Patterns in completion of colorectal cancer screening using fecal immunochemical tests in a health maintenance organization setting

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Abstract

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Epidemiology

Background: Fecal immunochemical test (FIT) is a home-based stool test for colorectal cancer (CRC) screening and an effective means to improve rates of CRC screening overall, and thus reduce CRC mortality. We investigated and described patient characteristics associated with completion of FIT once a physician order has been placed.

Methods: Enrollees of Kaiser Permanente Washington between ages 50 and 75 years who were given an order for FIT during 2011 through 2012 for CRC screening were observed for receipt of FIT (N=64,148). Patient characteristics were ascertained through administrative and electronic health record data sources. We compared patient characteristics using prevalence ratios, described time from order to return of FIT, and estimated differences in completion of FIT screening with Kaplan-Meier and Cox regression.

Results: Greater than half (53.7%) of all study subjects returned FIT within one year from the date of the first order. The median time to return of FIT for those who completed screening was 13 days from the date of order (mean: 44.5 days: Q1, Q3: 6, 42). Patient factors associated with decreased completion of FIT included: younger age (50-55 years vs. 70-75 years adjusted HR: 0.56; 95% CI: 0.54, 0.59), obesity (vs. normal BMI adjusted HR: 0.82; 95% CI: 0.82, 0.88), and higher Charlson comorbidity index score (3+ vs 0 adjusted HR: 0.87; 95% CI: 0.83, 0.92). There was significant evidence of increased completion of FIT compared to whites among Asian (adjusted HR: 1.36; 95% CI: 1.30, 1.42), Black (adjusted HR: 1.13; 95% CI: 1.07, 1.21), and Hispanic (adjusted HR: 1.12; 95% CI: 1.05, 1.19) race/ethnicities.

Conclusion: We observed greater FIT completion among minority race/ethnicities, suggesting that disparities in CRC screening within these groups is likely due to failure of provider initiation rather than patient completion of the test. However, additional interventions in other groups, such as obese individuals, to improve screening should be considered.

Impact: Our results can be used to develop targeted interventions based on patient characteristics that would improve CRC screening compliance.

Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the second leading cause of cancer death among men and women combined in the United States (US).[1] Available screening options have been demonstrated to effectively reduce the burden of this disease among adults age 50 to 75 years old.[2,3] Screening has been shown to effectively reduce CRC mortality by facilitating detection of early stage cancers for an improved prognosis.[4] While the US has successfully achieved the target age adjusted mortality of 14.5 CRC deaths per 100,000 people set by the Healthy People 2020 initiative,[5] with only 63% screening adherence in 2015, public health efforts have yet to achieve the American Cancer Society (ACS) goal of 80% by 2018.[6]

The US Preventive Services Task Force (USPSTF) continues to recommend three evidence-based screening options for US adults aged 50 to 75 years old: 1) guaiac-based fecal occult blood testing (gFOBT) or fecal immunochemical testing (FIT) once every year; 2) flexible sigmoidoscopy (FS) every five years with gFOBT/FIT every three years; or 3) colonoscopy every ten years.[2] These screening options received the highest grade by the USPSTF, reflecting the strength of evidence that shows high certainty of substantial benefit from CRC screening. [7-9]

From a clinical care perspective, FIT has consistently been shown to be a preferred screening tool for individuals at average risk of CRC.[10] Compared to colonoscopy, FIT is less invasive, less expensive, and carries less risk of adverse events, having the potential to translate into increased CRC screening participation by underscreened groups and a lower overall cost to screening programs.[11-14] Over the last several years, the FIT replaced gFOBT as the preferred stool test, due to a higher sensitivity in detection of CRC and reduced burden on patients (i.e., FIT requires only one stool test whereas gFOBT requires three).[15-21] Furthermore, both FIT and gFOBT have been shown to be more accepted by patients than FS screening;[22] they have also been shown to better detect proximal tumors, which are associated with greater mortality in colon cancer than distal tumors, as compared to FS.[23,24] Areas where FIT-based screening programs have been actively implemented have shown a 22% reduction in CRC-specific mortality.[25]

The process of screening consists of several steps, from identification of the eligible population to completion of test and follow-up of testing results.[26] Previous research has highlighted the deficits in overall compliance with CRC screening recommendations, without allowing for the identification of deficits within steps of the screening process.[27] In a previous study, we noted the prominent utilization of stool tests (either FOBT or FIT) among first-time screenees, with 72% of study participants using a stool-based test for their first CRC screening after age 50.[27] Further, the retrospective cohort showed that important patient characteristics, including higher body mass index and being a woman, were associated with lower uptake of any CRC screening tests when considering all screening methods combined. Such findings encompass two critical aspects in the cancer care continuum: 1) the administration of screening options to patients by clinicians as part of regular primary care, resulting in CRC screening order, and 2) the follow-through of screening on the part of the patient once given a screening order.

Building on previous findings regarding the acceptability and performance of FIT, we characterized patterns of return of a FIT following clinician order, and identified patient characteristics associated with lower rates of FIT screening completion within a healthcare delivery system.

Methods

Study setting

The Population-based Research Optimizing Screening through Personalized Regimens (PROSPR) consortium was created to allow multiple study sites to coordinate transdisciplinary research for the improvement of screening practices for breast, cervical, and colorectal cancers in community settings.[28] In 2011, Kaiser Permanente Washington Health Research Institute (KPWHRI), was funded as part of the expansive consortium created by the National Cancer Institute's PROSPR consortium for CRC screening. KPWHRI is a mixed model health insurance and care delivery system in Washington State. The aim of the consortium is to understand CRC screening processes and potential failures and successes of the screening process to improve overall patient health. The collection of data throughout the screening process can further inform comparative effectiveness research questions for CRC screening.[29] Data were accessible through the Virtual Data Warehouse (VDW) for Kaiser Permanente Washington (KPWa). The VDW houses patient information in separate content areas: enrollment/demographics, utilization, laboratory, pharmacy, census, tumor registry, and vital/social history.[30] Information regarding the covariates and outcomes of interest were extracted from VDW records and data systems for all study participants.

The study protocol received Institutional Review Board approval through KPWHRI Human Subjects Division for waiver of consent to enroll participants, link study data, and perform statistical analyses.

Identification of FIT orders and test return

CRC screening guidelines at Kaiser Permanente Washington (KPWa) follow USPSTF recommendations as described.[2] In 2011, KPWa providers replaced offering of the 3-sample SENSA® gFOBT for the one-sample FIT due to the improved diagnostic characteristics of the test. From clinical laboratory data, we identified the date of receipt of FIT with Current Procedural Terminology (CPT) codes (i.e., 82270, 82271, 82272, 82273, 82274) and Health Common Procedure Coding System (HCPCS) codes (i.e., G01017, G0328, G0394).[31,32] These codes differentiated screening FIT from diagnostic tests, which are assumed to be rare. Information was available on dates the test was ordered and when the test was received by laboratories (if returned).

We identified 86,076 physician orders for FIT between January 1, 2011 and January 1, 2013 among men and women enrollees aged 50 and older at KPWa. We excluded FIT orders due to: 1) standing future orders (i.e., automatic orders for future receipt of FIT) (n=104); 2) orders for which there were a valid reason for being cancelled (see appendix A) (n=2,358); 3) inpatient orders (n=44); 4) and orders included in the treatment arm of an ongoing randomized control trial (n=81).[33] Remaining orders were merged with cohort data containing patient characteristics. Orders were collapsed so that there was a single record per subject, retaining the date of the first FIT order during the time period, the total

number of orders over the study period, and the date of receipt for the first completed FIT (if applicable).

