# Bridging the pain gap after cancer surgery - Evaluating the feasibility of transitional pain service to prevent persistent postsurgical pain - A systematic review and meta-analysis

### Address for correspondence:

Dr. Raghu S. Thota,
Department of Palliative
Medicine, MB-75, Ground
Floor, Tata Memorial
Hospital, E. Borges Road,
Parel, Mumbai - 400 012,
Maharashtra, India.
E-mail: ragstho24@gmail.com

Submitted: 12-Apr-2024 Revised: 03-Jun-2024 Accepted: 23-Aug-2024 Published: 14-Sep-2024 Raghu S. Thota, S Ramkiran¹, Aveek Jayant², Koilada Shiv Kumar², Anjana Wajekar³, Sadasivan Iyer⁴, Ashwini M⁵

Palliative Medicine, Tata Memorial Centre (Tata Memorial Hospital), Homi Bhabha National Institute, 
<sup>1</sup>Department of Onco-Anaesthesiology and Critical Care, Sri Shankara Cancer Hospital and Research Center, Bengaluru, Karnataka, <sup>2</sup>Anaesthesiology, Critical Care and Pain, Homi Bhabha Cancer Hospital and Research Centre, Vishakapatnam, Andhra Pradesh, <sup>3</sup>Anaesthesiology, Critical Care, Pain, Tata Memorial Centre (ACTREC), Homi Bhabha National Institute, <sup>4</sup>Anaesthesia and Pain Management, Manipal Hospital, Bengaluru, 
<sup>5</sup>Department of Biostatistics, ICAR-NIVEDI, Ramagondanahalli, Yelahanka, Bengaluru, Karnataka, India

#### **ABSTRACT**

Background and Aims: The lack of a dedicated pain service catering to the postsurgical period has resulted in the origination of the pain-period gap. This has led to a resurgence of transitional pain service (TPS). Our objective was to evaluate the feasibility of TPS in pain practice among postsurgical cancer patients and its prevention of persistent postsurgical pain (PPSP), culminating in chronic pain catastrophising. Methods: The protocol for this meta-analysis was registered in the International Prospective Register of Systematic Reviews (ID: CRD42023407190). This systematic review included articles involving all adult cancer patients undergoing cancer-related surgery experiencing pain, involving pharmacological, non-pharmacological and interventional pain modalities after an initial systematic pain assessment by pain care providers across diverse clinical specialities, targeting multimodal integrative pain management. Meta-analysis with meta-regression was conducted to analyse the feasibility of TPS with individual subgroup analysis and its relation to pain-related patient outcomes. Results: Three hundred seventy-four articles were evaluated, of which 14 manuscripts were included in the meta-analysis. The lack of randomised controlled trials evaluating the efficacy of TPS in preventing PPSP and pain catastrophising led to the analysis of its feasibility by meta-regression. The estimate among study variances  $\tau^2$  was determined and carried out along with multivariate subgroup analysis. A regression coefficient was attained to establish the correlation between the feasibility of TPS and its patient outcome measures and opioid-sparing. Conclusion: TPS interventions carried out by multidisciplinary teams incorporating bio-physical-psychological pain interventions have resulted in its successful implementation with improved pain-related patient outcomes mitigating the occurrence of PPSP.

**Keywords:** Acute pain service, chronic postsurgical pain, opioid-sparing, onco-anaesthesia, pain catastrophising, palliative care, persistent postsurgical pain, transitional pain service

# Access this article online

Website: https://journals.lww. com/ijaweb

DOI: 10.4103/ija.ija\_405\_24

Quick response code



## INTRODUCTION

Most cancer centres have well-established acute pain services (APSs) and chronic pain services. The most vulnerable time patients experience postsurgical pain is after hospital discharge and while resuming their routine activities. Ironically, the transition between discharge from hospital to This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow\_reprints@wolterskluwer.com

**How to cite this article:** Thota RS, Ramkiran S, Jayant A, Kumar KS, Wajekar A, Iyer S, *et al.* Bridging the pain gap after cancer surgery – Evaluating the feasibility of transitional pain service to prevent persistent postsurgical pain – A systematic review and meta-analysis. Indian J Anaesth 2024;68:861-74.

home and follow-up visits to hospital results in a pain gap. The pain gap could be attributable to the absence of a dedicated pain service, and the inability to address this gap has contributed to the evolution of persistent postsurgical pain (PPSP). The failure to recognise the pain and period gap has resulted in poor quality of life and physiological implications with adverse physical and psychological effects.<sup>[1,2]</sup> This is where the need for a dedicated transitional pain service (TPS) emerges.<sup>[2,3]</sup>

TPS strives to bridge the 'pain gap' and the 'period gap' (hospital care progressing to home care and transitioning back), providing a care continuum among postsurgical patients and modulating pain trajectories. [2-7] TPS has evolved as a new paradigm for preventing PPSP transformation by including multidisciplinary integrative pain modulation and intervention pathways utilising bio-psychosocial interventions. [4] This review aims to evaluate the feasibility of TPS in bridging the perioperative pain gap and prevention of PPSP after major cancer surgery.

### **METHODS**

Protocol for the review was registered prospectively in the International Prospective Register of Systematic Reviews (PROSPERO) database (ID: CRD42023407190) reported according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement. The analysis included patients undergoing pain-eliciting oncological treatment and surgical procedures. The TPS intervention is used to bridge perioperative analgesia and prevent PPSP. Standard-of-care cancer pain practice involving APSs and chronic pain clinics in the perioperative period was included for comparison.

## Study design

This systematic review included randomised clinical trials and observational cohort studies. Relevant manuscripts about editorial reviews, letters to the editor and narrative review articles were not considered. Isolated case reports/series, institution protocols, educational media, non-indexed internet publications, abstract-only papers and studies on human volunteers were excluded.

All the manuscripts were evaluated in their full available version. Emphasis was placed upon extracting high-quality data and rigorous internal independent quality assessment utilising inter-rater reliability agreement between two authors regarding the risk of bias (ROB) based on the Kappa statistical table. [9,10]

# Search strategy and data collection

The search strategies were defined to include title, abstract and full text published to include publications on TPS from January 2012 till March 2023, published in English about 'transitional pain service' with full text available for retrieval. The keywords included 'TPS', 'TPS feasibility', 'PPSP', 'Pain catastrophising' and '2012-2023'. Web-based tools Zotero 5.0 and Rayyan Qatar Computing Research Institute (QCRI) were utilised to conduct systematic reviews and compilations, and a comprehensive and robust exploration of the research topic was used along with a back-reference search[11,12] [Appendix 1]. Two independent authors interpreted and validated the data. The disagreements were resolved after discussion. In addition, the agreement was subjected to intraclass coefficient (ICC) (interobserver correlation by an ICC) and the 'Cohen's kappa' value towards literature search with selection of primary studies for inclusion in the meta-analysis and inter-rater reliability was derived to be 0.79, which was considered to be 'substantial agreement'.[9,10] Both authors agreed upon including 14 studies in a meta-analysis from among the 27 studies [Figure 1].

