OREGON HEALTH & SCIENCE UNIVERSITY
SCHOOL OF MEDICINE—GRADUATE STUDIES

IMPACTS OF CHRONIC DISEASE ON BREAST, CERVICAL, AND COLORECTAL CANCER SCREENING IN RURAL OREGON

By

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A THESIS

Presented to the Department of Public Health & Preventive Medicine
and the Oregon Health & Science University
School of Medicine
in partial fulfillment of the requirements for the degree of

Master of Public Health

April 2012

Department of Public Health and Preventive Medicine

School of Medicine

Oregon Health & Science University

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TABLE OF CONTENTS

List of Tables and Figures

Abbreviations

BMI	Body Mass Index
BRFSS	Behavioral Risk Factor Surveillance System
DCBE	Double Contrast Barium Enema
FOBT	Fecal Occult Blood Test
FQHC	Federally Qualified Health Center
HIPAA	Health Insurance Portability and Accountability Act (of 1996)
IRB	Institutional Review Board
Pap	Papanicolaou test
SEER	Surveillance Epidemiology and End Results
USPSTF	United States Preventive Services Task Force

Acknowledgements

I am very grateful for the support, guidance, and insights of my thesis committee: Patty Carney, PhD, Tomi Mori, PhD, and LJ Fagnan, MD. I am also very thankful for the statistical help from Jean O'Malley, MPH. This project is supported by the American Cancer Society, Oregon Rural Practice-based Research Network, and the Oregon Clinical and Translational Research Institute's Oregon Students Learn and Experience Research program. Finally, I would like to acknowledge my parents and friends for their support.

Abstract

Background: Cancer is a leading cause of morbidity and mortality in the United States. Screening can prevent the incidence and mortality for colorectal and cervical cancer, and mortality for breast cancer. Chronic conditions may play a role in the receipt of patients' cancer screening. How those conditions affect cancer screening in rural patients have not been well studied.

Objective: To examine the association between the number and type of patients' chronic conditions and the likelihood those patients are up-to-date for appropriate screening for breast, cervical, and colorectal cancer in rural Oregon.

Design, Participants, Main Measures: We reviewed medical charts from four primary care clinics in rural Oregon from 2008-2009. Up-to-date status was constructed on risk status based on USPSTF guidelines. Eight chronic conditions were examined. Variables associated with those conditions were examined with random effect logistic regression analysis and odds ratios were calculated.

Results: We had 3,433 patients for our analysis of colorectal cancer screening, 1859 women for breast cancer screening, and 740 women for colorectal cancer screening analysis. We identified a total of 584 (17%) patients with no condition, 802 (23%) with one, 815 (24%) with two, and 1,232 (36%) with three or more conditions. Patients with three or more conditions were less up-to-date for screening, especially for cervical cancer (OR=0.40, 95% CI: 0.23-0.70). For colorectal cancer screening in men, those with cardiovascular disease were less likely to be up-to-date (OR=0.61, 95% CI: 0.45-0.82) and those with chronic digestive disease were more likely (OR=1.80, 95% CI: 1.35-2.41). For women, those with depression were less likely to

be up-to-date (OR=0.76, 95% CI: 0.60-0.97) and those with chronic digestive disease were more likely (OR=1.70, 95% CI: 1.33-2.15). For breast cancer, those with asthma and cardiovascular disease were less likely to be up-to-date (OR=0.60, 95% CI: 0.44-0.81; OR=0.70, 95% CI: 0.53-0.93), and those with digestive disease were more likely (OR=1.28, 95% CI: 1.01-1.63). For cervical cancer, those with arthritis/joint disease, diabetes mellitus, and hypertension were all less likely to be up-to-date for screening (OR=0.64, 95% CI: 0.43-0.94; OR=0.56, 95% CI: 0.33-0.96; OR=0.53, 95% CI: 0.36-0.77).

Conclusions: With a more detailed understanding of cancer screening in rural primary care setting, we hope to address potential barriers for patients and modify physician practice behaviors to increase conversations for appropriate screening and adherence to guidelines.

BACKGROUND

Cancer remains the second leading cause of death in the United States, close in mortality rates to the leading cause, heart disease. (1) Breast and colorectal cancers are the second leading cancer causes of death in women, and men and women, respectively. While cervical cancer mortality has significantly decreased for the majority of women in the US, it remains as the tenth leading cancer cause of mortality for Black and Hispanic women. (1) Researchers have shown a mortality benefit from screening for breast cancer, decrease in incidence of late stage diseases, and mortality of cervical and colorectal cancers. (2-6) Although the benefits of screening have been widely established for these three cancers, screening continues to be less than optimal. From 2005 to 2008, colorectal cancer screening has slightly increased from 43.1% to 50.2%, with the primary change being a rise in receipt of colonoscopies. (7) However, 2010 data from the National Health Interview Survey showed that breast cancer and cervical cancer screenings have been steadily declining from 2000 to 2010. (8) Progress is still needed to achieve the Healthy People 2020 goals of colorectal, breast, and cervical cancer screening rates of 70.5%, 81.1%, and 93%, respectively. (9)

Along with leveling screening rates, health disparities exist between different populations of America that require our attention. Rural residents have lower screening rates for breast, cervical and colorectal cancers than urban residents. (10-14) External factors, such as distance from metropolitan areas, lack of health insurance, lack of usual source of care, lack of health maintenance visits, (15) socioeconomic factors, and lack of physician recommendation, have been shown to act as barriers to receipt of available

cancer screening test that have been shown to be effective in decreasing cancer mortality. (2, 16) Despite national emphasis and increases in the use of cancer screening tests since the 1990s, large disparities still exist among underserved groups, such as minority and rural populations. (17)

Patients' chronic diseases not only serve as further barrier in the utilization of screening services, they may also be an independent risk factor for certain cancers. Type-two diabetes mellitus has been associated with increased risk of breast and colorectal cancers, after adjustment for risk factors like obesity. (18-20) An independent increase in mortality of several cancers, including breast and colorectal, has been associated with diabetes as well. (21) Extra consideration of the benefits of screening should be noted for these patients.

Not only are certain chronic diseases associated with increase in cancer risks, they have also been associated with decrease in receipt of screening of breast, cervical and colorectal cancers. Managing comorbidities may serve as competing demands in a busy primary care clinic. (22-23) As the number of chronic diseases increases in the US, time to care for complex conditions in a time-restricted primary care office may overshadow prevention or early detection of other diseases. Fontana's study of patient-reported data showed that patients with diabetes, hypertension and heart disease were less likely to receive preventive services such as clinical breast exam, mammography, Pap test, sigmoidoscopy and FOBT. (24) Among female patients with diabetes mellitus, rates of never having had a pap or mammogram are higher than those without diabetes, and these women tend to have these screening tests less frequently at the appropriate

intervals. (25) A large Canadian retrospective cohort study also found that women with diabetes were less likely to receive mammograms at timely intervals than those without diabetes. (26) Kiefe's study of two primary care clinics based out of University of Alabama, Birmingham showed that screening for breast and cervical cancers decreased with each unit increase in the Charlson index of comorbidity. (27) Comorbidities such as obesity and depression have also been associated with decreased cervical and breast cancer screening, respectively. (28)

Yet, recent studies using national datasets have shown conflicting results of cancer screening utilization and burden of comorbidities. Researchers using a survey-based study of elders in North Carolina showed that comorbidities did not lower screening rates of cancers; hypertension was associated with higher rates of breast exams, pap tests and FOBT, and the presence of three or more conditions were associated with increased rates of mammogram, breast exam, and pap test. (29) Yasmeen's study using SEER-Medicare data found that use of mammography increased with increasing comorbidity score, 27% screening with score of zero compared to 56% screening with score of 3 and above. (22) Zhao's study using Behavioral Risk Factor Surveillance System (BRFSS) showed that women with diabetes had similar screening rates for breast cancer, lower screening rates for cervical cancer and higher screening rates for colorectal cancer. (30)

How chronic disease affect screening of breast, cervical and colorectal cancers remains controversial. Researchers have used national datasets, such as SEER or BRFSS, to analyze the relationship between up-to-date status of cancer screening and chronic

diseases status. However, authors have shown that studies using BRFSS tend to overestimate rates of screening due to bias. (31) Past studies also have also focused on specific disease populations, such as diabetic patients, or urban and national areas. Breast cancer screening has been well studied in relations to chronic disease, but cervical and colorectal cancers have not been well studied. We focused our study on four primary clinics, through medical chart review, in two rural Oregon sites. As rural patients are already at a disadvantage in terms of cancer screening, we focused on rural patients' profile, specifically on their comorbidities, to help better understand the under-utilization of cancer screening tests in rural settings. We know that physician recommendation is a crucial catalyst for patients to receive screening. (16, 23) As multiple authors have shown that a health maintenance visit is important to cancer screening, (14) our results will help physicians understand how to target patients with complex medical conditions to have such a visit and to consider how structural changes could increase utilization of screening tests proven to decrease mortality and morbidity of common cancers.

