

# Social Deprivation is Associated with Increased Pain in Patients Presenting with Neuropathic Pain

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**Background:** Neuropathic pain following nerve injury can be debilitating and negatively impact quality of life. Targeted muscle reinnervation (TMR) is an efficacious technique for the management of neuropathic pain. However, this technique may be unequally available for many geographical locations. Therefore, the aim of this study was to evaluate the association between Area Deprivation Index (ADI) and preoperative pain in patients undergoing TMR for treatment of neuropathic pain.

**Methods:** Patients who underwent TMR for neuropathic pain in the lower and upper extremities were prospectively enrolled at our tertiary care clinic. A chart review was conducted to obtain socioeconomic, surgery, and comorbidity parameters. Preoperative pain scores (0–10 pain score index), and the ADI, reflecting deprivation status on a 0–100 scale, were collected.

**Results:** A total of 162 patients from 13 different states were included, of which 119 were amputees (74%). The median ADI was 25 (IQR: 16–41) and the median preoperative pain score was 6 (IQR: 5–8). A higher ADI was independently associated with higher preoperative pain. The time interval from nerve injury to TMR was not associated with ADI.

**Conclusions:** Patients undergoing surgical treatment of neuropathic pain from more socially deprived settings have increased pain experience upon initial evaluation, despite having similar time from nerve injury or amputation to TMR. These findings highlight the importance of identifying patients presenting from socially deprived settings, as this may impact their physical and mental health along with their coping mechanisms, resulting in increased pain. (*Plast Reconstr Surg Glob Open* 2024; 12:e5931; doi: [10.1097/GOX.0000000000005931](https://doi.org/10.1097/GOX.0000000000005931); Published online 27 June 2024.)

## INTRODUCTION

Neuropathic pain following nerve injury may be debilitating and negatively impact the overall quality of life.<sup>1</sup> Although the management of neuropathic pain remains challenging, active nerve surgical techniques developed over the past two decades have shown to decrease neuropathic pain. One such technique is targeted muscle

reinnervation (TMR), where a nerve end is coapted to a terminal motor nerve branch of a muscle that is in close proximity.<sup>2–4</sup> As a relatively novel modality, TMR has gained popularity for the treatment of these sequela and its utilization as a prophylactic modality is being more widely adopted across the United States.<sup>5</sup> However, it has been identified that access to this technique at time of amputation (primary TMR) is not always available for many geographical locations.<sup>6</sup>

Differences in location and socioeconomic factors, expressed as Area Deprivation Index (ADI) score,<sup>7</sup> have been linked to worse pain coping and social support.<sup>8</sup> Additionally, preoperative disability (pain and function) was demonstrated to be different for race and demographical location in patients undergoing total joint arthroplasty.<sup>9</sup> However, it is not known whether such factors might influence accessibility of TMR for the treatment

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of neuropathic pain in the amputee and nonamputee population.

The primary aim of this study was to evaluate the association between ADI and preoperative pain in patients undergoing TMR for treatment of neuropathic pain. Additional aims included the evaluation of whether ADI was associated with the time interval from amputation or peripheral nerve injury to TMR surgery, along with evaluating the association between ADI and preoperative pain with other patient factors.

## MATERIALS AND METHODS

Following approval by the institutional review board (approval no.: 2020P003555), patients who were evaluated for neuropathic pain at a tertiary care center were prospectively enrolled in a data repository between November 2017 and August 2023. For the present study, all patients who underwent TMR and who were enrolled in this repository were screened for eligibility. All patients were evaluated by plastic and reconstructive peripheral nerve surgeons in a specialized peripheral nerve clinic.<sup>10</sup>

### Study Population

A total of 317 patients were enrolled in the repository at the time of this study. These were patients who were scheduled for TMR surgery for treatment of neuropathic pain of the lower or upper extremity, caused by a previous amputation or peripheral nerve injury due to surgery or trauma. Patients were excluded if they underwent TMR at or around time of amputation for pain prophylaxis ( $n = 122$ ), if patients were younger than 18 years of age at time of TMR surgery ( $n = 3$ ), if no preoperative pain data were available ( $n = 23$ ), or if patients presented with neuropathic pain of bilateral extremities and pain outcomes were not distinguishable per limb ( $n = 7$ ). A total of 162 patients were included in this study, of whom 119 patients (73.5%) presented with neuropathic pain following limb amputation, and 43 nonamputee patients (26.5%) had neuropathic pain related to a peripheral nerve injury.

