Patient-maintained propofol sedation for adult patients undergoing surgical or medical procedures: a scoping review of current evidence and technology

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Summary

Patient-maintained propofol sedation (PMPS) is the delivery of procedural propofol sedation by target-controlled infusion with the patient exerting an element of control over their target-site propofol concentration. This scoping review aims to establish the extent and nature of current knowledge regarding PMPS from both a clinical and technological perspective, thereby identifying knowledge gaps to guide future research. We searched MEDLINE, EMBASE, and OpenGrey databases, identifying 17 clinical studies for analysis. PMPS is described in the context of healthy volunteers and in orthopaedic, general surgical, dental, and endoscopic clinical settings. All studies used modifications to existing commercially-available infusion devices to achieve prototype systems capable of PMPS. The current literature precludes rigorous generalisable conclusions regarding the safety or comparative clinical effectiveness of PMPS, however cautious acknowledgement of efficacy in specific clinical settings is appropriate. Based on the existing literature, together with new standardised outcome reporting recommendations for sedation research and frameworks designed to assess novel health technologies research, we have made recommendations for future pharmacological, clinical, behavioural, and health economic research on PMPS. We conclude that high-quality experimental clinical trials with relevant comparator groups assessing the impact of PMPS on standardised patient-orientated outcome measures are urgently required.

Keywords: anxiolytic; conscious sedation; equipment design; hypnotics; propofol; sedatives; target-controlled infusion

Editor's key points

- Patient control over analgesic or sedative agent administration may improve safety and patient satisfaction.
- Patient-maintained propofol sedation (PMPS) is a technique which combines target-controlled infusion and patient control technologies to provide a patient with some control over the depth of their sedation.
- The authors performed a scoping review to establish the extent and nature of current knowledge regarding PMPS.
- The current literature is limited, and high-quality clinical trials are needed to assess the impact of PMPS on standardised patient-orientated outcome measures.

The relief of anxiety and the provision of analgesia during awake surgical and medical procedures forms a large and increasing part of anaesthetic service delivery.[1] The relief of perioperative anxiety and stress is one of the standardised endpoints for perioperative medicine research proposed by the Standardised Endpoints in Perioperative Medicine - Core Outcome Measures in Perioperative and Anaesthetic Care (StEP-COMPAC) Group[2] and is an outcome measure of high priority for patients. Procedural sedation is commonly achieved using propofol delivered by target-controlled infusion (TCI), non-TCI ml h^{-1} or µg kg^{-1} min^{-1} infusion, or intermittent i.v. bolus techniques. Such techniques are typically titrated to effect (i.e. sedation level) by healthcare professionals supervising the drug regimen. It is established clinical practice for patients to be given some element of titration control when using nitrous oxide, methoxyflurane, and i.v. opioid analgesia systems. No equivalent system exists to allow patients to exert

direct control over their depth of sedation during propofol TCI sedation regimes. Such a technique can be termed patient-maintained propofol sedation (PMPS).

Given the importance of procedural anxiolysis to patients, the increase in the number of procedures being performed using sedation, and the varied approaches to propofol sedation undertaken worldwide (including instances of new propofol delivery systems being brought to and withdrawn from market)[3] we have conducted a formal scoping review of the current literature on PMPS.

The aim of this scoping review is to establish the extent and nature of evidence regarding PMPS and to identify gaps in the existing literature. The objectives of this review are three-fold. First, to establish the populations and clinical settings in which PMPS has been studied. Second, to examine the range of pharmacokinetic models, sedation algorithms, and technologies that have delivered PMPS. Third, to explore studies of clinical efficacy or effectiveness and thereby recommend future research and technology development in this field.

Methods

This scoping review was performed according to the methodological principles described by Levac and colleagues[4] and conforms to the 2018 Preferred Reporting Items for Systematic Review and Meta-analysis Extension for Scoping Reviews (PRISMA-ScR) reporting standards.[5] Although the objectives of the review and the plan for its conduct were determined *a priori*, scoping review protocols are not accepted by the International Prospective Register of Systematic Reviews (PROSPERO) database, therefore the review was registered via ResearchRegistry.com (Reference: Researchregistry5389).

