Project PREVENT: A Randomized Trial to Reduce Multiple Behavioral Risk Factors for Colon Cancer

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Abstract

Background: **This report examines the outcome data for Project PREVENT, a two-site randomized control trial designed to reduce behavioral risk factors for colorectal cancer among individuals who have been diagnosed with adenomatous colon polyps.**
Methods: **The study sample included 1,247 patients with recent diagnosis of adenomatous colorectal polyps. Within 4 weeks following the polypectomy, participants completed a baseline survey by telephone, and were randomized to either Usual Care (UC) or the PREVENT intervention, which was designed to target multiple risk factors. The intervention consisted of a telephone-delivered intervention plus tailored materials, and focused on the six primary behavioral risk factors for colorectal cancer, including red meat consumption, fruit and vegetable intake, multivitamin intake, alcohol, smoking, and physical inactivity.**
Results: **Participation in the PREVENT intervention was associated with a significantly greater reduction in prevalence of multiple risk factors for colorectal cancer compared with UC. Only about one third of UC participants dropped any risk factors during the study period, compared with almost half of the PREVENT participants. PREVENT participants were also significantly more likely to change more than one behavior than UC participants.**
Conclusions: **The PREVENT intervention was effective in helping patients change multiple risk factors. These results provide further support that more comprehensive interventions that move beyond emphasis on a single risk factor are acceptable to patient populations, can result in improvements, and are cost effective.** (Cancer Epidemiol Biomarkers Prev 2005;14(6):1453–9)

Introduction

Colorectal cancer is a prevalent and costly disease. Over 150,000 adults in the United States are diagnosed with colorectal cancer annually. In 2004, an estimated 151,000 cancer cases and 56,000 deaths and will be attributable to colorectal cancer (1), making it the second leading cause of cancer mortality among men and women. The vast majority of colorectal cancer arises from benign and asymptomatic colonic polyps, which are highly prevalent among American adults (1, 2). Polyps can be identified and removed via sigmoidoscopy or colonoscopy, depending on their size and location. However, 30% to 50% of polyp patients experience a recurrence (2).

There are a number of behavioral risk factors that have been associated with the development of polyps and colorectal cancer. Physical activity has been consistently found to be protective against colorectal cancer (3-17). Level of physical activity also is inversely associated with relative risk of having large polyps (16), which are most likely to have malignant potential (18). A number of studies have identified an association between cigarette smoking, polyp size, colorectal cancer incidence, and mortality (19-22). A review of 22 studies concluded that evidence accumulating over the past decade strongly supports a causal link between smoking and colorectal cancer risk (23). Diet has also been thought to increase risk for colorectal cancer (24-27, 24, 28-30). However, the evidence is most consistent for increases in risk associated with red meat consumption. The potential risk-reducing benefits of fruit, vegetable, and fiber consumption for colorectal cancer are less clear (31-33). Several studies have established the use of multivitamin, and folate in particular, as protective for colorectal cancer (34, 35). In addition, alcohol use has also been found to increase colorectal cancer risk (15).

Several ongoing epidemiologic studies will further clarify the complex interrelationships between these risk factors and colorectal cancer. In the mean time, prudent recommendations for improving diet quality, increasing physical activity, and smoking cessation are consistent with general recommendations for lowering overall cancer risk. Identification of adenomatous polyps may increase perceptions of risk for colorectal cancer and as such, these individuals, particularly those who are engaging in behavioral risk factors that increase their colorectal cancer and other cancer risk, may be especially responsive to related health messages and interventions.

The multiple behavioral risk factors described above that increase risk for polyps and colorectal cancer are interrelated in terms of the psychological, social, and environmental factors that reinforce them (36). Thus, it is not surprising that consistent evidence shows that those who eat high-fat diets are also more likely to lead sedentary lifestyles and to be cigarette smokers (37-39). Despite evidence that these risk behaviors may be mutually reinforcing, few studies have intervened on multiple behaviors simultaneously, encouraged change in overall risk profiles, or evaluated interrelationships among risk factors. Indeed, it has been argued that intervening on multiple risk factors simultaneously may undermine

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success at changing individual behaviors (40, 41). However, our work (37, 42, 43) and that of others (44) suggest that change in one behavioral risk factor may serve as a stimulus or gateway for change in the other health behaviors. Whereas intervening on multiple risk behaviors simultaneously represents a challenge from an intervention perspective, the interrelationships among risk behaviors cannot be ignored and may provide an important opportunity to maximize the potency of cancer prevention interventions. Moreover, the complex and multifactorial process of carcinogenesis suggests that overall lifestyle changes may be needed to significantly reduce risk. Thus, multiple risk factor interventions warrant further study.

