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Non-compliance with the initial screening exam visit in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial

Pamela M. Marcus[a], **Sheryl L. Ogden**[b], **Lisa H. Gren**[c], **Jeffery C. Childs**[d], **Shannon M Pretzel**[e], **Lois E. Lamerato**[f], **Kayo Walsh**[g], **Heather M. Rozjabek**[a,h], **Jerome Mabie**[i], **Brett Thomas**[i], and **Tom Riley**[i]

Pamela M. Marcus: marcusp@mail.nih.gov; Sheryl L. Ogden: Sheryl.ogden@ucdenver.edu; Lisa H. Gren: Lisa.gren@hsc.utah.edu; Jeffery C. Childs: jeff.childs@hsc.utah.edu; Shannon M Pretzel: Shannon.pretzel@ucdenver.edu; Lois E. Lamerato: llamera1@hfhs.org; Kayo Walsh: walsh@hcp.med.harvard.edu; Heather M. Rozjabek: heather.rozjabek@gmail.com; Jerome Mabie: mabiej@imsweb.com; Brett Thomas: thomasb@imsweb.com; Tom Riley: rileyt@imsweb.com

[a]National Cancer Institute, Division of Cancer Control and Population Sciences, 9609 Medical Center Dr, Room 4E-608, Bethesda, MD, USA 20892-9763

[b]Colorado Colorectal Screening Program, University of Colorado Cancer Center, University of Colorado Anschutz Medical Campus, 13001 E 17th Pl, Aurora, CO, USA 80045

[c]University of Utah, Department of Family and Preventive Medicine. 375 Chipeta Way, Salt Lake City, UT, USA 84108

[d]University of Utah, Division of Oncology. 2000 Circle of Hope, Room LL376, Salt Lake City, UT, USA 84112

[e]University of Colorado Anschutz Medical Campus.13001 E 17th Pl, Aurora, CO, USA, 80045

[f]Department of Public Health Sciences, Henry Ford Health System, 1 Ford Place, Detroit, MI, USA 48202

[g]Harvard Medical School, 180 Longwood Ave. Boston, MA, USA 02115

[h]Drexel University School of Public Health, 1505 Race St., Philadelphia, PA, USA 19102

[i]Information Management Systems. 6110 Executive Blvd, Rockville, MD, USA 20852

Abstract

Corresponding author: Pamela M. Marcus, National Cancer Institute, Division of Cancer Control and Population Sciences, 9609 Medical Center Dr, Room 4E-608, Bethesda, MD 20892-9763, 240-276-6901; marcusp@mail.nih.gov.

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Objective—Identify predictors of non-compliance with first round screening exams in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial.

Method—PLCO was conducted from 1993–2011 at 10 US institutions. A total of 154,897 healthy men and women ages 55–74 years were randomized. Intervention arm participants were invited to receive gender-appropriate screening exams for prostate, lung, colorectal and ovarian cancer. Using intervention-arm data (73,036 participants), non-compliance percentages for 13 covariates were calculated, as were unadjusted and adjusted odds ratios (ORs), and 95% confidence intervals. Covariates included demographic factors as well as factors specific to PLCO (e.g., method of consent, distance from screening center).

Results—The rate of non-compliance was 11% overall but varied by screening center. Significant associations were observed for most covariates but indicated modest increases or decreases in odds. An exception was use of a two-step consent process (consented intervention arm participants for exams after randomization) relative to a one-step process (consented all participants prior to randomization) (OR: 2.2, 95% CI: 2.0–2.5). Non-compliance percentages increased with further distance from screening centers, but ORs were not significantly different from 1.

Conclusions—Many factors modestly influenced compliance. Consent process was the strongest predictor of compliance.

Keywords

Mass screening; adherence; compliance; cancer; randomized controlled trial as subject

BACKGROUND

The success of randomized controlled trials (RCTs) depends upon many accomplishments, including meeting or exceeding pre-specified levels of compliance with interventions. Failure to meet compliance goals can reduce statistical power, which may necessitate recruitment of more participants than originally planned or extension of follow-up. These changes can be deleterious, particularly if funds are not available for unanticipated activities or the pool of potential participants has become limited. Therefore, it is critical to identify characteristics that affect compliance.

