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**Patient-reported allergies predict postoperative outcomes and psychosomatic markers  
following spine surgery**

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IRB approval (16-153) was obtained prior to start of study.

### Abstract

Background Context: Prior studies have shown that patient-reported allergies can be prognostic of poorer postoperative outcomes.

Purpose: To investigate the correlation between self-reported allergies and outcomes after cervical or lumbar spine surgery.

Study Design/Setting: Retrospective cohort study at a single tertiary-care institution.

Patient Sample: All patients undergoing cervical or lumbar spine surgery from 2009-2014.

Outcome Measures: The primary outcome measure was change in the EuroQol-5 Dimensions (EQ-5D) following surgery. Secondary outcomes included change in the Pain Disability Questionnaire (PDQ) and Patient Health Questionnaire-9 (PHQ-9), achieving the minimal clinically important difference (MCID) in these measures, as well as cost of admission.

Methods: Prior to and following surgery, EQ-5D, PDQ, and PHQ-9 were recorded for patients with available data. Paired student's *t*-tests were used to compare change in these measures following surgery. Multivariable linear and logistic regression were used to assess the relationship between the log transformation of the total number of allergies and outcomes.

Results: 592 cervical patients and 4,465 lumbar patients were included. The median number of reported allergies was two. The EQ-5D index increased from 0.539 to 0.703 for cervical patients and from 0.530 to 0.676 for lumbar patients ( $p<0.01$  for both). Patients experienced significant pain improvement by the PDQ (80.1 to 58.2 for cervical patients, 79.4 to 58.1 for lumbar patients;  $p<0.01$ ). Using multivariable logistic regression, the log transformation of number of allergies predicted significantly higher odds of achieving the PDQ MCID (OR = 2.09, 95% CI 1.05-4.15,  $p=0.02$  for cervical patients; OR = 1.30, 95% CI 1.03-1.68,  $p=0.03$  for lumbar patients). However, this relationship was not durable for patients with follow-up exceeding 1 year. The log transformation of number of allergies for lumbar patients predicted significantly increased cost of admission ( $\beta=\$3,597$ ,  $p<0.01$ ) and trended towards significance among cervical patients ( $\beta=\$1,842$ ,  $p=0.10$ ).

Conclusions: Patient-reported allergies correlate with subjective improvement in pain and disability following spine surgery and may serve as a marker of postoperative outcomes. The relationship between allergies and PDQ improvement may be secondary to the short-term expectation-actuality discrepancy, as this relationship was not durable beyond 1 year.

Key Words: Patient-reported allergies; somatization; spine surgery; admission costs; patient outcomes

## 1 Introduction

2 Collecting an accurate list of allergies from the medical history is critical for patient care.

3 Importantly, it is unclear whether patient-reported allergies represent true allergic reactions,  
4 adverse effects, or other factors. For example, the most common patient-reported drug allergy is  
5 to penicillin. However, in one hospital cohort, only a minority of patients who reported or had a  
6 documented penicillin allergy in the medical record proved to be positive for penicillin via  
7 allergy testing or drug challenge.<sup>1</sup> Even if patient-reported allergies have not been verified  
8 through testing, they still can still influence patient care. For example, patients who report  
9 penicillin allergies have increased broad-spectrum antibiotic use, greater antibiotic costs, and  
10 more frequent drug-resistant infections compared to those without the allergy as less optimal  
11 antimicrobial therapies may be used in treatment due to this reported allergy. These patients also  
12 experience longer hospital stays, more complicated hospital courses, increased likelihood of an  
13 ICU admission, and increased risk of mortality during the hospitalization.<sup>1-3</sup>

14  
15 In addition, patient-reported allergies are also correlated with significant underlying  
16 psychosomatic burden. In a Canadian cohort, patient-reported allergies correlated with Axis I  
17 psychological disorders including major depression, bipolar, panic, and social phobia disorders.<sup>4</sup>  
18 Other studies have shown a correlation between drug hypersensitivity reactions and anxiety,<sup>5</sup> as  
19 well as allergies and suicide mortality. The association with nonfatal suicidal behaviors is still  
20 unclear.<sup>6</sup> Finally, a cohort study of patients suffering from drug intolerance or insect venom  
21 allergies showed that patients reporting these reactions scored significantly higher on  
22 questionnaires measuring somatization and had worse health-related quality of life (QOL),  
23 frequently reporting higher levels of anxiety relative to the normal population.<sup>7</sup>

In the present study, we investigated whether or not patients who self-report more allergies prior to undergoing cervical or lumbar spine surgery have worse outcomes after surgery. We hypothesized that patient-reported allergies are associated with poorer postoperative outcomes and higher admission costs and thus may serve as a prognostic factor for outcomes after spinal surgery.

## Methods

### *Data Collection*

IRB approval was obtained prior to study initiation. No patient consent was required given the retrospective nature of this study. A retrospective cohort study of all patients undergoing cervical or lumbar spine surgery at a tertiary-care center between January 2009 to December 2014 was performed. Queried data were collected from institutional audited data warehouses and included demographics, comorbidities, insurance status, length of hospital stay, and operative data. Patient-reported allergies were collected from institutional audited data warehouses and included all allergies recorded in the medical chart, including allergies without confirmatory testing (e.g. skin or patch testing) had been obtained. Patient comorbidities were used to derive the Charlson Comorbidity Index (CCI) using established ICD-9 coding algorithms.<sup>8</sup> QOL data were collected both preoperatively and through last follow-up (LFU). To represent costs of admission corresponding with spine surgery, we collected charge data from the institution's financial database. Charges reflect patient-level resource utilization and include all components of care including imaging, laboratory diagnostics, and therapies. To represent costs from the payer's

perspective, billed charges were normalized to Medicare reimbursement rates based upon institutional cost-to-charge ratios (CCR)<sup>9,10</sup> and presented in 2016 U.S. dollars.

