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## A Community-Based Feasibility Study Using Wheat Bran Fiber Supplementation to Lower Colon Cancer Risk<sup>1,2</sup>

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**Methods.** In this feasibility study, free-living older adults ( $n = 180$ ;  $\bar{x} = 67.5$  years old) were randomly assigned to one of three levels of a 3-month standardized compliance enhancement program.

**Results.** Regarding subject compliance with the 18 g/day wheat bran fiber supplement, the high compliance enhancement group had a superior regimen compliance rate (88%) versus the medium and low groups, (66 and 29%, respectively) ( $P = 0.01$ ), with similar attrition rates.

**Conclusion.** No significant gastrointestinal side effects and changes in body weight were reported. For similar efficacy, the comprehensive compliance enhancement group had the greatest cost effectiveness. © 1991 Academic Press, Inc.

### INTRODUCTION

Colorectal cancer remains a leading cause of death in the United States with an estimated 155,000 new cases and 61,000 deaths each year (1). The protective effect of fiber-containing foods on colon cancer has been noted in epidemiological, animal, and case-control studies (2). The study reported here tested the feasibility of a community-based wheat bran fiber intervention. Kritchevsky (3, 4) postulated several related protective mechanisms, e.g., increased fecal weight, decreased fecal pH, decreased transit time, and decreased fecal mutagenic activity. Even in populations consuming similar levels of total dietary fat and animal protein, the fiber intake difference is associated with significant changes of the above stool parameters in the predicted directions. Additionally, although stool parameters such as total bile acid concentration and fecal mutagenic activity are substantially affected by other dietary factors (e.g., total fat intake), increasing fiber

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intake can lower their levels independently and therefore lower the risk for colon cancer. Sufficient evidence supports the adenoma to carcinoma progression to justify trials of fiber intervention among high-risk populations (5).

The choice of wheat bran as the dietary fiber supplement providing the most protective effect from colon cancer is consistent with the findings of Reddy *et al.* (6, 7) and prior studies (8). When Reddy compared subjects in New York and Kuopio, Finland who consumed similar quantities of fat and protein, the Kuopio subjects consumed higher levels of dietary fiber and had a higher fecal fiber output. The Kuopio subjects are considered at lower risk for colon cancer. The higher fecal excretion of cholesterol metabolites may partially explain the protective effect of the dietary fiber. In addition, Reddy *et al.* (9) studied the effect of different types of supplemental fiber on fecal mutagens and bile acids in 19 human volunteers, who at baseline were found to excrete high levels of mutagens. They then consumed a controlled diet plus 10 g of dietary fiber from alternately wheat bran, oat fiber, or cellulose for 5-week periods. Concentrations of fecal secondary bile acids and mutagenic activity were significantly lower during the wheat bran and cellulose but not the oat bran fiber supplemental periods. Wheat bran fiber is composed primarily of cellulose, an insoluble, nonfermentable fiber, and hemicellulose, a soluble, somewhat fermentable fiber. Wheat bran fiber holds considerable water and its action in the bowel is to create a soft stool of fairly uniform consistency resulting in smooth peristalsis, decreased transit time, and less gas production than soluble fibers such as oat bran (10).

Amid varied research-based human dietary recommendations (11–13), the current U.S. dietary fiber intake is estimated to be 10–20 g/day (12). The National Cancer Institute recommends at least doubling current daily consumption to 25 to 35 g of dietary fiber (12). Wheat bran fiber supplementation ranging from 8 g to more than 35 g of fiber per day above baseline has been used in adults for several weeks in various metabolic studies (10, 14–16).

In this study, the feasibility of implementing a chemoprevention trial using 18 g of supplemental wheat bran fiber was investigated three ways: (a) regimen compliance rate, (b) cost effectiveness, and (c) safety with regard to side effects. The study was modeled on the decision-making process recommended for clinical trials (17), and the state-of-the-science for fiber and colon cancer, as a basis for chemoprevention trials (18).

