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Estimated effects of potential interventions to prevent declines in self-rated health among breast cancer survivors

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Abstract

Purpose—To estimate the effect of hypothetical changes in modifiable predictors on the incidence of fair-poor self-rated health (SRH) in breast cancer survivors.

Methods—In 2007-2008, we interviewed 832 breast cancer survivors 1 year after diagnosis (baseline) and 1 year later. First, multivariable logistic regression models estimated the association between the predictors (sociodemographic factors, access to medical care, comorbid conditions, psychosocial factors, perceived neighborhood conditions, cancer-related behaviors, clinical factors) and SRH. Second, we estimated the probabilities of fair-poor SRH for values of the predictors for each breast cancer survivor. Third, we estimated the population-wide effect of potential changes in modifiable predictors on the incidence of fair-poor SRH.

Results—7.6% of participants (92.4% white; mean age: 58.0 years) whose SRH was rated good-excellent at baseline reported fair-poor SRH one year later. The largest potential reduction in incidence of fair-poor SRH could be obtained by eliminating surgical side effects (27.8% reduction) and comorbidity (21.8% reduction) and by engaging in any physical activity (19.6% reduction).

Conclusions—A significant portion of the decline in SRH can be avoided by reducing surgical side effects, preventing comorbidity and improving physical activity using evidence-based strategies.

Keywords

Breast Cancer; Intervention; Disability

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Introduction

Although breast cancer is increasingly viewed as a chronic illness and many survivors are in good health, survivors can experience various adverse medical and psychosocial outcomes after diagnosis. Thus, patient-reported outcomes, in general, and quality of life outcomes, in particular, in breast cancer survivors have increased in importance (1). While many generic and cancer-specific multi-item measures have been used to examine health-related quality of life among breast cancer survivors (2), a single-item measure of self-rated health (SRH) has been used less frequently in studies of cancer survivors. In cancer survivors, SRH, in addition to sociodemographic and clinical measures, can help predict survival (3). There is growing recognition that routine measurement of SRH in oncology practice has the potential to improve cancer care planning, monitoring, and management for cancer survivors (1).

Most studies of SRH have used multivariable logistic regression models and cross-sectional analyses to identify factors associated with SRH. While informative, this approach provides little information about how SRH might change if the underlying population distribution of these factors were modified (4). A complementary perspective would be to estimate how hypothetical *changes* in the population distribution of different potentially modifiable predictors might serve to improve SRH using a prospective design and a population intervention framework. By using population intervention models as part of the counterfactual framework (5), we can gain insights into the potential changes in the distribution of SRH a population could experience if interventions focused on modifying a particular factor. Use of population intervention models can provide information that is relevant for public health practitioners, policy makers, and clinicians by providing quantitative results that estimate effects of potential interventions. They may then use this information to identify specific evidence-based interventions that could achieve such change. This approach will be increasingly relevant given the increasing interest in comparative effectiveness research and translation of evidence-based interventions into clinical practice. Thus, in this study we estimated the effect of potential changes in the modifiable predictors on reducing the incidence of fair-poor SRH using a population-level approach. We contrasted the results across these predictors.

Methods

Study sample

Missouri women age 25 or older diagnosed with first primary breast cancer during June, 2006 through June 2008 were identified from the statewide Missouri Cancer Registry. Women were recruited by mail; at least seven phone calls were made among those who did not respond to our mailings. Following Institutional Review Board approval at both Washington University and the University of Missouri-Columbia (where the Missouri Cancer Registry is housed) and obtaining participants' informed consent, specially trained interviewers administered baseline, computer-assisted telephone interviews one year after diagnosis. Women who participated in the baseline interview were invited to participate in the follow-up interview one year later (2 years after diagnosis).

Self-rated health

Self-rated health was based on responses to the question, “In general, would you say your health is excellent, very good, good, fair, or poor?” Analyses were based on dichotomizing self-rated health responses as “fair-poor” versus all three other categories combined, following common practice in the general population (6, 7). SRH, assessed by a single self-report item, has been found to be a strong predictor of health-care utilization, functional ability, and mortality in the general population (8-10). Test-retest kappa was 0.75 when self-rated health was reassessed 2-3 weeks later among an age-race-geography matched sample of Missouri women without breast cancer.

