

# The Long-term Post-operative Pain Course Following Primary and Secondary Targeted Muscle Reinnervation for Neuropathic Pain in Amputees

Authors: Floris V. Raasveld, MD | Maximilian Mayrhofer-Schmid | Justin McCarty, DO | Ian L. Valerio, MD, MS, MBA, FACS | Kyle R. Eberlin, MD

Hand and Arm Center, Department of Orthopaedic Surgery, Massachusetts General Hospital, Boston, MA

Presented by: Floris V. Raasveld, MD - Research Fellow/PhD Candidate

## Introduction

Targeted muscle reinnervation (TMR) has been demonstrated to be effective in the surgical treatment of neuropathic pain for amputees.<sup>1,2</sup> However, the long-term postoperative pain course for patients that undergo **Primary TMR** (<14 days since amputation) or **Secondary TMR** (≥14 days) TMR surgery is not clearly known. This study aims to describe the **long-term post-operative pain course** for these patients to aid in **managing pain expectations**.

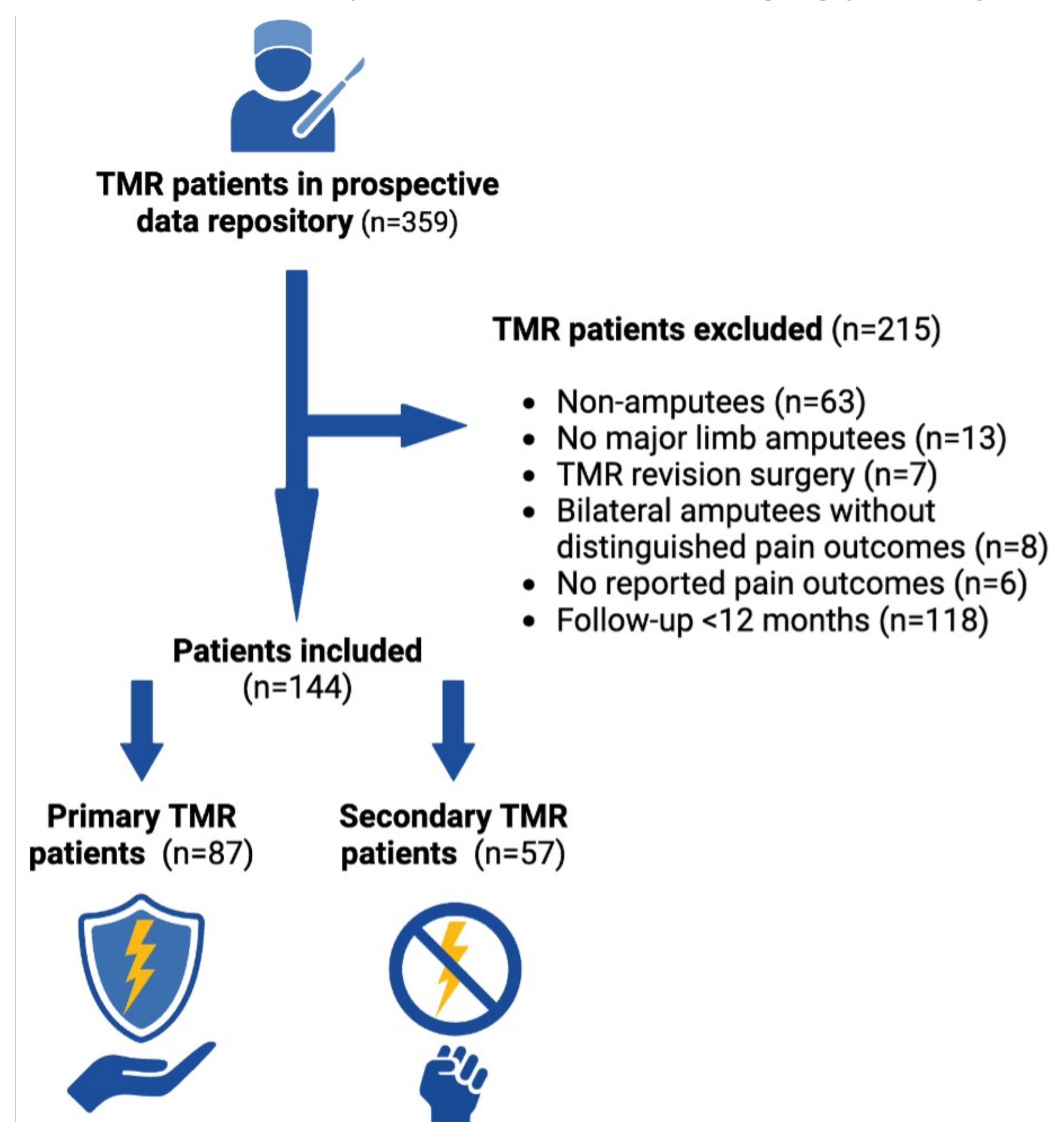


Figure 1 – Flowchart of included patients and in-/exclusion criteria

## Methods

Chart review was performed for amputees who underwent primary and secondary TMR and who were prospectively enrolled between 2018 and 2024, with a **minimum follow-up up of 12 months**. Pain scores reported on the