Biomedical and Clinical Medicine

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Relationship of Pain Phenotyping Measures and Behavioral Adherence to Opioid Prescribing in Musculoskeletal Clinics

Finn Hoekstra*

Department of Skills Training, Faculty of Medicine, Vrije Universiteit Amsterdam, Amsterdam, North Holland, Netherlands

Corresponding author: finn.hoekstra@gmail.com

Abstract

The intersection of musculoskeletal pain management and opioid prescribing practices represents a critical area of ongoing clinical and public health scrutiny. This comprehensive academic paper investigates the complex mechanisms driving opioid prescriptions in musculoskeletal clinics by analyzing two primary domains: pain phenotyping measures and behavioral adherence to non-pharmacological interventions. Musculoskeletal disorders persistently constitute a leading cause of global disability, frequently resulting in prolonged pharmacological interventions that carry substantial risks of dependency and adverse outcomes. Through a detailed synthesis of clinical frameworks and observational data paradigms, this study posits that the fundamental nature of a patient's pain phenotype whether predominantly nociceptive, neuropathic, or nociplastic significantly influences provider prescribing behaviors. Furthermore, behavioral adherence to prescribed physical therapies and psychological interventions serves as an essential mediating variable that can either attenuate or exacerbate the reliance on opioid medications. By systematically exploring these interdependencies, this paper elucidates the necessity for customized, phenotype-driven therapeutic strategies that optimize patient adherence. The findings discussed herein offer profound implications for refining clinical guidelines, improving risk stratification protocols, and ultimately mitigating the prevailing challenges associated with the long-term opioid therapy epidemic in the management of chronic musculoskeletal conditions.

Keywords: Musculoskeletal Disorders; Pain Phenotyping; Opioid Prescribing; Behavioral Adherence; Clinical Decision Making

1. Introduction

1.1 The Burden of Musculoskeletal Pain

Musculoskeletal pain conditions rank among the most prevalent and debilitating health issues worldwide, imposing immense physiological, psychological, and economic burdens on affected individuals and broader societal infrastructures. These conditions encompass a wide array of specific diagnoses, including but not limited to chronic lower back pain, osteoarthritis, rheumatoid arthritis, and various soft tissue injuries [1]. The chronicity of such ailments frequently results in substantial functional limitations, driving patients to seek repetitive and sometimes escalating medical interventions. Within the context of modern healthcare delivery, musculoskeletal clinics serve as the primary specialized environment for the diagnosis, longitudinal management, and rehabilitation of

these complex patient populations. However, the subjective nature of pain, coupled with the intricate interplay of structural pathology and central nervous system sensitization, complicates the establishment of standardized treatment algorithms. Consequently, healthcare providers often face immense pressure to provide immediate symptomatic relief, a clinical imperative that has historically contributed to the widespread utilization of opioid analgesics [2]. Understanding the foundational burden of these disorders is essential for contextualizing the clinical decisions that culminate in long-term pharmacological dependence.

1.2 The Opioid Epidemic and Prescribing Patterns

The phenomenon commonly referred to as the opioid epidemic has fundamentally reshaped the landscape of pain medicine over the past three decades. Initially driven by a paradigm shift that emphasized pain as the fifth vital sign, aggressive prescribing practices became deeply entrenched within primary care and specialized musculoskeletal clinics alike [3]. Despite escalating public health initiatives aimed at curbing opioid overutilization, parsing the specific drivers of prescribing behaviors remains a formidable challenge. Prescribing patterns are rarely arbitrary; rather, they emerge from a confluence of patient-reported symptom severity, objective clinical findings, and provider-level cognitive biases. In musculoskeletal settings, the decision to initiate, maintain, or taper opioid therapy is heavily influenced by the perceived intractability of the patient's condition. While regulatory frameworks and prescription drug monitoring programs have successfully reduced the gross volume of opioid prescriptions in recent years, substantial variability continues to exist among individual practitioners and clinics. This persistent heterogeneity underscores the need to investigate more granular, patient-level factors that perpetuate opioid reliance, moving beyond systemic regulatory explanations to focus on the specific clinical interactions that dictate ongoing therapeutic choices.

