Evidence-based clinical practice guidelines on postdural puncture headache: a consensus report from a multisociety international working group

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ABSTRACT

Introduction Postdural puncture headache (PDPH) can follow unintentional dural puncture during epidural techniques or intentional dural puncture during neuraxial procedures such as a lumbar puncture or spinal anesthesia. Evidence-based guidance on the prevention, diagnosis or management of this condition is, however, currently lacking. This multisociety guidance aims to fill this void and provide practitioners with comprehensive information and patient-centric recommendations to prevent, diagnose and manage patients with PDPH.

Methods Based on input from committee members and stakeholders, the committee cochairs developed 10 review questions deemed important for the prevention, diagnosis and management of PDPH. A literature search for each question was performed in MEDLINE (Ovid) on 2 March 2022. The results from each search were imported into separate Covidence projects for deduplication and screening, followed by data extraction. Additional relevant clinical trials, systematic reviews and research studies published through March 2022 were also considered for the development of guidelines and shared with contributors. Each group submitted a structured narrative review along with recommendations graded according to the US Preventative Services Task Force grading of evidence. The interim draft was shared electronically, with each collaborator requested to vote anonymously on each recommendation using two rounds of a modified Delphi approach.

Results Based on contemporary evidence and consensus, the multidisciplinary panel generated 50 recommendations to provide guidance regarding risk factors, prevention, diagnosis and management of PDPH, along with their strength and certainty of evidence. After two rounds of voting, we achieved a high level of consensus for all statements and recommendations. Several recommendations had moderate-to-low certainty of evidence.

Conclusions These clinical practice guidelines for PDPH provide a framework to improve identification, evaluation and delivery of evidence-based care by physicians performing neuraxial procedures to improve the quality of care and align with patients' interests. Uncertainty remains regarding best practice for the majority of management approaches for PDPH due to the paucity of evidence. Additionally, opportunities for future research are identified.

INTRODUCTION

Postdural puncture headache (PDPH) is a recognized complication following unintentional dural puncture during epidural analgesia, or intentional dural puncture for spinal anesthesia, diagnostic or interventional neuraxial procedures. Its incidence varies widely, with rates ranging from <2% to 40%, depending on procedural and patient factors.[1–3]

PDPH is usually postural and presents within first 5 days of witnessed or suspected dural puncture.[4] Headache is often accompanied by neck stiffness and/or subjective hearing symptoms. Although headache may resolve within 2 weeks, its severity may interfere with daily activities; this becomes especially important for postpartum patients caring for the newborn child. Furthermore, PDPH is associated with complications including subdural hematoma (SDH), cerebral venous sinus thrombosis (CVST), depression, cranial nerve dysfunction, chronic headache and backache.[5]

Despite numerous reviews on the prevention and management of PDPH, most lack structured recommendations. This is because data are inconclusive, as studies are generally small and heterogeneous, often mixing preventative and therapeutic treatments. In 2013, Bradbury *et al* presented evidence on preventative modalities for PDPH.[6] Subsequently in 2019, Russell *et al* summarized evidence on conservative management and the use of an epidural blood patch (EBP) for PDPH in an obstetrics.[7 8] More recent studies have added to the current body of the literature.[9] Furthermore, there is a lack of practice guidelines covering both perioperative and diagnostic or interventional settings. Current multisociety guidelines aim to fill this void and provide comprehensive information with strength and certainty of evidence.

METHODS

Delegates from the American Society of Regional Anesthesia and Pain Medicine (ASRA Pain Medicine), European Society of Regional Anesthesia (ESRA), Society for Obstetric Anesthesia and Perinatology (SOAP), Obstetric Anaesthetists' Association

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Postdural puncture headache (PDPH) is a recognized complication following unintentional dural puncture during epidural analgesia, or intentional dural puncture for spinal anesthesia, diagnostic or interventional neuraxial procedures. It is usually postural and presents within the first 5 days of witnessed or suspected dural puncture. Although the headache usually resolves within 2 weeks, it may be associated with significant complications including persistent or chronic headache, backache, cranial nerve dysfunction, subdural hematoma and cerebral venous sinus thrombosis.

WHAT THIS STUDY ADDS

⇒ In these evidence-based and consensus-based guidelines from a multidisciplinary group, recommendations from a panel of 21 experts outline comprehensive guidance on prevention, identification and management of PDPH with strength and certainty of evidence on various patient, procedural, diagnostic and management aspects of PDPH.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These guidelines provide a framework for individual clinicians to assess risk, confirm diagnosis and provide a systematic approach to PDPH management. A discussion regarding the possibility of PDPH should be part of the informed consent process, and institutions should have a policy to identify and manage PDPH. We recommend local efforts are made at each facility performing neuraxial procedures to disseminate and discuss the information shared in this document, providing necessary education to all patient care teams, including, but not limited to, members of the anesthesiology, emergency medicine, neurology, chronic pain and any other medical specialties performing procedures that either risk dural puncture or intentionally breach the dura.

(OAA), American Society of Spine Radiology (ASSR) and American Interventional Headache Society contributed to these multisociety guidelines (figure 1). The committee cochairs (VU and SN) initially obtained approval from the ASRA Pain Medicine Guidelines Committee and Board of Directors.

The ASRA Pain Medicine Executive Director (AS) contacted each society to nominate representatives to contribute to the guidelines. Based on input from the committee members and stakeholders, the committee cochairs developed 10 review questions that were refined during conference calls. After an initial virtual meeting, contributors were divided into writing groups, and a person from each group was designated as a group leader.

A health sciences librarian conducted literature searches for each question in MEDLINE All (Ovid) on 2 March 2022. The search block for the 'PDPH' concept, common to all searches, was combined with search blocks specific to each review question (online supplemental appendix S1A). A publication date limit of 1960 onwards was set, as this was when PDPH was increasingly recognized as a clinical problem and studies started emerging. An English language limit was also applied due to team members' language abilities. Animal studies were excluded from all searches.

The results from each search were imported into separate Covidence projects for deduplication and screening. One reviewer from each group conducted title/abstract and full-text screening followed by data extraction either directly from Covidence or after exporting to Microsoft Excel. In addition, systematic reviews on PDPH were searched and shared with contributors. Each group was requested to screen references of systematic reviews relevant to their question to ensure no essential references were missed.

Each group submitted their work as a structured narrative review. Recommendations for each topic were graded according to the US Preventative Services Task Force (USPSTF) grading of evidence guidelines.[10] The grade of evidence was classified as A, B, C, D or I, whereas the level of certainty was rated as high, medium or low (tables 1 and 2).[11] Statements were presented when recommendations were not possible (eg, for patient factors) or when there was insufficient evidence to make recommendations. Statements were assigned a level of certainty without grading, whereas recommendations were assigned both level of certainty and grading. The editing team (RR, VU and RSV) reviewed submissions, which underwent multiple iterations with contributors to formulate an interim draft.

The interim draft was shared with all collaborators electronically, and each collaborator was requested to vote anonymously on each recommendation using a modified Delphi approach.[12] We used Microsoft Excel (Microsoft, Redmond, Washington, USA) for two rounds of electronic voting. The Delphi evaluation criteria were simplified, and collaborators were requested to indicate whether they 'agree' or 'disagree' or would like to 'abstain' from each recommendation.[13] Collaborators were also invited to provide mandatory comments and reasons for their decision if they disagreed or abstained.

The editing team refined and clarified the statements and recommendations after the first round of voting. Recommendations with 100% agreement were accepted, and recommendations with <100% agreement were revised considering contributors' comments. The aim was to increase the consensus in the second round.

In the second round, statements and recommendations with a predefined>75% agreement were accepted. Both USPSTF grading and >75% agreement threshold hve been previously used in ASRA Pain Medicine consensus guidelines.[14] Language recommendations were refined considering contributors' comments. The subsequent draft was shared with all the collaborators for final approval.

RESULTS

The number of results retrieved in Medline for each search and duplicates removed is shown in online supplemental appendix S1A. After two rounds of voting, we obtained the predefined>75% consensus for all statements and recommendations. In fact, 90%–100% consensus was obtained for almost all recommendations after the second round of voting (online supplemental appendix S2B). The final manuscript was approved by each collaborator, the ASRA Pain Medicine Board of Directors and participating societies listed in the methods section. The key recommendations are summarized in figure 2. A summary report of statements and recommendations is published elsewhere.[15]

Question 1: when should PDPH be suspected?

Definition

According to the most recent International Classification of Headache Disorders, 3rd edition (ICHD-3) published in 2018, PDPH is a headache attributed to low cerebrospinal fluid (CSF) pressure occurring within 5 days of a lumbar puncture (LP), caused by CSF leakage through the dural puncture.[16] Headache

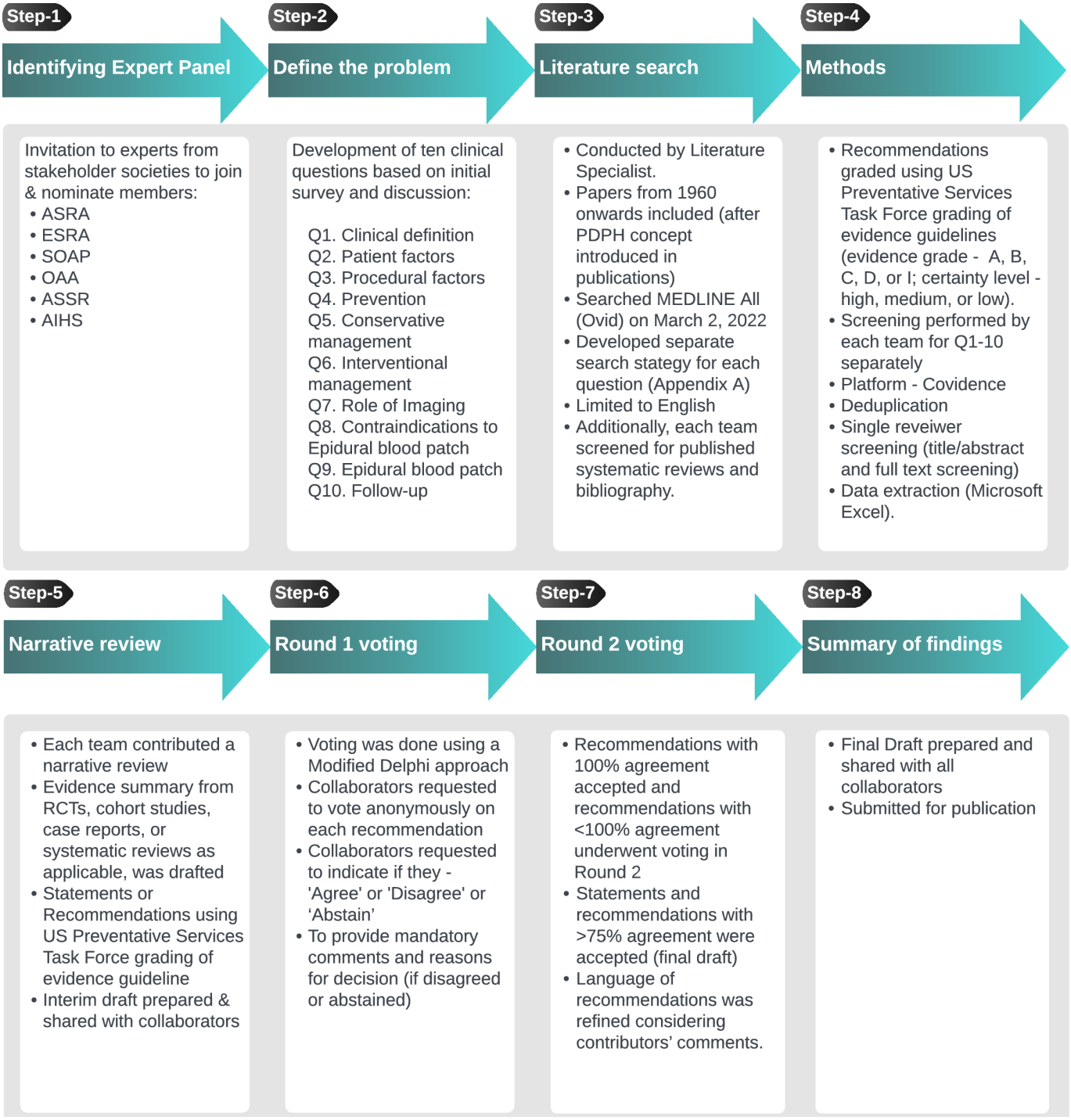

Figure 1 Summary of methods used for the development of guidelines. AIHS, American Interventional Headache Society; ASRA, American Society of Regional Anesthesia; ASSR, American Society of Spine Radiology; ESRA, European Society of Regional Anesthesia; OAA, Obstetric Anaesthetists' Association; PDPH, postdural puncture headache; RCTs, randomized controlled trials; SOAP, Society for Obstetric Anesthesia and Perinatology.