Multiple strategies are required to deal with the various aspects of the complex behavior called subject compliance to treatment regimen (19). Research indicates people can comply to a high-fiber diet despite the magnitude of the recommended increase and problems associated with quantification of fiber consumption (20). For population-based trials the minimum compliance enhancement program required to achieve a reasonable compliance rate needs to be defined (16, 22). This feasibility study addresses the issue of the minimum needed.

Since life expectancy in the United States is over 70 years, lifestyle-modifying interventions may have several decades to protect against tumorigenesis in high-risk populations (23, 24). This feasibility study of compliance, cost, effectiveness, and safety of free-living older adults is therefore vital.

## MATERIALS AND METHODS

### *Recruitment of Subjects*

The recruitment technique comprised telephone interviews with older individuals from a retirement community in southern Arizona who responded to a randomized community mail survey inquiring about colon cancer prevention and related health behaviors (25). Sixty-five percent of those who returned the questionnaire ( $n = 345$ ) agreed to participate, and 87% of those who agreed to participate met the following subject selection criteria: age over 50, residence in the target community (i.e., >6 months/year), free-living and ambulatory, and no history of invasive cancer. Subjects reporting history of chronic diseases or gastrointestinal diseases were instructed to consult with their own physicians before participation. The project physician reviewed each of these cases and disqualified those with potential complications. The mean age in each group was no different from the total of 67.5 years ( $SD = 6.4$ , range 50–92) with a male to female ratio equal to 1, 1, and 0.6 for Groups A, B, and C, respectively. Each group had 15 married couples.

### *Treatment*

The 180 eligible subjects were randomly assigned to three compliance intervention treatment groups: low and high interventions plus the “normal condition” in the United States, i.e., an environment in which key groups recommend that people eat some kind of bran to reduce their cancer risk. Of course, the “normal controls” were expected to do least well in adhering to fiber intake recommendations. However, it was vital to document how much worse they would do. The three groups which varied in degree of compliance enhancement activity were:

Group A: Comprehensive educational program including compliance enhancement program and free fiber supplement, plus personalized problem-solving assistance (high intervention)

Group B: Free fiber supplement only (low intervention)

Group C: Letter only (control)

For Groups B and C, study personnel contact was limited to pre- and poststudy only to minimize effects on compliance behavior. At the beginning of the 3-month study, Group C subjects received the least compliance enhancement in the form of a letter encouraging them to double their dietary fiber intake to lower colon cancer risk as recommended by the National Cancer Institute, e.g., adding 2 oz ( $\frac{2}{3}$  cup) of 100% bran cereal daily.

Subjects in Group B received additional compliance enhancement. To improve treatment efficacy (26), a free, 3-month supply of fiber supplement was provided. The fiber supplement was 100% wheat bran cereal (Kellogg's All Bran) individually packaged in 1-oz unmarked boxes. To provide 18 g of wheat bran fiber, subjects were asked to consume two boxes daily. The fiber supplement was delivered to the homes of Group B subjects at the beginning of the study and unused supplement was picked up when the study was completed.

Group A also received the free fiber supplement, picked up during monthly

interviews, plus a comprehensive educational program developed to meet the needs of: (a) general compliance maintenance and (b) individual problems related to compliance (27). The standardized program also incorporated findings on compliance enhancers and detractors identified in the recruitment survey (28). Several compliance enhancement approaches were employed: contingency contract, monthly newsletters, two group meetings, daily record keeping, a recipe contest, and a recipe book consisting of recipes submitted by subjects. The specific variables addressed by these activities included health status, health threat, social support, health and personal benefits, and physiological and psychosocial barriers to compliance, all based on a Health Behavior in Cancer Prevention Model for compliance prediction (29).

Portions of the compliance enhancement program for Group A were personalized, based upon monthly self-reports of the fiber supplement intake. Subjects were classified as "good" if their mean daily intake was at least 75% of the recommended daily dose (1.5 oz fiber supplement), "marginal" (between 50 and 74%), or "poor" (<50%; <1 oz). The protocol for the marginal compliers involved a letter which acknowledged their participation in the study and encouraged them to increase their intake of the fiber supplement. For the poor compliers, the individualized problem-solving protocol assured a timely work-up of their cases, while minimizing these costly procedures for others. This protocol included individualized problem assessment and monitoring, counseling for physiological or psychosocial problems, and referral as needed. Subject time was estimated to be a total of 15 hr (5 hr/month) for subjects in Group A, 6 hr (2 hr/month) for Group B, and 2 hr for the whole study for Group C.

