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Chronic postsurgical pain and transitional pain services: a narrative review highlighting European perspectives

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ABSTRACT

Background/Importance Chronic postsurgical pain (CPSP) is a significant, often debilitating outcome of surgery, impacting patients' quality of life and placing a substantial burden on healthcare systems worldwide. CPSP (pain persisting for more than 3 months postsurgery) leads to both physical and psychological distress. Recognized as a distinct chronic pain entity in International Classification of Diseases, 11th Revision, CPSP enables better reporting and improved management strategies. Despite advancements in surgical care, CPSP remains prevalent, affecting 5%–85% of patients, with higher rates following thoracotomies, amputations, mastectomies and joint replacements.

Objective The acute to chronic pain transition involves complex interactions between peripheral and central mechanisms, with central sensitization playing a key role. Identifying high-risk patients is crucial for prevention, with factors such as surgical type, nerve injury, neuropathic elements in acute postoperative pain, and psychosocial conditions being significant contributors.

Evidence review Current pain management strategies, including multimodal therapy and regional anesthesia, show limited effectiveness in preventing CPSP. Neuromodulation interventions, though promising, are not yet established as preventive modalities.

Findings Transitional pain services (TPSs) offer a comprehensive, multidisciplinary approach to managing CPSP and reducing opioid dependence, addressing both physical and psychosocial aspects of functional recovery. While promising results have been seen in Canada and Finland, TPSs are not yet widely implemented in Europe. There is also growing interest in pain biomarkers, through initiatives such as the A2CPS program, aiming to improve CPSP prediction and develop targeted interventions.

Conclusions Future research should focus on large-scale studies integrating various factors to facilitate CPSP prediction, refine prevention strategies and reduce its long-term impact.

INTRODUCTION

Chronic postsurgical pain (CPSP) has become a silent epidemic and represents a significant, often debilitating outcome of surgery, affecting a substantial number of patients worldwide, within the context of an aging population and increasingly complex procedures. Defined as pain persisting for more than 3 months postsurgery, it severely impacts patients' quality of life (QoL), leading to physical and psychological distress, ultimately affecting their functional status.[1 2] CPSP results in a disproportionate consumption of healthcare resources, escalating costs and contributing to the global healthcare burden. These patients have limited treatment options and often rely on opioids, leading to psychosocial problems, mainly sleep disturbances.

In Europe, where surgical procedures are prevalent, and healthcare systems sophisticated yet diverse, CPSP is a major public health issue, requiring comprehensive management strategies. Despite advancements in surgical care, many patients experience CPSP beyond the expected healing period, profoundly affecting healthcare utilization, and increasing socioeconomic costs. Hence, there is a growing focus on multidisciplinary approaches, including the development of transitional pain services (TPS), to mitigate the CPSP long-term impact.[3–6]

In the latest edition of International Classification of Diseases (ICD-11), driven by the collaborative initiative and combined efforts of the WHO and the International Association for the Study of Pain (IASP), CPSP has been classified as a distinct chronic pain entity, rather than merely a symptom.[7] This critical step forward enables more precise reporting of its incidence in future studies. Therefore, the problem is formally recognized, raising awareness of the condition, and fostering interdisciplinary research for its prevention and management.

On behalf of the European Society of Regional Anaesthesia and Pain Therapy, this narrative review explores briefly CPSP complexities, such as epidemiology, underlying mechanisms, risk factors, and the potential preventive role of regional anesthesia-analgesia (RA) techniques and multimodal analgesia protocols. It also examines the rationale, principles, structure, impact and challenges of TPS on the evolving landscape of pain management in Europe.

CPSP OVERVIEW

Definition

CPSP definition was updated and standardized in 2019 and included in ICD-11,[7] as a distinct type of pain. It is characterized by its development or increase in intensity following surgery, persistence beyond the usual healing period (typically 3 months after the triggering event), and a significant negative

impact on QoL. CPSP may be localized to the surgical field or projected onto a referred area and may be associated with ongoing acute postoperative pain or develop after an asymptomatic period. Other causes (infection, cancer recurrence, pre-existing chronic pain) are excluded. CPSP often exhibits neuropathic pain (NP) characteristics. While CPSP inclusion in ICD-11 was regarded as a significant advancement, some researchers argue for rethinking the definition, to incorporate a broader range of patient-reported and pain-related outcomes, to better differentiate between functional CPSP and ongoing chronic pain.[7–12]