Patient-related predictors of compliance with therapeutic drug regimens for cancer, both in experimental and community-based settings, have been studied extensively, demonstrating the clinical community's recognition of the importance of compliance when patients or subjects are ill. Compliance with chemopreventive regimens has been reported for RCTs of persons at above-average risk of cancer of the breast [1,2] and lung [3], as well as RCTs like the Women's Health Initiative, which enrolled average risk women and had breast and colon cancer as primary endpoints [4]. Predictors of screening regimen compliance in RCTs of persons at average risk who reside in the developed world have been published for only one trial (the UK flexible sigmoidoscopy trial) [5][1], but only race and attitudes concerning

[1]Results have been published from the French component of the European Randomized Study of Prostate Cancer Screening [6], but are not available in English, and thus are not considered.

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colorectal cancer and screening for that cancer were examined. Also, this trial randomized persons prior to consenting them for screening exams, and thus did so without their knowledge.

To explore multiple predictors of compliance in mass screening RCTs conducted in the US, we analyzed data from the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO), an RCT of cancer screening efficacy in men and women ages 55–74 years [7]. Roughly half the 154,897 participants were randomly assigned to an intervention arm and offered specific screening exams multiple times during their first six years of enrollment. These exams required a clinic visit that included a blood draw and, at certain study visits, other invasive and non-invasive clinical procedures.

METHODS

The PLCO Trial

PLCO, a multiphasic RCT, began in 1992, enrolled participants through mid-2001, screened through 2006, and followed each participant until withdrawal, death, 13 years of follow-up, or December 31, 2009 (whichever occurred first) [7]. Final primary results were published in 2011 and 2012 [8–11]. A total of 154,897 participants, aged 55–74 years at entry, were enrolled at one of ten screening centers nation-wide and were randomized to either an intervention or control arm [12]. At baseline, control arm participants were advised to receive their usual medical care, and intervention arm participants were offered a blood-based PSA exam and digital rectal exam (prostate, men only), a single view chest x-ray (lung), a flexible sigmoidoscopy (colorectal), and a blood-based CA-125 exam and transvaginal ultrasound (ovarian, women only). For prostate and ovarian cancer, blood-based exams were offered annually for five more years, and invasive exams were offered annually for three more years. For lung cancer, ever smokers were offered chest x-ray annually for three more years; never smokers were offered that test annually for two more years. For colorectal cancer, one additional flexible sigmoidoscopy was offered at either year 3 or 5, with year of exam dependent on date of enrollment due to a mid-study protocol change. In almost all instances, all exams for a given study year were performed at a single clinic visit that lasted no more than 2 hours. All screening exams were offered at no cost to the participant; some screening centers provided gas cards or taxi vouchers to offset the cost of transportation to the screening center. Either at or prior to the first screening visit, participants were asked to complete the Baseline Questionnaire Form (BQF), which was gender-specific and queried participants about numerous factors, including demographics, prior and current health history, and family history of cancer.

Informed consent

All screening centers received Institutional Review Board approval to conduct trial activities. Two methods of consent were used: single and dual. Seven centers used a single consent process, which consented for enrollment and randomization at the same time. The remaining three (Henry Ford Health System, Washington University School of Medicine, and Pacific Health Research and Education Institute) initially used a dual consent process. This process began with consent for administration of the BQF and follow-up for cancer

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incidence and vital status. Consented participants were then randomized, without their knowledge, to the intervention or control arm, and only participants randomized to the intervention arm were told of their assignment; they also received a second consent, which consented for administration of screening exams. The single consent method was expected to increase compliance in the intervention arm but lead to contamination in the control arm; the dual consent method, while expected to decrease participation in the intervention arm, was expected to decrease contamination in the control arm. Contamination refers to the receipt of the screening exams under study by control arm participants. Because the rate of refusal to participate among dual-consent participants randomized to the intervention arm was unacceptably high, the three screening centers switched to the single consent process, with two switching in 1995 and one in 1997.

Compliance

We examined compliance with the first screening round, because all intervention arm participants were offered all screening exams. We chose not to create a compliance index that reflected compliance across study years for a number of reasons: participant relocation, changes in eligibility for exams due to protocol changes and cancer diagnoses, and expected-to-be important compliance predictors, such as declining health status, for which we had no or incomplete data. Participants were classified as non-compliant if no screening exams were completed within 11 months of randomization, and compliant otherwise.

