Exploring the Determinants of Prescription Opioid Use Among Chronic Pain Patients with Pain-Associated Medical Illnesses: A Comprehensive Predictive Modeling Approach

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INTRODUCTION

The elevated prevalence of opioid prescriptions for individuals suffering from chronic noncancer pain (CNCP) has prompted inquiries into the various factors that shape physicians' choices when it comes to opioid prescriptions. It has been proposed that the prescription of opioids follows a concerning trend referred to as "adverse selection." In this pattern, patients with CNCP who have more extensive medical diagnoses, higher comorbidity scores, and consequently, a heightened risk of unfavorable outcomes, tend to be prioritized by physicians for opioid therapy. **In this study, we aim to assess the contribution of pain-associated non-cancer illnesses (NCIs) to prescription opioid use among a large cohort of CNCP patients. Predictive modeling was used to understand the patients' characteristics determining increased opioid use across NCIs.**

METHODS

Population: This study used data from the UK Biobank, a prospective cohort of over 500,000 participants. CNCP patients were considered as those reporting pain interfering with their usual activities for more than 3 months. Data was analyzed from 195,808 CNCP participants.
**Measures:** Regular use (i.e., most days of the week for the last 4 weeks) of prescription opioids and self-reported non-cancer illnesses were identified at data collection visit.
Analysis: Associations between opioid use and 11 major NCIs were described using odds ratios (ORs) with 95% confidence intervals(95%CI). Also, associations between the total number of reported NCIs with opioid use were described using ORs. A machine learning approach was used to develop two separate predictive models of opioid use. A total of 77 pain agnostic features, including sociodemographic, lifestyle, mental health, mood, and anthropometric measures (i.e., pain-agnostic model), and a total of 16 pain-related features, including the location of the acute and chronic pain (i.e., pain model) were entered in the predictive models. Differences in pain and pain-agnostic risk scores for prescription opioid use were evaluated using Cohen's *d* effect sizes comparing each NCI group with the NCI-free group.
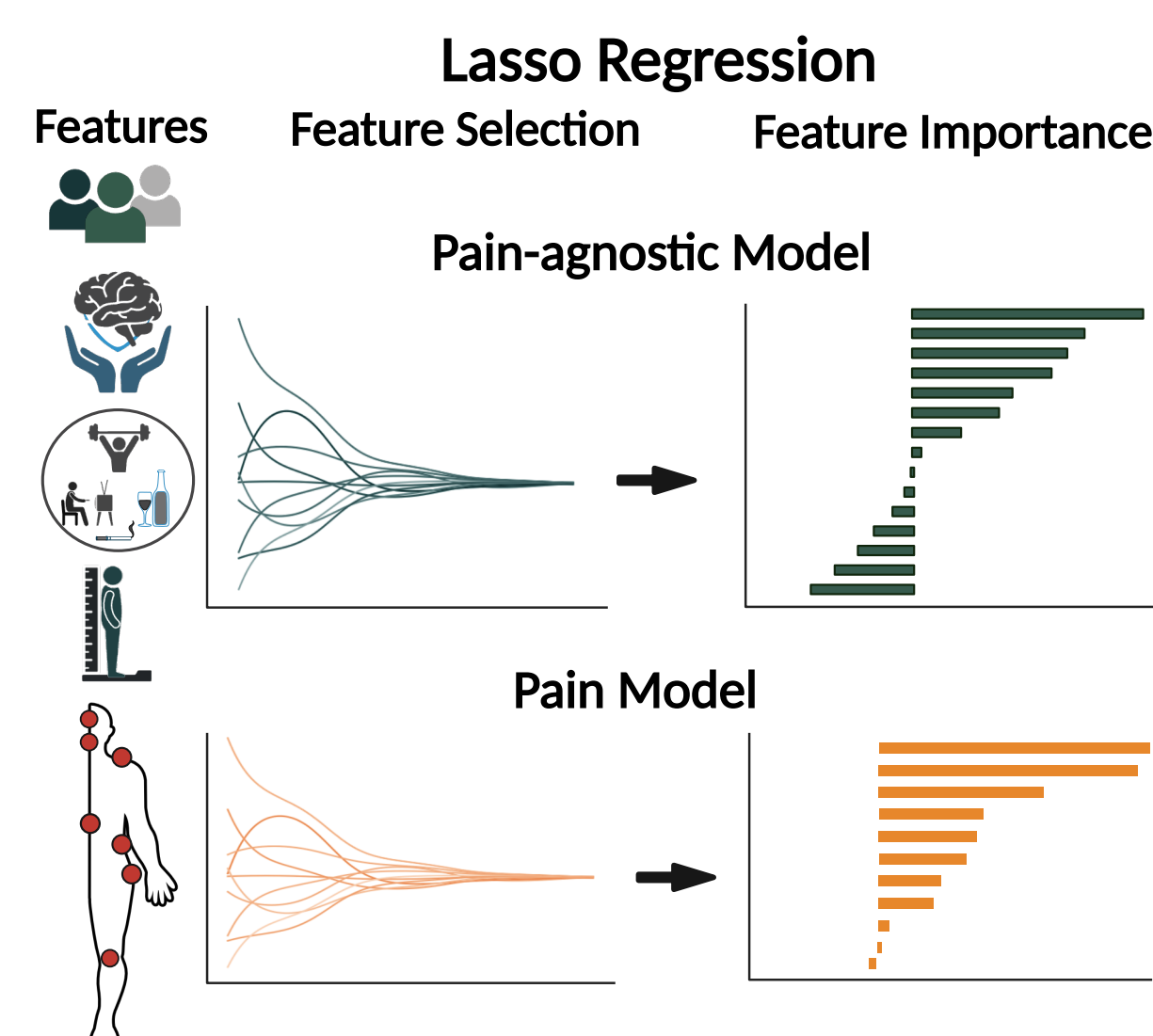