METHODS

Study Design, Setting and Population

We performed a medical chart review study in collaboration with the Oregon Rural Practice-based Research Network (OPBRN). Study design and data collection have been detailed in a recent publication. (14) Briefly, data were collected from medical charts at four primary care clinics in two rural Oregon communities. Each community had a private clinic and a federally qualified health center (FQHC), for two public and

two private clinics total. Eligibility criteria for patients included being at least 55 years of age to ensure they meet screening criteria and also to allow time for completion of screening tests, having had at least one clinic visit in the last two years, and having medical records extending to five years prior to the year of medical chart review. In three of the four clinics, all medical charts of patients 55 years and older were abstracted, while in the fourth clinic, a large well-established practice, 1,000 patients were selected at random. No patient identifiers were collected, and all study activities were approved by the Institutional Review Board of Oregon Health & Science University, and conducted under a HIPAAA waiver for collection of personal health information without consent.

Data Collection/Medical Chart Review

Medical charts were reviewed from October 2008 to August 2009. Two chart reviewers were specifically trained and independently collected data on-site using a database designed for chart review purposes on lap top computers. Chart review materials were tested on two non-study clinics that used paper and electronic medical records. A third independent reviewer examined 10% of the reviewed charts to assess the quality and establish reliability for data collected. We collected retrospective data on dates of receipt of colorectal, breast, and cervical cancer screening, for up to ten years. Colorectal cancer screening tests included fecal occult blood test (FOBT), colonoscopy, flexible sigmoidoscopy, and double contrast barium enema (DCBE); breast cancer screening test included mammography; and cervical cancer screening test included the Papanicolaou test (Pap).

We collected patient information including age, gender, total clinic visit counts, length of contact with a clinic in years, health maintenance visits, marital status, occupation, race/ethnicity, last insurance status and type, weight, height, smoking history, alcohol use history, personal history of cancers and type, family history of cancers and type, prior abnormal screening test results associated with colorectal, breast or cervical cancers, and numbers and types of comorbid chronic conditions. Comorbid conditions included arthritis/musculoskeletal disease/degenerative joint disease, asthma/emphysema/COPD/chronic lung disease, cardiovascular disease, hypertension, chronic digestive disease, chronic pain, low back pain, diabetes mellitus, depression/anxiety, and substance abuse. We divided the number of chronic diseases into four categories—none, one, two, and three or more conditions—to further analyze the burden of chronic disease on cancer screening in these clinics. Unlike the Charlson index, our category of number of conditions variable is not an aggregated predictor of mortality risk from comorbid conditions. Our variables are shown in Table 1.

Statistical Analysis

The initial data abstraction included 3,593 patients. For this analysis, we excluded patients whose age was missing (n=5), those with any prior personal history of ovarian, breast, colon cancers (n=155). With these exclusions, the final analysis file included a total of 3,433 patients. For our up-to-date status of cancer screenings, we used USPSTF guidelines.(32-34) Subjects were considered up to date if the most recent screening in the record—any of the four tests for colorectal, mammography for breast,

and Pap test for cervical cancer—was within the appropriate time duration according to risk status (abnormal screenings for colorectal cancer and family history for all).

Among women, we excluded patients with a recent history of abnormal mammograms because we could not be certain whether a patient had returned for screening or diagnostic mammography. Short interval follow-up after an abnormality is found is typically done at 3, 6, or 9 months to evaluate the stability of an abnormal finding, which can turn out to be cancer. Similarly, we excluded women with recent abnormal pap tests, as the follow-up could include other pap, invasive sampling or HPV testing and there is uncertainty of a diagnosis of cancer. These circumstances could indicate an impending cancer diagnosis, making these patients more similar to those we excluded because of a prior personal history of cancer. For colorectal cancer screening, we did not exclude those for whom a polyp had been removed, because the return to surveillance or screening is clearer than it is for mammography and the time interval for return is longer than it is for abnormal mammography and Pap tests.

We calculated kappa coefficients between our two reviewers for the variables abstracted from the records. The variables we included in our analysis had kappa values between 0.5 and 0.9, indicating moderate to almost perfect agreement.(35) (36) For chronic conditions, we excluded two conditions with kappa values below 0.4, substance abuse and chronic pain. For continuous variables, age at last contact and calculated BMI values, we looked at the distribution of the values and categorized them into clinically relevant categories. BMI was divided into four categories according to WHO guidelines: less than 25 kg/m^2, between 25 and 30 kg/m^2, greater than or equal to 30 kg/m^2, and

not noted. The underweight category of less than 18.5 kg/m^2 had only 30 individuals, considered too small for accurate estimation in the regression model. A sensitivity analysis done with regressions that included and excluded those 30 individuals did not alter the ORs or p-values of any of the variables; thus, we collapsed the underweight individuals into the category of less than 25 kg/m^2 to preserve the overall sample size. For age, we divided it into four categories according to its histogram distribution and lowess graph of smoothness: 50-59 year-old, 60-64 year-old, 65-75 year-old, and greater than 75 year-old. For cervical cancer screening, we had no applicable individuals greater than 65 year-old. We also categorized the total clinic visit counts in 5 years and the length of patient contact with a clinic. Visit counts were divided into four categories: <5 visits, 5 to 10 visits, 11-20 visits and >20 visits. Patient's overall length of contact with a clinic in years was divided into five categories: <6 months, 6 months to <1 year, 1 year to <2 years, 2 years to <5 years, 5 years and greater.

STATA statistical software version 11.2 was used to analyze the effect of chronic disease on the up-to-date screening status of colorectal, breast and cervical cancers. As screening practices may be related within each clinical practice, we treated the clinics as a random effect in our logistic regression models, adjusting for potential confounders. We used Pearson's chi test to look at association between patient demographics and each number category of comorbidity. We created a random effect logistic regression model, using backwards elimination process, to evaluate the effect of specific chronic diseases and also of number of chronic diseases for each cancer screening, from which we calculated ORs and 95% CI. We stratified colorectal cancer modeling by gender. We

also looked for interactions between insurance type, ethnicity, visit count and length of contact and each chronic disease, but no significant effect modifications were found. After modeling, we further analyzed each chronic disease and up-to-date status by adjusting for a standard set of potential confounders that included: age, marital status, ethnicity, BMI class, occupation, insurance status, alcohol history, smoking history, length of contact with clinic, and number of clinic visits. Rather than excluding subjects with missing values, we created a missing category to classify those with missing values in each covariate. We adjusted each chronic disease by the previous set of confounders and the rest of the chronic conditions. We also explored which covariate and which chronic condition could be driving the unadjusted and adjusted odds ratios for the number of conditions. We adjusted our category of number of conditions by the number of visit counts, and created a separate category of number of conditions without digestive disease to further examine the relationship of number of conditions and screening status.

RESULTS

Study Population:

We identified a total of 503 (15%) patients with no condition, 646 (19%) with one, 786 (23%) with two, and 1,498 (44%) with three or more conditions. Baseline characteristics of our study population are presented in Table 2. Our screening rates were 49% for breast cancer, 37% for colorectal cancer and 52% for cervical cancer screening. Of those with no chronic conditions, 53% were females, 8% were Hispanic, 63% had private insurance, and 7% were uninsured. Of those with one condition, 54%

were females, 14% were Hispanic, 56% had private insurance, and 7% were uninsured. Of those with two conditions, 53% were females, 14% were Hispanic, 51% had private insurance, and 10% were uninsured. Of those with three or more conditions, 56% were females, 12% were Hispanic, 50% had private insurance, and 8% were uninsured. We had a large proportion of people with missing information, especially for race and ethnicity. Younger patients had less chronic disease than older patients. The median length of contact with a clinic and the median number of clinic visits both increased with increasing number of conditions.

The mean and median number of comorbid conditions was 2.44 and 2, respectively (range 0-10). We initially had 10 categories of comorbid conditions, but two were excluded due to kappa value below 0.40. The distribution of the eight remaining comorbid conditions is shown in Figure 1. The number of each individual disease increases with increasing number of conditions. Of those patients with one condition, many had hypertension (30%). Of those patients with two conditions, a large portion of patients had arthritis or other joint diseases (33%), and hypertension (56%). Of those patients with three or more conditions, a large portion of patients had arthritis or joint diseases (63%), cardiovascular disease (46%), chronic digestive disorders (45%), depression (49%), hypertension (78%) and low back pain (55%). Figure 2 shows the distribution of screening rates by number of conditions. Those with no conditions had low screening rates as well as those with three or more conditions.