Patient data on socioeconomic, surgery, and comorbidity parameters were collected retrospectively through chart review. Socioeconomic factors included gender, time from injury or amputation to TMR surgery, age at the time from TMR surgery, race, insurance type, and ADI based on nine-digit ZIP code data. The ADI data for patients were retrieved for all states in the United States using the Wisconsin UO Neighborhood Atlas 2021 data, which represent a nationwide index of deprivation status, assigned per ZIP code, where 1 indicates a low deprived and 100 indicates a highly deprived status.<sup>7</sup> This score is based on 17 indicators, which encompass income, employment, housing, and education conditions, as reported through the American Community Survey. Surgery and treatment characteristics included were amputation status, indication and level of amputation, and preoperative use of opioids and neuromodulators. Comorbidity factors and other factors demonstrated to influence neuropathic pain by Lans et al<sup>11,12</sup> were BMI, smoking, alcoholism, diabetes (type 1 and type 2), peripheral vascular disease, chronic

## Takeaways

**Question:** The study aimed to assess the relationship between social deprivation, measured by the Area Deprivation Index, and preoperative pain in patients presenting with neuropathic pain.

**Findings:** Patients from more socially deprived areas experienced higher preoperative pain levels, despite similar time intervals from amputation or nerve injury to targeted muscle reinnervation surgery.

**Meaning:** Social factors may play a significant role in pain experience. Identifying and addressing these social disparities seems crucial for optimizing patient care and pain outcomes.

kidney disease, hypothyroidism, psychiatric comorbidity, history of chronic pain, and chronic regional pain syndrome, which were assessed at the time of TMR surgery. All data were stored using Research Electronic Data Capture, which is an online and HIPAA-compliant data collection instrument.

### Primary Outcome

The primary outcome for this study was preoperative pain at time of preoperative clinical evaluation using the numeric rating scale pain score, and the Defense & Veterans Pain Rating Scale, both of which consist of a 0–10 pain scale where 0 indicates no pain and 10 indicates most severe pain. Both scales have previously demonstrated correlation and have been validated for concomitant assessment.<sup>13</sup> Following study enrollment, patient-reported pain data were prospectively collected through clinicians during the clinic visit, focusing on neuropathic pain in the residual limb. The most recent pain score before surgery was included.

### Secondary Outcomes

Secondarily, it was assessed whether the time since amputation or since peripheral nerve injury was associated with differences in ADI. Moreover, patient factors previously established to affect nerve regeneration and neuropathic pain were evaluated for their association with preoperative pain.

### Statistical Analysis

All collected data were assessed for normality and presented as mean and SD for parametric data, median, and interquartile range (IQR) for nonparametric data, and frequency and percentage for dichotomous and categorical data. Additionally, ADI was analyzed by quartile. Depending on normality, continuous variables were tested for association with preoperative pain using a linear regression and Pearson or Spearman test, and categorical variables were assessed using analysis of variance or Kruskal-Wallis tests. All factors indicating statistical significance were assessed for independent association using a multivariable linear regression analysis. Level of significance was set at a  $P$  value less than 0.05. Additionally, a locally weighted scatterplot smoothing regression curve was generated using the results

**Table 1. Patient Demographics, Surgery, and Comorbidity Characteristics**

Demographics and Surgery Characteristics	All Patients (n = 162)
Age at TMR surgery, y, median (IQR)	54.0 (41.4–64.7)
Injury to TMR interval, y, median (IQR)	4.4 (1.5–11.3)
Female gender, n (%)	64 (39.5)
White race, n (%)	143 (88.3)
<b>Insurance, n (%)</b>	
Medicaid	62 (38.3)
Medicare	10 (6.2)
Private	81 (50.0)
None	9 (5.6)
Area Deprivation Index, years, median (IQR)	25 (16–41)
<b>Cause of neuropathic pain, n (%)</b>	
Nerve injury	43 (26.5)
Amputation upper extremity	13 (8.1)
Amputation lower extremity	106 (65.4)
Trauma as indication for amputation	70 (59.3)
<b>Comorbidities</b>	
Body mass index, kg/m <sup>2</sup> , median (IQR)	27.5 (23–31.3)
Alcoholism, n (%)	12 (7.4)
Smoking, n (%)	38 (23.5)
Opioid use, preoperative, n (%)	121 (74.7)
Neuromodulator use, preoperative, n (%)	128 (79.0)
Diabetes, n (%)	39 (24.1)
Hypothyroidism, n (%)	22 (13.6)
Peripheral vascular disease, n (%)	38 (23.5)
Chronic kidney disease, n (%)	16 (9.9)
History of chronic pain, n (%)	154 (95.6)
Chronic regional pain syndrome, n (%)	12 (7.4)
Psychiatric disorder, n (%)	97 (59.9)