is usually accompanied by neck stiffness and/or subjective hearing symptoms, remitting spontaneously within 2 weeks or after sealing of the leak with autologous epidural lumbar patch. As such, the International Headache Society (IHS) definition requires evidence of low pressure or of CSF leakage on cerebral imaging (showing brain sagging or pachymeningeal enhancement or spine imaging (MRI, CT or digital subtraction myelography) showing extradural CSF). This definition has several potential weaknesses:

1. Neither opening nor closing pressure has been shown to differ in studies of patients with PDPH compared with controls.[17 18]
2. Patients with intracranial hypertension can have PDPH.[19]
3. Case reports and series have shown that PDPH may become apparent more than 5 days after dural puncture,[20–22] or after hospital discharge.[23 24]
4. The omission of the postural component in ICHD-3 is controversial. The previous ICHD definition contained a pos-

Table 1 US Preventative Services Task Force (USPSTF) grade definitions*

Grade	Definition	Suggestions for practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

*https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/grade-definitions.

tural component[25]: 'a headache that worsens within 15 min after sitting or standing and improves within 15 min after lying down after dural puncture has occurred or is suspected'. An analysis of electronic charts from 27 064 parturients having a neuraxial procedure over a 10-year period found that only 8 of 142 parturients with PDPH had no postural component.[4] Furthermore, the ICHD-3 diagnostic criteria V.7.2 (headache attributed to low CSF pressure criterion) states: 'headache has developed in temporal relation to the low CSF pressure or CSF leakage, or led to its discovery'.

5. A dural puncture may not be noticed during the procedure.[26]
6. There is an increasing body of evidence suggesting that headache can persist for longer than 2 weeks.[27–31]

Clinical features

In 2021, the American Society of Anesthesiologists released a statement in which the diagnosis of PDPH is based on both the clinical presentation and a detailed history and physical examination.[32] Typical symptoms include the following: neck stiffness; pain in the cervical, thoracic or lumbar vertebral area; subjective hearing symptoms; visual disturbances; and vertigo. Headaches are frequently reported after childbirth, but only a minority may be attributed to PDPH.[33] Headache may be worse with coughing or a Valsalva maneuver.

A recent observation of 1001 laboring women with PDPH revealed that only 40% showed classical signs (postural component and at least one of the following symptoms: neck stiffness, tinnitus, hypoacusia, photophobia and nausea).[34] Nausea/vomiting were present in 20%, auditory symptoms in 18%, dizziness in 24%, diplopia in 2%, other visual symptoms in 13% and tinnitus in 10%. Nevertheless, the pain location and associated symptoms in post-LP headache may be variable.[35]

Visual disturbances may be associated with cranial nerve palsy, of which the most affected are the abducens and facial nerve.[36] Typically, patients with PDPH do not exhibit fever, meningism, altered alertness or focal neurologic findings. Following an inadvertent dural puncture, the extent of CSF spread in the epidural space, extensive CSF leak on MRI and MRI scores correlate with the severity of PDPH symptoms.[37]

PDPH can be classified as mild, moderate and severe based on the amount of rest and physical activity per day and associated auditory and vestibular symptoms.[21] Atypical presentation of PDPH has been increasingly recognized. Loures *et al* reported a non-postural PDPH in 5.6% of obstetric

Table 2 Levels of certainty regarding net benefit

Level of certainty*	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: The number, size or quality of individual studies. Inconsistency of findings across individual studies. Limited generalizability of findings to routine primary care practice. Lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: The limited number or size of studies. Important flaws in study design or methods. Inconsistency of findings across individual studies. Gaps in the chain of evidence. Findings not generalizable to routine primary care practice. Lack of information on important health outcomes. More information may allow estimation of effects on health outcomes.

*The US Preventative Services Task Force (USPSTF) defines certainty as 'likelihood that the USPSTF assessment of the net benefit of a preventive service is correct'. The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Figure 2 Infographic showing recommendations with level A or B grading. EBP, epidural blood patch; LP, lumbar puncture; NSAIDs, non-steroidal anti-inflammatory drugs; PDPH, postdural puncture headache.

patients, the most significant predictor of which was identification of dural puncture is by aspiration of CSF from the epidural catheter.[4] In an observational study of 77 patients with PDPH, 55% exclusively reported a postural component to their headache. However, 45% occasionally experienced a non-postural headache when rising from the recumbent to the upright position.[38] Seizures have been reported with PDPH due to cerebral vasoconstriction.[39]

In the obstetric population, about one-third of women develop headaches in the first postpartum week. It is essential to differentiate PDPH from other causes of headache. In a prospective study, nearly 75% of headaches were classified as primary headaches (eg, migraines or tension headaches) and the remainder were due to secondary causes such as PDPH, hypertensive disorders of pregnancy or intracranial pathology.[33] PDPH accounted for only 4.7% of all the postpartum headaches. The other differential diagnoses of PDPH include caffeine withdrawal, sepsis, meningitis, sinusitis, CVST, cerebral ischemia, arterial dissection, pre-eclampsia and pneumocephalus.[31 39] Additional differential diagnoses may include intracranial pathology, such as an intracranial, subarachnoid or SDH; intracranial tumor; aneurysm; cerebral infarction; spontaneous intracranial hypotension; benign intracranial hypertension; cerebral edema; pituitary apoplexy; neurotoxicity of drugs; reversible cerebral vasoconstrictive syndrome; and posterior reversible encephalopathy syndrome (PRES).[32 40] Appropriate clinical and neurological examination, imaging studies and regular follow-up should be performed based on the clinical presentation to ensure correct diagnosis and treatment of headache.

Frequency of observation

The frequency with which patients should be observed after a neuraxial block or an LP is unclear. Inpatients should be seen by a member of the healthcare team at least once per day to ensure full neurological recovery and absence of headache. After a neuraxial procedure and before discharge, patients should be given verbal and written advice on when and who to contact if complications appear.

If PDPH is suspected, a member of the healthcare team should see the patient more often and within 24 hours[31] and treatment initiated immediately. An analysis of more than 22 million deliveries showed that delayed treatment was the strongest risk factor associated with a cranial SDH.[24] Follow-up with patients is required until symptoms resolve.

- **Statement**: *PDPH should be suspected if headache or neurological symptoms, which may be relieved when lying flat, occur within five days of a neuraxial procedure (Moderate Level of Certainty).*
- **Recommendation**: *Inpatients who have received a neuraxial procedure should be reviewed and evaluated for symptoms of PDPH. Outpatients should be instructed to report symptoms of PDPH to their physicians (Grade A; High Level of Certainty).*

Question 2: what patient factors are associated with the incidence of PDPH?

Overview

PDPH is a known complication of intentional dural puncture during an LP, spinal procedure or inadvertent dural puncture during an epidural procedure.[1] Its incidence, as reported in the literature, varies widely. Following spinal anesthesia, rates ranging from <2% to 40% have been described, depending on needle gage.[1–3] In the obstetric population, a meta-analysis showed a risk of dural puncture of 1.5% with epidural insertion, with half of these patients developing PDPH.[41] Subsequent studies have shown inadvertent dural puncture rates in obstetric patients as low as 0.5%, and subsequent PDPH rates as high as 80%.[5] PDPH may follow labor epidural analgesia in which dural puncture was not recognized.[26]

A variety of risk factors for PDPH have been studied, often retrospectively, via chart review. Some prospective studies have followed cohorts of patients after dural puncture, but there are few relevant randomized, controlled trials. Risk factors include patient demographic variables (eg, age and sex), comorbidities and obstetric factors. Articles feature a myriad of patient populations, including males and females, obstetric and non-obstetric surgical patients receiving neuraxial anesthetics or medical patients undergoing diagnostic LP.

Patient risk factors that have been most well-studied are age, sex, body mass index (BMI) and history of headache.[20 42–45]

These factors are examined, along with several more recently investigated obstetric factors and maternal habits, such as smoking and depression.

Studies evaluating patient factors

Age

A large number of studies have investigated whether age influences the risk of developing PDPH.[46–49] Fourteen studies, comprizing both adult[50] and pediatric[3] patients, reported the association between age and incidence of PDPH.[20 43 50–57] Historically, PDPH has been thought to have its highest incidence in the age group of 20–30 years and rarely occurs after the age of 60 years.[55 58]

In adult patient studies, younger age was defined specifically as <40 years in three studies.[47 56 57] Nielsen and Vamosi reported that older patients were less likely than younger patients (age<40 years) to develop PDPH (OR, 0.95; 95% CI, 0.94 to 0.97).[56] Pirbudak *et al* reported that patients between 25 and 40 years were more likely to experience PDPH than older patients.[57] Vilming *et al* reported the same for patients<40 years (without ORs).[47] In two studies, age<50 years was reported to be associated with a higher risk of PDPH.[20 59] Amorim *et al* reported that age between 31 and 50 years was associated with an OR of 2.21 (95% CI, 1.12 to 4.36) of developing PDPH.[20] Finally, Wadud *et al* reported PDPH in 30 patients, with an incidence of 30% in patients aged 30–50 years and 5% in patients aged 51–75 years.[59]

Six additional studies reported younger mean ages for patients with PDPH.[43 46 49 50 55 60] In a retrospective study of 2655 obstetric and non-obstetric patients undergoing spinal and epidural anesthesia, Kim *et al* reported that patients with PDPH tended to be younger (OR, 0.979; 95% CI, 0.960 to 0.997); however, there were relatively few cases of PDPH in the sample and the technique was heterogeneous.[60] In an earlier prospective study of patients undergoing LP, Kuntz *et al* reported that patients with versus without PDPH had a mean age of 46 and 54 years, respectively.[50]

The adolescent population warrants special commentary. A recent study by DelPizzo *et al* including 656 patients aged 12–45 years receiving either spinal or combined spinal–epidural (CSE) anesthesia for ambulatory surgery found that patients aged 12–19 years had an almost threefold increase in the odds of developing PDPH (adjusted OR (aOR) 2.8; 95% CI, 1.1 to 7.3) compared with the 20–45 year age group.[52] Previously, Egbohou *et al* described 500 healthy patients receiving non-urgent surgery with spinal anesthesia in which patients from ages 16–30 years had an increased risk of PDPH with an OR 2.1 (95% CI, 1.1 to 2.2) in comparison with patients>30 years.[53]

- **Statement**: *The preponderance of evidence suggests that in the adult population, younger age may be associated with an increased risk of PDPH (High Level of Certainty).*

Sex

Female sex has long been considered an independent risk factor for the development of PDPH. Theories citing differences in biological and psychosocial factors between the sexes are suggested as to why females report more postoperative headaches than males.[58] The relationship between sex and development of PDPH in non-pregnant patients has been examined in 11 studies.[20 43 47 48 50 55 58–62]

The incidence of PDPH between males and non-pregnant females has been compared in nine prospective studies and one meta-analysis.[20 43 47 48 50 55 58 59 61] Most studies report a higher likelihood of developing PDPH in females.[20 43 47 48 50 55 58 59 61] An adjusted OR (OR, 2.25; 95% CI, 1.07 to 4.73) was reported by Amorim *et al*.[20] Wu *et al* performed a meta-analysis including 18 randomized studies that evaluated non-obstetric patients of both sexes and determined that males had a lower risk of developing PDPH than non-pregnant females (OR, 0.55; 95% CI, 0.44 to 0.67).[58]

- **Statement**: *The preponderance of evidence suggests that female sex is associated with an increased risk of PDPH (High Level of Certainty).*

Body mass index

There is a preponderance of studies that address BMI and PDPH, many of which suggest that obesity is associated with a lower incidence of PDPH. It is postulated that the higher intra-abdominal pressure that accompanies an increased BMI increases epidural pressure, thus decreasing the intrathecal-to-epidural-space pressure gradient and reducing CSF leak through the dural hole. Lower BMI was found to be associated with a higher risk of PDPH in seven studies (three prospective,[49 50 53] four retrospective[63–66]). Peralta *et al* retrospectively analyzed data from 518 obstetric patients who had a witnessed inadvertent dural puncture during epidural or CSE neuraxial labor analgesia procedures.[66] They found that patients with a higher BMI had a lower incidence of PDPH after inadvertent dural puncture (39% for BMI≥31.5 kg/m^2 vs 56% for BMI<31.5 kg/m^2), a difference of −17% (95% CI, −7% to −26%).[66] Neither the initial nor maximum headache intensity differed between groups. Costa *et al* performed a 10 year retrospective study on over 32 000 obstetric patients receiving epidural or CSE labor analgesia.[65] Patients with a BMI<31.5 kg/m^2 were more likely to develop a PDPH after dural puncture compared with patients with a BMI≥31.5 kg/m^2. Chekol *et al* published a meta-analysis that concluded that normal BMI was positively associated with PDPH (aOR, 1.22; 95% CI, 1.09 to 1.35) in parturients who delivered by cesarean section under spinal anesthesia.[67] However, a single study[64] appears to have contributed most of the data accounted for in this meta-analysis due to the large sample (172 599 patients).