Logistic Regression Analysis:

Colorectal Cancer Screening in Males:

This analysis included 1,563 men. Results from our random effect logistic regression modeling with clinic as a random effect are shown in Table 3. Cardiovascular disease and chronic digestive disorder were significant in the model of colorectal cancer screening in males (Table 3). Those with cardiovascular disease were 41% less likely to be up-to-date ($p < 0.001$), and those with chronic digestive disorders were 83% more likely to be up-to-date for colorectal cancer screening ($p < 0.001$). For individual chronic conditions, we found in our univariate analysis similar results, where those with cardiovascular disease were 23% less likely to be up-to-date ($p=0.036$), those with digestive disorders were twice as likely to be up-to-date ($p < 0.001$), and those with low back pain were 29% more likely to be up-to-date ($p=0.042$) (Table 4). After adjusting for potential confounders of patient characteristics and demographics, the results among those with cardiovascular disease and digestive disorder did not change, though those with low back pain now had an odds ratio closer to 1.0. In the same analysis, we also showed our assessments of each chronic condition with previously adjusted confounders and the other chronic conditions. The finding for cardiovascular disease and digestive disorder persisted, OR=0.59 ($p=0.001$) and OR=1.86 ($p < 0.001$), respectively. Those with diabetes mellitus were somewhat less likely to be up-to-date for screening, through our adjustments, though not statistically significant, OR=0.77 ($p=0.113$).

Looking at categories of number of comorbid chronic diseases, the unadjusted odds of being up-to-date for colorectal cancer screening in males increased with increasing number of conditions: 44% more likely in those with three or more conditions

compared to those with no conditions, (p=0.033) (Table 5). Having one condition had the same odds of being up-to-date as having no conditions, OR=1.07 (p=0.747). However, as we saw in our earlier analysis, having digestive disorder indicated a significant effect of being up-to-date for colorectal cancer screening. Thus, it is likely that the increase and decrease in odds ratio by individual conditions created a dilution of effects when grouped into categories of number of conditions. We analyzed the categories of number of conditions further by separating out those with chronic digestive disorders. Without those in the categories of number of conditions, the likelihood of being up-to-date with increasing number of conditions disappears. Our adjusted odds ratios showed that having one or more chronic conditions lowered the likelihood of being up-to-date, though not statistically significantly so (p=0.544). Though this finding is more significant in the categories of number of conditions without digestive disorder with an OR=0.54 for those with three or more conditions (p=0.017). From our modeling process, the covariate of number of clinic visits was strongly associated with our outcome variable. We further adjusted the categories of number of conditions by the number of clinic visits only; the results were very similar to the fully adjusted odds ratio. Those with three or more conditions were 39% less likely to be up-to-date, (p=0.016). This suggests that this covariate is a strong driver for the change in direction of the odds ratio of being up-to-date with increasing number of conditions. This finding persisted to a greater degree for the categories of number of conditions without digestive disorder.

<u>Colorectal cancer screening in females:</u>

This analysis included 1,870 women. Our random effect logistic regression modeling with clinic as a random effect showed that chronic digestive disorder, diabetes mellitus type 1 or type 2, and depression/anxiety were significant in a predictive model for colorectal cancer screening in females (Table 3). Those with diabetes mellitus were 27% less likely to be up-to-date (p=0.051), those with depression were 31% less likely to be up-to-date (p=0.003), and those with chronic digestive disorders were 71% more likely to be up-to-date for colorectal cancer screening (p <0.001). For individual chronic conditions, we found in our univariate analysis slightly different results, where those with depression were as likely to be up-to-date as those without disease (p=0.844), those with digestive disorders were more than twice as likely to be up-to-date (p <0.001), those with diabetes were 11% less likely to be up-to-date (p=0.401), and those with low back pain were 70% more likely to be up-to-date (p<0.001) (Table 4). When adjusted for potential confounders of patient characteristics and demographics, the finding was similar to that found in the model, those with digestive disorder had an OR=1.70 (p<0.001) and those with depression had an OR=0.76 (p-0.026). Those with low back pain were 26% more likely to be up-to-date, though p=0.068. Those with diabetes were 25% less likely to be up-to-date (p=0.073). In our assessment of each chronic condition with previously adjusted confounders and the rest of the chronic conditions, we found this finding to persist.

Looking at categories of number of comorbid chronic diseases, the unadjusted odds of being up-to-date for colorectal cancer screening in females increased with increasing number of conditions: 37% more likely in those with three or more conditions

compared to those with no conditions, (p=0.039) (Table 6). However, as we saw in the analysis of individual conditions similar to that of males, digestive disorder played a significant role in one's odds of being up-to-date. Without those in the categories of number of conditions, being more likely to be up-to-date with increasing number of conditions as a finding disappears. Our adjusted odds ratios showed that having one or more chronic conditions lowered one's odds of being up-to-date, though not statistically so (p=0.118). T his finding is more significant in the categories of number of conditions without digestive disorder, OR=0.58 for those with three or more conditions (p=0.018). We again adjusted for number of clinic visits, as the covariate was also strongly significant with our outcome for females. The results were very similar to the fully adjusted odds ratio. Those with three or more conditions were 38% less likely to be up-to-date, (p=0.008). This covariate is again a strong driver for the change in direction of the odds ratio of being up-to-date with increasing number of conditions. This finding persisted to a greater degree for the categories of number of conditions without digestive disorder, as it did for males.

Breast cancer screening:

Of the 1,870 women in the study, 1859 of them were included in the analysis. Six women were excluded due to having an abnormal mammogram within 2 years of chart review, four women had bilateral mastectomies and one woman was transgendered. Our predictive modeling showed that asthma/COPD/chronic lung disease, cardiovascular disease and chronic digestive disorder were significant for breast cancer screening (Table 7). Those with asthma/chronic lung disease were 41% less likely

to be up-to-date (p=0.001), those with cardiovascular disease were 29% less likely to be up-to-date (p=0.015), and those with chronic digestive disorder were 31% more likely to be up-to-date for mammography screening (p=0.029). For individual chronic conditions, we found in our univariate analysis similar results, where those asthma were 29% less likely to be up-to-date (p=0.016), those with cardiovascular disease were 29% less likely to be up-to-date (p=0.006), and those with digestive disorder were 64% more likely to be up-to-date (p <0.001) (Table 8). Those with low back pain were 23% more likely to be up-to-date, though only marginally significant (p=0.072). When adjusted for potential confounders of patient characteristics and demographics, the finding was consistent for asthma, cardiovascular disease and digestive disorder. Those with low back pain now had an odds ratio around unity. In our assessment of each chronic condition with previously adjusted confounders and the rest of the chronic conditions, the finding persisted with similar odds ratio as those adjusted without the rest of the chronic conditions.

Looking at categories of number of comorbid chronic diseases, the unadjusted odds of being up-to-date for mammography increased with increasing number of conditions: 30% more likely in those with three or more conditions compared to those with no conditions, (p=0.069) (Table 9). As digestive disorder again had an effect on one's up-to-date status, we analyzed the categories of number of conditions without those with chronic digestive disorders. Being more likely up-to-date with increasing number of conditions disappears again in the univariate analysis (Table 9). Our adjusted odds ratios showed that having one or more chronic conditions lowered one's odds of

being up-to-date, though not statistically significant (p=0.421). This finding is more significant in the categories of number of conditions without digestive disorder, OR=0.68 for those with three or more conditions (p=0.071). We further adjusted the categories of number of conditions by the number of clinic visits only; the results were very similar to the fully adjusted odds ratio. Those with three or more conditions were 38% less likely to be up-to-date, (p=0.005). The number of clinic visits again serving as the greatest factor that masks the effect of having increased number of conditions on up-to-date status of mammography screening. This finding persisted to a greater degree for the categories of number of conditions without digestive disorder (p<0.001).

Cervical cancer screening:

Of the 1,870 women in the study, 740 were included in the analysis. The rest were excluded due to age over 65 and no longer eligible for screening, history of hysterectomy, missing data and abnormal cervical screenings within last 2 years. Our modeling showed that arthritis/joint disease, diabetes mellitus type 1 or 2, and hypertension were significant in a predictive model for being up to date for cervical cancer screening (Table 10). Those with arthritis were 34% less likely to be up-to-date (p=0.035), those with diabetes mellitus were 40% less likely to be up-to-date (p=0.043), and those with hypertension were 47% less likely to be up-to-date for a Pap test (p=0.001). For individual chronic conditions, we found in our univariate analysis slightly different results: those with arthritis were 16% less likely to be up-to-date (p=0.323), those with diabetes mellitus were 30% less likely to be up-to-date (p=0.100), those with hypertension were 35% less likely to be up-to-date (p=0.006), and those with

cardiovascular disease were 29% less likely to be up-to-date (p=0.193) (Table 11). When adjusted for potential confounders of patient characteristics and demographics, the finding was similar to that of our model. Those with arthritis were 36% less likely to be up-to-date (p=0.023), those with diabetes mellitus were 44% less likely to be up-to-date (p=0.035), those with hypertension were 47% less likely to be up-to-date (p=0.001), and those with cardiovascular disease were 43% less likely to be up-to-date (p=0.060). In our joint assessment of each chronic condition with previously adjusted confounders and the rest of the conditions, the finding persisted, but only hypertension was statistically significant, OR=0.57 (p=0.004).

