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Hand/Peripheral Nerve

Managing Neuroma and Phantom Limb Pain in Ontario: The Status of Targeted Muscle Reinnervation

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Background: Painful neuromas (PN) and phantom limb pain (PLP) are common following amputation and are unreliably treated, which impacts quality of life. Targeted muscle reinnervation (TMR) is a microsurgical technique that repairs the severed proximal nerve end to a redundant motor nerve in the amputated stump. Evidence supports TMR as effective in treating PN and PLP; however, its adoption has been slow. This study aimed to characterize: (1) the populations experiencing post-amputation PN/PLP; (2) current trends in managing PN/PLP; and (3) attitudes toward routine use of TMR to manage PN/PLP.

Methods: A cross-sectional survey was distributed to all orthopedic surgeons, plastic surgeons, and physiatrists practicing in Ontario, via publicly available emails and specialty associations. Data were collected on demographics, experience with amputation, managing post-amputation pain, and attitudes toward routine use of TMR.

Results: Sixty-six of 698 eligible participants submitted complete surveys (9.5% response rate). Respondents had a greater experience with surgical management of PN (71% PN versus 10% PLP). However, surgery was considered a 3rd-line option for PN and not an option for PLP in 57% and 59% of respondents, respectively. Thirty participants (45%) were unaware of TMR as an option, and only 8 respondents have currently incorporated TMR into their practice. Many (76%) would be willing to incorporate TMR into their practice as either an immediate or delayed surgical technique.

Conclusions: Despite its promise in managing post-amputation pain, awareness of TMR as a surgical option is generally poor. Several barriers to the widespread adoption of this technique are defined. *(Plast Reconstr Surg Glob Open 2020;8:e3287; doi: 10.1097/GOX.0000000000003287; Published online 21 December 2020.)*

INTRODUCTION

The incidence of lower limb amputation in Canada is approximately 22.9 per 100,000, representing, on average, more than 7000 amputations per year.[1] Further, many Canadians will undergo upper limb amputation. Among amputees, the prevalences of painful neuroma (PN) and phantom limb pain (PLP) are reported as high as 76% and 80%, respectively.[2–4] PN is characterized by a localized area of neuropathic pain within the amputated stump, resulting from disordered growth and aggregation of severed sensory axons.[5,6] PLP, meanwhile, is a neuropathic pain perceived in the amputated part that is thought to result from combined derangement of central and peripheral nervous systems.[7,8] Adding to the physical and psychosocial challenges of limb loss, PN and PLP are important detractors from patient quality of life after amputation,[9–11] limiting ability or desire to use prostheses, reducing mobility and impeding ability to return to normal activities of daily living.[12–15]

Targeted muscle reinnervation (TMR) is an emerging surgical technique that shows promising results in treating PN and PLP. The technique involves isolating and coapting the distal end of severed sensory nerves in

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the amputated stump to nearby motor nerves that innervate now redundant muscles. TMR may be performed at the time of amputation (primary) or delayed. Originally developed to improve myoelectric prosthetic control,[16] TMR has been shown, in several studies (including a randomized controlled trial), to reduce development of PN and PLP, improving post-amputation quality of life.[17–19]

Despite its promising results and increasing use in other countries,[17,18,20] TMR has yet to be adopted widely in Canada for treating amputation-related pain. The reasons behind this slow incorporation into practice are unknown and unexplored. Currently, we have little insight into practice patterns for PN and PLP management, incidence of amputation-related pain,[21] or feasibility of incorporating TMR into routine care of patients with PN or PLP. To address these knowledge gaps, this study aimed to survey plastic and reconstructive surgeons (PRS), orthopedic surgeons (OS), and physiatrists in Ontario (Canada's most populous province), with the following objectives: (1) characterizing the amputee population experiencing post-amputation PN and PLP; (2) surveying current management of PN and PLP by specialists; and (3) evaluating current awareness of and attitudes toward routine use of TMR in managing post-amputation PN and PLP. We hypothesize that, among the Ontarian amputee population, the need for TMR is high but that this procedure is used by few clinicians.

METHODS

A province-wide, cross-sectional survey targeted all Ontarian OS, PRS, and physiatrists. This study was reviewed and approved by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board.

Survey Design

Survey questions were developed through a multistep process and informed by the survey objectives and literature around PN, PLP, and TMR. A representative panel of specialists reviewed the survey to ascertain content validity. This panel consisted of 2 OS, 2 PRS, (one who whom had experience performing TMR), and 3 physiatrists, including 1 amputee rehabilitation specialist. A revised survey was constructed electronically using Qualtrics software (Provo, Utah). The finalized, online survey was fine-tuned after pre-testing by a new PRS and physiatrist. (**See questionnaire, Supplemental Digital Content 1**, which displays the final survey. http://links.lww.com/PRSGO/B520.)

Recruitment Plan and Participants

Eligible participants were currently practicing PRS, OS, or physiatry in Ontario and could complete the survey in English. Participants were contacted by email invitation. The Royal College of Physicians and Surgeons of Canada online directory provided a list of Ontarian specialists.[22] Physician emails were then gathered using several strategies: internet search of publicly accessible emails; Ontario hospital and medical school websites; professional societies willing to provide emails for active members (Canadian Society of Plastic Surgeons) or distribute invitations to their membership via email [Ontario and Canadian Orthopedic Associations (OOA and COA)] or e-newsletters (Canadian Association of Physical Medicine and Rehabilitation). Finally, the survey was designed as a public link to allow specialists to share access with relevant colleagues.

Email invitations provided the survey purpose, implied consent process, and survey link. All participants were blind-copied to protect confidentiality. Email invitations were addressed from the senior author, JMH, as peer-influence may improve response rates.[23] Likewise, survey completion was modestly incentivized with an optional draw for a tablet computer.[24–26] Finally, 2–3 reminder emails were sent after initial contact.