The purpose of this work is to report on the outcomes of Project PREVENT, a multisite, randomized clinical trial designed to reduce behavioral risk factors for colorectal cancer among patients who have been diagnosed with adenomatous polyps. The primary goal of Project PREVENT was to determine if it was possible to stimulate simultaneous change in the multiple risk factors that pose risk for colorectal cancer and other cancer development. Project PREVENT was a telephone-based counseling intervention that incorporated tailored print materials to promote simultaneous change in multiple risk behaviors. The behavioral targets included increasing physical activity, fruit and vegetable consumption, multivitamin intake, and decreasing red meat consumption, alcohol intake, and smoking. The primary outcome variable was a multiple risk factor index that was based on not meeting recommendations for each of the individual risk factors. Secondary outcomes evaluated change in risk status on each of the risk factors. We hypothesized that the PREVENT intervention would lead to a significant reduction on the multiple risk factor index, compared with the Usual Care (UC) intervention. We also hypothesized that there would be greater change on the individual risk factors in the PREVENT condition.

Materials and Methods

Sample. The study sample was drawn from patients who had undergone either flexible sigmoidoscopy or colonoscopy through the gastroenterology department in four health care systems, two in Boston, Massachusetts, and two in North Carolina. Eligibility criteria included (*a*) having an adenomatous colon polyp removed within 4 weeks of recruitment, (*b*) having no personal history of colorectal cancer, (*c*) of ages 40 to 75 years, (*d*) being able to read and speak English, (*e*) being mentally capable of informed consent, and (*f*) being reachable by telephone. Institutional review boards at all participating institutions approved the study methods, and informed consent was obtained from participants.

Eligible patients were identified from fall of 1999 through the fall of 2001 via the Health Center databases and sent an introductory letter that described the project. The patients who did not call a toll-free number to refuse contact were telephoned by a survey research firm and asked to complete the baseline survey. Those deemed eligible were asked to give verbal consent to participate in the PREVENT trial. Participants who agreed to participate were stratified by site (North Carolina versus Massachusetts), age (40-59 and 60+), and gender, and randomly assigned within strata to either the Project PREVENT Intervention or UC. Enrollment was conducted during the telephone survey; randomization was conducted by the study biostatistician following collection of baseline data. The final study outcomes were assessed at the 8-month post-baseline follow-up. All data collectors were blind to condition assignment.

A total of 1,979 individuals were identified as being potentially eligible by the participating health care systems during the recruitment period and were sent an initial letter about study participation (see Fig. 1). The final sample was composed of 1,247 participants who completed the baseline survey (response rate: 61% of invited, 67% of eligible, and 75% of those contacted). Our sample size was determined based on power analysis to detect differences at the 0.05 level in our primary and secondary outcomes.

Intervention Conditions. The intervention activities of Project PREVENT were ongoing from fall of 1999 through the winter of 2002. The components of each intervention condition are described below.

Usual Care Control Group. The standard of care offered by the participating gastroenterologists served as the UC intervention. In addition, all participants received a letter from their gastroenterologist endorsing the behavior change targets, plus a Colorectal Cancer Prevention tip sheet via mail or in the procedure room of their health center.

Project PREVENT Multiple Risk Factor Intervention. The PREVENT intervention was theory driven, designed to promote change across multiple health behaviors simultaneously. The intervention was designed to address the limited literature on studies that have intervened on multiple behaviors simultaneously or encouraged change in overall risk profiles. The intervention was grounded in the Social Cognitive Theory (38), which suggests that health habits have common underpinnings [i.e., a constellation of intrapersonal (e.g., response and self-efficacy) and interpersonal factors (e.g., social support)]. Accordingly, the cognitive and behavioral skills needed to change these behaviors also are similar. Thus, the PREVENT intervention had three overarching objectives. The first was to capitalize on the identification of an adenomatous polyp as a cue to frame the importance of, and prompt motivation for, risk factor reduction for colorectal cancer and other chronic diseases. A second objective was to bolster patient's self-efficacy to change multiple risk behaviors by helping them recognize natural intersections among their risky health habits that could make it easier to change more than one habit at a time. The third objective was to help them learn general skills that could be used to change any of their risk factors. To this end, those in the PREVENT condition received (*a*) a motivational and goal-setting telephone session delivered by a health educator within a month of the polyp identification; (*b*) four follow-up telephone counseling calls at monthly intervals conducted over the 4 subsequent months, tailored to the patient's level of motivation for change using detailed

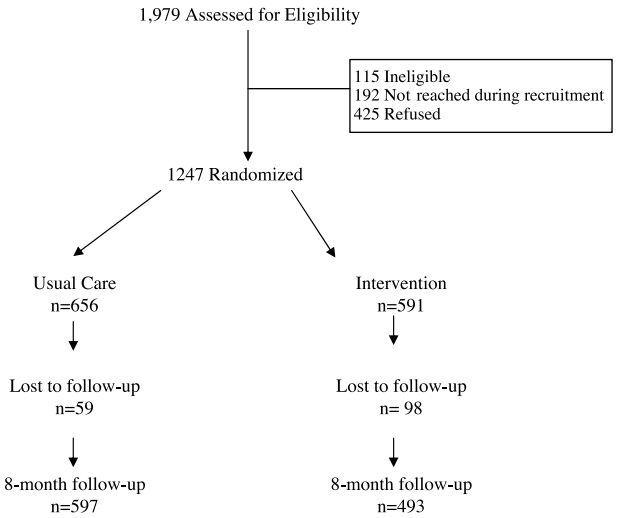

Figure 1. Recruitment for Project PREVENT (consort figure).