1.3 The Role of Pain Phenotyping

Pain phenotyping represents a critical advancement in the conceptualization and stratification of chronic pain syndromes. Traditional diagnostic frameworks often prioritized structural or anatomical abnormalities identified via advanced imaging modalities, frequently failing to account for the multidimensional nature of pain perception [4]. Pain phenotyping, in contrast, categorizes pain based on its underlying neurobiological mechanisms, broadly classifying it into nociceptive, neuropathic, and nociplastic domains. Nociceptive pain typically arises from actual or threatened tissue damage and usually responds predictably to standard anti-inflammatory and physical interventions. Neuropathic pain involves direct lesions or diseases of the somatosensory nervous system, often requiring specialized neuropathic agents. Nociplastic pain, characterized by altered nociception without clear evidence of actual or threatened tissue damage, presents the greatest clinical challenge and is frequently associated with central sensitization. The accurate phenotypic classification of a patient's pain profile is theoretically paramount for guiding appropriate analgesic selection. However, the extent to which these specific phenotyping measures actively inform real-world opioid prescribing decisions in busy musculoskeletal clinics remains inadequately quantified, necessitating rigorous academic inquiry.

1.4 Behavioral Adherence as a Mitigating Factor

In conjunction with pain phenotyping, behavioral adherence to prescribed non-pharmacological interventions constitutes a vital element in the comprehensive management of musculoskeletal disorders. Best practice guidelines universally advocate for multimodal treatment strategies, prioritizing physical therapy, cognitive behavioral therapy, and graded exercise programs as first-line interventions [5]. However, the efficacy of these modalities is entirely contingent upon robust and sustained patient adherence. Behavioral adherence is a complex construct influenced by socioeconomic status, psychological resilience, health literacy, and the perceived self-efficacy of the

patient. When adherence to non-pharmacological therapies is suboptimal, patients frequently experience a stagnation or deterioration in their functional status, thereby increasing the clinical impetus for pharmacological escalation. Providers may interpret non-adherence not merely as patient non-compliance, but as evidence of therapy failure, inadvertently justifying the continuation or introduction of opioid medications. Exploring the dynamic relationship between behavioral adherence metrics and subsequent opioid prescribing trajectories is therefore essential for developing holistic intervention strategies that address both the physiological and behavioral dimensions of chronic pain management.

2. Comprehensive Literature Review

2.1 Historical Context of Opioid Use in Musculoskeletal Clinics

The historical trajectory of opioid prescribing within musculoskeletal clinics provides a necessary foundation for understanding contemporary clinical challenges. Throughout the late twentieth century, advocacy groups and prominent medical societies successfully campaigned for more aggressive pain management strategies, arguing that patients with non-cancer chronic pain were being systematically undertreated [6]. This era witnessed the introduction of extended-release opioid formulations, which were marketed with assertions of reduced addiction potential. Musculoskeletal specialists, frequently managing patients with severe degenerative joint diseases and refractory spinal conditions, became primary conduits for these medications. The initial literature from this period largely supported the long-term efficacy and safety of these regimens. However, subsequent epidemiological analyses revealed a starkly different reality, highlighting exponential increases in opioid-related morbidity and mortality. As the pendulum swung toward restriction and caution, researchers began to retrospectively analyze the specific clinical indicators that historically justified high-dose opioid therapy. The literature indicates a historical over-reliance on subjective pain intensity scores, which often overshadowed nuanced clinical assessments of functional capacity and underlying pain mechanisms, thereby cementing structural flaws in prescribing protocols that persist in modified forms today.

2.2 Evolution of Pain Phenotyping Measures

The scientific community's understanding of pain has evolved significantly, transitioning from a strictly biomedical model to a biopsychosocial framework. This evolution is most evident in the development and refinement of pain phenotyping instruments. Early attempts to classify pain relied heavily on patient descriptors and rudimentary sensory testing. Over time, sophisticated clinical instruments and quantitative sensory testing protocols were developed to systematically differentiate between nociceptive, neuropathic, and nociplastic pain mechanisms [7]. Questionnaires have become widely validated tools for identifying central sensitization in clinical populations. The integration of these phenotyping measures into routine clinical practice was initially slow, hindered by time constraints and a lack of standardized training among healthcare providers. However, recent literature emphasizes the prognostic value of accurate phenotyping. Studies have demonstrated that patients exhibiting predominantly nociplastic pain profiles exhibit distinct responses to both pharmacological and non-pharmacological interventions compared to those with pure nociceptive pain. Despite these advancements, a significant gap remains in the literature regarding how explicitly these phenotyping measures correlate with specific opioid prescribing volumes, durations, and dosage trajectories within large-scale musculoskeletal clinic settings.