Despite significant progress in basic pain research and the increasing volume of surgeries worldwide, CPSP prevalence has remained unchanged over the past decades, raising concerns regarding the effectiveness of applied preventive strategies.[1 2 4 12–14] Its incidence varies widely (5%–85%, mean 10%–40%), depending on the type of surgery, patient characteristics, and diagnostic criteria.[7] Higher rates (>40%) are observed after limb amputation, inguinal hernia repair, spine surgery, thoracotomy and mastectomy.[11 12]

Historically, CPSP was largely an under-recognized, underreported and neglected surgical consequence, until it gained attention, as an alarming postsurgical complication, after the publication of Crombie *et al* in PAIN, in 1998. The study surveyed 5.130 patients, attending Outpatient Pain Clinics in Scotland & North England, reporting that 22.5% of patients attributed their pain to previous operations, with 50% identifying surgery as the sole cause of their chronic pain condition.[15]

Since then, multiple, retrospective or prospective studies have assessed CPSP prevalence, with incidence varying according to study designs and chronic pain definitions used. In 2008, literature data highlighted that 10% of surgical patients developed CPSP, with 1% suffering from severe CPSP.[13 16] A 2015 multicenter European study reported similar findings.[17] In 2021, a cohort study (14,000 non-cardiac surgery patients) concluded a 3.3% incidence of incisional pain at 1 year, with nearly half reporting moderate (35%) to severe (14%) pain. 85% of patients reported daily activities interference and over 50% focused on analgesics consumption.[18] Such observations align with earlier findings showing that 14%–24% of surgical patients experience suboptimal physical and emotional recovery at 6–1 2 months postsurgery, with 5%–7% reporting severe disabling pain at 1 year, stressing that CPSP pain intensity and impact on functional and emotional QoL needs investigation.[17 19–21] The clinical significance of CPSP extends beyond patients' immediate discomfort, affecting sufferers and their families, leading to a cascade of negative outcomes (physical disability, psychological distress, social isolation, and reduced QoL). CPSP further increases healthcare costs due to the need for ongoing pain management, physical therapy, psychological support, and additional surgeries/interventions, compounded by lost productivity and long-term disability. Unfortunately, suboptimal pain management in high-risk patients, inappropriate opioid treatment and lack of proper follow-up are common, further exacerbating the problem.[1–4]

Pathophysiology: mechanisms underlying CPSP

The transition from acute to chronic pain is complex, heterogeneous and multifactorial, varies among individuals, and involves interactions between peripheral and central pain processing mechanisms. The understanding of underlying pathophysiology comes largely from preclinical studies. Nerve and tissue damage trigger inflammatory and immune responses, leading to peripheral (pain nociceptors at injury site) and central (spinal cord, brain) sensitization.[22–24] This process lowers the pain activation threshold, making the affected area more sensitive to stimuli, and its comprehension is essential for developing effective prevention and management strategies.

Surgical trauma can cause NP, with abnormal sensations such as burning, tingling, or shooting pain, due to nerve damage.[24 25] Central sensitization amplifies pain signals within the central nervous system (CNS), particularly the spinal cord and brain. Therefore, repetitive nociceptive stimuli induce permanent CNS changes, resulting in altered and enhanced pain sensations (hyperalgesia, allodynia, dysaesthesia and other).[1] Central sensitization plays a key role in pain persistence after the initial injury has healed, contributing to the CPSP chronic nature.[1–6 22–25] Blocking nociceptive stimuli during surgery by multimodal analgesia or RA may prevent this altered nociceptive processing.[26] While the concept of preemptive analgesia focuses on interventions before surgery, preventive analgesia refers to a broader approach, where timing is less critical.[27] Conditional pain modulation offers another theory to explain acute pain chronification, suggesting a dysregulation/imbalance between pronociceptive and antinociceptive systems, often evident in chronic pain sufferers and chronic opioid users, manifested as opioid-induced hyperalgesia.[3]

Risk factors: identifying high-risk populations

Identifying patients at high risk for CPSP is crucial for its prevention. Predisposing factors are broadly categorized into surgical, patient-related, and perioperative ones.[1 2 6 12 28] The type and extent of surgery are primary determinants, with procedures involving major tissue disruption, prolonged recovery times, or significant nerve damage (thoracotomies, mastectomies, amputations, joint replacements) posing higher CPSP rates. Procedural invasiveness, surgical skill, duration of operations and the need for repeated/revision surgeries also influence CPSP likelihood.[1 6 24 28] Intraoperative nerve injury carries a higher risk, often linked to acute NP, a significant component of CPSP, particularly in patients undergoing limb amputation (60%), and mastectomy or thoracotomy (20%–40%).[6 24 29] Individual patient characteristics (age, gender, genetic predisposition, pre-existing chronic pain conditions) may modulate CPSP risk, with younger patients and females generally being more susceptible. Beyond physiological factors, psychological ones also determine pain experience. Perioperative anxiety, depression, sleep difficulties, substance abuse history, and pain catastrophizing are significant CPSP predictors. Social factors (support networks, work status, and socioeconomic conditions) also affect pain perception and coping strategies.[1 2 6 10 11 24 30]

