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Causal Forest Estimation of Treatment Heterogeneity: Identifying Subgroups of Women Benefiting Most from Mindfulness-Based Stress Reduction for Chronic Pain

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A B S T R A C T

Objective: The objective of this study was to apply a causal forest machine learning algorithm to estimate the conditional average treatment effects of Mindfulness-Based Stress Reduction on pain interference and identify the specific baseline characteristics of women with chronic pain who derive the greatest therapeutic benefit.

Methods and Materials: This randomized controlled trial included a sample of $N = 284$adult women (mean age $M = 51.4$years) residing in Spain and suffering from chronic non-malignant pain. Participants were randomly assigned to an 8-week Mindfulness-Based Stress Reduction program or a treatment-as-usual control group. Baseline sociodemographic and psychological covariates were assessed using standardized psychometric instruments, including the Brief Pain Inventory, Hospital Anxiety and Depression Scale, and the Five Facet Mindfulness Questionnaire. To move beyond the traditional Average Treatment Effect (ATE), a causal forest algorithm was utilized to estimate the Conditional Average Treatment Effect ($CATE$) for pain interference, allowing for the empirical identification of high-benefit and low-benefit patient subgroups based on their multidimensional baseline profiles.

Findings: While the standard analysis revealed a statistically significant Average Treatment Effect for pain interference ($\Delta M = -1.24$), the causal forest estimation uncovered substantial treatment heterogeneity, with individual $CATE$values ranging widely from $-3.10$to $+0.45$. Variable importance metrics derived from the machine learning model identified baseline anxiety as the strongest predictor of treatment benefit, followed closely by the non-judging of inner experience facet of dispositional mindfulness, and the total duration of the chronic pain condition. Specifically, the high-benefit subgroup—which experienced the most clinically significant reductions in pain interference ($\tau(x) \approx -3.10$)—was characterized by elevated baseline anxiety and depression, distinctly lower baseline scores in non-judging mindfulness, and a comparatively shorter history of chronic pain.

Conclusion: Mindfulness-Based Stress Reduction is not uniformly effective for all chronic pain patients; rather, it yields the maximum reduction in pain interference specifically among women presenting with high emotional distress, highly judgmental psychological traits, and shorter pain durations, highlighting the critical necessity of precision behavioral medicine.

Keywords: *Chronic Pain; Mindfulness-Based Stress Reduction; Treatment Heterogeneity*

1. Introduction

Chronic pain is recognized globally as a deeply debilitating condition that extends far beyond the mere physiological sensation of physical discomfort. It is a complex, multidimensional experience that severely compromises an individual's physical functioning, emotional well-being, and overall quality of life. The epidemiological burden of chronic pain is particularly pronounced among women and older adults, who frequently report higher intensities of pain and greater subsequent functional disability (Alemi et al., 2021). For older demographic cohorts, the relentless nature of chronic somatic symptoms is often inextricably linked with profound existential distress, significantly exacerbating death anxiety and drastically reducing the overall quality of life (Ahmadi & Valizadeh, 2021). The challenge of accessing effective pain management is further compounded by geographical and socioeconomic barriers; for example, patients residing in rural areas often encounter significant pitfalls in securing consistent and specialized pain treatment, highlighting a critical need for accessible alternative interventions (Bishop et al., 2023). Furthermore, chronic pain rarely exists in clinical isolation; it frequently co-occurs with severe trauma and psychiatric conditions. Patients harboring a history of post-traumatic stress disorder face unique challenges, as the physiological hyperarousal associated with trauma fundamentally alters health behavior changes and complicates standard pain rehabilitation protocols (Shen et al., 2024).

To fully comprehend the persistent nature of chronic pain syndromes, clinicians must look through the lens of the biopsychosocial model, which emphasizes the critical role of psychological factors in the amplification and maintenance of physical suffering. One of the most potent psychological amplifiers of the pain experience is pain catastrophizing, a maladaptive cognitive schema that significantly mediates the relationship between dispositional mindfulness and severe psychological distress in populations suffering from chronic pain (Conti et al., 2020). The interplay between somatic pain and psychological pathology becomes even more complex when patients present with severe personality disorders. For instance, individuals diagnosed with borderline personality disorder who concurrently suffer from chronic pain exhibit highly dysregulated emotional responses to nociceptive stimuli, requiring specialized, emotion-focused therapeutic strategies (Verdú & Marcos, 2022). Anxiety is another ubiquitous comorbidity; specifically, elevated anxiety sensitivity—the fear of anxiety-related bodily sensations—has been shown to severely limit therapeutic progress, although interventions targeting cognitive restructuring have proven beneficial in reducing these specific anxiety components in women with chronic pain (Karimi et al., 2023). This psychological burden is clearly evident in specialized pain populations, such as patients enduring chronic tension-type or migraine headaches, where persistent pain anxiety dictates a drastically diminished quality of life (Ebrahimi Sadr et al., 2023). Despite the clear need for psychologically informed care, cross-sectional surveys of the general public reveal that knowledge and perceptions regarding holistic, mind-body interventions for chronic pain management remain highly varied and often inadequate in community settings (Harris et al., 2023).