## **Primary outcome**

The primary outcome was to evaluate the feasibility of TPS in preventing PPSP after cancer surgery, thereby bridging both the pain and period gap in the context of an effective pain service.

# Subgroup analysis and synthesis of secondary outcomes

A meta-analysis was performed to assess the feasibility of TPS in the context of PPSP. Employing the R open-source scripting software version 3.2.5 for statistical analysis (v3.2.5; RCore Team 2021), the effect size was realised through a forest plot with its associated confidence intervals (CIs). The meta-analysis protocol included integrating fixed and random effects models to account for the diversity and inconsistency (I²) embedded within the collective studies. For heterogeneity among the studies, the meta-regression and subgroup analysis was done to address the issue of heterogeneity. Meta-regression was performed on the statistical software package using R open-source scripting software version 3.2.5 (The R Foundation, Vienna, Austria) to delineate

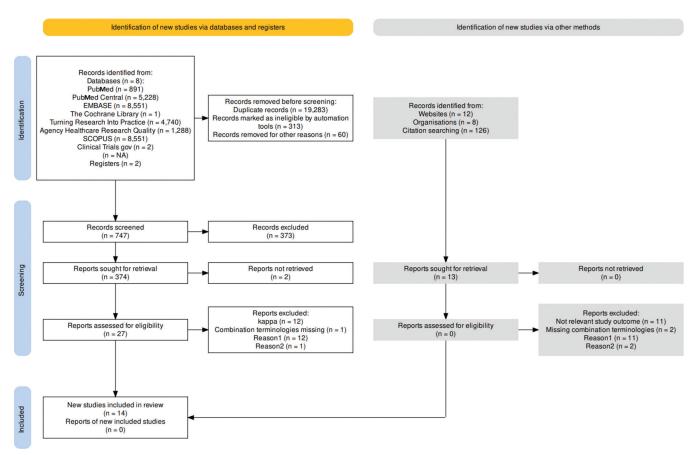


Figure 1: PRISMA flow chart deriving review synthesis. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses

the study characteristic with its intervention effect of TPS, and subgroup analysis was performed across various clinical settings involving diverse study populations. [16] Random effects analysis by meta-regression was principally employed as the number of studies was heterogeneous and very limited, as per the Cochrane guidelines for systematic intervention reviews. [17]

ROB was assessed by utilising the ROBVIS application tool (McGuiness LA 2019). Publication bias was assessed by a funnel plot, and its outliers were excluded from the final analysis.<sup>[18-23]</sup>

# **RESULTS**

Database and hand search yielded 29,252 titles and abstracts [Figure 1]. Of these, 27 articles were eligible, and a full article review was independently conducted by two authors on these 27 articles. An assessment of inclusion was contemplated after the quality content of studies using the kappa index was assessed for agreement. Fourteen manuscripts qualified to be included in the meta-analysis based on randomised controlled trials (RCTs) or observational

cohort studies evaluating the burden of PPSP and its prevention  $^{[24-37]}$  [Table 1].

Using the meta-regression approach, a subgroup analysis was performed. Variables such as geographical diversity, sample size, diagnostic test utility and quality scores related to its inherent potential bias were scrutinised using meta-regression to quantify the extent and magnitude of heterogeneity within the dataset [Table 2]. The findings of this meta-regression analysis underscored the influential role of specific covariates in the observed study heterogeneity. These covariates included the size of the sample (regression coefficient for events: Qm = 128.51, P < 0.001), the techniques employed for detection (tests; Om = 118.68, P < 0.001), the classification of study species (Qm = 11.79, P < 0.001) and countries in which the studies were conducted (Qm = 138.83, P < 0.001) (Qm represents meta-regression as a measure of the overall fit of the technologies used) [Table 2].

A regression coefficient was attained to establish the correlation between the feasibility of TPS and its outcome measures on patient satisfaction and opioid

		litative synthesis of high	•	•		
Author	Population	Intervention	Comparator	Outcome	Study design	Results and conclusion
Admiraal et al. <sup>[24]</sup>	176 patients at risk for CPSP	TPS	Standard of care	Quality of recovery (primary)	RCT	Short-term outcomes are not affected
(TRUSt)				Opioid consumption		Might improve long-term outcomes. Decreased opioid use
Liang <i>et al</i> . <sup>[25]</sup>	95 patients with ankylosing spondylitis	Nurse-led multidisciplinary transitional care	Routine nursing care	Clinical outcomes (short form 36) and quality of life	RCT	Improved clinical outcome and quality of life
Wang and Wu <sup>[26]</sup>	156 patients undergoing cancer pain management	Transitional care model in cancer pain management	Standard care	Pain score Quality of life Patient satisfaction Adequacy of opioids	RCT	Reduction in pain scores, higher satisfaction and quality of life and adequacy of opioids
Abid Azam et al. <sup>[27]</sup>	382 patients undergoing multidisciplinary TPS to manage CPSP	ACT as part of multidisciplinary TPS	No ACT	Behavioural pain management and opioid consumption	RCT	ACT as part of TPS resulted in reduced opioid use, improved mood and pain interference/ catastrophising
Featherall et al. <sup>[28]</sup>	208 patients undergoing total joint arthroplasty	TPS	Historical control	Opioid use at 90 days (primary) Postoperative outcome scores and opioid consumption (secondary)	RCT	TPS resulted in a reduction in opioid prescription consumption, leading to a reduction in persistent opioid use
Clarke et al. <sup>[29]</sup>	251 high-risk TPS patients	TPS among opioid naïve	TPS among opioid experience	Opioid use, opioid weaning rate and pain management	POS	Successful opioid weanin in 50% of opioid naïve and 25% of opioid experienced
Hussain et al. <sup>[30]</sup>	86 patients	Tele-TPS among opioid-naïve and exposed patients		Opioid tapering CBT achieving TPS efficacy on persistent opioid use and pain/ behavioural outcomes	POS	100% efficacy in opioid tapering among opioid naïve and in 52% among opioid exposed
Haynes et al. <sup>[31]</sup>	31 paediatric patients	To evaluate the risk factors and clinical features of PPSP in a paediatric complex pain service after introduction of TPS		TPS-based intervention	ROS	TPS-based non-pharmacological strategies and conservative use of opioids by TPS are the best ways of preventing PPSP
Buys <i>et al</i> . <sup>[32]</sup>	Observational study among 336 veterans undergoing major joint surgery	To evaluate the reduction in opioid use by TPS		TPS reduced the onset of new chronic opioid use	ROS	Implementation of TPS resulted in opioid consumption and opioid weaning among preexisting opioid users
Buys <i>et al</i> . <sup>[33]</sup>	Observational study among 213 veterans undergoing orthopaedic surgery	To evaluate reduction in opioid usage by TPS among 72% opioid naïve	Evaluate opioid usage by TPS among 28% chronic opioid users	TPS as an emerging concept in perioperative surgical home concept	ROS	Multidisciplinary TPS for veteran population decreased by 40% without affecting the pain intensity and physical function
Huang et al. <sup>[34]</sup>	Single-centre, observational cohort study on 200 APS patients by telephonic interview	To evaluate the incidence of PPSP and persistent opioid use utilising the pain disability index, brief pain inventory and health outcome questionnaire- EuroQol 5 Dimension 5 Level (EQ-5D-5L)	APS—TPS combination to evaluate opioid usage	Postoperative opioid use is associated with lower mood and functional interference, leading to pain-related daily life disability	POS	Utility of TPS in modifying pain trajectories and effective opioid weaning