from the multivariable regression analysis. All data analyses were conducted using Stata IC (version 16; StataCorp LLC, College Station, Tex.).

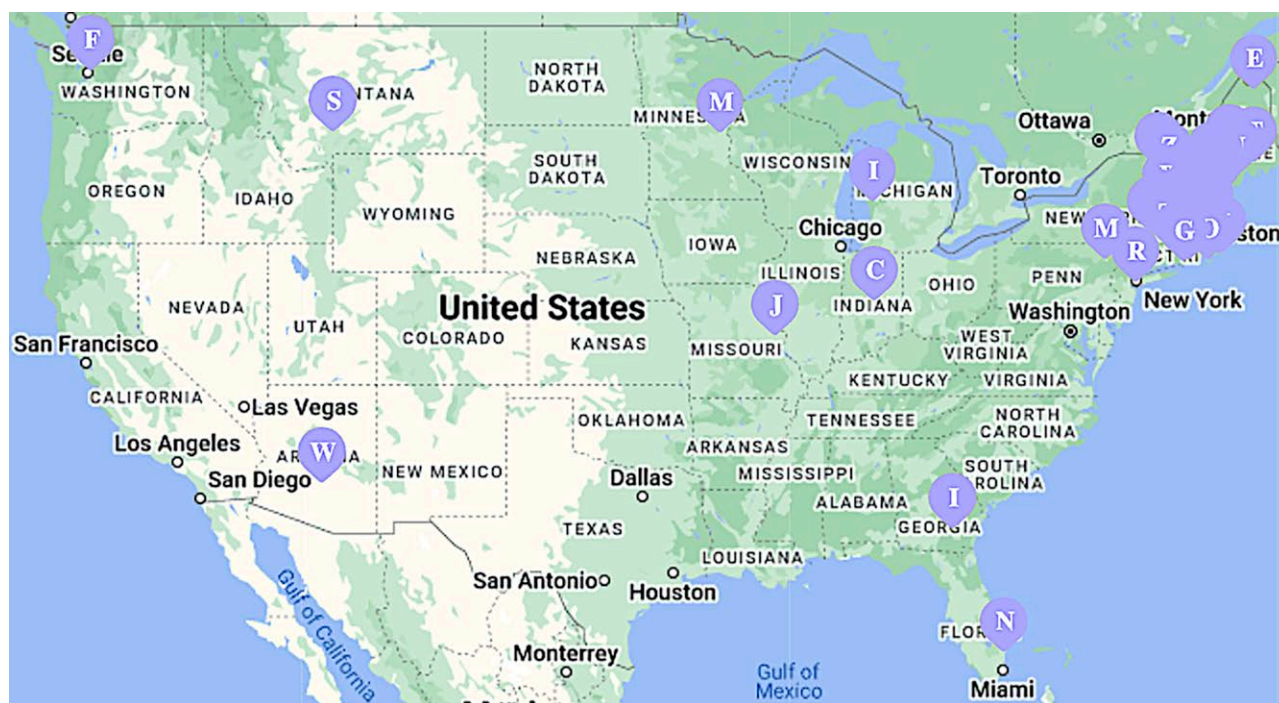
## RESULTS

### Study Population

Of the 162 patients who were included, 64 patients (39.5%) were women, and the median age at TMR surgery was 54.0 years (IQR: 41.4–64.7) (Table 1). Six patients were deceased during this study. One hundred nineteen patients (73.5%) were amputees, of whom 106 (89.1%) were lower extremity amputees, and trauma was the most common indication for amputation (59.3%). Of the patients with nonamputation-related neuropathic pain, 30 patients (67.4%) presented following peripheral nerve injury due to surgery, and 14 (32.6%) sustained a peripheral nerve injury due to trauma. The median ADI in this population was 25 (IQR: 16–41). At the time of TMR surgery, patients included in this study were residing in Massachusetts, Maine, Connecticut, Rhode Island, New Hampshire, Vermont, Indiana, Minnesota, Pennsylvania, New York, Georgia, Arizona, and Florida (Fig. 1).