Predictors of incidence of fair-poor self-rated health at follow-up

Patterned after other studies among cancer survivors (11-14), we examined baseline predictors of incidence of fair-poor self-rated health at the follow-up interview, including: 1) sociodemographic factors, 2) access to medical care, 3) chronic conditions, 4) psychosocial factors, 5) perceived neighborhood conditions, 6) cancer-related behaviors (15), and 7) cancer-related clinical characteristics and surgical side effects. First, sociodemographic factors included age group, race, Hispanic origin, income categories, educational attainment, employment, marital status, home ownership, length at residence in years, food security, and income adequacy. Household income was based on standard categories from the BRFSS. Food security was based on the question if participants reported having been concerned about having enough food in the past month. Income adequacy was measured by asking participants whether they felt their household income was comfortable, enough to make ends meet, or not enough to make ends meet. Second, access to medical care consisted of having health care insurance at the time of the interview, being unable to see a doctor during the 12 months prior to the interview because of cost, and having a place to go when sick or needing advice about health issues. All questions were from the Behavioral Risk Factor Surveillance System (BRFSS) (16). Third, Katz's validated adaptation of the Charlson comorbidity index was used to measure the presence and/or history of several comorbid conditions (17). Fourth, psychosocial factors included measures of perceived stress, personal stress, social support, and depressed mood. Four items from the Cohen stress scale were used to measure perceived stress (18), and two items from The National Opinion Research Center (NORC) National Health Survey were used to measure personal stress (19). Total scores were computed for each of the two stress scales. Perceived availability of social support was measured using the Medical Outcomes Study Social Support Survey (20). Depressive symptoms were measured using the 11-item version of the Center for Epidemiologic Studies Depression (CES-D) scale (21). Fifth, perceived neighborhood conditions were measured using four scales: perceived neighborhood disorder (22), collective efficacy (23), multidimensional measure of neighborliness (24), and neighborhood fear (25). Neighborliness consisted of four items focused on neighborhood attachment and social ties. Because of the distribution of responses on this variable, we contrasted women who reported at least one day of fear and those who reported no days of fear. Scale internal reliability was sufficiently high as was the test-retest reliability of all perceived neighborhood scales (26). Sixth, cancer-related behaviors consisted of current smoking status, participation in any physical activity in the past month from the BRFSS, and alcohol use during the past month (>1 drink versus ≤1 drink) (27). Seventh, cancer-related clinical characteristics consisted of collaborative stage at diagnosis, surgical side effects, and types of treatment received. Stage at diagnosis was obtained from the Missouri Cancer Registry and was categorized into early stage (stage 0 and I) and late stage (stage II-IV). Based on the literature (28) and surgeons' anecdotal reports of patients' complaints after surgery, we developed a five-item measure of breast-surgery-associated side effects with higher summed scores for the measure indicating more severe side effects (alpha=0.74; minimum factor loading=0.60). The five questions addressed limited arm mobility/frozen shoulder; chest tightness, tenderness; breast tightness, tenderness, discomfort; arm weakness; and lymphedema of the arm. The five-point ordinal response scale for each question ranged from “not at all” to “very much.” Treatment received consisted of type of surgery, axillary lymph node removal, receipt of chemotherapy, receipt of radiotherapy, and taking hormonal therapy (Tamoxifen or Rolaxifen) at the time of the interview. Self-reported treatment is accurate relative to medical record review (29).

Statistical analysis

There are four steps for estimating the effects of potential changes in predictors (population intervention parameter on interest) on SRH based on an algorithm for computing missing counterfactual observations, called the “g-computation algorithm” (30, 31). See additional studies for a more in-depth discussion of counterfactual models (4, 5, 32). First, we estimated the association between all factors and SRH using multivariable logistic regression. We used the Hosmer-Lemeshow goodness-of-fit statistic and the c-statistic to describe the fit and discriminatory power of a model. We included all variables in the model because one of the assumptions of the g-algorithm is that there are no unmeasured confounders. Second, we used the model from step 1 to calculate the probabilities of fair-poor SRH for each study participant for the modifiable predictors, incorporating all of the factors included in the logistic model. We estimated these counterfactual probabilities of fair-poor SRH for each breast cancer survivor while fixing the modifiable predictor of interest to different levels that correspond to the range of the observed data, taking into account other predictors included in the logistic model. Third, by averaging the probabilities across all survivors and comparing to the observed incidence of fair-poor SRH, we estimated the population-wide, estimated effect of potential changes in modifiable predictors on the incidence of fair-poor SRH. Fourth, we calculated confidence intervals around the population-level effect estimate using bootstrapping. We then repeated steps 2-4 for different, modifiable predictors of interest predicting incidence of fair-poor SRH, which will allow for the comparison of the effect of changes in the predictors on SRH incidence. Multivariable logistic regression may produce biased odds ratios when there are fewer than 10 events per variable analyzed (33). From the prediction standpoint, it is important to include all variables since our results concern the accuracy of the prediction and not the hypothesis testing of the parameter estimates (34).