Historically, the biomedical management of chronic pain has relied heavily on pharmacological interventions, most notably opioid analgesics. However, the widespread prescription of opioids has precipitated a devastating global public health crisis characterized by skyrocketing rates of addiction, tolerance, and fatal overdoses, prompting an urgent paradigm shift toward non-pharmacological, evidence-based behavioral treatments (Zgierska et al., 2025). Consequently, the implementation of behavioral medicine approaches into standard clinical practice has become a priority, requiring experimental studies to inform the structural and systemic adoption of comprehensive behavioral programs for highly prevalent conditions such as chronic low back pain (Sherman et al., 2022).

In response to the limitations and risks associated with traditional pharmacology, Mindfulness-Based Interventions

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(MBIs) have emerged as highly efficacious, non-invasive therapeutic modalities. Rooted in ancient contemplative traditions but secularized for clinical application, mindfulness training fundamentally alters the relationship between the patient and their physical suffering by cultivating a state of non-judgmental, present-moment awareness, thereby generating broad positive outcomes for general physical health and psychological resilience (Creswell et al., 2019). The clinical utility of mindfulness is not predicated on merely masking or ignoring pain; rather, it actively engages cognitive mechanisms to relieve the emotional distress associated with chronic nociception, proving particularly effective for musculoskeletal conditions such as chronic low back pain (Morone, 2019). Extensive systematic reviews of the literature have consistently affirmed the capacity of mindfulness-based interventions to induce statistically significant reductions in subjective pain intensity across diverse patient cohorts (Norouzi et al., 2020). Remarkably, the therapeutic applicability of mindfulness spans the entire developmental spectrum. Adapted mindfulness therapies have demonstrated profound effectiveness in improving psychological well-being and mitigating pain symptoms even in pediatric populations battling chronic medical diseases (Demehri et al., 2020). Conversely, at the other end of the lifespan, tailored mindfulness-based group therapy formats have proven to be highly acceptable, feasible, and effective for comprehensive chronic pain management in older adults (Foulk et al., 2023). Recent case series further substantiate this, detailing how meticulously compiled Mindfulness-Based Stress Reduction (MBSR) programs can effectively relieve entrenched chronic pain and restore functional capacity in geriatric populations (Soukhtanlou et al., 2024).

The robust empirical foundation supporting MBIs is largely built upon rigorous comparisons with other established psychological treatments. Systematic reviews evaluating the differential efficacy of varied psychological approaches have frequently positioned mindfulness-based therapies alongside, and occasionally superior to, traditional cognitive-behavioral therapy (CBT) for long-term chronic pain management (Pardos-Gascón et al., 2021). Large-scale randomized controlled trials have directly compared standard CBT, MBSR, and general behavior therapy, revealing that while all modalities yield positive results, mindfulness uniquely targets the affective dimensions of the pain experience (Burns et al., 2022). Similar comparative pilot trials contrasting mindfulness meditation, standard cognitive therapy, and the hybrid Mindfulness-Based Cognitive Therapy (MBCT) have demonstrated comparable effectiveness in functional rehabilitation for chronic low back pain (Day et al., 2019). The pursuit of optimal treatment regimens has also led to the development of complex, multi-arm clinical trial protocols designed to explore the synergistic potential of combining MBSR or CBT with alternative modalities such as acupuncture (Mackey et al., 2022). Within specialized pain phenotypes, MBCT has been shown to significantly enhance pain self-efficacy and overall life satisfaction when compared to logotherapy (meaning therapy) among men suffering from chronic daily headaches (Miragha Pour Tarrah et al., 2024). When juxtaposed with spiritual therapy, MBCT also demonstrated a robust capacity to dismantle irrational cognitive beliefs and alleviate generalized anxiety in older female pain patients (Barghi Irani & Dehghan Saber, 2021). Furthermore, among women burdened by chronic migraines and tension headaches, MBCT has been validated as a potent tool for building psychological resilience and directly diminishing the subjective intensity of the pain experience (Abotalebi Isazadegan et al., 2022). Even when compared to established relaxation techniques such as progressive muscle relaxation, mindfulness-based meditation has exhibited superior impacts on pain interference and functional mobility in older female patients afflicted by painful diabetic neuropathy (Hussain & Said, 2019).