### *Outcome Assessment*

Outcomes in all three treatment groups were measured four ways: self-reports of fiber supplement intake, operational costs for carrying out the intervention protocol, gastrointestinal side effects, and changes in body weight. Instruments administered to all subjects at the beginning of the study included questions on general health history, bowel function (25), health behaviors (29), and usual food intake (30). When the study was completed, all subjects were asked to complete instruments related to compliance behavior, bowel function, health behaviors, and usual food intake.

*Compliance.* Several possible compliance indices were explored: self-reported intake records, box count of unused fiber supplement, and compliance score based on the intake records and telephone and/or face-to-face interviews for applicable groups. However, the assignment of compliance enhancement protocol for Group A was based solely on the intake records.

*Cost and effectiveness.* The cost analysis for this feasibility study was kept very basic and simple. Unit cost per compliant subject is used here for a relative measure of success in the three different treatment groups. It is more appropriate to use the cost per unit change in impact (i.e., effectiveness) than the cost per unit of output (i.e., efficiency) used in clinical trials because a high rate of conversion from program output to outcome (e.g., a high compliance rate) cannot be ensured (31). Costs for Treatment Groups A, B, and C included subject recruitment,

treatment randomization, postage fees, phone, travel, supplies, data management (coding and quality control of questionnaires), and related personnel costs (study coordinator, physician, and interviewers). The costs for Groups A and B also included the estimated current local market value of the fiber supplement provided free to study subjects, in addition to the cost of delivering the fiber supplement to and collecting it from the homes of those in Group B. The operational cost for Group A included the comprehensive compliance enhancement program, i.e., two group meetings, a recipe contest, monthly newsletters, contingency contract, and telephone interviews. Biochemical tests and the highly variable developmental costs related to research protocols, data collection instruments, overhead, and client time were not part of the cost analysis.

*Safety.* Short-term safety for gastrointestinal side effects (15) and metabolic function (4) was monitored using the Side Effects Monitoring Scale, adapted from the Southwest Oncology Group (32). The adapted scale is based upon (a) the perceived frequency of related gastrointestinal side effects; diarrhea, flatulence, constipation, and abdominal pain; (b) self-reports of body weight change; and (c) blood and urine chemistry profiles. Due to budgetary limitations, only Group A subjects were given the option of participating in the latter. For these 38 volunteers, biochemical tests of blood (SMA 20, serum triglyceride, total cholesterol, high- and low-density lipoprotein levels, CBC) and urine were conducted before and after fiber supplementation. In general, level 0 on the Side Effects Monitoring Scale indicates no evidence of the specified side effect due to the fiber supplementation, level 1 indicates mild side effects, level 2 indicates moderate side effects, and level 3 indicates severe side effects. The relationship between the frequency and/or magnitude of the side effect and the level of side effect is illustrated in Table 1.

## RESULTS

### *Compliance Evaluation*

Compliance outcomes are discussed here in terms of rate of attrition, number of persons consuming fiber, amount of fiber supplement intake, and individual level of compliance. Study drop-out, defined by failure to return any end-of-study questionnaires (regardless of the amount of fiber consumed), was not significantly different among Groups A (18%), B (29%), and C (18%). (Table 2). The normal controls in Group C were invaluable in assessing 3-month compliance and costs. Overall regimen compliance rate, defined as the percentage of subjects who reported consuming any of the fiber supplement, among the three groups was significantly different ( $\chi^2 = 8.7$ ;  $df = 2$ ;  $P = 0.01$ ). The high-intervention group (A) was 22% higher (88%) than the low-intervention group (B) (66%). In the control group (C), the regimen compliance rate (29%) was based upon a reported average daily increase of wheat bran fiber equivalent to 4.5 g, approximately the amount of dietary fiber provided by 0.5 oz of bran cereal.