Thota, et al.: Transitional pain services to prevent persistent postsurgical pain

		Ta	ble 1: Contd			
Author	Population	Intervention	Comparator	Outcome	Study design	Results and conclusion
Montbriand et al.[35]	Retrospective study of 239 patients	Association of smoking status and pain along with opioid use	Non-smokers	Higher pain intensities and opioid consumption among smokers are associated with higher pack-years	ROS	TPS-initiated smoking cessation as a modifiable risk for opioid use after surgery
Liu <i>et al.</i> <sup>[36]</sup>	Prospective cohort study among 279 patients undergoing thoracic surgery	To evaluate pain trajectories among elective thoracic surgery patients until 1 year after surgery	Regional anaesthesia techniques and psychological assessed interventions for reducing pain catastrophising	Pain-related outcomes and complications among three subgroup pain trajectories constituted as mild or moderate and associated with pain catastrophising	POS	Higher preoperative pain catastrophising and occurrence of immediate postoperative pain progress to severe CPSP
Yu et al. <sup>[37]</sup>	TPS retrospective cohort study among 140 patients undergoing solid organ transplant surgery	Opioid consumption, pain catastrophising and psychological attributes evaluated	TPS in transplantation surgery evaluated	Association between opioid consumption, psychological characteristics and pain incorporating psychology and physiotherapy	ROS	Treatment by the multidisciplinary TPS team was associated with significant improvement in pain severity and a reduction in opioid consumption

ACT=acceptance and commitment therapy, APS=acute pain service, CBT=cognitive behavioural therapy, CPSP=chronic postsurgical pain, POS=observational studies based on prospective cohort population, PPSP=persistent postsurgical pain, RCT=randomised controlled trial, ROS=observational studies based on mixed cohort population, TPS=transitional pain service

Group	Particulars	SE	Z	Estimated (95% CI)	Qm	P
Sample size	High	0.15	8.71	1.23 (0.99, 1.57)	128.51	<0.001
	Low	0.15	7.26	1.08 (0.78, 1.37)		
Detection	Observational Study (P)	0.20	5.43	1.10 (0.70, 1.50)	118.68	< 0.001
techniques	RCT	0.18	7.28	1.33 (0.97, 1.68)		
	Observational study®	0.18	6.01	1.10 (0.73, 1.45)		
Category of	(ACT- TPS)	0.43	3.68	1.57 (0.73, 2.40)	11.79	< 0.001
species	(APS- TPS)	0.43	3.67	1.57 (0.73, 2.40)		
	Pain catastrophising and psychological interventions	0.43	2.74	1.17 (0.33, 2.01)		
	Tele-TPS on opioid naive	0.43	1.84	0.79 (-0.04, 1.62)		
	TPS on opioid naive	0.43	2.10	0.89 (0.05, 1.73)		< 0.001
	TPS-based weaning	0.15	7.42	1.12 (0.82, 1.41)		
	Transitional care nurse based	0.43	3.67	1.57 (0.73, 2.40)		
Country	Australia	0.38	1.29	0.49 (-0.25, 1.24)	138.83	< 0.001
	Canada	0.16	7.51	1.17 (0.86, 1.48)		
	China	0.27	4.89	1.33 (0.79, 1.86)		
	Veteran USA	0.38	4.09	1.57 (0.81, 2.32)		
	The Netherlands	0.38	2.21	0.84 (0.09, 1.59)		
	USA	0.22	5.92	1.31 (0.87, 1.74)		

ACT=acceptance and commitment therapy, APS=acute pain service, CI=confidence interval, SE=standard error, TPS=transitional pain service

consumption, enabling us to find whether a linear relationship was demonstrable. The estimate among study variances  $\tau^2$  was determined using the most extreme probability assessment [Figure 2]. Effect size (sample size) was regressed against the moderator variable. Several moderators were considered, including the diagnostic assay, geographical region, year of publication and relative sample size while performing univariate meta-regression analysis. While

transitioning to the multivariable meta-regression phase, only those variables that demonstrated a P value below 0.05 in the univariate analysis were retained [Table 2]. The estimate among study variances  $\tau^2$  was determined, and the P value from each regression coefficient was further analysed to find differences among subgroups from TPS intervention. The final model included factors that exhibited statistical significance (P value threshold of  $\leq$ 0.05) [Table 3].

## Risk of bias and publication bias

RCTs were evaluated utilising the ROB2 tool, and observational studies using the ROBINS-E tool [Figures 3 and 4]. The funnel plot reveals asymmetry attributed to publication bias, potentially arising from the variability that causes smaller studies to report effects that notably deviate from larger ones [Figure 5]. Among the research articles, the majority were dispersed outside the funnel, with only a few falling within it, indicating presence of publication bias. the To address the potential ramifications of publication bias, we employed meta-regression, integrating sample size as a parameter for assessing ROB. The analysis yielded outcomes that were not statistically significant (P < 0.05), thus mitigating the impact of publication bias on the study's conclusions. The outcome indicated non-significance (P > 0.05),

nullifying publication bias's impact within the study.

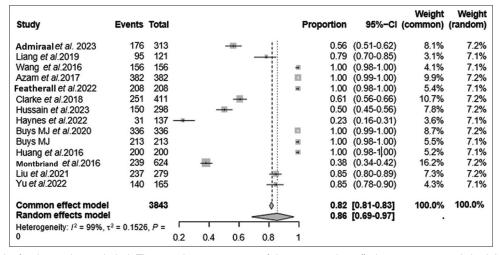
The stratification of sample sizes revealed notable disparities in feasibility rates of TPS pain-related interventions among patients. Studies falling below the median sample size reported a higher percentage of 92% (95% CI: 71%, 100%,  $I^2=100$ ,  $\tau^2=0.14$ , P<0.01), while those exceeding the median sample size exhibited a lower feasibility percentage of 77% (95% CI: 99%, 96%,  $I^2=99$ ,  $\tau^2=0.16$ , P<0.01) [Tables 2, 3 and Figure 6].