We calculated the absolute and relative reduction in fair-poor SRH incidence. Absolute reduction is the difference between the predicted (counterfactual) and observed incidence of fair-poor SRH. Defined as the reciprocal of the absolute risk reduction, the number needed to intervene is the estimated average number of patients needed to be exposed to an intervention to prevent a decline to fair-poor SRH in one additional breast cancer survivor (35). Lower numbers indicate potentially more effective interventions. Relative reduction is the absolute reduction expressed as a percentage from the average incidence. All analyses were implemented in STATA version 11.

We performed several sensitivity analyses to determine the robustness of our findings. We estimated a multivariable logistic regression model of whether or not participants were included in the analytic sample, and computed their predicted probability of inclusion based on age, race, and stage at diagnosis using Missouri Cancer Registry data in order to examine potential nonresponse bias. With these data we determined the probability of participation (i.e., inclusion in the analytic sample) and subsequently used the inverse to re-weight the data (36). This method gives greater weight to participants included in the analytic sample who are similar to women who were not included in the sample (36). The total of the weighted participants reflects the actual number of women interviewed, implying that some women received weights that were greater than 1 while others received weights that were less than 1. Also, we examined the effect of the OMC test score among the follow-up interview by comparing the results when including and excluding women who scored too high on the OMC test. Finally, we examined the effect of potential selection bias due to loss to follow-up for each of the predictors of SRH decline (37, 38).

Results

Study sample

During the study period, 4020 women with first primary breast cancer were identified by the Missouri Cancer Registry as potentially eligible to participate, 675 of whom we were unable to contact after seven attempts. Of the remaining women, 1164 women completed the baseline telephone interview for a participation rate of 34.8 percent. Seventy women were excluded upon screening because of high scores on the OMC test. Nonparticipants were statistically more likely to be older and African American. There was no significant difference in stage at diagnosis between study participants and non-participants.

Overall, 16.4% of breast cancer survivors reported their health as fair-poor at baseline and were subsequently excluded from further analysis. Among the 929 remaining women at baseline, seven died before the follow-up interview and 89 (9.6%) did not complete the follow-up interview, leaving 832 women for inclusion in the study. Women with the following baseline characteristics were more likely to be lost to follow-up: those not physically active (OR: 2.18; 95% CI: 1.33; 3.54), reported depressive symptoms (OR: 2.11; 95% CI: 1.21; 3.57), were unable to see a doctor because of cost (OR: 2.84; 95% CI: 1.08; 6.66), had concerns about having enough food (OR: 3.61; 95% CI: 1.82; 6.82). Those who were lost to follow-up were statistically ($p<0.05$) on average 3 years younger, reported slightly more fear, higher stress, and had higher average surgical side effects (1 point higher). None of the other 21 variables were statistically associated with a women's loss to follow-up. Table 1 describes the characteristics of the 832 women in the current analysis. In univariate analysis, several characteristics were associated with incident fair-poor SRH at follow-up (Table 2).

Multivariable model

Of 832 women who reported good-excellent health at baseline, 7.6 percent developed fair-poor health one year later. Of the modifiable predictors, only comorbidity (OR: 1.53 per point; 95% CI: 1.17; 1.99), surgical side effects (OR: 1.13 per point on the scale; 95% CI: 1.03; 1.24) and lack of participation (vs. any participation) in physical activity (OR=2.07; 95% CI: 1.09; 3.92) were statistically associated with incidence of fair-poor SRH in the multivariable model. The model's goodness-of-fit ($p=0.9273$) and discriminatory power were high (c-statistic: 0.82).