The mean daily fiber supplement intake of regimen compliant subjects reporting at least 2 months of fiber consumption from Groups A ( $n = 51$ ) and B ( $n = 38$ ) was 13.1 and 13.0 g, respectively, which approximated 1.5 oz per day over the 3 months. On the basis of individual monthly means shown in Table 3, Group B

TABLE 1  
SIDE EFFECTS MONITORING SCALE<sup>a</sup>

	Level of side effect			
	0 (none)	1 (mild)	2 (moderate)	3 (severe)
<b>Gastrointestinal side effects</b>				
A. Diarrhea	Almost never/never	25–50% of stool	75% of stool	With every stool
B. Constipation	Daily bowel movements (BM)	4–6 BM/week	2–3 BM/week	<2 BM/week
C. Flatulence	Usually none	Daily	Usually every hour	Almost continuously
D. Abdominal pain	Almost never/never	Not more than once per week	Several times per week	Daily
Body weight	No change	<5% change	5–10% change	>10% change
Blood and urine chemistry profiles	No change	<2 SD <sup>b</sup>	2–3 SD	>3 SD

<sup>a</sup> Based on Southwestern Oncology Group (1987).

<sup>b</sup> SD, standard deviation.

initially reported a higher intake but exhibited a downward trend for the duration of the study. The mean daily intake between Groups A and B was not significantly different at any point in the study. Mean daily intake was not significantly higher among males ( $\bar{x} = 13.8$ ,  $SD = 3.2$ ,  $n = 43$ ) than females ( $\bar{x} = 12.4$ ,  $SD = 4.1$ ,  $n = 46$ ). To avoid a profound Hawthorn effect, Group C participants were included in the single, post-trial compliance measure only.

Classification of regimen compliant subjects as good, marginal, or poor based upon reported average daily intake revealed that Group B had significantly more

TABLE 2  
COMPLIANCE AND COST ANALYSIS OUTCOME MEASURES OF THE THREE TREATMENT GROUPS

	Group A Fiber supplement plus compliance enhancement program ( $n = 60$ )	Group B Fiber supplement only ( $n = 59$ )	Group C Letter only ( $n = 58$ )
Study drop-out rate <sup>a</sup> (at Month 3)	18%	29%	18%
Percentage of regimen compliant subjects <sup>b</sup>	88% ( $n = 53$ )	66% ( $n = 39$ )	29% ( $n = 17$ )
Total operational cost	\$3,021	\$2,118	\$361
Unit cost per regimen compliant subject	\$57	\$54	\$21

<sup>a</sup>  $\chi^2 = 2.8$ ;  $df = 2$ ;  $P = 0.24$ .

<sup>b</sup>  $\chi^2 = 8.7$ ;  $df = 2$ ;  $P = 0.01$ .

TABLE 3  
MEAN DAILY FIBER SUPPLEMENT INTAKE (g) AND STANDARD DEVIATION, AND SAMPLE SIZE (n)  
AMONG REGIMEN COMPLIANT SUBJECTS IN TREATMENT GROUP A AND B

	Group A	Group B
Month 1 <sup>a</sup>	12.9 ± 4.4 (n = 53)	14.4 ± 3.6 (n = 39)
Month 2 <sup>b</sup>	13.8 ± 4.3 (n = 51)	12.6 ± 3.8 (n = 38)
Month 3 <sup>c</sup>	12.5 ± 4.3 (n = 49)	11.9 ± 4.4 (n = 37)

<sup>a</sup>  $t = -1.67$ ;  $df = 90$ ;  $P = 0.099$ .

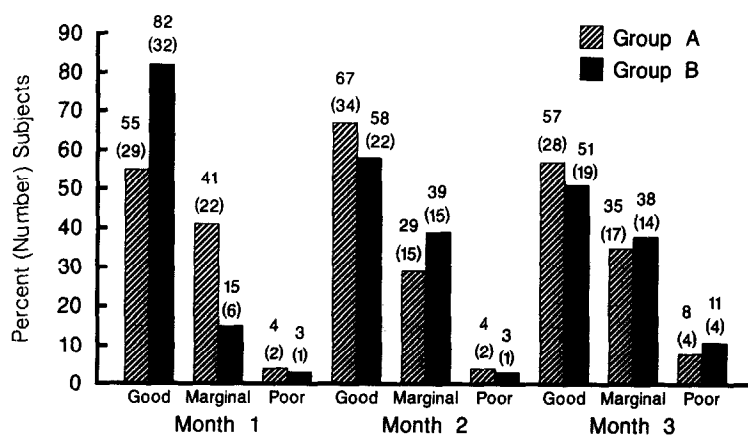
<sup>b</sup>  $t = 1.48$ ;  $df = 87$ ;  $P = 0.142$ .