Analysis

All intervention arm participants who did not die or withdraw between randomization and the first screening visit were included in our analyses, although we excluded those who did not complete the BQF or omitted an answer for at least one of the questions under consideration. We examined the relationship between non-compliance and age at randomization, gender, race, educational attainment, body mass index (BMI), presence or history of a co-morbidity at baseline (bronchitis, cirrhosis, diabetes, emphysema, heart attack, hepatitis, stroke, or personal history of cancer), smoking status, marital status, occupation at baseline, family history of a PLCO cancer, screening center, consent type, and year of randomization. The three screening centers (University of Colorado Anschutz Medical Campus, Henry Ford Health System, University of Utah Health Sciences Center) with an interest in the relationship of travel distance and non-compliance used Mapquest.com to calculate, for 1500 randomly selected participants who were eligible for the first screening visit (500 at each center), the distance from the participants' baseline home addresses to the screening center. Distance was categorized using screening center-specific tertile values due to variation in population density in the catchment areas of the three centers. We used logistic regression models to calculate both unadjusted and adjusted odds ratios. SAS statistical software (Version 9) was used for all statistical analyses.

RESULTS

Entire cohort

Of the 77,445 participants randomized to the intervention arm, 77,436 were eligible for the first screening visit. Our analyses included the 73,036 participants with complete covariate

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information, or 94% of those eligible for the first screening visit. The average rate of non-compliance in this group was 11%. Rates of non-compliance varied by screening center: they were very low at the University of Alabama at Birmingham (2%) and the University of Minnesota School of Public Health (2%) screening centers, but high at the Henry Ford Health System screening center (26%). For factors other than screening center, the lowest non-compliance rates were observed for males (8%), participants with college degrees or post-graduate training (8%), and persons enrolled using the single consent method (9%); the highest non-compliance rates were observed for participants enrolled using the dual method (29%), participants with a BMI of 18.5 or less (21%) and participants who classified their occupational status as disabled/extended sick leave (20%). (Table 1)

Unadjusted odds ratios for consent type, race, smoking status, and occupation were attenuated after adjustment for all variables in multivariate logistic regression models. In some instances, adjustment resulted in a change from a statistically significant association to one that was not. An example is the odds of non-compliance for Black, non-Hispanic participants: the unadjusted odds ratio was 1.6 (95% CI: 1.5–1.8) and the adjusted odds ratio was 0.9 (95% CI: 0.8–1.0). (Table 2)

A number of adjusted odds ratios were significant but indicated modest increases or decreases in risk of non-compliance. A notable exception was use of the dual consent method (OR: 2.2, 95% CI: 2.0–2.5), relative to the single consent method. Significant odds ratios of 1.5 or greater also were observed for those with a BMI of 18.5 or less, relative to those who had a BMI of 18.6–25.0 (OR: 1.6, 95% CI: 1.3–2.0), and those who were disabled or on extended sick leave, relative to those who were working (OR: 1.5, 95% CI: 1.3–1.7). Significant odds ratios less than 1 were observed for Asian participants relative to White, non-Hispanic participants (OR: 0.8, 95% CI: 0.6–0.9), persons with college degrees or post-graduate training relative to those whose highest attained education was high school (OR: 0.8, 95% CI: 0.7–0.8), males (OR: 0.7, 95% CI: 0.7–0.8), and participants randomized in 1993 or 1994 (OR: 0.4, 95% CI: 0.4–0.5) and 1999 or 2000 (OR: 0.8, 95% CI: 0.8–0.9), relative to participants randomized in 1995 or 1996. Many screening centers had significant odds ratios less than 1, as the University of Colorado Anschutz Medical Campus screening center was used as the reference category and had one of the higher rates of non-compliance. (Table 2)

Distance subset

Of the 1500 randomly selected participants for distance analyses, 1425 (95%) had complete covariate information and were included. Non-compliance in the distance subset was 18%, which was the same as non-compliance among the totality of participants from those three centers. Patterns of non-compliance were similar in the subset to those in the entire cohort, although rate of non-compliance for the dual consent method was 37% (OR: 7.4, 95% CI: 3.0–18.3). The non-compliance percentages for the tertiles of distance from the screening center were 14% (nearest), 18% (midrange), and 20% (furthest), respectively. The odds ratios for the midrange and far categories, relative to the bottom tertile, were 1.2 and 1.4, respectively, but neither was significantly different from 1.0 (95% CIs: 0.8–1.8 and 1.0–2.1, respectively).