Patient characteristics

Patient characteristics were selected based on identified risk factors for CRC and availability within our data systems.[34] We obtained patient characteristics through administrative patient files including gender (female/male) and race/ethnicity. The calculated variable of BMI, based on the weight and height from the measurement date closest to the FIT order, was extracted by the VDW from vital signs recorded at the corresponding clinical visit. Charlson comorbidity index score is calculated as a count of the number of specific diagnoses identified from physician claims data.[35]

One individual for whom gender was unknown was excluded from analysis. Consistent with current screening guidelines, we further excluded individuals younger than 50 or older than 75 years of age at the time of the first FIT (n=5,562). Our study was focused on average risk adults; hence, patients were excluded if they had a prior diagnosis of CRC (n=66), full or partial colectomy, ileostomy, or proctectomy (n=79), Crohn's disease (n=457), or ulcerative colitis (n=496). The final sample population included 64,148 unique patients eligible for CRC screening who received a FIT order and kit.

Statistical analysis

In this retrospective cohort study, we evaluated the association of various demographic features (i.e., race, gender, age, BMI) and medical conditions (i.e., Charlson index scores and specific comorbidities) on the return rates of FIT kits for CRC screening. Self-reported race and ethnicity was grouped as non-Hispanic white, non-Hispanic black, Hispanic (all races), non-Hispanic Asian, and non-Hispanic. Gender was binary as male and female. Age groups were divided into five-year increment groupings between 50 and 74 years. The most recent BMI measurement (within the past year) at the time of the first FIT order was categorized as underweight (below 18.5 kg/m^2), normal or healthy weight (18.5-24.9), overweight (25.0-29.9), and obese (30.0 and above).[36] The Charlson comorbidity index was calculated for all patients with comorbid conditions, with the lowest score (0) as the referent group and compared to groups of higher scores as indicators (1, 2, and 3 or more). Additional analyses were done for three comorbidities with the highest prevalence in the sample population, namely: diabetes, chronic pulmonary disease, and myocardial infarction. Our outcome of interest was dichotomized as affirmative or negative for return of FIT by one year from the date of test order. Additionally, a continuous variable to describe the time in days between FIT order and laboratory receipt was used to determine hazard ratios using Cox regression, with censoring for disenrollment, reorder for screening, death and 365 days from FIT order date, whichever came first.

Model 1 used a generalized linear model to estimate the unadjusted prevalence ratio (PR) and 95% confidence interval comparing the completion of FIT by patient level factors to the previously described reference group within each variable. Model 2 included all variables, without the specific comorbidities. Patients for which information on a covariate was missing were dropped from multivariate analyses (N=23,248). To estimate the adjusted PR for specific comorbidities, Charlson Index score was removed from the model and replaced by each of the comorbidities in separate models. While we are interested in describing disparities of incompletion, we used completion of FIT order

rather than incompletion as the outcome of interest in this binary analysis in order to maintain consistency of interpretation with the results of the time-to-event analysis. Therefore, a PR greater than one indicates a higher proportion of FIT completion, a clinically positive outcome, and conversely, a PR less than one indicates a higher proportion of the adverse outcome (i.e. incomplete FIT).

We performed time-to-event analysis from the date recorded of first FIT order until the date recorded for a received FIT. Individuals were censored for death, disenrollment from KPWa, and at 365 days from the date of the first FIT order. Time to completion was described using non-parametric Kaplan-Meier estimates and differences between groups within variables were initially estimated by Log-rank tests, graphical display through 180 days from first FIT order. A univariate analysis was used to describe the mean, median, and interquartile range of time to completion of FIT among those with a returned order. Cox proportional hazard models were used to estimate unadjusted (Model 3) and adjusted (Model 4) hazard ratios (HR) and 95% confidence intervals comparing the time from order to receipt of FIT by patient level factors to the variable specific referent category. We used the Breslow's method for ties.

All analysis and figures were performed using SAS version 9.4 (SAS Institute). Additional analyses of each model were conducted in which categorical variables for age, BMI, and Charlson scores were replaced with the corresponding continuous variable and tested for trends.

Results

Among 64,148 adults with a FIT order between 2011 and 2012, over half (54%) of the sample population returned a FIT to the laboratory within a year of order date. The proportion of patients who returned a completed FIT varied by patient race/ethnicity, age, and BMI (Table 1). There were statistically significant differences in completion by gender and specific comorbidities, but the differences were marginal. In our sample population, nearly 60% of FIT order recipients were female, and approximately 75% were white. There was a fairly even distribution of subjects in each age group. For those with a recorded BMI (76.2%), nearly 30% were obese. Approximately a quarter of our patients had a Charlson index score of one or greater. Patients for whom BMI or a Charlson score was missing were more likely to have an incomplete FIT.

With respect to time to completion of FIT order, we observed that 50% of patients who returned a completed FIT kit did so within 13 days. There was little variation in the median time to completion by patient characteristics. The substantial difference between the mean and median across groups, along with the difference between the median and third quartile, suggest a heavily right skewed distribution of time to return (Table 2). The Kaplan-Meier curves display the time-to-completion experience comparing within variable groups (figure 1). Multivariate-adjusted Cox proportional hazards models based on these completion times generated HR's estimates that were more pronounced than the previously described PR's (Table 4). Of note, those in the lower age category (50-55 years of age) were 44% less likely to return their FIT than compared to those of the oldest age group (70-75 years of age), after adjusting for other variables. Differences in return by gender were more dramatic when looking at the adjusted Cox model compared to the binary outcome and account for differences in time from FIT order to return.

The unadjusted and adjusted generalized linear models yielded similar PRs (table 3). The most dramatic change with adjustment was for the unknown/missing race/ethnicity (Model 1 PR = 0.68; Model 2 PR = 0.87), although still in the same direction of less likely to complete FIT within a year following order. Patients of Asian race were approximately 20% more likely to have completed FIT screening within a year as compared to non-Hispanic whites. There was a clear positive association with age and completion showing that younger patients are less likely to complete compare to hose between 70 – 75 years old. Obesity was associated with a decreased likelihood of FIT completion, with a statistically significant p-value when testing for trend with increasing BMI ($p<0.001$). Charlson score was modestly associated with FIT completion: those with a Charlson score of three or greater were 7% less likely to return a FIT within one year as compared to those with comorbidity scores of zero.

The results of the analyses testing trends in the continuous variables for age, BMI, and Charlson score were consistent with the results in the categorical models (Appendix B1 and B2). Notably, we see an increased likelihood of completion with every year increase in age, and a decrease in likelihood of completion as BMI increases, both in the unadjusted and adjusted models. The unadjusted models did not indicate a trend between Charlson score and completion of FIT. However, models 2 and 4 both show a decreased likelihood of FIT completion with increasing Charlson index scores.

Conclusion

Among those opting for a stool kit, completion of colorectal cancer screening begins with the return of the FIT kit. Our study is among the first to suggest that just more than 50% of adults who receive a stool kit return it within one year, and if they do return the kit, the majority of participants are returning the FIT within 2-3 weeks of order date. Hence, if adults are planning to participate in CRC screening with a stool kit, the first few weeks after test order are most important in completion of this first step. If they do not return a kit within 2 weeks, the rate at which they are returned diminishes over time. Patient factors associated with completion of testing included Asian race, older age, and normal BMI. Our results indicate that systems, clinics, screening programs, and clinical teams should consider interventions to encourage return of the stool kit.

