	8.2	18.1	12.8				
% of energy from saturated fat				0.34	−0.09 to 0.77	NS	< .001
Mean	11.2	9.8	10.2				
SE	0.2	0.20	0.20				
Participants meeting goal (< 10%)				—		NS	< .001
No.	87	129	121				
%	35.8	53.1	49.8				
Physical activity (moderate + vigorous), min/wk				−0.17	−18.2 to 17.8	NS	< .001
Mean	33.3	101.1	100.9				
SE	2.9	7.3	8.3				
Participants meeting goal (≥ 150 min/wk)				—		NS	< .001
No.	0	46	43				
%	0	18.9	17.7				
Body weight, kg				0.25	−0.17 to 0.67	NS	< .001
Mean	85.55	83.09	83.31				
SE	0.85	0.83	0.87				
BMI, kg/m^2				0.03	−0.13 to 0.19	NS	< .001
Mean	29.1	28.2	28.2				
SE	0.2	0.2	0.2				
Participants with normal weight (BMI, 18.5-24.9)						NS	< .001
No.	0	20	24				
%	0	8.2	10.0				
Delayed intervention							
Diet quality score				5.2	3.4 to 7.0	< .001	< .001
Mean	59.3	61.1	66.2				
SE	0.9	0.9	0.8				
Daily servings of fruits and vegetables, No.				1.01	0.66 to 1.36	< .001	< .001
Mean	3.6	3.8	4.8				
SE	0.1	0.1	0.2				
Participants meeting goal (women ≥ 7; men ≥ 9)				—		< .001	< .001
No.	14	11	33				
%	5.7	4.5	13.5				
% of energy from saturated fat				−0.99	−1.43 to −0.55	< .001	< .001
Mean	11.2	11.0	10.0				
SE	0.2	0.2	0.2				
Participants meeting goal (< 10%)				—		.0016	< .001
No.	86	93	123				
%	35.1	38.0	50.2				
Physical activity (moderate + vigorous), min/wk				45.8	26.9 to 64.6	< .001	< .001
Mean	37.5	69.0	114.8				
SE	3.2	7.8	9.0				
Participants meeting goal (≥ 150 min/wk)				—		.003	< .001
No.	0	29	52				
%	0	11.8	21.2				
Body weight, kg				−1.46	−1.97 to −0.95	< .001	< .001
Mean	84.43	83.49	82.03				
SE	0.82	0.84	0.86				
BMI, kg/m^2				−0.56	−0.75 to −0.36	< .001	< .001
Mean	29.1	28.8	28.3				
SE	0.2	0.2	0.2				
Participants with normal weight (BMI, 18.5-24.9)				—		.004	< .001
No.	0	18	32				
%	0	7.4	13.1				

Abbreviations: BMI, body mass index; NS, not significant; RENEW, Reach Out to Enhance Wellness.
**P* values for unadjusted tests are reported; *P* values for adjusted tests were similar and did not affect significance.
†Change in status over time was assessed using the McNemar test.
‡Intent-to-treat analyses that imputed zero change for dropouts did not appreciably change results or affect significance.

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Table 3. Change in Physical Function From Baseline to Year 1 and From Year 1 to Year 2 in the RENEW Immediate-Intervention Versus Delayed-Intervention Arms

Function	Slope: Baseline to Year 1		Slope: Year 1 to Year 2		
	Mean	SE	Mean	SE	P^*
Immediate intervention					
Physical function (SF-36 subscale)	−1.71	1.09	−3.77	1.10	.044
Basic lower extremity function	0.61	0.74	−1.75	0.61	< .001
Advanced lower extremity function	−0.26	0.62	−2.37	0.63	< .001
Delayed intervention					
Physical function (SF-36 subscale)	−5.52	1.10	−1.02	1.25	< .001
Basic lower extremity function	−1.82	0.76	0.32	0.68	.002
Advanced lower extremity function	−2.60	0.68	0.30	0.71	< .001

Abbreviations: RENEW, Reach Out to Enhance Wellness; SF-36, Short Form-36.

*P values for year 1 to year 2 slopes were derived using univariate t tests with the null location defined as the baseline to year 1 slope for the same intervention group.

Therefore, our results for weight loss are likely to be generalizable (at least to cancer survivors). Additionally, although RENEW was aimed at promoting only modest weight loss, the improvements of −0.8 to −0.9 units in BMI were similar to the mean loss of −0.87 units found by Wu et al[14] in their pooled analysis of 17 diet and exercise studies. More importantly, the mean rate of weight regain in RENEW of 0.03 BMI units over the course of 1 year is far lower than the mean regain of 0.30 units found in a meta-analysis of dietary counseling interventions over the same period.[9] This suggests that the weight loss produced by the RENEW intervention was indeed durable. Given data that show a 1.9% increase in health care costs over an 18-month period with each BMI unit above normal, there are both health and economic reasons to support such an intervention.[44] The durability of RENEW may be attributed to the longer duration (1 year) and its multiple-component nature, factors identified as enhancing long-term weight management.[45,46] Durability also may be attributed to the target population (ie, cancer survivors), and evidence suggests that this may be an exceptionally engaged and motivated population.[47] That being said, the clinical guidelines established for the treatment of overweight and obesity, which recommend continued long-term management, still may be appropriate for cancer survivors.[48]

