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Patient trust-in-physician and race are predictors of adherence to medical management in inflammatory bowel disease

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Abstract

BACKGROUND—Adherence plays an important role in the therapeutic effectiveness of medical therapy in IBD. We assessed whether trust-in-physician and Black race were predictors of adherence.

METHODS—We performed a cross-sectional study of Black (n=120) and White (n=115) IBD patients recruited from an outpatient IBD clinic. Self-reported adherence to taking medication and keeping appointments, trust-in-physician, and health-related quality of life were measured using the validated instruments, the modified Hill-Bone Compliance Scale (HBCS), the Trust-in-Physician Scale (TIPS), and the Short IBD Questionnaire (SIBDQ) respectively.

RESULTS—Overall adherence was 65%. Higher adherence correlated with greater trust-inphysician (R=-0.30; P<0.0001), increasing age (R=-0.19; P=0.01), and worsening health-related quality of life (R=-0.18; P=0.01). Adherence was also higher among White IBD patients compared to Blacks (HBSC: 15.6 versus 14.0, P=0.0002). Trust-in-physician, race, and age remained predictors of adherence to medical management after adjustment for employment, income, health insurance, marital and socioeconomic status, and immunomodulator therapy. The adjusted odds ratio for adherence in Blacks compared to Whites was 0.29 (95% CI: 0.13 - 0.64). Every half standard deviation increase in trust-in-physician and every incremental decade in age were associated with 36% and 47% higher likelihood of adherence, respectively.

CONCLUSIONS—Trust-in-physician is a potentially modifiable predictor of adherence to IBD medical therapy. Black IBD patients exhibited lower adherence compared to their White counterparts. Understanding the mechanisms of these racial differences may lead to better optimization of therapeutic effectiveness.

Keywords

adherence; African American; Black; Crohn's disease; inflammatory bowel disease; race, trust in physician; ulcerative colitis

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INTRODUCTION

Inflammatory bowel disease (IBD), which comprises Crohn's diseases and ulcerative colitis, is a chronic and relapsing condition that substantially diminishes quality of life and frequently leads to major abdominal surgery. One study has shown that adherence to medical therapy decreases the risk of recurrence to disease, particularly in ulcerative colitis (1). However, self-reported non-adherence to medical therapy among IBD patients ranges from 40% to 60% (2–4). Thus, optimizing adherence may reduce overall morbidity from IBD.

Several studies have evaluated the determinants of adherence to IBD therapy. Factors that predict adherence vary among studies but include age, gender, complexity of medication regimen, and disease activity (2–5). In other chronic diseases, the patient-physician relationship, particularly patients' trust-in-physicians, is an important predictor of medical adherence (6–9), though this association has yet to be shown in IBD. Race and ethnicity have also been shown to be predictors of adherence in the general population (10;11). In addition, prior studies suggest that trust-in-physicians varies within different races and ethnicities and is particularly low among Blacks (12–15).

Based on these previous studies, we sought to determine whether trust-in-physicians correlates with adherence in the IBD population. Furthermore, our goals were to assess whether adherence differs among Black and White IBD patients and if race is a predictor of medical adherence independent of trust-in-physicians and other demographic factors.

METHODS

Study Population

We recruited consecutive White and Black IBD patients who attended the outpatient clinics at Johns Hopkins who: had a confirmed diagnosis of IBD by pathology, endoscopy, and medical records; were at least 18 years of age; and were accessible by telephone for interview. Patients were recruited between October of 2005 and August of 2007.

Study Protocol

This study is a cross-sectional component of an ongoing longitudinal cohort study of Black and White IBD patients. Following initial enrollment from clinic, participants were contacted over the phone by a single interviewer who administered a 40 - 45 minute questionnaire that incorporated validated scales to measure medical adherence, trust-in-physician, socioeconomic status (employment status, marital status, education, and income), health-related quality of life, disease severity, and concurrent medication use.