Inadequate perioperative pain control is recognized as a critical, potentially modifiable risk factor for CPSP and prolonged opioid use. Patients experiencing severe acute postoperative pain are at higher risk of developing CPSP. Some individuals are inherently predisposed to severe postoperative pain ("pain begs for pain"), making postoperative pain a key CPSP determinant, necessitating targeted preventive measures.[1 6 24 28] Evidence linking acute pain and CPSP is only moderate,[26] and correlation does not necessarily imply causality, as different types of persistent pain may pre-exist and/or develop, parallel to acute postoperative pain resolution.[4 31] Nevertheless, effective acute postoperative pain management is widely regarded by anesthesiologists and pain specialists, as essential for CPSP prevention. Factors such as intensity and duration of acute perioperative pain, overall pain trajectories, and predominance of severe neuropathic-like or visceral pain (as

opposed to incisional one) significantly contribute to CPSP development.[32]

The severity of acute postoperative pain during mobilization is a strong predictor of CPSP intensity/severity, challenging the predictive value of commonly used single pain scores. Indeed, postoperative pain should be seen as true dynamic process, best understood through the concept of "pain trajectories", which are further evolving into "recovery trajectories". These trajectories are dichotomized to optimal and non-optimal ones, with the latter being linked to persistent acute pain and higher CPSP rates.[4 33] This perspective aligns with earlier observations, reporting that time spent in severe pain immediately after surgery increases CPSP risk.[34] Assessing pain impact on recovery parametres (mobilization, mood, sleep and analgesic medications utilization) is more important than relying solely on traditional pain scores. Mobilization is crucial for overall recovery and the cornerstone of Fast-Tracking and Enhanced Recovery after Surgery (ERAS) programs. Recent studies show that 14%–24% of patients experience suboptimal physical and emotional recovery 6–12 months postsurgery, indicating that pain intensity should be considered alongside its effects on patient's functional and emotional QoL.[18]

The perioperative journey is a critical period, as some patients are particularly vulnerable to long-term effects of poorly controlled pain. While most patients recover smoothly and discontinue opioids quickly, a significant minority deviates from this typical trajectory and develops CPSP. Early identification of CPSP risk factors can enable effective risk stratification and application of evidence-based preventive strategies. Despite numerous studies, evidence on CPSP risk factors remains inconclusive. Recent efforts focus on developing CPSP predictive models, based on patient characteristics and perioperative variables.[35–37] CPSP may develop after any surgery and, with individual factors playing a major role in pain chronification, and clinical risk factors showing better predictive value than genetic predisposition.

Mitigating the CPSP risk: preventive strategies

Preventive analgesia, aimed at minimizing the impact of noxious stimuli, reducing pain intensity and preventing peripheral and central sensitization perioperatively, has gained popularity over traditional preemptive analgesia, which focuses on the timing of analgesics administration, relative to incision.[25] Both strategies have shown some success in reducing CPSP incidence and intensity,[6 38] though the optimal duration for postoperative analgesia to prevent sensitization still remains uncertain.

Multimodal therapy, using at least two different drugs/interventions, to reduce or eliminate opioid consumption, is particularly important because opioids may exacerbate neuroinflammation, and intensify/prolong postoperative pain. Therefore, multimodal analgesia use should be prioritized.[39] Non Steroidal Anti Inflammatory Drugs (NSAIDs), COX2 inhibitors, acetaminophen, steroids, alpha-2 agonists, ketamine, intravenous lidocaine, or gabapentinoids are typically used in multimodal pain management. While their efficacy in acute postoperative pain management is well documented, evidence regarding their long-term effects is limited. According to a 2013 systematic review of 40 RCTs, examining the impact of various pharmacological interventions on CPSP prevalence, and a 2021 update (adding 70 new RCTs), the effect of all medications on pain prevalence, 3–6 months postsurgery, was minimal and of uncertain clinical relevance. Consequently, no drug studied is recommended for CPSP prevention.[38–40]