Survey Content and Outcomes

This anonymous survey included no identifying questions and covered 3 main topics. First, physician demographics (eg, specialty, subspecialty, experience, and practice setting) were collected. The second section inquired about experience in managing amputation, PN, and PLP, including questions regarding frequency of amputation, current amputees in their practice, proportion of patients developing PN and PLP, impression of impact on patient quality of life (domains informed by the Prosthesis Evaluation Questionnaire and the 36-Item Short Form Survey[27,28]) and management strategies for PN and PLP. The final section queried willingness to consider using or referring for TMR and perceived barriers to its adoption. Pertinent terms, such as upper- and lower-limb amputation, PN, PLP, and TMR, were defined to ensure uniform understanding.

Analysis

Only submitted surveys were analyzed, as unsubmitted surveys did not meet implied consent criteria. Demographics and responses regarding quality of life, TMR adoption, and barriers were analyzed using descriptive statistics in Microsoft Excel. Response rate was calculated by dividing the number of surveys submitted by number of invitations sent. Chi-square tests were used to compare specialty response rates and proportions of respondents willing to adopt TMR before versus after reading about it in our survey. Fisher's exact tests measured associations between specialty and exposure to amputation and PN/PLP, and association between exposure to PN/PLP and duration of follow-up after amputation. PN and PLP prevalence estimates and the number of treatments chosen per respondent were not normally distributed (Shapiro-Wilks test). Hence, PN/PLP prevalence estimates were compared across specialties and number of years in practice using the Kruskal-Wallis test. The mean number of treatments selected for PN versus PLP were compared using the Wilcoxon Signed Rank test. Mean ± SD is presented where appropriate.

Table 1. Overview of Survey Distribution and Response Rates

	Total	Plastic and Reconstructive Surgery	Orthopedic Surgery	Physiatrists
No. emails sent (to valid emails)	698	182	375	141
Complete responses	66	18	25	20
Total eligible respondents by specialty	—	37.9%	27.3%	30.3%
Analyzable responses rate	9.5%	9.9%	6.7%	14.2%

Specialty-specific breakdown shows response rates that were not significantly different (Chi-square test, $P < 0.05$).

RESULTS

Participant Demographics

Of the 1161 licensed OS, PRS, and physiatrists practicing in Ontario, we secured email addresses for 698. Of the 96 who started the survey, 66 completed it (Table 1). Response rates did not differ significantly between specialties ($P = 0.27$). The sample included both academic and non-academic clinicians. Participants worked in various settings, though academic centers with a level 1 trauma center predominated. Mean clinical experience among participants was 17.8 years (Table 2). All subspecialties within PRS, OS, and physiatry were represented, except orthopedic oncology, spine, and cancer rehabilitation (Fig. 1). Over half of the physiatrists subspecialized in amputee rehabilitation.

Experience with Amputation, PN, and PLP

Experience with amputation varied (Fig. 2). Significantly more physiatrists managed a higher number of amputees annually compared with surgical cohorts ($P < 0.05$), but volume did not differ significantly between PRS and OS ($P = 0.07$). Half of the physiatrists followed >50 amputees annually, while surgeons managed fewer (Fig. 2A). Most commonly, surgeons performed <5 primary and <5 revision amputations annually. In total, 3 surgeons (1 OS, 2 PRS) performed no primary amputations, and an additional 4 OS performed no revision amputations. Trauma was the most common indication for amputation: 12 surgeons (29%) reported amputating >5 times per year, while 16 (39%) amputated 1–5 times per year (Fig. 2B). Infection and diabetes were other common indications. Malignancy was least common. Other reported indications included polydactyly, Dupuytren's contractures, and brachial plexus injury.

More participants had encountered PN (90.4%) compared with PLP (82.5%), though this difference was not statistically significant ($P = 0.445$). Among PRS, 94% had encountered PN, while 56% encountered PLP. Conversely, 88% of OS had encountered PLP compared with 76% observing PN. An estimated 85% of OS and 59% of PRS followed patients for ≤6 months after amputation. Meanwhile, 60% of physiatrists working with amputees reported 3- to 6-month follow-up intervals, and none went >12 months without follow-up. Among surgeons, duration of follow-up after amputation (ie, 1–3 months, 3–6 months, 6–12 months, or >12 months) was not significantly associated with whether clinicians had encountered PN ($P = 0.431$) or PLP ($P = 0.705$).

Estimates of the proportion of amputees developing PN and PLP varied by specialty (Fig. 3). OS estimated 10% ± 9% of their patients developed PN, which did not differ significantly from PRS's mean estimate of 12% ± 18% ($P = 0.928$). Both surgical specialties' estimates, however, differed significantly from physiatrists' mean estimate of 22% ± 19% ($P < 0.05$) (Fig. 3A). Conversely, PRS's mean estimate of PLP prevalence was lower at 6% ± 6%, followed by OS estimating 24% ± 24% and physiatrists estimating the highest at 43% ± 24%. Mean estimates of PLP prevalence did not differ significantly between OS and PRS ($P = 0.075$) but both differed significantly from physiatrists' estimate ($P < 0.05$) (Fig. 3B). PN and PLP prevalence estimates were not associated with respondents' experience with amputation ($P = 0.228$).

A majority of clinicians estimated that all quality of life domains, except for "hygiene/self-care," were moderately to severely affected by PN/PLP (Fig. 4). Domains most

Table 2. Overview of Practice Type and Setting of Respondents

		Overall
Practice setting	Community health center	3
	Office-based practice	17
	Outpatient hospital (ambulatory center)	17
	Community hospital with inpatient beds (less than level 1 trauma center)	22
	Community hospital with level 1 trauma center	1
	Academic hospital (less than level 1 trauma center)	14
	Academic hospital with level 1 trauma center	26
Practice type	Non-academic community clinician or surgeon	24
	Academic clinician/surgeon—academic focus on research	14
	Academic clinician/surgeon—academic focus on education	17
	Academic clinician/surgeon—academic focus on administration	7
	Academic work only	1
Years of clinical experience	Mean (±SD)	17.8 (11.8)
	Range	0–42

The proportion of academic to non-academic clinician responders was 1.6:1. There was moderately even representation in the sample population, from nearly all practice environments, with the exception of community health centers and community hospital with level 1 trauma services.