### Association between Pain and ADI

The median patient-reported pain score upon preoperative evaluation was 6 (IQR: 5–8). In bivariate analysis, a higher ADI score was associated with increased pain score ( $P = 0.0023$ , Spearman  $\rho = 0.24$ ), along with smoking ( $P = 0.019$ ), preoperative use of opioids ( $P = 0.016$ ),

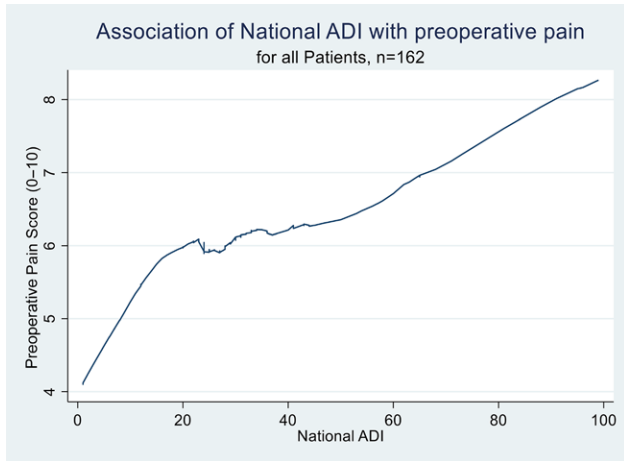


**Fig. 1.** Areas indicating the ZIP codes of residence of patients who underwent TMR. ZIP codes are indicated with unique letter combinations. Created with BioRender.com.

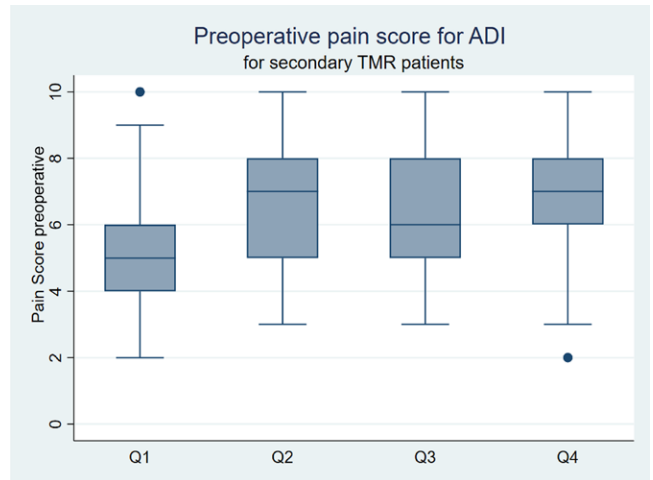
**Table 2. Multivariable Analysis of Factors Associated with Increased Preoperative Pain**

Characteristic	All Patients (n = 162)			
	$\beta$	SE	P	95% CI
Smoking	0.4687238	0.4840807	0.334	-0.4874748 to 1.424922
Opioid use preoperative	0.5498008	0.4084965	0.194	-0.2741599 to 1.341003
Diabetes	0.9372509	0.4768078	0.510	-0.0045816 to 1.879083
Psychiatric disorder	0.4113990	0.4136414	0.321	-0.4056617 to 1.228460
National ADI	0.0226835	0.0089767	<b>0.013</b>	0.004952 to 0.040415

P value in bold demonstrates significance.  
 CI, confidence interval; SE, standard error;  $\beta$ , beta coefficient.



**Fig. 2.** LOWESS curve of association between ADI and preoperative pain. LOWESS, locally weighted scatterplot smoothing.