Study Instruments

Disease-specific health-related quality of life (HRQL) was measured by the Short Inflammatory Bowel Disease Questionnaire (SIBDQ), an abbreviated validated version of the IBDQ (16). For Crohn's disease patients, disease severity was measured using the Chapel Hill Index, a validated self-report instrument, that is based on and correlates with the Crohn's Disease Activity Index (17). Similarly, the Simple Colitis Clinical Activity Index was used to measure disease severity in ulcerative colitis (18). For both continuous scales, higher values reflected greater disease severity. We assessed patients trust in their physicians using the Trust-in-Physician Scale (TIPS), a validated and reliable 11-item questionnaire on a 5-point Lickert scale with scores that can range between 5 (lowest level of trust) and 55 (highest level of trust). This instrument correlates with patient satisfaction and continuity of care when assessed at 6 months (6;19). The primary outcome was self-reported

nonadherence which was measured using the modified Hill-Bone Compliance Scale (HBCS). This instrument was developed for chronic diseases such as hypertension and has been validated in the Black population (20). We modified the original scale by removing an item that queried adherence to dietary recommendations which was not relevant to IBD. Another item that asked whether patients took IBD medications belonging to another patient was also removed during analysis due to low prevalence of IBD relative to other chronic conditions. Our preliminary analysis showed that the response to this item was uniformly "no." Our modified questionnaire contained 10 items on a 4-point Lickert scale along two behavior domains: medication taking and prescription refill (8 items) and appointment keeping (2 items). A summary score is generated, ranging from 10 (most adherent/least nonadherent) to 40 (least adherent/most nonadherent). Adherence was also dichotomized with a threshold score of less than 16 reflecting adherence versus non-adherence, based on the cutoff for the bottom tertile of the HBCS score (top-third for adherence). For the medication taking behavior subscale, the cutoff for adherence was similarly defined as less than 11. Two questions were also introduced to query patient attitudes toward the difficulty

and importance of taking IBD medications during quiescent disease. These questions were not validated and not part of the HBCS score. Both the TIPS and HBCS have been validated for face-to-face interview and for self-administration. However, neither has been validated specifically for administration via telephone interview.

Statistical Analysis

All analyses were conducted using Stata 10.0 software (StataCorp LP, College Station, Texas). We used the unpaired Student t- test to compare differences in means of continuous variables and the chi-square statistic for difference in proportions. The primary outcome adherence was analyzed as both a continuous and dichotomous variable. We first used multiple logistic regression to determine the independent associations between adherence (as a dichotomous variable) and the two primary exposure variables, race and trust-in-physician, while adjusting for attained age, health-related quality of life, gender, employment status, household income, type of health insurance, marital status, use of immunomodulators, and education. To ensure that these results did not substantially differ with analysis of adherence as a continuous variable, we conducted a sensitivity analysis using multiple linear regression which incorporated the same predictors as the logistic regression model. Interaction terms between trust-in-physician and other factors including race, gender, IBD diagnosis (CD vs. UC), and quality of life were determined *a priori* and incorporated into these models to assess for effect modification between predictor variables. We also conducted a logistic regression analysis in which only the medication-taking behavior subscale of the HBCS score was included.

RESULTS

The baseline demographic and clinical characteristics of the study population are shown in Table 1 stratified by race. Blacks differed from White IBD patients with respect to educational background, type of health insurance coverage, and use of immunomodulators or infliximab. There was no racial difference in health-related quality of life or disease severity. There was a marginally statistically significant difference in trust-in-physician score between Blacks and Whites (43.0 versus 44.4; P=0.06).

Attitudes toward medical therapy during quiescent disease

When asked to rate on 4-point Lickert scale (1=disagree; 4=agree) how difficult it was to take medications when there were no active symptoms, there was no difference between Whites and Blacks (1.5 versus 1.7, P=0.12). Similarly, when participants were asked to rate

on the same scale the importance of taking medications while in remission, Whites and Blacks responded similarly (3.8 versus 3.8, P=0.83).

Univariate Analysis

The average HBCS score was higher (indicating higher non-adherence) among Blacks compared to Whites (16.6 vs. 15.0, P=0.0002). This racial difference was greater than half a standard deviation in the HBCS score for the entire study population (half SD=1.5). When the HBCS was categorized as adherent versus non-adherent, the overall proportion of subjects classified as adherent was 65%. Blacks were significantly less likely to be adherent than Whites (50% versus 80%, P<0.0001; OR 0.25, 95% CI: 0.14 - 0.48) and these differences were similar using only the medication-taking behavior subscale (44% versus 68%, P<0.0001; OR 0.36, 95% CI: 0.20 - 0.64). IBD patients who were employed were more likely to be classified as adherent to medical care (68% versus 33%, P=0.008). When adherence was measured as a dichotomous outcome, ulcerative colitis patients were more likely to be categorized as adherent than those with Crohn's disease (75% versus 60%, P=0.03).