RA, including central neuraxial techniques, peripheral nerve blocks, and local anesthesia wound infiltration, is a key element of multimodal analgesia, targeting multiple sites along the pain pathway, activated by surgery.[41] However, most clinical data do not demonstrate that RA prevents effectively the CPSP development.[42] A Cochrane review provided moderate-quality evidence that epidural anesthesia reduces CPSP risk 3–18 months post-thoracotomy, with only low-quality evidence supporting RA effectivity in reduce CPSP 3–12 months after breast cancer surgery.[43 44] A recent systematic review concluded that only paravertebral blocks were associated with a significant CPSP risk reduction postmastectomy, but not thoracotomy.[45] The question on the efficacy of continuous RA versus single injections for CPSP prevention remains unanswered.[46]

TPS: AN INSIGHTFUL APPROACH

Beyond acute postoperative pain: the importance of transitional pain

In addition to acute postoperative pain, attention must be given to pain that persists after hospital discharge, known as "subacute" postoperative or "transitional" pain (TP). Key questions include (a) Does TP correlate with CPSP prevalence? (b) Can TP predict poor recovery postsurgery? and (c) Could TP guide CPSP prevention? Pain evolution and resolution are dynamic, multifaceted, and complex processes. TP is considered as a subset of acute pain and is typically defined by timeframes, though it should be understood by its fundamental etiology and prognosis. TP occupies a "gray zone" between hospital discharge and the suggested CPSP cut-off (10 days to 3 months postsurgery) and has recently gained attention for its potential in CPSP prediction. While therapeutic interventions during TP might prevent CPSP, it remains unclear whether they are more effective than early, aggressive perioperative pain management. This uncertainty may stem from the oversimplified and potentially misleading concept of acute to chronic pain transitioning, as some CPSP forms are a continuum of acute pain, due to a shift from physiological to pathological states, although other pain types potentially coexist/develop postoperatively.[4 47 48]

The TP period is often overlooked in clinical research, despite its importance in rehabilitation.[4 48] Some studies have successfully proven a TP–CPSP link, following various surgeries. Few prospective studies identified 30-day or 6-week postoperative pain intensity as a CPSP predictor, particularly after inguinal hernia and cosmetic breast surgery. Patients with high-intensity postoperative pain within 30 days after hernia repair are more vulnerable to develop CPSP at 3 months.[49 50] During examination of long-term pain trajectories, in total knee arthroplasties (TKA), TP intensity at 30 days is a risk factor for severe CPSP at 3 and 6 months, whereas at 1 month serves as a reliable CPSP predictor at 1 year.[51–53] Pain intensity can escalate during the "subacute" period, indicating NP presence, as observed after hernia repair or orthopedic surgery in rehabilitation units. Similar observations are reported in thoracotomy patients,[54] where the emotional aspect of pain also predicts subsequent CPSP development, particularly in children undergoing major operations, where delayed pain recovery, encompassing both pain intensity and unpleasantness at 2 weeks postsurgery, negatively affects long-term outcomes at 4 months or later.[55 56]

TPS: conceptual framework

Disappointingly, current perioperative pain management is fragmented and problematic. During the transition period, neither acute nor chronic pain specialists are typically involved, leaving

the primary surgeon, who is not trained in pain management, to handle TP not following the normal postoperative course. This model is reactive rather than proactive, focusing on short-term solutions, instead of a comprehensive approach, often leading to escalated opioid use, due to unfamiliarity with other modalities.[2 5 32 48 57 58]

A significant number of patients experience moderate to severe pain for days to weeks postsurgery, and many could potentially be identified preoperatively, by assessing patient-specific, procedural and environmental risk factors. Addressing these factors through intervention at each phase (preoperative, intraoperative, postoperative and postdischarge) can be achieved by a holistic approach via the establishment of a "TPS", a multidisciplinary team composed of anesthesiologists, acute pain nurse practitioners, clinical psychologists, palliative care specialists, exercise physiologists, and patient-care coordinators. Integrating TPS into "perioperative medicine", is crucial for effective pain management and prompt identification of CPSP risk factors, particularly since the most severe pain episodes occur at home and during rehabilitation, especially in the vast majority of orthopedic patients.[6 32 48] TPS was introduced to provide comprehensive, interdisciplinary care throughout the entire perioperative period and represent a soft place to "land" for patients at increased risk for long term, excessive opioid consumption and dependency, and/or CPSP development. TPSs focus on preventing transitioning from acute to chronic pain following surgery, thereby reducing the associated disability.[48 57 58]