# Subgroup analysis after meta-regression

Subgroup analysis helps identify potential effect modifiers or factors influencing outcomes due to TPS, resulting in the development of tailored interventions or treatment strategies [Table 3 and Figures 6, 7]. The

Group	Subgroup	<b>I</b> <sup>2</sup> %	<b>T</b> <sup>2</sup> %	P	Total no. of studies	Total no. of samples	Feasibility (%)	95% CI
Events	High	99	0.16	<0.01	7	1390	77	(0.99, 0.96)
	Low	100	0.14	<0.01	7	2453	92	(0.71, 1.00)
Detection	POS	99	0.12	<0.01	4	1188	80	(0.48, 0.98)
techniques	RCT	99	0.12	0	5	1180	99	(0.74, 1.00)
	Other observational studies (ROS)	100	0.25	<0.01	5	1475	79	(0.37, 1.00)
Species	Subspecific TPS	100	0.18	0	9	2499	85	(0.61, 0.69)
Country	Canada	100	0.13	<0.01	6	2061	85	(0.60, 0.99)
	China	98	0.11	<0.01	2	277	94	(0.57, 1.00)
	USA	100	0.20	< 0.01	3	842	93	(0.51, 1.00)

CI=confidence interval, POS=observational studies based on prospective cohort population, RCT=randomised controlled trial, ROS=observational studies based on mixed cohort population, TPS=transitional pain service



**Figure 2:** Forest plot for the studies included. The visual representation of the meta-analysis findings was accomplished through forest plots. These plots depict each study's effect size and corresponding Cls. Within these plots, each study is portrayed as a square, indicating the point estimate of the effect size. In addition, extending from the square is a horizontal line that represents the 95% Cl. Each square's size indicates the study's weight within the broader meta-analysis context. The diamond represents heterogeneity, and its increasing width depicts increased heterogeneity. The outcome evaluated was the feasibility of TPS, estimated at 86% (0.86 proportion depicted on the random effects model). Cl = confidence interval, TPS = transitional pain service

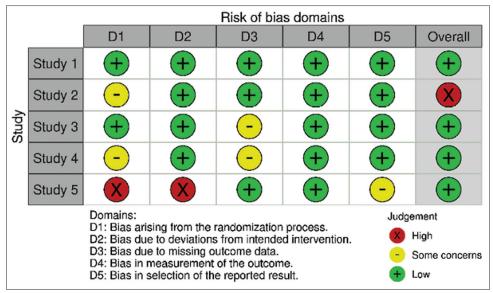


Figure 3: Risk of bias (ROB2) for randomised controlled studies. Risk of bias domains (ROB2) represented on the X-axis; and randomised controlled studies included in the meta-analysis represented on the Y-axis

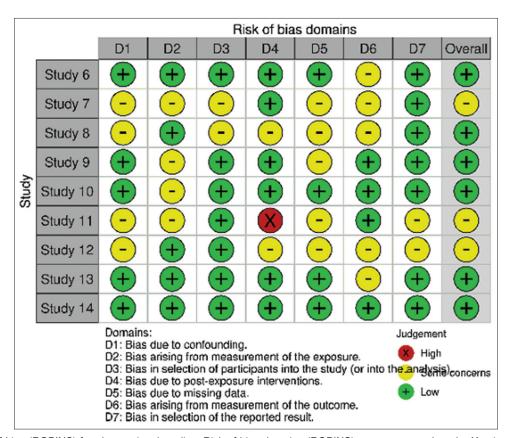
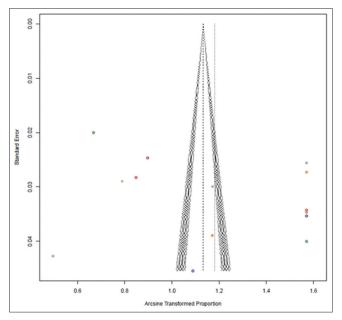


Figure 4: Risk of bias (ROBINS) for observational studies. Risk of bias domains (ROBINS) are represented on the X-axis; and observational studies included in the meta-analysis represented on the Y-axis

RCT, although showing a high effectiveness feasibility rate with 99% (95% CI: 74%, 100%,  $I^2 = 99$ ,  $\tau^2 = 0.12$ , P < 0.01), needed further investigation towards refinement in its study design. The observational studies involving prospective cohorts showed 80%

feasibility efficacy (95% CI: 48%, 98%,  $I^2 = 99$ ,  $\tau^2 = 0.12$ , P < 0.001), a substantial effectiveness rate, signifying their potential utility in identifying patients who may benefit from TPS interventions. We also analysed observational studies with random mixed cohort,

which showed 79% efficacy in feasibility (95% CI: 37%, 100%,  $I^2 = 100$ ,  $\tau^2 = 0.25$ , P < 0.001), again a notable effectiveness rate, also providing valuable insights into



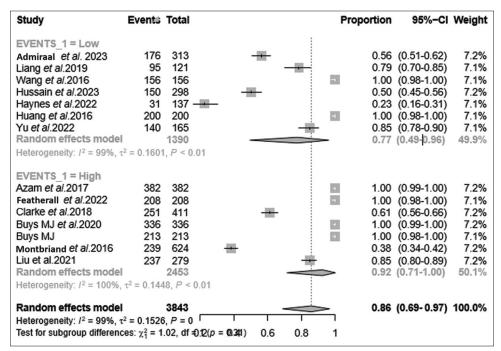
**Figure 5:** Funnel plot representing publication bias among the included studies. The X-axis is represented by the proportion of the arcsine transformation of the study fraction, and the standard error represents the Y-axis. Symmetry of funnel plot is established. The outliers in the study are represented in dotted colour, and their associated asymmetry is depicted, contributing to the heterogeneity of studies

early identification of pain catastrophising within TPS feasibility studies [Table 3, Figure 7]. This refinement becomes particularly crucial when considering various countries, varied diagnostic test methodologies and distinct categorisations of study species. Focusing on subspecific TPS groups within TPS feasibility studies revealed a percentage of 85% (95% CI: 61%, 69%,  $I^2 = 100$ ,  $\tau^2 = 0.18$ , P = 0). Its high effectiveness rate emphasises the relevance and applicability of TPS interventions in addressing pain-related challenges among subspecific TPS [Table 3 and Figures 6, 7]. However, the subspeciality and subspecific TPS domains did not achieve significance with the *P* value. This finding highlights the need for patient-centred approaches and the customisation of TPS strategies to suit individual patient needs and preferences.