#### *Quality of Life Measures*

QOL data were prospectively collected in an institutional database of patient-reported health status measures (HSM) including validated questionnaires administered at each outpatient visit. These questionnaires include the EQ-5D,<sup>11–13</sup> Pain Disability Questionnaire (PDQ),<sup>14,15</sup> and Patient Health Questionnaire-9 (PHQ-9).<sup>16–18</sup> The EQ-5D contains five dimensions of a patient's health state: Mobility, Self-Care, Completion of Usual Activities, Pain/Discomfort, and Anxiety/Depression, with each dimension scored on a scale from 1 to 3. An EQ-5D index is subsequently derived from the five subscores and represents the patient's overall health state ranging from 0 (death) to 1 (perfect health). The minimal clinically important difference (MCID) for the EQ-5D index following spine surgery has been reported to be 0.1.<sup>19,20</sup> The PDQ is used to evaluate chronic disabling musculoskeletal and spinal disorders, focusing on disability and patients' abilities to perform activities of daily living. It records functional (FC) and psychosocial components (PC) of pain for a total score between 0 and 150. The MCID for the PDQ has been reported to be 20.<sup>21</sup> The PHQ-9 assesses for depression based on nine criteria for major depressive disorder established in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-V).<sup>22</sup> Each of the nine questions is scored from 0 to 3 for a total score ranging from 0 to 27. The MCID for the PHQ-9 has been reported to be 5.<sup>23</sup>

#### *Statistical Analysis*

All statistical analyses were performed using R statistical software version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria).<sup>24</sup> Quantitative statistics are presented as means with standard deviations or medians with interquartile ranges, while qualitative statistics are represented as counts with percentages. Continuous variables were compared using Student's *t*-tests. Multivariable linear regression was used to model postoperative change in QOL questionnaires, cost of admission, and length of hospital stay, while multivariable logistic regression was used to model changes in QOL measures greater than the MCID. For each of these models, pertinent covariates were included to adjust for confounding and minimize bias. Only covariates demonstrating association ( $p < 0.20$  via simple regression) with outcome variables of interest were evaluated in multivariable models. Backward stepwise regression was used to arrive at the final model, with  $p < 0.10$  as the stopping criterion. Additional separate multivariable regressions were performed with the number of allergies included as a continuous variable using restricted cubic splines with five knots to represent a nonlinear relationship between the number of allergies and modeled outcomes.<sup>25</sup> Regression coefficients ( $\beta$ ) and odds ratios (OR) were reported for linear and logistic models, respectively. All values of  $p < 0.05$  were considered statistically significant.

## Results

Five hundred ninety-two cervical spine patients and 4,465 lumbar spine patients were included in the present study (Table 1). Patients had an average age of 56.2 and 60.8 years for cervical and lumbar procedures, respectively. The patient demographics were slightly predisposed towards males in both cervical (43% female) and lumbar (48% female) patient groups. However, when subset by the presence of allergies, females less often had no allergies among cervical (26%) and

1 lumbar (29%) patients (Tables S1 and S2). The most common spine conditions in cervical spine  
 2 patients were degenerative disc disease (31%), spondylosis (29%), stenosis (24%), disc  
 3 herniation (16%), and spondylolisthesis (15%), whereas the most common lumbar spine  
 4 conditions were stenosis (60%), degenerative disc disease (60%), spondylosis (53%), disc  
 5 herniation (20%) and spondylolisthesis (33%). Patients with at least 1 allergy consistently were  
 6 diagnosed with multiple spine pathologies (Tables S1 and S2; cervical patients with at least 1  
 7 allergy more often were diagnosed with degenerative disc disease (35% v. 23%) and spondylosis  
 8 (32% v. 22%), as were lumbar patients who more often had degenerative disc disease (63% v.  
 9 53%) and spondylosis (57% v. 44%). Median length of stay was 1 day for cervical patients and 3  
 10 days for lumbar patients. Average cost of hospital admission was \$15,105 for cervical patients  
 11 and \$19,123 for lumbar patients. For both groups of patients, the most common type of reported  
 12 allergy was a medication allergy (median of 1 reported allergy), with a median number of 2 total  
 13 reported allergies. Approximately two thirds of both cervical and lumbar spine surgery patients  
 14 reported at least one allergy (cervical patients, 67%, lumbar patients, 71%). The distribution of  
 15 the number of allergies for both cervical and lumbar patients is illustrated in Figure 1. Median  
 16 follow-up time was 7.8 months for both cervical and lumbar patients with 98% of all patients  
 17 meeting at least 90-day follow-up and 63% of cervical patients and 64% of lumbar patients  
 18 meeting at least 180-day follow-up.

19  
 20 For unadjusted QOL outcomes, both cervical and lumbar patients improved in several factors as  
 21 measured with the EQ-5D, PDQ, and PHQ-9 (Table 2). Both patient groups showed significant  
 22 postoperative improvement in all five dimensions of their health status in the EQ-5D following  
 23 surgery, with the EQ-5D index increasing from 0.539 to 0.703 for cervical patients and from

0.530 to 0.676 for lumbar patients ( $p<0.01$  for both). Additionally, both patient groups showed significant improvement in their pain symptoms as measured by the PDQ. Cervical spine surgery patients improved from an average score of 80.1 to 58.2 after surgery ( $p<0.01$ ), while lumbar patients improved from 79.4 to 58.1 after surgery ( $p<0.01$ ). Depressive symptoms as measured by PHQ-9 scores were also significantly improved in both cervical (8 to 4) and lumbar (7 to 4) patients ( $p<0.01$  for both).

For both cervical and lumbar patients, multivariable linear regression was used to adjust for covariates associated with modeled outcomes. Preoperative PDQ and follow-up time were included in our models for change in PDQ burden while age and CCI were included in our models predicting admission cost and length of stay. We first performed these models using restricted cubic splines to represent the number of allergies as a continuous variable with a nonlinear relationship with modeled outcomes (Figure 2). Despite the general trend towards increased allergies predicting larger improvement in PDQ, this trend was not significant for cervical or lumbar patients (Figures 2A and 2E). However, when modeling achievement of PDQ MCID with multivariable logistic regression, the number of allergies became a significant predictor of increased odds of PDQ MCID for cervical spine patients with greater than 7 allergies and lumbar patients with greater than 6 allergies (Figures 2B and 2F). A larger number of allergies was found to be associated with increased cost of admission, though this was only found to be consistently significant for lumbar patients (Figures 2C and 2G). Similarly, a larger number of allergies predicted a longer length of stay, but this was only consistently significant for lumbar patients (Figures 2D and 2H). Despite the observed relationship between the number

of allergies and outcomes reported above, no significant relationship was observed between total number of allergies and changes in postoperative EQ-5D or PHQ-9.