Definitions

There is no consensus definition of PMPS, however we propose to use the following definitions in this review. The delivery of propofol sedation by fixed bolus dose (measured in mg) with or without concurrent ml hr^{-1} infusion, where the delivery of bolus doses is determined by the patient (typically using a handheld trigger), is called 'patient-controlled propofol sedation' (PCPS). Commercially available infusion devices (e.g. patient-controlled analgesia devices) can be re-purposed to deliver propofol sedation in this manner, although such modification typically requires formal regulatory authority approval since the device is then used beyond its intended use.

The delivery of propofol sedation by TCI, when the patient can influence their target-site concentration of propofol (in μg ml^{-1}) using a handheld trigger, is called patient-maintained propofol sedation (PMPS). The theoretical advantages of PMPS over PCPS are conferred by the use of target-controlling, which uses automated pharmacokinetic modelling to achieve rapid, reliable, and stable propofol compartment concentrations and therefore a stable and easily titratable depth of sedation.

Data sources and search for evidence

We searched MEDLINE and EMBASE databases from inception to May 1, 2020 via the Ovid® interface. The search terms 'propofol', 'sedation', 'patient-led', and 'patient-maintained' were applied with search truncation, wildcards, and Boolean operators as appropriate (see Supplementary online Appendix

Fig 1. PRISMA flow diagram [5] of literature search and study selection. PMPS, patient-maintained propofol sedation.
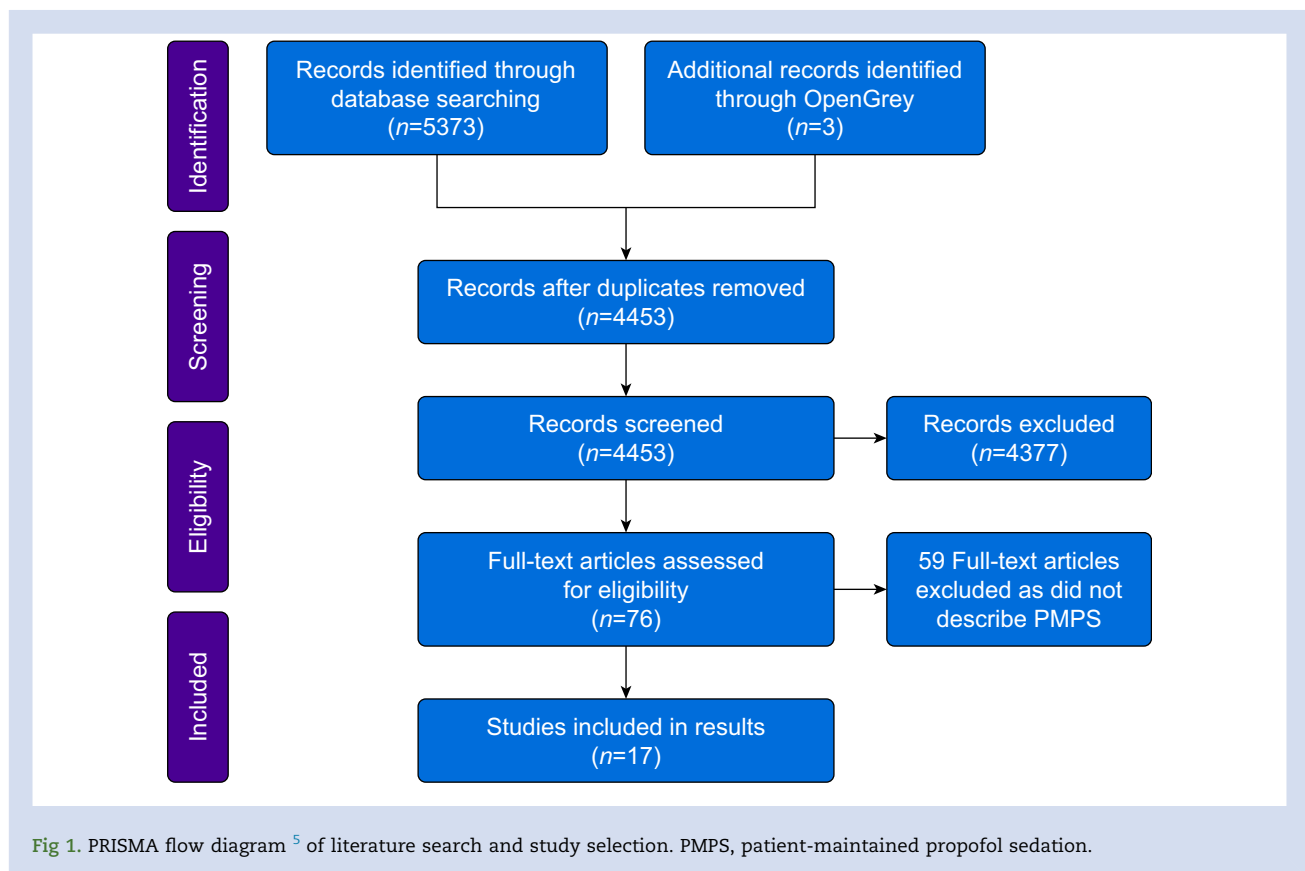
Table 1 Identified articles, study design, participants and settings.