computer-based counseling protocols; (*c*) computer-generated tailored print progress reports in tandem with the follow-up calls to reinforce their goals and address areas that needed further consideration; and (*d*) tailored self-help materials. The self-help materials were provided in a Project PREVENT binder, which included a personalized health behavior profile, a tailored guidebook, a logbook (e.g., a personal diary for the participant to record their goals, keep track of their progress, and keep ''to do'' lists), and behavior-specific tip sheets (e.g., smoking cessation guide, a walking for fun and fitness brochure, and common questions about multivitamin use). The personalized profile included customized graphs that displayed the participant's current status and the recommended levels for each of the six risk factors (red meat, fruit and vegetables, alcohol, multivitamin, physical activity, and smoking). The tailored guidebook gave detailed background information about the relevant risk factors and illustrated connections among the individual's health habits, offering personalized suggestions for strategies that could help the individual jointly accomplish recommended changes in all of their identified risk behaviors. For example, skill recommendations for individuals who were identified at lower than recommended levels of physical activity and daily servings of fruits and vegetables were given messages that integrated both behaviors. After each counseling call, materials were sent summarizing the calls and goals.

The intervention was delivered by health advisors based in North Carolina and Massachusetts. Health advisors at both sites were trained together and received 16 hours of training and ongoing supervision from an expert in motivational interviewing. To ensure standardization of intervention delivery across sites, training and supervision sessions were conducted via an initial joint on-site meeting and on an ongoing basis via conference calls that included supervisors and health advisors from each of the sites. In addition, counseling sessions were selected at random and reviewed by supervisors to guide continuous training.

Outcome Measures. The baseline survey included socioeconomic and demographic variables such as age, gender, education, marital status, race/ethnicity, height, weight, medical history, and characteristics of the household. The behavioral outcomes were assessed at baseline and follow-up, and included dietary intake, multivitamin intake, physical activity, smoking, alcohol use, and a multiple risk factor index.

Dietary Intake. Fruit/vegetable and red meat consumptions were assessed using an abbreviated form of the semiquantitative food frequency questionnaire (3), which captures the key dietary constituents of interest related to colorectal cancer risk. The 22-item food frequency questionnaire includes a list of fruits, vegetables, red meats, poultry, and fish with specified serving sizes that are described using usual portion sizes (e.g., one medium orange) or the standard weight and volume measures of the servings commonly consumed. For each food item, participants indicate their average frequency of consumption by choosing one of 11 categories for fruits and vegetables and 12 categories for red meat, ranging from never or less than once per month, to six or more per day.

Multivitamin Intake. Multivitamin use was assessed with a single-item question in which participants indicated their average intake of multivitamins or folic acid supplements by choosing one of nine categories ranging from never to 7 days per week. The item used is the measure of multivitamin intake used in the Nurse's Health Study (34).

Alcohol Intake. Alcohol consumption was measured using the quantity frequency index (45). This measure assesses frequency of alcohol consumption during the past 30 days, in addition to the average number of alcoholic drinks per drinking day.

Physical Activity. Physical activity was measured using a modified version of the CHAMPS Activities Questionnaire for Older Adults (46). This 24-item instrument assesses the average frequency and duration of moderate-intensity activities done in the past week or a typical week. Participants first responded to an open-ended question about frequency of the activity in the past week. If the activity was done, the participant responded to a duration question on a six-point scale from <1 hour per week to ≥9 hours per week. The psychometric properties of the CHAMPS are adequate (46).

Smoking. Smoking status was assessed by self-report using standardized questions concerning lifetime smoking (e.g., having smoked at least 100 cigarettes in lifetime), current smoking, number of cigarettes smoked per day, number of quit attempts made in the past 12 months, and nicotine dependence (47).

Multiple Risk Factor Index. A categorical measure was designed to evaluate the relationships between six behavioral risk factors (37). This risk factor index was based on current smoking status (smoking, no smoking), consumption of fewer than five servings of fruits and vegetables per day, consumption of more than three servings per week of red meat, taking a multivitamin less than 7 days per week, drinking more than one (women) or two (men) servings of alcohol per day, and exercising at least moderately less than 150 minutes per week. Subjects were assigned a score of 1 if they had the risk factor and a score of 0 if they did not have the risk factor. These categorizations were based on what is generally accepted in the field as the minimum requirements for risk factor reduction and/or cardiorespiratory benefit. The individual risk factor scores were then summed to yield a categorical multiple risk factor assessment (0 = no risk factors; 6 = all risk factors).

Cost Data. Although we collected costs related to both research requirements and intervention delivery, our cost analyses are restricted to those intervention-related costs needed to replicate the intervention. To estimate the costs of the PREVENT intervention, we used time sheets to track the time spent on different activities and the materials used for the intervention. We also tracked time and materials spent for the control arm. For 2 randomly selected weeks, the health advisors were instructed to record the time spent in each of a number of categories and the total number of participants contacted during that week. These time sheets were completed for the three phases of the intervention: (*a*) preparation (i.e., ''pre-randomization'' period), (*b*) initial telephone call (''call 1''), and (*c*) subsequent telephone calls (''calls 2-5'').