The correlation coefficients between the HBCS for adherence and age, health-related quality of life, disease severity, income, years of education, and trust-in-physician are shown in Table 2. The variable exhibiting the strongest correlation with adherence was trust-inphysician (R=-0.30; P<0.0001). The correlation between trust-in-physician and adherence was not different between Blacks and Whites (R=-0.25 versus -0.30; P=0.8). Increasing attained age (R=-0.19; P=0.01) and worsening health-related quality of life as measured by the SIBDQ (R=-0.18; P=0.01) also inversely correlated with the HBS Compliance Score. Ulcerative colitis disease severity did not correlate with adherence. There was a weak correlation of adherence with disease severity among CD patients, though the level of significance of this association was less than that for the SIBDQ score. Black race was also associated with a one-half standard deviation greater non-adherence compared to Whites (HBCS Score: 15.6 versus 14.0, P<0.001). Participants who were unemployed at the time of the interview also demonstrated higher non-adherence compared to those unemployed (16.7 versus 14.6, P=0.009). There were no differences in adherence scores by gender, diagnosis (CD versus UC), marital status, or immunomodulator use, or type of health insurance (Table 3).

Predictors of Overall Adherence

When adherence was analyzed as a dichotomous outcome in a multiple logistic regression model, Blacks were less likely to be adherent to medical therapy compared to Whites (OR 0.29; 95% CI: 0.13 - 0.64) after adjustment for confounders. Trust-in-physician was also independently associated with adherence with every half standard deviation in the TIPS scale (half SD = 2.9) correlating with a 36% increase in the likelihood of adherence (OR 1.36; 95% CI: 1.09 - 1.69). Additionally, every decade increase in age was associated with a 47% increased odds of adherence (P=0.02). Health-related quality of life, IBD diagnosis, number of years of education, employment status, household income, marital status, having private health insurance, and use of immunomodulators or infliximab were not statistically significant predictors of adherence in the multivariate model.

The results of multiple linear regression with adherence analyzed as a continuous variable were similar to those obtained from the logistic model and are shown in Table 4. There was no statistical interaction between race and trust-in-physician or between IBD symptomatology and either race or trust-in-physician. Similarly, gender and IBD diagnosis (CD versus UC) did not modify the effect of Black race, trust-in-physician, age, or IBD symptoms on adherence.

Predictors of Medical Adherence

Our analysis of the medical adherence subscale which excluded components of adherence pertaining to appointment keeping revealed similar results as analysis of overall adherence. After multivariate analysis, Blacks were less likely than Whites to adhere to taking medications (OR 0.34; 95% CI: 0.16 - 0.71). Every half standard deviation increase in trust-in-physician was associated with a 41% increase in odds of adherence to taking medications (OR 1.41; 95% CI: 1.14 - 1.75), while every decade increase in age was associated with a 55% increase in odds of adherence (OR 1.55; 95% CI: 1.15 - 2.09). IBD-specific health-related quality of life (SIBDQ) was, however, not associated with adherence. Analysis of the adherence medication subscale as a continuous variable yielded similar results.

DISCUSSION

We have demonstrated in this cross-sectional study that trust-in-physician and Black race are among the multi-dimensional factors that influence self-reported adherence to medical management in IBD patients. Kane et al. have shown that nonadherence to maintenance mesalamine therapy during quiescent UC increased the risk clinical relapse more than fivefold.(1) In addition, a clinical trial has shown withdrawal of azathioprine in CD even after longstanding remission resulted in higher relapse (21). Thus, our findings provide additional insights into factors that potentially impact the overall effectiveness of medical therapy in IBD.

Though patient trust-in-physician has not been previously shown to be a predictor of medical adherence in IBD, our findings are consistent with those of other studies that have shown that physician trustworthiness correlates with patient satisfaction, continuity of care, and adherence in the general population and other chronic diseases such as diabetes.(6;8) Trust-in-physician is one of several dimensions of the physician-patient relationship that may also include patients' perceived respect from physicians, effectiveness of communication, and physician participatory decision-making styles (22;23). Certain factors such as length of patient-physician interactions and the degree to which physicians explored how their patients experienced their illness are associated with higher levels of trust (24). In addition, Sewitch et al. have demonstrated that concordance between physician and patient with respect to perceptions of a patient's symptoms, health status, and quality of communication predicts better adherence (25). Thus, a better understanding of the potentiators of physician trust and the subsequent development of behavioral interventions that may enhance the physician-patient relationship may lead to higher overall effectiveness of IBD medical therapy.