A TPS assists patients with complex medical needs manage pain and de-escalate opioid use, improving their coping strategies and overall functioning. Transitional care begins before surgery and extends through the entire postoperative period and beyond, whereas substance use/abuse, polypharmacy, and frailty are simultaneously addressed. The team encompasses a multidisciplinary approach, including physician-guided pharmacotherapy, physiotherapy, alternative therapies (like acupuncture), clinical psychology, e-health mobile self-management tools and patient education. For patients at risk to develop CPSP, TPS optimizes care by reducing opioid use, providing individualized education, and offering behavioral therapy to ease surgery-related anxiety while setting realistic expectations. Perioperative pain control is optimized via individualized multimodal and RA techniques, with related strategies prioritizing weaning from opioids, following initial pain control. Follow-up care includes a clinic visit 6–12 weeks postdischarge, to review treatment progress, coordinate care, by liaising with the patients' general practitioner, and consider referrals to services, like rehabilitation, addiction medicine, mental health services, and multidisciplinary chronic pain clinics, as needed, alongside ongoing surgical assessments.[6 32 38 48 59 60]

Neuromodulation techniques as a component of TPS

Various analgesic interventions were introduced to enhance RA and multimodal analgesia efficacy, currently being applied for both CPSP treatment and prevention, early targeting TP. Percutaneous peripheral nerve stimulation and stimulating peripheral nerve block catheters have been used for neuromodulation, with promising results on immediate postoperative pain,[61 62] although the underlying mechanisms remain unclear. Theoretical background supports CNS effects, through suppression of dorsal horn activity, or due to a conduction block of small-diameter fibers.[63] Cryoneurolysis (based on thermal neurolysis and prolonged disruption of pain signals conduction) has been effective in managing pain in procedures, including thoracotomy, TKA, and shoulder arthroplasty.[64] In contrast, radiofrequency therapy has shown no significant analgesic or functional benefits in recent pilot studies, 6 weeks post-TKA.[65] To date, none of these methods have yet demonstrated long-term analgesic effects or reduced CPSP, although they may be the focus of future research.

Similar to trials on multimodal analgesia and RA, those on neuromodulation techniques are inadequately designed to address the CPSP complexity and multifactorial nature. Future studies with larger sample sizes, longer follow-up, and a focus on individual pain trajectories could yield better results. High pain responders may benefit most from analgesic modalities in both the short-term and longer-term perspective. Instead of solely focusing on CPSP incidence, outcomes like pain characteristics and intensity might be more relevant. Nonetheless, preventing iatrogenic nerve injury during surgery is likely more crucial,[66] than any neuromodulation technique, as nerve injury is a major CPSP risk factor.

TPS: the European experience

Centers, such as the Toronto General Hospital TPS, established a successful history and hold a strong track record in reducing CPSP and minimizing opioid reliance, with their three-stage approach, driven by the alarming opioid crisis.[32 48 57–60] Similarly, Finland implemented an acute pain outpatient clinic to address the high-risk CPSP syndrome, highlighting a significant unmet need for better pain management worldwide. At hospital discharge, many patients were prescribed pain medications (54% weak opioids, 32% strong opioids, 71% gabapentinoids), but following clinic visits percentages dropped significantly (20%, 6%, and 43%, respectively). Additionally, 22% of patients were referred to multidisciplinary chronic pain clinics, emphasizing the complexity of pain management needs.[67] Effective TPS follow-up also addresses the psychosocial pain dimensions, including family dynamics and patient attitudes, to improve overall care that is influenced by pain perception and management.[32 48 55–60]

TPS utility and potential benefits versus standard of care (SoC) have been explored in several cohort studies, predominantly from North America, showcasing reduced opioid consumption or/and successful opioid tapering in both opioid-naive and opioid-non-naive patients, at 90-day to 6--month postsurgery follow-ups.[5 68–71] In Europe, TPS efficacy in patients at higher risk for CPSP development was compared with SoC in the Netherlands' TRUSt Study. Unlike prior trials, this RCT primary outcome focused on quality of recovery (QoR) on day 3 postsurgery, whereas secondary outcome measures included intergroup differences in postoperative opioid consumption. Although TPS did not significantly affect short-term QoR, it showed potential for improving long-term outcomes, such as CPS incidence, opioid consumption, and daily life functioning up to 6 months postsurgery.[72] Additionally, 81% of the TRUSt study staff endorsed TPS as an advancement in care, with 88% recommending the program continuation.[72] In Germany, the ongoing prospective POET–PAIN trial, involving almost 2000 patients across 6 university hospitals, is evaluating the TPS effectiveness and feasibility in elective surgeries associated with elevated CPSP risk, particularly for patients with somatic and/or psychosocial risk factors for its development. The study results are eagerly awaited to provide valuable insights once published.[73]