Based upon the shapes of the curves obtained using restricted cubic splines, we chose to also model these outcomes using the log transformation of the total number of allergies (Tables 3 and 4). To adjust for the “ceiling effect,” higher preoperative PDQ was significantly associated with postoperative decreases in both patient groups (cervical  $\beta=-0.34$ ,  $p<0.01$ , lumbar  $\beta=-0.36$ ,  $p<0.01$ ). Longer follow-up time was also associated with worse postoperative improvement in both patient groups (cervical  $\beta=0.50$ ,  $p=0.02$ , lumbar  $\beta=0.28$ ,  $p<0.01$ ). Similar to our findings using restricted cubic splines, the log transformation of the total number of allergies in both patient groups trended towards predicting greater postoperative improvement in PDQ, but this was not significant (cervical  $\beta=-6.36$ ,  $p=0.21$ , lumbar  $\beta=-3.32$ ,  $p=0.11$ ). Furthermore, again after adjusting for numerous covariates, higher total costs during the hospital admission were significantly associated with the log transformation of the total number of allergies for lumbar patients ( $\beta=\$3,597$ ,  $p<0.01$ ) and trended towards statistical significance among cervical patients ( $\beta=\$1,842$ ,  $p=0.10$ ). Similar findings were observed when modeling length of stay, as the log transformation of the total number of allergies significantly predicted longer length of stay for lumbar patients ( $\beta=1.01$ ,  $p<0.01$ ) and trended towards significance among cervical patients ( $\beta=0.36$ ,  $p=0.08$ ).

Notably, the log transformation of the total number of allergies was found to be correlated with an improvement in the postoperative PDQ score above the MCID (Table 4). For cervical patients, again after adjusting for the “ceiling effect” with preoperative PDQ and follow-up time,

the log transformation of the total number of allergies predicted significantly higher odds of an improvement in PDQ greater than the MCID (OR = 2.09, 95% CI 1.05-4.15,  $p=0.02$ ). After identical adjustments in lumbar patients, log transformation of the total number of allergies was again significantly predictive of higher odds of improvement in PDQ above the MCID (OR = 1.30, 95% CI 1.03-1.68,  $p=0.03$ ). However, when repeat analyses were performed among patients subset by follow-up time (less than or greater than 1 year), log transformation of the total number of allergies was inconsistently associated with achieving the PDQ MCID. For both cervical (OR 2.38, 95% CI 1.02-5.58,  $p=0.04$ ) and lumbar (OR 1.57, 95% CI 1.02-1.92,  $p=0.04$ ) patients with less than 1-year follow-up, log transformation of the total number of allergies predicted achieving the PDQ MCID. In contrast, both cervical (OR 1.70, 95% CI 0.51-5.65,  $p=0.38$ ) and lumbar (OR 1.20, 95% CI 0.78-1.83,  $p=0.41$ ) patients with more than 1-year follow-up did not demonstrate this relationship.

## Discussion

In the present study of over 5,000 patients undergoing cervical and lumbar spine surgery, we identified numerous patients with extensive self-reported allergies. In this cohort, the number of patient-reported allergies was associated with superior postoperative improvements in pain-related QOL as measured by the PDQ. Additionally, total number of allergies significantly correlated with higher admission costs and longer lengths of stay.

Previous studies have identified potential relationships between patient-reported allergies and outcomes following surgery. Within spine surgery, one previous study reported an association between patient-reported allergies and poorer postoperative pain and disability following surgery

for degenerative lumbar spine diseases.<sup>26</sup> Within this study, patients increasing numbers of patient-reported medication allergies demonstrated worse outcomes by the Oswestry Disability Index, Short Form-12 Physical Composite Score, and Visual Analog Scale for Back and Leg Pain. Increased self-reported allergies was also significantly correlated with depression and anxiety in this cohort as measured by the Zung Depression Scale and Modified Somatic Perception Questionnaire. Previous studies have shown that patient-reported allergies correlate with poorer functional outcomes in both hip and knee arthroplasties. Patients with self-reported allergies who have undergone total knee arthroplasty reported inferior postoperative outcomes in knee function as measured by WOMAC and KSS scores compared to patients who did not report any allergies, though this effect was not associated with depression.<sup>27</sup> Patients with multiple (>3) reported allergies in the medical record experienced poorer patient-reported functional outcomes in both knee and hip arthroplasty as measured by the physical component of the SF-36 and functional WOMAC scores, as well as increased lengths of hospital admissions.<sup>28,29</sup>

In addition to affecting hospital admission and postoperative outcomes in surgical patients, self-reported allergies have also been associated with various psychiatric comorbidities. Patient-reported allergies correlate with a significant burden of various psychosomatic processes across studies, including major depression, bipolar, panic, social phobia disorders, anxiety, suicide mortality, and somatization.<sup>4-7</sup> Patient-reported allergies are also correlated with other clinical considerations and conditions such as psychogenic non-epileptic seizures (PNES)<sup>30-32</sup> and drug intolerance,<sup>33</sup> which may be reflective of higher levels of somatization in these patients.