Authors	Year	Title	Country	Study type	Study design	Participants (*n*)	Clinical setting
Irwin and colleagues[8]	1997	Patient-maintained propofol sedation: assessment of a target-controlled infusion system	Hong Kong	Efficacy	Case series	36	General and orthopaedic surgery
Murdoch and Kenny[9]	1999	Patient-maintained propofol sedation as premedication in day-case surgery: assessment of a target-controlled system	UK	Efficacy	Case series	20	Day case surgery
Murdoch and colleagues[10]	2000	Safety of patient-maintained propofol sedation using a target-controlled system in healthy volunteers	UK	Efficacy	Healthy volunteer study	10	N/A
Gillham and colleagues[11]	2001	Patient-maintained sedation for endoscopic retrograde cholangiopancreatography with a target-controlled infusion of propofol: a pilot study	UK	Efficacy	Case series	20	Endoscopic retrograde cholangiopancreatography
Henderson and colleagues[12]	2002	Patient-maintained propofol sedation: a follow-up safety study using a modified system in volunteers	UK	Efficacy	Healthy volunteer study	20	N/A
Leitch and colleagues[13]	2003	Patient-maintained sedation for oral surgery using a target-controlled infusion of propofol: a pilot study	UK	Efficacy	Case series	20	Oral surgery
Rodrigo and colleagues[14]	2003	A randomised crossover comparison of patient-controlled sedation and patient-maintained sedation using propofol	Hong Kong	Effectiveness	Randomised crossover trial	23	Oral surgery
Campbell and colleagues[15]	2004	Patient-maintained sedation for colonoscopy using a target-controlled infusion of propofol	UK	Efficacy	Case series	20	Colonoscopy

Continued

Table 1 Continued

Authors	Year	Title	Country	Study type	Study design	Participants (n)	Clinical setting
Leitch and colleagues[16]	2004	A partially blinded RCT of patient-maintained propofol sedation and operator controlled midazolam sedation in third molar extractions	UK	Effectiveness	RCT	110	Oral surgery
Rodrigo and colleagues[17]	2004	Patient maintained propofol sedation for dental surgery	Hong Kong	Efficacy	Case series	50	Oral surgery
Anderson and colleagues[18]	2005	Effect-site controlled patient maintained propofol sedation: a volunteer safety study	UK	Efficacy	Healthy volunteer study	20	N/A
Chapman and colleagues[19]	2006	Evaluation of a new effect-site controlled, patient-maintained sedation system in dental patients	UK	Efficacy	Case series	40	Oral surgery
Stonell and colleagues[20]	2006	Effect-site targeted patient-controlled sedation with propofol: comparison with anaesthetist administration for colonoscopy	Australia	Effectiveness	RCT	40	Colonoscopy
Allam and colleagues[21]	2013	Patient-maintained propofol sedation using reaction time monitoring: a volunteer safety study	UK	Efficacy	Healthy volunteer study	20	N/A
O'Brien and colleagues[22]	2013	Reaction time-monitored patient-maintained propofol sedation: a pilot study in oral surgery patients	UK	Efficacy	Case series	20	Oral surgery
Hewson and colleagues[23]	2019	A prospective observational study of effect-site targeted, patient-maintained propofol sedation for lower limb orthopaedic surgery performed under spinal anaesthesia	UK	Efficacy	Case series	25	Orthopaedic surgery
Hewson and colleagues[24]	2019	Anaesthetist-controlled vs patient-	UK	Effectiveness	Protocol for RCT	80	Orthopaedic surgery