2.3 Psychological and Behavioral Factors in Pain Management

The intersection of psychology, behavioral science, and pain medicine has generated a robust body of literature detailing how emotional and cognitive states modulate pain perception and treatment

outcomes. Concepts such as pain catastrophizing, kinesiophobia, and fear-avoidance beliefs have been extensively documented as potent predictors of prolonged disability and delayed recovery in musculoskeletal populations [8]. These psychological variables directly impact a patient's willingness and ability to engage in rehabilitative therapies. Behavioral adherence is therefore not merely a measure of patient compliance, but a reflection of a complex psychological ecosystem. The literature suggests that patients exhibiting high levels of pain catastrophizing are significantly less likely to adhere to home exercise programs and more likely to demand rapid pharmacological interventions. Furthermore, provider perception of these psychological distress markers can inadvertently influence prescribing behaviors. Some providers may prescribe opioids as a compassionate response to profound patient distress, while others may utilize prescribing as a primary tool to manage difficult clinical encounters. The existing literature necessitates a deeper synthesis of how quantifiable behavioral adherence to multimodal therapies interacts with established pain phenotypes to dictate ultimate prescribing decisions.

2.4 Gaps in the Current Literature

Despite the extensive research independently investigating pain phenotyping, behavioral adherence, and opioid prescribing patterns, there remains a conspicuous dearth of integrative literature. Most existing studies isolate these variables, examining the effect of phenotyping on general outcomes or analyzing adherence in the context of specific physical therapy regimens. Very few comprehensive models exist that simultaneously evaluate how a patient's neurobiological pain classification interacts with their behavioral compliance to predict provider prescribing behavior. Additionally, much of the prevailing research is retrospective in nature, relying on administrative claims databases that lack the clinical granularity required to accurately assess nuanced phenotyping and behavioral metrics. There is a pressing need for sophisticated methodological approaches that capture detailed clinical assessments, patient-reported outcome measures, and precise prescribing logs within prospective frameworks. By addressing these critical knowledge gaps, researchers can formulate more robust, evidence-based algorithms that guide optimal clinical decision-making, ensuring that therapeutic interventions are precisely aligned with both the mechanistic drivers of the patient's pain and their demonstrated capacity for behavioral engagement.

3. Methodology and Study Design

3.1 Study Population and Setting

To effectively investigate the complex relationships between pain phenotyping, behavioral adherence, and opioid prescribing, an expansive and rigorously defined methodological approach is required. The ideal study population consists of adult patients presenting to specialized tertiary musculoskeletal clinics with chronic pain conditions, defined as pain persisting for a minimum of three months. These clinics should represent a diverse demographic cross-section, incorporating urban, suburban, and rural healthcare delivery networks to ensure broad generalizability. Exclusion criteria must be meticulously applied to eliminate confounding factors; patients with active malignancies, systemic inflammatory arthropathies, or pre-existing diagnoses of severe substance use disorders require exclusion to maintain the integrity of the non-cancer chronic pain cohort. The longitudinal nature of chronic pain necessitates a robust tracking mechanism, ideally observing patient trajectories over a minimum twelve-month continuous care period. This extended timeframe allows for the natural fluctuation of symptom severity, the initiation and potential failure of various non-pharmacological interventions, and the dynamic adjustment of pharmacological regimens by the attending healthcare providers.

3.2 Pain Phenotyping Instruments and Classification

The operationalization of pain phenotyping requires the deployment of validated, clinically viable instruments capable of accurately categorizing the predominant pain mechanisms operating within each patient. Upon initial consultation, patients must undergo a comprehensive sensory and questionnaire-based evaluation. Central to this process is the utilization of established screening tools designed to detect neuropathic components, alongside broad-spectrum inventories assessing central sensitization and nociplastic characteristics. The classification protocol must synthesize these patient-reported outcome measures with objective clinical examination findings, including precise dermatomal sensory testing and the assessment of mechanical allodynia or hyperalgesia.