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DISCUSSION

Compliance with PLCO's first screening visit was nearly 90%. Few factors impacted non-compliance in a more-than-modest manner. Our strongest finding, that a dual-step consent process increased the odds of non-compliance more than two-fold, suggests that willingness to participate in observational research does not guarantee willingness to participate in interventional research, and that processes that consent participants for activities after they are randomized should be carefully considered before use.

The UK flexible sigmoidoscopy trial, which examined the association of compliance and race, observed that relative to whites, blacks were more likely to be compliant and Asians less likely to be compliant, but odds ratios were not significantly different from 1 [5]. These patterns are opposite those in the PLCO cohort. Given the minimal data available for compliance in screening RCTs, we compared our findings to RCTs of cancer chemoprevention. In the CARET trial, a trial of lung cancer conducted in above-average risk males and females, patterns of non-compliance by age and gender were comparable to those seen in PLCO [3]. BCPT, a trial of women at above-average risk of breast cancer, observed patterns similar to those of PLCO for age, smoking status, and education [2]. In the WHI supplemental calcium and vitamin D trial, a study of healthy women that examined multiple endpoints including breast and colorectal cancer, patterns of non-compliance for marital and smoking status were similar to PLCO in terms of direction, but patterns of non-compliance for race (in particular, for African-Americans) and age were not [4]. In the aforementioned chemoprevention studies, magnitude of associations was typically modest, as in our data. The fact that in our data certain unadjusted odds ratios for variables typically thought to be associated with non-compliance, like smoking and race, were attenuated after adjustment indicates that it may be misleading to examine and draw conclusions about these variables in other studies without consideration of factors that correlate with them.

The expected benefit of the dual-consent method was to keep contamination low, but low rates of participation among those randomized to the intervention arm were higher than expected. Therefore, the centers that began with the dual-consent method ultimately changed to the single-consent method. There are two lessons to be learned: that participation in an observational study should not be taken to mean willingness to participate in interventional research, and that it is best for to consent participants for interventional activities, especially those that are invasive, prior to randomization so that non-participation, including non-compliance, is minimized and study power can be maintained. If a situation arises in which a "randomize-before-consent" approach must be used, researchers and study coordinators must go to extra efforts to ensure that trial integrity is not compromised due to non-compliance. The fact that the strength of the association of the dual-consent method and non-compliance was meaningfully attenuated after adjustment suggests that targeted approaches to decrease non-compliance in such situations might be effective.

Our restriction to compliance with the first screen limits the generalizability of our results. Risk of non-compliance is likely to change over time as life events, such as aging, disease development, and change in employment, occur. Our findings, therefore, only are relevant to non-compliance soon after trial enrollment. In addition, the BQF was not designed to

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capture reasons for non-compliance, so we have no data on factors that are certain to impact non-compliance, such as mobility difficulties and other impediments to traveling to a screening center. We would like to note, however, that in our experience the most important factor is the relationship between participants and study staff, something that is multi-dimensional and thus difficult, if not impossible, to measure.

Strengths of our study include a large sample size, one that allowed us to examine odds of non-compliance for some covariate levels that typically have low prevalence, such as low levels of education. We also were able to include many covariates in multivariate models to account for potential confounding.

CONCLUSIONS

In PLCO, a large multi-phasic cancer screening RCT, many factors significantly influenced non-compliance with the first round of exams, including BMI, employment status, and race, but did so only modestly. A process that consented intervention arm participants for screening exams after randomization increased odds of non-compliance two-fold, suggesting that use of this method should be carefully considered before its implementation.