The relationship between race and adherence is more complex, confounded by socioeconomic and cultural factors. Lower adherence to medical therapy has been demonstrated among Blacks for other chronic conditions such as hypertension.(26) The underlying mechanisms are likely multifactorial. Importantly, in our study we were able to adjust for factors such as employment, education, and general perception of well-being which varied between races and could potentially influence adherence. Trust-in-physician has also been shown to be lower among non-Hispanic Blacks compared to Whites and may contribute to racial differences in adherence (12). In our study, trust-in-physician did partially contribute to race effects on adherence. However, the racial gap in adherence persisted despite adjustment for physician trust. The residual association between Black race and adherence even after accounting for these other confounders suggest that unmeasured factors are at play. These potential determinants may include cultural factors and aspects of the physician-patient relationship beyond just trust-in-physician (27). One study has shown that patients who are of the same race as their physicians rate their providers as more participatory in decision-making (23), while another study suggest racial concordance

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between physician and patient results in longer patient visits, more positive patient affect, and greater patient satisfaction (28). Thus, having an IBD physician of the same race may play an important role in patient adherence. A limitation of this current study is that all the IBD physicians at our IBD clinic are White. This unilateral racial discordance between patient and physician among our Black and not White IBD patients may significantly contribute to the observed racial disparities in adherence and is not accounted for in this study design. This hypothesis needs to be addressed in larger multi-centered studies with physicians of greater racial diversity. Racial differences in adherence may also arise from variations in attitudes toward taking medications particularly in asymptomatic phases in chronic diseases. In our study, we surveyed participants on their perceptions of the difficulty and importance of taking medications while they were asymptomatic, and found no differences by race.

We also found older age to be an important predictor of better adherence. These findings are consistent with those of previous studies in which younger IBD patients have been shown to exhibit lower adherence (3;5). Increasing age has also been found to be a predictor of medical compliance in other chronic conditions such as hypertension and diabetes mellitus (26;29;30). This association may reflect greater maturity, responsibility, independence, and acceptance of chronic disease by older individuals. Older patients may also have had longer enduring patient-physician-patient relationships than their younger counterparts which could also contribute to greater adherence. Unfortunately, we do not have data on the duration of the physician-patient relationship to address this hypothesis. The relationship between age and adherence may also reflect a potential selection bias arising from an oversampling of inherently adherent older individuals because these are the ones who still remained in follow-up over a longer period of time and thus available to be studied. In contrast, younger patients in our study were more likely to have had shorter duration of physician follow-up allowing for a lesser degree of self-selection of adherent individuals. After adjustment for confounders, we did not find quality of life scores to be associated with adherence which is consistent with previous studies (4;5). Unlike, previous reports which showed that the effect of age and IBD diagnosis varied by gender (5), we observed no effect modification of predictors of adherence by gender. Our study also showed no effect by marital status either in univariate or multivariate analysis as previously reported (4).

One of the limitations of the study is the use of self-reported adherence without corresponding validation by objective measures. The ideal and most rigorous measurement of adherence outcomes would be through direct observation or pill counts. The latter is typically employed in clinical trials and not feasible for a cross-sectional observational study. Validated instruments that rely on self-reported adherence such as that used in our study are not perfect but are suitable for observational studies because of their versatility, efficiency, and correlation with pill counts and health outcomes (31-33). The HBCS queries not only medication-taking behaviors, but also incorporates dimensions of adherence to clinical follow-up. Because this study is the first to address IBD adherence in Blacks, we selected the HBCS because it was validated specifically in Blacks. (20). Unfortunately there are no self-report adherence instruments that are validated in both Blacks and Whites. However, the HBCS does contain items from the widely used Morisky scale for selfreported adherence that has been validated in the White population (34).. Regardless, there may be bias introduced if the accuracy of reporting is different between Blacks and Whites. The HBCS also does not quantify the proportion of medications taken, which does not allow comparison to other adherence studies that report this measure. It should also be noted that the two primary instruments in our study, the HBCS and the TIPS have been validated for administration by face-to-face interview but not telephone interview. These questionnaires do not incorporate any visual aids that would lead to dramatic differences face-to-face and telephone administration. However, we cannot exclude potential biases that may arise from