Population-level effect

The reduction in incidence of fair-poor SRH would be slightly higher for preventing surgical side effects compared to reducing physical inactivity and prevalence of comorbid conditions in the multivariable-adjusted models (Table 3). Eliminating all surgical side effects relative to the current prevalence of surgical side effects in the study population would reduce the incidence of fair-poor SRH by 27.8% in relative and by 2.1% in absolute terms (observed incidence is 7.6%). The average for the side effects scale was 7.7 (standard deviation: 3.0, median: 7) with 26.6% of women reporting “not at all” to all of the five questions comprising the scale. Incidence of fair-poor SRH would be reduced by 19.6% (absolute reduction: 1.5%) if women who were inactive at baseline had reported any physical activity participation. At baseline, 21.3% of women reported not participating in any physical activity during the prior month. Incidence of fair-poor SRH would be reduced by 21.8% (absolute reduction: 1.7%) when eliminating comorbid conditions from the current prevalence pattern in the study population. In the population, 72.5% of women reported no comorbid conditions, 16.4% reported one comorbid condition, and 11.2% reported at least two comorbid conditions. Incidence of fair-poor SRH would be reduced by 14.0% when reducing comorbid conditions by one point from the current prevalence pattern in the study population. We performed several sensitivity analyses, but our findings appeared to be robust.

Discussion

Our results show that eliminating surgical side effects, comorbid conditions, or physical inactivity one year after diagnosis would subsequently reduce the incidence of fair-poor SRH among breast cancer survivors by 20-28% one year later. Other, potentially modifiable predictors, including access to medical care, psychosocial factors, perceived neighborhood conditions, other cancer-related behaviors (alcohol use, smoking), type of treatment received, and stage at diagnosis, would not be expected to affect the incidence of fair-poor SRH. Using this population intervention approach can provide insights into the potential changes in the distribution of SRH that a population of breast cancer survivors could experience if interventions focused on a particular factor, going beyond traditional logistic regression models that focus solely on the identification of predictors.

Our analysis shows that a significant portion of the decline in SRH can be avoided. A growing body of evidence-based preventive strategies is available to reduce the preventable burden of disease, that is, the amount of disease that could be averted if preventive and therapeutic services were universally delivered. The gap between what is avoidable through interventions, and what we currently achieve represents the translation gap, namely the failure to translate effective clinical and community-level services into practice (39). The relative balance and prioritization of interventions should be based, at least in part, on a clear understanding of what can be achieved. Typically, setting priorities among preventive services has been challenging because of the lack of comparative data (40), which our population intervention approach was able to provide in terms of absolute and relative reductions in fair-poor SRH incidence. The population intervention approach effectively standardizes the effect of potential changes in the predictors, allowing for the comparison of their values directly and determining which changes will have the greatest impact on SRH. Thus, the population intervention approach can be a valuable tool, particularly with the increasing interest in comparative effectiveness research and with translation and implementation of evidence-based interventions into routine clinical and community practice.

Reducing surgical side effects, particularly breast tightness, tenderness and discomfort one year after diagnosis would prevent the decline in SRH one year later by 27%. Although it may not be possible entirely to eliminate breast tightness, tenderness and discomfort, even reducing it by one point on the five-point scale would prevent the decline in SRH in 18% of women. Other studies have described the high prevalence of persistent breast pain in survivors, though the type of pain and mechanism may differ (41). Reasons for chronic discomfort after surgery are varied and complex, but nerve damage associated with axillary lymph node dissection is the most commonly reported cause although chemotherapy and radiotherapy may also play a role (42) Improvements in the delivery of radiotherapy through partial or intra-operative therapy may result in reduced breast pain and chest tightness (43, 44).

By taking a population-level approach in this study, we have quantified the hypothetical benefits of reducing or eliminating comorbidity across a population of breast cancer survivors. A lower prevalence in comorbidity at baseline would significantly affect subsequent incidence in fair-poor SRH. This provides an additional reason for the importance of preventing comorbidity, above and beyond its effect on other breast health outcomes (45). Clearly, it is not feasible to eliminate all comorbidities among breast cancer survivors, however, even reducing comorbidity by one point among those who scored one or more on the comorbidity measure would reduce the incidence of fair-poor SRH by 14%. While it would be difficult or even impossible to eliminate comorbidity in an existing individual patient, it is hypothetically possible to *prevent* comorbidity in future populations of breast cancer survivors. In addition to reducing comorbidity, alternative strategies may include managing some of the comorbidities to the extent to which it reduces its effect on the decline on SRH. It is possible that the effect of comorbidity at baseline on SRH is underestimated, since women might have developed comorbid conditions in the ensuing year. For example, a woman who had a heart attack in the year after the baseline interview would likely report lower SRH at the follow-up. In addition, the comorbidity measure used in this study does not include questions about some debilitating conditions, like osteoarthritis, which is a strong predictor of SRH and functional status (46).