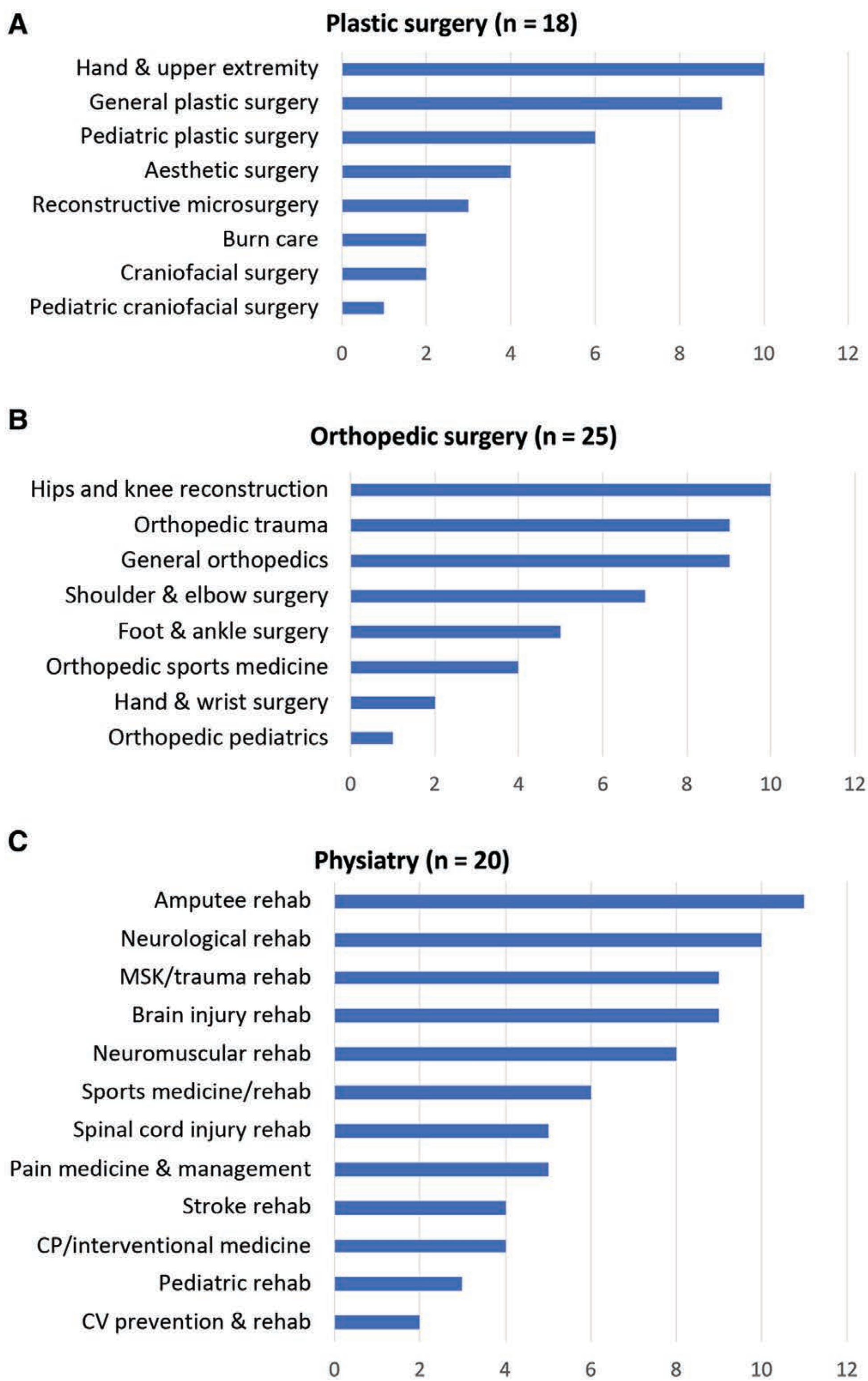

Fig. 1. Overview of clinical background of respondents. A, Plastic Surgery (n = 18); B, Orthopedic Surgery (n = 25); C, Physiatry (n = 20). Nearly all subspecialties were represented in the cohort of respondents among the 3 target physician groups. The only subspecialties that did not contribute to the dataset were orthopedic oncology, orthopedic spine, and cancer rehabilitation physiatrists. Respondents were permitted to identify with more than 1 subspecialty in this component of the questionnaire. Rehab, rehabilitation; CV, cardiovascular; MSK, musculoskeletal; CP, chronic pain.