Our observation that women are less likely to complete screening using FIT is consistent with previous studies which suggest gender-specific factors that influence CRC screening, such as competing screening for breast cancer.[37] In our population, many more women than men were given a clinician order for FIT. However, on the whole, women have been shown to be less likely to participate in CRC screening, possibly due to the additional need to participate in screening programs for breast and cervical cancers.[30] When considering the clinical implications of these findings, it is also important to consider the meaning in the context of differing test performance. Another study has reported that fecal occult blood testing diagnostic accuracy varies significantly by gender, showing greater accuracy in detection of adenomas in men than in women.[38] Gender differences in CRC screening performance are not unique to FIT. Women have been shown to receive a shorter and more limited flexible sigmoidoscopy.[39] These factors should be considered at the point of physician communication of screening choice and could impact the ability of primary care provider to facilitate timely completion of screening with FIT.

The most notable difference in completion of FIT is the effect of age. We demonstrated that the youngest age group was nearly half as likely to return a FIT within a year of the first order, and we see a consistent linear trend across all models. Interventions aimed at improving initiation of CRC screening though referrals, tracking of patient outcomes, and mitigating patient barriers have been shown to be effective at increasing CRC screening among adults younger than 64 years old.[46] A recent study conducted at KPWa using mailed FIT tests and support over the phone was shown to double the number of adults who were currently compliant with CRC screening recommendations.[33] Mailed outreach was effective for improving rates of CRC screening among underserved populations, and had a markedly higher effect on screening with FIT as compared to invitation for colonoscopy.[40] Another study suggested that improved CRC screening will most likely be achieved through optimizing the time during current primary care visits rather than through outreach to encourage patients to attend primary care visits.[44,41]

Obesity was associated with reduced return of FIT following physician order, consistent with previous research which has shown that being overweight and obese is associated with reduced participation in CRC screening as compared to normal weight patients.[46,47] Participation for this group should be emphasized, as obesity has also been shown to be a strong risk factor for CRC.[48] Additional research should also look at whether such difference in FIT completion by obesity status depends on patient gender, as previous research has suggested this association to only be present in obese women and not in men.[37,49] Comorbidities overall was associated with a slight reduction in completion of FIT kits. For breast cancer screening, a diagnosis of diabetes has been shown to be an independent barrier for screening even after adjusting for socio-economic status.[35] We did not specifically evaluate interactions between patient characteristics, but important subgroups, such as overweight women with diabetes could be potential target populations for screening follow-up.

Our findings regarding differences by race/ethnicity contrast with previous studies which have suggested lower rates of CRC screening among minorities, and lower receipt of FIT specifically for blacks and Hispanics.[42] Although our population is comprised of a relatively small proportion of non-white patients, we observed significantly increased completion of FIT for Asians, blacks, and Hispanics in our adjusted models. In our population, non-Hispanic blacks were more likely to complete screening than non-Hispanic whites (adjusted HR: 1.13; 95% CI: 1.07, 1.21). This is contrary to previous studies which have stated that a considerable proportion of the disparities in overall CRC survival between blacks and whites could be attributed to differences in screening.[43] If the results of our study are also true, it would indicate that differences in screening are predominantly due to disparities in provider initiation of screening, as opposed to failure to complete screening once the recommendation is received.[42] However, our results are consistent with a recent randomized clinical trial which found that non-white participants were more likely to adhere to gFOBT than white participants, while white participants adhered more often to colonoscopy.[44] As colonoscopy is generally more common than FOBT/FIT, this would explain the overall disparity in CRC screening adherence among minority populations. Patients with unknown/missing race/ethnicity were the least likely to complete CRC screening with FIT (PR 0.68: 95% CI: 0.64, 0.72). The clinical significance of this finding is likely a reflection of engagement with

medical care, rather than an effect of having an unknown race/ethnicity. A similar conclusion can be drawn for those with a missing BMI.

While we show various patient factors associated with return of FIT, there are some limitations as a result of our study population. It is important to recognize that this is a fully insured population. The effects of generalizability due to this characteristic are two-fold. First, screening for these patients is covered by insurance, thus, they should not experience any direct expense associated with performing FIT. However, economic barriers around transportation to primary care clinics and follow-up remain. Previous research has highlighted the low prevalence of CRC screening in the uninsured population and should look at barriers to completing FIT once a patient has received an order to do so.[45] For those who are uninsured, FIT may be the most economically feasible method to receive CRC screening. Second, it is likely that the participants included in this study tend to be somewhat wealthier than the general population. As a result, the mechanisms through which lower-income populations may encounter barriers in completing screening may not be reflected by those in this study population. Unfortunately, there is limited ability to assess disparities by socio-economic status in our population, though it has been demonstrated in European populations.[46] Lastly, it is important to note that FIT is only a step in the CRC screening continuum, and a positive FIT requires a follow-up colonoscopy. Our study did not consider completion of follow-up screening; however, the potential for disparities in such follow-up merits further investigation.

To our knowledge, this is the first study to assess screening completion based on return of FIT following physician order. This research is important in order to reach the Healthy People goal of 80% completion of CRC screening by 2018 and is an important contribution to the existing knowledge on CRC screening to reduce underuse.[47] Targeted interventions should focus on those patient characteristics associated with non-completion of CRC with FIT (i.e., women, younger age, obesity, and comorbidities) to considerably improve compliance to screening recommendations.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed

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Table 1. Descriptive characteristics of Kaiser Permanente Washington members with an order for FIT in 2011-2012 by completion status of test within one year of order.

	Complete		Incomplete		Total
Patient characteristics	**34,417**	**(%)**	**29,731**	**(%)**	**64,148**
Gender					
Male	15,109	(43.9%)	12,539	(42.2%)	27,648
Female	19,308	(56.1%)	17,192	(57.8%)	36,500
Race/ethnicity					
White, non-Hispanic	25,770	(74.9%)	22,304	(75.0%)	48,074
Asian, non-Hispanic	3,577	(10.4%)	1,980	(6.7%)	5,557
Black, non-Hispanic	1,552	(4.5%)	1,243	(4.2%)	2,795
Other, non-Hispanic	415	(1.2%)	453	(1.5%)	868
Multi-racial, non-Hispanic	442	(1.3%)	419	(1.4%)	861
Unknown/missing, non-Hispanic	1,224	(3.6%)	2,154	(7.2%)	3,378
Hispanic	1,437	(4.2%)	1,178	(4.0%)	2,615
Age groups					
50-55	7,771	(22.6%)	8,502	(28.6%)	16,273
55-60	7,699	(22.4%)	8,184	(27.5%)	15,883
60-65	8,053	(23.4%)	6,635	(22.3%)	14,688
65-70	6,771	(19.7%)	4,317	(14.5%)	11,088
70-75	4,123	(12.0%)	2,093	(7.0%)	6,216
BMI					
Underweight (=<18.5)	200	(0.6%)	158	(0.5%)	358
Normal or Healthy Weight (18.5-25)	6,976	(20.3%)	4,477	(15.1%)	11,453
Overweight (25-30)	8,962	(26.0%)	6,170	(20.8%)	15,132
Obese (>=30)	10,088	(29.3%)	8,538	(28.7%)	18,626
Missing	8,191	(23.8%)	10,388	(34.9%)	18,579
Charlson scores					
0	20,874	(60.7%)	16,913	(59.9%)	37,787
1	4,560	(13.2%)	3,857	(13.0%)	8,417
2	2,571	(7.5%)	1,957	(6.6%)	4,528
3+	2,136	(6.2%)	1,689	(5.7%)	3,825
Missing	4,276	(12.4%)	5,315	(17.9%)	9,591
Comorbidities					
Diabetes	4,091	(11.9%)	3,388	(11.4%)	7,479
Chronic pulmonary disease	2,708	(7.9%)	2,400	(8.1%)	5,108
Myocardial infarction	961	(2.8%)	721	(2.4%)	1,682

Table 2. Univariate description of time in days from first FIT order in 2011-2012 till return among tests completed within a year for Kaiser Permanente Washington members by patient characteristics.