facial or behavioral cues that may be absent in a telephone interview. Though we showed that adherence was associated with trust-in-physician, race, and age, the strength of these associations are uncertain due to the fairly wide confidence intervals that surround them. An additional limitation of this study is that it arises from a tertiary referral center and is perhaps not as representative as population-based data (5). However, one of the focuses of this study was to assess the relationship between race and adherence. Due to lack of a population-based registry of Black IBD patients, it became necessary to recruit these participants from a tertiary care setting.

In this study, we have demonstrated that physician trust is an important aspect of the physician-patient relationship that relates to adherence to medical care among IBD patients. In addition, this study is, to our knowledge, the first to evaluate adherence in the Black IBD population It is important to further understand the mechanisms of lower adherence among Blacks and to determine their long-term consequences through longitudinal studies. Because adherence is an important predictor of disease relapse, our findings reinforce the importance of physician-patient interactions in overall therapeutic effectiveness. Thus, future directions in IBD healthcare should consider efforts toward fostering long-term longitudinal care and increased contact time with healthcare providers – perhaps feasibly through physician extenders. These approaches may be particularly important for Blacks who have demonstrated greater general mistrust in physicians (12;14). Such strategies to promote trust-in-physicians may provide additional avenues with which to optimize IBD medical care.

Abbreviations

| CD | Crohn's disease |
|-------|----------------------------|
| HBCS | Hill-Bone Compliance Scale |
| IBD | inflammatory bowel disease |
| SD | standard deviation |
| SIBDQ | short IBD Questionnaire |
| TIPS | Trust-in-Physicians Scale |
| UC | ulcerative colitis |

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Demographic and clinical characteristics of inflammatory bowel disease patients

| | All Patients (N = 235) | White (N = 115) | African American (N = 120) |
|--|---------------------------|--------------------|-------------------------------|
| Mean age (yrs) (SD) | 41.2 (14.2) | 41.7 (14.3) | 40.6 (14.1) |
| Mean age at diagnosis (yrs) (SD) | 29.2 (13.7) | 29.9 (14.0) | 28.5 (13.4) |
| Female (%) | 57% | 51% | 63% |
| Education (yrs) (SD) | 14.9 (2.2) | 15.2 (2.2) | 14.5 (2.2)* |
| Unemployed (%) | 21% | 19% | 24% |
| Median income (\$ in thousands) (Interquartile range) | 65 (35 – 100) | 80 (50 - 120) | 45 (25 – 84) [*] |
| Married (%) | 54% | 64% | 43%* |
| Health Insurance $(\%)^{\dagger}$ | | | |
| Private | 79% | 86% | 71%* |
| Medicare | 9% | 10% | 8% |
| Medicaid | 13% | 6% | 20%* |
| Diagnosis (%) | | | |
| Crohn's disease | 63% | 60% | 67% |
| UC/inderterminate | 37% | 40% | 33% |
| Immunomodulator use (%) | 44% | 55% | 35%* |
| Disease Severity \ddagger | | | |
| Chapel Hill Index (SD) | 142 (120) | 140 (121) | 144 (155) |
| SCCAI Score (SD) | 4.2 (3.5) | 3.6 (3.5) | 4.9 (3.5) |
| SF-12v2 | | | |
| Physical (SD) | 48.1 (6.3) | 48.2 (5.7) | 47.8 (6.7) |
| Mental (SD) | 48.5 (11.2) | 48.4 (10.9) | 48.4 (11.4) |
| Short IBDQ (SD) | 51.1 (13.9) | 52.4 (12.5) | 49.8 (15.0) |
| Trust in physician (SD) | 44.7 (5.8) | 45.4 (5.8) | 44.0 (5.7) |

* P<0.05

 † Health insurance categories are non-exclusive since individuals may have more than one type of coverage

[‡]Disease severity was assessed using the Chapel Hill Index for Crohn's disease patients and the Simple Colitis Clinical Activity Index (SCCAI) score for ulcerative colitis.