For the time spent during the delivery of the intervention (except for the telephone calls which were tracked automatically), we considered five different activities: (*a*) database management (e.g., time spent tracking participants); (*b*) material preparation (e.g., time spent running algorithms to prepare materials such as the baseline tailored feedback report); (*c*) mailing (e.g., time spent mailing tailored feedback report); (*d*) supervision of health educators (e.g., time spent discussing cases); and (*e*) others. From the time sheets, we summed the time spent in each activity and calculated the average number of minutes per contact. Time per contact was separately estimated for Dana-Farber Cancer Institute and Duke Comprehensive Cancer Center. We then assigned a unit cost per hour of time of $15.82 for Dana-Farber Cancer Institute and $14.00 for Duke Comprehensive Cancer Center. The overall cost estimates were obtained by taking a weighted average of the per-contact costs for the two sites, weighted by the number of contacts reported.

Time spent on counseling was collected via a telephone tracking system that recorded the total number of completed calls (n_c), the average time spent on completed calls (t_c), the total number of attempted calls (n_a), and the average time

spent on attempted calls (t_a). This was separately done for both sites for each call. The time spent on completed calls was adjusted for the declining number of calls from the first to the final call (i.e., drop outs). The mean time per contact spent on telephone calls at each site was calculated as follows: $t_c + (n_a / n_c) * t_a$. The overall cost estimate of the telephone calls was obtained by taking a weighted average of the per-contact costs of the two sites, weighted by the number of completed calls recorded.

Statistical Analyses. All demographic and outcome variables were compared across intervention groups at baseline. Bivariate associations between change in outcome measures and intervention were calculated using χ^2 analyses. If a measure was missing or unknown at baseline or follow-up, it was assumed that no change took place in that time period. Thus, for all participants that were lost to follow-up the intention-to-treat principle was applied and their baseline values were assumed to be unchanged. Polytomous logistic regression (using generalized logits) was used to assess the association between intervention and change in risk factors (positive and negative changes versus no change) adjusting for age, gender, race, and site. Seasonal effects were tested and found to be not significant and thus do not appear in the final model. All analyses were conducted using SAS Version 8.2 software.

Results

Demographics and Behavioral Risk Factors at Baseline. Baseline demographic characteristics are presented by condition in Table 1. The only demographic difference between the two conditions was in income; there were slightly more lower income individuals in UC compared with the PREVENT condition, and slightly more moderate income individuals in the PREVENT group than in UC ($P < 0.02$). Income was included as a covariate in outcome analyses.

Table 1. Demographic variables by intervention condition

Variable	Total (%)	UC (%)	PREVENT (%)	*P*
Age				0.19
40-59	47.6	49.3	45.6	
60+	52.4	50.6	54.3	
Gender (% male)	58.1	59.9	56.0	0.16
Marital status				0.65
Married/cohabiting	75.6	74.8	76.1	
Divorced/separated	11.3	11.0	11.7	
Widowed	7.4	8.2	6.5	
Never married	5.8	6.0	5.6	
Race/ethnicity				0.98
White non-Hispanic	82.9	83.1	82.7	
Black non-Hispanic	12.1	12.0	12.2	
Other	5.0	4.9	5.1	
Education				0.85
≤HS	24.9	24.0	26.0	
Some college	22.6	22.6	22.6	
College graduate	20.9	21.1	20.7	
Postgraduate work	31.6	32.4	30.7	
Household income				0.01
≤$15,000	7.3	9.1	5.2	
$25,001-$30,000	12.9	13.3	12.5	
$30,001-$45,000	12.8	11.0	14.9	
$45,001+	57.7	58.5	56.7	
Don't know/refused	9.3	8.1	10.7	
Health status				0.15
Excellent	31.6	30.4	33.0	
Good	51.2	53.8	48.4	
Fair/poor	17.1	15.8	18.6	
Risk factor status				
Red meat (as a risk factor)	58	58	58	ns
Fruit and vegetable	63	63	63	ns
Multivitamin intake	54	52	55	ns
Physical activity	43	43	44	ns
Alcohol use	9.2	7.8	10.7	ns
Smoking	14.3	14.3	14.4	ns

NOTE: ns, not significant.

As expected, there were significant differences between the sites on most of the demographic factors. Patients seen at the North Carolina sites had lower income, less education, were more likely to be African American, and reported poorer health status than patients seen at the Massachusetts sites. Site was included as a covariate in all analyses.

Table 1 also illustrates the high prevalence of colorectal cancer risk factors at baseline among this sample. The average number of risk factors at baseline on the multiple risk factor score was 2.4. Only 6% of participants had zero risk factors, 20% had one risk factor, 54% had two to three risk factors, 15% had four, and 5% had five or six risk factors.

Intervention Outcomes. The outcomes on the multiple risk factor index and the individual risk factors are presented in Table 2. Patients in the PREVENT condition reported significantly greater improvement than those in UC in total number of risk factors; 47% of the PREVENT group reduced their multiple risk factor score compared with 35% of the UC group ($P < 0.0001$). On individual risk factors analyzed as discrete variables (i.e., within the risk cut point or not), the PREVENT group experienced significantly greater improvement in multivitamin intake and reduction in weekly servings of red meat than the UC condition. Patients in the PREVENT condition also tended to have a lower rate of regression in their levels of physical activity over the course of the study than the UC condition (8% adding the risk factor versus 13% adding the risk factor in the respective conditions); there were no between-condition differences in smoking, alcohol, or fruit and vegetable consumption. We also evaluated change over time in continuous levels of the target health behaviors, and the patterns of results were the same.