Continued

Table 1 Continued

Authors	Year	Title	Country	Study type	Study design	Participants (n)	Clinical setting
		maintained effect-site targeted propofol sedation during elective primary lower-limb arthroplasty performed under spinal anaesthesia (ACCEPTS): study protocol for a parallel-group randomised comparison trial					

I for details of the search strategy).[6] 'Patient-controlled' was included in the search terms since there is variation in the nomenclature used by researchers to describe patient-led propofol sedation techniques. Tangential electronic exploration using citations to related texts was performed. To maximise search exposure, a supplemental search of grey literature was conducted using OpenGrey.[7] Studies were limited to clinical trials reported in English. Animal studies were excluded, however opinion papers, case reports, and editorials were included if found. No existing reviews on this topic were identified in the Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, National Institute for Health Research Health Technology Assessment Programme (NIHR HTA), NIHR i4i Programme, or the National Institute for Health and Care Excellence (NICE) websites.

All observational and experimental studies that addressed PMPS as defined above were considered for inclusion. All surgical and medical disciplines were considered including non-operative medical procedures such as colonoscopy and sedation in the emergency department or dental chair. We included studies with participants aged 18 yr or older either as healthy volunteers or patients. Studies were excluded if they described PCPS as defined above.

Screening and data extraction

All titles and abstracts identified by the initial search were screened for inclusion according to the selection criteria for detailed review. Discrepancies in data screening and extraction were resolved by consensus among the authors. Data on the following characteristics were extracted from included studies: titles, authors, publication year, study design, primary objectives, population characteristics and group allocations (including comparator group) if relevant, clinical setting, hardware used to deliver PMPS, pharmacokinetic model used for propofol delivery, compartment targeted during sedation, starting concentration of propofol targeted, incremental increase in propofol concentration triggered by patient request, lock-out time, maximum propofol concentration obtainable by patient during sedation, decrement in propofol concentration and decrement time if applicable, and minimum propofol concentration during sedation.

Results

A total of 4453 non-duplicate records were identified by the search, from which 76 full text articles were retrieved and evaluated (Fig. 1). Of the 76 identified texts, 17 describe PMPS. These articles, all of which are original research publications, are summarised in Table 1.
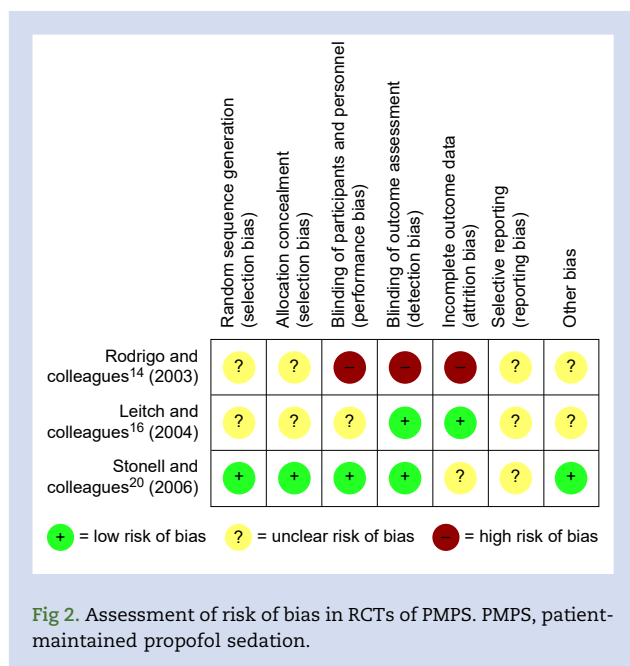
Population and clinical settings

PMPS has been examined in four healthy volunteer studies (a total of 70 participants),[10,12,18,21] nine observational clinical studies (251 participants),[9,11,13,15,17,19,22,23] and three prospective RCTs (150 participants).[15,17,20] One RCT protocol, published by the authors of this review, comparing PMPS with anaesthetist-controlled propofol sedation in lower limb arthroplasty surgery was identified.[24] The studies identified have taken place in the setting of general surgery,[17] orthopaedic surgery,[17,23] endoscopic retrograde cholangiopancreatography (ERCP),[11] colonoscopy,[15,20] and oral surgery.[13,14,16,17,19,22]