Correlation of continuous predictor variables with the modified Hill-Bone Compliance Scale

| | Correlation coefficient | P-value |
|--|-------------------------|----------|
| Trust-in-physician Scale | -0.30 | < 0.0001 |
| Short IBD Questionnaire | -0.18 | 0.009 |
| Disease Severity | | |
| Chapel Hill Index* | +0.18 | 0.03 |
| SCCAI Score ^{\ddagger} | +0.09 | 0.45 |
| Education (yrs) | +0.02 | 0.82 |
| Income | -0.10 | 0.21 |
| Attained age | -0.19 | 0.008 |

* For Crohn's disease patients

 ‡ For ulcerative colitis patients

Univariate analysis of association of categorical variables with the modified Hill-Bone Compliance Scale

| | ADHERENCE | | | | |
|--------------------|--------------------|-----------------|---------------------|-----------------|--|
| | Continuous outcome | | Dichotomous outcome | | |
| | HBCS Score | <i>p</i> -value | % Adherent | <i>p</i> -value | |
| Race | | | | | |
| White | 14.0 | 0.0001 | 80% | 0.0001 | |
| African American | 15.6 | <0.0001 | 50% | <0.0001 | |
| Gender | | | | | |
| Male | 14.5 | | 67% | 0.54 | |
| Female | 15.1 | 0.27 | 63% | 0.54 | |
| Diagnosis | | | | | |
| Crohn's disease | 15.0 | 0.17 | 75% | 0.03 | |
| Ulcerative colitis | 14.5 | | 60% | | |
| Marital Status | | | | | |
| Married | 14.6 | 0.27 | 69% | 0.27 | |
| Single/divorced | 15.0 | 0.27 | 61% | 0.27 | |
| Health Insurance | | | | | |
| Private | 14.7 | | 67% | 0.12 | |
| Non-private | 15.4 | 0.29 | 54% | 0.12 | |
| Employment status | | | | | |
| Employed | 14.6 | 0.000 | 68% | 0.003 | |
| Unemployed | 16.7 | 0.009 | 33% | 0.003 | |
| Medication | | | | | |
| Immunomodulator | 14.6 | 0.22 | 68% | 0.19 | |
| No immunomodulator | 14.9 | 0.23 | 63% | | |

HBCS = Hill Bone Compliance Scale

Multivariate regression models for predictors of patient adherence

| | Logistic R | Linear Regression | | |
|----------------------------------|--------------------|-------------------------|-----------------------|---------|
| | Overall Adherence | Medication Adherence | β coefficient (SE) | p-value |
| | OR (95% CI) | OR (95% CI) | | |
| Trust-in-physician* | 1.36 (1.09 – 1.69) | 1.41 (1.14 – 1.75) | -0.41 (0.13) | 0.003 |
| Race | | | | |
| White | ref | ref | ref | |
| African American | 0.29 (0.13 – 0.64) | 0.34 (0.16 - 0.71) | 1.02 (0.49) | 0.037 |
| Age (per 10 years) | 1.47 (1.08 – 2.02) | 1.55 (1.15 – 2.09) | -0.46 (0.18) | 0.01 |
| Diagnosis | | | | |
| Crohn's disease | ref | ref | ref | |
| Ulcerative colitis | 1.93 (0.85 – 4.35) | 1.36 (0.63 – 2.91) | -0.26 (0.50) | 0.60 |
| SIBDQ Score [*] | 1.04 (0.85 – 1.27) | 1.08 (0.89 – 1.31) | -0.25 (0.13) | 0.05 |
| Education (yrs) | 0.92 (0.76 – 1.11) | 0.89 (0.74 - 1.08) | 0.16 (0.11) | 0.16 |
| Married vs. non-married | 0.68 (0.29 - 1.60) | 0.63 (0.28 - 1.43) | 0.40 (0.53) | 0.45 |
| Employed vs unemployed | 1.95 (0.44 - 8.60) | 1.44 (0.33 – 6.39) | -0.59 (0.97) | 0.54 |
| Household Income (US dollars) | 1.00 (0.99 – 1.00) | 1.00 (0.99 – 1.00) | 0 (0) | 0.96 |
| Private vs non-private insurance | 1.06 (0.32 - 3.48) | 1.04 (0.33 – 3.23) | -0.15 (0.66) | 0.94 |
| Immunomodulator Use | 0.87 (0.40 - 1.88) | 0.95 (0.45 - 2.00) | 0.19 (0.49) | 0.70 |

*Expressed in increments of half standard deviation units