Polytomous logistic regression model results are shown in Table 3. We modeled the intervention effect on the change in the number of risk factors (a positive change/dropping risk factors versus negative change/adding risk factors versus no change) while controlling for site, gender, age, and the number of risk factors present at baseline. All possible confounders and effect modifiers were tested for significance in bivariate models controlling for site, gender, and age. The number of baseline risk factors was the only confounder shown to be associated significantly with outcomes in bivariate analyses. We tested a site by condition interaction and found it to be nonsignificant for positive change ($P = 0.776$) and negative change ($P = 0.07$). Intervention condition was significant; the odds of having a positive change were 1.5 times greater for the PREVENT condition than for UC ($P = 0.001$). The odds of having a negative change for the PREVENT condition were 0.6 that of the UC condition ($P = 0.004$).

Baseline number of risk factors was also a significant predictor of change. Regardless of condition, participants with more risk factors at baseline were significantly more likely to have made a positive change and significantly less likely to have made a negative change (odds ratio, 1.67 and 0.60, respectively). Moreover, after controlling for gender, age, condition, and number of baseline risk factors, patients in North Carolina were 1.48 times more likely than Massachusetts patients to report negative change.

Lastly, we assessed whether those in the PREVENT condition were more successful at changing multiple risk behaviors simultaneously. We were also interested in exploring change patterns among those with a substantial number of risk factors to determine whether there was a negative effect of having more behaviors to change. We examined the number of risk factors at follow-up among those patients who had four or more risk factors at baseline ($n = 203$). Overall, 30% of those

Table 2. Intervention effect on risk factors

Risk factor status	UC	PREVENT	*P*
	n (%)	*n* (%)	
Multiple risk factor score			
Dropped one or more risk factor	228 (35)	279 (47)	0.000
No change	302 (46)	248 (42)	
Added one or more risk factor	126 (19)	64 (11)	
Multivitamin Intake			
Dropped this risk factor	94 (14)	179 (30)	0.000
No change	527 (80)	398 (67)	
Added this risk factor	35 (5)	14 (2)	
Red meat			
Dropped this risk factor	80 (12)	104 (18)	0.002
No change	511 (78)	452 (76)	
Added this risk factor	65 (10)	35 (6)	
Fruit and vegetables			
Dropped this risk factor	114 (17)	118 (47)	ns
No change	488 (74)	426 (72)	
Added this risk factor	54 (8)	47 (8)	
Alcohol			
Dropped this risk factor	15 (2)	22 (4)	ns
No change	633 (96)	556 (94)	
Added this risk factor	8 (1)	13 (2)	
Smoking			
Dropped this risk factor	11 (2)	18 (3)	0.11
No change	645 (98)	573 (97)	
Added this risk factor	—	—	
Physical activity			
Dropped this risk factor	97 (15)	76 (13)	0.007
No change	476 (73)	469 (79)	
Added this risk factor	83 (13)	76 (8)	

with four or more risk factors at baseline had two or fewer risk factors at the follow-up, reflecting a reduction of at least two risk factors (see Table 4). Further, the intervention had a significant effect on promoting multiple risk factor change among those with four or more risk factors at baseline ($P < 0.0001$).

Intervention Participation. Overall participation in the intervention was good. Sixty percent of intervention participants received four or five intervention calls, with an average of 3.4 calls per participant. The intervention materials were rated extremely high. Only 3% of intervention participants did not recall receiving the materials. Of those who did recall the materials, 89% rated them as either very helpful (44%) or helpful (45%); 3% indicated that they were unhelpful or very unhelpful. There were similar ratings regarding the helpfulness of the counseling calls, with 91% of participants rating them as very helpful or helpful, and only 2% rating them as unhelpful or very unhelpful.

Table 4. Intervention effect on change in number of risk factors for those with four or more risk factors at baseline (*n* = 211)

Study condition*	No. risk factors at 8-month follow-up			
	≤2 (*n* = 65)	3 (*n* = 76)	4 (*n* = 58)	5+ (*n* = 12)
Usual care	19%	36%	38%	7%
Intervention	43%	36%	16.%	5%
Total	31%	36%	27%	6%

*$P = 0.0002$.

Cost-Effectiveness. The total amount of time spent by health educators on telephone calls per contact was 75.2 minutes at Dana-Farber Cancer Institute and 75.0 minutes at Duke Comprehensive Cancer Center, which includes preparatory time, contact attempts, and time on the phone with participants. The overall cost per contact for telephone calls was $18.86. Thus, the cost of labor associated with delivering the intervention in the study was $37.10 (lower bound) to $42.61 (upper bound). The cost of materials was estimated to be $5.09 per participant. This includes costs of stationary, envelopes, postage, pamphlets, and incentives.