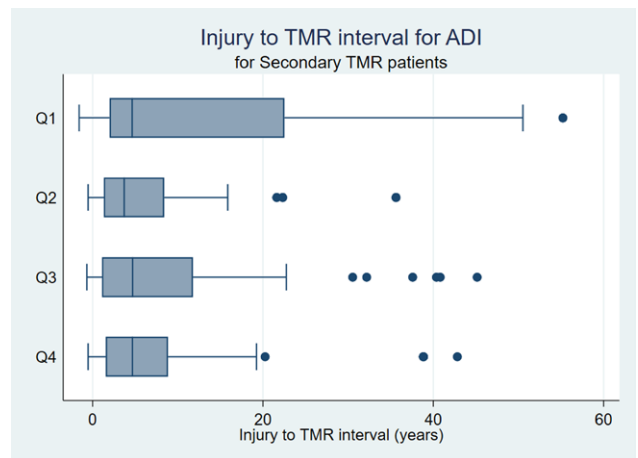


**Fig. 3.** Box plot of association between ADI and preoperative pain.

and with presence of diabetes ( $P = 0.013$ ). (See table, **Supplemental Digital Content 1**, which displays the bivariable analysis of factors associated with increased preoperative pain. <http://links.lww.com/PRSGO/D314>.) In multivariable analysis, ADI demonstrated an independent association with increased preoperative pain [ $\beta = 0.023$ ,  $P = 0.013$ , 95% confidence interval (0.005–0.040)] (Table 2 and Fig. 2). When comparing the different preoperative pain scores per ADI quartile, the first quartile was significantly associated with lower pain [5 (IQR: 4–6),  $P = 0.0034$ ], compared with the second [7 (IQR: 5–8)], third [6 (IQR: 5–8)], and fourth [7 (IQR: 6–8)] quartiles (Fig. 3). The median time from amputation or peripheral nerve injury to TMR was 4.4 years (IQR: 1.5–11.3). There was no association between ADI and time to TMR. When comparing time with TMR per ADI quartile, this was equally distributed (Fig. 4).

**DISCUSSION**

Prospectively, 162 patients who presented to a specialized peripheral nerve clinic at a tertiary referral center and underwent TMR for neuropathic pain were included. Patients presented with neuropathic pain either related to a preexistent limb amputation (73.5%) or peripheral nerve injury in the absence of amputation (26.5%). Increased social deprivation, as determined by the ADI, was an independent predictor for higher preoperative pain scores. An interesting finding that was not anticipated is that the time



**Fig. 4.** Box plot of ADI vs the injury to TMR interval.

since amputation or peripheral nerve injury was not associated with ADI.

The findings of this study demonstrate that patients seeking surgical care for neuropathic pain who reside in areas with increased social deprivation present with higher preoperative pain. The ADI takes into account several sociodemographic and psychosocial aspects. We hypothesize that an overall less-favorable position regarding access to health care, economic constraints, psychosocial stressors, education and health literacy, environmental factors,

delayed medical intervention, and health disparities may contribute to this observed relationship. These aspects are complex and interrelated and therefore may have a negative impact on each other.”

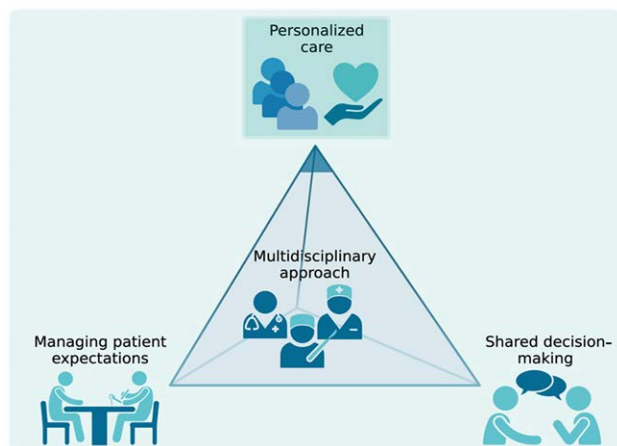
Previous studies have reported that patients from deprived areas have higher opioid prescription rates and higher dosage of opioids used.<sup>14–16</sup> This may indicate the magnitude of overall socioeconomic status on surgical accessibility and associated pain levels. Patients with limited resources may have social and financial restraints to seek care, although given that there was no relationship between ADI and time to TMR, this is not clear in this study population. Especially in patients with chronic pain, it is important to be conscientious of the relationship with ADI to allocate adequate resources to manage the pain experience. Understanding how patients from different geographic areas present their pain is important when setting patient expectations. In our study, bivariable analysis demonstrated a significant association between preoperative opioid use and preoperative pain. However, the lack of significance in the multivariable model may suggest that the initially identified association may be influenced by other factors, such as the ADI. When looking at this potential relationship, we indeed observed a clear trend of increased usage rate for higher ADI, which is reflected by the four ADI quartiles, namely Q1, 21/38 (55.3%); Q2, 29/40 (72.5%); Q3, 32/41 (78.1%); Q4, 37/42 (88.1%).

