

## Time to Screening in the Systems of Support to Increase Colorectal Cancer Screening Trial

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### Abstract

Understanding how interventions affect time to completion of colorectal cancer screening might assist in planning and delivering population-based screening interventions. The Systems of Support to Increase Colorectal Cancer Screening (SOS) study was conducted between 2008 and 2011 at 21 primary care medical centers in Western Washington. Participants in the study, ages 50 to 73 years, were eligible if they were enrolled in Group Health (Seattle, WA) and were due for colorectal cancer screening. Of note, 4,675 recruited participants were randomized to usual care or one of three interventions with incremental levels of systems of support for completion of colorectal cancer screening. We conducted time to screening analyses of the SOS data in years 1 and 2. We investigated whether these effects were time-varying. For year 1, the intervention effects on the time to completion of colorectal cancer screening were the strongest during the first two post-randomization months and then decreased, with no significant effect after the fifth month. For year 2, the intervention effects on the time to colorectal cancer screening increased from the first to the third month and then decreased, with no significant effect after the fifth month. Hence, each of the interventions to increase colorectal cancer screening had its greatest effect within the first 3 months after being offered to participants. Future studies should test whether booster interventions offered later could increase screening rate among those who remain unscreened. Additional research is needed to develop intervention strategies for colorectal cancer screening that focus on sustained behavior over time. *Cancer Epidemiol Biomarkers Prev*; 23(8); 1683–8. ©2014 AACR.

### Introduction

Colorectal cancer is the second most common cause of cancer-related death in the United States (1, 2). Large randomized trials provide evidence that colorectal cancer screening reduces colorectal cancer-related mortality (3–5). Hence, the U.S. Preventive Services Task Force screening guidelines recommend annual high-sensitivity fecal occult blood testing (FOBT), flexible sigmoidoscopy every 5 years with interval FOBT, or colonoscopy every 10 years for Americans of ages 50 to 75 years (4). Because of less than satisfactory adherence (<66%) to colorectal cancer screening among the age-eligible adults (6, 7), considerable effort has been made to promote colorectal cancer screening. The Systems of Support to Increase Colorectal Cancer Screening (SOS) was a four-arm parallel random-

ized controlled trial comparing usual care with three interventions designed to enhance colorectal cancer screening (1). The trial enrolled 4,675 participants in Washington State and was conducted in 21 medical centers in the Puget Sound region from August 2008 to November 2011. The main article from the SOS study (8) showed that all three interventions were more effective than usual care at increasing the proportion of randomized patients who participated in colorectal cancer screening. In this report, we conducted time to colorectal cancer screening analyses of the SOS data among all randomized participants in year 1, and among those who remained eligible for screening in year 2. Knowledge of the time to complete screening might inform population-based efforts for improving screening rates, particularly for FOBT, which is recommended annually.

### Materials and Methods

#### Study participants and design

The participants and design of the SOS study have been previously described in detail (1). Briefly, participants of ages 50 to 73 years were eligible if they were due for colorectal cancer screening, defined as no FOBT within 9 months, no flexible sigmoidoscopy within 4 years, and no colonoscopy within 9 years, had no first-degree relative with colorectal cancer before the age of 60 years, and had no history of colorectal cancer or life-threatening diseases.

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The Group Health Institutional Review Board approved all study procedures. Recruited participants were randomized to usual care or one of three interventions with incremental levels of systems of support for completion of colorectal cancer screening. The randomization was stratified on age group (50–64 or 65–73), medical center, and prior receipt of colorectal cancer screening as self-reported on the baseline telephone survey.

As part of routine usual care, Group Health (Seattle, WA) patients are reminded to complete preventive health screening tests by an outreach birthday letter reminding them of screening tests that are due (including colorectal cancer screening) as well as efforts by health care providers at medical visits. In addition to usual care, those randomized to the first intervention group (Automated) were given automated support in the beginning of each study year, including mailed reminders, FOBT screening cards, information about colorectal cancer screening options, and a phone number to call in case they had questions or wanted to discuss screening preferences. Patients in the second intervention group (Assisted) were offered assisted support in addition to usual care and automated support. Assisted support included a phone call from a medical assistant (soon after automated support was provided), who documented elected screening options and sent patients' requests to their assigned physicians. Participants in the third intervention group (Navigated) received usual care, automated support, and assisted support plus care management from a nurse who provided telephone counseling about screening options, action plans, and follow-up to assure screening completion.