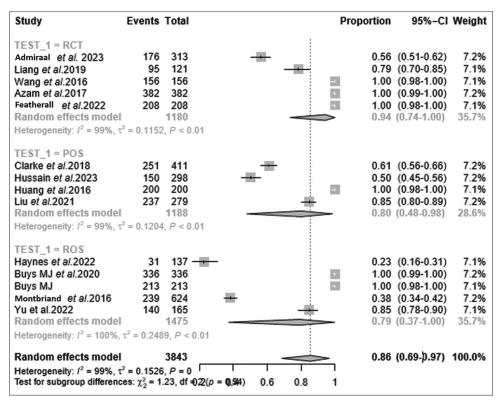
## **DISCUSSION**

We evaluated the feasibility of TPS and its efficacy in preventing PPSP and achieving opioid sparing during its process.

It is catastrophic that 5%–60% of postoperative patients bear the burden of PPSP across various surgeries, leading to debilitated recovery. The median prevalence of PPSP is 20% in the paediatric



**Figure 6:** Subgroup analysis based on forest plot for event occurrence. Forest plot portraying subgrouping of sample size based on the events (high-occurrence vs. low-occurrence events) among the studies evaluated. TPS feasibility was estimated to be 77% among studies with low occurrence of events (PPSP, PCS), whereas the feasibility attained 92% among studies with high occurrence of events (PPSP, PCS). The overall feasibility of TPS was 86% on the random effects model. PCS = pain catastrophising, PPSP = persistent postsurgical pain, TPS = transitional pain service



**Figure 7:** Subgroup analysis based on forest plot portraying subgrouping by detection techniques based on the study type involved. Random effects model depicting efficacy proportions for each study subtype involved. Feasibility of TPS was estimated among studies involving RCT at 94%, POS at 80% and ROS at 79%. CI = confidence interval, POS = observational studies based on prospective cohort population, RCT = randomised controlled trial, ROS = observational studies based on mixed cohort population, TPS = transitional pain service

population undergoing surgery.[39] PPSP contributes up to 25% workload of pain clinics, which could instead be diverted to TPS. The prevalence of PPSP is extremely variable (3%-85%) across multiple studies, with an incidence of about 10%.[2,40,41] Amputation (85%), thoracotomy (65%), craniotomy (65%), hernia (63%), mastectomy (57%), spine surgery (56.5%) and joint replacement (48.7%) reported the highest prevalence of PPSP.[4,42,43] PPSP has been linked with higher preoperative pain scores, lower pro-nociceptive conditioned pain modulation and enhanced temporal pain summation.[3,41,44] The prevalence of persistent pain after breast cancer treatment (surgery, hormonal, immuno-chemo-radiation) was reported to be 21.8% among breast cancer survivors, leading to a negative impact on recovery, quality of life, functional limitation and psychological distress.[1,44-49] Persistent pain following cancer surgery always needs to be differentiated from the possibility of a local recurrence. It is important to note that a high pain catastrophising score has been considered an independent risk factor for PPSP.[4,5,33,41,44,46,50]

Qualitative pain-related patient outcomes in the form of quality of recovery, patient satisfaction,

quality of life, early return to intended oncological treatment (RIOT), evaluating return to baseline activities of daily routine and patient disability interference need to be considered as TPS quality indicators. Pain-psychological interventions and coping strategies by TPS prevent PPSP, with an emphasis on perioperative opioid-sparing strategies and opioid de-escalation in substance use [Table 4]. The intervention of TPS in the causation of heterogeneous outcome effects like improved pain-related patient outcomes and achieving opioid sparing, as well as considering multiple explanatory variable factors in its causation, like pain catastrophising and antecedent clinical predispositions, were analysed.

The stratification of sample sizes revealed notable disparities in the feasibility rates of TPS pain-related interventions among patients. Studies falling below the median sample size reported a higher percentage of 92%, while those exceeding the median sample size exhibited a lower feasibility percentage of 77%. The high events subgroup, with a significant effectiveness rate and a narrow CI, suggests a substantial need for TPS interventions among these patients. Conversely, despite a higher effectiveness rate, the low events

	Table 4: Interventions in TPS	
Non-pharmacological	Pharmacological	Pain interventions
Physical therapy	Tricyclic antidepressants	Head and neck
Acupuncture, Acupressure	Amitriptyline	Cervical plexus block, TMJ injection
Myofascial trigger	SNRI	Buccal infiltration, dental intraligamental injection, inferior alveolar nerve
TENS	Venlafaxine, duloxetine	Infraorbital, mandibular nerve, suprazygomatic maxillary nerve blocks
Whole body exercise (walking, cycling)	Antiepileptics	Breast
Yoga	Levetiracetam	Thoracic paravertebral block (radiofrequency ablation, steroids)
Resistance training	Gabapentinoids	Intercostobrachial nerve, pectoralis-II, serratus anterior plane
Targeted functional exercises (shoulder exercise)	Gabapentin, pregabalin	Proximal intercostal, erector spinae blocks
Laser therapy	NMDA antagonist	Thoracic
Magnetic stimulation	Low-dose ketamine, magnesium, memantine, nitrous oxide	Thoracic epidural, thoracic paravertebral, erector spinae plane
	Opioids	Intercostal, serratus anterior plane blocks
Psychological therapy	Oxycodone, tramadol, tapentadol, morphine, fentanyl patch	Upper abdomen
CBT	Opioid substitutes	Thoracic epidural, thoracic paravertebral
ACT	Buprenorphine, buprenorphine- naloxone, methadone, cannabis	Erector spinae plane, subcostal transversus abdominis plane
Pain neuroscience education	Steroids	Quadratus lumborum, rectus sheath blocks
MBI	Dexamethasone, depot methylprednisolone	Abdominopelvic
Dialectical behavioural therapy	NSAIDs	Lower thoracic/lumbar epidural, paravertebral block
Desensitisation	Randomised	Transversus abdominis plane, quadratus lumborum
Sensory discrimination training	Alpha-2-agonist	Ilioinguinal, fascia iliaca, rectus sheath blocks
Guided imagery	Clonidine, dexmedetomidine	Miscellaneous
Music therapy	Local anaesthetics	Sympathetic-mediated blocks, epidural steroid, spinal cord stimulation
Relaxation techniques	Intravenous lignocaine, liposomal bupivacaine	Intra-articular local anaesthetic, continuous wound infiltration devices
Clinically induced hypnosis	Topical Capsaicin, prilocaine, eutectic mixture	Subcutaneous infusion pumps, transdermal drug delivery and subperiosteal catheters

ACT=acceptance and commitment therapy, CBT=cognitive behavioural therapy, MBI=mindfulness-based intervention, NMDA=N-methyl-d-aspartate, NSAIDs=nonsteroidal anti-inflammatory drugs, SNRI=serotonin–norepinephrine reuptake inhibitor, TENS=transcutaneous electrical nerve stimulation, TMJ=temporomandibular joint, TPS=transitional pain service

subgroup indicated a wider range of effectiveness, possibly influenced by patient characteristics and treatment modalities. This variation underscores the need for tailored TPS interventions based on the severity and nature of patients' individualised perioperative pain experiences.