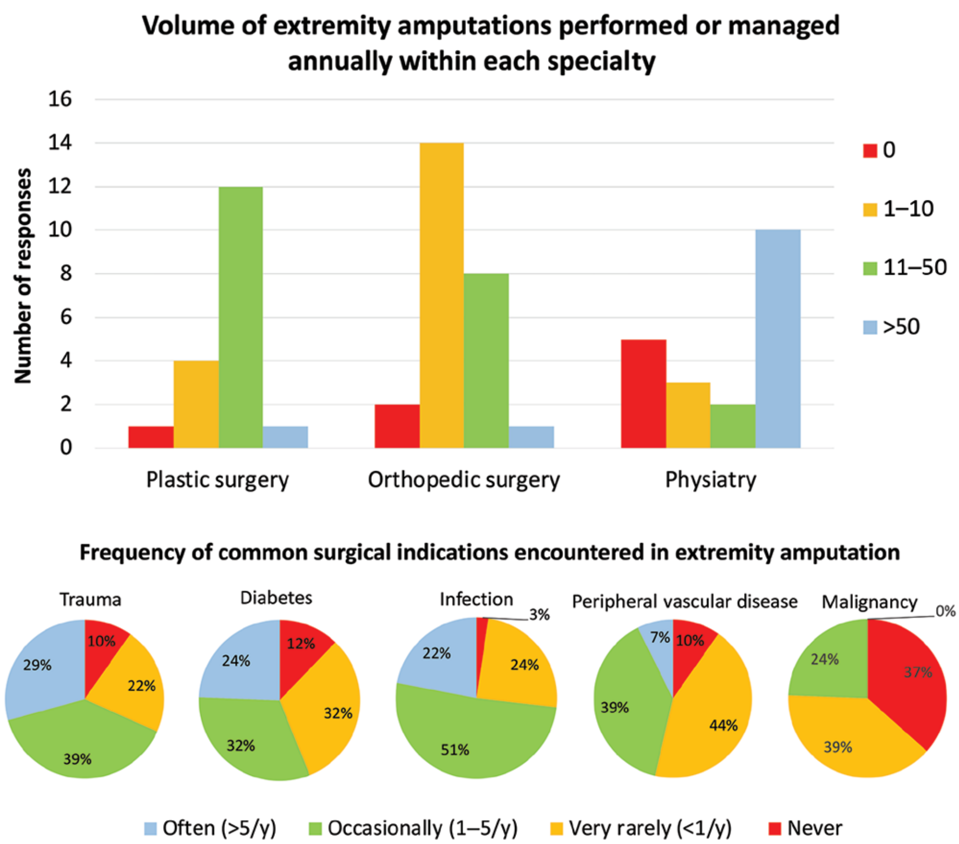

Fig. 2. Clinician experience with managing or performing amputations among respondents. A, Histogram depicting the volume of amputations carried out or managed within each specialty. Participants indicated how many they performed annually on average, and these responses were categorized into the intervals presented (n = 63). B, Among surgeons who stated that they performed amputation (n = 40), frequency of surgical indication is presented for each diagnosis.

commonly deemed severely affected were prosthetic use, ability to cope with amputation, and mental health and stress (Fig. 4).

PN and PLP Management

Respondents indicated their "typical" pharmacological and non-pharmacological strategies for managing PN and PLP (Fig. 5). Across all specialties, respondents identified significantly more management strategies for PN than for PLP ($P < 0.05$). The most common management strategies for PN were anticonvulsants (65%), NSAIDs (60%), referral for rehabilitation therapy or exercise (57%), and injection with local anesthetic (57%) (Fig. 5A). Conversely, top management strategies for PLP were pain clinic referral (50%), anticonvulsants (46%), and tricyclic antidepressants (44%) (Fig. 5B).

Among surgeons performing amputations, 68% had managed PN surgically, while none had managed PLP surgically. Preferred surgical techniques to manage PN included neuroma excision combined with nerve ending burial in muscle (39.5%), and neuroma stump resection alone (25.6%) (Fig. 6A). OS were least familiar with acellular nerve grafting, while PRS were least familiar with TMR. Forty percent of both PRS and OS were aware of but had never used TMR (Fig. 6A).

Among physiatrists, 90% had referred patients with PN for surgical management, with 4 reporting experience referring for TMR (Fig. 6A). Fewer physiatrists (65%) had referred for surgical management of PLP.

Although 86% would consider operating (surgeons) or referring for surgery (physiatrists) to manage PN, only 29% considered surgery as a 1st- or 2nd-line option (Fig. 6B). The 8% who would not consider surgical management for PN were all OS. Far fewer participants (32%) would consider surgical management for PLP, with only 3% considering it 1st- or 2nd-line.

Willingness, Conditions, and Barriers to Adopting TMR for PN and PLP Treatment

After reading a brief explanation of TMR with supporting literature, 48 participants reported they would consider incorporating TMR (or TMR referral) into their practice (Fig. 7A) compared with 10 willing participants previously, representing a statistically significant increase ($P < 0.05$) (Fig. 7A). (**See questionnaire, Supplemental Digital Content 1**, which displays the final survey. http://links.lww.com/PRSGO/B520.) Nonacademic surgeons represented 50% of those willing to adopt primary TMR, whereas only 1 physiatrist, an academic clinician, would not consider referral for TMR,

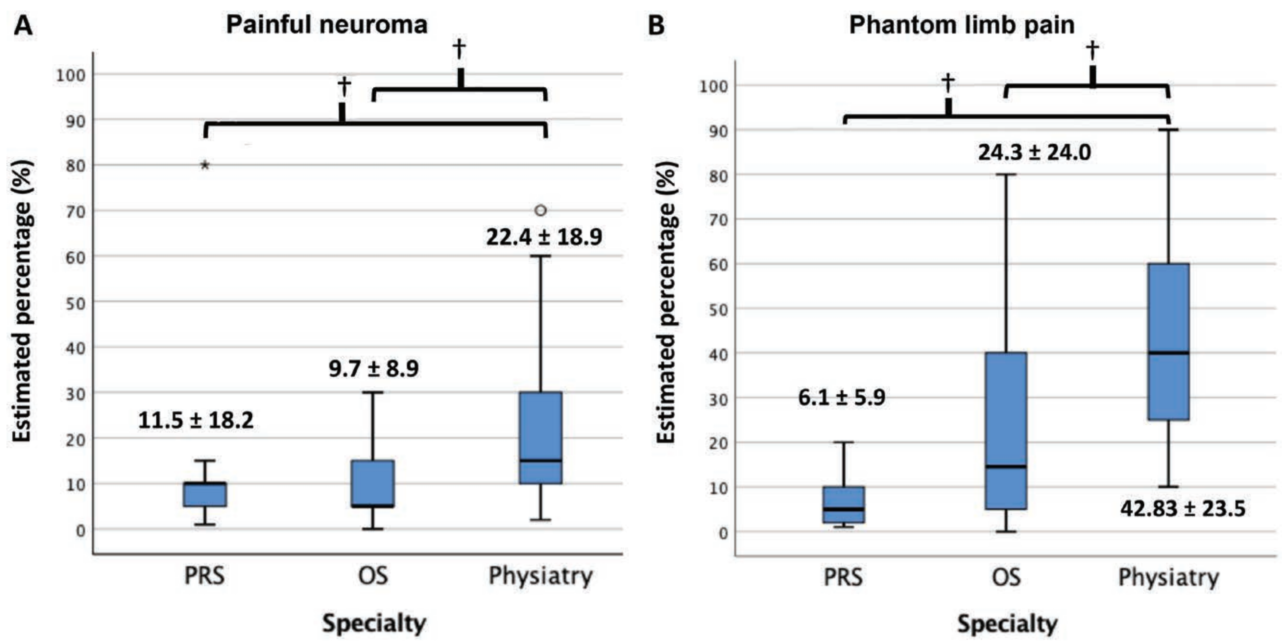

Fig. 3. Participants' perceived incidence of PN and PLP among amputees in their practice. A, Estimates of the proportion of patients developing painful neuroma (PN) after amputation organized in a box plot. B, Estimates of the proportion of patients developing phantom limb pain (PLP) after amputation organized in a box plot. The "°" indicates an outlier (1.5 x IQR), while the "*" indicates an extreme outlier (3 x IQR). The "†" indicates a statistically significant difference (Kruskal-Wallis test, $P < 0.05$).

preferring referral to an amputation specialist to decide appropriateness of TMR.