In contrast, several other investigators found no difference in the incidence of PDPH related to BMI.[43 48 62 67–70] Song *et al* investigated 17 497 parturients receiving labor epidural analgesia before vaginal delivery, 164 of whom experienced an inadvertent dural puncture.[69] Although, 51.2% developed PDPH, there was no significant relationship between BMI and PDPH incidence or intensity of headache. Miu *et al* retrospectively analyzed over 18 000 parturients receiving epidural or CSE for labor analgesia who developed PDPH, with or without inadvertent dural puncture.[68] Again, the women in BMI≥30 group (n=60) and BMI<30 group (n=65) did not significantly differ with respect to incidence or intensity of PDPH (overall, 82% vs 80%; severe, 36% vs 23%, respectively) or need for an EBP. The groups also did not differ significantly in a subgroup analysis of those who had a witnessed inadvertent dural puncture (n=93) or in women with a BMI>40 kg/m^2 (n=10). There was also no difference in mode of delivery for these patients, thus eliminating an important potential confounding variable. In a prospective study of 464 women in Turkey receiving spinal anesthesia for cesarean delivery with 27G Quincke needles, there was no difference in PDPH between those with BMI<30 or ≥30 kg/m^2.[70] This finding was supported by a study of 144 patients undergoing LP in which BMI was similar in those with and without headaches.[43] In another diagnostic LP study with a >50% PDPH rate, BMI was also not associated with PDPH, although mean BMI was 28.9 kg/m^2.[62]

In light of the inconsistency of findings, Russell *et al* have published a protocol outlining a systematic review to determine if there is a difference in the incidence of PDPH in the obese parturient compared with the non-obese parturient after an inadvertent dural puncture.[71]

- **Statement**: *Evidence does not suggest that BMI consistently correlates with an increased risk of PDPH (Moderate Level of Certainty).*

Comorbidities

Headache

Numerous studies have investigated the association of various classifications of headache prior to dural puncture and the subsequent development of PDPH based on a potential, common physiological pathway involving vasodilation of intracranial vessels and/or hypersensitivity to substance P.[42] Three studies of patients undergoing large-bore dural punctures found a positive association between pre-existing or recent headache and PDPH.[46 50 62] In a prospective cohort of 252 men and women studied by Ljubisavljevic *et al*, pre-existing headaches were found to be an independent risk factor for PDPH (aOR, 4.23; 95% CI, 1.27 to 14.1) after LP with 18G and 20G cutting spinal needles.[62] In a retrospective review of patients receiving spinal drains for thoracic aortic aneurysm repair, a history of preoperative headache was found to significantly increase the risk of PDPH (27.9% vs 8.3%; p≤0.001).[46] A third review of 501 consecutive LPs with 20G or 22G needles found that headache in the week preceding the procedure was a risk factor for developing a PDPH.[50] In a study of Jordanian women receiving spinal anesthesia for cesarean delivery (25G Whitacre or 27G cutting needles), the presence of tension but not migraine headache increased the risk of PDPH 4.6-fold.[72]

When a history of headache rather than a contemporaneous headache is studied, the association with PDPH persists. Goldszmidt *et al* found that having more than 12 headaches (type not specified) per year was associated with an aOR of 2.25 (95% CI, 1.63 to 3.11) of PDPH.[33] In a population of 144 patients undergoing diagnostic LP with 20G or 22G Quincke needles, Khlebtovsky *et al* found that a history of headaches of heterogenous types before their acute illness was reported by 67% of the post-LP headache group and 38% of the no-headache group.[43] In a study of 160 migraineurs and 53 age-matched and sex-matched healthy controls before and after LP, being a migraineur did not increase the risk of PDPH.[49]

Finally, it has been speculated that a history of PDPH increases the risk of future PDPH, perhaps due to host effects. Two studies confirm this conjecture. When Lybecker *et al* prospectively investigated 873 consecutive patients undergoing spinal anesthesia (1021 procedures), multivariate analysis showed a history of previous PDPH to be a significant predictor of PDPH.[55] Amorim *et al* confirmed this finding; after 640 nonpregnant women and men had received spinal anesthesia with Quincke 25G or 27G needles, a history of PDPH increased the odds of subsequent PDPH (26.4% vs 6.2% (OR 4.30; 95% CI 1.99 to 9.31)).[20]

- **Statement**: *The preponderance of evidence suggests that a history of headaches (chronic, contemporaneous, or prior PDPH) may be associated with an increased risk of PDPH. The association specifically with migraine is less clear (Moderate Level of Certainty).*

Smoking

Perhaps related to nicotine's vasoconstrictive properties, cigarette smoking may influence the development of PDPH, as reported in two studies. Using multivariate analysis, Ljubisavljevic *et al* reported that among smokers, patients with a longer smoking history had a lesser risk of PDPH than those with a shorter smoking history.[62] Dodge *et al* reported in a single-center retrospective study that smokers exhibited a lower incidence of PDPH versus non-smoker controls (13.7% to 34.1%, p=0.009).[73]

► **Statement**: *Limited evidence suggests that cigarette smoking might be associated with a decreased risk of PDPH (Low Level of Certainty).*

Depression

In a single study, Makito *et al* found that depression was associated with a higher incidence of PDPH in obstetric and non-obstetric female patients after spinal anesthesia.[64]

► **Statement**: *There is insufficient evidence to conclude that depression is a risk for PDPH (Low Level of Certainty).*

Obstetric factors

There are a several retrospective cohort studies that associate obstetric factors with the likelihood of developing PDPH. Three of these studies found an association between pushing during labor and an increased risk of developing PDPH. In an early study of 33 patients with unintentional dural puncture during labor epidural procedures, 74% of women who subsequently pushed, versus 10% of those who did not, developed PDPH.[74] Increasing the duration of pushing was associated with an increased likelihood of developing PDPH. In their study of 518 obstetric patients with documented unintentional dural puncture during epidural or CSE neuraxial labor analgesia, Peralta *et al* found an increased odds of developing PDPH in women who pushed compared with those who did not push during delivery (OR, 2.4; 95% CI, 1.2 to 3.9).[66] Franz *et al* also found that parturients who pushed during active labor after a witnessed dural puncture during CSE or epidural labor analgesia procedures exhibited an increased risk of PDPH (OR, 2.1; 95% CI, 1.1 to 4.0), longer duration of headache and increased need for an EBP, although these findings were not reproduced in multivariate analysis.[75]

A retrospective analysis of over 1.7 million privately insured patients identified a potential protective effect for cesarean delivery in the risk of developing PDPH following labor neuraxial analgesia. The authors suggested that this may be due to the avoidance of pushing during the second stage of labor.[76]

Studies with dissenting results had some important inherent differences. Ravindran *et al* assigned women to either a 'push' or 'no push' group after suffering an inadvertent dural puncture and found no difference in the PDPH rate between groups.[77] However, in contrast to the previously cited studies, this study featured intentional dural puncture with a 22G spinal needle rather than inadvertent dural puncture with a larger, 17–18G epidural needle. In addition, the duration of pushing was short (≤10 pushes) and may not have been adequate to result in a detectable difference. Goldszmidt *et al* prospectively studied 985 women delivering over a 3-month period in a single tertiary care institution.[33] They concluded that a shorter duration of pushing was associated with an increased risk of PDPH (aOR 0.90; 95% CI, 0.81 to 1.00), although the CI included '1'.

Orbach-Zinger *et al* retrospectively found that patients with increased cervical dilation had an increased risk of unintentional dural puncture (OR, 1.23; 95% CI, 1.04 to 1.42), but not necessarily headache.[78] Bardon *et al* reported that cervical dilation of ≥7 cm was associated with an increased risk of PDPH and blood patch (OR, 6.5; 95% CI, 1.5 to 29.3).[79]

► **Statement**: *Evidence regarding the effect of active pushing on PDPH during the second stage of labor following dural puncture with an epidural needle is conflicting (Low Level of Certainty).*

Question 3: what procedural characteristics are associated with PDPH?

Studies evaluating performer and procedural characteristics

Needle type

Spinal needles are classified as cutting (conventional or traumatic) or non-cutting (atraumatic or pencil point) based on their tip configuration.[2] Cutting needles (eg, Quincke) have a sharp, slanted tip that cuts through the dura, with a distal opening. Non-cutting needles (eg, Whitacre) have a closed pencil point tip with a side port distal aperture. Non-cutting needles reduce the incidence of PDPH by limiting CSF leakage after dural puncture.[80 81]

In studies across obstetric, non-obstetric and neurological populations, compared with cutting needles, non-cutting needles reduced the risk of PDPH (4.2% vs 11%), the incidence of severe PDPH (1.2% vs 4.2%) and the need for an EBP (1.1% vs 3.0%).[82–85] These differences are retained irrespective of population subtypes (obstetric vs non-obstetric).[82–86] In the most extensive published meta-analysis to date, Nath *et al* pooled results from 110 trials (31 412 patients). They showed that non-cutting needles retained procedural efficiency (similar success at the first attempt, overall failure, and risk of backache) while reducing the need for a return to the hospital for further management (eg, fluid administration, analgesics or EBP).[84] Their subgroup analysis also revealed that the non-cutting needles retained their effect of reducing rates of PDPH across various needle sizes. Finally, despite a higher material cost, evidence supports the use of non-cutting needles as they reduce overall healthcare utilization through harm reduction.[87] Evidence suggests that various types of non-cutting needles are associated with a similar PDPH risk profile.[88 89]

► **Statement**: *Compared to cutting needles, non-cutting spinal needles are associated with decreased risk of PDPH (High Level of Certainty). However, there is limited evidence regarding a particular design of non-cutting spinal needle (Low Level of Certainty).*

► **Recommendation**: *Routine use of non-cutting spinal needles for LP for all populations is recommended (Grade A; High Level of Certainty).*

Needle size

The impact of needle size on PDPH risk is likely a result of interaction among needle size, needle type and the risk of multiple redirections (for narrower gage needles). Moreover, this risk is likely non-linear, more profound for mid-gaged to wider-gaged needles, and less for narrower needles.

Ten studies have compared cutting needles of different sizes: five randomized controlled trials (RCTs),[2 54 90–92] three prospective cohort studies,[48 62 93] one non-randomized study[94] and one survey.[95] Eight studies[2 48 54 90 92–95] demonstrated a reduction in PDPH risk with a narrower gage cutting needle. Of the nine studies comparing non-cutting needles of different sizes,[17 96–103] five RCTs failed to demonstrate a significant difference,[17 96–98 103] while the remaining four showed a modest benefit of narrower gage non-cutting needles over larger non-cutting types.[99–102] Six studies compared cutting and non-cutting needles of different sizes (three retrospective,[104–106] two prospective[107 108] and one RCT[109]) involving diagnostic LP showed that non-cutting needles of narrower-gage reduced PDPH risk. Seven[100 110–115] out of ten studies[116–118] that compared a narrower gage cutting needle to a wider non-cutting needle concluded that there was a lower risk of PDPH with the non-cutting design.