Table 2 Pharmacokinetic models and sedation algorithms used in published studies. Terms are defined as follows: *Starting concentration*, the concentration of propofol at which participants commence the sedation regime; *Increment concentration*, the increase applied to the target-site concentration of propofol obtained by each participant handheld trigger activation; *Lock-out time*, the time after an increment in target-site concentration during which a subsequent handheld trigger activation will not cause a further increment; *Maximum obtainable concentration*, the 'ceiling' target-site concentration, above which the sedation will not increment regardless of handheld trigger activations; *Decrement concentration*, the target-site concentration reduction which is automatically applied in the event of no handheld trigger activations within the decrement time; *Decrement time*, the time which must expire with no handheld trigger activations before the decrement concentration is automatically applied; *Minimum concentration*, the target-site concentration below which the sedation will not decrement during the sedation period.

Authors	Year	Propofol model	Target-site	Starting concentration ($\mu g\ ml^{-1}$)	Increment concentration ($\mu g\ ml^{-1}$)	Lock-out (sec)	Maximum obtainable concentration ($\mu g\ ml^{-1}$)	Decrement concentration ($\mu g\ ml^{-1}$)	Decrement time (s)	Minimum concentration ($\mu g\ ml^{-1}$)
Irwin and colleagues[8]	1997	Marsh	Plasma	1.0	0.2	120	3.0	0.2	Variable	0.2
Murdoch and Kenny[9]	1999	Marsh	Plasma	1.0	0.2	120	3.0	Unspecified	360	0.2
Murdoch and colleagues[10]	2000	Marsh	Plasma	1.0	0.2	120	3.0	Unspecified	360	0.2
Gillham and colleagues[11]	2001	Marsh	Plasma	1.0	0.2	120	3.0	0.2	360	Unspecified
Henderson and colleagues[12]	2002	Marsh	Plasma	0.5	0.1	240	3.0	Unspecified	Unspecified	Unspecified
Leitch and colleagues[13]	2003	Marsh	Plasma	1.0	0.2	120	3.0	0.2	360	Unspecified
Rodrigo and colleagues[14]	2003	Marsh	Plasma	1.4	0.2	120	3.0	0.2	Variable	0.2
Campbell and colleagues[15]	2004	Marsh	Plasma	1.0	0.2	120	4.5	Unspecified	Unspecified	Unspecified
Leitch and colleagues[16]	2004	Marsh	Plasma	1.0	0.2	120	3.0	Unspecified	360	Unspecified
Rodrigo and colleagues[17]	2004	Marsh	Plasma	1.4	0.2	120	3.0	0.2	Variable	0.2
Anderson and colleagues[18]	2005	Marsh	Effect-site	1.0	0.2	Variable	No maximum	0.2	360	Unspecified
Chapman and colleagues[19]	2006	Marsh	Effect-site	1.0	0.2	Variable	No maximum	No decrement	N/A	Unspecified
Stonell and colleagues[20]	2006	Schnider	Effect-site	0.8	0.1	180	No maximum	0.1	300	Unspecified
Allam and colleagues[21]	2013	Marsh	Effect-site	1.0	0.2	Variable	3.0	Variable	Variable	Unspecified
O'Brien and colleagues[22]	2013	Marsh	Effect-site	1.0	0.2	Variable	3.0	No decrement	N/A	Unspecified
Hewson and colleagues[23]	2019	Schnider	Effect-site	0.5	0.2	Variable	2.0	0.1	360	0.5
Hewson and colleagues[24]	2019	Schnider	Effect-site	0.5	0.2	120	2.0	0.1	900	0.5

Fig 2. Assessment of risk of bias in RCTs of PMPS. PMPS, patient-maintained propofol sedation.

Pharmacokinetic models, sedation algorithms, and technologies

With the exception of two studies that used Schnider modelling,[20,23] all completed studies used the Marsh model of propofol TCI. All studies published before 2005 were conducted using plasma-compartment targeting, whereas those studies published after 2005 all used effect-site targeting. Until more recently published propofol TCI models, such as the Eleveld model,[25] become available on commercial infusion devices or via open source software[26] it is likely that Marsh or Schnider modelling will remain standard for PMPS research techniques.