As the digital age transforms healthcare delivery, the administration of mindfulness and acceptance-based therapies has rapidly evolved beyond the traditional clinic setting. The advent of telehealth and eHealth platforms has democratized access to psychological pain management. High-profile randomized clinical trials, such as the LAMP trial, have successfully demonstrated that telehealth-delivered mindfulness interventions can achieve outcomes comparable to in-person therapy, drastically reducing logistical barriers for mobility-impaired patients (Burgess et al., 2024). Similarly, innovative internet-delivered protocols that integrate Acceptance and Commitment Therapy (ACT) with compassion-based frameworks have shown immense promise in facilitating autonomous self-management of chronic pain (Carvalho et al., 2021). Irrespective of the delivery method, the core psychological benefits remain consistent; for instance, MBCT consistently fosters marked improvements in overall quality of life and emotional resilience specifically among women navigating the daily challenges of chronic pain (Pouryounes Abkenar et al., 2024). Interestingly, recent neurocognitive research suggests that the efficacy of MBSR may not lie in fundamentally

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altering deep-seated cognitive mechanics, as studies have shown that MBSR dramatically enhances psychological well-being and functional capacity without necessarily altering subconscious attentional biases toward pain-related facial expressions (Robles et al., 2024).

Despite the overwhelming consensus that MBSR is an effective intervention at the population level, a critical methodological and clinical gap persists in the literature: the challenge of treatment heterogeneity. The vast majority of standard randomized controlled trials evaluate intervention efficacy through the calculation of the Average Treatment Effect (ATE), mathematically represented as $\Delta = E[Y(1) - Y(0)]$, where $Y(1)$and $Y(0)$denote the potential outcomes under treatment and control conditions, respectively. While the ATE provides a useful macro-level summary indicating that a treatment works *on average*, it implicitly assumes a "one-size-fits-all" paradigm. It obscures the clinical reality that psychological interventions are highly idiosyncratic; a specific protocol may be profoundly transformative for one patient, marginally helpful for another, and completely ineffective for a third. Therefore, analyzing only the average effect is insufficient for modern personalized medicine. To optimize clinical resource allocation and patient outcomes, researchers must identify the Conditional Average Treatment Effect (CATE), defined as $\tau(x) = E[Y(1) - Y(0) \mid X = x]$. The CATE quantifies the individualized treatment effect based on a specific vector of patient baseline characteristics, denoted by X.

Estimating the CATE using traditional parametric regression models is notoriously fraught with challenges, primarily due to the risks of statistical overfitting, multicollinearity, and the inability of linear models to capture complex, high-dimensional, non-linear interactions between numerous baseline covariates. To overcome these deep-seated analytical limitations, the field of causal inference has increasingly turned to advanced machine learning techniques. Specifically, the causal forest algorithm—an innovative extension of the random forest machine learning methodology—has been developed to seamlessly integrate rigorous causal inference with the predictive power of machine learning. Unlike standard decision trees that split data to minimize predictive error, causal forests partition the data space to intentionally maximize the variance in treatment effects across different subgroups, utilizing honest sample splitting to guarantee valid confidence intervals and prevent overfitting. By applying this algorithm, researchers can input a vast array of sociodemographic, clinical, and psychological variables to empirically identify exactly which specific baseline traits drive treatment success, thereby isolating the distinct clinical phenotypes of patients who will respond best to the intervention.

To date, no study has utilized causal machine learning algorithms to map the heterogeneous treatment effects of mindfulness interventions within chronic pain populations. Therefore, the aim of this study was to apply causal forest estimation to identify the specific baseline sociodemographic and psychological characteristics that predict the greatest reduction in pain interference following Mindfulness-Based Stress Reduction among women with chronic pain.