Increasing participation in baseline physical activity would significantly affect subsequent decline in fair-poor SRH. Several evidence-based interventions are available that would be able to achieve this (47). Because the survey question asked about participation in “any physical activities or exercises such as running, calisthenics, golf, gardening, or walking for exercise in the past month,” even interventions that would increase participation in light physical activity (e.g., walking) at modest frequency/duration could theoretically affect the incidence of fair-poor SRH.

Our study was limited by the low response rate, increasing the likelihood for selection bias. However, our sensitivity analysis shows that potential selection bias as a result of age, race, and stage at diagnosis did not affect our findings. An assumption of the population intervention approach is no unmeasured confounding. Even though we adjusted for many potential confounders, we cannot rule out bias due to unmeasured or mismeasured confounders. Generalizability of our results is limited to participants who reported having good-excellent self-rated health at baseline measurement, recognizing the limitations of the relatively small number of women whose SRH declined by the follow-up interview. Future research with larger samples could also examine potential predictors of elevation in SRH among women who self-reported fair-poor SRH at baseline. Strengths of our study included a statewide sample of breast cancer survivors, the extensive list of predictors of self-rated health that were included, and our novel approach toward quantifying the effect of changes in modifiable on incidence of fair-poor SRH.

In conclusion, interventions that focus on reducing surgical side effects, preventing comorbidity and on improving physical activity can prevent the decline in SRH of breast cancer survivors by 20-28% assuming a causal and unbiased relationship.

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Table 1

Prevalence of selected characteristics at baseline for breast cancer survivors.

	Prevalence at baseline (%) (n=832)
Sociodemographics	
Age (mean [s.e.])	57.7 (0.4)
Race	
White	93.9
African American	4.5
Education	
Less than high school	3.0
High school	27.4
More than high school	69.6
Income adequacy	
Comfortable	66.2
Have just enough to make ends meet	26.3
Do not have enough to make ends meet	7.0
Concerned about having enough food for family (yes vs no)	4.9
Marital status (married vs not)	72.0
Employed (yes vs. no)	57.3
Length of time at current address (mean [s.e.])	15.5 (0.4)
Access to medical care	
Health insurance (No vs yes)	2.8
Unable to afford dr because of cost (yes vs no)	3.4
Unable to afford prescription in 12 months (yes vs no)	6.6
Chronic conditions	
Comorbidity (>=1)	27.5
Body mass index	
<25.0	31.9
25.0-29.9	34.7
30.0-34.9	19.8
35.0+	12.7

	Prevalence at baseline (%) (n=832)
Psychosocial factors	
Cohen stress (mean [s.e.])	7.1 (0.1)
Personal stress (mean [s.e.])	4.5 (0.06)
Social support (mean [s.e.])	4.4 (0.02)
Depressive symptoms (yes vs no)	14.9
Perceived neighborhood conditions	
Social disorder (mean [s.e.])	12.5 (0.1)
Physical disorder (mean [s.e.])	7.7 (0.08)
Collective efficacy (mean [s.e.])	2.0 (0.01)
One of more days of fear (yes vs no)	2.9
Cancer-related behaviors	
Current smoker (yes vs no)	8.3
Alcohol use (yes vs no)	19.8
Physical activity (no vs yes)	21.3
Cancer-related clinical characteristics and surgical side effects	
Stage	
In situ-localized	74.8
Regional-distant	24.5
Surgical side effects (mean [s.e.])	7.7 (0.1)
Lymph node removed (yes vs no)	76.8
Chemotherapy received (yes vs no)	43.8
Radiotherapy received (yes vs no)	72.8
Hormonal therapy received (yes vs no)	66.6

Table 2

Unadjusted risk of incident fair-poor self-rated health for breast cancer survivors at follow-up.