Effective TPS workflow [Figure 8] implementation begins during a preoperative visit, during which patient education, multimodal prehabilitation and pain coping skills are imparted. APSs involve intraoperative regional anaesthesia techniques and the adaptation of enhanced recovery after surgery protocols, thereby facilitating early RIOT. Intensive physical therapy involving progressive resistance training, functional aerobic exercise and psychological interventions by combined APS-TPS further enhance recovery. The goal of the combined APS-TPS is to recognise acute

postoperative pain persisting beyond the conventional tissue healing duration, predisposing further to PPSP and chronic pain if not intervened.<sup>[2,4]</sup>

Patients on preexisting opioids presenting for surgery need titrated dose optimisation, opioid alternatives, behavioural counselling and pain coping strategies towards achieving meaningful opioid weaning. [3,5] TPS attributes the highest potential to de-escalate opioids even in complex postsurgical pain, which offers the critical window to de-escalate opioids by regional anaesthesia and non-opioid analgesic strategies. The surrogate goal of TPS would strive to prevent persistent opioid usage and mitigate opioid crisis. [5,29,32,34,51-53] Introduction of TPS results in overall opioid prescription reduction from 27.3% to 13.4% among both opioid-naïve and chronic opioid users. [32] Tele-TPS reduces frequent hospital visits and

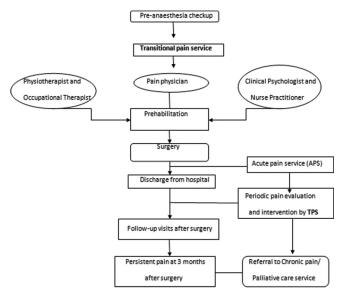


Figure 8: Workflow in TPS. TPS = transitional pain service

possesses immense future potential in cancer pain management.[2,4,5,54] Cognitive behavioural therapies, mindfulness-based interventions, mind-body exercises for stress reduction and acceptance commitment therapy (ACT) have revolutionised TPS and improved the quality of life.[29,33,34,41,52-58] ACT incorporates acceptance and committed action towards achieving a value-based goal by imparting pain education, pain coping skills and mindful acceptance towards the pain experience.[1,5,47,52,59-61] Pharmacological therapy and interventions in continuous wound infiltration, regional anaesthetic blocks, central neuraxial block, spinal cord stimulation, fascial plane blocks, targeted nerve blocks, ganglion and sympathetic blocks have all added new dimensions for pain intervention in TPS [Table 4].[1,3,5,44,62-65]

## Strength and limitations

The strength of our study was evaluating the feasibility of establishing TPS. The incorporation of an independent TPS team augurs well for bridging the pain gap after cancer surgery, involving both APSs and chronic pain services. However, the review has limitations in that the administrative/economic/ financial/managerial/human resource and functional logistics of the institution or hospital were not considered in establishing dedicated TPS. An already overburdened pain department would be required to double up to establish TPS. Our study could not perform a sensitivity analysis, which accounts for its limitation. Further RCTs and future meta-analyses are needed to establish whether the inculcation of TPS would positively impact reduction in PPSP upon

opioid sparing and by what quantitative/qualitative extent of the effect.

### CONCLUSION

TPS involves individualised preoperative pain evaluation, identification of pain catastrophising, implementation of pain education, and imparting multimodal prehabilitation and early pain coping interventions to modify pain trajectory perioperatively. The feasibility of TPS has been established with meta-regression analysis by stratification of median sample sizes, with feasibility rates ranging from 77% up to 92%, achieving clinical significance for establishing a dedicated TPS.

# Financial support and sponsorship Nil.

#### Conflicts of interest

There are no conflicts of interest.

### **ORCID**

Raghu S Thota: https://orcid.org/0000-0001-8945-2174 S Ramkiran: https://orcid.org/0000-0002-1669-4268 Aveek Jayant: https://orcid.org/0000-0002-3465-1229 Koilada Shiv Kumar: https://orcid.org/0000-0002-1530-1768

Anjana Wajekar: https://orcid.org/0000-0002-0665-668X Sadasivan Iyer: https://orcid.org/0000-0001-5750-139X Ashwini M: https://orcid.org/0009-0006-6490-5687

# **REFERENCES**

- Khan JS, Ladha KS, Abdallah F, Clarke H. Treating persistent pain after breast cancer surgery. Drugs 2020;80:23-31.
- Admiraal M, Hermanides J, Meinsma SL, Wartenberg HCH, Rutten MVH, Ward-van der Stam VMC, et al. Current multidisciplinary approaches to preventing chronic postoperative pain. Br J Anaesth 2021;127:331-5.
- Steyaert A, Lavand'homme P. Prevention and treatment of chronic postsurgical pain: A narrative review. Drugs 2018;78:339-54.
- Glare P, Aubrey KR, Myles PS. The transition from acute to chronic pain after surgery. Lancet 2019;393:1537-46.
- Mikhaeil J, Ayoo K, Clarke H, Wąsowicz M, Huang A. Review of the transitional pain service as a method of postoperative opioid weaning and a service aimed at minimizing the risk of chronic postsurgical pain. Anaesthesiol Intensive Ther 2020;52:148-53.
- Katz J, Weinrib A, Fashler SR, Katznelzon R, Shah BR, Ladak SS, et al. The Toronto General Hospital Transitional Pain Service: Development and implementation of a multidisciplinary program to prevent chronic postsurgical pain. J Pain Res 2015;8:695-702.
- Clarke H, Weinrib A, Kotteeswaran Y, Katz J, Yu A, Tanguay R. Remote buprenorphine-naloxone initiation as an essential service for people with chronic pain and opioid dependence during the COVID-19 pandemic: Case reports, clinical