<sup>c</sup>  $t = 0.60$ ;  $df = 84$ ;  $P = 0.550$ .

good compliers than Group A for the first month ( $\chi^2 = 7.67$ ,  $P = 0.02$ ), but that this compliance level was not sustained for there were no significant differences among the groups in Months 2 or 3. Figure 1 shows the distribution of compliers within each group. The percentage of good/marginal compliers was similar in both groups for all 3 months (>89%). However, the more comprehensive compliance intervention retained more subjects than the less comprehensive one and was characterized by steadier compliance levels. Both compliance interventions promoted higher fiber intake than the control.

#### Validation of Compliance Measures

In Group A, self-reported supplement intake was highly correlated with unused



Results of Significance Tests Between Groups A and B

	Chi-Square	df	Significance
Month 1	7.67	2	0.02
Month 2	1.03	2	0.60
Month 3	.84	2	3.44

FIG. 1. Monthly percentage (number) of good, marginal, and poor compliers by compliance intervention group.



package count ( $r = -0.85$ ) and the mean compliance score assigned by interviewers ( $r = 0.83$ ). There appeared to be no evidence of gross misreporting by individuals, although no physiological measure was available for validation. The small discrepancy between self-reported intake and package count may have been due to waste of unfinished cereal. Daily intake records of fiber foods were not useful as a compliance measure, since 25% of regimen compliant subjects did not fill out the forms satisfactorily. There was no indication that failure to comply to paper work was related to oral misreports of regimen intake.

### *Cost and Effectiveness*

The total operational cost and unit cost per regimen compliant subject for each treatment group were calculated from costs incurred in implementing the particular protocol and collecting data (Table 2). The comprehensive compliance enhancement program received by Group A was most expensive per compliant subject but yielded higher overall number of good compliers with more subjects eating fiber. (Without a standard deviation for the computed vector of group means, statistical tests of significance are not feasible.) Cost incurred for Group A was only a few dollars more than that for Group B, (\$57 vs \$54). However, Group B showed a downward shift from good to poor compliers over the 3 months due in part to a decrease of 31% in the number of good compliers ( $P = 0.03$ ). Although the total operational costs for the control group were the lowest, the effect on individual behavior change was also the smallest. The difference between the 66% compliance rate in Group B and the 29% in Group C can be attributed to a free supply of supplement. An additional cost of less than \$1,000 for implementing the educational program in Group A (about \$15 extra costs per recruited subject per 3 months) resulted in a further 22% increase from Group B's regimen compliance rate. The comprehensive compliance enhancement regimen had the greatest community impact and is the desirable regimen for future trials.

### *Evaluation of Side Effects*

*Gastrointestinal effects.* The severity of reported gastrointestinal side effects by regimen compliant subjects according to criteria of Side Effects Monitoring Scale was basically similar from pre- to postintervention in all three treatment groups. Flatulence and abdominal pain increased less than 15% and diarrhea increased 15.4 and 15.8% in Groups A and B, respectively. In summary, 0 to 15.8% of the subjects reported an increase of at least one level of gastrointestinal side effects after the fiber supplementation with no significant differences noted (see Table 4).