Numerical Rating Scale (**NRS, pain on a 0-10 scale**) were collected up to latest follow-up. Mean NRS pain levels were compared between primary and secondary TMR cohorts. **Multilevel mixed-effects models** were utilized to analyze the difference in pain and visualize average postoperative pain courses.

## Results

A total of **144 amputees** (60.4.% male; 60.4% Secondary TMR patients) were included. The median **follow-up was 3.2 years** (IQR: 2.6-4.1).

- **Primary TMR** patients demonstrate a more rapid decline in pain, typically achieving **average mild pain levels at 12 months** (NRS = 3.0, versus 4.1 for Secondary TMR patients ( $p < 0.001$ )) before stabilizing at an average level of 2.5.
- **Secondary TMR** patients demonstrate a less rapid, yet consistent decrease in pain, reaching an **average mild pain level at the 36-month mark** (NRS = 2.7, versus 2.3 for Primary TMR patients ( $p < 0.001$ )).
- The difference in pain between Primary and Secondary TMR patients is significantly different over the compete 36-month, trajectory ( $p < 0.001$ ).
- On average, Secondary TMR patients reached the **Minimally Clinically Important Difference (MCID)** at the 36-month mark, compared to pain at baseline (NRS=6.0 to NRS=2.7,  $\Delta$ NRS=-3.3,  $p < 0.001$ ).