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ABBREVIATIONS

PLCO	Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial
BQF	Baseline Questionnaire Form

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HIGHLIGHTS

- Many factors modestly affected non-compliance with the first screening exam visit
- The strongest predictor was method of consent
- Consent after randomization significantly increased non-compliance two-fold.
- These results are relevant for RCTs of healthy persons ages 55–74

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Table 1

Non-compliance by baseline characteristics in PLCO (10 US screening centers; 1993–2011)

	All					Sampled for distance questions				
	Eligible* for any T0 screen	Compliant		Not compliant		Eligible* for any T0 screen	Compliant		Not compliant	
	N	N	%	N	%	N	N	%	N	%
All intervention arm participants	77,436	67,466	87.1	9970	12.9	1500	1223	81.5	277	18.5
Complete covariate information	73,036	65,243	89.3	7793	10.7	1425	1176	82.5	249	17.5
Characteristics										
Age at randomization (years)										
Younger than 59	24,450	21,932	89.7	2518	10.3	425	349	82.1	76	17.9
60–64	22,470	20,201	89.9	2269	10.1	465	393	84.5	72	15.5
65–69	16,413	14,631	89.1	1782	10.9	315	263	83.5	52	16.5
70 or older	9703	8479	87.4	1224	12.6	220	171	77.7	49	22.3
Gender										
Female	36,998	32,213	87.1	4785	12.9	755	606	80.3	149	19.7
Male	36,038	33,030	91.7	3008	8.3	670	570	85.1	100	14.9
Race										
White, non-Hispanic	64,756	58,160	89.8	6596	10.2	1230	1018	82.8	212	17.2
Black, non-Hispanic	3623	3059	84.4	564	15.6	109	84	77.1	25	22.9
Hispanic	1358	1154	85.0	204	15.0	70	61	87.1	9	12.9
Asian	2719	2399	88.2	320	11.8	8	8	100	0	.
Pacific Islander	384	310	80.7	74	19.3	0	.	.	0	.
American Indian	196	161	82.1	35	17.9	8	5	62.5	3	37.5
Education										
Less than high school	5305	4490	84.6	815	15.4	119	84	70.6	35	29.4
High school grad	16,692	14,732	88.3	1960	11.7	304	248	81.6	56	18.4
Post HS/some college	25,109	22,248	88.6	2861	11.4	516	423	82.0	93	18.0

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	All					Sampled for distance questions				
	Eligible* for any T0 screen	Compliant		Not compliant		Eligible* for any T0 screen	Compliant		Not compliant	
	N	N	%	N	%	N	N	%	N	%
College grad/postgrad	25,930	23,773	91.7	2157	8.3	486	421	86.6	65	13.4
BMI (kg/m^2)										
0 – 18.5	552	439	79.5	113	20.5	10	8	80.0	2	20.0
18.6 – 25.0	23,950	21,273	88.8	2677	11.2	467	377	80.7	90	19.3
25.1 – 30.0	30,792	27,771	90.2	3021	9.8	613	527	86.0	86	14.0
> 30	17,742	15,760	88.8	1982	11.2	335	264	78.8	71	21.2
Comorbidity score										
No	52,994	47,879	90.3	5115	9.7	1003	847	84.4	156	15.6
Yes	20,042	17,364	86.6	2678	13.4	422	329	78.0	93	22.0
Cigarette smoking status										
Never smoker	34,207	30,799	90.0	3408	10.0	699	592	84.7	107	15.3
Current smoker	7792	6622	85.0	1170	15.0	153	115	75.2	38	24.8
Former smoker	31,037	27,822	89.6	3215	10.4	573	469	81.8	104	18.2
Marital status										
Married/living as married	55,450	50,205	90.5	5245	9.5	1082	895	82.7	187	17.3
Formerly married	15,111	12,897	85.3	2214	14.7	303	251	82.8	52	17.2
Never married	2475	2141	86.5	334	13.5	40	30	75.0	10	25.0
Current occupation										
Homemaker	8303	7252	87.3	1051	12.7	177	133	75.1	44	24.9
Working	29,381	26,438	90.0	2943	10.0	527	442	83.9	85	16.1
Unemployed	757	643	84.9	114	15.1	11	9	81.8	2	18.2
Retired	31,326	28,136	89.8	3190	10.2	641	542	84.6	99	15.4
Disabled /extended sick leave	1704	1360	79.8	344	20.2	32	21	65.6	11	34.4
Other	1565	1414	90.4	151	9.6	37	29	78.4	8	21.6
Family history of PLCO cancer										