The comparison of RENEW data related to PA and dietary change with other extant data is challenging because of a paucity of reported studies that have assessed these behaviors long term. RENEW increased DQ from the 75th to the 85th percentiles, which is clinically significant,[49] yet there are few dietary interventions that have targeted global changes in dietary patterns and none that have assessed impact long term. For PA, slightly more comparative data exist, with three trials reporting outcomes at 2-year follow-up.[10] Even so, results were mixed, and issues related to quasiexperimental designs and overestimated effects as a result of the prevalent practice of last observation carried forward are problems that cloud clear comparisons.[10,46] Three recently published articles on older adults with designs similar to RENEW (ie, 1-year intervention followed by 1 to 2 years of observation) show that PA remains above baseline levels and above those observed for controls.[50-52] However, declines in PA did occur and ranged from 30% to 60% during the postintervention period. These declines in PA stand in stark contrast to the durable effects observed in the RENEW trial.

Perhaps, the most salient comparison of RENEW lies with findings of the FRESH START trial, in which 543 breast and prostate cancer survivors received eight installments of print materials over a 1-year period and then were observed for an additional year.[53] After the baseline assessment, participants were randomly assigned to standardized print materials or to an arm that received a tailored workbook and a series of tailored newsletters. Like this intervention, it was multicomponent in nature, but only a subset of participants in the experimental arm received tailored materials on exercise. Mean weekly minutes of PA were as follows: baseline, 55 minutes (SD, 116 minutes); 1 year, 117 minutes (SD, 129 minutes); and 2 years, 113 minutes (SD, 145 minutes). Although the mean age of the FRESH START sample was 57 years and the study reported baseline and follow-up values for PA that were 10 to 20 minutes per week higher, the patterns are similar and suggest that home-based interventions can produce significant and durable increases in PA among cancer survivors. Given variable responses and wide CIs, it is clear that although exercise interventions are embraced strongly by many survivors, some remain untouched. Therefore, future studies are needed to determine those most likely to benefit, while developing additional interventions to target the recalcitrant.[6]

Finally, for PF, it must be remembered that this intervention was placed not only against the backdrop of functional decline characteristic in the elderly,[54] but also the even steeper decline noted among older adults with cancer.[55] Although RENEW study participants were overweight and physically inactive at study enrollment, other factors beyond behaviors influence functional trajectories, and unfortunately, preservation of attenuated decline in function was not sustained long term. Nonetheless, our findings from the main outcomes analysis[19] and this secondary analysis show that the RENEW intervention significantly and positively reoriented the trajectory of functional decline during intervention delivery and did so repeatedly (ie, in the immediate-intervention arm and again in the delayed-intervention arm). Because PF was measured using three different scales, each of which tap distinct functional domains related to independent living, the accelerated functional decline noted once the intervention ended points to the need for a longer intervention or boosters to enhance improved maintenance of PF.

Continued research is important because older cancer survivors represent a patient population that now numbers over 7 million and is rapidly expanding.[56,57] Findings of the current study help inform future research and practice for this vulnerable segment. In doing so, this study's limitations must be kept in mind, including the reliance on self-reported data and potential bias resulting from attrition and low proportional enrollment. Although attrition was comparatively lower than other 2-year lifestyle interventions and sensitivity analyses indicated no differences between dropouts and completers, the low proportional accrual of less than 6% is a larger issue and may suggest that RENEW trial enrollees may have differed from cancer survivors in general. These concerns are balanced by the following strengths: enrollment in three countries and 21 states through population-based cancer registries, and previous study findings showing negligible influence of social desirability in responses to a home-based diet and exercise intervention that is evaluated through telephone survey.[58]

In conclusion, RENEW was the first reported trial to test a multicomponent diet and exercise intervention aimed at promoting

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weight loss and favorably influencing the trajectory of functional decline among older, overweight, long-term survivors of breast, prostate, and colorectal cancer.[19,21] The intervention was theoretically grounded and specifically addressed common barriers that exist in this high-risk and high-need population (functional deficits, transportation issues, and low vision).[10,41,59-62] It also is one of the few diet and exercise trials to follow participants over 2 years. Data from long-term follow-up suggest that the intervention was not only reproducible but also durable. In contrast to a majority of lifestyle interventions, significant improvements in diet and exercise behaviors were observed and maintained over the 2-year study period; moreover, the modest weight loss that was promoted in this overweight sample of high-risk elders was sustained over the same period. Finally, although data suggest that the RENEW intervention slowed functional decline during delivery, the inexorable influence of aging and other factors on function remains a challenge.[20,54,63,64] More research is needed to combat this problem, especially given the aging of the population and the health care burden that is imposed when functional status threatens independence. This is an area in which scalable and sustainable interventions are greatly needed[65] and in which home-based interventions, such as RENEW and others,[41,53] can make a difference.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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