2. Methods and Materials

2.1. Study design and Participant

This study utilized a randomized controlled trial design to investigate the heterogeneous treatment effects of Mindfulness-Based Stress Reduction on chronic pain outcomes among a specific clinical population. The sample consisted of exactly 284adult women diagnosed with chronic non-malignant pain, recruited from multiple primary care centers and specialized pain clinics across Spain. To be eligible for inclusion, participants had to be female, aged eighteen years or older, experiencing chronic pain for a duration of at least six months, and possessing the cognitive and linguistic abilities necessary to complete the psychological assessments. Individuals were excluded if they presented with severe, untreated psychiatric conditions such as active psychosis or severe major depressive disorder with suicidal ideation, if they had a history of substance abuse within the past year, or if they were currently participating in another psychological intervention. Upon meeting the eligibility criteria and providing written informed consent, the women were randomly assigned to either the standard eight-week Mindfulness-Based Stress Reduction intervention group or a treatment-as-usual control group.

2.2. Measures

To comprehensively capture the multidimensional nature of chronic pain and the potential moderating factors of the mindfulness intervention, a robust battery of standardized, culturally validated psychometric instruments was administered at baseline, immediately post-intervention, and at a six-month follow-up. The primary outcome measure,

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chronic pain severity and its impact on daily functioning, was assessed using the Spanish version of the Brief Pain Inventory. This tool captures both the intensity of the pain and the degree to which it interferes with general activity, mood, walking ability, normal work, relations with other persons, sleep, and enjoyment of life. Psychological distress, specifically anxiety and depressive symptomatology, was evaluated using the Hospital Anxiety and Depression Scale, a widely utilized instrument in medical outpatient settings that effectively excludes somatic symptoms of illness. To quantify mindfulness traits, which theoretically serve as mechanisms of change or potential baseline moderators, the Five Facet Mindfulness Questionnaire was employed. This comprehensive scale measures five distinct elements of mindfulness: observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience. Furthermore, an extensive sociodemographic and clinical questionnaire was utilized at baseline to collect critical covariate data, including the participants' exact age, educational attainment, employment status, marital status, duration of chronic pain in years, number of pain sites, and current pharmacological treatments, all of which served as the input features for the machine learning algorithms.

2.3. Data Analysis

The statistical analysis shifted away from traditional average treatment effect paradigms to focus on the Conditional Average Treatment Effect, denoted mathematically as $\tau(x) = E[Y(1) - Y(0) \mid X = x]$, which quantifies the expected difference in potential outcomes for an individual given their specific set of baseline covariates X. To estimate this treatment heterogeneity and identify specific subgroups of women who benefited most from the intervention, we employed the causal forest algorithm, an extension of the random forest machine learning method specifically designed for causal inference. The causal forest algorithm constructs a large number of decision trees, splitting the data in a manner that maximizes the variance of the treatment effect across the resulting nodes rather than simply predicting the outcome. To ensure valid statistical inference and prevent overfitting, the algorithm utilizes an "honest" tree-building approach, wherein the training dataset is split into two distinct halves: one half is used to determine the optimal splits for the trees, and the other half is used to estimate the treatment effects within those newly formed leaves. Prior to training the forest, orthogonalization was achieved by estimating the propensity scores and the expected outcomes using separate regression forests, effectively removing confounding bias and isolating the causal signal. Following the estimation of the individualized treatment effects, we analyzed the variable importance metrics generated by the causal forest to determine which baseline sociodemographic and psychological characteristics were the strongest drivers of treatment heterogeneity. Finally, we categorized the women into high-benefit and low-benefit subgroups based on their estimated conditional average treatment effects and conducted comparative analyses between these data-driven subgroups to generate actionable clinical profiles of the optimal responders. All computational procedures were executed using the generalized random forests framework within the R statistical computing environment.

3. Findings and Results

The total sample consisted of $N = 284$adult women residing in Spain, randomized into the MBSR intervention group ($n = 142$) and the Treatment-As-Usual (TAU) control group ($n = 142$). Preliminary analyses confirmed that randomization was successful, with no statistically significant differences between the two groups on any baseline sociodemographic, clinical, or psychological variables. The mean age of the participants was $M = 51.4$years ($SD = 10.2$), and the average duration of chronic pain was $M = 7.3$years ($SD = 4.8$). Baseline characteristics for the full sample, divided by treatment allocation, are detailed in Table 1. Before examining individualized effects, an Average Treatment Effect (ATE) was calculated using standard linear regression models controlling for baseline scores. For the primary outcome of pain interference measured by the Brief Pain Inventory (BPI), the overall ATE indicated a statistically significant reduction in the MBSR group compared to the TAU group at post-intervention ($\Delta M = -1.24$, 95% CI$[-1.65, -0.83]$, $p < .001$). Similar overall improvements were observed for BPI pain severity ($\Delta M = -0.98$, $p < .01$) and psychological distress on the Hospital Anxiety and Depression Scale (HADS). However, these average effects masked significant underlying variability in how individual women responded to the mindfulness program.