	Unadjusted risk of incident fair-poor self-rated health at follow-up interview	
	Odds ratio	**95% confidence interval**
Sociodemographics		
Age (mean [s.e.])	1.00	0.98 ; 1.03
Race		
White	1.95	0.73; 5.19
African American		
Education		
Less than high school	0.41	0.14; 1.11
High school	0.18	0.07; 0.48
More than high school	1.00	
Income adequacy		
Comfortable	1.00	
Have just enough to make ends meet	2.71	1.52; 4.83
Do not have enough to make ends meet	6.08	2.91; 12.68
Concerned about having enough food for family (yes vs no)	4.55	2.09; 9.66
Marital status (married vs not)	0.56	0.33; 0.96
Employed (yes vs. no)	0.50	0.29; 0.83
Length of time at current address (mean [s.e.])	1.00	0.98; 1.02
Access to medical care		
Health insurance (No vs yes)	2.68	0.88; 8.12
Unable to afford dr because of cost (yes vs no)	1.49	0.44; 5.08
Unable to afford prescription in 12 months (yes vs no)	3.48	1.70; 7.14
Chronic conditions		
Comorbidity (>=1)	3.03	1.78; 5.05
Body mass index		
<25.0	1.00	
25.0-29.9	1.36	0.66; 2.82
30.0-34.9	2.23	1.05; 4.71

	Unadjusted risk of incident fair-poor self-rated health at follow-up interview	
	Odds ratio	95% confidence interval
35.0+	2.71	1.21; 6.06
Psychosocial factors		
Cohen stress (mean [s.e.])	1.19	1.10; 1.28
Personal stress (mean [s.e.])	1.20	1.05; 1.38
Social support (mean [s.e.])	0.95	0.64; 1.39
Depressive symptoms (yes vs no)	2.29	1.26; 4.13
Perceived neighborhood conditions		
Social disorder (mean [s.e.])	1.07	1.00; 1.14
Physical disorder (mean [s.e.])	1.14	1.04; 1.25
Collective efficacy (mean [s.e.])	1.23	0.62; 2.47
One of more days of fear (yes vs no)	0.52	0.07; 3.94
Cancer-related behaviors		
Current smoker (yes vs no)	0.44	0.21; 0.91
Alcohol use (yes vs no)	1.03	0.54; 1.99
Physical activity (no vs yes)	3.33	1.96; 5.64
Cancer-related clinical characteristics and surgical side effects		
Stage		
In situ-localized	1.04	0.58; 1.88
Regional-distant	1.00	
Surgical side effects (mean [s.e.])	1.16	1.08; 1.24
Lymph node removed (yes vs no)	1.22	0.64; 2.35
Chemotherapy received (yes vs no)	1.18	0.71; 1.98
Radiotherapy received (yes vs no)	0.62	0.36; 1.06
Hormonal therapy received (yes vs no)	0.68	0.40; 1.16

Table 3

Effects of potential changes in modifiable predictors on incidence of fair-poor self-rated health among breast cancer survivors (n=832).

Characteristic	Absolute reduction in incidence (%)		Number needed to intervene	Relative reduction in incidence	
	Unadjusted	Adjusted*		Unadjusted	Adjusted*
Physical activity (everyone physically active)	2.2 (1.0; 3.5)	1.5 (0.1; 2.9)	66.7 (34.5; 1000.0)	29.4 (14.1; 44.8)	19.6 (1.9; 37.3)
Surgical side effects					
Elimination	2.8 (1.4; 4.2)	2.1 (0.3; 3.8)	47.6 (26.3; 333.3)	36.4 (19.1; 53.8)	27.8 (5.6; 49.9)
Reduction by 1 on scale	1.4 (0.5; 2.4)	1.4 (0.4; 2.3)	71.4 (43.5; 250.0)	18.8 (6.8; 30.8)	18.2 (5.5; 31.0)
Comorbid conditions					
Elimination	1.9 (0.9; 2.9)	1.7 (0.4; 2.9)	58.8 (34.5; 250.0)	25.0 (12.7; 37.3)	21.8 (5.5; 38.2)
Reduction by 1 point	1.2 (0.5; 1.8)	1.1 (0.2; 2.0)	90.9 (50.0; 500.0)	15.6 (7.7; 23.5)	14.0 (2.1; 26.0)

*Adjusted for all variables