### Statistical methods

In our analyses, participants were followed until diagnosis with colorectal cancer, death, or disenrollment from Group Health, whichever occurred first. The end of follow-up time for year 1 analysis was the end of the 12th month after randomization, and for year 2 analysis it was the end of the 24th month after randomization. Participants were analyzed on the basis of the randomization group (i.e., intention-to-treat), with all patients included in the analyses except those who left Group Health before randomization ( $n = 10$ ), or withdrew consent after randomization ( $n = 1$ ). For year 2 analyses, we excluded participants who were no longer eligible: those with a colonoscopy ( $n = 686$ ), positive FOBT ( $n = 82$ , with or without a colonoscopy or flexible sigmoidoscopy), flexible sigmoidoscopy ( $n = 229$ ), colorectal cancer diagnosis ( $n = 9$ ), and those who died ( $n = 12$ ), or disenrolled ( $n = 197$ ) during year 1, with some participants having more than one exclusion reason. The total number of participants in the analyses for years 1 and 2 were 4,664 and 3,583, respectively.

The primary outcome in the analysis was the time to colorectal cancer screening. Kaplan–Meier survival curves (9), stratified by study groups, are presented. Cox proportional hazards regression models (10) were used to

estimate hazard ratios (HR) with Wald 95% confidence intervals (CI), and  $P$  values comparing each intervention group with usual care, adjusting for age, sex, race/ethnicity, and education. Clinic was included as a random effect (11) to account for correlations in observed screening times for participants within clinics and to accommodate potential heterogeneity of the intervention effects on time to completion of any colorectal cancer screening across clinics. We assessed the proportionality of the hazards for Cox regression based on the Schoenfeld residuals (12). We presented the smoothed time-varying effects for any colorectal cancer screening by weighted smoothing of monthly HRs (13).

In a subgroup analysis, Wald tests were used to assess whether intervention effects were different between the group that had ever completed screening (53.7%) and the group that had never completed screening (46.3%) before the study. Analyses were performed using R statistical software, version 3.0.1 (Free Software Foundation available at <http://www.r-project.org>).

## Results

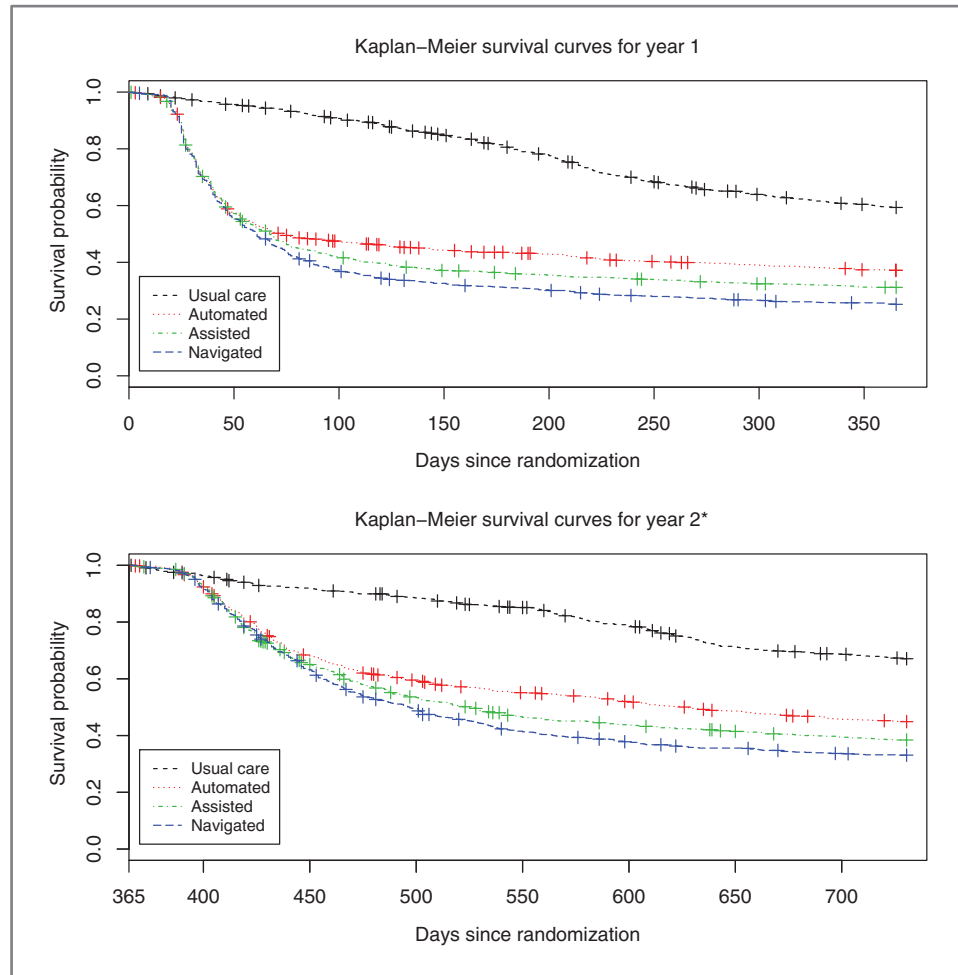
### Baseline characteristics of the participants