Patient characteristics	Mean	Median	Q1, Q3
Total	44.5	13	6, 42
Gender			
Male	42.7	12	6, 38
Female	45.9	13	6, 45
Race/ethnicity			
White, non-Hispanic	45.5	13	6, 44
Asian, non-Hispanic	35.5	9	5, 25
Black, non-Hispanic	44.8	12	6, 41
Other, non-Hispanic	44.5	13	6, 52
Multi-racial, non-Hispanic	49.9	14	6, 56
Unknown/missing, non-Hispanic	45.4	12	6, 42
Hispanic	46	12	6, 48
Age groups			
50-55	48.2	14	6, 48
55-60	48.7	14	6, 52
60-65	44.1	13	6, 42
65-70	40.6	11	6, 36
70-75	36.7	10	6, 30
BMI			
Underweight (=<18.5)	34.8	11	5, 33
Normal or Healthy Weight (18.5-25)	39.5	11	6, 34
Overweight (25-30)	41.2	12	6, 37
Obese (>=30)	47.7	13	6, 48
Missing			
Charlson scores			
0	43.6	12	6, 41
1	48.7	13	6, 49.5
2	46.8	13	6, 48
3+	47	13	6, 50.5
Missing			
Comorbidities			
Diabetes=no	43.8	12	6, 41
Diabetes=yes	49.4	14	6, 51
Chronic pulmonary disease=no	44	12	6, 41
Chronic pulmonary disease=yes	50.4	15	6, 56
Myocardial infarction=no	44.4	13	6, 42
Myocardial infarction=yes	49.2	13	6, 56

Table 3. Prevalence ratios (PR) for completion of FIT within one year following first order in 2011-2012 among members of Kaiser Permanente Washington.*

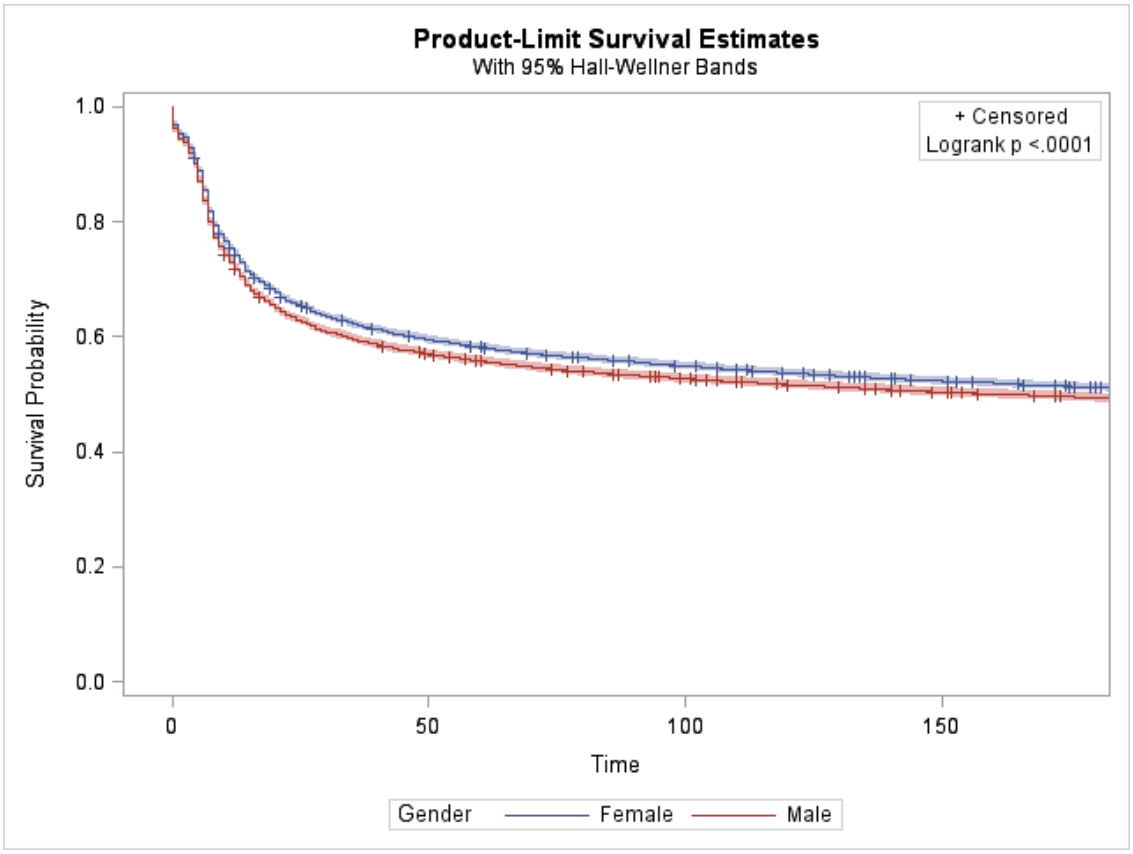
Patient characteristics	Unadjusted PR	(95% CI)	Adjusted PR[a]	(95% CI)
Gender				
Male	Ref		Ref	
Female	**0.97**	(0.95, 0.99)	**0.97**	(0.95, 1.00)
Race/ethnicity				
White, non-Hispanic	Ref		Ref	
Asian, non-Hispanic	**1.20**	(1.16, 1.24)	**1.17**	(1.12, 1.23)
Black, non-Hispanic	1.04	(0.98, 1.09)	**1.08**	(1.01, 1.15)
Other, non-Hispanic	**0.89**	(0.81, 0.98)	0.94	(0.84, 1.06)
Multi-racial, non-Hispanic	0.96	(0.87, 1.05)	0.98	(0.88, 1.09)
Unknown/missing, non-Hispanic	**0.68**	(0.64, 0.72)	**0.87**	(0.81, 0.94)
Hispanic	1.03	(0.97, 1.08)	1.06	(1.00, 1.13)
Age groups				
50-55	**0.72**	(0.69, 0.75)	**0.71**	(0.68, 0.75)
55-60	**0.73**	(0.70, 0.76)	**0.75**	(0.72, 0.79)
60-65	**0.83**	(0.80, 0.86)	**0.83**	(0.79, 0.87)
65-70	**0.92**	(0.89, 0.96)	**0.92**	(0.88, 0.96)
70-75	Ref		Ref	
BMI				
Underweight (=<18.5)	0.92	(0.80, 1.06)	0.88	(0.75, 1.02)
Normal or Healthy Weight (18.5-25)	Ref		Ref	
Overweight (25-30)	0.97	(0.94, 1.00)	**0.97**	(0.94, 1.02)
Obese (>=30)	**0.89**	(0.86, 0.92)	**0.91**	(0.88, 0.94)
Missing	0.72		-	
Charlson scores				
0	Ref		Ref	
1	0.98	(0.95, 1.01)	0.97	(0.94, 1.00)
2	1.03	(0.99, 1.07)	0.98	(0.98, 1.03)
3+	1.01	(0.97, 1.06)	**0.93**	(0.89, 0.98)
Missing	0.81		-	
Comorbidities				
Diabetes	1.02	(0.99, 1.06)	0.98	(0.94, 1.02)
Chronic pulmonary disease	0.99	(0.95, 1.03)	**0.95**	(0.91, 0.99)
Myocardial infarction	**1.1**	(1.07, 1.14)	0.96	(0.90, 1.03)