Regarding somatization, the DSM-V currently includes somatoform disorders under the category of somatic symptom and related disorders, and aims to redefine somatic disorders as typically having multiple somatic complaints that significantly impact QOL (e.g. pain, fatigue, lethargy) rather than the absence of an organic medical cause of the symptoms. The prevalence of somatoform disorders is significant at nearly 10%, similar to that of other well-known psychiatric disorders like depression and anxiety, which are often comorbid with somatoform disorders.<sup>34</sup> Given the association between somatoform disorders and medical conditions, it is possible that patient-reported allergies may be a proxy for somatization and somatoform disorders. With this increased burden of psychiatric conditions, there should also be a significant overlap between patient-reported allergy burden and somatic symptoms and related disorders. In fact, these patients may seek out care with greater expectations or desires for therapies to benefit their condition, though this may be a double-edged sword, as individuals with a tendency towards somatization are oftentimes more likely to develop the nocebo response and report more adverse effects from therapy, possibly due to hyperawareness of adverse effects.<sup>35,36</sup>

Recent studies and meta-analyses have shown that patient expectations of spine surgery contribute significantly to surgical outcomes. Higher preoperative expectations are associated with improved postoperative outcomes. This may be related to a placebo-like effect. However, when patients' expectations are unrealistic, this is associated with poorer postoperative outcomes in patients undergoing elective spine surgery.<sup>37,38</sup> This may be the phenomenon underlying patient response to surgical therapies, with the best outcomes achieved at a healthy balance of patient expectations.

In the present study, patients with higher levels of self-reported allergy burden may have greater levels of behavioral health comorbidities and therefore greater expectations of surgical management alleviating their disability and pain. Patients with more self-reported allergies showed greater improvements in perceived postoperative pain and disability burden as measured by the PDQ without corresponding improvement of underlying psychiatric burden (PHQ-9) or other QOL measures (EQ-5D). However, this relationship between allergy burden and perceived pain improvement was predominantly observed in the brief follow-up window of less than one year following surgery, as patients with follow-up exceeding one year did not consistently demonstrate the same significant relationship. These patients may not be aware of their underlying psychiatric burden and may not see any significantly different biologic or mechanical difference in postoperative outcomes. Interestingly, this seems to align with aspects of the expectation-actuality discrepancy. Thus, patients report a short-term subjective improvement in their pain and disability postoperatively, even if this improvement may not be reflected on other behavioral or QOL measures and ultimately may not remain durable over extended follow-up. As spine surgery is oftentimes performed on an elective basis for the goal of improving specific symptoms such as pain and overall QOL, spine surgery may be uniquely subject to patient expectations of pain and disability relief. Thus, patient-reported allergies may serve as a predictor of short-term subjective improvements in pain and disability postoperatively, although they may not be as useful for predicting outcomes in other QOL measures.

Of course, significant correlations with increased cost of care and longer lengths of stay also reflect the greater complexities of caring for patients who report allergies in general. As medication allergies were the most common self-reported allergies in this study, and penicillin is

the most commonly reported drug allergy, it is reasonable to think that some of the additional costs of admission may be due to more complicated hospital courses with challenging postoperative management and complications due to these self-reported allergies, as has been previously reported in patients who self-report both confirmed and unconfirmed penicillin allergies.<sup>1-3</sup> Furthermore, while patients with allergies did not have any notable differences in overall medical comorbidities as measured by the CCI, nearly all of our recorded spine conditions and indications were more commonly diagnosed among our patients with listed allergies. Thus, it is possible that their histories of neck or back pain along with multiple spine conditions could alter both patient expectations and perceived treatment at a tertiary referral center.

Our study is limited by several factors. The chief limitation of this study was that it was retrospective, and thus limited in its ability to directly assess patient somatization levels. Going forward, future prospective studies could directly interrogate the link between somatization, patient-reported allergies, and spine surgery outcomes through the use of validated screening instruments such as the Screening for Somatoform Disorders (SOMS) or Somatosensory Amplification Scale (SSAS) questionnaires in addition to structured clinical interviews to determine patient somatization burden.<sup>39</sup> Allergies were assessed without differentiation between unconfirmed allergies and allergies confirmed by objective testing methods, and differences between perceived and confirmed allergies may affect patient perceptions of outcome. Indeed, patients with validated allergies may be affected by biologic processes such as altered immune regulation or inflammatory states that might alter their responsiveness to surgical therapy as well as lead to different outcomes (i.e. inadvertent allergen exposures leading to medical

complications) compared to individuals who do not have validated allergies. In addition, patients with validated allergies may also suffer from increased levels of anxiety and depression as a result of their allergies, perhaps due to various possible immunologic mechanisms, in addition to the psychologic stress in avoiding allergens and the corresponding impact on quality of life.<sup>40,41</sup> This may serve as a possible confounder in this and future studies, and indeed, many prior studies on this subject have not differentiated between patients with and without validated allergies.<sup>41</sup> Further investigation and analysis of differences in patient outcomes comparing individuals with validated allergies against those without validated allergies would be highly informative in this aspect. Additional analyses of the root causes of increased admission costs and the role of managing complications (i.e. prolonged ICU stays, infection) incurred related to the patient's allergies in increased admission costs for spinal surgery may also be valuable in further exploring the impact of allergies on clinical outcomes and healthcare systems. In addition, although we examined both lumbar and cervical spine surgical patients, ultimately it is unclear if cervical spine surgical patients have a significantly different profile than lumbar spine surgical patients given the discrepancy. Furthermore, our sample size of patients with longer allergy lists was fairly limited, as most patients had fairly few reported allergies, which resulted in wider confidence intervals at larger allergy numbers. Finally, given that this was a study conducted in a single healthcare system, the results may not be generalizable to other systems, especially if patient expectations of surgery differ significantly.

## **Conclusion**

In conclusion, patient-reported allergy burden is significantly correlated with reductions in postoperative pain burden, as well as increased costs of care during the hospital admission and

1 longer lengths of stay, and thus may serve as a useful prognostic factor for these postsurgical  
2 outcomes. The relationship between patient-reported allergies and reduction in PDQ may be  
3 secondary to the effects of the expectation-actuality discrepancy, as this relationship was  
4 observed for patients with shorter follow-up but not durable beyond 1 year. No significant  
5 associations were found with changes in mental health or overall QOL.

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## Figure Legends

Figure 1. Distribution of allergies. Among patients with reported allergies, the provided histograms illustrate the distribution of the number of allergies per patient among (A) cervical and (B) lumbar patients.