Over half of surgeons willing to adopt primary TMR would do so under any conditions. The remainder would only incorporate TMR if it: only added 30 min to the case (n = 4), only added an hour (n = 3), or required another surgeon (n = 3). Four surgeons would only consider performing delayed TMR (Fig. 7B).

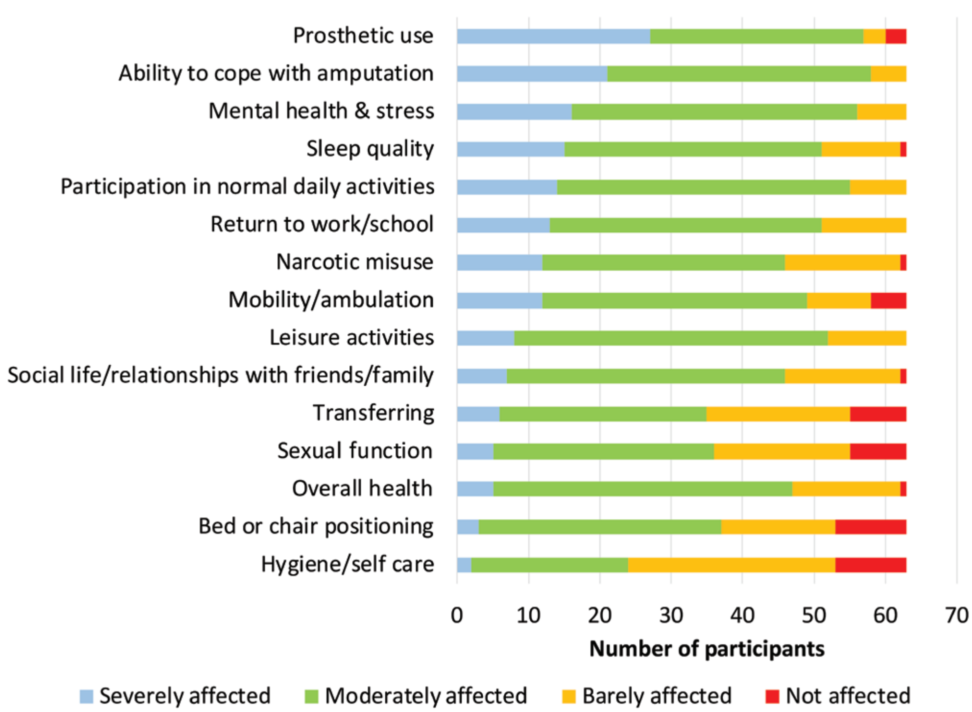

Fig. 4. Extent to which quality of life is impacted by PN and PLP. Respondents were asked to rate the degree to which each domain impacted quality of life. The list of quality-of-life domains was developed based on a combination of items included in the 36-Item Short Form Survey Instrument and the Prosthesis Evaluation Questionnaire as well as expert input.

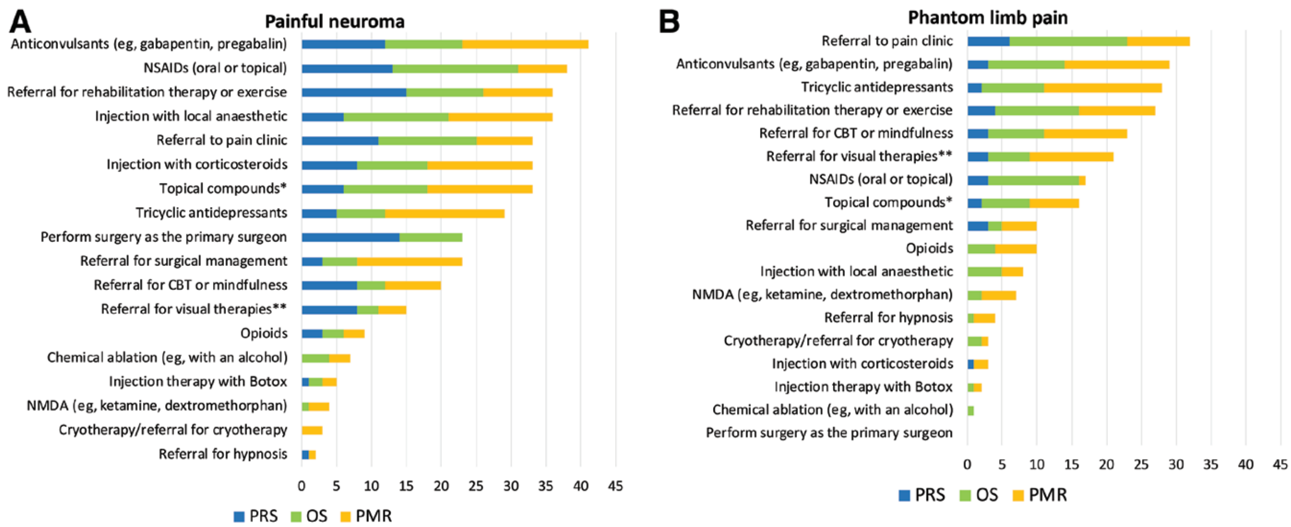

Fig. 5. Comprehensive overview of strategies to manage PN and PLP among PRS, OS, and physiatrists. A, Strategies most commonly used to treat painful neuroma (PN). B, Strategies most commonly used to treat phantom limb pain (PLP). Topical treatments trended toward being more commonly used in managing PN, whereas managing PLP involved putting relatively more emphasis on behavioral and rehabilitative techniques. Medical treatments were commonly used to manage both PN and PLP across all specialty groups. NMDA, N-methyl-D-aspartate receptor antagonists; CBT, cognitive behavioral therapy. *Topical compounds refer to agents such as lidocaine, TCAs, and NSAIDs. **Guided imagery, visual-kinetic feedback therapy, or mirror therapy.