For categories of number of comorbid chronic diseases, the unadjusted odds of being up-to-date for cervical cancer screening decreased slightly with increasing number of conditions, though not statistically significant (p=0.888) (Table 12). Digestive disorder did not influence receipt of cervical cancer screening. As the age range for cervical cancer screening was skewed towards older patients, about half of those with digestive disorders were excluded in this analysis. Without patients with digestive disorder in the categories of number of conditions, the odds ratios remained about the same as those with digestive disorder included in the number of conditions (Table 12). Our adjusted odds ratios showed that having progressively increased number of conditions lowered one's odds of being up-to-date for cervical cancer screening (p=0.011). Those with three or more conditions were 60% less likely to be up-to-date (p=0.001). Adjusting the categories of number of conditions by the number of clinic visits only, the results were very similar to the fully adjusted odds ratio. Those with three or more conditions were

58% less likely to be up-to-date, ($p<0.001$). This again supported that this covariate served as a strong driver for the change in the odds ratios of being up-to-date with increasing number of conditions. This finding persisted for the categories of number of conditions without digestive disorder, though not to a greater degree as was previously seen for colorectal and breast cancer screenings.

DISCUSSION

This study examined the effects of comorbid conditions in rural patients and the likelihood of them being up-to-date for colorectal, breast, and cervical cancer screenings, according to the USPSTF guidelines. We looked at both individual types of chronic conditions as well as number of conditions. Our study found that not only do the number of comorbid conditions have an impact on one's screening status, but the type of disease also has an effect. No effect modifications were found between individual conditions, and ethnicity, insurance status, length of contact, and number of clinic visits. The overall screening rates were found to be low in our study population, below national rates. Our screening rates were 49% for breast cancer, 37% for colorectal cancer and 52% for cervical cancer screening, compared to national rates of 72%, 59%, and 83% in 2010, respectively. (8) In general, as in our study and previous studies, an increasing number of comorbid conditions had been associated with decreased screening rates. (27, 37) This was especially the case for cervical cancer screening in our study.

We found a different set of comorbid conditions to be significant in driving one's up-to-date status for each cancer screening. For colorectal cancer screening in men, we

found that cardiovascular disease and chronic digestive disorder influenced being up to date. In women, we found diabetes mellitus, chronic digestive disorder and depression to be significant. For breast cancer screening, we found asthma/chronic obstructive pulmonary disease (COPD)/chronic lung disease, cardiovascular disease, and chronic digestive disorder to be important. Lastly, for cervical cancer screening, we found arthritis/musculoskeletal disease/degenerative joint disease, diabetes mellitus, and hypertension to be significant. Of the individual diseases that were significant in driving one's up-to-date status, chronic digestive disorder was the only one to be significant in increasing one's odds of being up to date for screening. The remaining conditions were all associated with decreased screening among patients. These results persisted after adjustments for potential confounders such as BMI, insurance status, number of clinic visits and length of contact with clinic.

For some of the individual conditions, we could easily hypothesize why one would have a higher or lower screening rate. A patient with chronic digestive disorder would likely have a higher rate of completion of tests for colorectal cancer screening. These patients carry a diagnosis of a gastrointestinal disease or are symptomatic; and what we found to be a higher likelihood of being up to date may actually indicate tests were done for diagnostic purposes, which altered the time when they would need to have their next screening test. We tried to control for this bias by excluding patients with personal history of colorectal cancers, but the finding persisted. In our up-to-date status of colorectal cancer screening, we also stratified higher risk category by including family history of colorectal cancer. These patients may also frequent the physician's

office, which increased the window of opportunity for having a conversation about screening. Although, after adjusting for number of visit counts, having digestive disorder still led one to have an increased odds of screening. The reason why men with cardiovascular disease had a lower screening rate may be due to their poorer health status, and thus less benefit from screening, or that more time might be spent in the clinic on managing medications for patients' cardiovascular disease. Authors of past studies have shown that having heart disease is associated with lower colorectal cancer screening. (24) As heart disease management have been more prominently targeted for men, who tend to have higher rates of the disease, we postulate that physicians spend more time counseling men and managing their disease in clinic than for women.

We found it interesting that women with depression were less likely to be up-to-date for colorectal cancer screening, but not for breast or cervical cancer screenings. Depression in these patients might be severe and dominate most of clinic visits that conversations about preventive care were of lower priorities. Colorectal screening tends to be perceived as more of an unpleasant experience for most patients that this might have been an extra barrier to overcome for these patients. (2) Colorectal screening is referred to a specialty clinic and prep work is involved prior to the procedure; these may be extra hurdles and work for a depressed patient with likely low energy levels. We also note that low back pain, though not statistically significant, was associated with being more likely to be up-to-date for colorectal cancer screening for women. This was surprising and hard to explain. Low back pain is a common diagnosis and often difficult to manage. It could be that physicians would be more prone to offer

other services, such as preventive services, to provide more comprehensive for these patients. Low back pain could also lead physicians to speculate possible tumors around the region, which would include colon cancer spread, that prompted conversations of colorectal cancer screening. As we did not have information regarding physician-patient conversations, we could only speculate on the reasons of such a protective effect.

We found individual conditions to be associated with lower cervical cancer screening rates in women. This may be due to the fact that Pap tests are in-office procedures, which would compete for time with other health priorities at a clinic visit. Those with arthritis might have difficulty with pain and movement to be in position for a Pap test. As mentioned earlier, other authors have also found those with diabetes mellitus and hypertension to have lower screening rates. (24) These conditions may involve more in-clinic management, thus serve as competing demands for physicians and patients. Despite perhaps more frequent visits, the lower odds ratios persisted after our adjustments for length of contact and number of clinic visits. We also did not find a statistically significant effect modification of length of contact and number of visit counts for these conditions.

For breast cancer screening, those with asthma or chronic lung disease and cardiovascular disease were less likely to be up-to-date for mammography. Again, these patients may have severe disease or a poor quality of life that such preventive service would have minimal benefit and more discomfort. However, as these diseases can now be managed chronically and effectively, physicians should not disregard screening for these patients readily. Breast cancer is still a leading cause of death among women;

mortality and morbidity would be even higher for patients with comorbidities. We found it surprising that digestive disorder was associated with an increased rate of mammography screening. We could not readily surmise the reason for this relationship. Perhaps, as gastrointestinal complaints are difficult to treat and determine their causes, physicians might more readily offer ways to find other causes for their symptoms.

Individual conditions had a larger effect on one's up-to-date status of cancer screening than the number of conditions did. When conditions were aggregated into categories of number of conditions, the change in likelihood often disappeared as we saw with the category of having one comorbid condition. Even though this category was not significant, we saw that having digestive disorder or cardiovascular disease had a big effect on one's up-to-date status. We also saw that the number of clinic visits was the most significant confounder. The number of clinics visits was significantly associated with a patient's number of conditions. It changed the direction of the effect of number of conditions on up-to-date status. For every patient with a significant number of comorbid conditions, a physician should readily question whether screening for these three cancers would yield benefit to the patient. Screening considerations should weigh the benefits and harm, rather than be hastily disregarded for a patient with a large burden of conditions. Similarly for each individual disease that we examined, especially as they are prevalent conditions in the US today, a physician should be mindful of having screening conversations with their patients with these diseases. If screening has not been done for a patient with cardiovascular disease, the physician should have had that

conversation with the patient, and determined that the benefits did not overweigh the risks.