Figure 1. Predictive models. Using the patients' characteristics, we derived pain and pain-agnostic models that predicted the use of prescription opioids in CNCP patients.Models were trained using a sample of 178,763 CNCP patients from the Uk Biobank baseline data (2006-2011) (i.e., train set) and validated using a left-out sample of 17,045 CNCP patients attending in a follow-up visit (9 years later) (i.e., test set). Selected features correspond to the most predictive variables with non-zero weights after penalization. Positive weights indicate positive correlation,while negative weights indicate negative correlation with opioid use.

RESULTS
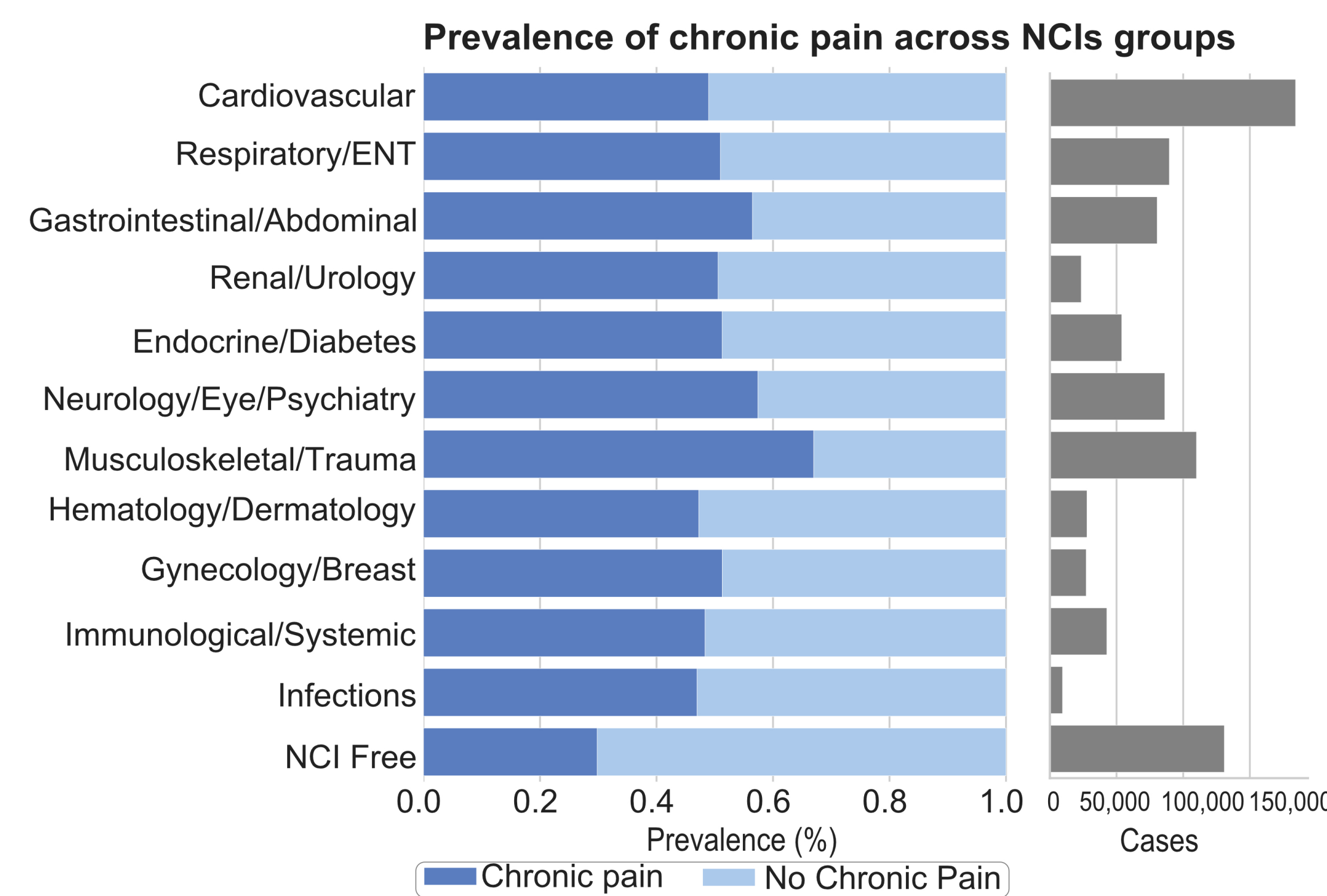
Figure 2. Prevalence of chronic pain stratified by 11 major NCIs. Chronic pain was more prevalent in participants diagnosed with at least one non-cancer illness than diagnosis-free (NCI-free) participants.
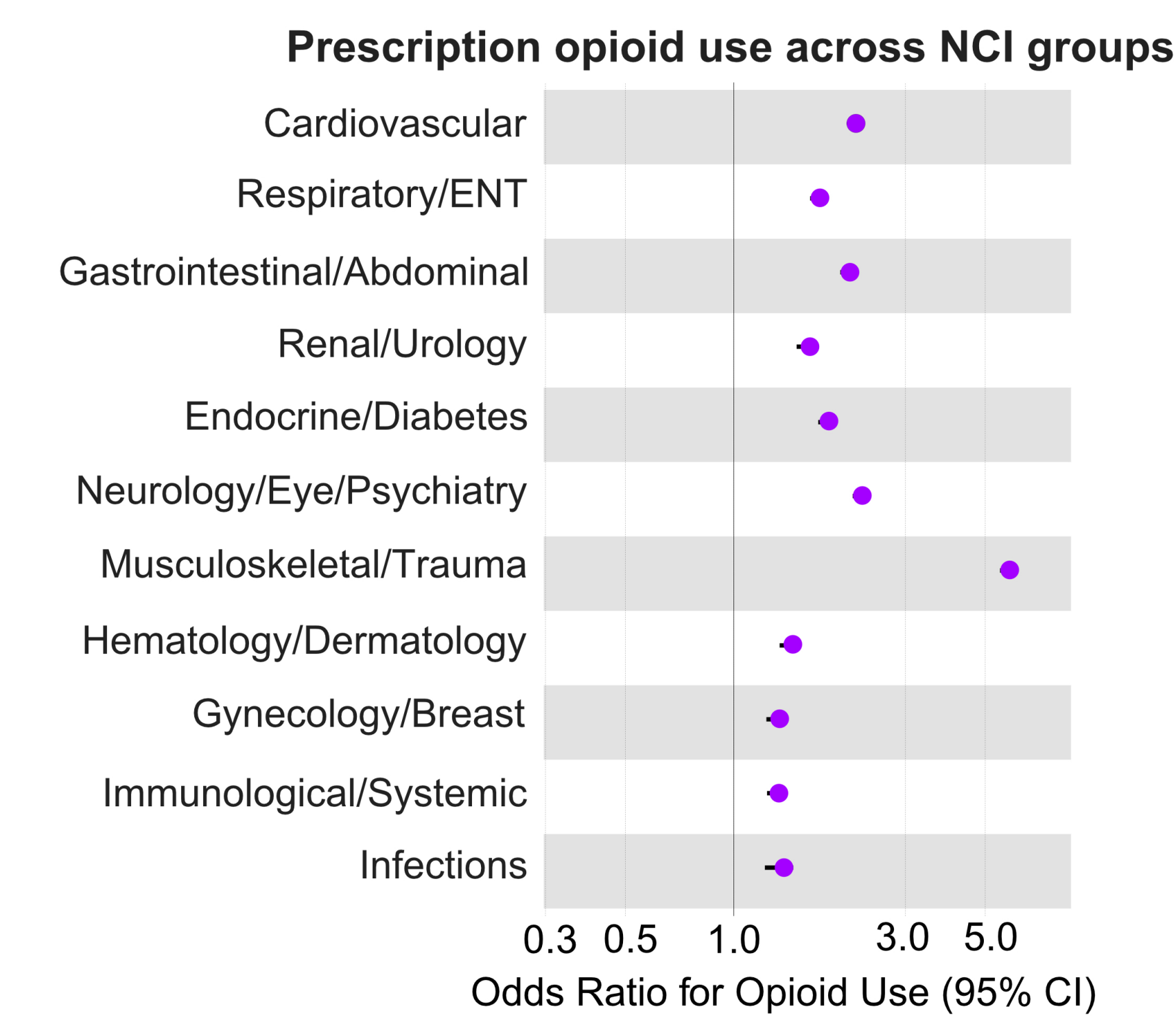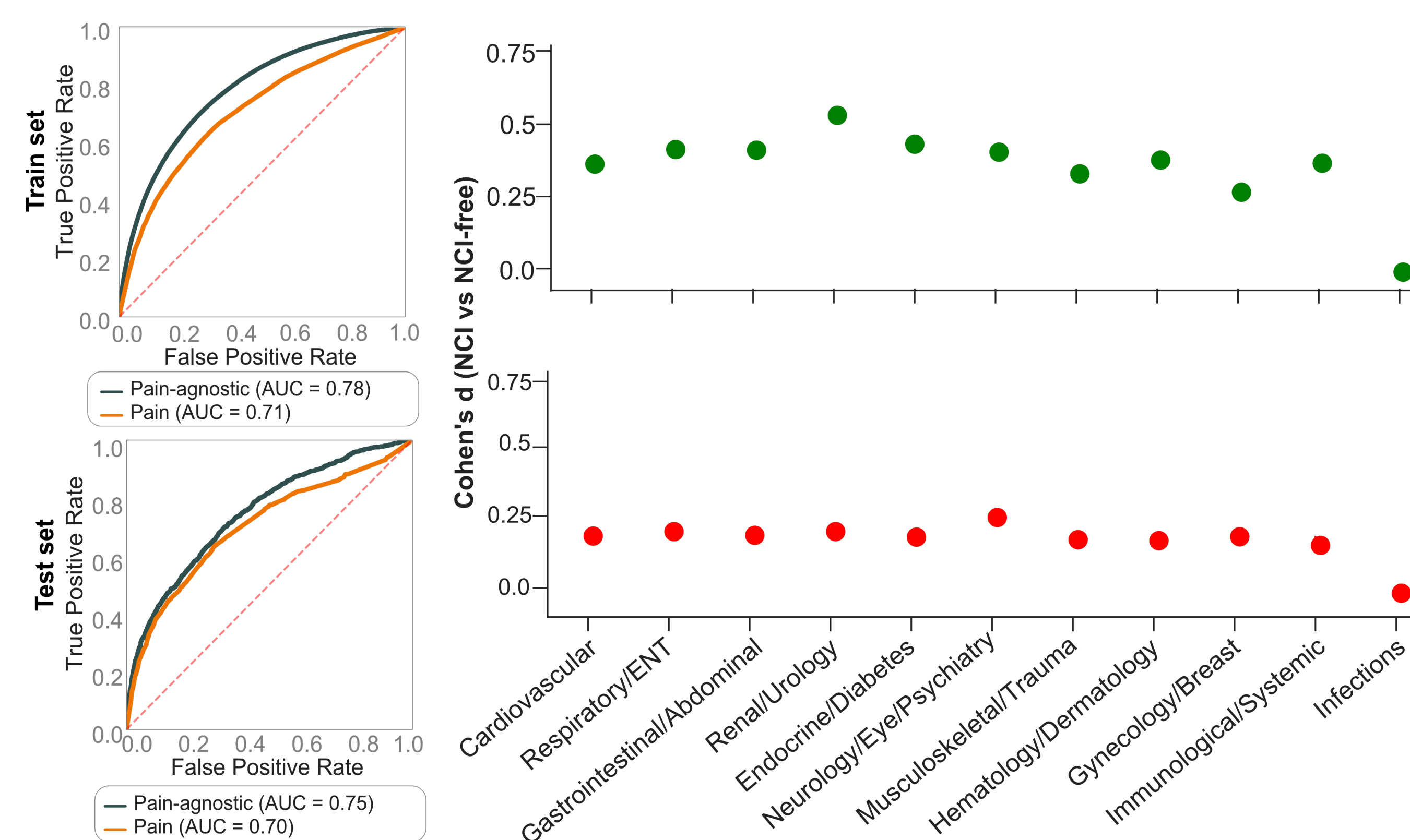