Figure 2. Non-linear relationships between number of allergies and patient outcomes. Restricted cubic splines were used to represent number of allergies as a continuous variable with a nonlinear relationship with modeled outcomes in both cervical (left) and lumbar (right) patients. (A, E) Increased allergies trended towards predicting larger improvement in PDQ for cervical and lumbar patients. (B, F) Greater than 7 allergies predicted increased odds of PDQ MCID for cervical patients, whereas greater than 6 allergies predicted increased odds for PDQ MCID. (C, G) More allergies predicted increased cost of admission, consistently found to be significant among lumbar patients. (D, H) More allergies also predicted a longer length of stay, consistently significant among lumbar patients.

1 Table 1. Patient Characteristics

| Characteristic             | Cervical      | Lumbar        |
|----------------------------|---------------|---------------|
| N                          | 592           | 4465          |
| Age at Surgery (years)     | 56.2±12.1     | 60.8±14.5     |
| Female                     | 252 (43%)     | 2,123 (48%)   |
| Race                       |               |               |
| White                      | 520 (88%)     | 4,011 (90%)   |
| Black                      | 55 (9%)       | 281 (6%)      |
| Other                      | 17 (3%)       | 173 (4%)      |
| Marital Status             |               |               |
| Single                     | 106 (18%)     | 694 (16%)     |
| Married                    | 403 (68%)     | 3,063 (69%)   |
| Separated                  | 50 (8%)       | 388 (9%)      |
| Widowed                    | 26 (4%)       | 300 (7%)      |
| Unknown                    | 7 (1%)        | 20 (1%)       |
| BMI                        | 28.9±5.9      | 29.6±6.1      |
| CCI                        | 0 [0, 1]      | 0 [0, 1]      |
| Spine Conditions           |               |               |
| Degenerative Disc Disease  | 184 (31%)     | 2,671 (60%)   |
| Spondylosis                | 171 (29%)     | 2,362 (53%)   |
| Stenosis                   | 142 (24%)     | 2,690 (60%)   |
| Disc Herniation            | 92 (16%)      | 1,806 (40%)   |
| Spondylolisthesis          | 86 (15%)      | 1,461 (33%)   |
| Scoliosis                  | 55 (9%)       | 906 (20%)     |
| Kyphosis                   | 28 (5%)       | 304 (7%)      |
| Lordosis                   | 4 (1%)        | 42 (1%)       |
| Length of Stay (days)      | 1 [1, 2]      | 3 [1, 4]      |
| Cost of Hospital Admission | 15,105±10,239 | 19,123±15,466 |
| Presence of Allergy        |               |               |

|                         |                 |                 |
|-------------------------|-----------------|-----------------|
| Animals                 | 12 (2%)         | 84 (2%)         |
| Food                    | 49 (8%)         | 367 (8%)        |
| Insects                 | 16 (3%)         | 111 (2%)        |
| Medication              | 351 (59%)       | 2,846 (64%)     |
| Environmental           | 46 (8%)         | 395 (9%)        |
| Skin                    | 54 (9%)         | 524 (11%)       |
| Other                   | 6 (1%)          | 64 (1%)         |
| Any                     | 398 (67%)       | 3,181 (71%)     |
| Number of Allergies     |                 |                 |
| Animals                 | 0 [0, 0]        | 0 [0, 0]        |
| Food                    | 0 [0, 0]        | 0 [0, 0]        |
| Insects                 | 0 [0, 0]        | 0 [0, 0]        |
| Medication              | 1 [0, 3]        | 1 [0, 3]        |
| Environmental           | 0 [0, 0]        | 0 [0, 0]        |
| Skin                    | 0 [0, 0]        | 0 [0, 0]        |
| Other                   | 0 [0, 0]        | 0 [0, 0]        |
| Total                   | 2 [0, 4]        | 2 [0, 4]        |
| Follow-up Time (months) | 7.8 [4.3, 14.5] | 7.8 [4.3, 14.7] |
| 95% Range (months)      | (3.0, 36.1)     | (3.0, 41.4)     |
| 90-day follow-up        | 581 (98%)       | 4359 (98%)      |
| 180-day follow-up       | 373 (63%)       | 2850 (64%)      |

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N, Number; BMI, body mass index; CCI, Charlson Comorbidity Index. Continuous variables reported as mean  $\pm$  standard deviation or median [interquartile range] unless otherwise specified; categorical variables reported as count (percent).

1 Table 2. Unadjusted Quality of Life Outcomes

| Characteristic     | Cervical    |             |                              |        | Lumbar      |             |                              |
|--------------------|-------------|-------------|------------------------------|--------|-------------|-------------|------------------------------|
|                    | Pre-op      | Post-op     | <i>p</i> -value <sup>†</sup> |        | Pre-op      | Post-op     | <i>p</i> -value <sup>†</sup> |
| EQ-5D (N=562)      |             |             |                              | N=4161 |             |             |                              |
| Mobility           | 2 [2, 2]    | 2 [1, 2]    | <0.01*                       |        | 2 [2, 2]    | 2 [1, 2]    | <0.01*                       |
| Self-Care          | 1 [1, 2]    | 1 [1, 2]    | <0.01*                       |        | 1 [1, 2]    | 1 [1, 2]    | <0.01*                       |
| Usual Activities   | 2 [2, 2]    | 2 [1, 2]    | <0.01*                       |        | 2 [2, 2]    | 2 [1, 2]    | <0.01*                       |
| Pain/Discomfort    | 2 [2, 3]    | 2 [2, 2]    | <0.01*                       |        | 2 [2, 3]    | 2 [2, 2]    | <0.01*                       |
| Anxiety/Depression | 2 [1, 2]    | 1 [1, 2]    | <0.01*                       |        | 2 [1, 2]    | 1 [1, 2]    | <0.01*                       |
| Index              | 0.539±0.220 | 0.703±0.202 | <0.01*                       |        | 0.530±0.222 | 0.676±0.218 | <0.01*                       |
| MCID               |             | 298 (53%)   |                              |        |             | 2090 (50%)  |                              |
| PDQ (N=268)        |             |             |                              | N=1782 |             |             |                              |
| Function           | 51.7±18.7   | 38.1±24.1   | <0.01*                       |        | 51.1±19.6   | 37.8±23.4   | <0.01*                       |
| Psychosocial       | 28.5±13.0   | 20.0±14.8   | <0.01*                       |        | 28.4±13.5   | 20.3±15.5   | <0.01*                       |
| Total              | 80.1±30.0   | 58.2±37.0   | <0.01*                       |        | 79.4±31.1   | 58.1±37.2   | <0.01*                       |
| MCID               |             | 123 (50%)   |                              |        |             | 889 (50%)   |                              |
| PHQ-9 (N=217)      |             |             |                              | N=1854 |             |             |                              |
| Total              | 8 [4, 14]   | 4 [2, 9]    | <0.01*                       |        | 7 [3, 12]   | 4 [1, 9]    | <0.01*                       |
| MCID               |             | 80 (37%)    |                              |        |             | 602 (32%)   |                              |