These findings are consistent with existing systematic reviews. While Choi *et al*[41] demonstrated a reduction in PDPH with narrower gage needle sizes, Chekol *et al*[67] concluded that multiple attempts were associated with a higher risk of PDPH. Zorrilla-Vaca *et al* performed a meta-regression using data from 57 trials and demonstrated a significant relationship between needle gage and PDPH for cutting needles, but not non-cutting needles. Based on this, the authors recommended that providers consider selecting wider-gage non-cutting needles to maximize technical proficiency without an increased risk of PDPH.[86 119] Finally, the recent evaluation by Nath *et al* showed a decreasing incidence of PDPH with needle size for both cutting (28.11%, 11.3% and 3.9% with 20–22G, 23–26G and >26G, respectively) as well as non-cutting needles (12.4%, 3.45% and 1.1% with 20–22G, 23–26G and >26G, respectively).[84]

The inadvertent dural puncture rate has been reported in many studies. Using a 16G Tuohy needle, Sprigge and Harper[26] found a rate of 0.9% in 18 337 obstetric patients. The rates of 0.5% have been described by both van de Velde *et al*[120] (n=17 158) and Sadashivaiah and McLure[121] (n=21 466) using an 18G Tuohy needle. Caution is, however, advised when comparing outcomes between different studies. Furthermore, McNeill and Thorburn compared 685 obstetric patients undergoing lumbar epidural analgesia and found no differences in block-related complications between 16G and 18G Tuohy needles.[122]

- **Statement**: *When using cutting needles, narrower gauge needles decrease the risk of PDPH (High Level of Certainty).*
- **Statement**: *For non-cutting needles, limited evidence suggests narrower gauge needles decrease the risk of PDPH (Moderate Level of Certainty).*
- **Recommendation**: *If using a cutting needle for LP, use of a narrower gauge needle is recommended to decrease the risk of PDPH (Grade A; High Level of Certainty).*
- **Recommendation**: *Limited evidence supports use of narrower gauge non-cutting needles over larger needles for LP to decrease the risk of PDPH (Grade C; Moderate Level of Certainty).*

Needle insertion

Janik and Dick used 25G Whitacre needles to compare midline and paramedian insertion in 250 patients undergoing transurethral prostate surgery and did not identify a difference in PDPH risk.[123] Mosaffa *et al* used 25G Crawford needles to compare midline and paramedian insertion of a spinal needle in the orthopedic population (n=150) and again failed to find a significant difference in the incidence of PDPH.[61] Similarly, Uluer *et al* used 25G Quincke needles and reported no significant difference in PDPH rates for midline versus paramedian insertion of spinal needles in the obstetric population (n=200).[124] However, Viitanen *et al* used 27G Quincke needles in 212 parturients in a prospective cohort study and found an association between paramedian needle insertion and increased PDPH risk,[125] although needle insertion technique was not randomized. A prospective study comparing epidural catheter insertion in obstetric patients using either the midline or paramedian approach did not demonstrate a difference in PDPH.[126]

- **Statement**: *Evidence does not support the paramedian over the midline approach to decrease the risk of PDPH when performing LP (Moderate Level of Certainty).*

Bevel direction

It has been proposed that parallel (longitudinal) bevel orientation could reduce PDPH based on the hypothesis of the longitudinal arrangement of elastic and collagen fibers in the dura mater.[127] However, electron microscopy shows no specific arrangement of such fibers.[128] Three RCTs that concluded a lower risk of PDPH with cutting needles in parallel bevel orientation to the dural fibers (longitudinal insertion) versus perpendicular orientation (transverse insertion) were identified.[129–131] This is also supported by 1 prospective[55] (n=873) and 1 retrospective study (n=92).[132] However, two small RCTs did not support this conclusion.[133 134] Richman *et al*, in their meta-analysis, concluded that insertion of a cutting needle with the bevel oriented in a parallel/longitudinal fashion resulted in a significantly lower incidence of PDPH compared with that oriented in a perpendicular/transverse fashion (PDPH rates of 10.9% vs 25.8%; OR 0.29, 95% CI 0.17 to 0.50).[135] Recent in vitro electron microscopy studies have challenged the belief that parallel bevel orientation is responsible for reducing the incidence of PDPH.[136]

Norris *et al* evaluated the effect of epidural needle bevel orientation in 41 women with dural puncture.[137] In total, 14 of the 20 women in the group in which the needle bevel was perpendicular to dural fibers developed a moderate-to-severe headache, whereas only 5 of 21 in the group in which the needle bevel was parallel to dural fibers did so ($p<0.05$). The authors concluded that identifying the epidural space with the needle bevel oriented parallel to the longitudinal dural fibers limits the size of the subsequent dural tear and, therefore, lowers the incidence of headache should dural perforation occur. However, rotation of the needle within the epidural space to facilitate catheter insertion may increase the likelihood of dural trauma.

- **Recommendation**: *If using a cutting needle for LP, insertion with the bevel parallel to the long axis of the spine is preferred as it may decrease the risk of PDPH (Grade B; Moderate Level of Certainty).*

Needle advancement

When performing an epidural procedure, the epidural space is usually identified by a loss of resistance technique using a syringe either filled with air or saline. Needle advancement may be either continuous or intermittent. There is minimal evidence on the effect of the technique on the incidence of dural puncture, inadvertent intrathecal catheter placement and PDPH.[138]

- **Statement**: *Evidence is insufficient to confirm benefit of any technique used to identify the epidural space on reduction of the incidence of PDPH (Low Level of Certainty).*

Number of attempts

Multiple attempts at spinal anesthesia or LP may result in numerous unrecognized dural punctures, contributing to an increased likelihood of PDPH. Khraise *et al* conducted a prospective study of 680 women undergoing cesarean section under spinal anesthesia with a non-cutting needle using either a 27G Spinostar (n=345) or a 25G Whitacre needle (n=335).[72] The adjusted effects in the logistic regression model showed that use of the Spinostar needle increased the risk of a repeated puncture attempt 28-fold compared with use of the 25G Whitacre needle. They reported that repeated attempts at spinal anesthesia increased the PDPH rate from 4.7% to 10% (OR, 2.55; 95% CI, 1.09 to 5.93). In two studies, Harrison and Langham demonstrated higher rates of PDPH following multiple attempts at spinal anesthesia.[114 139] Seeberger *et al* analyzed prospectively collected data on 8034 spinal anesthetics and found the incidence of PDPH increased from 1.6% to 4.2% if a subarachnoid block was repeated after a failed spinal.[140]

- **Statement**: *Evidence suggests an association between the number of attempts at LP and the risk of PDPH (Moderate Level of Certainty).*

Operator experience

Trainees are likely to have a higher rate of PDPH during their initial years of training. Dittmann *et al* reported a lower PDPH rate among consultants compared with trainees (0.5% vs 2%) in a prospective observational study of 2378 spinal anesthetics.[141] Haller *et al* reported a reduced risk of PDPH with anesthetist training>3 years (OR, 0.20; 95% CI, 0.55 to 0.76) in a case–control study including spinal, epidural and CSE procedures.[142] Sidhu *et al* demonstrated higher PDPH rates following blocks done by registrars and fellows (compared with consultant anesthetists) in their retrospective cohort study of 7976 labor epidurals.[143] Tien *et al* reviewed 43 434 records of labor epidurals and estimated a decreasing rate of PDPH with increasing experience.[144] Michaan *et al* did not find a difference in experience level between cases and controls in their study (n=147),[145] possibly due to the fact that both cases and controls were performed by anesthesiologists with over 10 years of experience.

- **Statement**: *Evidence suggests that increased operator experience level decreases the incidence of PDPH, but net benefit may be small (Moderate Level of Certainty).*

Type of neuraxial block

Three extensive retrospective analyses of databases demonstrate a similar risk of PDPH following CSE, spinal or epidural.[26 120 146] By contrast, in a randomized study of 224 patients<55 years old undergoing minor non-obstetric surgery, Flatten *et al* showed a higher risk of PDPH following spinal anesthesia with a 27G Quincke needle (15.5%) than with an epidural using an 18G Tuohy needle (1.8%).[147] In both groups, headaches were of similar duration and intensity. Puolakka *et al* found no difference in PDPH rates following spinal, continuous spinal and CSE in a prospective study of 3230 orthopedic patients.[148] Finally, Simmons *et al* conducted a meta-analysis and showed similar rates of PDPH between CSE versus epidural (nine RCTs)[149] and CSE versus spinal (five RCTs).[150] Similar rates of PDPH have been reported after epidural and dural-puncture epidural techniques but numbers are too small to draw firm conclusions.[151]

- **Statement**: *Evidence suggests that all neuraxial techniques (ie, spinal, epidural, and CSE) have similar PDPH risk profiles (Moderate Level of Certainty).*

Level of neuraxial block

Makito *et al* analyzed over 1.8 million epidurals and did not find a significant difference in the risk of PDPH between thoracic versus lumbar epidural (multivariate OR, 1.31; 95% CI, 1.00 to 1.72).[64]

- **Statement**: *Evidence does not suggest an association of PDPH with the level of epidural insertion (Moderate Level of Certainty).*

Patient position

While the sitting position may be associated with the ease of performing LP or a neuraxial block, a higher CSF pressure may also result in a greater leak and an increased risk of PDPH.[152 153] The results from two RCTs indicate a lower rate of PDPH with the lateral decubitus than with the sitting for spinal anesthesia.[154 155] Zorrilla-Vaca and Makkar conducted a meta-analysis (7 studies, n=1101) and demonstrated a significant reduction of the incidence of PDPH (relative risk (RR), 0.61; 95% CI, 0.44 to 0.86, p=0.004; I^2=25%; p for heterogeneity=0.42) with the lateral decubitus compared with the sitting position during dural puncture.[156] However, for operators relatively unfamiliar with procedures conducted in the lateral position, an increased number of attempts may be necessary which could increase the risk of PDPH.

- **Statement**: *Evidence suggests a decreased risk of PDPH with techniques performed with the patient in the lateral decubitus position. (Moderate Level of Certainty)*

Traumatic versus atraumatic tap

Visualization of blood during a neuraxial block resulting from vascular trauma may be referred to as a traumatic tap. The initial description of an EBP by Gormley, resulted from the observation that traumatic taps were associated with a reduced PDPH rate.[157] Nath *et al*[84] included 9 RCTs (n=1585) in a meta-analysis of spinal anesthesia, which included the incidence of traumatic tap between cutting and non-cutting needles, in both adults and children. There was no significant difference in the incidence of traumatic tap between the two needles. No reports assessing the risk of PDPH after traumatic taps during epidural blocks were identified.

- **Statement**: *Evidence suggests that the choice of needle for LP does not alter the risk of traumatic tap and the risk of PDPH (Moderate Level of Certainty).*

Question 4: what measures may be used to prevent PDPH?

Continuous spinal or epidural analgesia following inadvertent dural puncture

There is a significant variation in clinical practice regarding the immediate management of inadvertent dural puncture during epidural anesthesia or analgesia. Options include abandoning the procedure (and proceeding with another mode of analgesia or anesthesia), placing an intrathecal catheter to enable continuous spinal anesthesia or resiting the epidural at a different lumbar interspace.

The role of intrathecal catheters in preventing PDPH after an observed inadvertent dural puncture has been evaluated in several systematic reviews and meta-analyses. Apfel *et al* considered six studies (five full papers and one abstract) and found no reduction in the incidence of headache or the need for an EBP in patients who had received an intrathecal catheter.[158] In a 2013 meta-analysis (nine studies, six full papers, three abstracts), Heesen *et al* found no difference in headache rates but a reduced requirement for an EBP.[159] Heesen updated the analysis in 2020 (13 studies, 12 full papers, 1 abstract),[160] finding that the RR for the incidence of PDPH was 0.82 (95% CI, 0.71 to 0.95), and the RR for the need for an EBP was 0.62 (95% CI, 0.49 to 0.79). However, this was negated by trial sequential analysis, which suggested insufficient data to exclude a type 1 error of statistical analysis. The authors concluded that there was, despite increasing use in clinical practice, no firm evidence on which to base a definite conclusion. Deng *et al*, in a retrospective study and meta-analysis conducted in 2019 (13 full papers),[161] found that an intrathecal catheter significantly reduced the incidence of PDPH (pooled RR, 0.823; 95% CI, 0.700 to 0.967; p=0.018) and the requirement for an EBP (pooled RR, 0.616; 95% CI, 0.443 to 0.855; p=0.004). However, only two of the studies included were prospective.