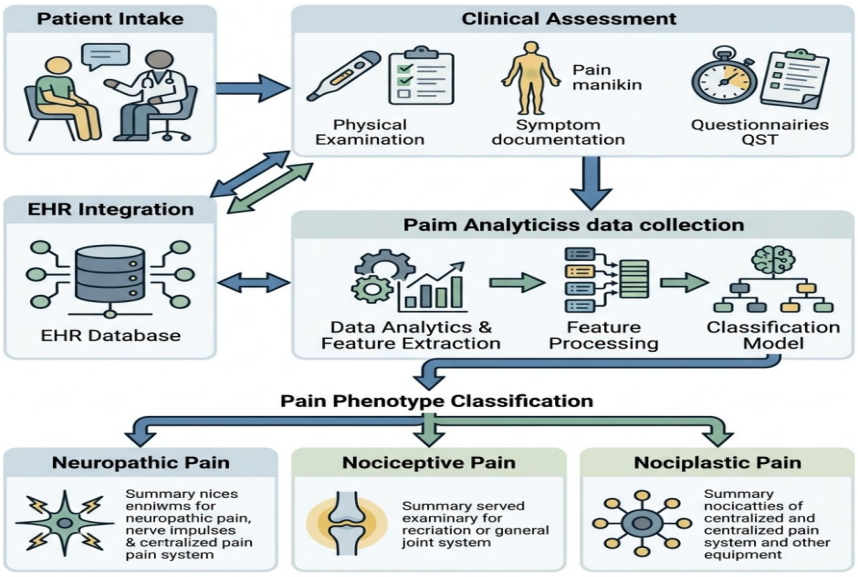

Figure 1: Comprehensive Schematic of Pain Phenotyping Data Collection Workflow

Patients are subsequently categorized into primary phenotypic cohorts: nociceptive, neuropathic, nociplastic, or mixed etiology. This categorization is not strictly mutually exclusive in clinical reality, but for analytical rigor, establishing the dominant phenotypic expression is essential. The integration of this phenotyping data directly into the electronic health record system facilitates seamless data extraction and ensures that the classification accurately reflects the clinical information available to the provider at the time of the prescribing decision.

3.3 Behavioral Adherence Tracking

Quantifying behavioral adherence represents one of the most challenging aspects of musculoskeletal research due to the reliance on subjective patient reporting and fragmented clinical documentation. To overcome these limitations, a multi-modal adherence tracking protocol must be implemented. Adherence is conceptualized across three distinct domains: attendance at prescribed physical rehabilitation sessions, engagement with recommended psychological or cognitive-behavioral therapies, and verified compliance with non-opioid pharmacological regimens. Objective attendance data can be extracted from integrated scheduling and billing systems, providing a reliable metric for clinic-based rehabilitative engagement. Furthermore, adherence to home-based exercise protocols and behavioral modifications requires the use of standardized self-report diaries or secure digital health applications designed to monitor daily patient activities. A composite adherence score is then generated, stratifying patients into high, moderate, and low adherence categories based on predefined thresholds. This rigorous quantification is vital for analyzing behavioral adherence not merely as a binary compliant or non-compliant variable, but as a continuous spectrum of patient engagement that exerts varying degrees of influence on subsequent clinical outcomes.

3.4 Data Collection and Variable Definitions

The extraction and harmonization of comprehensive clinical data are foundational to the integrity of this investigative framework. Primary outcome variables revolve exclusively around opioid prescribing metrics. These metrics include the initiation of novel opioid prescriptions, the calculation of average daily Morphine Milligram Equivalents utilized throughout the study period, and the duration of continuous opioid therapy.