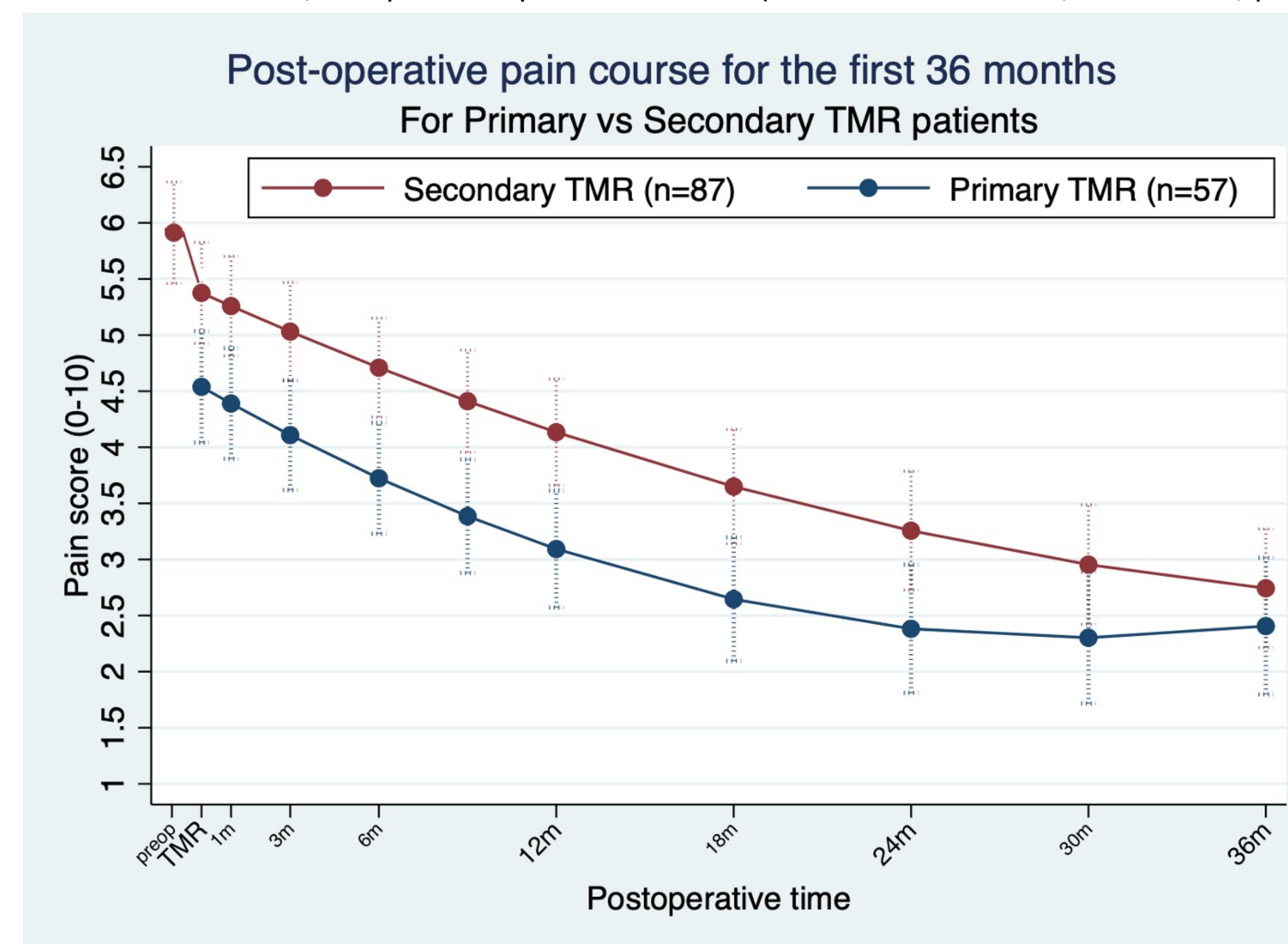


Figure 2: Post-operative Pain Course for amputees following TMR, for Primary TMR patients (blue) versus secondary TMR patients (red). Adjusted linear prediction of the average post-operative pain with 95% confidence intervals. Abbreviation: TMR = Targeted Muscle Reinnervation

## Discussion

Primary TMR patients illustrated a consistent post-operative decrease in pain score, reaching low levels of pain at 12 months before stabilizing at these mild pain levels. Secondary TMR patients demonstrate slower but consistent decline in pain levels. Although not significant at every time point, Primary TMR patients demonstrate lower pain levels over the whole trajectory. Since patients undergoing Secondary TMR have pre-existent pain following sensitization, these sequela are rooted deeper and will be more difficult to treat.<sup>3</sup> This contrast between Primary and Secondary TMR demonstrates the potential that this preventive strategy has compared to treatment of the same issue. Therefore, in this patient population, we believe a shift from treatment to prevention is justified and even encouraged. Since this study demonstrates the average pain course of TMR patients, there will be patients responding less optimal to TMR surgery, but there will also be well-responders or even cases achieving complete absence of pain. We are working on identifying such cohorts of less- and well responders. Being able to accurately stratify and predict which patient will benefit most versus which patient may not benefit at all, will allow for patient-tailored surgical treatment trajectories and would decrease overtreatment of patient who may not develop post-amputation neuropathic pain in the first place.

## Conclusion

These trends may assist in illustrating and understanding the long-term post-operative pain course and counseling patients in pain expectations following TMR. This data reinforces the durability of both primary and secondary TMR over a long timeframe. Moreover, we recommend TMR to be conducted in Primary, prophylactic, setting when possible. After all, an ounce of prevention is worth a pound of cure

## References

1. Hwang CD, Hoftiezer YAJ, Raasveld FV et al. Biology and Pathophysiology of Symptomatic Neuromas. *Pain*. Published online 2023. doi:PAIN-D-22-01167R1
2. Reid RT, Johnson CC, Gaston RG, Loeffler BJ. Impact of Timing of Targeted Muscle Reinnervation on Pain and Opioid Intake Following Major Limb Amputation. *Hand (N Y)*. Published online 2022. doi:10.1177/15589447221107696
3. Goodyear G, O'Brien AL, West JM, et al. Targeted Muscle Reinnervation at the Time of Amputation Decreases Recurrent Symptomatic Neuroma Formation. *Plast Reconstr Surg*. Published online May 18, 2023:Online ahead of Print