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Table 1

Baseline Sociodemographic and Clinical Characteristics of the Study Sample

Variable	MBSR Group ($\boldsymbol{n = 142}$)	TAU Group ($\boldsymbol{n = 142}$)	$\boldsymbol{p}$-value
Age (years), $\boldsymbol{M(SD)}$	51.2(10.5)	51.6(9.9)	.742
Education Level, $\boldsymbol{n}$(%)			.815
Primary or less	38(26.8%)	41(28.9%)	
Secondary	62(43.7%)	58(40.8%)	
University	42(29.5%)	43(30.3%)	
Pain Duration (years), $\boldsymbol{M(SD)}$	7.1(4.6)	7.5(5.0)	.481
BPI Pain Severity, $\boldsymbol{M(SD)}$	6.4(1.5)	6.5(1.4)	.553
BPI Pain Interference, $\boldsymbol{M(SD)}$	6.8(1.6)	6.7(1.7)	.602
HADS Anxiety, $\boldsymbol{M(SD)}$	11.4(3.2)	11.2(3.4)	.610
HADS Depression, $\boldsymbol{M(SD)}$	9.8(3.5)	10.1(3.3)	.458
FFMQ Total Score, $\boldsymbol{M(SD)}$	115.4(14.2)	114.8(13.8)	.715

To explore this variability, a causal forest model was trained with 2,000honest trees to estimate the Conditional Average Treatment Effect (CATE) for each participant regarding BPI pain interference. The estimated CATEs ranged widely from $-3.10$to $+0.45$, confirming substantial treatment heterogeneity. A negative CATE indicates a reduction in pain interference (a beneficial treatment effect). The out-of-bag omnibus test for the presence of heterogeneity was highly significant ($p < .001$). Having established that the treatment effect varied across individuals, we examined the variable importance metrics generated by the causal forest to identify the baseline features driving this variance. Variable importance is measured as the proportion of splits in the forest where a specific variable was utilized, indicating its relative influence on determining the personalized treatment effect. As shown in Table 2, baseline anxiety levels (HADS Anxiety), specific mindfulness facets (FFMQ Non-judging of inner experience), and pain duration were the most critical determinants of the heterogeneous treatment response. Sociodemographic variables such as age and educational level demonstrated comparatively low variable importance, suggesting that clinical and psychological profiles were better predictors of MBSR efficacy than basic demographics.

Table 2

Variable Importance Measures from the Causal Forest Model for Pain Interference

Baseline Feature	Importance Weight	Rank
HADS Anxiety	0.214	1
FFMQ Non-judging	0.185	2
Pain Duration (years)	0.142	3
FFMQ Acting with Awareness	0.110	4
BPI Baseline Pain Interference	0.095	5
HADS Depression	0.082	6
FFMQ Observing	0.061	7
Age	0.045	8
Number of Pain Sites	0.038	9
Education Level	0.028	10

Following the estimation of individual CATEs, the sample was stratified into empirical subgroups to facilitate clinical interpretation. Participants whose estimated CATE fell below the median of the CATE distribution (i.e., those exhibiting larger reductions in pain interference) were classified into the "High-Benefit Subgroup" ($n = 142$), while those above the median were classified into the "Low-Benefit Subgroup" ($n = 142$). An inferential comparison of these two data-driven subgroups revealed the distinct clinical profiles of women who responded optimally to the MBSR intervention. As detailed in Table 3, women in the high-benefit subgroup had significantly higher baseline levels of anxiety ($M = 13.1$ vs. $M = 9.5$, $p < .001$) and depression ($M = 11.2$ vs. $M = 8.7$, $p < .001$) compared to those in the low-benefit subgroup. Furthermore, optimal responders exhibited significantly lower baseline scores on

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the FFMQ Non-judging facet ($M = 18.4$ vs. $M = 24.1$, $p < .001$) and had been suffering from chronic pain for a shorter duration ($M = 5.2$ years vs. $M = 9.4$years, $p < .001$). There were no significant differences between the high-benefit and low-benefit subgroups regarding baseline BPI pain severity ($p = .124$) or sociodemographic characteristics.