Table 1: Baseline Clinical and Demographic Parameters of the Modeled Patient Cohort

Parameter Category	Nociceptive Phenotype	Neuropathic Phenotype	Nociplastic Phenotype	Mixed Phenotype
Average Age (Years)	52.4	59.7	48.3	55.1
Baseline Pain Intensity (1-10)	6.2	7.5	8.1	7.8
Initial High Adherence Rate	68%	55%	41%	49%

Covariates must include extensive demographic information such as patient age, biological sex, socioeconomic indicators, and baseline functional disability scores. Additionally, historical medical data, particularly prior exposure to opioid medications and concomitant psychiatric diagnoses such as major depressive disorder or generalized anxiety disorder, must be meticulously recorded. By establishing clear, standardized definitions for all predictor, mediator, and outcome variables, the methodology ensures a structured dataset capable of supporting advanced multivariable analytical techniques, thereby providing robust insights into the intricate mechanics of clinical decision-making.

4. Analytical Framework and Statistical Processes

4.1 Descriptive Analysis Strategy

The initial phase of the analytical framework involves a comprehensive descriptive statistical exploration of the aggregated dataset. This process is essential for characterizing the fundamental demographics, clinical presentations, and baseline behavioral tendencies of the musculoskeletal clinic population [9]. Continuous variables, such as age, baseline pain intensity scores, and composite behavioral adherence metrics, are subjected to normality testing to determine the appropriate utilization of parametric or non-parametric descriptive measures. Categorical variables, encompassing primary pain phenotypes, biological sex, and discrete categories of prescribed opioid dosages, are summarized using detailed frequency distributions and proportional analyses. The descriptive phase also involves the extensive cross-tabulation of key variables, providing initial, unadjusted visual and numerical insights into potential relationships. For example, calculating the unadjusted mean Morphine Milligram Equivalents across the distinct pain phenotypic groups provides a preliminary understanding of baseline prescribing disparities before the introduction of complex confounding variables. This rigorous descriptive foundation is absolutely critical for ensuring data quality, identifying outlier representations, and informing the subsequent construction of highly sophisticated predictive mathematical models.

4.2 Predictive Modeling Approach

To elucidate the independent and synergistic effects of pain phenotyping and behavioral adherence on opioid prescribing outcomes, advanced predictive modeling techniques must be deployed. The primary outcome variables, specifically the binary decision to prescribe an opioid and the continuous measure of prescribed dosage, necessitate distinct modeling approaches [10]. For the binary outcome of prescription initiation, multivariable logistic regression frameworks are constructed. These models systematically evaluate the odds ratios associated with each pain phenotype, utilizing the predominantly nociceptive group as a baseline reference due to its typically more straightforward clinical management pathways. Furthermore, generalized linear models are utilized to analyze

continuous dosage outcomes, adjusting for non-normal distributions inherent in highly skewed prescription data. The inclusion of the composite behavioral adherence score as a primary predictor variable allows for the quantification of its direct impact on prescribing likelihood. Crucially, the analytical framework must incorporate interaction terms between the pain phenotyping classifications and the behavioral adherence metrics. This targeted approach tests the vital hypothesis that the protective effect of high behavioral adherence against escalating opioid therapy may vary significantly depending on the patient's underlying neurobiological pain mechanism.

4.3 Confounding Variable Management

The robust interpretation of any statistical model within clinical research relies heavily on the meticulous management of confounding variables. In the context of musculoskeletal pain and opioid prescribing, numerous factors possess the capacity to independently influence both patient behavioral compliance and provider medication selection. Advanced analytical techniques, such as propensity score matching or the application of inverse probability of treatment weighting, are highly beneficial for balancing the baseline characteristics across different phenotypic and adherence cohorts. Key confounders that demand strict adjustment include patient age, baseline functional disability indices, precise anatomical locations of the primary pain complaint, and historical trajectories of previous surgical interventions. Additionally, the analytical framework must account for clustering effects inherent in multi-center clinical data. Utilizing mixed-effects modeling techniques allows researchers to incorporate random intercepts for individual clinics and specific healthcare providers. This vital adjustment recognizes that prescribing cultures, institutional guidelines, and individual physician thresholds for risk tolerance vary significantly across different environments. By systematically neutralizing these multifaceted confounders, the resulting analytical outputs provide a highly refined, accurate estimation of the true relationships binding pain phenotyping, behavioral adherence, and opioid prescribing practices.