For the UC condition, the average cost of the time spent delivering the ''placebo'' intervention was $2.02 (lower bound) to $2.17 (upper bound) per contact. Thus, the net cost (upper bound) of the intervention is $42.61 + $5.09 − $2.17 = $45.53.

Cost related to dropping risk factors was calculated by dividing the net intervention cost ($45.53) by the difference in proportions that dropped at least one risk factor across the two conditions (0.12). Thus, the cost-effectiveness estimate related to multiple risk factor reduction was $379 per risk factor dropped. However, this estimate only considers intervention benefit and does not consider that some who received the intervention regressed. Thus, we computed a second cost-effectiveness estimate considering both regression and progression in terms of risk factors, which yielded a cost-effectiveness estimate of $228 per unit change in the multiple risk factor score.

Discussion

This report describes the outcomes of Project PREVENT, a multisite randomized clinical trial timed to take advantage of clinical identification of adenomatous polyps, the precursors to colorectal cancer, to encourage behavior changes that reduce risk for colorectal cancer, other cancers, and chronic disease.

Table 3. Intervention effect on change in number of risk factors adjusted for site, gender, age group, and number of baseline risk factors

	No change	Positive change/dropping risk factors	Negative change/adding risk factors
	n = 540	*n* = 507	*n* = 190
Intervention vs usual care			
OR (95% CI)	1.00 (—)	1.53 (1.19-1.98)	0.59 (0.42-0.85)
P		0.001	0.004
Baseline risk factors (increase of 1)			
OR (95% CI)	1.00 (—)	1.67 (1.50-1.87)	0.60 (0.52-0.71)
P		<0.0001	<0.0001
Site: North Carolina vs Massachusetts			
OR (95% CI)	1.00 (—)	1.23 (0.95-1.59)	1.48 (1.05-2.09)
P		0.11	0.03
Gender: female vs male			
OR (95% CI)	1.00 (—)	1.02 (0.79-1.33)	1.20 (0.85-1.70)
P		0.86	0.30
Age: 60+ vs 40-59			
OR (95% CI)	1.00 (—)	0.88 (0.68-1.13)	0.89 (0.63-1.25)
P		0.32	0.48

NOTE: OR, odds ratio; 95% CI, 95% confidence interval.

To our knowledge, no other studies have targeted this clinical event and emphasized change in multiple risk factors simultaneously. A multiple risk factor approach has great potential to maximize risk reduction because it is becoming increasingly clear that colorectal cancer and other cancers arise from a complex interplay of behavioral and genetic risk factors. It is likely that maximum benefit in risk reduction would be achieved by more comprehensive changes in lifestyle. Accordingly, these risk factors are associated with a number of other cancers, coronary artery disease, and other chronic conditions. Thus, the benefits of behavior change can be generalized to other conditions.

Indeed, 74% of the patients with adenomatous polyps had two or more risk factors for colorectal cancer. Participation in the PREVENT intervention was associated with a significantly greater reduction in prevalence of multiple risk factors for colorectal cancer compared with UC. Only about one third of UC participants dropped any risk factors during the study period, compared with almost half of the PREVENT participants. Almost one fifth of the UC group added risk factors, compared with only one tenth of the PREVENT participants. Moreover, PREVENT participants were significantly more likely to change more than one behavior than UC participants. In terms of individual risk factor change, there were significantly greater rate increases in multivitamin intake and decreases in weekly servings of red meat in the PREVENT group. The PREVENT group also had less regression in terms of physical activity compared with the UC group. No group differences were seen in smoking or alcohol consumption, which were quite low in prevalence at baseline, nor in daily servings of fruits and vegetables. Overall, these results are particularly encouraging because those with more risk factors at baseline were significantly more likely to adopt positive changes and less likely to add new risk factors. Thus, it does not seem that those with a poorer risk profile were too demoralized to benefit from the intervention.

The intervention effect should be considered in relation to the intervention intensity and cost. This intervention was delivered via mail and telephone, without the need for in-person contact. The net per-person cost of the PREVENT intervention over UC was $45.53, which is at the low end of the range of costs reported in the literature. The intervention was very cost-effective, particularly when both regression and progression of risk factors were considered. The cost-effectiveness estimate of $228 per unit change in multiple risk factor score compares favorably with the cost of smoking cessation intervention, which is in the range of $3,000 to $7,000 per quit (48). Of note, there are no cost-effectiveness analyses on multiple risk factor change in the literature with which to compare our findings.

One important issue to consider in future research is how to define the multiple risk factor index. One possibility is to use high levels of behavioral attainment that would confer the most benefit to an at-risk population, in contrast to our use of the minimum standards that are suggested by current risk reduction recommendations for the general population. However, there are no evidence-based guidelines in the literature to suggest what these standards should be for polyp patients or for most other high-risk groups. If epidemiologic evidence becomes available to suggest alternative guidelines for at-risk groups, it would be important to consider these in the calculation of the multiple risk factor index.

Some limitations of the present study should be noted. First, although the response rate was relatively high given that participants were proactively approached for participation rather than first screened for interest in health behavior change, 25% of those contacted refused to participate. We conducted the outcome analyses using both intention-to-treat analyses and the complete data set only. The findings were identical, although the odds ratios were lower with the more conservative intention-to-treat approach. Study participants were primarily well educated, likely a reflection of the fact that this was largely an insured population, and thus, the findings are generalizable only to other groups with similar levels of education and insurance coverage.