*Results in bold indicate significance as p<0.05

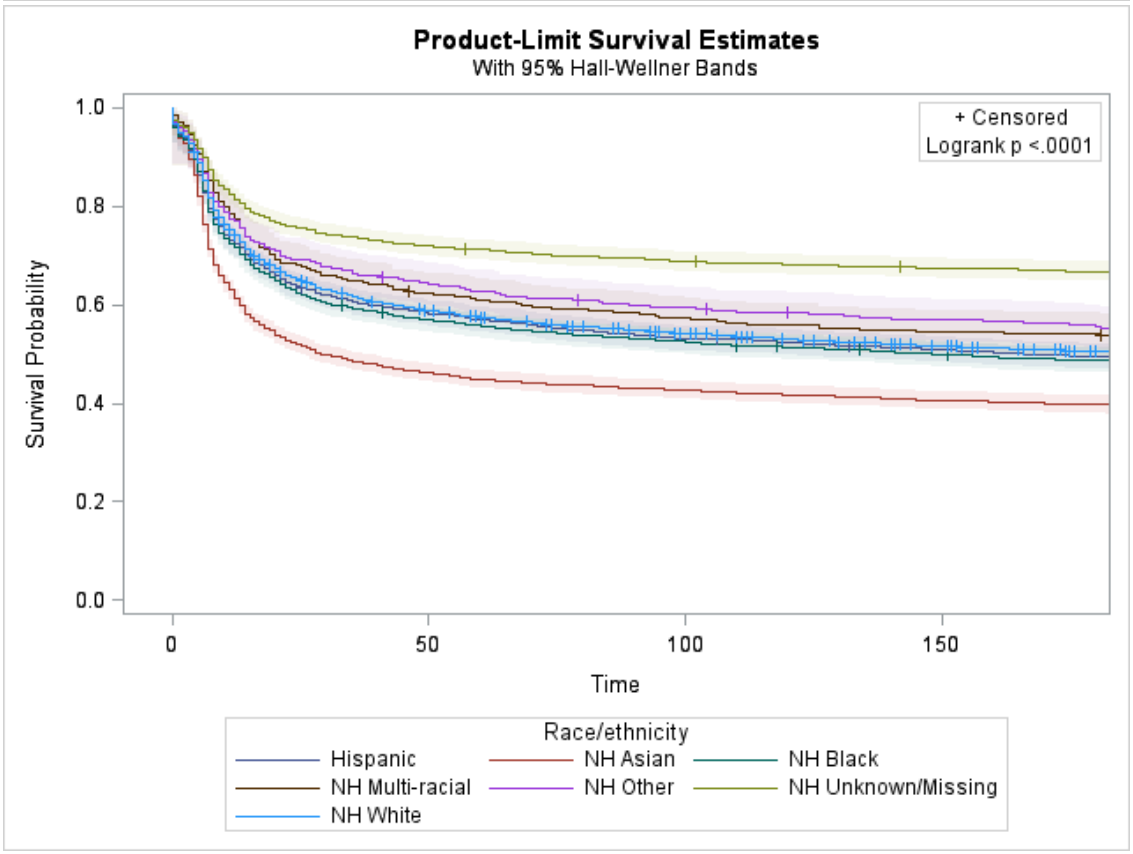
[a]Analyses are adjusted for all variables presented in the table, excluding specific comorbidities.

[b]Specific comorbidities replaced Charlson scores in the adjusted model, each was estimated separately.

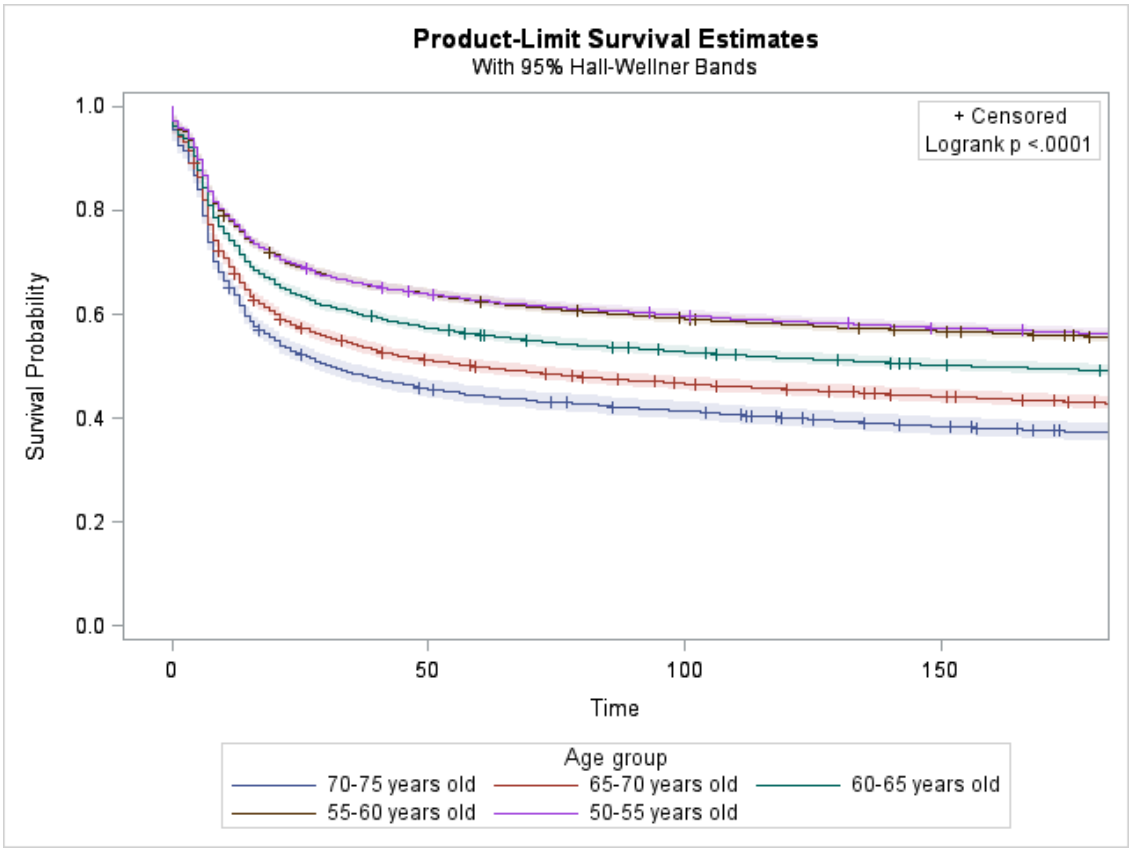
A.