Deprived socioeconomic status has previously been associated with worse outcomes following surgery. Wan et al demonstrated an increased risk of postoperative complications, and of 3-year mortality for more socioeconomically deprived patients, in a cohort of 9051 patients undergoing elective surgery.<sup>17</sup> Also, preoperative pain and function status may be influenced, as Cohen-Levy et al demonstrated that increased median household income and White race were associated with higher preoperative patient-reported outcome measure scores in 1371 patients undergoing primary total joint arthroplasty.<sup>9</sup> This suggests that socioeconomic deprivation has a profound influence on disparities in orthopedic postsurgical outcomes. Delivered perioperative care, impact of social aspects on health, and perhaps differences in access to health care and the severity of disease at time of presentation may be influencing factors.<sup>18</sup> In patients presenting with plastic and reconstructive surgical problems, these trends have been identified as well. More deprived patients presenting for craniostylosis had a higher risk for poor speech outcomes,<sup>19</sup> increased socioeconomic deprivation was associated with poor health outcomes in oncological reconstructive head and neck patients,<sup>20</sup> and socially deprived patients underwent fewer occupational hand therapy sessions and worse range of motion following flexor tendon repair,<sup>21</sup> implying that deprivation may be associated with disparities in health-care access, leading to a decline in compliance and subsequent worse outcomes. Although we did not demonstrate a difference in ADI between insurance types, Medicaid coverage was previously associated with increased pre- and early postoperative pain in patients undergoing upper extremity surgery.<sup>22</sup> It is possible that patients from a less-favorable socioeconomic background are more likely to obtain government funded

insurance, in contrast to private insurance, which may demonstrate the relationship between Medicaid coverage and an overall more socially deprived status.

Moreover, the relationship between social deprivation and psychosocial well-being has been well established. This was demonstrated by Wright et al in their 2019 study of 7500 adult patients who presented to an orthopedic center. Patients living in areas with the highest deprivation had worse mean scores across pain interference and physical function, but also anxiety and depression scores of Patient-Reported Outcomes Measurement Information System assessments.<sup>23</sup> Additionally, Wall et al found that in a population of 375 pediatric patients with congenital upper extremity differences, anxiety and depression were worse in more socially deprived areas, which suggests more psychosocial challenges amongst these patients.<sup>24</sup> Although we have not assessed for mental well-being factors in our study, it is well known that limb amputations and neuropathic pain affect mental wellbeing.<sup>25</sup> These studies suggest this would be enhanced for patients living in more socially deprived areas. Therefore, social deprivation status should be considered as an integral part of delivered care and understanding patients' needs in this population. Allocating adequate resources such as social workers, pain psychologists, and other specialists among these patients should be emphasized.

A combination of increased preoperative pain levels and a lower social deprivation index may predict a more challenging postoperative trajectory, compared with patients with a more favorable baseline social condition, despite similar time from injury to TMR or regenerative peripheral nerve interface. Nonetheless, understanding that patients from deprived settings experience higher pain scores is valuable for the treating physician to allocated additional resources, which may impact not only the treatment for neuropathic pain but also the patient's overall health. Future studies investigating the impact of social deprivation on postoperative outcomes will further elucidate these relationships and the optimal treatment pathways. To reduce the gap between surgical care provided for amputee patients from more deprived areas and their potentially different needs, personalized care should be provided in an attempt to understand individual needs based on differences in preoperative pain and mental well-being. In our clinic, we value shared decision-making during the diagnosis<sup>26,27</sup> and treatment trajectory. Our multidisciplinary approach enables us to identify the specific needs that exist, and in which areas additional help can be provided to manage patient expectations and provide an optimally personalized treatment plan, through the combined approach of psychiatric, rehabilitation, and ortho-plastic surgical care (Fig. 5). This approach might lead to personalized differences in analgesic regimens, length of postoperative hospital admission, and frequency of pre- and postoperative consultation, tailored to the patients' needs and starting situation. This may assist in improved identification of patients with disparities in health-care access due to logistic or financial issues, for improvement of early patient–physician engagement and recognition of required care.<sup>28</sup>