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	All					Sampled for distance questions				
	Eligible* for any T0 screen	Compliant		Not compliant		Eligible* for any T0 screen	Compliant		Not compliant	
	N	N	%	N	%	N	N	%	N	%
Yes	20,470	18,530	90.5	1940	9.5	393	326	83.0	67	17.0
No	50,808	45,177	88.9	5631	11.1	991	819	82.6	172	17.4
Possibly	1758	1536	87.4	222	12.6	41	31	75.6	10	24.4
Screening center**										
Colorado	6194	5351	86.4	843	13.6	480	411	85.6	69	14.4
Georgetown	3470	3335	96.1	135	3.9	0	0	.	0	.
Pacific Health	4992	4271	85.6	721	14.4	0	0	.	0	.
Henry Ford	11,585	8573	74.0	3012	26.0	448	311	69.4	137	30.6
Minnesota	12,786	12,512	97.9	274	2.1	0	0	.	0	.
Washington University	7333	6371	86.9	962	13.1	0	0	.	0	.
Pittsburgh	8405	7855	93.5	550	6.5	0	0	.	0	.
Utah	7144	6526	91.3	618	8.7	497	454	91.3	43	8.7
Marshfield	8074	7454	92.3	620	7.7	0	0	.	0	.
Alabama	3053	2995	98.1	58	1.9	0	0	.	0	.
Consent type										
Single	65,971	60,210	91.3	5761	8.7	1075	954	88.7	121	11.3
Dual	7065	5033	71.2	2032	28.8	350	222	63.4	128	36.6
Randomization year										
1993–1994	7950	7244	91.1	706	8.9	221	190	86.0	31	14.0
1995–1996	24,563	21,572	87.8	2991	12.2	541	408	75.4	133	24.6
1997–1998	22,330	19,865	89.0	2465	11.0	397	346	87.2	51	12.8
1999–2000	16,855	15,382	91.3	1473	8.7	248	216	87.1	32	12.9
2001	1338	1180	88.2	158	11.8	18	16	88.9	2	11.1
Distance from screening center										
Tertile 1	N/A	N/A	N/A	N/A	N/A	478	410	85.8	68	14.2
Tertile 2						476	391	82.1	85	17.9

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	All					Sampled for distance questions				
	Eligible* for any T0 screen	Compliant		Not compliant		Eligible* for any T0 screen	Compliant		Not compliant	
	N	N	%	N	%	N	N	%	N	%
Tertile 3						471	375	79.6	96	20.4

*Excludes participants who withdrew or died between randomization and the first screening visit.

**Complete names and locations of screening centers can be found in the Funding section of this manuscript.

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Table 2

Odds ratios (OR) and 95% confidence intervals (CI) of non-compliance according to baseline characteristics in PLCO (10 US screening centers; 1993–2011)

	% Non-compliant	Unadjusted* OR (95% CI)	Adjusted*,** OR (95% CI)
Age at randomization (years)			
Younger than 50	10.3	Reference	Reference
60–64	10.1	1.0 (0.9–1.0)	1.0 (0.9–1.1)
65–59	10.9	1.1 (1.0–1.1)	1.1 (1.0–1.2)
70 or older	12.6	**1.3 (1.2–1.4)**	**1.3 (1.2–1.4)**
Gender			
Female	12.9	Reference	Reference
Male	8.3	**0.6 (0.6–0.6)**	**0.7 (0.7–0.8)**
Race			
White, non-Hispanic	10.2	Reference	Reference
Black, non-Hispanic	15.6	**1.6 (1.5,1.8)**	0.9 (0.8–1.0)
Hispanic	15.0	**1.6 (1.3–1.8)**	1.1 (0.9–1.3)
Asian	11.8	1.2 (1.0–1.3)	**0.8 (0.6–0.9)**
Pacific Islander	19.3	**2.1 (1.6–2.7)**	1.2 (0.9–1.6)
American Indian	17.9	**1.9 (1.3–2.8)**	1.2 (0.8–1.8)
Education			
Less than high school	15.4	**1.4 (1.2–1.5)**	**1.2 (1.1–1.3)**
High school grad	11.7	Reference	Reference
Post HS/some college	11.4	1.0 (0.9–1.0)	1.0 (0.9–1.0)
College grad/postgrad	8.3	**0.7 (0.6–0.7)**	**0.8 (0.7–0.8)**
BMI (kg/mˆ2)			
0 – 18.5	20.5	**2.0 (1.7–2.5)**	**1.6 (1.3–2.0)**
18.6 – 25.0	11.2	Reference	Reference
25.1 – 30.0	9.8	**0.9 (0.8–0.9)**	1.0 (0.9–1.0)
> 30	11.2	1.0 (0.9–1.1)	1.0 (0.9–1.0)
Comorbidity score			
No	9.7	Reference	Reference
Yes	13.4	**1.4 (1.4–1.5)**	**1.3 (1.2–1.4)**
Cigarette smoking status			
Never smoker	10.0	Reference	Reference
Current smoker	15.0	**1.6 (1.5–1.7)**	**1.3 (1.2–1.4)**
Former smoker	10.4	1.0 (1.0–1.1)	1.1 (1.0–1.1)
Marital status			
Married/living as married	9.5	Reference	Reference