There are several important strengths of this study. This sample was drawn from several large gastroenterology clinics representing several different health care systems. The large study sample made it possible to evaluate both individual and multiple risk factor change. Both the outcome and cost-effectiveness data were analyzed using intention-to-treat, so that the findings would be conservative. The intervention was designed to have multiple components to maximize intervention effect; however, as a result, it is not possible to disentangle the contribution of individual intervention components to the study outcomes. Relatively high uptake of the intervention components suggests that the high intensity and multiple components PREVENT may be needed for patients to change multiple health behaviors.

This study shows the effectiveness of the PREVENT multiple risk factor intervention for reducing behavioral risk factors among patients who have experienced adenomatous polyps. Even among those with high levels of baseline risk factors, behavior change was possible, and the intervention has a significant effect on the level of change observed. Individuals who have had adenomatous polyps are an at-risk population who should take advantage of every opportunity to reduce their risk factors for colorectal cancer and other cancers. It is significant that the PREVENT intervention was effective in helping patients change multiple risk factors. These results provide further support that more comprehensive interventions that move beyond emphasis on a single risk factor are acceptable to patient populations, can result in improvements, and are cost-effective. Although our data do not permit us to address this specifically, previous work (49, 50) suggests that the acceptability of the PREVENT intervention may have been due to the tailored approach that enabled personalized feedback regarding individual patterns of health habits rather than more generic approaches.

References

1. Pignone M, Levin B. Recent developments in colorectal cancer screening and prevention. Am Fam Physician 2002;66:297–302.
2. Yood M, Oliveria S, Boyer J, Wells K, Stang P, Johnson C. Colon polyp recurrence in a managed care population. Arch Intern Med 2003;163:422–6.
3. Willett W, Sampson L, Stampfer M, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am J Epidemiol 1985;122:51–65.
4. Fraser G, Pearce N. Occupational physical activity and risk of cancer of the colon and rectum in New Zealand Males. Cancer Causes Control 1993;4:45–50.
5. Lynge E, Thygesen L. Use of surveillance systems for occupational cancer: Data from the Danish National System. Int J Epidemiol 1988;17:493–500.
6. Wu A, Paganini-Hill A, Ross R. Alcohol, physical activity and other risk factors for colorectal cancer: A prospective study. Br J Cancer 1987;55:687–94.
7. Gerhardsson M, Floderus B, Norell S. Physical activity and colon cancer risk. Int J Epidemiol 1988;17:743–6.
8. Gerhardsson de Verdier M, Steineck G, Hagman U. Physical activity and colon cancer: A case-reference study in Stockholm. Int J Cancer 1990;46:985–9.
9. Severson R, Nomura A, Grove J, Stemmermann G. A prospective analysis of physical activity and cancer. Am J Epidemiol 1989;13:522–9.
10. Albanes D, Blair A, Taylor PR. Physical activity and risk of cancer in the NHANES I population. Am J Public Health 1989;79:744–50.
11. Ballard-Barbash R, Schatzkin A, Albanes D, et al. Physical activity and risk of large bowel cancer in the Framingham Study. Cancer Res 1990;50:3610–3.
12. Lee I, Paffenbarger R, Hsieh C. Physical activity and risk of developing colorectal cancer among college alumni. J Natl Cancer Inst 1991;83:1324–9.
13. Longnecker M, De Verdier M, Frumkin H, Carpenter C. A case-control study of physical activity in relation to risk of cancer of the right colon and rectum in men. Int J Epidemiol 1995;24:42–50.