The baseline characteristics (socio-demographics, general health conditions, personal colorectal cancer screening history, and family history with colorectal cancer) for study participants by the randomization group have been previously published (8). Baseline characteristics did not vary substantively by group. Overall, the majority of the study participants were of age 50 to 64 years (85.2%), female (54.5%), White (80.1%), employed (71.8%), or attended college (84.9%).

### Primary outcome

Overall, 2,853 (61.2%) and 1,901 (53.1%) of eligible patients received colorectal cancer screening in years 1 and 2, respectively. The screening rates for the usual care/Automated/Assisted/Navigated groups were 39.7%, 62.2%, 68.3%, and 74.4% for year 1 and 32.1%, 54.0%, 60.2%, and 65.9% for year 2. Figure 1 shows the Kaplan–Meier survival curves corresponding to completion of any colorectal cancer screening events by group in years 1 and 2. For year 1, all the Kaplan–Meier survival curves indicated that time to screening differed in the intervention groups versus usual care [global  $P < 0.001$ ; Mantel and Haenszel (14); log-rank test]. The six log-rank tests for pairwise comparisons of the survival rates between groups resulted in  $P$  values that were mostly smaller than 0.001, except for Automated versus Assisted ( $P = 0.015$ ) and Assisted versus Navigated ( $P = 0.009$ ). Rate of colorectal cancer screening completion was ordered, with lowest rates among usual care, with stepped increases, and participants in the Navigated group having the highest colorectal cancer screening completion rate compared with other groups. The Kaplan–Meier survival curves in year 2 were similar to year 1.

**Figure 1.** Kaplan–Meier survival (nonscreened) curves for time to completion of any colorectal cancer screening for year 1 or year 2. \*, Curves for year 2 excluded participants who had colonoscopy, positive FOBT, flexible sigmoidoscopy, colorectal cancer diagnosis, died, or disenrolled before year 2.



We conducted multivariate Cox proportional hazards regression to assess the intervention effects on time to completion of any colorectal cancer screening, adjusting for age, sex, race/ethnicity, and education variables and considering clinical center as a cluster variable (Table 1). Interventions were significantly associated with time to completion of any colorectal cancer screening in both years 1 and 2 ( $P < 0.001$ ). In year 1, participants in the Automated group had a higher rate of completing any

colorectal cancer screening than those in the usual care (adjusted HR, 2.46; 95% CI, 2.19–2.77;  $P < 0.001$ ). Participants in the Assisted group also completed colorectal cancer screening at a higher rate than participants in the usual care (HR, 2.82; 95% CI, 2.50–3.16;  $P < 0.001$ ) as did participants in the Navigated group (HR, 3.23; 95% CI, 2.88–3.62;  $P < 0.001$ ). The analysis results for year 2 were similar to those for year 1, although the HRs for year 2 were generally smaller than those for year 1.

**Table 1.** Adjusted HRs for time to completion of any colorectal cancer screening for year 1 or year 2<sup>a</sup>

		Automated vs. usual care	Assisted vs. usual care	Navigated vs. usual care
Any colorectal cancer testing	Year 1			
	HR (P value)	2.46 (<0.001)	2.82 (<0.001)	3.23 (<0.001)
	95% CI	(2.19–2.77)	(2.50–3.16)	(2.88–3.62)
	Year 2			
	HR (P value)	2.25 (<0.001)	2.68 (<0.001)	3.06 (<0.001)
	95% CI	(1.94–2.61)	(2.32–3.10)	(2.65–3.53)

<sup>a</sup>Models were adjusted for age, sex, race/ethnicity, and education, with clinical center as a cluster variable.