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	% Non-compliant	Unadjusted* OR (95% CI)	Adjusted*,** OR (95% CI)
Formerly married	14.7	**1.6 (1.6–1.7)**	**1.3 (1.2–1.3)**
Never married	13.5	**1.5 (1.3–1.7)**	**1.3 (1.2–1.5)**
Current occupation			
Working	10.0	Reference	Reference
Homemaker	12.7	**1.3 (1.2–1.4)**	1.0 (0.9–1.1)
Unemployed	15.1	**1.6 (1.3–2.0)**	**1.3 (1.1–1.7)**
Retired	10.2	1.0 (1.0–1.1)	0.9 (0.9–1.0)
Disabled/extended sick leave	20.2	**2.3 (2.0–2.6)**	**1.5 (1.3–1.8)**
Other	9.6	1.0 (0.8–1.1)	0.9 (0.8–1.1)
Family history of a PLCO cancer			
No	11.1	Reference	Reference
Yes	9.5	**0.8 (0.8–0.9)**	**0.8 (0.8–0.9)**
Possibly	12.6	1.2 (1.0–1.3)	1.1 (1.0–1.3)
Screening center***			
Colorado	13.6	Reference	Reference
Georgetown	3.9	**0.3 (0.2–0.3)**	**0.3 (0.2–0.3)**
Hawaii	14.4	1.1 (1.0–1.2)	1.0 (0.9–1.2)
Henry Ford	26.0	**2.2 (2.1–2.4)**	**1.4 (1.3–1.5)**
Minnesota	2.1	0.1 (0.1–0.2)	**0.1 (0.1–0.2)**
Washington	13.1	1.0 (0.9–1.1)	**0.8 (0.7–0.9)**
Pittsburgh	6.5	**0.4 (0.4–0.5)**	**0.4 (0.4–0.5)**
Utah	8.7	**0.6 (0.5–0.7)**	**0.6 (0.5–0.6)**
Marshfield	7.7	**0.5 (0.5–0.6)**	**0.5 (0.4–0.5)**
Alabama	1.9	**0.1 (0.1–0.2)**	**0.1 (0.1–0.1)**
Consent type			
Single	8.7	Reference	Reference
Dual	28.8	**4.2 (4.0–4.5)**	**2.2 (2.0–2.5)**
Randomization year			
1993–1994	8.9	**0.7 (0.6–0.8)**	**0.4 (0.4–0.5)**
1995–1996	12.2	Reference	Reference
1997–1998	11.0	**0.9 (0.8–0.9)**	0.9 (0.9–1.0)
1999–2000	8.7	**0.7 (0.6–0.7)**	**0.8 (0.8–0.9)**
2001	11.8	1.0 (0.8–1.1)	0.9 (0.7–1.0)

* Adjusted for all covariates listed in table

** Complete names and locations of screening centers can be found in the Funding section of this manuscript.

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Table 3

Odds ratios (OR) and 95% confidence intervals (CI) of non-compliance according to baseline characteristics for the distance subset (3 screening centers) in PLCO (10 US screening centers; 1993–2011) (n=1425)