Significant heterogeneity exists in all studies evaluating intrathecal catheters (eg, randomization, utilization (continuous spinal anesthesia vs no infusion) and duration of intrathecal

catheters (long-term vs short-term catheter placement)). In addition, most studies are retrospective and predominantly include obstetric patients, potentially limiting the generalizability of the findings. In one of the few prospective investigations, Russell did not observe a reduction in headache incidence or the need for an EBP in the protocol-compliant or intention-to-treat groups.[162]

The potential mechanism of action of intrathecal catheters is infrequently considered. One suggestion has been that leaving a catheter in situ promotes a fibrotic reaction aiding closure of the dural hole. However, like all medical devices, epidural catheters are extensively tested and inert, so they are unlikely to promote a tissue reaction. A more plausible explanation is that leaving a catheter in situ reduces CSF leakage.

- **Statement**: *Following inadvertent dural puncture during attempted epidural catheter insertion, evidence is insufficient to confirm that placement of an intrathecal catheter decreases the risk of PDPH and EBP (Low Level of Certainty).*
- **Recommendation**: *After inadvertent dural puncture during epidural catheter placement, an intrathecal catheter may be considered to provide anesthesia/analgesia. This decision must consider potential risks associated with intrathecal catheters (Grade B; Low Level of Certainty).*

Prophylactic EBP

A prophylactic EBP, in which blood is injected into the epidural space via an existing catheter before its removal or as a standalone procedure, may be performed in patients after inadvertent dural puncture but before the development of PDPH.

Three RCTs and one systematic review have approached the topic.[163–166] Colonna-Romano and Shapiro studied the effect of an EBP via the epidural catheter inserted after unintentional puncture of the dura in laboring parturients. They reported a significant decrease in headache incidence in the study group, although some patients were monitored by telephone after discharge and only for 4 days after the procedure. The anesthesiologist making the diagnosis of PDPH was not blinded.[163] Trivedi *et al* showed a significant decrease in PDPH after prophylactic EBP when compared with no treatment or saline injection via an epidural catheter.[164] Patients were not blinded as those in the control group were aware that no prophylactic measure was performed. Scavone *et al* compared a prophylactic blood patch with no intervention. In their study, 64 parturients who experienced an inadvertent dural puncture were randomized to receive a prophylactic EBP with 20 mL of autologous blood or a sham patch.[166] An unblinded investigator observed patients for a minimum of 5 days after the procedure. The incidence of PDPH was similar for both groups. However, a prophylactic EBP shortened the length and severity of PDPH symptoms without increasing the incidence of backache or other adverse effects.

In a prospective trial, Stein *et al* randomized obstetric patients who had sustained an inadvertent dural puncture during epidural analgesia for labor or cesarean delivery to receive a prophylactic EBP or conservative treatment with a therapeutic EBP if required.[167] They found that 11/60 (18.3%) patients in the prophylactic EBP group developed a PDPH compared with 39/49 (79.6%) in the therapeutic EBP group ($p<0.0001$). The number of patients who needed a second EBP did not differ significantly between the two groups. They concluded that a prophylactic EBP effectively reduced the development of PDPH in obstetric patients. In the conservative treatment with therapeutic EBP if required group, it is noteworthy that treatment was not standardized, with the decision to proceed to an EBP being made at the clinician's discretion.

- **Statement**: *Prophylactic EBPs via an existing epidural catheter or as a standalone procedure have been performed following inadvertent dural punctures in both obstetric and non-obstetric populations with variable success. Not every patient who experiences a dural puncture develops a PDPH. Therefore, a policy of routine prophylactic blood patching exposes some patients to unnecessary potential risks.*
- **Recommendation**: *A prophylactic EBP is not recommended as routine as there is insufficient evidence to support its effectiveness in preventing PDPH (Grade C; Low Level of Certainty).*

Bed rest

The symptoms of PDPH are classically positional and usually improve when supine and worsen with an upright position. Hence, bed rest and the supine position have been conventionally promoted to improve symptoms, although these benefits are often transient.

Three RCTs and three systematic reviews have studied the effectiveness of bed rest in preventing PDPH or decreasing severity of symptoms.[168–174] There is consistent evidence that bed rest has a minimal role in preventing the incidence of PDPH and, therefore, should not be recommended for prophylaxis. Whether bed rest decreases the severity of PDPH is controversial: in 1 RCT of 80 obstetric patients,[168] best rest for 24 hours increased the incidence of severe headache with compared with ambulation (15.7% vs 2.4%). However, in a study of 208 non-obstetric patients randomized to early ambulation or 24 hours bed rest, the incidence of severe headache was higher in the ambulant group (57% vs 12%).[173]

Prolonged bed rest can increase the risk of thromboembolism, particularly in obstetric patients. Therefore, thromboprophylaxis should be considered in any patient confined to bed for longer than 24 hours because of PDPH. If pharmacological thromboprophylaxis is started and the patient subsequently requires an EBP, adequate time between the last dose of anticoagulant and the EBP must have elapsed to reduce the risk of vascular complications.

- **Statement**: *Evidence of a reduction in severity of PDPH with prophylactic bed rest is inconclusive (Moderate Level of Certainty).*
- **Recommendation**: *Bed rest is not routinely recommended as prophylaxis against PDPH. (Grade D, Moderate Level of Certainty).*

Epidural and spinal injections

Several authors have studied the efficacy of epidural or spinal injection of different substances (excluding blood) to prevent PDPH. Al-Metwalli studied the effectiveness of epidural morphine in preventing PDPH in a prospective, randomized, double-blind trial in 25 parturients after inadvertent dural puncture with a 17G epidural needle.[175] Women were randomly allocated to receive two epidural injections, 24 hours apart, of either morphine 3 mg in 10 mL saline (morphine group) or 10 mL saline (saline group). A limitation of the study was that sample size analysis was based on the intrinsic PDPH rate of 75%, whereas the observed rate was 48% in the saline group.

Peralta *et al* injected either morphine 150 µg or equal volume of saline through an intrathecal catheter placed in obstetric patients who had suffered inadvertent dural puncture during the placement of a labor epidural.[176] Injections were performed soon after delivery and catheters were removed after injection. Their results showed no benefit in preventing PDPH. They reported

an increased incidence of PDPH for both groups suggesting that placing the intrathecal catheter after unintentional dural puncture may be responsible, but they do not provide information about the type and size of the catheter.

The impact of intrathecal morphine and diamorphine on developing PDPH was evaluated in a long-term, retrospective audit by Martlew.[177] The author suggested a reduced incidence of PDPH following a change from fentanyl (0.88%) to diamorphine (0.49%), with other elements of spinal anesthesia remaining the same (eg, needle type). However, no information was provided about how PDPH was diagnosed or the incidence of side effects from intrathecal opioids.

Hydroxyethyl starch solutions (HES), dexamethasone and saline, given via the epidural or spinal route, have been evaluated as prophylactic agents for PDPH following inadvertent dural puncture. Najafi *et al* injected dexamethasone 8 mg (in 2 mL of saline) or 2 mL saline after uneventful spinal anesthesia without noting any beneficial effect in reducing the incidence of PDPH.[178] In a retrospective case series, Song *et al* assessed the effectiveness of injecting HES 6% solution 15 mL into the epidural space to prevent PDPH after an inadvertent dural puncture.[179] The authors concluded that this was highly effective in preventing the occurrence of PDPH. However, a limitation was that the injection of HES was performed 24 hours after using an epidural catheter to provide analgesia; therefore, it is unclear which intervention was effective.

In a randomized trial of 100 women, Faridi Tazeh-Kand *et al* investigated the effect of intrathecal saline 5 mL injected before hyperbaric bupivacaine compared with hyperbaric bupivacaine alone, for spinal anesthesia for elective cesarean section.[180] The incidence and severity of PDPH were assessed after 48 hours and again 3–7 days postoperatively. The incidence of moderate and severe PDPH during the first postoperative 48 hours was no different between groups. However, the frequency of PDPH after 3–7 days was significantly higher in the bupivacaine-alone group compared with the saline/bupivacaine group (16% vs 2%, p=0.03). No information on other effects of the addition of saline, such as block extension or duration of anesthesia, was reported.

In an observational study, three consecutive groups of 50 obstetric patients received spinal anesthesia. The control group received no prophylactic treatment for PDPH, the second group received an epidural saline injection of 20–25 mL and the third group received an abdominal binder. There was no statistically significant difference between the two intervention groups (6% vs 4%), but results showed that applying either intervention could significantly reduce the incidence of PDPH.[170] However, the study was small and did not describe the use of abdominal binders to ensure reproducibility. Additionally, the technique of injecting epidural saline after spinal injection (while retracting the spinal needle) was questionable and likely to produce variable results.

- **Recommendation**: *Routine injection of any substance intrathecally or epidurally to prevent PDPH is not recommended (Grade I; Low Level of Certainty).*

Pharmacological measures

Several authors have studied the effect of paracetamol, caffeine, morphine, dexamethasone and aminophylline in preventing PDPH following uneventful spinal anesthesia and reported no benefit.[181–184] Hakim evaluated the effect of intravenous cosyntropin in an RCT and noted a significant benefit in preventing PDPH.[185] Following inadvertent dural puncture with either a 16G or 18G epidural needle, 90 obstetric patients were randomly assigned to receive cosyntropin 1 mg intravenously or an equal volume of normal saline. There was a significant difference in the proportion of patients who developed PDPH in the cosyntropin group, 15/45 (33%) compared with 31/45 (68.9%) in the control group (p=0.001). Significantly fewer patients in the cosyntropin group required an EBP compared with the control group (5 (11.1%) vs 13 (28.9%), p=0.035).

In an RCT, Vahabi *et al* compared the effect of regular gabapentin versus placebo in 120 patients after spinal anesthesia and found a reduction in headache incidence and severity, and morphine consumption.[186] However, the nature of headaches in all patients was unclear. There were no differences between groups in the incidence of adverse side effects.

Okpala *et al* reported a reduction in PDPH with preoperative intravenous dexamethasone 8 mg compared with placebo following uneventful spinal anesthesia for cesarean section.[187] However, this finding contradicts those from a meta-analysis (four RCTs)[183] and an RCT in cesarean section patients,[188] which indicated that dexamethasone does not produce a statistically significant effect and may in fact aggravate the severity of PDPH. The meta-analysis has several methodological heterogeneities, such as limited sample size, duration of follow-up and needle size variations, all of which make any strong inferences difficult.

- **Recommendation**: *There is insufficient evidence to recommend routine systemic drug administration for PDPH prophylaxis (Grade I; Low Level of Certainty).*

Question 5: what conservative measures may be used to treat PDPH?

Non-pharmacological measures

Bed rest

There are no published RCTs examining the effect of bed rest in the treatment of PDPH. Some temporary relief of headache is often obtained, but prolonged bed rest is undesirable because of the risks associated with immobilization.

- **Recommendation**: *Evidence does not support routine use of bed rest to treat PDPH, but it may be used as a temporizing measure for symptomatic relief (Grade C; Low Level of Certainty).*

Fluid therapy

Increased oral intake of fluids is often encouraged, or intravenous fluid therapy is started to maintain or increase CSF production in patients with PDPH. While a single clinical trial noted no benefit of fluid therapy for prophylaxis,[189] no other studies have evaluated the benefit of either oral or intravenous fluid therapy exclusively for treating PDPH. Dehydration could worsen CSF production and headache.

- **Recommendation**: *Adequate hydration should be maintained with oral fluids; intravenous fluid should be used when oral hydration cannot be maintained (Grade C; Low Level of Certainty).*

Abdominal binders

Abdominal binders are thought to work by increasing pressure within the spinal canal, pushing CSF cephalad, thereby reducing headache. There are few data to support the use of abdominal binders for either prophylaxis or treatment of PDPH, with only one study showing benefit.[170] Abdominal binders are likely impracticable after recent abdominal or truncal surgery and unacceptable to patients.