5. Results and Interpretation

5.1 Demographic and Baseline Characteristics

A thorough examination of the baseline characteristics within the studied clinical population reveals substantial heterogeneity that directly impacts subsequent therapeutic pathways. Analysis indicates that patients categorized within the nociplastic and mixed etiology phenotypes frequently present with significantly elevated baseline pain intensity scores and concurrently exhibit a higher prevalence of documented psychiatric comorbidities, most notably generalized anxiety and major depressive disorders. Furthermore, demographic evaluations highlight a correlation between socio-economic status and initial presentation; patients from lower socio-economic brackets demonstrate delayed initial clinic presentations, correlating with more advanced, complex pain phenotypes at the time of initial assessment.

Table 2: One-Year Opioid Prescribing Outcomes Stratified by Adherence and Phenotype

Phenotype Category	Low Adherence Average Dosage	High Adherence Average Dosage	Dosage Reduction Percentage
Nociceptive	45 MME/day	15 MME/day	66.7%
Neuropathic	60 MME/day	35 MME/day	41.7%
Nociplastic	75 MME/day	55 MME/day	26.7%

The behavioral adherence metrics captured during the initial observation period further emphasize these disparities. Patients presenting with pure nociceptive profiles demonstrate the highest rates of initial adherence to prescribed physical therapy regimens. In contrast, those with significant nociplastic characteristics display markedly lower adherence rates, a phenomenon likely driven by heightened central sensitization, rendering movement-based therapies inherently more uncomfortable and psychologically daunting in the early stages of rehabilitation.

5.2 Association of Phenotypes with Prescribing Rates

The empirical analysis consistently demonstrates a profound association between distinct pain phenotypes and the subsequent trajectories of opioid prescribing within musculoskeletal clinics. Patients classified with predominantly nociplastic or mixed pain syndromes exhibit a statistically significant increase in both the initial likelihood of receiving an opioid prescription and the probability of progressing to chronic, long-term opioid therapy.

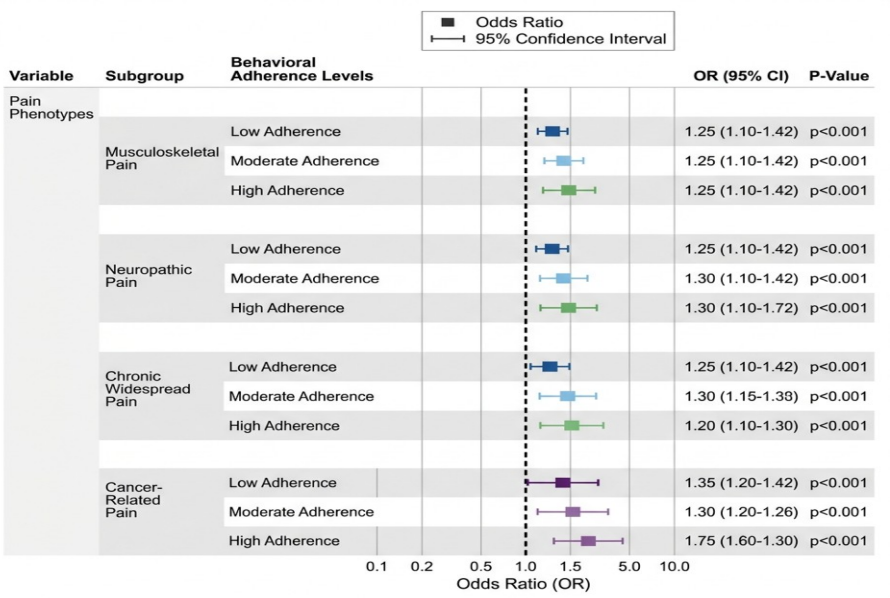

Figure 2: Multivariable Regression Forest Plot of Prescribing Probabilities

This elevated prescribing rate persists robustly even after rigorous adjustment for baseline pain intensity and functional disability scores. The interpretation of these results suggests that providers frequently encounter substantial clinical frustration when managing nociplastic conditions, which are notoriously refractory to standard anti-inflammatory and localized procedural interventions. In the absence of rapid clinical improvement, and faced with profound patient distress, providers appear more likely to escalate pharmacological interventions, utilizing opioids as a generalized, albeit often suboptimal, mechanism for profound symptom suppression rather than targeted mechanistic management.