The sedation algorithms used in individual studies are defined and summarised in Table 2. There was wide variation in the published starting concentrations of propofol (0.5–1.4 μg ml^{-1}), increment concentrations (0.1–0.2 μg ml^{-1}), lock-out times (120–240 s), maximum obtainable concentrations (2.0–4.5 μg ml^{-1}), decrement concentrations (0.1–0.2 μg ml^{-1}), decrement times (300–900 s), and minimum obtainable concentrations (0–0.5 μg.ml^{-1}).

In the absence of a commercially available infusion device capable of PMPS, researchers report a variety of infusion devices modified by serial-port connection to bespoke software in order to deliver PMPS. The Omheda 9000 device (BOC Healthcare, Manchester, UK),[8] Graseby 3400 (Smiths Medical Ltd, Ashford, UK),[8,9–18] Graseby 3500 (Smiths Medical Ltd, Ashford, UK),[21,22] Asena GH (BD Ltd, Wokingham, UK),[20] Alaris PK (BD Ltd, Wokingham, UK),[23] and the Perfusor fm (B. Braun Medical, Melsungen, Germany)[24] have all been modified in this manner. One study did not specify the technology by which their PMPS algorithm was delivered.[19]

Clinical efficacy of PMPS

The concepts of efficacy (the operation of the sedation technique under ideal conditions, usually in closely supervised conditions) and effectiveness (the comparative operation of the technique in a pragmatic clinical environment) are fundamental to the potential adoption of new medical techniques and technologies and as such the literature can be broadly divided into examinations of efficacy[8–13,15,18,19,21–23] and comparative effectiveness[14,16,20] with the acknowledgement that the two concepts are a continuum rather than a dichotomy in clinical research.[27]

All four healthy volunteer studies have assessed efficacy and safety by instructing participants to render themselves unconscious using the PMPS handheld trigger. In addition to direct modifications of the parameters of the sedation algorithm (as defined in Table 2), the authors of these studies suggest the risk of over-sedation can be reduced by the use of a handheld trigger which must be pressed twice within 1 s to successfully increment the target-site concentration,[10] the direct supervision of PMPS by an anaesthetist,[9] and the integration of a user-reaction time monitor.[21]

Efficacy has been further assessed in nine case-series. While these studies universally describe high patient 'satisfaction' or 'willingness to repeat the procedure' after the PMPS technique,[8,11,13,15] none reported outcome measures relating to patient comfort to a standard which would facilitate generalisable analysis or conclusions.[28] These studies additionally demonstrate that under- and over-sedation can occur using PMPS if the sedative properties of propofol and the sedation algorithm used are not matched to the particular clinical setting. For example, in the case series of PMPS used for ERCP, Gillham and colleagues[11] describe three of their 20 patients being insufficiently sedated to tolerate the procedure. Patients undergoing painful procedures, such as ERCP, are likely to benefit from an analgesic component to their sedation regime which propofol alone cannot provide. Although several studies present data demonstrating stability of physiological parameters (participant HR, arterial oxygen saturations, BP) during the sedation period,[8,16,19] data arising from small and heterogeneous observational trials (251 participants in total) on the safety of anaesthetic techniques must be interpreted carefully, since much larger samples are required to conclusively demonstrate safety in specific clinical settings.[29]

Comparative clinical effectiveness of PMPS

There are three published randomised trials of PMPS addressing comparative effectiveness.[15,17,20] Two trials compared PMPS with control groups that could be described as 'standard care': physician-delivered midazolam sedation in Leitch and colleagues[16] and anaesthetist-controlled propofol sedation in Stonell and colleagues.[20] In the third trial, Rodrigo and colleagues[14] compared PMPS with a PCPS technique using a crossover design.

Leitch and colleagues[16] randomised 110 participants to PMPS or midazolam sedation for oral surgery performed under local anaesthetic infiltration with joint primary outcome measures of minimum arterial oxygen saturations during sedation and time until discharge from the theatre suite. PMPS offered superior reduction in mean (standard deviation [SD]) VAS-rated intraoperative anxiety compared with physician-controlled midazolam (21 [21] vs 11 [18] mm; P=0.010). Depth of sedation, as reported by the unblinded operating surgeon, was less in the PMPS group, and so the authors discuss the possibility that PMPS provides superior intraoperative anxiolysis, but less deep sedation, compared with midazolam under physician control. Recall of surgical events was similar

Table 3 Research suggestions for patient-maintained propofol sedation.