Other gastrointestinal changes observed by the compliant subjects included an increase in stool bulk among 36, 33, and 47% of the subjects in Groups A, B, and C, respectively. In addition, many reported an increase in the number of bowel movements per week, reducing the number with constipation. The magnitude of this increase was greatest in Group A who also had the highest percentage of regimen compliant subjects. They reported an increase from 8.3 BM/week (SD = 3.1) to 10.1 BM/week (SD = 3.5) ( $t = -3.75$ ;  $P = 0.001$ ). Subjects from Group B, the second highest regimen compliance rate, reported an increase from 7.6 BM/week (SD = 3.6) to 8.5 BM/week (SD = 4.4) ( $t = -1.76$ ;  $P = 0.09$ ). No

TABLE 4  
 PERCENTAGE (AND NUMBER) OF REGIMEN COMPLIANT SUBJECTS REPORTING AN INCREASE IN THE SEVERITY OF GASTROINTESTINAL SIDE EFFECTS (BASED UPON THE SIDE EFFECTS MONITORING SCALE) FOLLOWING THE FIBER SUPPLEMENTATION

	Group A	Group B	Group C
Diarrhea <sup>a</sup>	15.4 (6)	15.8 (3)	6.3 (1)
Constipation <sup>b</sup>	2.2 (1)	3.7 (1)	0
Flatulence <sup>c</sup>	14.3 (6)	14.8 (4)	12.5 (2)
Abdominal pain <sup>d</sup>	11.4 (5)	11.8 (3)	11.8 (2)

<sup>a</sup>  $\chi^2 = 0.63$ ;  $df = 2$ ;  $P = 0.63$ .

<sup>b</sup>  $\chi^2 = 0.65$ ;  $df = 2$ ;  $P = 0.72$ .

<sup>c</sup>  $\chi^2 = 0.05$ ;  $df = 2$ ;  $P = 0.98$ .

<sup>d</sup>  $\chi^2 = 0.00$ ;  $df = 2$ ;  $P = 0.99$ .

increase was noted for Group C, the least compliant group, from prestudy ( $\bar{x} = 8.7$  BM/week;  $SD = 3.6$ ) to poststudy ( $\bar{x} = 8.6$  BM/week;  $SD = 3.1$ ). Reports of stool flotation showed no change.

*Body weight.* There was no significant changes observed in self-reported body weight from pre- to poststudy among the regimen compliant subjects ( $t = -0.04$ ,  $P = 0.964$ ,  $n = 90$ ). Based upon the criteria from the Side Effects Monitoring Scale shown in Table 1, 63% ( $n = 24$ ) of the subjects in Group A, 68% ( $n = 27$ ) from Group B, and 66% ( $n = 8$ ) from Group C had experienced <5% weight change (mild). A 5–10% change (moderate) was observed by 5% ( $n = 2$ ), 10% ( $n = 4$ ), and 17% ( $n = 2$ ) of the subjects in Groups A, B, and C, respectively, while only one subject (Group A) experienced >10% change (severe). The remaining subjects reportedly did not show a change in body weight over the 3 months. These changes are similar to what would be expected in the general population.

*Biochemical parameters.* Among biochemical parameters measured in subjects from Group A who volunteered for pre- and postintervention blood and urine tests ( $n = 38$ ), significant increases were noted for sodium ( $P < 0.01$ ) and chloride ( $P < 0.001$ ) while a significant decrease was noted for calcium ( $P < 0.001$ ). All other parameters showed no significant differences.

The number of subjects exhibiting level 2 and 3 side effects (according to the Side Effects Monitoring Scale) among selected biochemical parameters at both pre- and post-test was not different than what would be expected in the general population. There was no increase in the number of subjects exhibiting level 3 side effects (greater than three standard deviations from the mean) for albumin, total protein, glucose, phosphorus, sodium, potassium, triglyceride, or high-density lipoproteins. An increase of one level 3 side effect was found for serum chloride and serum total cholesterol. Regarding level 2 side effects (two to three standard deviations from the mean), the number of subjects exhibiting increases from pre- to poststudy were noted for albumin, potassium, and triglyceride with a maximum increase of two subjects.

#### Supplement Usage Patterns

When subjects in Groups A and B were asked how they had incorporated the

fiber supplement into their daily meal patterns, monthly reports showed no significant differences between the two groups. At least 90% of the subjects reportedly consumed the fiber at breakfast with fewer than 23 and 15% consuming the supplement at lunch and dinner, respectively. The proportion eating the supplement as a snack ranged between 15 and 27%. Significantly more subjects in Group A tried incorporating the supplement into recipes (a monthly average of 51.3%) compared to Group B (27.6%). This difference was attributed to several of the compliance enhancement activities (e.g., recipe contest, newsletter) provided only to Group A. A large proportion of subjects from both groups (75–87%) reported using it in the same manner every day. There was no significant difference in the proportion of regimen compliant subjects who considered the supplement appetizing (Group A = 83%; Group B = 78%). Ninety-five percent of both Groups A and B perceived the supplement as convenient to use.