- **Recommendation**: *Evidence does not support routine use of abdominal binders to treat PDPH (Grade D; Low Level of Certainty).*

Aromatherapy

Aromatherapy with lavender has shown to have a small and temporary benefit in decreasing severity of PDPH in a small sample of patients with established PDPH.[190] In total, 50 patients with PDPH post spinal anesthesia were randomized to receive either 15 min inhalations of lavender oil or liquid paraffin as a placebo. It is to be noted that the benefit of aromatherapy in this trial was present only immediately after the intervention. Given the small sample of patients and limited evidence on the topic, recommendations cannot be made either in favor of or against aromatherapy for PDPH management.

- **Recommendation**: *Evidence does not support routine use of aromatherapy to treat PDPH (Grade D; Low Level of Certainty).*

Pharmacological measures

Oral analgesia

No placebo-controlled trials have examined the role of simple oral analgesia including acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs) or weak opioids, (including codeine) in preventing or treating PDPH. They are usually included in the control group when other therapies are investigated.

While opioids have been shown to have no role in the prevention of PDPH,[191] they are often recommended as a part of a multimodal analgesic regimen for managing pain, especially if conservative and simple analgesics are insufficient. Long-term opioids are not recommended because of the high incidence of side effects.

Routine caffeine administration has not been shown to prevent PDPH after dural puncture. A recent Cochrane systematic review of systemic analgesics for conservative management of PDPH stated that caffeine was effective in decreasing the persistence of symptoms and the need for supplementary treatment interventions.[192] However, this is based on limited evidence as the review contained very few studies including caffeine therapy (three RCTs, two of which were in obstetric populations), theophylline (three RCTs), hydrocortisone (two RCTs), gabapentin (two RCTs) and four different RCTs assessing sumatriptan, adrenocorticotropic hormone (ACTH), pregabalin and cosyntropin, respectively.[192]

In a randomized trial of 41 patients with PDPH, intravenous caffeine 500 mg was compared with placebo.[193] The authors reported significant improvement in headache 2 hours after caffeine administration. In a study of obstetric patients, Camann *et al* randomized 40 women with PDPH following epidural or spinal anesthesia to receive either oral caffeine 300 mg or placebo.[194] The severity of headache was significantly better after 4 hours in the caffeine group, but there was no difference between groups at 24 hours or in the number of women who received an EBP. In addition, excessive caffeine administration may lead to untoward side effects such as withdrawal, dehydration and even seizures. Therefore, a dose maximum of 900 mg per day has been recommended by some authors.[7] In breastfeeding women, a maximum dose of 200 mg is recommended in the UK[195] and 300 mg in the USA.[195 196]

Other medications shown to decrease the severity of symptoms include gabapentinoids,[186] theophylline[197–199] and hydrocortisone,[200–202] but multiple study weaknesses such as small numbers, patient demographics (obstetric/non-obstetric, age, gender, etiology of dural puncture not specified, insufficient methodology and potential for bias) limit their interpretation. Other medications, including triptans,[203–205] ACTH/cosyntropin,[206–208] neostigmine/atropine,[209] piritramide[210] and methergine,[211] have been evaluated for the treatment of PDPH. While they show benefit in terms of reduced severity and duration of headache, these treatment modalities again demonstrate poor-quality evidence.

- **Recommendation**: *Regular multimodal analgesia including acetaminophen and NSAIDs, unless contraindicated, should be offered to all patients with PDPH (Grade B; Low Level of Certainty).*
- **Recommendation**: *Short-term use of opioids may be considered in the treatment of PDPH if regular multimodal analgesia is ineffective (Grade C, Low Level of Evidence); long-term opioid use is not recommended in the treatment of PDPH (Grade D, Moderate Level of Certainty).*
- **Recommendation**: *Caffeine may be offered in the first 24 h of symptoms with a maximum dose of 900 mg per day (200–300 mg if breastfeeding) and avoiding multiple sources to prevent untoward side effects (Grade B; Low Level of Certainty).*
- **Recommendation**: *Evidence does not support the routine use of hydrocortisone, theophylline, and gabapentin in the management of PDPH (Grade D; Low Level of Certainty).*

Question 6: what procedural interventions may be used to treat PDPH?

Acupuncture

The efficacy of acupuncture in treating various forms of headache is uncertain.[212] Acupuncture is thought to act by increasing release of enkephalin and substance P, which suppress the trigeminal nucleus caudalis and spinal dorsal horn neurons.[213] Various needle insertion sites have been suggested, although not all reports use the same technique. Evidence for acupuncture in PDPH is limited to observational studies and case reports containing fewer than 50 patients.[213–217] Other forms of treatment were not standardized and, when reported, most patients received concurrent oral analgesia. Headache severity improved after acupuncture in nearly all cases although the duration of effect was variable. Two patients subsequently required an EBP. No significant side effects were reported.

With such limited evidence, the benefit of acupuncture in PDPH is difficult to establish. Reduction in headache severity may reflect actual clinical efficacy, a placebo effect or the expected resolution in symptoms over time. Without RCTs, it is difficult to be certain which mechanism is most relevant.

- **Recommendation**: *Evidence does not support routine use of acupuncture to treat PDPH (Grade I; Low Level of Certainty).*

Sphenopalatine ganglion block

The treatment of headache with sphenopalatine ganglion blocks (SPGBs) was first described in 1908.[218] Its use in PDPH has only recently been investigated with mixed findings. The proposed mechanism of action is by blocking parasympathetic outflow from the sphenopalatine ganglion resulting in cerebral vasoconstriction and downregulation of neurogenic inflammatory mediators.[219 220]

Supporting evidence consists of five observational studies and several case series and reports: evidence showing no benefit or equivocal results includes one meta-analysis and one RCT. The

role of SPGB in PDPH has also been assessed in a systematic review.[221] All publications relied on history and physical examination to diagnose PDPH, and SPGBs were performed via a bilateral, intranasal approach. The heterogeneity of patients included differences in sex, age, mechanism of dural puncture and other medical comorbidities, with a predilection toward postpartum patients.

There were differences in the performance of intranasal SPGBs, with some using a cotton swab saturated with local anesthetic positioned adjacent to the nasopharynx, with or without ongoing medication delivery.[9 222] Others injected[219 223] or sprayed[224 225] local anesthetic into the nasopharynx with the patient supine until medication was felt at the back of the throat. In a randomized, single-blind comparison of transnasal SPGBs in obstetric patients using the cotton swab applicator technique versus spray, better outcomes were observed with the applicator.[226]

Composition and volume of local anesthetic differed with some reports using one agent, while others included a mixture of short-acting and long-acting formulations with injected volumes ranging from 0.5 to 5 mL per nostril. In most studies, patients were treated with a combination of conservative measures including bed rest, acetaminophen, caffeine, NSAIDs, hydration, and in one case, opioids before intervention.[227] Conservative care was maintained throughout most studies; however, in others, it was stopped when interventions were employed.[228 229] In most cases, rescue blocks were permitted, including within the only RCT, in which it was also allowed in the placebo group.[9] There was no consistency in the defined endpoint among cases, and no clear assessment of a successful block. One observational study using transcranial Doppler found a correlation between pulsatile index and mean flow velocity of intracranial arteries when SPGBs provided pain relief versus those that did not.[222] This method may be able to determine the success of an SPGB; however, further studies are needed to ensure its validity. The transcutaneous approach remains the most direct means of performing an SPGB; however, there are no published studies where this approach is used.

A double-blind RCT comparing transnasal SPGB with placebo for treatment of PDPH used a 1:1 mixture of 4% lidocaine and 0.5% ropivacaine and a total volume of 1 mL per nostril.[9] The use of a hollow, saturated cotton swab positioned adjacent to the nasopharynx and delivering additional local anesthetic or saline 0.5 mL resulted in no statistically significant difference in pain intensity after 30 min compared with placebo. Limitations included the potential for unblinding, unreliable verification of block efficacy, use of rescue blocks for both treatment and placebo arms and the possibility of an active placebo. A meta-analysis, including this RCT and two additional retrospective studies,[11 230] concluded there was no significant therapeutic advantage of SPGB over medical management or EBP.[231] Reported limitations included small numbers, differences in study design and local anesthetic use, definition of pain relief and inconsistent therapeutic intervention protocols.

In summary, the lack of RCTs and heterogeneity of reported cases preclude the ability to generalize outcomes. Furthermore, in the absence of an objective means of validating successful intranasal SPGB, clinical outcome cannot be reliably ascribed.[9 232] No study included an objective means of diagnosing PDPH, which limits the establishment of a cause-and-effect relationship. The reported reduction, or lack thereof, in headache severity may reflect an actual clinical effect, placebo or the expected resolution in symptoms over time. Further clarity is required from robust RCTs.

- **Recommendation**: *Evidence does not support routine use of SPGBs to treat PDPH (Grade I; Low Level of Certainty).*

Greater occipital nerve block

The greater occipital nerve, a branch of the C2 dorsal ramus, carries sensory input from a large part of the posterior scalp extending to the vertex. Greater occipital nerve blocks (GONBs) are thought to work by providing symptomatic relief of low-pressure headaches. Bilateral blocks are usually performed with a mixture of local anesthetic and steroid. There are five RCTs,[233–237] a systematic review[221] and a meta-analysis[238] evaluating their efficacy.

In 90 patients with PDPH after spinal anesthesia for cesarean delivery, ultrasound-guided GONBs with lidocaine and dexamethasone produced significantly better headache relief than saline placebo at 24 hours.[233] Nausea resolved in all patients following GONB, but none of the control group showed improvement. Ultrasound-guided GONB with lidocaine, bupivacaine and triamcinolone was compared with no intervention in an RCT of 30 surgical patients with PDPH after spinal anesthesia.[234] At 12 hours, pain scores were significantly lower in the GONB group with an EBP performed in six of the control group compared with one in the GONB group. Side effects included injection site hematoma and pain, dizziness and vasovagal episodes.

In an RCT of 47 mixed surgical patients with PDPH after spinal anesthesia, nerve stimulator-guided GONB with lidocaine, bupivacaine, fentanyl and clonidine was compared with conservative management.[235] Blocks were repeated daily if visual analog scale (VAS) scores remained above four out of ten during the 8-day follow-up. Patients received lesser occipital nerve blocks if pain extended to frontal and temporal areas. Headache resolved completely in 68% of patients receiving treatment after one or two injections, and in all cases after four injections. In the conservative management group, only 8% had complete relief after 2 days rising to 36% after 4 days.

Ultrasound-guided GONB with lidocaine and dexamethasone was compared with conservative management in an RCT of 50 mixed surgical patients with PDPH after spinal anesthesia.[236] Median pain scores at 24 hours were lower in the 25 patients in the GONB group, although headache recurred in 6 patients.

A total of 93 patients with PDPH after spinal anesthesia for cesarean delivery were randomized to receive either bilateral landmark-guided GONB with lidocaine and dexamethasone or bilateral SPGBs with the same mixture.[237] Both treatments significantly reduced pain scores from baseline but there was no difference between groups at 24 hours.

In an observational study, 19 patients who experienced inadvertent dural puncture during epidural catheter insertion, in whom conservative management had failed, were offered a GONB with lidocaine and dexamethasone or an EBP.[239] One patient chose an EBP and had a complete resolution of symptoms. Of 18 patients who opted for GONB, 6 had a partial resolution of symptoms and were treated successfully with an EBP, although 1 patient had a recurrent headache successfully treated with a GONB.

In total, 42 obstetric patients with PDPH after spinal, epidural or CSE in whom conservative measures had failed, received SPGBs with or without GONBs and trigger point infiltration.[240] Of these, 27 required 1 course of blocks, with 15 receiving 2 courses. Nine patients required a rescue EBP after two courses of blocks.

Ultrasound-guided bilateral GONBs were evaluated retrospectively in 21 patients with PDPH who did not respond to conservative treatment 48 hours after spinal anesthesia.[241] Patients with milder PDPH had a more sustained effect from GONB; when headache was more severe, initial improvement was often followed by a return of symptoms. Data regarding the need for EBP were not presented. Retrospective data from 16 patients with PDPH following spinal anesthesia for cesarean delivery who received GONBs showed a significant reduction in pain scores.[242] Similarly, other small case series have reported partial or complete relief of PDPH symptoms following GONB.[243–246]

With the exception of one observational study,[239] all reports of GONB are for PDPH following spinal anesthesia. The majority of investigators used a mixture of local anesthetic and steroid. The performance of blocks was heterogeneous, including the use of ultrasound-guided, nerve stimulator-guided or landmark-guided techniques. The comparator groups included either a sham block, no block, SPGB or EBP. Most patients had partial to complete improvement in symptoms following GONB, although at least 25% ultimately required an EBP. It is unclear if efficacy was a direct effect of the block, systemic absorption of steroid, placebo, expected resolution over time or a combination of each. Subcutaneous hematoma and pain at the injection site were commonly reported adverse effects.