Product-Limit Survival Estimates
With 95% Hall-Wellner Bands
+ Censored
Logrank p <.0001
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
50
100
150
Time
Gender
Female
Male

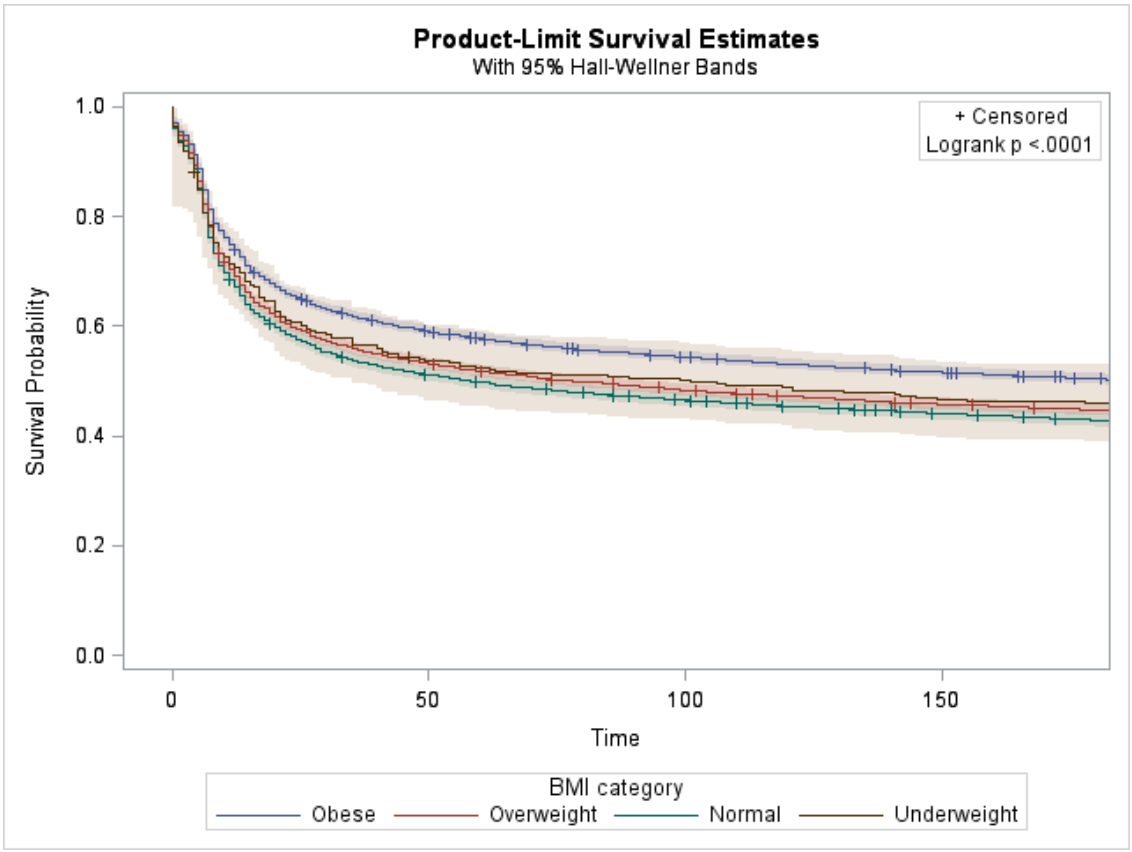
B.


Product-Limit Survival Estimates
With 95% Hall-Wellner Bands
+ Censored
Logrank p <.0001
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
50
100
150
Time
Race/ethnicity
Hispanic
NH Asian
NH Black
NH Multi-racial
NH Other
NH Unknown/Missing
NH White

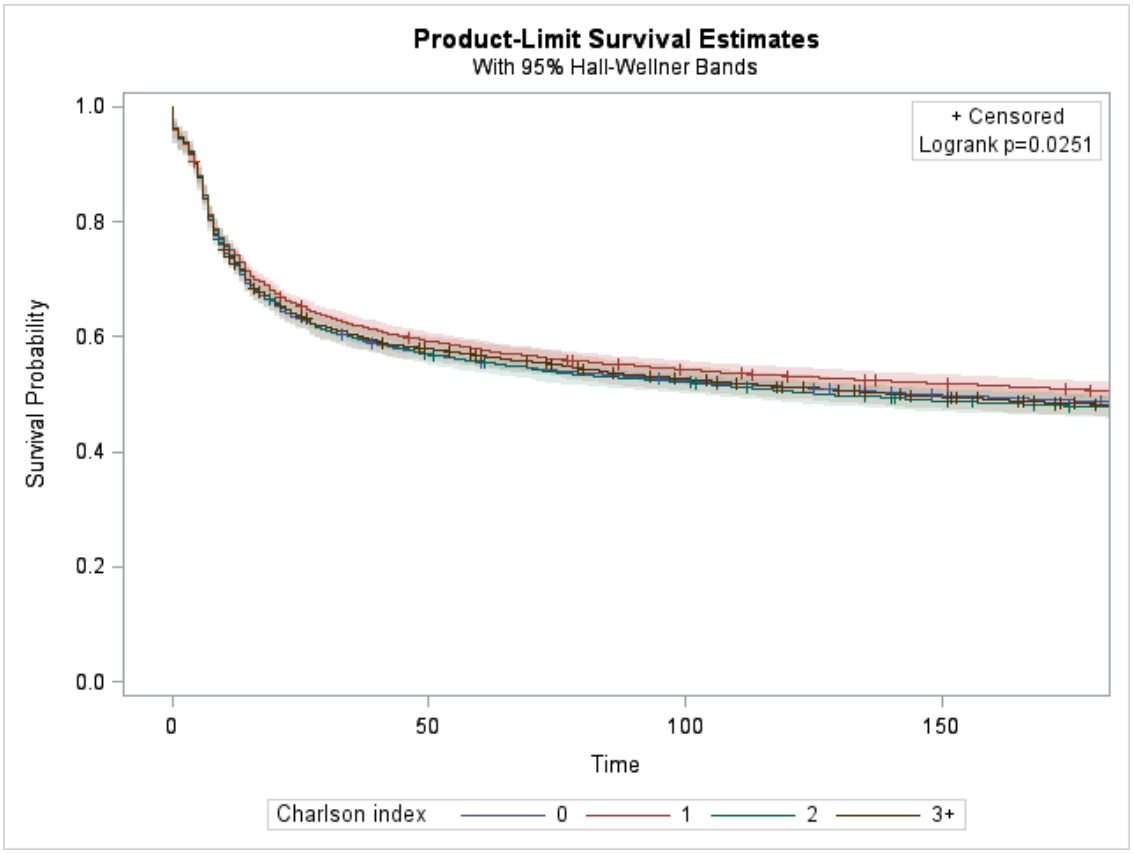
C.