To examine whether the intervention effects on time to completion of colorectal cancer screening remained constant over time, we conducted tests of the proportional hazards assumption based on Schoenfeld residuals. The *P* values associated with the tests for proportional hazards in both years 1 and 2 were smaller than 0.001, indicating that the effect of the intervention may vary with time. We further estimated the monthly HRs for the completion of any colorectal cancer screening in years 1 and 2 (Fig. 2). HRs increased from randomization to the second post-

randomization month, and then decreased. The ratios were generally large (greater than 8) during the first 2 months after randomization, suggesting that the intervention effects on the time to completion of colorectal cancer screening were stronger during the first 2 post-randomization months compared with later times. The HRs appeared to decrease gradually and the intervention effect disappeared by the sixth month after randomization in year 1. Similar time trends with smaller HRs were found in year 2, but with the largest effect at the third month.

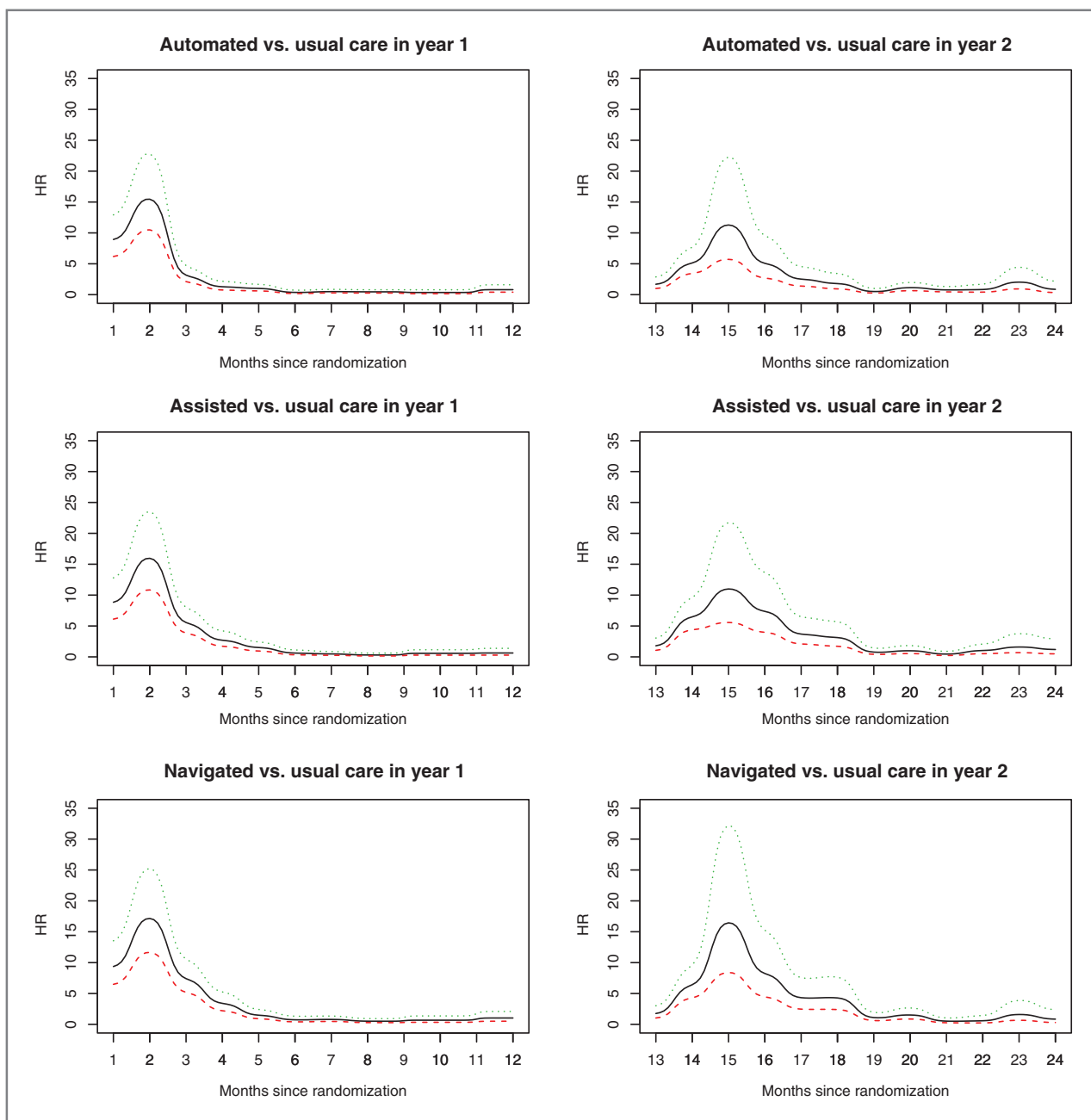


Figure 2. Time-varying adjusted HRs for time to completion of any colorectal cancer screening in years 1 and 2: the solid curves are the estimated HR curves and the dashed curves represent the 95% CIs.

In subgroup analyses, the overall colorectal cancer screening rates for the group with prior screening were higher than the group without prior screening ( $P < 0.001$ ; ref. 8). There was a difference in screening rate by prior screening within each group ( $P < 0.001$ ). However, the intervention effects among the individuals with prior screening were not significantly different from those without prior screening (data not shown).

## Discussion

To our knowledge, very few studies have examined the duration of intervention effects on colorectal cancer screening or other preventive health behaviors. We found that each of the interventions to increase colorectal cancer screening had its greatest effect within the first few months after being offered to participants. The intervention effects for colorectal cancer screening compared with usual care changed over time, with the greatest effects in the first 2 months of year 1. For year 2, the intervention effects for colorectal cancer screening peaked at the third month. The difference between the two years is likely because in year 1, interventions were delivered immediately after randomization as all participants were overdue for colorectal cancer screening. However, in year 2, timing of interventions depended on screening in the prior year. For those completing FOBT in year 1, interventions would not begin until 12 months after the test, with those taking more time to complete FOBT being offered year 2 interventions later. Delay in screening time would become more prominent in a longer study on average. In subgroup analysis, although individuals with prior screening had higher screening rates for each randomization group, intervention effects were similar to those without prior screening. This implies that intervention strategies would not need to differ by prior screening.