Figure 3. Associations between each NCI group and prescription opioid use. Forest plots show ORs of using opioids given each NCI group. Opioid use was associated with all NCIs, with ORs ranging from 5.5, [95%CI:5.49,5.84] for neurological and psychiatric illnesses and 1.29, [95%CI:1.24-1.35] for immunological comorbidities.
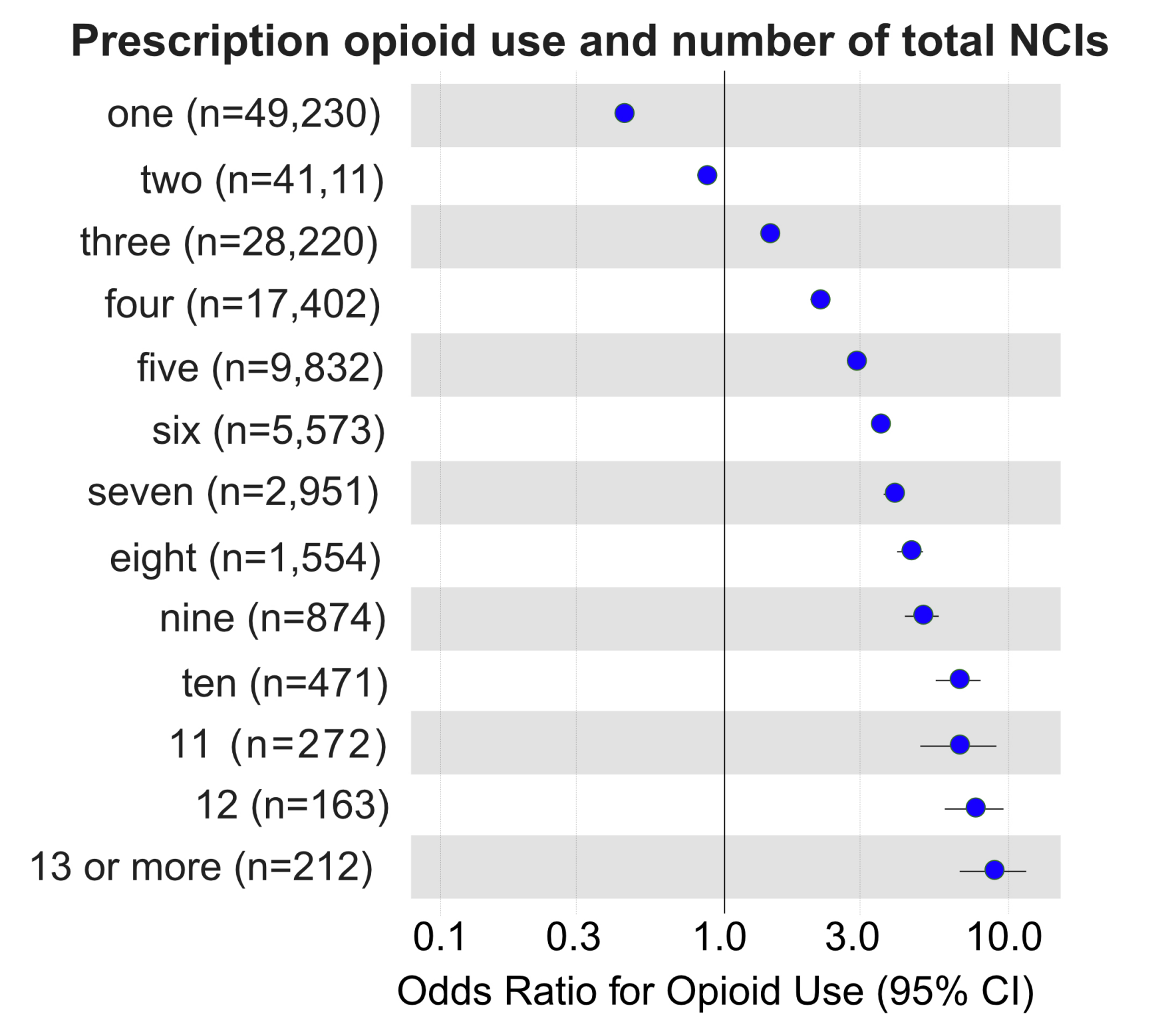
Figure 4. Associations between number of reported NCIs and opioid use in CNCP patients. Prescription opioid use was strongly associated with the number of non-cancer medical illnesses in CNCP patients, and the likelihood of using opioids linearly increased with the number of illnesses.