Table 3

Comparison of Baseline Characteristics Between High-Benefit and Low-Benefit Subgroups

Variable	High-Benefit Subgroup ($n = 142$)	Low-Benefit Subgroup ($n = 142$)	t-statistic	p-value
Estimated CATE (BPI Interference)	−2.15(0.45)	−0.33(0.38)	−36.84	<.001
Pain Duration (years), $M(SD)$	5.2(3.1)	9.4(5.2)	−8.21	<.001
HADS Anxiety, $M(SD)$	13.1(2.5)	9.5(2.8)	11.45	<.001
HADS Depression, $M(SD)$	11.2(3.0)	8.7(3.1)	6.92	<.001
FFMQ Non-judging, $M(SD)$	18.4(4.2)	24.1(4.5)	−11.05	<.001
FFMQ Acting with Awareness, $M(SD)$	22.1(3.8)	26.5(4.1)	−9.38	<.001
BPI Pain Severity, $M(SD)$	6.6(1.4)	6.3(1.5)	1.74	.083
Age (years), $M(SD)$	50.8(10.1)	52.0(10.4)	−0.98	.328

In summary, the causal forest analysis isolated a specific phenotype of women with chronic pain who are most likely to experience substantial therapeutic gains from MBSR. These data strongly suggest that women experiencing elevated psychological distress (particularly anxiety) combined with lower baseline mindfulness traits (specifically a tendency to judge their own inner experiences) and a relatively shorter history of chronic pain derive the maximum clinical benefit from the MBSR curriculum. Conversely, women with long-standing chronic pain, low baseline distress, and naturally high dispositional mindfulness demonstrated minimal to no clinically meaningful improvement relative to standard care.

4. Discussion

The present study aimed to elucidate the heterogeneous treatment effects of Mindfulness-Based Stress Reduction on pain interference among women suffering from chronic non-malignant pain. While standard statistical analyses demonstrated a statistically significant average treatment effect, indicating that the mindfulness intervention effectively reduces pain severity and interference on average, the application of causal forest machine learning revealed substantial underlying variance in individual responses. Specifically, the estimation of the conditional average treatment effect, mathematically denoted as $\tau(x)$, identified a distinct high-benefit subgroup. This empirical subgroup, which experienced the most profound and clinically meaningful reductions in pain interference, was characterized by elevated baseline psychological distress in the form of anxiety and depression, lower baseline levels of dispositional mindfulness, specifically the non-judging of inner experience facet, and a comparatively shorter duration of the chronic pain condition. These findings underscore the critical limitation of relying solely on average effects in randomized controlled trials and highlight the absolute necessity of personalized behavioral medicine to optimize chronic pain management.

The overall finding that the mindfulness intervention is an efficacious treatment for chronic pain aligns robustly with the broader literature on mind-body therapies. Previous systematic reviews have consistently demonstrated the capacity of mindfulness-based interventions to significantly diminish subjective pain intensity and improve functional outcomes across diverse clinical populations (Norouzi et al., 2020). By cultivating a state of present-moment awareness, mindfulness fundamentally alters the cognitive and affective processing of nociceptive signals, a mechanism that has been validated across numerous psychosomatic outcome studies (Creswell et al., 2019). Furthermore, the observed improvements in global psychological well-being and quality of life in our sample mirror findings from recent clinical trials demonstrating the high efficacy of both standard mindfulness and related cognitive therapies among women navigating the debilitating daily realities of chronic pain syndromes (Pouryounes Abkenar et al., 2024). Similar positive average outcomes have been rigorously documented in specialized populations, including geriatric cohorts undergoing culturally adapted mindfulness programs (Foulk et al., 2023; Soukhtanlou et al., 2024) and pediatric patients managing the psychological burden of chronic medical diseases (Demehri et al., 2020). The average treatment effect observed in our preliminary analysis further

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solidifies mindfulness as a potent, non-pharmacological alternative capable of addressing both the somatic and psychological dimensions of chronic physical suffering (Morone, 2019).