Topic	Suggested research strategy
Health economic evaluation	Cost-consequence, cost-utility analysis, or both
Health system efficiency	Healthcare resource use analysis
Clinical safety and effectiveness	High-quality experimental trials with relevant comparator group(s) assessing the impact of PMPS on standardised patient-orientated outcome measures.[33,34]
User credibility, acceptability, and engagement	Assessments of technology and technique to supervising health professionals, patients, and commissioners of health services
Behavioural assessment	Qualitative psychological evaluations of patient and healthcare professional experience of PMPS
Pharmacological validation studies	Pharmacodynamic and pharmacokinetic predictive performance of specific propofol TCI models when adopted for PMPS

PMPS, patient-maintained propofol sedation; TCI, target-controlled infusion.

between groups, but PMPS patients had a shorter mean (SD) time to readiness for discharge compared with the patients who had received midazolam (18 [5.5] *vs* 25 [9.0] min; P=0.001). The mean (SD) lowest arterial oxygen saturation was lower in the midazolam group than in the PMPS group (97.0 [2.0] *vs* 97.8 [1.8] %; P=0.026), however there is no clinical significance to this difference.

In 2006, Stonell and colleagues[20] published an RCT of Schnider effect-site targeted PMPS *vs* anaesthetist-controlled propofol sedation by intermittent bolus in 40 patients undergoing colonoscopy. There was no difference in primary outcome measure, procedural satisfaction measured on VAS, between groups (91 *vs* 90 mm; P=0.779). The PMPS group was less sedated than the control group, with higher mean (SD) bispectral index (88 [9] *vs* 78 [11]; P=0.011) and median (interquartile range [range]) Observer Assessment of Alertness/Sedation scores 4 (4−5 [3−5]) *vs* 3 (2−4 [1−5]).

A single randomised trial has been conducted comparing PMPS with PCPS.[14] The trial recruited 23 patients undergoing bilateral oral surgery scheduled as two separate surgical procedures. On their first operative visit patients were randomly assigned to either plasma-compartment targeted Marsh model PMPS or to a PCPS system delivering propofol 18 mg with a 60 s lock-out. On the second operative visit, participants received the alternate allocation. The authors conclude that PMPS and PCPS result in similar mean (SD) total propofol doses during the sedation period (84.3 [38.6] *vs* 93.7 [20.4] μg kg^{-1} min^{-1}; P=0.13) but PMPS was preferred by more patients compared with PCPS (15 *vs* 7; P=0.02).

Heterogeneity in the trial settings and PMPS algorithms, together with inconsistent reporting standards for outcome data, render meta-analysis to assess clinical effectiveness inappropriate.

Risk of bias assessment

Although scoping reviews do not always include an assessment of internal validity, it was deemed appropriate to do so in the context of the available literature on PMPS. Each trial was assessed using predefined criteria specified in the Cochrane Risk of Bias Tool for Randomised Controlled Trials[30] and a summary is presented in Figure 2. The overall quality of the trials was low with inadequate descriptions of methods undertaken to reduce selection, attrition, and reporting bias in two of the three trials. [14,16] Effective blinding of participants, surgeons, anaesthetists, and outcome assessors is a complex area in sedation trials. There may be justifiable reasons for not blinding participants since some of the anxiolytic effect of PMPS may result from the psychological empowerment they obtain from knowing they can control their sedation using a button. To blind participants (with sham buttons or similar) may therefore alter the impact of the intervention itself. The extent to which psychological empowerment facilitates anxiolysis during PMPS should be a topic of future research.

Discussion

This scoping review has identified the extent of research undertaken on PMPS. Sixteen healthy volunteer, observational, or RCTs of PMPS were published between 1997 and 2020. One RCT protocol has been published. The completed studies involved a total of 471 participants. We identified assessments of PMPS in medical and surgical procedural settings, using both Marsh and Schnider modelling and using a wide range of sedation algorithms. All PMPS research to date has been conducted using research-group specific software modifications to existing commercially available infusion devices, repurposing these devices for PMPS delivery.