Both surgeons willing and unwilling to adopt TMR reported barriers to incorporating it. Overall, TMR was most commonly reported to be outside respondents' scope or skill set (Fig. 8A, B). Of 11 surgeons unwilling to adopt TMR, 9 cited this barrier. Seven of those 9 were OS, and, therefore, were unlikely to have microsurgical training (Fig. 8B). Surgeons willing to adopt TMR most commonly indicated insufficient general knowledge about TMR. Only 1 surgeon considered their current techniques effective enough and another reported insufficient demand for TMR (Fig. 8A).

PMR specialists most often cited no barriers, with "insufficient general knowledge about TMR" being the second most commonly chosen option (Fig. 8C). Physiatrists also submitted "other" barriers: "Surgeons' willingness to perform [TMR]," "Not knowing who to refer to and wait times," and "lack of familiarity with amputation medicine." Two respondents offered pertinent comments: "several" patients had been successfully treated in a physiatry-PRS collaborative program; TMR may be used to treat neuropathic pain associated with spinal cord injury.

DISCUSSION

This study successfully administered a cross-sectional survey to gain perspective on current management of amputation-related PN and PLP. Despite modest response rates, participants represented nearly all relevant subspecialties and practice types within PRS, OS, and physiatry. (**See table, Supplemental Digital Content 2,** which displays a comparison of survey and underlying populations. http://links.lww.com/PRSGO/B521.) All clinician groups had substantial experience performing amputations or managing amputee care, with the greatest number of high-volume providers being physiatrists. Despite comparable experience, physiatrists estimated a significantly higher prevalence of both PN and PLP ($P < 0.05$). Given that PN can be a late-developing phenomenon,[6,29] this discrepancy in estimated prevalence may be explained by a longer follow-up duration among physiatrists.[30] However, our study found no significant association between duration of follow-up and exposure to PN/PLP. Another explanation for different prevalence estimates could be specialty-specific biases related to expertise, differences in understanding the pathophysiology of PN/PLP, or stringency in diagnostic criteria.

The significance of PN and PLP in the amputee population may be underappreciated. Study participants identified that 10%–22% of amputees may be developing PN and 6%–43% may develop PLP—values within the range reported in the literature.[3,30–35] When our survey estimates are extrapolated to the 3000 lower limb amputations performed annually in Ontario,[1] for example, the absolute prevalence of PN and PLP among lower limb amputees alone may be as high as 660 and 1290 cases per year, respectively.

Despite discrepant prevalence estimates, participants uniformly identified that nearly all quality-of-life domains are impacted moderately to severely by PN and PLP. Post-amputation PN and PLP impose a burden on quality of life, in addition to the inherent challenges of limb loss. The quality-of-life domains most commonly considered to be severely impacted, including prosthetic fitting and psychological well-being, correspond to those described in the literature.[9,13,36] As such, developing a reliable repertoire of treatments is necessary to avoid and manage these painful, and potentially devastating, sequelae of amputation.