- **Statement**: *The efficacy of GONB for PDPH following dural puncture with wider gauge needles is unclear (Low Level of Certainty).*
- **Recommendation**: *GONBs may be offered to patients with PDPH following spinal anesthesia with a narrower gauge (22G or less) needle, although headache may recur in a significant proportion with more severe headache requiring an EBP (Grade C; Moderate Level of Certainty).*

Epidural and spinal morphine

Cases of PDPH treated with epidural and spinal morphine have been reported from one center; all publications are over 25 years old.[247–250] The specific mechanism by which epidural and spinal morphine relieves PDPH is unclear. Cases were not adequately described with few details on patient characteristics, other forms of treatment and pain scores. Side effects, which were likely to have been clinically significant, were not adequately reported. Large, repeated doses of intrathecal morphine (1.5 mg over 16 hours) are concerning and monitoring for respiratory depression was not discussed.[251]

- **Recommendation**: *Evidence does not support use of spinal and epidural morphine to treat PDPH (Grade D, Low Level of Certainty).*

Epidural crystalloids

Relief of PDPH from the injection of epidural crystalloid solutions is presumed to occur by elevation in intracranial pressure reducing tension on pain-sensitive structures.

In an RCT comparing epidural saline 30 mL with a 10 mL EBP, 42 of 43 obstetric patients achieved dramatic pain relief at 60 min.[252] At 24 hours, headache had returned in 15 patients, more commonly in the saline group and more commonly after use of a 17G versus a 25G needle. In total, 9 of 21 patients randomized to epidural saline ultimately received an EBP. Another RCT compared a 10–15 mL EBP with epidural saline 15–20 mL followed by saline 20 mL/h for 3 hours, in 16 patients with PDPH following spinal anesthesia with a 23G or 25G needle.[253] Pain scores improved in both groups and were significantly better in the EBP group at 3 hours but not at 15 min or 24 hours. Two of eight patients in the saline group required an EBP. Lower limb pain during the initial injection was reported by four of eight patients in the EBP group and five of eight in the saline group.

Observational work demonstrated that up to 100 mL of caudal or lumbar epidural saline provided effective pain relief in the majority of 24 patients with PDPH, although headache returned in over 50% requiring further saline injections.[254] In another study, complete relief of symptoms was achieved after one or two caudal saline injections of 10–120 mL without complication in 243 patients who underwent spinal anesthesia or diagnostic LP.[255] Immediate relief of PDPH after spinal anesthesia was also reported in 10 of 11 non-obstetric patients following lumbar epidural saline injection of 10–30 mL.[256] Eight patients had no further headache; the others required repeat saline injection.

Outcomes in 56 patients with PDPH who received caudal saline injection of up to 220 mL over 20 min one or two times per day for 1–2 days were presented in another observational study.[257] Conservative management included 24 hours bed rest, 2 L fluid per day and analgesia, although this was not defined. Four patients ultimately required an EBP; others had a 'satisfactory' outcome. An unpleasant warmth or leg tightness during injection was reported but its incidence was not stated. Intrascapular pain has been reported during epidural crystalloid infusion.[258 259] The development of lower back discomfort, similar to that seen during an EBP, is not uncommon, its incidence appearing to be related to volume and speed of injection. Gill and Heavner identified 12 cases of retinal hemorrhage after epidural saline injection, which was related to increased CSF pressure proportional to the rate and volume of fluid injected. Recovery occurred in 80% of patients.[260] Cases of successful epidural saline injection as an alternative to an EBP have been described.[261–265]

- **Statement**: *Epidural saline may be of temporary benefit but should not be expected to provide long-lasting relief of PDPH (Low Level of Certainty).*

Epidural dextran

Successful use of epidural dextran has been described in observational studies and case reports in fewer than 100 patients with PDPH.[266–271] No cases of anaphylaxis have been reported. Human safety data on epidural injection of dextran 40 are lacking, although in a rat model there was no evidence of toxicity 30 days after intrathecal dextran injection.[272]

- **Recommendation**: *Evidence does not support routine use of epidural dextran to treat PDPH (Grade I; Low Level of Certainty).*

Epidural gelatin

Epidural gelatin has been reported in three cases of PDPH: two using Gelfoam powder mixed with the patient's plasma to make a 10 mL viscous solution[273] and one with Plasmion (a fluid gelatin) 10 mL in a sickle cell patient.[274] Other than transient lumbar pain during injection, no adverse effects were reported. No safety data on the use of the epidural administration of gelatin are available.

- **Recommendation**: *Evidence does not support routine use of epidural gelatin to treat PDPH (Grade I; Low Level of Certainty).*

Epidural hydroxyethyl starch

Four cases of successful PDPH treatment with epidural HES 15–30 mL have been reported.[275–277] In three cases, a second

epidural injection of HES was required. In one case, an infusion of HES at 5 mL/hour was started after the initial bolus.[277] In another, sufentanil 5 µg was added to the HES bolus.[276] Human safety data are lacking but in a rat model, there was no evidence of neurotoxicity following intrathecal HES injection.[278 279]

- **Recommendation**: *Evidence does not support routine use of epidural HES to treat PDPH (Grade I; Low Level of Certainty).*

Fibrin glue

First described in 1987,[280] epidural fibrin glue has been predominantly used for PDPH refractory to an EBP or when autologous epidural blood injection have been contraindicated.[281–285] The proposed mechanism of action is sealing of the dural tear, which prevents further CSF leakage. Where described, it is usually injected under fluoroscopic or CT guidance. There are no studies directly comparing fibrin glue with other treatment modalities. Evidence on efficacy comes from one observational study[286] and multiple case reports[284 287–290] describing its use following diagnostic LP or intrathecal drug delivery system (IDDS) or spinal cord stimulator insertion.

In an observational study of 73 patients with PDPH after IDDS insertion,[286] 79% were managed conservatively with 21% requiring an EBP or fibrin glue patch for full resolution of headache. Of this latter group, 88% had complete relief following one EBP, although it is unclear how many received fibrin glue.

The successful use of an epidural injection of platelet-rich plasma in a septic patient has been reported.[284] The 20 mL injection contained platelets, plasma and a contrast agent and was followed by fibrin glue, 1 mL. This resulted in immediate relief of symptoms, but follow-up was not reported.

A study of prophylactic epidural injection of Tissucol 1.0–1.8 mL during the withdrawal of the 20G needle immediately following dural puncture was stopped after the seventh patient developed possible aseptic meningitis and brachial plexus neuritis.[280] Anaphylaxis has been reported in 2 of 10 patients who underwent repeated applications of epidural fibrin glue.[291] The authors recommend waiting for 3–6 months before repeat fibrin glue injection and administering prophylactic antihistamine and corticosteroid before injection. Evidence to support this management plan was not presented.

- **Statement**: *The use of fibrin glue in the treatment of PDPH has been associated with anaphylaxis and aseptic meningitis, although it not possible to quantify risk (Low Level of Certainty).*
- **Recommendation**: *Evidence does not support routine use of fibrin glue to treat PDPH. (Grade I; Low Level of Certainty).*
- **Recommendation**: *Fibrin glue should be reserved for management of PDPH refractory to EBP or when autologous blood injection is contraindicated (Grade I; Low Level of Certainty).*

Question 7: is imaging required in PDPH management?

Imaging to confirm a diagnosis of PDPH

The diagnosis of PDPH is established on clinical presentation, and cranial imaging is usually not needed for routine assessment of patients with typical PDPH symptoms. Most patients with PDPH show no abnormalities on brain or spine imaging, and therefore the absence of abnormal imaging findings should not mitigate a diagnosis.

In a minority of patients with PDPH, signs of intracranial hypotension may be seen on brain imaging.[292] Manifestations of decreased CSF volume can be summarized with the mnemonic SEEPS: Sagging of the brainstem, Enhancement of the dura, Engorgement of venous structures (specifically, distension of the transverse venous sinus), Pituitary hyperemia and Subdural fluid collections.[293 294] One study containing 44 patients with PDPH found that the most common feature was distension of the transverse venous sinus (39%), followed by dural enhancement (26%).[292]

Imaging for alternative diagnoses

In some cases, cranial imaging may help to establish alternative diagnoses to PDPH (see Question 1). Case reports describe other or coexistent etiologies for headache that may occur subsequent to dural puncture, including the development of subdural hygromas or hematomas,[295] CVST or cortical vein thrombosis[296] and PRES.[297–299]

Subdural hygromas or hematomas may develop following dural puncture. When intracranial CSF volume decreases, fluid may accumulate passively in the subdural space, in accordance with the Monro-Kellie doctrine.[300] In some cases, rupture of associated veins may produce hemorrhage within these subdural hygromas. Drainage may be required if there is sufficient mass effect, but collections may reaccumulate if the underlying CSF leak is not addressed,[301 302] and thus should not preclude prompt treatment of PDPH with an EBP. CVST may also complicate spinal CSF leakage.[303 304] It is postulated to result from intracranial venous stasis in the setting of CSF volume depletion. However, in obstetric patients prothrombotic factors in the peripartum period increase the risk of CVST,[305] independent of CSF leakage and may account for cases among parturients who receive neuraxial blocks. Finally, PRES may occur in the setting of eclampsia.[306] PRES is often accompanied by headache, but other symptoms, including visual changes, seizures and decreased level of consciousness, may also be present.

Several case reports have emphasized the importance of a change in the nature of headache from orthostatic to non-orthostatic when complicating conditions such as SDH, CVST or PRES develop after an initial diagnosis of PDPH.[295 307–310] In the postpartum period, hypertension and proteinuria may indicate pre-eclampsia.[311] The development of focal neurological deficits, visual changes or seizures should prompt neuroimaging to evaluate for PRES.[310 311] Most PDPHs develop within 5 days of dural puncture, so alternative diagnoses should be considered when headache onset is outside this period.[311 312] Finally, although lack of response to an EBP does not preclude a diagnosis of PDPH, alternative diagnoses may be considered if no symptomatic response is observed following repeat EBPs.

Preprocedural imaging

No experimental or observational studies have directly addressed whether cranial imaging is required before an EBP for PDPH. In the absence of direct evidence from the literature, a reasonable approach is to perform cranial imaging after suspected dural puncture when headaches are associated with 'red-flag' symptoms such as new neurological deficits, when headache symptoms change from orthostatic to non-orthostatic, or when patients are otherwise at high risk for conditions that may coexist with PDPH such as SDH, CVST or PRES.[313]

- **Statement**: *Current evidence is insufficient to assess the risk-benefit balance for routine cranial imaging before EBP for PDPH (Low Level of Certainty).*

Imaging selection

Both CT scan of the head and MRI of the brain may be appropriate for patients with new-onset headaches. MRI of the brain is

preferred over CT scan when PRES is suspected.[314] Furthermore, the changes of intracranial hypotension due to postdural puncture CSF leakage are much more commonly seen with MRI than CT scan, and some of the findings are only apparent on postcontrast MRI of the brain.[292] Therefore, MRI of the brain with and without intravenous contrast is the preferred imaging modality when available in most cases of headache following suspected dural puncture. The addition of MRI venography or CT venography is indicated in the setting of concern for CVST.[313] Spinal imaging is usually not needed in routine PDPH, but may occasionally show abnormalities in cases of refractory PDPH.[315]

- **Recommendation**: *Brain imaging may be considered when non-orthostatic headache is present or develops after initial orthostatic headache, or when headache onset is more than five days after suspected dural puncture (Grade C; Low Level of Certainty).*
- **Recommendation**: *Focal neurological deficits, visual changes, alterations in consciousness, or seizures, especially in the postpartum period, should prompt neuroimaging to evaluate alternative diagnoses (Grade A; Moderate Level of Certainty).*

Question 8: what are the contraindications to an EBP?