**Fig. 5.** Suggested cornerstones for personalized surgical care. Created with BioRender.com.

However, it is notable that the time from peripheral nerve injury or amputation to TMR surgery was not associated with differences in preoperative pain in our study. Several clinical studies have demonstrated the difference in efficacy when TMR is performed at the time of amputation, in contrast to longer intervals, when chronic neuropathic pain may become more established and, therefore, more challenging to treat.<sup>29</sup> Reid et al<sup>30</sup> demonstrated the prophylactic effect of direct, primary TMR conducted at the time of amputation versus secondary TMR in a delayed fashion, and intermediate follow-up within the first postoperative year demonstrated significantly better pain outcomes for primary TMR patients. Furthermore, Goodyear et al<sup>31</sup> demonstrated better pain-related outcomes in patients with primary TMR compared with those undergoing secondary TMR. Moreover, a rodent study has demonstrated that the postoperative timing of intervention following nerve injury also influences the postoperative efficacy of TMR. TMR performed at the time of neurotomy/nerve injury, or after 3 weeks prevented or reversed pain behavior to baseline. However, when TMR was performed at 12 weeks following peripheral nerve injury, pain behaviors persisted. This is in accordance with theories on centralization of pain and transition of pain pathways in chronic pain types, amplifying neural signals within the central nervous system that elicit pain hypersensitivity.<sup>32,33</sup> In our study, we did not identify a relationship in time to presentation with ADI. All patients included presented for surgery due to chronic neuropathic pain sequela, and, although certain types of neuropathic pain like diabetic polyneuropathy<sup>34</sup> might evolve over time, this may reflect that increased time does not have a profound impact on severity of neuropathic pain in this population (once chronic pain has been established this may not per se get worse over time). Another potential influencing factor could be limited availability of surgical neuropathic pain treatment options in the surrounding region. Our specialized multidisciplinary pain clinic provides individualized care for this patient population.<sup>10</sup> This circumstance may narrow the timeframe and limit the exploration of

alternative centers, particularly given that a significant proportion of patients in this cohort are situated in the New England area.

This study has several limitations. First, as pain is subjective per definition, and although pain outcomes were recorded according to protocol under the treatment of our peripheral nerve surgery team, patients might not only report neuropathic pain and might not always be able to discriminate between different components and sources of pain. Furthermore, the pain assessment tool utilized considers the pain experienced at the time of the clinic encounter. It is possible that the reported pain score might be affected by frustration arising from logistical challenges associated with clinic attendance, particularly for patients residing in socioeconomically deprived areas who may be more vulnerable to such challenges.

Also, no pain catastrophizing or mental health assessment were included in this study; thus, we were not able to correct the reported pain for coping mechanisms. Moreover, the ADI includes several socioeconomic factors such as income, employment, education, and housing, but we did not assess for association of these factors separately. Finally, ADI was calculated based on retrospectively acquired ZIP codes at the time of data analysis. Although efforts were made to verify the relocation status of patients, the potential for address changes occurring between the time of surgery and the subsequent data analysis cannot be fully eliminated.

In conclusion, patients from socially deprived backgrounds present with higher degrees of neuropathic pain when undergoing TMR, despite having a similar time from amputation to TMR. These findings highlight the importance of identifying patients presenting from socially deprived settings, as this may impact their physical and mental health along with their coping mechanisms, resulting in increased pain.

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## DISCLOSURES

*Dr. Lans is a consultant for Axogen Inc. Dr. Valerio is a consultant for Axogen Inc, Integra Lifesciences Corporation, and Checkpoint Surgical Inc. Dr. Eberlin is a consultant for Axogen Inc, Integra Lifesciences Corporation, Checkpoint Surgical Inc, and Tulavi Therapeutics Inc, Tissium, and BioCircuit. Dr. Rassveld has nothing to disclose. This work was supported in part by the Jesse B. Jupiter Research Fund/Wyss Medical Foundation.*

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