- pathways, and implications for the future. Can J Pain 2020;4:224-35.
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.
- Hallgren KA. Computing inter-rater reliability for observational data: An overview and tutorial. tutor quant methods psychol 2012:8:23-34.
- Li M, Gao Q, Yu T. Kappa statistic considerations in evaluating inter-rater reliability between two raters: Which, when and context matters. BMC Cancer 2023;23:799. doi: 10.1186/ s12885-023-11325-z.
- Guimarães NS, Ferreira AJF, Ribeiro Silva RC, de Paula AA, Lisboa CS, Magno L, et al. Deduplicating records in systematic reviews: There are free, accurate, automated ways to do so. J Clin Epidemiol 2022;152:110-5.
- McKeown S, Mir ZM. Considerations for conducting systematic reviews: Evaluating the performance of different methods for de-duplicating references. Syst Rev 2021;10:38. doi: 10.1186/ s13643-021-01583-v.
- Stanley TD, Doucouliagos H. Neither fixed nor random: Weighted least squares meta-regression. Res Synth Methods 2017;8:19-42.
- Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539-58.
- Baker WL, White CM, Cappelleri JC, Kluger J, Coleman CI. Health Outcomes, Policy, and Economics (HOPE) Collaborative Group. Understanding heterogeneity in meta-analysis: The role of meta-regression. Int J Clin Pract 2009;63:1426-34.
- Geissbühler M, Hincapié CA, Aghlmandi S, Zwahlen M, Jüni P, da Costa BR. Most published meta-regression analyses based on aggregate data suffer from methodological pitfalls: A metaepidemiological study. BMC Med Res Methodol 2021;21:123. doi: 10.1186/s12874-021-01310-0
- Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, et al. Updated guidance for trusted systematic reviews: A new edition of the Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst Rev 2019;10:ED000142. doi: 10.1002/14651858.ED000142.
- Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928. doi: 10.1136/bmj.d5928.
- Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. Rob 2: A revised tool for assessing the risk of bias in randomised trials. BMJ 2019;366:l4898. doi: 10.1136/ bmj.l4898.
- Bero L, Chartres N, Diong J, Fabbri A, Ghersi D, Lam J, et al. The risk of bias in observational studies of exposures (ROBINS-E) tool: Concerns arising from application to observational studies of exposures. Syst Rev 2018;7:242. doi: 10.1186/ s13643-018-0915-2.
- Lin L, Chu H. Quantifying publication bias in meta-analysis. Biometrics 2018;74:785-94.
- Zwetsloot PP, Van Der Naald M, Sena ES, Howells DW, IntHout J, De Groot JA, et al. Standardized mean differences cause funnel plot distortion in publication bias assessments. Elife 2017;6:e24260. doi: 10.7554/eLife.24260.
- Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in metaanalysis. Biometrics 2000;56:455-63.
- 24. Admiraal M, Hermanides J, Meinsma SL, Wartenberg HCH, Rutten MVH, Heine Y, et al. The effectiveness of a transitional pain service in patients undergoing surgery with an increased risk of developing chronic postsurgical pain (TRUSt study). A randomized clinical trial. J Clin Anesth 2023;91:111262. doi: 10.1016/j.jclinane.2023.111262.
- Liang L, Pan Y, Wu D, Pang Y, Xie Y, Fang H. Effects of multidisciplinary team-based nurse-led transitional care

- on clinical outcomes and quality of life in patients with ankylosing spondylitis. Asian Nurs Res (Korean Soc Nurs Sci) 2019;13:107-14.
- Wang X, Wu X-C. Application of transitional care model in cancer pain management after discharge: A randomized controlled trial. Chin Nurs Res 2016;3:86-9.
- 27. Abid Azam M, Weinrib A Z, Montbriand J, Burns L C, McMillan K, Clarke H, et al. Acceptance and commitment therapy to manage pain and opioid use after major surgery: Preliminary outcomes from the Toronto general hospital Transitional pain service. Can J Pain 2017;1:37-49.
- Featherall J, Anderson JT, Anderson LA, Bayless K, Anderson Z, Brooke BS, et al. A multidisciplinary transitional pain management program is associated with reduced opioid dependence after primary total joint arthroplasty. J Arthroplasty 2022;37:1048-53.
- Clarke H, Azargive S, Montbriand J, Nicholls J, Sutherland A, Valeeva L, et al. Opioid weaning and pain management in postsurgical patients at the Toronto General Hospital Transitional Pain Service. Can J Pain 2018;2:236-47.
- Hussain M, Norgeot B, Zaafran A, Stark J, Caridi J, Fenoy A, et al. Virtual transitional pain service delivered via telehealth is effective in preventing new and persistent opioid use amongst postsurgical spine patients. medRxiv 2023;2023.08.18.23294272.doi:10.1101/2023.08.18.23294272.
- 31. Haynes N, Mclean C, Collins J, de Lima J. Persistent postoperative pain in children An argument for a transitional pain service in pediatrics. Pain Manag Nurs 2022;23:784-90.
- 32. Buys MJ, Bayless K, Romesser J, Anderson Z, Patel S, Zhang C, et al. Opioid use among veterans undergoing major joint surgery managed by a multidisciplinary transitional pain service. Reg Anesth Pain Med 2020;45:847-52.
- Buys MJ, Bayless K, Romesser J, Anderson Z, Patel S, Zhang C, et al. Multidisciplinary transitional pain service for the veteran population. Fed Pract 2020;37:472-8.
- 34. Huang A, Azam A, Segal S, Pivovarov K, Katznelson G, Ladak SS, *et al.* Chronic postsurgical pain and persistent opioid use following surgery: The need for a transitional pain service. Pain Manag 2016;6:435-43.
- Montbriand JJ, Weinrib AZ, Azam MA, Ladak SSJ, Shah BR, Jiang J, et al. Smoking, pain intensity, and opioid consumption 1-3 months after major surgery: A retrospective study in a hospital-based transitional pain service. Nicotine Tob Res 2018;20:1144-51.
- Liu C W, Page M G, Weinrib A, Wong D, Huang A, McRae K, et al. Predictors of one year chronic postsurgical pain trajectories following thoracic surgery. J Anesth 2021;35:505-14.
- 37. Yu H C, Kleiman V, Kojic K, Slepian PM, Cortes H, McRae K, et al. Prevention and management of chronic postsurgical pain and persistent opioid use following solid organ transplantation: Experiences from the Toronto General Hospital Transitional Pain Service. Transplantation 2023;107:1398-405.
- Levy N, Mills P, Rockett M. Postsurgical pain management: Time for a paradigm shift. Br J Anaesth 2019;123:e182-6.
- Williams G, Howard RF, Liossi C. Persistent postsurgical pain in children and young people: Prediction, prevention, and management. Pain Rep 2017;2:e616. doi: 10.1097/ PR9.00000000000000616
- Geil D, Thomas C, Zimmer A, Meissner W. Chronified pain following operative procedures. Dtsch Arztebl Int 2019;116:261-6.
- 41. Gulur P, Nelli A. Persistent postoperative pain: Mechanisms and modulators. Curr Opin Anaesthesiol 2019;32:668-73.
- 42. Simanski CJ, Althaus A, Hoederath S, Kreutz KW, Hoederath P, Lefering R, *et al.* Incidence of chronic postsurgical pain (CPSP) after general surgery. Pain Med 2014;15:1222-9.
- 43. Laufenberg-Feldmann R, Kappis B, Mauff S, Schmidtmann I, Ferner M. Prevalence of pain 6 months after surgery: A prospective observational study. BMC Anesthesiol 2016;16:91. doi: 10.1186/s12871-016-0261-7