	% Non-compliant	Unadjusted* OR (CI)	Adjusted*,** OR (CI)
Age at randomization (years)			
Younger than 50	17.9	Reference	Reference
60–64	15.5	0.8 (0.6–1.2)	1.0 (0.7–1.5)
65–59	16.5	0.9 (0.6–1.3)	1.4 (0.8–2.2)
70 or older	22.3	1.3 (0.9–2.0)	1.7 (1.0–2.9)
Gender			
Female	19.7	Reference	Reference
Male	14.9	**0.7 (0.5–0.9)**	0.8 (0.6–1.2)
Race			
White- non-Hispanic	17.2	Reference	Reference
Black, non-Hispanic	22.9	1.4 (0.9–2.3)	0.7 (0.4–1.2)
Hispanic	12.9	0.7 (0.3–1.4)	0.6 (0.3–1.3)
Asian	0.0	–	–
Pacific Islander	0.0	–	–
American Indian	37.5	2.9 (0.7–12.1)	1.8 (0.4–8.8)
Education			
Less than high school	29.4	**1.8 (1.1–3.0)**	1.4 (0.8–2.4)
High school grad	18.4	Reference	Reference
Post HS/some college	18.0	1.0 (0.7–1.4)	1.1 (0.8–1.7)
College grad/postgrad	13.4	0.7 (0.5–1.0)	0.9 (0.6–1.4)
BMI (kg/mˆ2)			
0 – 18.5	20.0	1.0 (0.2–5.0)	0.9 (0.2–5.7)
18.6 – 25.0	19.3	Reference	Reference
25.1 – 30.0	14.0	**0.7 (0.5–0.9)**	0.7 (0.5–1.0)
> 30.0	21.2	1.1 (0.8–1.6)	1.0 (0.7–1.4)
Comorbidity score			
No	15.6	Reference	Reference
Yes	22.0	**1.5 (1.2–2.0)**	1.3 (0.9–1.8)
Cigarette smoking status			
Never smoker	15.3	Reference	Reference
Current smoker	24.8	**1.8 (1.2–2.8)**	1.4 (0.9–2.4)
Former smoker	18.2	1.2 (0.9–1.6)	1.0 (0.7–1.4)
Marital status			
Married/living as married	17.3	Reference	Reference
Formerly married	17.2	1.0 (0.7–1.4)	0.9 (0.6–1.3)

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	% Non-compliant	Unadjusted* OR (CI)	Adjusted*,** OR (CI)
Never married	25.0	1.6 (0.8–3.3)	1.6 (0.7–3.6)
Current occupation			
Working	16.1	Reference	Reference
Homemaker	24.9	**1.7 (1.1–2.6)**	1.3 (0.7–1.9)
Unemployed	18.2	1.2 (0.2–5.4)	0.9 (0.2–4.7)
Retired	15.4	1.0 (0.7–1.3)	0.7 (0.5–1.0)
Disabled/extended sick leave	34.4	**2.7 (1.3–5.9)**	1.7 (0.7–3.9)
Other	21.6	1.4 (0.6–3.2)	1.0 (0.4–2.6)
Family history of a PLCO cancer			
No	17.4	Reference	Reference
Yes	17.0	1.0 (0.7–1.3)	1.1 (0.8–1.5)
Possibly	24.4	1.5 (0.7–3.2)	1.8 (0.8–3.9)
Screening center***			
Colorado	14.4	Reference	Reference
Henry Ford	30.6	**2.6 (1.9–3.6)**	0.5 (0.2–1.2)
Utah	8.7	**0.6 (0.4–0.8)**	**0.5 (0.3–0.8)**
Consent type			
Single	11.3	Reference	Reference
Dual	36.6	**4.5 (3.4–6.1)**	**7.4 (3.0–18.3)**
Randomization year			
1993–1994	14.0	**0.5 (0.3–0.8)**	**0.5 (0.3–0.8)**
1995–1996	24.6	Reference	Reference
1997–1998	12.8	**0.5 (0.3–0.6)**	1.0 (0.7–1.7)
1999–2000	12.9	**0.5 (0.3–0.7)**	1.2 (0.7–2.1)
2001	11.1	0.4 (0.1–1.7)	1.4 (0.2–7.9)
Distance			
Tertile 1	14.2	Reference	Reference
Tertile 2	17.9	1.3 (0.9–1.9)	1.2 (0.8–1.8)
Tertile 3	20.4	**1.5 (1.1–2.2)**	1.4 (1.0–2.1)

* Bolding indicates statistically significant ORs.

** Adjusted for all covariates listed in table.

*** Complete names and locations of screening centers can be found in the Funding section of this manuscript.