However, the most vital and novel contribution of this study lies in the variable importance metrics generated by the causal forest algorithm, which identified baseline anxiety as the strongest predictor of treatment benefit. The finding that women with higher initial anxiety and depressive symptomatology derived the greatest therapeutic gains suggests a compensatory mechanism wherein the intervention precisely targets severe emotional dysregulation. Chronic pain is intimately linked with psychological distress, a relationship heavily mediated by maladaptive cognitive schemas such as pain catastrophizing (Conti et al., 2020). Mindfulness therapies actively dismantle these catastrophizing feedback loops. Consequently, patients burdened with high anxiety sensitivity—the intense fear of anxiety-related somatic sensations—stand to benefit immensely from therapeutic modalities that incorporate deep cognitive restructuring alongside mindfulness principles (Karimi et al., 2023). This is extensively supported by evidence showing that targeted mindfulness interventions drastically reduce pain-related anxiety in specialized chronic pain phenotypes, such as tension headaches and persistent migraines (Abotalebi Isazadegan et al., 2022; Ebrahimi Sadr et al., 2023). Essentially, patients with elevated baseline psychological distress possess a higher clinical ceiling for improvement; the emotion-regulation skills imparted by the intervention provide them with a transformative coping repertoire that patients with low baseline distress may not require as acutely (Ahmadi & Valizadeh, 2021). This targeted efficacy on the affective dimension of pain often distinguishes mindfulness approaches from standard physiological relaxation techniques (Hussain & Said, 2019) and heavily emphasizes its role as a superior alternative to opioid-centric biomedical treatments (Zgierska et al., 2025).

Another major driver of treatment heterogeneity was the baseline level of dispositional mindfulness, specifically the non-judging of inner experience. Paradoxically, women who scored lower on this facet at baseline—indicating a strong psychological tendency to critically evaluate, resist, or judge their own pain and emotional responses—comprised the optimal responder subgroup. This inverse relationship highlights the direct skill-acquisition model of mindfulness training. Patients who already possess naturally high levels of non-judgmental awareness may experience a behavioral ceiling effect, deriving limited additional benefit from an intervention designed to teach mental skills they already utilize implicitly (Alemi et al., 2021). Conversely, highly self-critical patients experience a massive paradigm shift when exposed to the core tenets of mindfulness, which systematically trains individuals to observe physical discomfort without layering it with secondary emotional judgments (Barghi Irani & Dehghan Saber, 2021). Interestingly, recent empirical investigations suggest that the profound psychological benefits of mindfulness do not necessarily stem from altering deep subconscious attentional biases toward pain, but rather from changing the conscious, evaluative relationship the patient has with their suffering (Robles et al., 2024). By identifying low non-judging traits as a prerequisite for maximum benefit, our causal forest model provides an actionable phenotypic marker for clinical triage, aligning with modern efforts to optimize the self-management of chronic pain through acceptance-based eHealth frameworks (Carvalho et al., 2021).

Finally, the causal machine learning model identified a relatively shorter duration of chronic pain as a significant predictor of enhanced treatment efficacy. This finding strongly suggests that there may be a critical therapeutic window for behavioral interventions. When chronic pain persists for decades, it often initiates profound neuroplastic changes and solidifies deeply entrenched, maladaptive illness behaviors that are exceptionally resistant to relatively brief eight-week psychological interventions (Shen et al., 2024). Patients with highly protracted pain histories frequently present with complex psychiatric overlays, necessitating much longer, integrated, and multimodal therapeutic approaches (Verdú & Marcos, 2022). By utilizing causal machine learning, this study moves decisively beyond the limitations of traditional comparative effectiveness research, which has historically focused almost exclusively on aggregate differences between mindfulness, cognitive-behavioral therapy, and standard medical care (Burns et al., 2022; Day et al., 2019; Pardos-Gascón et al., 2021). Furthermore, understanding exactly who benefits most is fundamentally crucial for the successful implementation of complex, multi-arm clinical trials (Mackey et al., 2022) and the systemic adoption of behavioral medicine in routine primary care (Sherman et al., 2022). As healthcare systems increasingly utilize modern telehealth platforms to overcome geographical barriers to specialized pain management (Bishop et al., 2023; Burgess et al., 2024), and as local community settings become primary hubs for behavioral health education (Harris et al.,

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2023), deploying sophisticated algorithms to match the right patient with the right intervention will inevitably become the gold standard of meaning-centered and cognitively-informed care (Miragha Pour Tarrah et al., 2024).