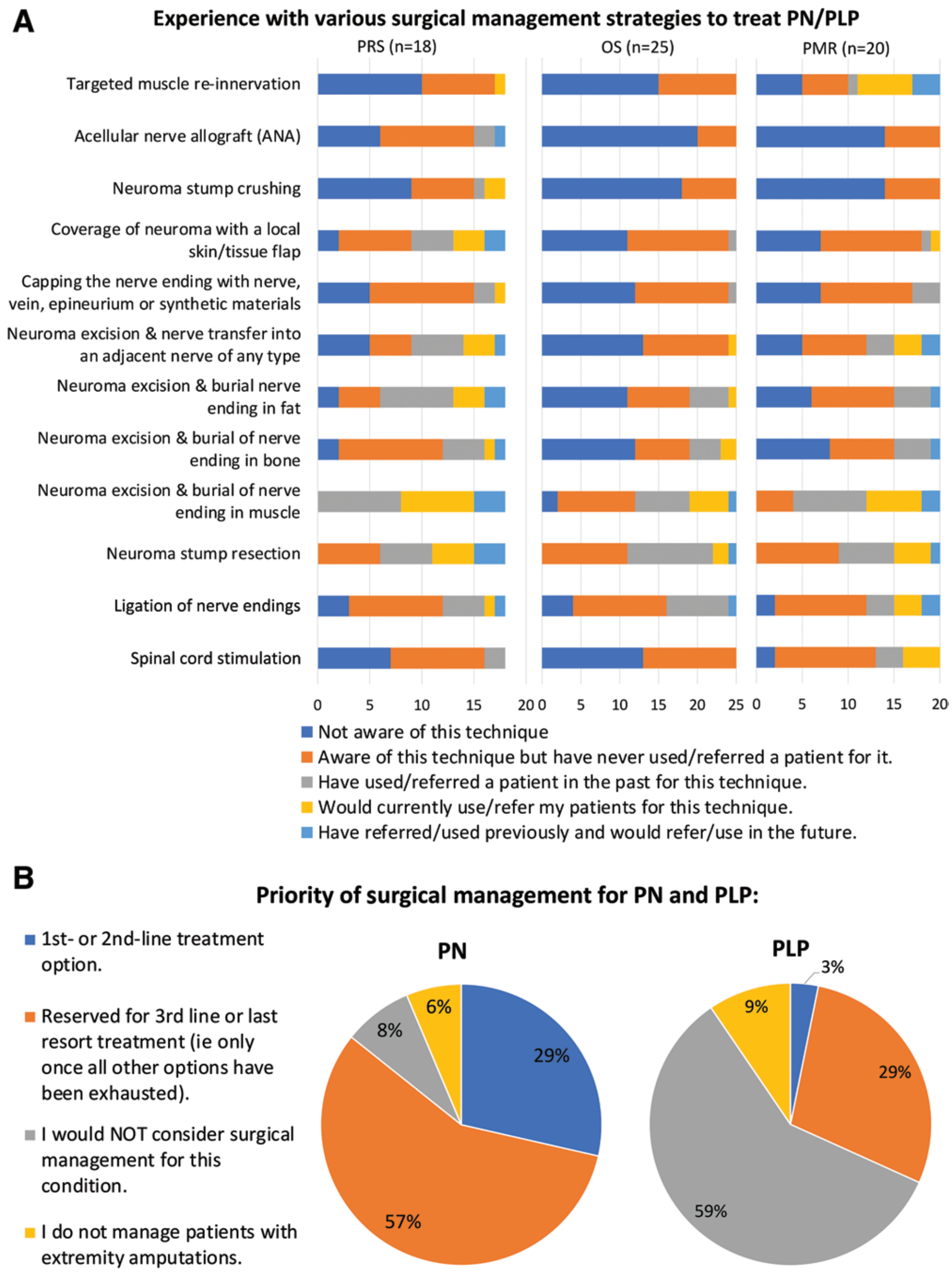

Fig. 6. Overview of current surgical practices in managing PN and PLP among respondents. A, Comprehensive list of known surgical techniques that depicts the degree of familiarity and use of each technique (PRS: n = 18; OS: n = 25; PMR: n = 20). B. Perceived priority of surgical management in treating PN and PLP.

Unfortunately, commonly used treatments for PN and PLP are currently diverse, unreliable, and without standardization.[19,37–39] Although respondents were familiar with most treatments in our comprehensive list, clear, distinct patterns of preferred management strategies for PN and PLP emerged. Injection, topical and surgical treatments were more commonly used for PN. Treatments selected for PLP were aligned with those reported in the literature and relied on pain clinics, neuroleptic medications, and tricyclic antidepressants.[37,39,40] Further, though familiar with numerous surgical options to treat PN/PLP, surgeons were more likely to operate for PN and most considered surgery no more than a 3rd-line or salvage option for both PN and PLP.

Pharmacological therapy alone is often insufficient. Surgical intervention, such as burial in muscle or bone, ligation, and restoration of nerve continuity, is often appropriate for intractable painful neuromas.[41,42] A majority of specialists, particularly surgeons, were unaware of TMR, favoring neuroma excision with or without burial in

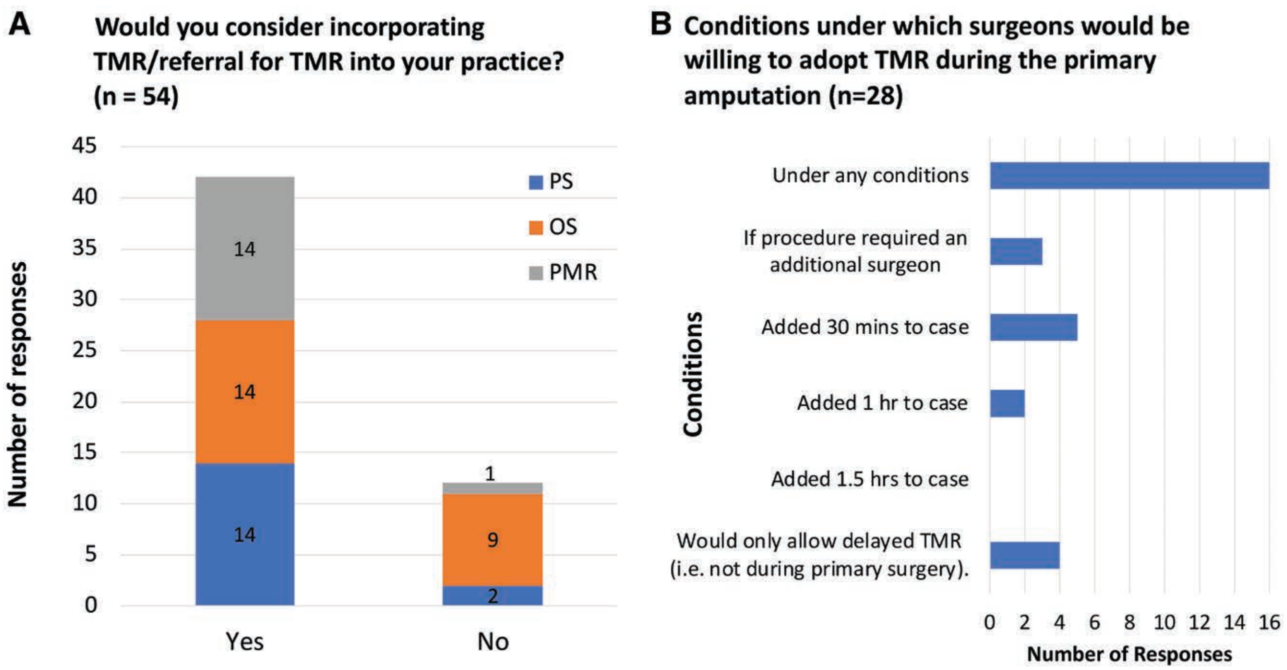

Fig. 7. Assessment of clinician willingness to incorporate TMR into their practice and under what conditions they would do so. A, Participants' responses to whether they would consider performing TMR (surgeons) or referring for TMR (physiatrists) in their practice (n = 54). B, Among surgeons who answered "Yes"(as indicated in panel A) (n = 28), a follow-up question explored under what time and supportive conditions they would consider performing TMR.

muscle, as described previously.[43] However, a majority were willing to consider incorporating TMR into their practice under any conditions, suggesting a growing acceptance of surgical options to complement conventional medical/therapy-based treatments.

Importantly, there appeared to be a hesitancy to manage PLP operatively that was less pronounced with PN. Eighty-six percent of surgeons considered surgical management for PN compared with 32% for PLP. This may be related to the inconsistent endorsement of evidence-based surgical options for PLP.[18,19,38,40,44–46] However, TMR is emerging as a viable option for treating both PN and PLP. In fact, a recent randomized control trial and meta-analysis have shown clinical improvement in PLP pain within a year after TMR.[18,47,48]

Despite demonstrated efficacy, adoption of TMR has been slow. That only half our respondents knew about TMR implies awareness of the concept is still spreading. Barkun et al described a 4-stage model of surgical innovation where TMR appears to be within the "early dispersion and exploration" stage, relying on opinions and experiences of a small number of leaders to drive the technique's diffusion.[49] Fortunately, as indicated by one respondent, small pockets of leaders are emerging, paving the way to push TMR toward widespread adoption and the final stage—long-term implementation and monitoring.[49] Participants identified other barriers potentially impacting TMR's adoption: (1) TMR was outside clinicians' practice scope or skill-set; (2) clinicians had insufficient comfort with microsurgery; and (3) clinicians lacked general knowledge about TMR.