Limitations of our study include only 2 years of observation. Also, we did not do chart audits to determine indication. Hence, most colorectal cancer tests were probably done for screening, but some were for diagnosis, surveillance, or treatment. Third, those most likely to adhere to screening might decide to have a colonoscopy, with those remaining eligible less likely to respond to stepped interventions, with differences between groups decreasing in subsequent years. Finally, the presentation

is for overall colorectal cancer screening, not specific tests. For FOBT, the intervention effects were similar to those for overall colorectal cancer screening. However, the study did not have sufficient power to examine time to colonoscopy or flexible sigmoidoscopy screening.

Our study has implications for resource utilization, as organizations may choose to do screening outreach as a one-time bolus or stagger outreach over time. Knowing that most people who respond to interventions will do so in a short time period is important for deciding how to structure and time outreach. Because intervention effects happen quickly but diminish over time, additive interventions might be offered later to boost screening among those who remain unscreened. One example of this might be adding a reminder to the electronic health record after 4 months post-due. This would identify a patient's lack of screening after population-based screening was offered, thus providing an opportunity at clinic visits to address issues related to nonadherence or add additional evidence-based interventions, such as providing FOBT kits at the time of a flu shot (15). Future assessments of time to screening might also include examining to what degree patterns of screening completion affect colorectal cancer outcomes, including detection of interval colorectal cancers and stage at detection.

## Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

## Authors' Contributions

**Conception and design:** C.-Y. Wang, S.W. Vernon, B.B. Green

**Development of methodology:** C.-Y. Wang, B.B. Green

**Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.):** S. Fuller

**Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis):** C.-Y. Wang, J.D. Tapsoba, J. Chubak, S. Fuller

**Writing, review, and/or revision of the manuscript:** C.-Y. Wang, J.D. Tapsoba, M.L. Anderson, S.W. Vernon, J. Chubak, S. Fuller, B.B. Green

**Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases):** S. Fuller, B.B. Green

**Study supervision:** B.B. Green

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