2 EQ-5D, EuroQol 5-Dimensions; N, Number; MCID, Minimal Clinically Important Difference; PDQ, Pain Disability Questionnaire; PHQ-9,  
3 Patient Health Questionnaire 9.

1 Continuous variables reported as mean  $\pm$  standard deviation or median [interquartile range]; categorical variables reported as count (percent).  
2 <sup>†</sup>Paired t-tests and Wilcoxon signed-rank tests used to compare preoperative measurements to postoperative measurements for parametric and  
3 nonparametric continuous variables, respectively.  
4 \*Statistically significant:  $p < 0.05$ .  
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1 **Table 3. Admission Cost and Quality of Life Improvement Multivariable Regression Models**

| Location | Outcome <sup>†</sup>  | Covariate                      | $\beta$ Coefficient | p-value |
|----------|-----------------------|--------------------------------|---------------------|---------|
| Cervical | $\Delta$ PDQ          | Preoperative PDQ               | -0.34               | < 0.01* |
|          |                       | Follow-Up (months)             | 0.50                | 0.02*   |
|          |                       | log(Total Number of Allergies) | -6.36               | 0.21    |
|          | Admission Cost (\$)   | Age                            | 93                  | < 0.01* |
|          |                       | CCI                            | 855                 | 0.02*   |
|          |                       | log(Total Number of Allergies) | 1,842               | 0.10    |
|          | Length of Stay (days) | Age                            | 0.04                | < 0.01* |
|          |                       | CCI                            | 0.13                | 0.05*   |
|          |                       | log(Total Number of Allergies) | 0.36                | 0.08    |
| Lumbar   | $\Delta$ PDQ          | Preoperative PDQ               | -0.36               | < 0.01* |
|          |                       | Follow-Up (months)             | 0.28                | < 0.01* |
|          |                       | log(Total Number of Allergies) | -3.32               | 0.11    |
|          | Admission Cost (\$)   | Age                            | 101                 | < 0.01* |
|          |                       | CCI                            | 786                 | < 0.01* |
|          |                       | log(Total Number of Allergies) | 3,597               | < 0.01* |
|          | Length of Stay (days) | Age                            | 0.04                | < 0.01* |
|          |                       | CCI                            | 0.25                | < 0.01* |
|          |                       | log(Total Number of Allergies) | 1.01                | < 0.01* |

2 PDQ, Pain Disability Questionnaire; BMI, Body Mass Index; CCI, Charlson Comorbidity Index.

3 <sup>†</sup>Decrease in PDQ represents improvement.

4 \*Statistically significant;  $p < 0.05$ .

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1 Table 4. Pain Disability Questionnaire Minimal Clinically Important Difference Multivariable  
 2 Regression Models

| Location | Subgroup                    | Covariate                      | OR [95% CI]        | p-value |
|----------|-----------------------------|--------------------------------|--------------------|---------|
| Cervical | All Patients (N=268)        | Preoperative PDQ               | 1.01 [1.00 – 1.02] | < 0.01* |
|          |                             | Follow-Up (months)             | 0.98 [0.94 – 1.01] | 0.13    |
|          |                             | log(Total Number of Allergies) | 2.09 [1.05 – 4.15] | 0.02*   |
| Cervical | < 1-Year Follow-up (N=167)  | Preoperative PDQ               | 1.01 [1.00 – 1.03] | < 0.01* |
|          |                             | Follow-Up (months)             | 1.08 [0.94 – 1.23] | 0.27    |
|          |                             | log(Total Number of Allergies) | 2.38 [1.02 – 5.58] | 0.04*   |
| Cervical | > 1-Year Follow-up (N=101)  | Preoperative PDQ               | 1.01 [1.00 – 1.03] | 0.14    |
|          |                             | Follow-Up (months)             | 0.97 [0.92 – 1.02] | 0.29    |
|          |                             | log(Total Number of Allergies) | 1.70 [0.51 – 5.65] | 0.38    |
| Lumbar   | All Patients (N=1782)       | Preoperative PDQ               | 1.01 [1.01 – 1.02] | < 0.01* |
|          |                             | Follow-Up (months)             | 0.98 [0.97 – 0.99] | < 0.01* |
|          |                             | log(Total Number of Allergies) | 1.30 [1.03 – 1.68] | 0.03*   |
| Lumbar   | < 1-Year Follow-up (N=1109) | Preoperative PDQ               | 1.01 [1.01 – 1.02] | < 0.01* |
|          |                             | Follow-Up (months)             | 1.03 [0.98 – 1.09] | 0.20    |
|          |                             | log(Total Number of Allergies) | 1.57 [1.02 – 1.92] | 0.04*   |
| Lumbar   | > 1-Year Follow-up (N=673)  | Preoperative PDQ               | 1.02 [1.01 – 1.02] | < 0.01* |
|          |                             | Follow-Up (months)             | 0.97 [0.95 –       | < 0.01* |

|  |  |                                |                             |      |
|--|--|--------------------------------|-----------------------------|------|
|  |  | log(Total Number of Allergies) | 0.98]<br>1.20 [0.78 – 1.83] | 0.41 |
|--|--|--------------------------------|-----------------------------|------|

OR, odds ratio; CI, confidence interval; PDQ, Pain Disability Questionnaire; MCID, Minimal Clinically Important Difference.