Product-Limit Survival Estimates
With 95% Hall-Wellner Bands
+ Censored
Logrank p <.0001
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
50
100
150
Time
Age group
70-75 years old
65-70 years old
60-65 years old
55-60 years old
50-55 years old

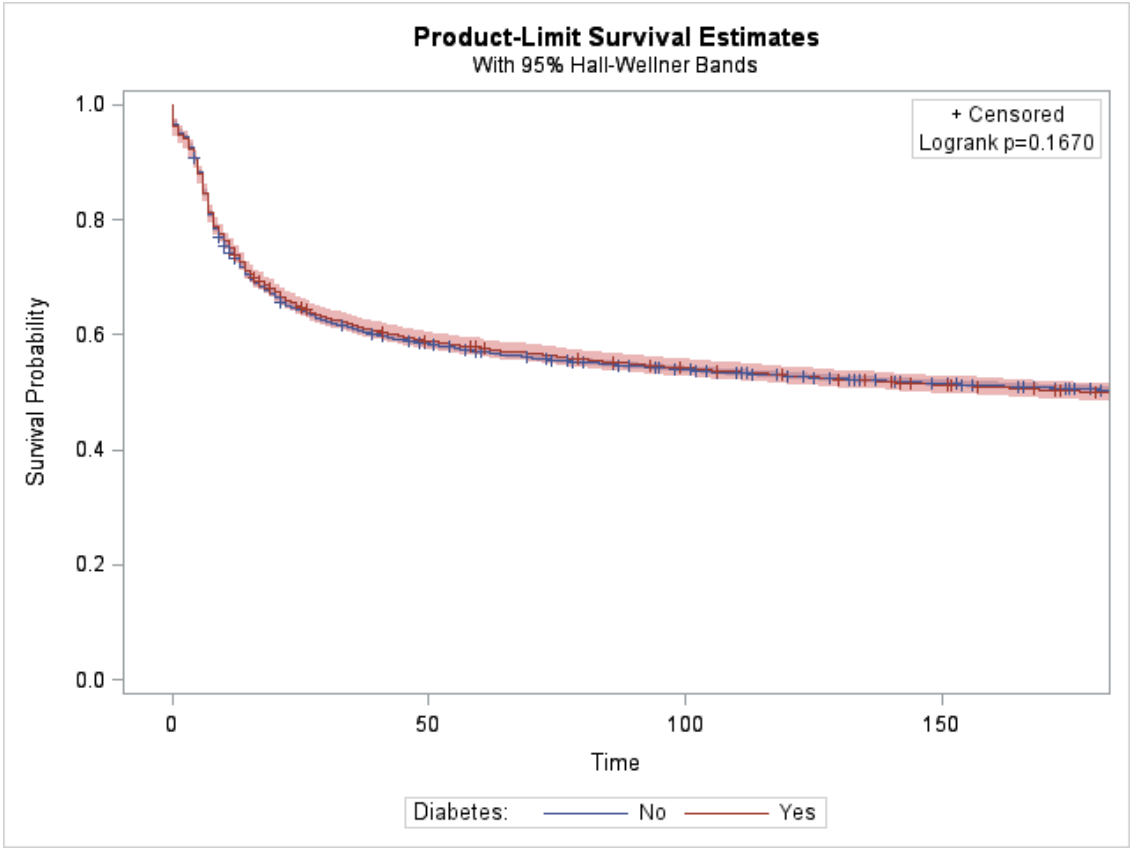
D.


Product-Limit Survival Estimates
With 95% Hall-Wellner Bands
+ Censored
Logrank p <.0001
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
50
100
150
Time
BMI category
Obese
Overweight
Normal
Underweight

E.


Product-Limit Survival Estimates
With 95% Hall-Wellner Bands
+ Censored
Logrank p=0.0251
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
50
100
150
Time
Charlson index
0
1
2
3+

F.


Product-Limit Survival Estimates
With 95% Hall-Wellner Bands
+ Censored
Logrank p=0.1670
Survival Probability
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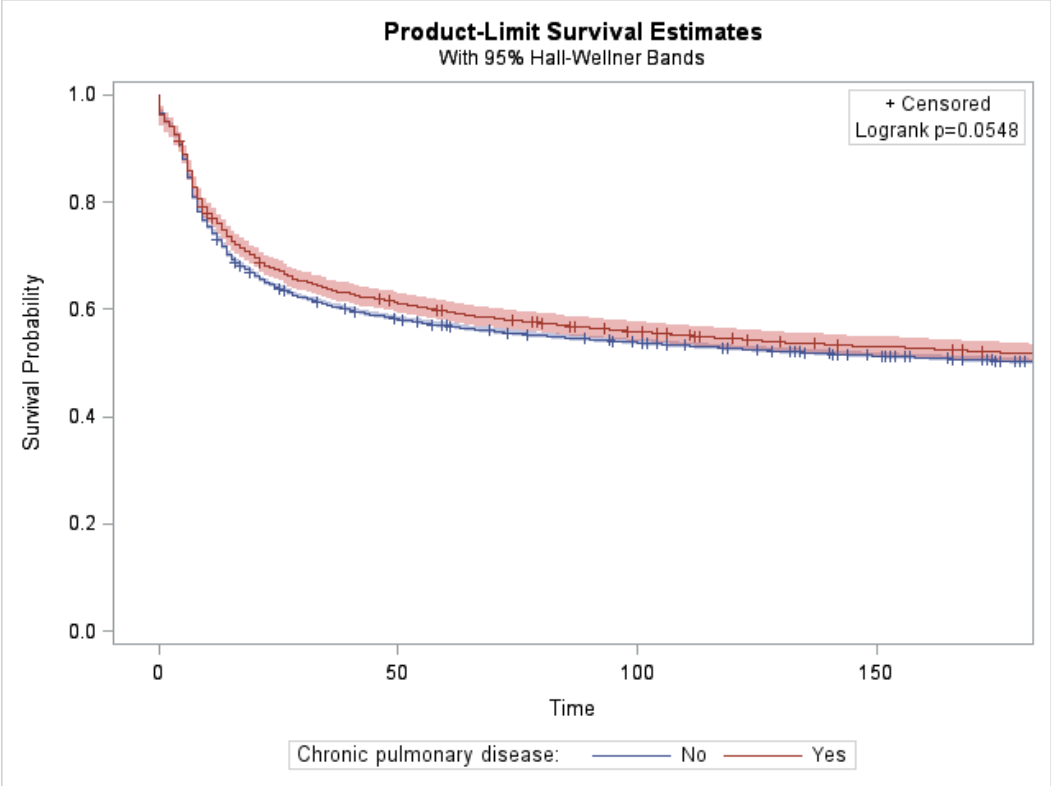
0.8
0.6
0.4
0.2
0.0
0
50
100
150
Time
Diabetes:
No
Yes

G.



H.