Figure 5. Pain and pain-agnostic risk scores across NCI groups. Area Under the Receiver Operating Curves (AUC-ROC) showing classification accuracy of the two Lasso regression models (i.e., pain-agnostic and pain) in the train (top) and test set (below). Both models obtained good performance in the test set. Differences in opioid use prediction scores (based on both models) between NCI and NCI-free groups were measured with Cohen's *d* effect sizes. Standard errors were estimated from 10,000 bootstrap resampling. Across all categories, medium effect sizes were found for the pain-agnostic risk scores and small effect sizes were found for the pain risk scores (average Cohen's $d_{pain-agnostic\ model}$ =0.40, P-value<0.001, and average Cohen's $d_{pain\ model}$ =0.19, P-value<0.001).

CONCLUSIONS

- Our findings suggest that opioid prescription and opioid-related disorders, are both associated with pain-agnostic characteristics that go beyond the physical pain experienced by the patients.
- Opioids are more frequently prescribed to patients suffering from comorbid conditions, and that associations between chronic pain and opioid use may be confounded by pain-associated illnesses.
- CNCP patients diagnosed with an NCI had significantly higher pain-agnostic risk scores compared to the NCI-free group, indicating that opioids may be prescribed to co-treat the patients' pain and overall poor functioning.

References

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