\*Statistically significant:  $p < 0.05$ .

(A) Distribution of Allergies among Cervical Patients

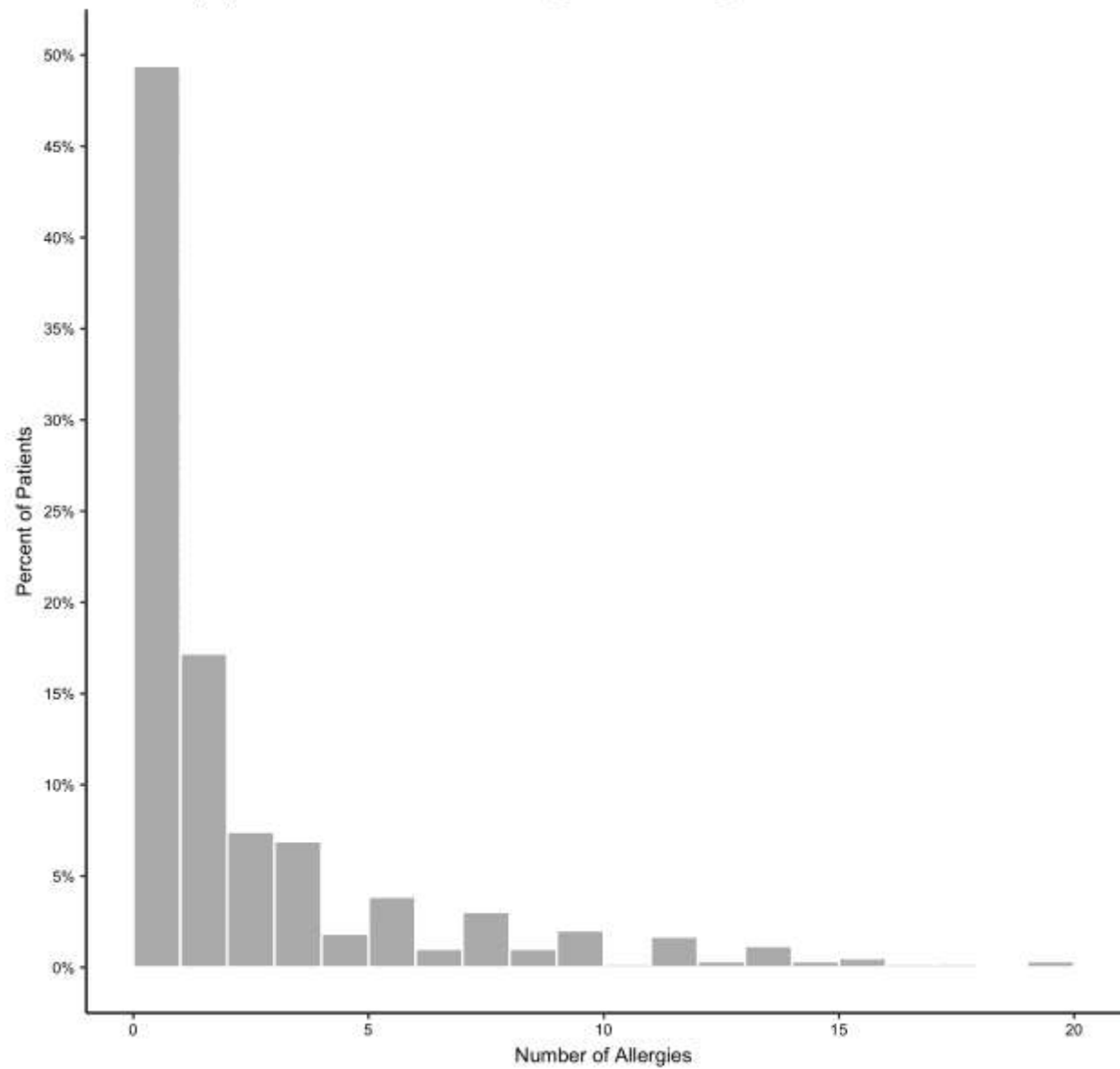


Figure 1A.tiff