14. Thun M, Calle E, Namboodiri M. Risk factors for fatal colon cancer in a large prospective study. J Natl Cancer Inst 1992;83:1324–9.
15. Giovannucci E, Ascherio A, Rimm E. Physical activity, obesity, and risk of colon cancer and adenoma in men. Ann Intern Med 1995;122:327–34.
16. Giovannucci E, Colditz GA, Stampfer MJ, Willett WC. Physical activity, obesity, and risk of colorectal adenoma in women (United States). Cancer Causes Control 1996;7:253–63.
17. Neuget A, Garbowski G, Lee W, et al. Dietary risk factors for the incidence and recurrence of colorectal adenomatous polyps: A case-control study. Ann Intern Med 1991;118:91–5.
18. DeCosse J, Tsioulias G, Jacobson E. Colorectal cancer: detection, treatment, and rehabilitation. CA Cancer J Clin 1994;44:27–42.
19. Chao A, Thun M, Jacobs E, Henley S, Rodriguez C, Calle E. Cigarette smoking and colorectal cancer mortality in the cancer prevention study II. J Natl Cancer Inst 2000;92:1888–96.
20. Terry P, Ekbom A, Lichtenstein P, Feychting M, Wolk A. Long-term tobacco smoking and colorectal cancer in a prospective cohort study. Int J Cancer 2001;91:585–7.
21. Giovannucci E, Colditz G, Stampfer M, et al. A prospective study of cigarette smoking and risk of colorectal adenoma and colorectal cancer in U.S. women. J Natl Cancer Inst 1994;86:192–9.
22. Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Ascherio A, Willett WC. Intake of fat, meat, and fiber in relation to risk of colorectal cancer in men. Cancer Res 1994;54:2390–7.
23. Giovannucci E. An updated review of the epidemiological evidence that cigarette smoking increases risk of colorectal cancer. Cancer Epidemiol Biomarkers Prev 2001;10:725–31.
24. Willett WC. Diet, nutrition, and avoidable cancer. Environ Health Perspect (supplement 8) 1995;103:165–70.
25. Giovannucci E, Stampfer M, Colditz G. Relation of diet to the risk of colorectal cancer in men. J Natl Cancer Inst 1992;84:91–8.
26. Trichopoulos D, Willett W. Nutrition and Cancer. Cancer Causes Control 1996;7:3–4.
27. Willett W, Trichopoulos D. Summary of the evidence: Nutrition and Cancer. Cancer Causes Control 1996;7:178–80.
28. Jarvinen R, Knekt P, Hakulinen T, Rissanen H, Heliovaara M. Dietary fat, cholesterol and colorectal cancer in a prospective study. Br J Cancer 2001; 85:357–61.
29. Schatzkin A, Lanza E, Corle D, et al. Lack of effect of a low fat, high fiber diet on the recurrence of colorectal adenomas. Polyp Prevention Trial Study Group. N Engl J Med 2000;342:1149–55.
30. Michels KB, Giovannucci E, Joshipura KJ, et al. Prospective study of fruit and vegetable consumption and incidence of colon and rectal cancers. J Natl Cancer Inst 2000;93:879.
31. Sesink A, Termont D, Kleibeuker J, Van der Meer R. Red meat and colon cancer: Dietary haem-induced colonic cytotoxicity and epithelial hyperproliferation are inhibited by calcium. Carcinogensis 2001;22:1653–9.
32. Sesink A, Termont D, Kleibeuker J, Van der Meer R. Red meat and colon cancer: Dietary haem, but not fat, has cytotoxic and hyperproliferative effects on rat colonic epithelium. Carcinogenesis 2000;21:1909–15.
33. Bingham S. High meat diets and cancer risk. Proc Nutr Soc 1999;58: 243–8.
34. Giovannucci E, Stampfer MJ, Colditz G, et al. Multivitamin use, folate, and colon cancer in women in the Nurse's Health Study. Ann Intern Med 1998; 129:517–24.
35. Glynn S, Albanes D. Folate and cancer: A review of the literature. Nutr Cancer 1994;22:101–19.
36. King T, Marcus B, Pinto B, Emmons K, Abrams D. Cognitive-behavioral mediators of changing multiple behaviors: Smoking and a sedentary lifestyle. Prev Med 1996;25:684–91.
37. Emmons K, Marcus B, Linnan L, Rossi J, Abrams D. Mechanisms in multiple risk factor interventions: Smoking, physical activity, and dietary fat intake among manufacturing workers. Prev Med 1994;23:481–9.
38. Bandura A. Social Foundations of Thought and Action: A Social Cognitive Theory. Englewood Cliffs, N.J.: Prentice-Hall; 1986.
39. Blair S, Jacobs D, Powell K. Relationships between exercise or physical activity and other health behaviors. Public Health Rep 1985;100:172–80.
40. Hall SM, Tunstall CD, Vila KL, Duffy J. Weight gain prevention and smoking cessation: cautionary findings. Am J Public Health 1992;82: 799–803.
41. Pirie P, McBride C, Hellerstedt W, Jeffery R, Hatsukami D. Smoking cessation in women concerned about weight. Am J Public Health 1992; 82:799–803.
42. Emmons K, Shadel W, Linnan L, Marcus B, Abrams D. A prospective analysis of change in multiple risk factors for cancer. Cancer Res Ther Control 1999;8:15–23.
43. Emmons KM, Shadel WG, Linnan LA, Marcus BH, Abrams DB. A prospective analysis of change in multiple risk factors for cancer. Cancer Res Ther Control 1999;8:15–23.
44. Unger J. Stages of change of smoking cessation: Relationships with other health behaviors. Am J Prev Med 1996;12:134–8.
45. Abrams D. Integrating Basic, Clinical and Public Health Research for Alcohol-Tobacco Interactions. Vol 30. Bethesda, MD: NIH Pub; 1995.
46. Stewart A, Mills K, King A, Haskell WL, Gillis D, Ritter P. CHAMPS physical activity questionnaire for older adults: outcomes for interventions. Med Sci Sports Exerc 2001;33:1126–41.
47. Fagerstrom KO. Measuring degree of physical dependence to tobacco smoking with reference to introduction of treatment. Addict Behav 1978;3: 235–41.
48. Levy DT, Friend K. A simulation model of policies directed at treating tobacco use a dependence. Med Decis Making 2002;22:6–17.
49. Rimer BK, Glassman B. Is there a use for tailored print communications in cancer risk communication? J Natl Cancer Inst Monogr 1999;25:140–8.
50. Kreuter M, Farrell D, Olevich L, Brennan L. Tailoring health messages: customizing communication with computer technology. Mahwah, NJ: Erlbaum; 1999.

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