5. Conclusion

The present study successfully transitions the evaluation of mindfulness-based interventions for chronic pain from a generalized assessment of average efficacy to a highly nuanced understanding of individualized treatment responses. By leveraging the advanced predictive capabilities of the causal forest algorithm, we empirically demonstrated that the therapeutic benefits of mindfulness are not uniformly distributed across the chronic pain population. Instead, the intervention is exceptionally effective for a specific clinical phenotype: women experiencing high levels of comorbid anxiety and depression, those who naturally exhibit highly judgmental attitudes toward their internal somatic experiences, and those whose chronic pain has not yet spanned multiple decades. For these specific individuals, mindfulness serves as a profound psychological catalyst, drastically reducing the interference of pain in their daily lives. Conversely, for patients lacking these baseline characteristics, the standard eight-week protocol may offer negligible clinical advantages over treatment as usual. These findings forcefully challenge the prevalent one-size-fits-all approach in behavioral medicine and provide a robust, data-driven foundation for precision psychotherapeutics in chronic pain management.

6. Limitations and Suggestions

Despite the methodological rigor introduced by the causal machine learning framework, several limitations must be carefully considered when interpreting these findings. First, the study sample was exclusively restricted to adult women residing in Spain, which inherently limits the cross-cultural and cross-gender generalizability of the individualized treatment effects. Chronic pain processing and psychological coping mechanisms are heavily influenced by gender socialization and cultural paradigms, meaning that the causal forest algorithm might identify completely different predictive covariates in male populations or in non-Western cultural contexts. Second, the study relied entirely on standardized self-report psychometric instruments to quantify highly subjective experiences such as pain interference and dispositional mindfulness. While these tools are validated, they remain susceptible to social desirability bias and momentary fluctuations in mood. Third, the longitudinal scope of the study was limited to a six-month follow-up period, leaving the long-term durability of the heterogeneous treatment effects unknown. Finally, while a sample size of several hundred participants is generally adequate for basic clinical trials, training robust machine learning models like causal forests ideally requires thousands of data points to ensure maximum algorithmic stability and to map out highly complex, higher-order interactions among dozens of covariates with absolute precision.

Future research must prioritize the replication of these causal forest models utilizing much larger, globally diverse, and multi-gender datasets to map the universal versus culture-bound drivers of treatment heterogeneity. Researchers should aim to integrate objective neurobiological markers into the machine learning algorithms alongside traditional psychological self-reports. By feeding baseline functional magnetic resonance imaging data, neuro-inflammatory biomarkers, and real-time physiological indicators gathered from wearable technology into the causal forest, researchers could generate exceptionally precise, multidimensional prognostic models. Furthermore, future randomized trials should transition to comparative heterogeneity designs, where causal machine learning is used not only to predict the response to mindfulness alone but to directly compare the individualized conditional average treatment effects of mindfulness against standard cognitive-behavioral therapy or acceptance and commitment therapy. Such comparative algorithmic mapping would allow researchers to definitively determine which specific psychological modality is optimal for which precise patient profile. Lastly, extending the longitudinal follow-up to multiple years will be essential to determine if the high-benefit subgroups maintain their therapeutic gains or if booster sessions are required over the lifespan of the chronic illness.

The findings from this machine learning analysis hold immediate, highly actionable implications for clinical practice and healthcare resource allocation. Pain clinics and primary care centers should seamlessly integrate rapid psychometric screening tools for anxiety, depression, and basic mindfulness traits into their standard intake procedures. Rather than indiscriminately referring all chronic pain patients to mindfulness programs, clinicians can use these baseline psychological profiles to actively triage patients. Women presenting with high emotional distress and a highly critical, judgmental relationship with

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their physical symptoms should be fast-tracked into mindfulness-based stress reduction programs, as they possess the ideal psychological architecture to extract maximum benefit from the curriculum. Conversely, patients presenting with a very long history of intractable pain combined with low baseline distress and naturally high non-judgmental awareness should not be routinely routed to standard mindfulness groups, as this could result in a misallocation of clinical resources and patient frustration. For these low-benefit individuals, clinical practices should implement stepped-care models, immediately prioritizing more intensive, multimodal pain rehabilitation programs, advanced pharmacological management, or specialized psychiatric interventions designed to address the deeply entrenched, structurally calcified nature of decades-long chronic pain.

Authors' Contributions

Authors contributed equally to this article.

Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

Transparency Statement

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Declaration of Interest

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The study protocol adhered to the principles outlined in the Helsinki Declaration, which provides guidelines for ethical research involving human participants.

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