(B) Distribution of Allergies among Lumbar Patients

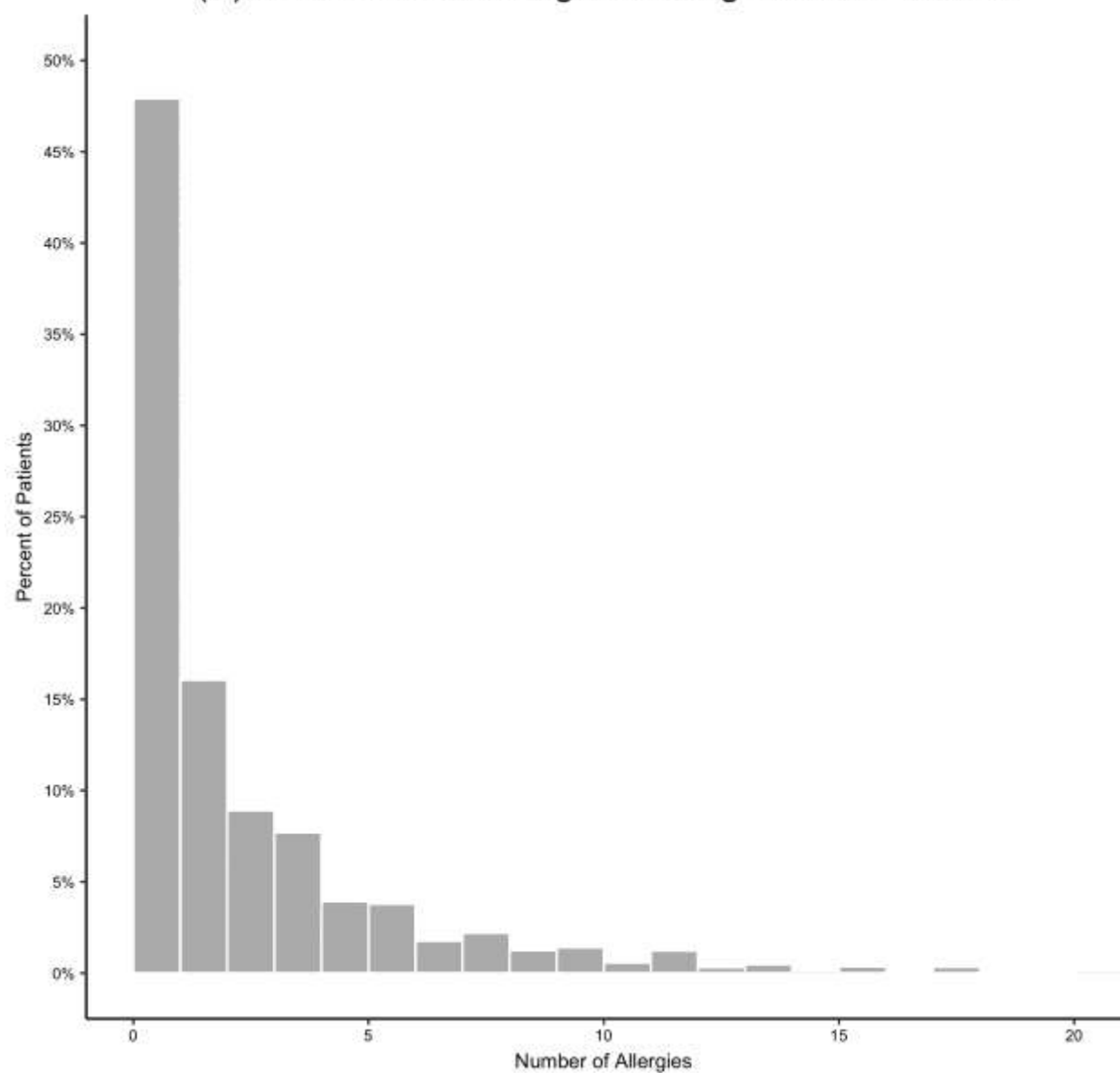
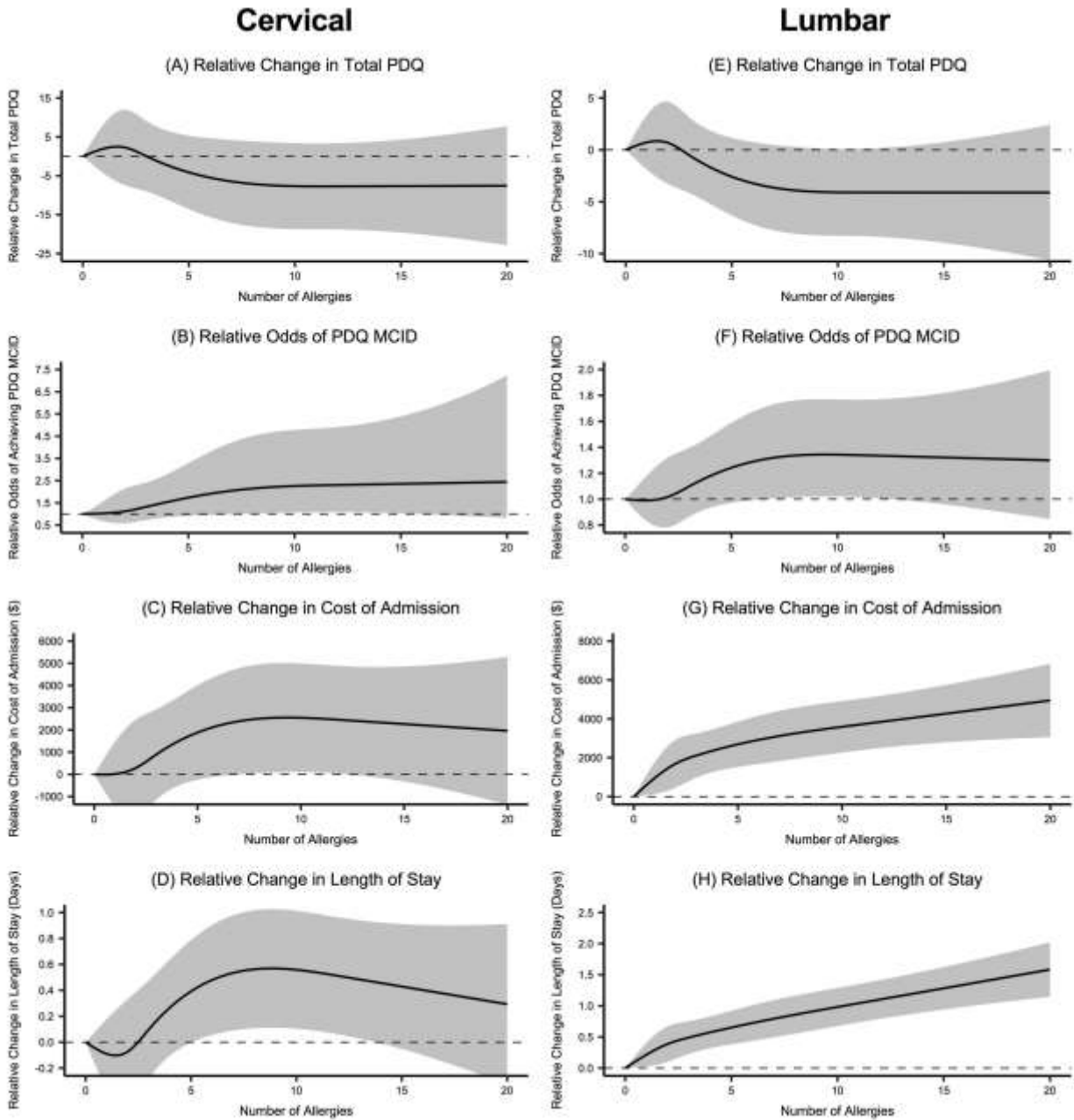


Figure 1B.tiff



1

2 Figure 2.tiff