TPS implementation across Europe varies due to the diversity of healthcare systems, resources, and patient populations, whereas limitations in the available literature could be partially

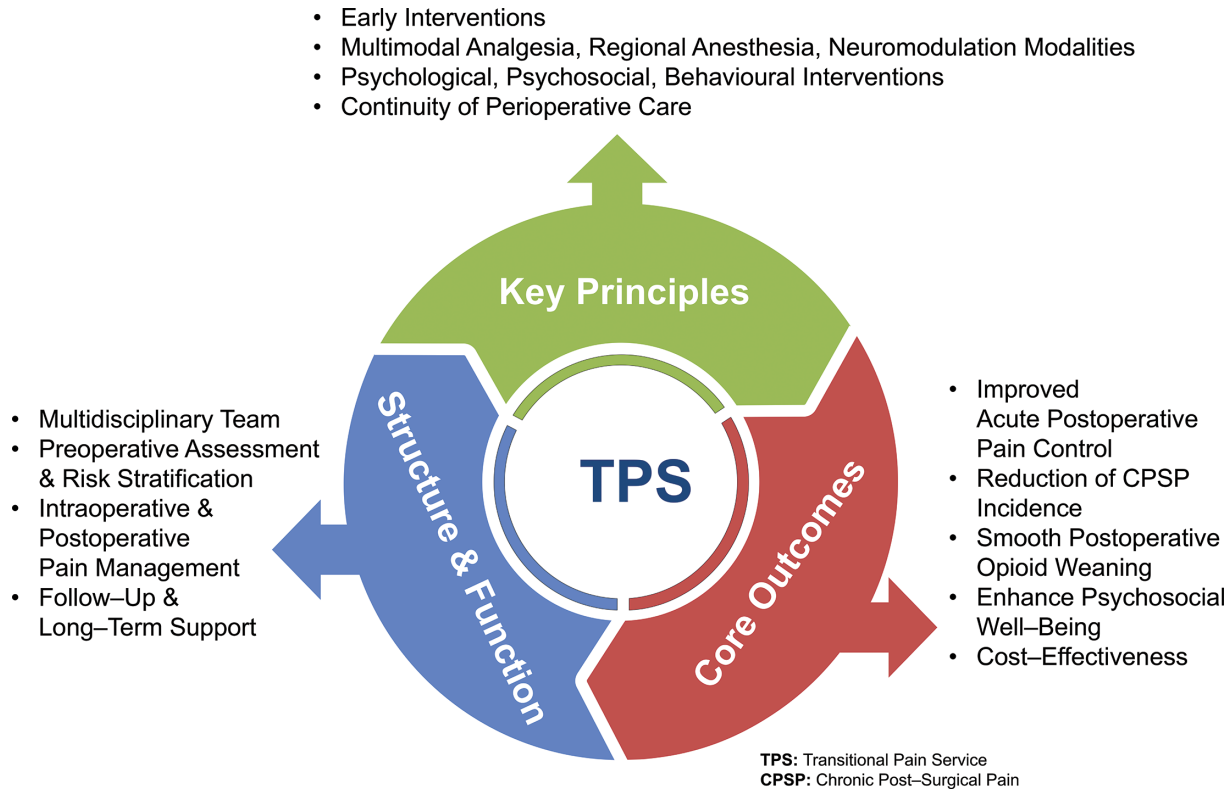

Figure 1 Key principles, structure and function and core outcomes of European transitional pain services (TPS).

attributed to methodological challenges and complexities in trial design, which may hinder full demonstration of TPS efficacy.[5 72] However, there is increasing recognition of TPS role in improving surgical outcomes and reducing CPSP burden. In this context, European TPS, also known as 'extended acute pain services (APS)', bridges the gap between traditional APS (developed in the 1990s) and chronic pain clinics. This gap emerged when CPSP was first reported over 25 years ago.[5 74] Key principles, structure and core outcomes of European TPSs are presented in figure 1. Although, from a publication point of view, the US and Canadian TPSs seem to focus primarily on preventing long-term opioid dependency, given the opioid epidemic,[5] their foundational goal is much broader. Like their European counterparts, North American TPS programs were created to address the management in relation to the transition from acute to chronic pain. While the opioid epidemic has heightened attention on opioid weaning, the original intent of US TPS aligns with the European model of preventing CPSP, by ensuring continuity of care across the entire pain management spectrum.[5 68 70 75]