The strengths of our study included our focus on individual disease conditions, our use of medical chart review, our study of three common cancer screenings, and our target on rural populations. Studies in the past often used a combined comorbidity index, such as the Charlson index, or focused on a specific group of diseased patients, such as the diabetic population. (20-21, 26, 30, 38) Our results showed that individual conditions have varied impact on one's up-to-date status for cancer screening. Understanding of why that is would facilitate more appropriate screenings and meeting the goals of Healthy People 2020. Our use of medical charts allowed us to avoid recall bias, as may be present with survey or self-reported results, whereas in a chart review the dates and results of screening tests are readily available. We focused on completion of screening tests rather than physician recommendations, to facilitate more accurate, objective records of when and if tests were done. We studied the results for all three cancer screening tests, as they are common and frequently discussed in a primary care clinic setting. We also focused our study on the rural population, which is often lagging in screening rates compared to its urban counterpart and under-studied. As studies have found in the past that access to physicians played a large barrier to receive the appropriate cancer screening, we tried to eliminate this factor by abstracting charts at primary care clinics, where patients have an established relationship. (39)

Potential limitations of our study included our missing information in regards to patient information, such as insurance and ethnicity, and that we did not have

information regarding patient and physician perspectives toward barriers of cancer screening. The latter would further elucidate potential barriers to screening. Our missing information regarding patient characteristics and demographics would lead to information bias; however, we included in our analysis a category of "not noted" to account for any impact this category would have on screening status. We had those with "no disease" as our referent group, which might have urged our results to show lower OR in those who are sick. However, we saw that the screening rates for those with "no disease" under the categories that we examined were low, below 50%, despite the opportunity for more preventive visits for those patients. For our cervical cancer screening analysis, we had a small sample size and also women towards the end of their screening criteria, from 55-65 year-old. This may have resulted in selection bias, as we had much older patients in our pool and likely to be less up-to-date for screening. We also were not able to collect information regarding patient's functional status and quality of life, which would help us further assess comorbidity's relationship to cancer screening status. We were able to adjust for many potential confounders, though we did not have information such as education or income. We were able to extrapolate socioeconomic status through occupation and insurance status. Even though we had patients in established primary care clinics, we surmised that those without that relationship would have even lower screening rates.

In the future, it would be interesting to gather information on patient's and physician's perspective of cancer screenings, and determine how best to fit cancer screening into opportunistic visits for those with multiple conditions. Information on

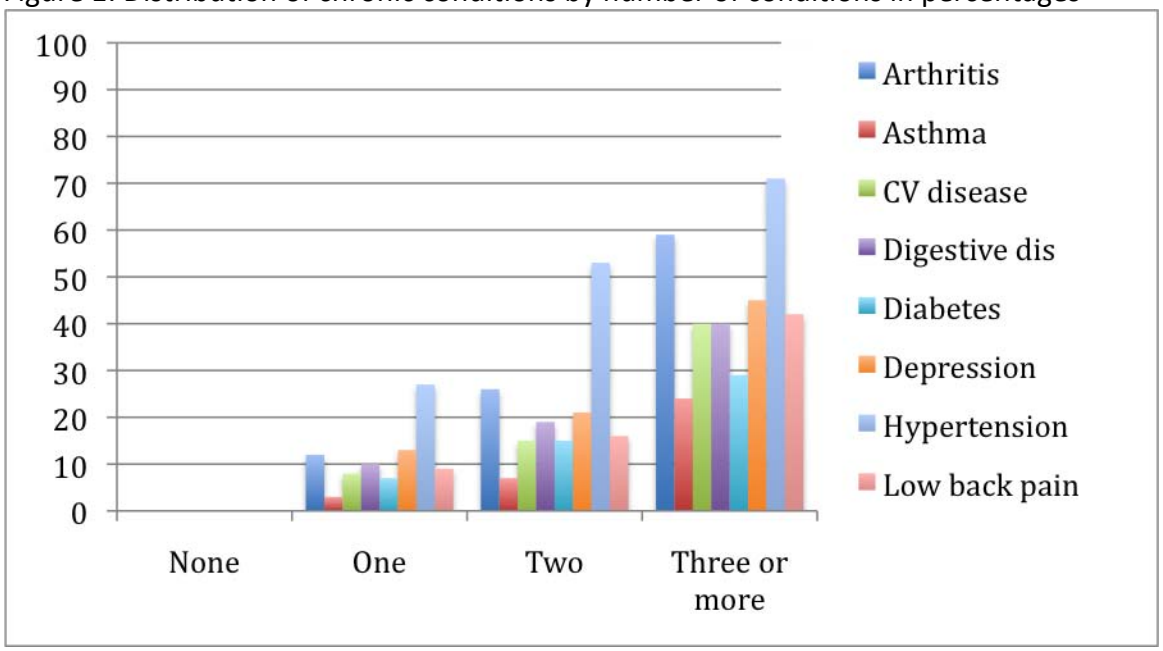
patient's quality of life and functional status would also help us to further understand a patient's up-to-date status. Interventional studies could also be done to evaluate how to best improve screening among those patients with conditions that bare less risk on mortality, such as depression and low back pain, as well as for those patients with multiple high-risk diseases in the context of their other health priorities.

CONCLUSION

In conclusion, we found that specific conditions have a larger impact on being up to date for cancer screening than the number of conditions. Although, when the number of conditions reached three or more, they also had an impact on screening status, especially for cervical cancer screening. We initially hypothesized that conditions that demand much of physicians' time in the clinic for acute management, such as diabetes or heart disease, would lower one's screening rate. Although this was true for some cancer screening tests, it was not the case for all three cancer screenings. Unique patient conditions, more than just their health status, played a role in getting the appropriate cancer screenings. Those with conditions that may not impose risk on a patient's mortality still had low screening rates. Screening conversations are important to be had in the primary care setting, especially among those who may be more ill. Understanding how individual diseases relate to cancer screening status in patients may help to decrease patient barriers to screening and help modify physician behaviors to increase adherence to screening guidelines in rural areas.

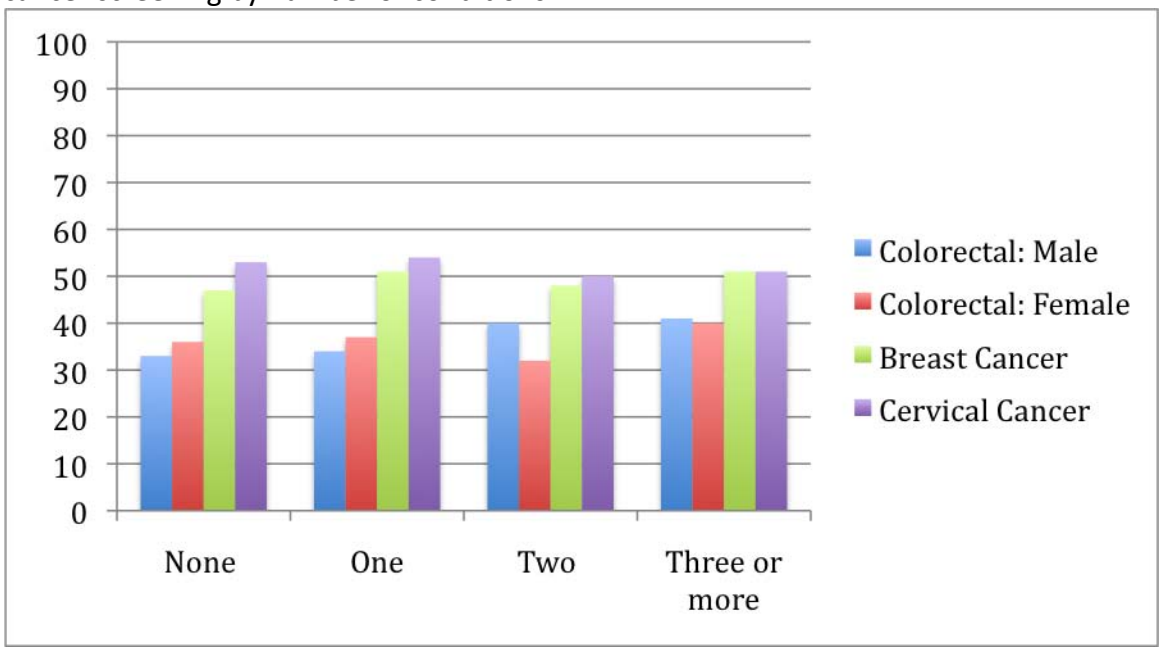
Figures

Figure 1: Distribution of chronic conditions by number of conditions in percentages



Y axis: percentages, X axis: number of conditions

Figure 2: Distribution of up-to-date percentages for colorectal, breast, and cervical cancer screening by number of conditions



Y axis: percentages, X axis: number of conditions

Tables

Table 1: Variables

Variable	Category	Type	Additional Description
Up to date status colorectal cancer screening	Outcome	Binary	• USPSTF 2002 Guidelines* • Based on risk status algorithm: personal and family history
Up to date status breast cancer screening	Outcome	Binary	• USPSTF 2002 Guidelines* • Based on risk status algorithm: family history
Up to date status cervical cancer screening	Outcome	Binary	• USPSTF 2003 Guidelines* • Based on risk status algorithm: family history
Chronic diseases:	Main effect		Kappa > 0.50
Arthritis	Predictor	Binary	• Chart diagnosis of arthritis, musculoskeletal, or degenerative joint diseases
Asthma	Predictor	Binary	• Chart diagnosis of asthma, emphysema, COPD or other chronic respiratory diseases
Cardiovascular disease	Predictor	Binary	• Chart diagnosis of cardiovascular disease
Hypertension	Predictor	Binary	• Chart diagnosis of hypertension
Chronic digestive disorders	Predictor	Binary	• Chart diagnosis of chronic digestive disorders
Low back pain	Predictor	Binary	• Chart diagnosis of low back pain
Diabetes mellitus	Predictor	Binary	• Chart diagnosis of diabetes mellitus type 1 or 2
Depression	Predictor	Binary	• Chart diagnosis of depression or anxiety
Categories of comorbid conditions	Predictor	Categorical	• Categorized based on histogram and significance • 4 categories: None, One condition, two conditions, three or more conditions • None as reference group
Potential Confounders:			
Age	Predictor	Categorical	• 4 categories based on histogram: 50-59 yo, 60-64 yo, 65-75 yo, 75+ yo • 50-59 yo as reference group
Marital status	Predictor	Categorical	• 3 categories:

			Partnered, Single, Not noted • Partnered as reference group
Occupation	Predictor	Categorical	• 4 categories: Employed, unemployed/disabled, retired, not noted • Employed as reference group
Ethnicity	Predictor	Categorical	• 3 categories: Not Hispanic, Hispanic, Not noted • Not Hispanic as reference group
Last insurance type	Predictor	Categorical	• 5 categories: Private, Medicare or Medicare/Private, Medicaid or Medicaid/Medicare, Uninsured, Unknown • Private insurance as reference group
BMI classification	Predictor	Categorical	• Calculated from weight and height • 4 categories based on clinical definition: normal: <25, pre-obese: 25 to <30, obese: 30 and up, not noted • Normal: <25 as reference group
Smoking status	Predictor	Categorical	• 4 categories: Never smoker, former smoker, current smoker, not noted • Never smoker as reference group
Alcohol status	Predictor	Categorical	• 4 categories: Non-user, former user, current user, not noted • Non-user as reference group
Length of contact	Predictor	Categorical	• Calculated from chart review date and earliest date on file in years • Categorized based on histogram • 4 categories: < 6 months, 6 months to < 1 year, 1 year to <2 years, 2 years to < 5 years, 5 years and more • < 6 months as reference group
Total visit count	Predictor	Categorical	• Categorized based on histogram • 4 categories: < 5 visits, 5-10 visits, 11-20 visits, >20 visits • < 5 visits as reference group

Table 2: Study patient characteristics

Table 2: Demographics by number of chronic diseases					
Characteristics	**No conditions**	**One**	**Two**	**Three or more**	p-value
N (%)	503 (15%)	646 (19%)	786 (23%)	1498 (44%)	
Community A (M)	121 (24%)	182 (28%)	302 (38%)	624 (42%)	<0.001
Community B (H)	382 (76%)	464 (72%)	484 (62%)	874 (58%)	
Gender:					0.547
Female	268 (53%)	346 (54%)	419 (53%)	837 (56%)	
Male	235 (47%)	300 (46%)	367 (47%)	661 (44%)	
Age:					<0.001
50-59	291 (58%)	287 (44%)	303 (39%)	465 (31%)	
60-64	94 (19%)	150 (23%)	159 (20%)	321 (21%)	
65-75	85 (17%)	138 (21%)	201 (26%)	382 (26%)	
75+	33 (7%)	71 (11%)	123 (16%)	330 (22%)	
BMI:					<0.001
<25	151 (30%)	133 (21%)	126 (16%)	215 (14%)	
25 to <30	138 (27%)	176 (27%)	211 (27%)	348 (23%)	
>=30	65 (13%)	165 (26%)	237 (30%)	522 (35%)	
Unknown	149 (30%)	172 (27%)	212 (27%)	413 (28%)	
Ethnicity:					0.015
Hispanic	42 (8%)	92 (14%)	109 (14%)	180 (12%)	
Non-Hispanic	154 (31%)	199 (31%)	224 (29%)	491 (33%)	
Unspecified	307 (61%)	355 (55%)	453 (58%)	827 (55%)	
Race:					<0.001
White	228 (45%)	332 (51%)	444 (56%)	1016 (68%)	
Other	14 (3%)	21 (3%)	25 (3%)	40 (3%)	
Unspecified	261 (52%)	293 (45%)	317 (40%)	442 (30%)	
Marital Status:					<0.001
Partnered	336 (67%)	423 (65%)	490 (62%)	890 (59%)	
Not partnered	99 (20%)	150 (23%)	223 (28%)	510 (34%)	
Unknown	68 (14%)	73 (11%)	73 (9%)	98 (7%)	
Occupation:					<0.001
Employed	288 (57%)	343 (53%)	342 (44%)	456 (30%)	
Unemployed/disabled	21 (4%)	48 (7%)	75 (10%)	256 (17%)	
Retired	104 (21%)	144 (22%)	237 (30%)	566 (38%)	
Unknown	90 (18%)	111 (17%)	132 (17%)	220 (15%)	
Insurance:					<0.001
Private	317 (63%)	363 (56%)	404 (51%)	756 (50%)	
Medicare or Medicare/Private	33 (7%)	93 (14%)	136 (17%)	311 (21%)	
Medicaid or Medicaid/Medicare	15 (3%)	19 (3%)	34 (4%)	122 (8%)	

Uninsured	34 (7%)	48 (7%)	81 (10%)	120 (8%)	
Unknown	104 (21%)	123 (19%)	131 (17%)	189 (13%)	
Smoking History:					<0.001
Non-smoker	350 (70%)	407 (63%)	451 (57%)	689 (46%)	
Former smoker	82 (16%)	143 (22%)	187 (24%)	454 (30%)	
Current smoker	20 (4%)	50 (8%)	105 (13%)	305 (20%)	
Unknown	51 (10%)	46 (7%)	43 (5%)	50 (3%)	
Alcohol Use:					<0.001
Non-user	170 (34%)	256 (40%)	331 (42%)	697 (47%)	
Former user	20 (4%)	32 (5%)	58 (7%)	136 (9%)	
Current user	245 (49%)	293 (45%)	329 (42%)	570 (38%)	
Unknown	68 (14%)	65 (10%)	68 (9%)	95 (6%)	
Length of Contact with Clinic:					
Median (25%, 75%) in years	7.7 (1.0, 18)	8.1 (2.7, 18)	9.5 (3.2, 20)	11 (5.9, 21)	
Health Care visit count in last 5 yrs:					
Median (range)	4 (1-33)	6 (1-46)	10 (1-254)	18 (1-407)	
Chronic Diseases:					
Arthritis/MS/Joint Disease	0 (0%)	76 (12%)	207 (26%)	884 (59%)	<0.001
* No Disease	503 (100%)	570 (88%)	579 (74%)	614 (41%)	
Asthma/COPD/ Chronic Respiratory	0 (0%)	22 (3%)	58 (7%)	353 (24%)	<0.001
* No Disease	503 (100%)	624 (97%)	728 (93%)	1145 (76%)	
Cardiovascular Disease	0 (0%)	49 (8%)	118 (15%)	598 (40%)	<0.001
* No Disease	503 (100%)	597 (92%)	668 (85%)	900 (60%)	
Chronic Digestive Disorders	0 (0%)	67 (10%)	153 (19%)	596 (40%)	<0.001
* No Disease	503 (100%)	579 (90%)	633 (81%)	902 (60%)	
Diabetes mellitus 1 or 2	0 (0%)	44 (7%)	116 (15%)	436 (29%)	<0.001
* No Disease	503 (100%)	602 (93%)	670 (85%)	1062 (71%)	
Depression/Anxiety	0 (0%)	81 (13%)	162 (21%)	673 (45%)	<0.001
* No Disease	503 (100%)	565 (87%)	624 (79%)	825 (55%)	
Hypertension	0 (0%)	173 (27%)	413 (53%)	1068 (71%)	<0.001
* No Disease	503 (100%)	473 (73%)	373 (47%)	430 (29%)	
Low Back Pain	0 (0%)	58 (9%)	129 (16%)	626 (42%)	<0.001
* No Disease	503 (100%)	588 (91%)	657 (84%)	872 (58%)	
Up-to-Date status:					
Colorectal Ca: Males	77 (33%)	103 (34%)	146 (40%)	271 (41%)	0.060
* Not up-to-date	158 (67%)	197 (66%)	221 (60%)	390 (59%)	

Colorectal Ca: Females	96 (36%)	128 (37%)	132 (32%)	331 (40%)	0.048
* Not up-to-date	172 (64%)	218 (63%)	287 (69%)	506 (60%)	
Breast Cancer	125 (47%)	176 (51%)	199 (48%)	420 (51%)	0.595
* Not up-to-date	142 (53%)	170 (49%)	217 (52%)	410 (49%)	
Cervical Cancer	87 (53%)	90 (54%)	77 (50%)	130 (51%)	0.817
* Not up-to-date	76 (47%)	76 (46%)	78 (50%)	126 (49%)	

Table 3: Random effect logistic regression models with significant individual conditions for colorectal cancer screening