#### *Subject Evaluation of Compliance Enhancement Program*

The components of the general compliance enhancement protocol used for Group A were evaluated as helpful or somewhat helpful by 74–100% of participants. The educational activities rated, in descending order of helpfulness to regimen compliance, were the initial orientation meeting, tasting party, receiving results of blood tests, monthly compliance interviews and daily fiber intake records, monthly newsletter, and recipe contest. Results did not indicate differential compliance rates between volunteers for the laboratory procedure and others. The individualized problem-solving protocol could not be evaluated due to the small number of poor compliers.

### DISCUSSION AND RECOMMENDATIONS

Feasibility issues investigated in this study included subject compliance to regimen, cost effectiveness of compliance enhancement strategies, and potential short-term side effects. The findings from this phase were used to identify needed modifications in the compliance protocol prior to initiation of an ongoing, randomized Phase II fiber–calcium trial at the Arizona Cancer Center (33). Randomized controlled cancer chemoprevention trials using specific types and amounts of fiber in defined populations, when feasible, will provide one of the most convincing types of scientific evidence to test the fiber and colon cancer hypothesis. Results may form definitive dietary recommendations with the most risk reduction potential for the population at large.

The compliance rate of 88% to the fiber supplement regimen in the comprehensive compliance group (A) prompted adoption of methods for the next trial. The comprehensive compliance program in the pilot study was designed to address the compliance barriers associated with the recommended study fiber dose level. These strategies were evaluated as helpful by the subjects and led to a demonstrated higher and consistent compliance rate in this group. The comprehensive program improved the overall regimen compliance rate over Group B and increased the daily dose of some subjects; however, for those who stayed in the trial, the mean daily dose was similar for both groups. The compliance enhancement program ultimately impacts on the retention rate of the group rather than on

individual dose. As expected, the provision of the fiber supplement without education in Group B (low intervention) and the provision of information alone in Group C did not produce a satisfactory compliance rate.

The recommended daily dose of approximately 2 oz of bran cereal is filling and may produce short-term side effects. However, to test the hypothesis that wheat bran fiber lowers colon cancer risk, it is important to select a dose which is not only biologically effective but with which the subjects can comply. The mean of the actual daily dose in Group A (high intervention) compliant subjects suggests that a daily regimen of ½ oz of bran cereal (13.5 g dietary fiber) is more feasible for future trials than the 2 oz (18 g) per day tested here.

Findings on comparative cost per successful case indicated that a comprehensive compliance enhancement program which addresses key compliance barriers and enhancers to a specific short-term intervention was most cost effective for subject yield. Starting the compliance intervention during a run-in period will likely increase compliance.

Findings suggest that self-reported gastrointestinal side effects were similar before and after the fiber supplementation. Consistent with human metabolic studies on wheat bran supplementation, each subject may self-adjust to a dose level with the maximal tolerable level of gastrointestinal (GI) side effects (16). Consequently, GI side effects do not appear to be a major barrier to regimen compliance at this dose. A remaining issue is how much participants reduced their daily dose as a result of GI side effects. The positive effect of decreased constipation is a clear benefit, especially for older people. Potential long-term side effects are being evaluated in a current trial.

## CONCLUSION

The use of wheat bran supplement as a possible chemopreventive agent in colon cancer prevention trials is feasible. Using the compliance enhancement program, self-reported subject compliance rate to the cereal fiber regimen was satisfactory and cost effective. Subjects' mean daily consumption of the supplement suggested that the feasible dose be lowered to approximately 13.5 g of wheat bran fiber. A National Cancer Institute-funded clinical trial based on the feasibility study is now in progress to test the fiber and colon cancer hypothesis with both the self-report and biological compliance markers.

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