Europe has not experienced an opioid crisis, despite an increase in opioid prescriptions since 2010.[76] A survey from the European Federation of IASP Chapters confirmed that "Europe, as a whole, is not facing an opioid crisis", despite differences across countries.[76] In contrast, the issue of persistent opioid use postsurgery (term with varying definitions across different reports) affects 3%–14% of previously opioid-naive US individuals.[5] Interestingly, a large cohort (N=129,379) found that the USA and Canada have a sevenfold higher postoperative opioid prescriptions rate, compared with Sweden.[77] Although European data on postoperative opioid use were previously inconclusive,[78] a European registry (Pain OUT, N=2326) revealed a decline in opioid consumption, from 5.5% before surgery to 3.5% 12 months after, with the highest long-term utilization risk among those with preoperative opioid use or non-surgery-related pain. Also, new opioid use postsurgery was 1.1%, with 0.7% being linked to CPSP.[79] Additionally, similar to the US practice, careful preoperative opioid weaning, where possible, has also gained popularity in Europe, as a potential intervention to help prevent CPSP, with related guidelines being available in the literature. Strong perioperative stewardship is recommended to address inappropriate opioid prescribing without affecting pain control, whereas opioids are advised to be judiciously prescribed before, during and after surgery.[80]

Patients with CPSP demonstrate a lower QoL regardless of opioid use. The ICD-11 new CPSP definition aims to improve CPSP identification, diagnosis, and treatment, recognizing it as a distinct disease.[7] A recent European survey (N=3297) reported 10.5% incidence 6 months after high-risk surgeries, including TKA, sternotomy, mastectomy, and endometriosis surgery.[81] CPSP severity encompasses a composite of patient pain-related outcomes (intensity, pain-related distress, and interference with daily activities), with a 3.3% of surgical patients being significantly affected.[9] Severe CPSP and NP components significantly impact psychological and functional well-being. Economically, similar to the USA and due to the large number of affected patients, in Europe, CPSP imposes a substantial burden of approximately €55,000/patient, including both direct and indirect costs (healthcare utilization, medication consumption, and lost income).[82 83]

Consequently, TPS establishment across Europe is logical and essential. While APS are well established,[84] TPS frameworks are still developing. A European TPS model could follow a similar approach to APS, focusing on key aspects, summarized in figure 2.