Adjusted Significant Comorbid Disease Affecting Colorectal Cancer Screening Based on Logistic Modeling

Males:		Up-to-date Colorectal Cancer Screening Status	
Individual Disease:		OR (95% CI)*	P-value
Cardiovascular Disease		0.59 (0.44-0.79)	<0.001
Digestive Disorders		1.83 (1.37-2.44)	<0.001
Females:			
Individual Disease:		OR (95% CI)**	P-value
Digestive Disorders		1.71 (1.34-2.18)	<0.001
Diabetes Mellitus		0.73 (0.54-1.00)	0.051
Depression		0.69 (0.55-0.88)	0.003

*These chronic diseases in the model adjusted for age, ethnicity, alcohol history, last insurance status, occupation, total visit counts in last 5 years, length of contact with the clinic

**These chronic diseases in the model adjusted for age, marital status ethnicity, alcohol history, last insurance status, BMI class, total visit counts in last 5 years, length of contact with the clinic

Table 4: Colorectal cancer screening univariate and adjusted odds ratios for individual conditions

Table 4: Individual Comorbid Condition's Effect on Colorectal Cancer Screening for Males According to USPSTF						
	Up-to-date Colorectal Cancer Screening Status					
Males:	Univariate		Adjusted for Demographics*		Adjusted for Demographics and Chronic Diseases**	
Chronic Disease:	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
(Referent=no disease)						
Arthritis	1.25 (0.99-1.58)	0.065	1.04 (0.80-1.36)	0.761	0.98 (0.74-1.28)	0.858
Asthma	1.12 (0.80-1.57)	0.510	1.01 (0.56-1.10)	0.164	1.01 (0.69-1.48)	0.971
Cardiovascular Disease	**0.77 (0.60-0.98)**	**0.036**	**0.61 (0.45-0.82)**	**0.001**	**0.59 (0.44-0.80)**	**0.001**
Digestive	**2.07 (1.60-2.69)**	**<0.001**	**1.80 (1.35-2.41)**	**<0.001**	**1.86 (1.39-2.49)**	**<0.001**
Diabetes Mellitus 1 or 2	0.88 (0.66-1.17)	0.373	0.73 (0.53-1.02)	0.062	0.77 (0.55-1.07)	0.113
Depression	1.24 (0.87-1.49)	0.359	0.95 (0.69-1.29)	0.724	0.90 (0.66-1.24)	0.530
Hypertension	1.18 (0.95-1.47)	0.135	0.96 (0.74-1.24)	0.730	1.06 (0.81-1.38)	0.695
Low Back Pain	**1.29 (1.01-1.66)**	**0.042**	1.05 (0.80-1.38)	0.741	1.01 (0.76-1.33)	0.972
Females:						
Arthritis	1.18 (0.96-1.45)	0.110	0.86 (0.68-1.09)	0.223	0.83 (0.65-1.06)	0.129
Asthma	1.24 (0.93-1.65)	0.135	1.07 (0.78-1.46)	0.690	1.04 (0.76-1.43)	0.801
Cardiovascular Disease	1.08 (0.85-1.38)	0.535	0.90 (0.68-1.20)	0.485	0.94 (0.71-1.26)	0.692
Digestive	**2.21 (1.77-2.75)**	**<0.001**	**1.70 (1.33-2.16)**	**<0.001**	**1.72 (1.34-2.19)**	**<0.001**
Diabetes Mellitus 1 or 2	0.89 (0.67-1.17)	0.401	0.75 (0.55-1.03)	0.073	0.77 (0.56-1.06)	0.115
Depression	1.02 (0.83-1.26)	0.844	**0.76 (0.60-0.97)**	**0.026**	**0.71 (0.56-0.91)**	**0.006**
Hypertension	1.04 (0.85-1.27)	0.700	0.87 (0.69-1.10)	0.255	0.90 (0.71-1.15)	0.399
Low Back Pain	**1.70 (1.36-2.13)**	**<0.001**	1.26 (0.98-1.62)	0.068	1.29 (0.99-1.67)	0.055

*Each disease adjusted for age, marital status, ethnicity, BMI class, occupation, alcohol history, smoking history, insurance status, length of contact with clinic, total visit counts in last 5 years

**Each disease adjusted for age, marital status, ethnicity, BMI class, occupation, alcohol history, smoking history, insurance status, length of contact with clinic, total visit counts in last 5 years, and rest of the chronic diseases

Table 5: Colorectal cancer screening univariate and adjusted odds ratios for number of conditions: Males

Table 5: Categories of comorbid conditions and its effect on colorectal cancer screening according to USPSTF: Males									
		Up-to-date colorectal cancer screening status							
Males:									
					Visit count				
Categories of		Univariate OR	p-value		Adjusted OR	p-value		Adjusted OR*	p-value
Conditions		(95% CI)			(95% CI)			(95% CI)	
			0.080			0.114			0.544
None		1.00 (Referent)			1.00 (Referent)			1.00 (Referent)	
One		1.07 (0.73-1.56)	0.747		0.72 (0.47-1.10)	0.125		0.75 (0.48-1.18)	0.212
Two		1.34 (0.93-1.93)	0.114		0.73 (0.48-1.09)	0.124		0.84 (0.53-1.31)	0.433
Three or more		**1.44 (1.03-2.02)**	**0.033**		**0.61 (0.41-0.91)**	**0.016**		0.74 (0.47-1.17)	0.200
					Visit count				
Cat of Conditions		Univariate OR	p-value		Adjusted OR	p-value		Adjusted OR*	p-value
without Digestive Dis		(95% CI)			(95% CI)			(95% CI)	
			0.591			0.011			0.086
None		1.00 (Referent)			1.00 (Referent)			1.00 (Referent)	
One		0.95 (0.64-1.42)	0.818		0.65 (0.42-1.01)	0.053		0.66 (0.41-1.05)	0.082
Two		1.22 (0.83-1.78)	0.314		0.67 (0.44-1.02)	0.064		0.75 (0.46-1.21)	0.233
Three or more		1.08 (0.75-1.55)	0.694		**0.48 (0.31-0.74)**	**0.001**		**0.54 (0.33-0.90)**	**0.017**

*Adjusted for age, marital status, ethnicity, BMI class, occupation, alcohol history, smoking history, insurance status, length of contact with clinic, total visit counts in last 5 years

Table 6: Colorectal cancer screening univariate and adjusted odds ratios for number of conditions: Females

Table 6: Categories of comorbid conditions and its effect on colorectal cancer screening according to USPSTF: Females								
		Up-to-date colorectal cancer screening status						
Females:								
					Visit count			
Categories of		Univariate OR	p-value		Adjusted OR	p-value		Adjusted OR*	p-value
Conditions		(95% CI)			(95% CI)			(95% CI)	
			0.016			0.012			0.118
None		1.00 (Referent)			1.00 (Referent)			1.00 (Referent)	
One		1.11 (0.79-1.56)	0.563		0.81 (0.57-1.17)	0.269		0.86 (0.58-1.26)	0.432
Two		0.94 (0.67-1.31)	0.697		**0.58 (0.40-0.83)**	**0.003**		**0.64 (0.43-0.95)**	**0.028**
Three or more		**1.37 (1.02-1.84)**	**0.039**		**0.62 (0.44-0.89)**	**0.008**		0.69 (0.46-1.02)	0.063
					Visit count				
Cat of Conditions		Univariate OR	p-value		Adjusted OR	p-value		Adjusted OR*	p-value
without Digestive Dis.		(95% CI)			(95% CI)			(95% CI)	
			0.601			<0.001			0.089
None		1.00 (Referent)			1.00 (Referent)			1.00 (Referent)	
One		0.99 (0.96-1.41)	0.957		0.73 (0.50-1.06)	0.098		0.81 (0.54-1.23)	0.325
Two		0.80 (0.56-1.15)	0.236		**0.51 (0.34-0.75)**	**0.001**		**0.64 (0.41-0.99)**	**0.043**
Three or more		0.94 (0.68-1.31)	0.722		**0.47 (0.32-0.69)**	**<0.001**		**0.58 (0.37-0.91)**	**0.018**

*Adjusted for age, marital status, ethnicity, BMI class, occupation, alcohol history, smoking history, insurance status, length of contact with clinic, total visit counts in last 5 years

Table 7: Random effect logistic regression model with significant individual conditions for breast cancer screening

Table 7: Adjusted Significant Comorbid Disease Affecting Breast Cancer Screening Based on Logistic Modeling			
		Up-to-date Mammography Status	
Individual Disease:		OR (95% CI)*	P-value
Asthma/COPD/chronic lung disease		0.59 (0.43-0.80)	0.001
Cardiovascular disease		0.71 (0.54-0.94)	0.015
Digestive disorder		1.31 (1.03-1.66)	0.029