Our recommendations follow from several observations. First, educating specialists involved in amputation care about emerging surgical treatments would be beneficial. Significantly more physicians reported they would be willing to consider using, or referring patients for, TMR after reading an educational description of TMR before completing the survey's final section. Improving awareness of evidence-based techniques does benefit patient care.[50] Second, many of the respondents who cited "lack of microsurgical expertise" as a barrier were OS with likely no microsurgical training. Ease of learning, low cost, and perceived magnitude of benefit of a new technique favor adoption of new surgical innovations.[50,51] With this in mind, institutional arrangements whereby plastic surgeons are available to support other services with timely access to TMR as well as regional referral networks may facilitate acceptance of the technique. That 50% of participants were willing to adopt TMR to manage PN/PLP under any conditions suggests key elements for widespread adoption, including clinician buy-in, are already in place.

We acknowledge several limitations of this study. First, despite efforts to maximize response rates using incentives, multiple reminders, and contact methods,[52–54] our response rate was low. Potential contributing factors include: (1) use of online surveys, which reportedly have lower response rates than do paper version[23,53,55,56]; (2) participant factors, including surgeons' notoriously low response rates[55,57,58]; (3) survey length, possibly leading nearly one-third respondents to abandon the survey before fully completing and submitting the same.[23,59] Another limitation relates to heterogeneity in development,

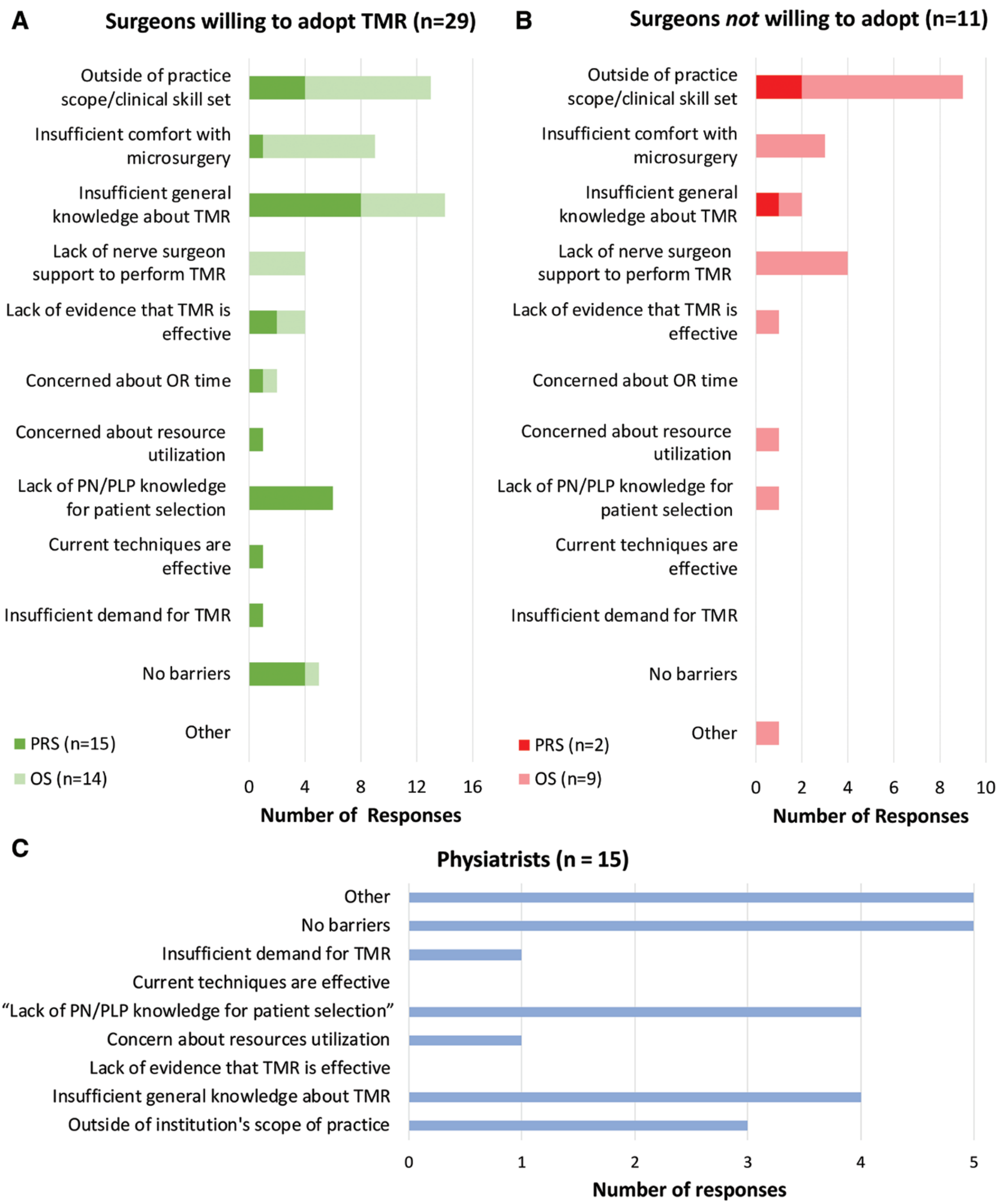

Fig. 8. Perceived barriers to incorporating TMR into practice, among OS, PRS, and physiatrists. A, Perceived barriers among surgeons willing to adopt TMR (n = 29); B, Perceived barriers among surgeons *not willing* to adopt TMR (n = 11); C, Barriers perceived by physiatrists (n = 15).

presentation, and impact on quality of life of PN and PLP. While this survey focused on questions around surgical treatment and the emerging role for TMR, we acknowledge that management for these sequelae is multimodal, multidisciplinary, and not necessarily amenable to 1 simple solution. Finally, future work should investigate knowledge and attitudes of other healthcare providers involved in amputation care, including vascular and general surgeons, as well as prosthetists, occupational, and physical therapists.

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