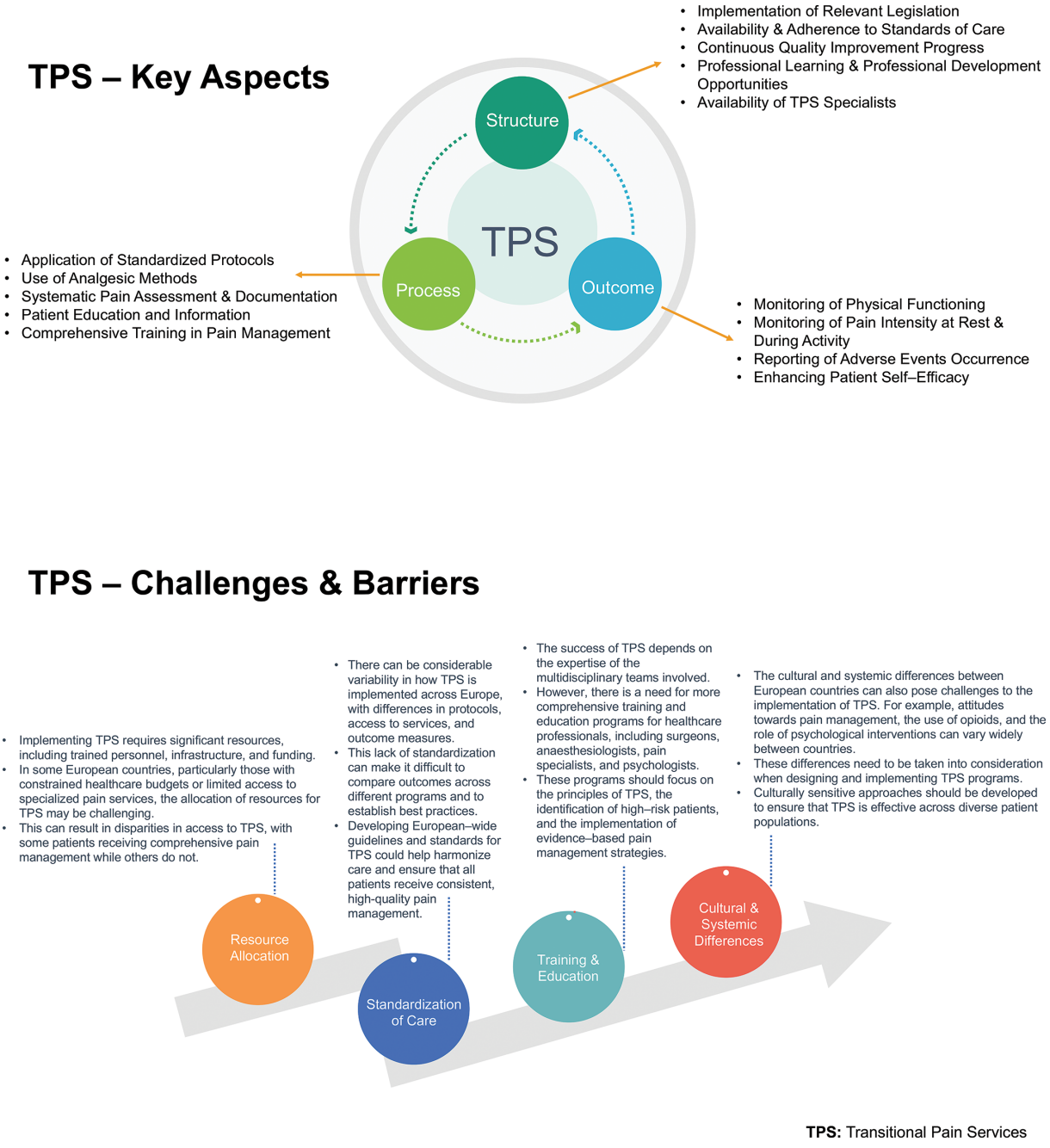

Figure 2 Organizational framework of European transitional pain services (TPS), following the model of acute pain services (APS)-related challenges and barriers.

Future directions: CPSP biosignature

CPSP severity is associated with NP components, in more than 50% of patients,[81 85] mainly observed after thoracic (thoracotomy, thoracoscopic surgery, sternotomy, breast surgery) and major orthopedic procedures (limbs, spine surgery). Recently, CPSP was reported after endometriosis surgery (16.2%), being associated with NP characteristics (41.4% of affected women).[81]

Such observations highlight the need for accurate CPSP assessment in all concerned patients. Initial TPS reports indicate that thoracic and orthopedic surgeries are the most common referral sources, with over 70% of CPSP patients suffering from NP, developing as early as 48 hours postsurgery (with a high chance of persistence after 2 months), or later, after a free interval.[67 86] Since preoperative predictive models have not led to effective prevention, identifying vulnerable patients postoperatively, during follow-up in TPS, may also be appropriate. Tailored therapeutic strategies should be promptly prescribed by pain specialists.[87] Although scientific evidence on TPS cost–benefit balance is limited, TPS could enhance CPSP mechanisms understanding and help stratifying patients into responders or non-responders to specific treatments.[72]

In this context, pain biomarkers could identify altered biological pathways and phenotypical expressions, offering treatment insights, and isolating at-risk individuals for early interventions. No biomarker has yet been validated for chronic pain. Recently, the Acute to Chronic Pain Signatures (A2CPS) program was launched, to develop biomarkers into biosignatures for pain chronification. A2CPS goal is to assess genomic, proteomic, metabolomic, neuroimaging, psychosocial and behavioral measures, aiming to extract valuable insights, covering the existing literature gaps.[88]

These approaches provide a system-level understanding of biological systems, enabling to uncover novel biomarkers and identify therapeutic targets. Combining unbiased proteome analysis with psychosocial and psychophysical factors can develop accurate CPSP predictive tools. Multivariate analyses, such as logistic regression or machine learning, might help determine the independent contribution of each factor in large-scale studies. Ultimately, integrating various preoperative, intraoperative, and postoperative factors in such studies could improve CPSP prediction, enable tailored preventive interventions, and reduce the CPSP burden.[89 90]

Indeed, the ongoing work on biosignatures underscores the growing necessity for personalized pain medicine, an approach that is expected to gain increasing support in the coming years. This represents a significant and much-needed shift away from the generalized ERAS-for-all strategy. It reinforces the idea that there is no "one-size-fits-all" model in perioperative medicine, advocating instead for individualized pain management plans to optimize patient outcomes.

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