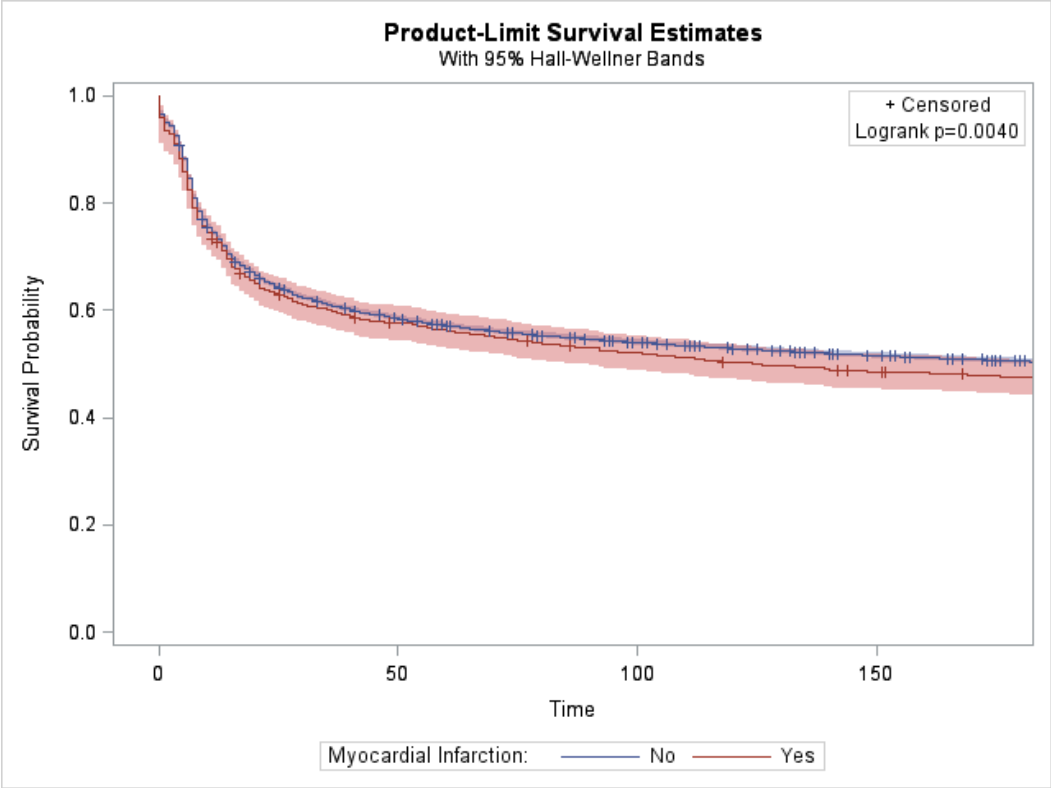


Figure 1A-H: Kaplan-Meier curves for time from first FIT order in 2011-2012 until receipt of test for Kaiser Permanente Washington members.

Table 4. Hazard ratios (HR) associated with completion of FIT within one year from first FIT order in 2011-2012 among Kaiser Permanente Washington members.*

Patient characteristics	Unadjusted HR	(95% CI)	Adjusted HR[a]	(95% CI)
Gender				
Male	Ref		Ref	
Female	**0.94**	(0.92, 0.96)	**0.93**	(0.91, 0.96)
Race/ethnicity0				
White, non-Hispanic	Ref		Ref	
Asian, non-Hispanic	**1.40**	(1.36, 1.46)	**1.36**	(1.30, 1.42)
Black, non-Hispanic	**1.07**	(1.01, 1.12)	**1.13**	(1.07, 1.21)
Other, non-Hispanic	**0.85**	(0.78, 0.94)	0.93	(0.83, 1.05)
Multi-racial, non-Hispanic	0.93	(0.84, 1.02)	0.97	(0.87, 1.09)
Unknown/missing, non-Hispanic	**0.60**	(0.59, 0.67)	**0.82**	(0.76, 0.88)
Hispanic	1.04	(0.98, 1.10)	**1.12**	(1.05, 1.19)
Age groups				
50-55	**0.59**	(0.57, 0.61)	**0.56**	(0.54, 0.59)
55-60	**0.60**	(0.58, 0.62)	**0.61**	(0.58, 0.63)
60-65	**0.72**	(0.70, 0.75)	**0.71**	(0.68, 0.74)
65-70	**0.86**	(0.83, 0.90)	**0.85**	(0.82, 0.89)
70-75	Ref		Ref	
BMI				
Underweight (=<18.5)	0.89	(0.78, 1.03)	**0.83**	(0.71, 0.96)
Normal or Healthy Weight (18.5-25)	Ref		Ref	
Overweight (25-30)	**0.95**	(0.92, 0.98)	**0.95**	(0.91, 0.98)
Obese (>=30)	**0.82**	(0.79, 0.84)	**0.85**	(0.82, 0.88)
Missing	-			
Charlson scores				
0	Ref		Ref	
1	**0.96**	(0.93, 0.99)	**0.94**	(0.90, 0.97)
2	1.03	(0.98, 1.07)	**0.94**	(0.90, 0.99)
3+	1.01	(0.96, 1.05)	**0.87**	(0.83, 0.92)
Missing	-			
Comorbidities				
Diabetes	1.02	(0.99, 1.05)	**0.94**	(0.90, 0.97)
Chronic pulmonary disease	0.96	(0.93, 1.00)	**0.9**	(0.86, 0.94)
Myocardial infarction	**1.1**	(1.03, 1.17)	**0.92**	(0.86, 0.99)

*Results in bold font indicate significance at p<0.05

[a]Models are adjusted for all variables presented in the table, excluding specific comorbidities.

[b]Specific comorbidities replaced Charlson scores in the adjusted model, each was estimated separately.

Appendix A: Reasons for FIT cancellation

Cancel Reason Name	Code	Frequency	Percent	
ABN signed, service refused	0	1	0	keep
Additional History Needed	5	2	0	keep
Auto Cancelled Per Protocol	6	1	0	keep
Canceled per attached Comment.	12	2226	3.64	keep
Canceled, lack of use	21	48579	79.42	keep
Changed order	24	231	0.38	drop
Consider Alternate Exam	28	29	0.05	drop
Data Entry Error by Lab - No Action Required	32	696	1.14	drop
Duplicate Procedure	41	4328	7.08	drop
Error	45	2084	3.41	drop
Improper Collection	46	1	0	keep
Inadequate Prep	47	2	0	keep
Invalid GHC Lab Test Code, please contact laboratory for more information	51	116	0.19	drop
Laboratory error - Procedure not performed.	52	24	0.04	drop
Laboratory error - Wrong medical history number used	61	9	0.01	drop
No show	71	4	0.01	keep
Not Indicated	75	3	0	drop
Other	77	877	1.43	drop
Patient Discharge	86	800	1.31	drop
Patient Expired	96	434	0.71	keep
Patient Returning for Collection	99	5	0.01	drop
Patient declined	104	97	0.16	keep
Patient not fasting - Patient to return	105	3	0	drop
Potential Error in Order	107	2	0	drop
Procedure cancelled per request	109	107	0.17	keep
Procedure not indicated per protocol.	110	16	0.03	drop
Replaced	111	35	0.06	drop
Specimen broken or lost in transit.	115	3	0	keep
Specimen mislabeled prior to receipt in Lab	123	9	0.01	keep
Specimen submitted in improper media.	141	17	0.03	drop
Technical difficulty - Test not Performed	152	7	0.01	keep
Unable to collect specimen	156	86	0.14	keep
Wrong Test Code	157	2	0	drop
Wrong procedure ordered - added correct procedure.	158	329	0.54	drop

Number missing = 76,261

Appendix B1: Generalized linear models for tests in trend of continuous variables.

Patient characteristics		Unadjusted PR	(95% CI)	Adjusted PR[a]	(95% CI)
Age					
	P_{trend}	**1.02**	(1.02, 1.02)	**1.02**	(1.02, 1.02)
BMI					
	P_{trend}	**0.99**	(0.99, 0.99)	**0.99**	(0.99, 0.99)
Charlson score					
	P_{trend}	1.00	(0.99, 1.01)	**0.98**	(0.97, 0.99)

Appendix B2: Cox proportional hazard models for tests in trend of continuous variables.

Patient characteristics		Unadjusted HR	(95% CI)	Adjusted HR[a]	(95% CI)
Age					
	P_{trend}	**1.03**	(1.03, 1.03)	**1.03**	(1.03, 1.03)
BMI					
	P_{trend}	**0.99**	(0.98, 0.99)	**0.99**	(0.99, 0.99)
Charlson score					
	P_{trend}	1.00	(0.99, 1.01)	**0.97**	(0.96, 0.98)

*Statistical significance is indicated by bolded point estimates.

[a] Continuous variables were replaced with the corresponding categorical variable in the full adjusted model and estimated separately.