The body of literature assessing PMPS is markedly smaller than that available for PCPS, where a recent systematic review conducted meta-analyses on clinical trial data for 1103 participants.[31] The ease with which PCPS can be administered (requiring no software or hardware modification to TCI infusion devices) may explain this difference. It is our contention, however, that the pharmacokinetic advantages of TCI propofol delivery (established from its widespread use as an anaesthetist-controlled sedative and agent of general anaesthesia) are such that PMPS, rather than PCPS, should be the focus of future technological development and sedation research.

Methodological considerations

Heterogeneity in clinical trial outcome measurement and reporting causes well known difficulties in evidence synthesis, and initiatives to encourage standardisation of outcomes measures[32] are comparatively new in the context of the available literature on PMPS. Studies identified in this review have typically used non-standardised measures of depth of sedation, physiological manifestations of over-sedation, patient satisfaction or anxiety, time to recovery from sedation, or propofol consumption, or all of these end-points, in their outcome reporting. There is, however, an emerging consensus led by groups such as the Sedation Consortium on Endpoints and Procedures for Treatment, Education and Research (SCEPTER) that procedural sedation should be evaluated using

consistent domains such as safety, effectiveness, patient-centeredness, and efficiency.[33] Furthermore, these domains should be evaluated using recommended instruments to provide consistency and facilitate subsequent meta-analysis.[33–35] The International Committee for the Advancement of Procedural Sedation has developed the Tracking and Reporting Outcomes Of Procedural Sedation (TROOPS) framework to promote consistency and standardised data collection for sedation research and quality improvement.[35]

Technological context

From a technological perspective we can infer from this scoping review that PMPS is in the well-known biotechnology 'valley of death', where novel technologies with early proof-of-concept prototype success delivered by individual research groups are not subsequently exploited by product development into healthcare technologies ready for commercialisation and market adoption. There is a circularity in the relationship between the technology required to deliver PMPS and the sedation method itself. The absence of an accessible infusion device capable of PMPS is a barrier preventing researchers from conducting rigorous clinical evaluations of the sedation technique, but the paucity of evidence to support clinical effectiveness likely deters potential investors from bringing the technology to market and making it available for research. Although novel technology development opportunities exist (e.g. in the role of fuzzy logic/machine learning applied to PMPS or the adoption of new propofol TCI models[25] for the PMPS technique), a basic commercially available infusion device capable of PMPS and approved by relevant regulatory authorities will be needed to conclusively demonstrate clinical effectiveness.

Recommendations for future research

Based on the evidence presented in this review, we have adapted the 2019 UK NICE Evidence Standards Framework for Digital Health Technologies[36] to provide future research suggestions for PMPS. These are shown in Table 3.

Review limitations

Although the conduct and reporting of our work conforms to current best-practice in scoping review methodology,[5] this approach to evidence synthesis is relatively new and our work is subject to several limitations. We used broad search criteria to identify all evidence relating to PMPS, but deliberately did not aim to critically appraise or systematically synthesise all results. Generalisable data-driven conclusions on the safety, efficacy, or effectiveness of PMPS (as would typically be found in systematic reviews) cannot be drawn from our work. Given the variety of nomenclature used to describe patient-led propofol sedation it is possible we have omitted sources of evidence which would have usefully contributed to our understanding of the current knowledge base of PMPS. Furthermore, our review is likely to have overlooked non-publicly accessible sources of information on PMPS, such as unpublished data (which may be commercially sensitive),patent applications or granted patents since a formal patent search was not undertaken.

Conclusions

Research evaluating the role of PMPS has been conducted on healthy volunteers and in observational and experimental clinical trials with participants from a range of medical and surgical settings. Results from an ongoing prospective RCT[24] are awaited. Although the heterogeneity and reporting quality of completed studies precludes meta-analysis to determine safety or comparative clinical effectiveness, cautious acknowledgement that PMPS appears to provide efficacious procedural sedation in adult patients is appropriate. Both SCEPTER and TROOPS recommendations on the evaluation of sedation techniques[33–35] and NICE guidelines in the assessment of healthcare technologies[36] should be used by researchers and device manufacturers to determine how PMPS should be implemented in clinical practice.

Authors' contributions

Study design, planning, conduct, writing, and revision of manuscript: all authors.

Declarations of interest

Funding

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.07.053.

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Handling editor: Tony Absalom