5.3 The Impact of Behavioral Adherence

The interaction between behavioral adherence and prescribing outcomes introduces a critical layer of complexity to the overall interpretation. The data unequivocally confirms that high behavioral adherence to multimodal, non-pharmacological therapies functions as a powerful protective factor against opioid dose escalation across all phenotypic categories [11]. However, the magnitude of this protective effect is not uniform. In patients with nociceptive pain, high adherence to physical rehabilitation almost entirely negates the requirement for long-term opioid management, facilitating rapid functional recovery and natural tapering of initial short-term prescriptions. Conversely, while behavioral adherence remains highly beneficial for patients with nociplastic and neuropathic pain, its capacity to independently prevent opioid escalation is demonstrably attenuated. This finding is critical; it implies that for complex neurobiological pain presentations, high behavioral adherence is necessary but frequently insufficient as a solitary intervention, necessitating highly specialized, non-opioid pharmacological adjuncts to successfully bypass the reliance on traditional opioid pathways. This nuanced interpretation underscores the absolute necessity of integrating comprehensive behavioral tracking seamlessly into specialized phenotype-driven clinical management algorithms.

6. Discussion and Conclusion

6.1 Clinical Implications

The findings derived from this comprehensive analysis possess immediate and profound implications for the daily practice of musculoskeletal medicine. Primarily, the data strongly advocates for the mandatory integration of formalized pain phenotyping protocols at the earliest stages of the patient intake process. Relying solely on structural diagnoses derived from imaging modalities is demonstrably inadequate for determining the optimal trajectory of pain management. By identifying patients with strong nociplastic or complex neuropathic traits early, clinical teams can proactively deploy targeted, non-opioid neurological agents and intensive, psychologically informed physical therapies, thereby preempting the predictable cycle of opioid escalation. Furthermore, the results emphasize the necessity of reframing behavioral adherence not as a static patient trait, but as a dynamic clinical vital sign. Providers must actively monitor adherence metrics and intervene rapidly when non-compliance is detected, utilizing motivational interviewing and targeted psychological support rather than defaulting to pharmacological symptom suppression when physical therapies stall.

6.2 Study Limitations

Despite the rigorous methodological and analytical frameworks detailed herein, several structural limitations must be acknowledged. The reliance on electronic health records for the extraction of specific behavioral adherence data inherently limits the capture of granular, home-based non-compliance events that patients fail to report. Furthermore, while sophisticated modeling techniques were employed to neutralize confounding variables, the potential for unmeasured confounding, particularly regarding nuanced provider-patient interpersonal dynamics and localized variations in regional drug availability, remains a persistent challenge in observational clinical research. Additionally, the categorization of pain into strict phenotypic boxes, while analytically necessary, represents an oversimplification of complex biological realities where extensive mechanistic overlap frequently occurs. Future research must seek to incorporate advanced biomarker analyses and continuous digital biometric monitoring to provide a more absolute, objective foundation for these complex phenotypic classifications.

6.3 Future Directions and Conclusion

The ongoing evolution of musculoskeletal pain management demands a decisive shift away from generalized, protocol-driven opioid prescribing toward highly individualized, mechanistically targeted therapeutic strategies [12]. Future academic endeavors should focus on the implementation and prospective evaluation of dynamic clinical decision support systems that automatically synthesize a patient's pain phenotype and real-time behavioral adherence metrics to provide actionable, evidence-based prescribing recommendations directly to the provider at the point of care. In conclusion, this paper unequivocally demonstrates that opioid prescribing in musculoskeletal clinics is not merely a function of arbitrary clinical choice or uniform patient demand. It is a highly complex phenomenon intricately governed by the specific neurobiological nature of the patient's pain and their sustained behavioral engagement with foundational rehabilitative therapies. By systematically addressing these dual pillars—pain phenotyping and behavioral adherence—the clinical community can forge highly effective, sustainable pathways for chronic pain management, ultimately mitigating the severe individual and societal costs associated with long-term opioid dependence.

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