- Richebé P, Capdevila X, Rivat C. Persistent postsurgical pain: Pathophysiology and preventative pharmacologic considerations. Anesthesiology 2018;129:590-07.
- Wang K, Yee C, Tam S, Drost L, Chan S, Zaki P, et al. Prevalence of pain in patients with breast cancer post-treatment: A systematic review. Breast 2018;42:113-27.
- Habib AS, Kertai MD, Cooter M, Greenup RA, Hwang S. Risk factors for severe acute pain and persistent pain after surgery for breast cancer: A prospective observational study. Reg Anesth Pain Med 2019;44:192-9.
- Osypiuk K, Ligibel J, Giobbie-Hurder A, Vergara-Diaz G, Bonato P, Quinn R, et al. Qigong mind-body exercise as a biopsychosocial therapy for persistent postsurgical pain in breast cancer: A pilot study. Integr Cancer Ther 2020;19:1534735419893766. doi: 10.1177/1534735419893766
- 48. Wang K, Moon DH, Amdur RJ, Dagan R, Sheets NC, Shen CJ, et al. Shoulder symptoms and quality of life impact of limited neck dissection after de-intensified chemo-radiotherapy: Secondary analysis of two prospective trials. Head Neck 2019;41:1213-19.
- Ammitzbøll G, Andersen KG, Bidstrup PE, Johansen C, Lanng C, Kroman N, et al. Effect of progressive resistance training on persistent pain after axillary dissection in breast cancer: A randomized controlled trial. Breast Cancer Res Treat 2020;179:173-83.
- Kojic K, Clarke H. Important considerations with respect to reducing the transition from acute to persistent postoperative pain. Expert Opin Pharmacother 2021;22:779-82.
- Clarke H, Soneji N, Ko D T, Yun L, Wijeysundera DN. Rates and risk factors for prolonged opioid use after major surgery: Population based cohort study. BMJ 2014;348:g1251. doi: 10.1136/bmj.g1251
- 52. Weinrib AZ, Burns LC, Mu A, Azam MA, Ladak SS, McRae K, et al. A case report on the treatment of complex chronic pain and opioid dependence by a multidisciplinary transitional pain service using the ACT Matrix and buprenorphine/naloxone. J Pain Res 2017;10:747-55.
- 53. Meng H, Hanlon JG, Katznelson R, Ghanekar A, McGilvray I, Clarke H. The prescription of medical cannabis by a transitional pain service to wean a patient with complex pain from opioid use following liver transplantation: A case report. Can J Anaesth 2016;63:307-10.
- Hunter OO, Mariano ER, Harrison TK. Leveraging video telehealth for the transitional pain service in response to COVID-19. Reg Anesth Pain Med 2021;46:460-1.
- 55. Roditi D, Robinson ME. The role of psychological interventions

- in the management of patients with chronic pain. Psychol Res Behav Manag 2011;4:41-9.
- Vowles KE, Fink BC, Cohen LL. Acceptance and commitment therapy for chronic pain: A diary study of treatment process in relation to reliable change in disability. J Contextual Behav Sci 2014;3:74-80.
- Syrjala KL, Jensen MP, Mendoza ME, Yi JC, Fisher HM, Keefe FJ. Psychological and behavioral approaches to cancer pain management. J Clin Oncol 2014;32:1703-11.
- 58. Hadlandsmyth K, Dindo LN, Wajid R, Sugg SL, Zimmerman MB, Rakel BA. A single-session acceptance and commitment therapy intervention among women undergoing surgery for breast cancer: A randomized pilot trial to reduce persistent postsurgical pain. Psychooncology 2019;28:2210-7.
- Veehof MM, Oskam MJ, Schreurs KMG, Bohlmeijer ET. Acceptance-based interventions for the treatment of chronic pain: A systematic review and meta-analysis. Pain 2011;152:533-42.
- Hughes LS, Clark J, Colclough JA, Dale E, McMillan D. Acceptance and Commitment Therapy (ACT) for chronic pain: A systematic review and meta-analyses. Clin J Pain 2017;33:552-68.
- Macfarlane TV, Wirth T, Ranasinghe S, Ah-See KW, Renny N, Hurman D. Head and neck cancer pain: Systematic review of prevalence and associated factors. J Oral Maxillofac Res 2012;3:e1. doi: 10.5037/jomr.2012.3101
- Evans SW, McCahon RA. Management of postoperative pain in maxillofacial surgery. Br J Oral Maxillofac Surg 2019;57:4-11.
- 63. Dort JC, Farwell DG, Findlay M, Huber GF, Kerr P, Shea-Budgell MA, et al. Optimal perioperative care in major head and neck cancer surgery with free flap reconstruction: A consensus review and recommendations from the enhanced recovery after surgery society. JAMA Otolaryngol Head Neck Surg 2017;143:292-03.
- 64. Kuo PY, Williams JE. Pain control in head and neck cancer. In: Agulnik M, editor. Head and Neck Cancer. 1st ed.: InTech; 2012:351-70. ISBN: 978-953-51-0236-6. Available from: http://www.intechopen.com/books/head-and-neck-cancer/pain-and symptom-control-in-head-and-neck-cancer. [Last accessed on 2024 Jun 03].
- 65. Brenin DR, Dietz JR, Baima J, Cheng G, Froman J, Laronga C, et al. Pain management in breast surgery: Recommendations of a multidisciplinary expert panel—The American Society of Breast Surgeons. Ann Surg Oncol 2020;27:4588-602.

# **APPENDIX 1**

#### Literature search

Keywords in Mesh terminology included population-based (persistent postsurgical pain after cancer surgery), 'cancer surgery pain', 'perioperative cancer pain', 'perioperative cancer pain intervention', 'persistent postsurgical pain', 'pain catastrophising', 'pain disability interference'; publication-based (transitional pain service) 'transitional pain service', 'establishing dedicated transitional pain services', 'feasibility of transitional pain service', 'integrated transitional pain service', 'acute pain service and transitional pain service', 'chronic pain and transitional pain service', 'oncoanaesthesia and transitional pain service', 'pain practice and transitional pain service'; and combination terms 'persistent postsurgical pain and transitional pain service', 'perioperative cancer surgery and pain catastrophising', 'transitional pain service and bridging pain gap in oncoanaesthesia'. Additional sources were obtained by searching the bibliography of included references.