*These chronic diseases in the model adjusted for age, marital status, BMI class, total visit counts in last 5 years, length of contact with clinic, alcohol history, smoking history, and insurance status

Table 8: Breast cancer screening univariate and adjusted odds ratios for individual conditions

Table 8: Individual Comorbid Condition's Effect on Breast Cancer Screening According to USPSTF								
		Up-to-date Mammography Status						
		Univariate			Adjusted for Demographics*		Adjusted for Demographics and Chronic Diseases**	
Chronic Disease:		OR (95% CI)	P-value		OR (95% CI)	P-value	OR (95% CI)	P-value
(Referent=no disease)								
Arthritis		1.10 (0.91-1.34)	0.325		0.93 (0.74-1.16)	0.519	0.94 (0.74-1.18)	0.585
Asthma		**0.71 (0.54-0.94)**	**0.016**		**0.60 (0.44-0.81)**	**0.001**	**0.60 (0.44-0.81)**	**0.001**
Cardiovascular Disease		**0.71 (0.56-0.91)**	**0.006**		**0.70 (0.53-0.93)**	**0.013**	**0.71 (0.54-0.94)**	**0.017**
Digestive		**1.64 (1.32-2.04)**	**<0.001**		**1.28 (1.01-1.63)**	**0.044**	**1.33 (1.04-1.70)**	**0.022**
Diabetes Mellitus 1 or 2		0.94 (0.72-1.21)	0.609		0.83 (0.62-1.11)	0.203	0.83 (0.62-1.13)	0.237
Depression		1.19 (0.98-1.45)	0.086		0.88 (0.70-1.11)	0.280	0.89 (0.71-1.12)	0.332
Hypertension		1.06 (0.87-1.27)	0.578		1.08 (0.86-1.35)	0.524	1.11 (0.88-1.40)	0.382
Low Back Pain		1.23 (0.98-1.53)	0.072		0.93 (0.73-1.20)	0.587	0.92 (0.71-1.19)	0.512

*Each disease adjusted for age, marital status, ethnicity, BMI class, occupation, alcohol history, smoking history, insurance status, length of contact with clinic, total visit counts in last 5 years

**Each disease adjusted for age, marital status, ethnicity, BMI class, occupation, alcohol history, smoking history, insurance status, length of contact with clinic, total visit counts in last 5 years, and rest of the chronic diseases

Table 9: Breast cancer screening univariate and adjusted odds ratios for number of conditions

Table 9: Categories of comorbid conditions and its effect on breast cancer screening according to USPSTF									
		Up-to-date Mammography Status							
					Visit count				
Categories of		Univariate OR	p-value		Adjusted OR	p-value		Adjusted OR*	p-value
Conditions		(95% CI)			(95% CI)			(95% CI)	
			0.301			0.010			0.421
None		1.00-Referent			1.00-Referent			1.00-Referent	
One		1.23 (0.89-1.71)	0.210		0.94 (0.66-1.33)	0.721		1.09 (0.75-1.59)	0.635
Two		1.15 (0.84-1.57)	0.393		0.74 (0.52-1.04)	0.079		0.93 (0.64-1.36)	0.725
Three or more		1.30 (0.98-1.73)	0.069		**0.62 (0.45-0.87)**	**0.005**		0.84 (0.57-1.22)	0.360
					Visit count				
Cat of Conditions		Univariate OR	p-value		Adjusted OR	p-value		Adjusted OR*	p-value
without Digestive Dis		(95% CI)			(95% CI)			(95% CI)	
			0.618			<0.001			0.066
None		1.00-Referent			1.00-Referent			1.00-Referent	
One		1.21 (0.86-1.68)	0.274		0.93 (0.65-1.32)	0.680		1.11 (0.75-1.63)	0.609
Two		0.99 (0.71-1.39)	0.961		**0.65 (0.45-0.93)**	**0.019**		0.85 (0.57-1.27)	0.432
Three or more		1.05 (0.77-1.43)	0.763		**0.51 (0.35-0.73)**	**<0.001**		0.68 (0.45-1.03)	0.071

*Adjusted for age, marital status, ethnicity, BMI class, occupation, alcohol history, smoking history, insurance status, length of contact with clinic, total visit counts in last 5 years

Table 10: Random effect logistic regression model with significant individual conditions for cervical cancer screening

Table 10: Adjusted Significant Comorbid Disease Affecting Cervical Cancer Screening Based on Logistic Modeling			
		Up-to-date Cervical Cancer Screening Status	
Individual Disease:		OR (95% CI)*	P-value
Arthritis/MS/DJD dis.		0.66 (0.45-0.97)	0.035
Diabetes Mellitus		0.60 (0.36-0.98)	0.043
Hypertension		0.53 (0.37-0.76)	0.001

*All of these chronic diseases in the model adjusted for marital status, BMI class, total visit counts in last 5 years

Table 11: Cervical cancer screening univariate and adjusted odds ratios for individual conditions

Table 11: Individual Comorbid Condition's Effect on Cervical Cancer Screening According to USPSTF								
		Up-to-date Cervical Cancer Screening Status						
		Univariate			Adjusted for Demographics*		Adjusted for Demographics and Chronic Diseases**	
Chronic Disease:		OR (95% CI)	P-value		OR (95% CI)	P-value	OR (95% CI)	P-value
(Referent=no disease)								
Arthritis		0.84 (0.60-1.18)	0.323		**0.64 (0.43-0.94)**	**0.023**	0.69 (0.46-1.03)	0.067
Asthma		1.06 (0.65-1.70)	0.821		0.86 (0.71-1.44)	0.596	0.90 (0.50-1.59)	0.709
Cardiovascular Disease		0.71 (0.43-1.19)	0.193		0.57 (0.32-1.02)	0.060	0.59 (0.32-1.08)	0.087
Digestive		1.04 (0.73-1.49)	0.813		0.69 (0.45-1.04)	0.079	0.70 (0.45-1.07)	0.098
Diabetes Mellitus 1 or 2		0.70 (0.47-1.07)	0.100		**0.56 (0.33-0.96)**	**0.035**	0.69 (0.39-1.20)	0.187
Depression		1.24 (0.90-1.70)	0.181		1.05 (0.72-1.53)	0.781	1.07 (0.72-1.58)	0.739
Hypertension		**0.65 (0.48-0.88)**	**0.006**		**0.53 (0.36-0.77)**	**0.001**	**0.57 (0.39-0.84)**	**0.004**
Low Back Pain		1.05 (0.73-1.50)	0.801		0.69 (0.46-1.05)	0.086	0.72 (0.47-1.12)	0.147

*Each disease adjusted for age, marital status, ethnicity, BMI class, occupation, alcohol history, smoking history, insurance status, length of contact with clinic, total visit counts in last 5 years

**Each disease adjusted for age, marital status, ethnicity, BMI class, occupation, alcohol history, smoking history, insurance status, length of contact with clinic, total visit counts in last 5 years, and rest of the chronic diseases

Table 12: Cervical cancer screening univariate and adjusted odds ratios for number of conditions

Table 12: Categories of comorbid conditions and its effect on cervical cancer screening according to USPSTF								
		Up-to-date cervical cancer screening status						
					Visit count			
Categories of		Univariate OR	p-value		Adjusted OR	p-value		Adjusted OR*	p-value
Conditions		(95% CI)			(95% CI)			(95% CI)	
			0.888			0.003			0.011
None		1.00-Referent			1.00-Referent			1.00-Referent	
One		1.05 (0.68-1.63)	0.814		0.79 (0.49-1.26)	0.318		0.76 (0.45-1.27)	0.294
Two		0.89 (0.57-1.40)	0.624		**0.58 (0.36-0.95)**	**0.029**		**0.58 (0.34-1.00)**	**0.049**
Three or more		0.94 (0.63-1.40)	0.748		**0.42 (0.26-0.68)**	**<0.001**		**0.40 (0.23-0.70)**	**0.001**
					Visit count				
Cat of Conditions		Univariate OR	p-value		Adjusted OR	p-value		Adjusted OR*	p-value
without Digestive Dis		(95% CI)			(95% CI)			(95% CI)	
			0.792			0.008			0.019
None		1.00-Referent			1.00-Referent			1.00-Referent	
One		1.05 (0.67-1.65)	0.830		0.80 (0.50-1.30)	0.370		0.80 (0.46-1.37)	0.406
Two		0.84 (0.52-1.39)	0.511		**0.58 (0.34-0.98)**	**0.043**		0.60 (0.33-1.09)	0.096
Three or more		0.88 (0.56-1.39)	0.581		**0.41 (0.24-0.70)**	**0.001**		**0.38 (0.20-0.71)**	**0.003**

*Adjusted for age, marital status, ethnicity, BMI class, occupation, alcohol history, smoking history, insurance status, length of contact with clinic, total visit counts in last 5 years

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