An EBP may be considered if PDPH affects the patient's ability to perform activities of daily living and conservative measures have failed to relieve symptoms.[7] It is a relatively safe procedure but not entirely without risk (see below). Consequently, before performing an EBP, factors that may increase risk, such as impaired coagulation and local or systemic infection, should be considered. These risks, together with the efficacy of the procedure and other forms of treatment, should be discussed with the patient as part of the consent process.

Antithrombotic agents and anticoagulants should be discontinued before an EBP in accordance with ASRA Pain Medicine or SOAP or ESAIC/ESRA guidelines.[316 317] Case reports suggest that it may be safe to perform an EBP in patients with acute varicella infections after receiving antiviral medications.[318] Studies have also found no signs of CNS spread in HIV-positive patients who required EBP.[319] Neuraxial anesthesia has been shown to be safe for orthopedic surgery in the setting of an infected joint but studies investigating EBPs in the setting of systemic bacterial infection have been sparse.[320 321]

An EBP should not be performed if the patient has evidence of systemic infection.[8] The value of routine blood cultures before an EBP has been questioned as subdural abscesses have been reported after an EBP even when blood cultures have been negative.[8 322] There are no studies addressing the efficacy of antibiotic prophylaxis prior to an EBP. Strict aseptic technique should be observed when performing an EBP.[322 323]

Hematologic malignancies, such as leukemia and lymphoma, have been considered contraindications to an EBP because of the theoretical risk of seeding malignant cells within autologous blood into the central nervous system. However, data supporting these concerns are tenuous and retrospective studies do not support the theory of neuraxial seeding.[324 325]

Thrombocytopenia is particularly prevalent in the obstetric population; >10% of patients have gestational thrombocytopenia, defined as a platelet count$<150\times10^9$/L.[326] Severe thrombocytopenia is a risk factor for epidural hematoma. A SOAP task force concluded that the risk of epidural hematoma was low when performing neuraxial procedures in obstetric patients with a platelet count$\geq70\times10^9$/L due to hypertensive disorders of pregnancy, immune thrombocytopenia or gestational thrombocytopenia.[327] Thrombocytopenia also increases the risk of an SDH following dural puncture; therefore, the risks and benefits of using an EBP should be weighed carefully.[328] Risks of non-intervention should be considered when patients decline treatment with EBP, including persistent PDPH and rare complications such as SDH and CVST.[329–331]

- **Statement**: *The risk of epidural hematoma is low when performing neuraxial procedures in obstetric patients with a platelet count$\geq70{,}000\times10^6$/L providing there is no defect in platelet function or other abnormality of coagulation (Moderate Level of Certainty).*
- **Statement**: *There is insufficient evidence for recommending prophylactic antibiotics before EBP (Low Level of Certainty).*
- **Recommendation**: *Clinicians should follow appropriate guidelines regarding neuraxial injection in patients on antithrombotics or with low platelet counts (Grade A; Moderate Level of Certainty).*
- **Recommendation**: *Caution should be exercised when considering an EBP in febrile patients or patients presenting with other systemic signs of infection. Deferring the procedure may be appropriate if there is risk of hematogenous infection (Grade C; Moderate Level of Evidence).*

Question 9: when and how should an EBP be performed?

Indications

Several factors support the use of an EBP. When the diagnosis of PDPH is established, the intensity and duration of symptoms require assessment. If headache is mild, conservative measures may be preferred with the expectation of symptom resolution without the need for a further invasive procedure. However, more severe headaches that affect activities of daily living, especially in the obstetric population, should lead to consideration of an EBP. Furthermore, improvements in the neurological sequelae of intracranial hypotension after dural puncture, such as changes in hearing loss[332 333] or optic nerve sheath diameter,[334] and cranial neuropathies[36] have been reported following EBP. In one study, hearing loss associated with PDPH improved by 10 dB in 12 of 16 (75%) patients within 1 hour of EBP.[332] In another study, optic nerve sheath diameter increased after EBP. Other authors reported that 13 of 17 (76%) patients showed resolution of cranial neuropathy within a few days or months after EBP.[36] Bechard, however, reported no improvement in abducens nerve palsy following dural puncture when EBP was performed more than 24 hours after the onset of symptoms.[335]

- **Recommendation**: *When PDPH is refractory to conservative therapy and impairs activities of daily living, an EBP should be considered to treat headache and other neurological sequelae of intracranial hypotension (Grade: B; Moderate Level of Certainty).*
- **Recommendation**: *In patients with PDPH with severe neurological symptoms (eg, hearing loss, cranial neuropathies), EBP should be considered as a therapeutic option (Grade: C; Moderate Level of Certainty).*

Efficacy

Several RCTs provide evidence of therapeutic efficacy for EBP.[336–338] In 1 RCT,[336] 32 patients with PDPH due to different etiologies received either a lumbar EBP or conservative therapy (fluids, analgesics, caffeine), with EBP resulting in statistically significant reductions in pain scores compared with conservative treatment (mean±SD VAS: EBP 0.7±0.16 vs conservative 7.8±1.2, $p<0.0001$) without any reported complications. In another RCT,[337] 42 patients with PDPH receiving EBP had lower

rates of headache within 24 hours versus conservative therapy (58% vs 90%, respectively; RR, 0.64; p=0.03). The EBP group (84%) had a higher probability of complete recovery at 1 week after treatment compared with the group receiving conservative therapy (14%) (p<0.001).

EBP success rates were originally reportedly between 89% and 91%.[339 340] Subsequent studies have suggested more variable rates.[341 342] Several studies indicate that a minority (2%–39%) of patients require repeat EBP after initial therapy.[338 341–350] After EBP, complete headache remission is estimated for 33%–91% of patients, with success primarily dependent on size of the needle or dural hole, although definitive evidence on remission rates after EBP is lacking.[341 342 348–350] Differences in reported efficacy rates may be due to variations in follow-up duration, variable definitions of 'failure,' differences in complete versus partial headache relief, or other management differences, such as delayed mobilization immediately post-EBP.

If an initial EBP produces no or partial relief of symptoms it may be repeated. In addition, many EBPs are repeated after the patient has complete relief from the first EBP with symptoms returning a few days later.[343] Various studies have shown that 14.5% of adult patients[343] and 8.4%[76] of obstetric patients, require more than one EBP is needed to achieve relief. It has been suggested that approximately 15% of patients with PDPH may require more than one EBP to achieve durable relief and that patients requiring≥2 EBP tended to be older or have a prior history of headaches or hypertension.[343]

Need for repeat EBP may be associated with the type of initial neuraxial procedure (eg, epidural vs spinal anesthesia). In a retrospective study[351] of 57 927 deliveries, the need for EBP was 0.16% after epidural, 1.2% after spinal, and 1.3% after CSE block. The initial EBP success rate was similar for parturients who had an epidural (89%), spinal (88%) or CSE (91%) (p=0.65). However, the recurrence rate was significantly higher in those who had epidural (31%) compared with that after spinal (5%) and CSE (7%) (p=0.001). The severity of supine symptoms correlated negatively with initial EBP success (p=0.016). BMI correlated negatively with symptom recurrence (p=0.049).

If an EBP produces no effect on the relief or resolution of the symptoms, or if the PDPH diagnosis is less certain, or if there is a change in the nature of the headache, then other headache etiologies and the involvement of other specialties should be considered before offering repeat EBP.

- **Statement**: *High success rates for EBP reported in early studies have not been reproduced in more recent publications with complete headache remission varying between 33% and 91% (Low Level of Certainty).*

Timing

EBP is considered to be the gold standard therapy for PDPH. Several publications (73 of 126, 58%)[36 46 158 166 167 240 261 335 337 338 342 343 346 347 351–399] directly or indirectly pertain to ideal timing for EBP, and most (69, 55%) are in the obstetric population. There are four RCTs[166 167 337 338] on this topic (two on prophylactic EBP,[166 167] covered elsewhere in these guidelines), while the remaining studies are case reports, observational case series, or retrospective studies. Studies results regarding EBP timing are conflicting and overall, there is opportunity for additional trials to improve evidence on this topic.

In obstetric settings, most observational studies suggest that EBP failure (defined as requiring more than one EBP) is more likely if EBP is performed within 24–48 hours of dural puncture.[36 46 158 166 167 240 261 335 337 338 342 343 346 347 351–399] However, the observation may be related to selection bias: patients with severe headaches within 24 hours of the puncture may represent situations where the dural hole is large enough to cause a severe CSF leak that requires more interventions (ie, repeat EBP) to treat. Furthermore, larger CSF leaks may initially displace the first EBP clot, necessitating repeat procedure. Another consideration is that if EBP is delayed, partial healing of the dura may have already occurred at the time of EBP, which might explain the better outcome.

Adverse consequences may be associated with delayed EBP.[372] These are thought to be secondary to prolonged uncorrected intracranial hypotension and include subsequent cranial nerve palsies from potential nerve stretch, venous dilation and stasis causing thromboembolic complications, or tearing of cranial bridging veins resulting in SDH. A large observational study of 26 million postpartum people found the rate of SDH after PDPH to be 147 (95% CI, 111 to 194) hematoma cases per 100 000 deliveries.[24] The authors attributed the risk to untreated intracranial hypotension causing traction and tearing of cranial vessels. In another case report, abducens nerve palsy after diagnostic LP manifested as diplopia with MRI findings consistent with intracranial hypotension.[335] An EBP relieved the headache, but diplopia persisted and did not resolve until 21 days after the dural puncture. The authors suggested that EBP should be performed within 24 hours of onset of diplopia to promote earlier symptom resolution, nevertheless ideal timing remains controversial. Although data are limited, long-term adverse symptomatic outcomes may occur with CSF leaks lasting>12 weeks in duration.[400]

- **Recommendation**: *If an EBP is performed within 48 h of dural puncture, patients should be counseled about a more likely need for repeat EBP to achieve symptom resolution (Grade B; Moderate Level of Certainty).*
- **Recommendation**: *Until symptom resolution, regular patient follow-up should be undertaken to determine the need for repeat EBP in cases of suspected persistent or severe CSF leak (Grade C; Low Level of Certainty).*

Intervertebral level, approach and blood volume

An EBP induces immediate headache relief from increased epidural pressure and redistribution of CSF (hydrostatic or mass effect). Delayed relief comes possibly from the clot sealing the dural hole and preventing CSF leakage (sealing effect).[401] Because the shape and size of the epidural space at each spinal level is not uniform,[402] optimal blood volume for a successful outcome may vary by spinal level. The level and type (interlaminar or transforaminal) of approach potentially affects EBP and results in specific patient cohorts.

Level of intervertebral injection and type of approach

The pattern of drug or blood disposition after epidural injection is affected by age; pregnancy (higher cranial extension); level of intervertebral injection (cervical, thoracic, or lumbar); volume; patient position; and gravity.[403] The epidural space has a pressure gradient with lower pressures at higher vertebral levels, which may explain preferential cephalic spread of epidural injectates.[403 404] Intracranial hypotension from PDPH causes secondary cranial venous dilation, potentiating this negative pressure gradient.[405] In a case series, two patients who underwent MRI after lumbar EBP in the Trendelenburg position revealed spread mostly to the upper cervical area.[406] In another case report, an MRI 10 days post lumbar EBP in the sitting position, demonstrated the presence of blood in the anterior cervical epidural space.[405]

Spread of the lumbar epidural injectate is proportional to the volume injected: 9–10 spinal levels are expected after 18–20 mL,[401] extending preferentially cephalad.[8] In one study, spread occurred 3–4 levels above and 1 level below the site of injection after 20 mL injectate.[352]

Case reports suggest PDPH after cervical procedures can be successfully treated with lumbar EBP[407–409] or fluoroscopic-guided caudal approach.[353] Caudal EBP can also be used,[353 410] particularly in severe lumbar deformity due to multiple surgeries[38] or after intrathecal pump placement.[410] However, the lumbar level is the most common (91%) reported site for EBP in patients with PDPH.[349 354]

Bilateral[355 411] or unilateral[356 357] transforaminal approach has been reported for cases of unsuccessful interlaminar EBP, such as for patients with epidural fibrosis after back surgery, anatomical deformity or when a ventral or far-lateral CSF leak is identified with imaging studies. The transforaminal approach can be used in the cervical, thoracic and lumbar spinal segments and requires image guidance (ie, CT for cervical and thoracic segments and fluoroscopy or CT for lumbar segments).[358]

- **Recommendation**: *When the site of dural puncture is known, an EBP should be performed ideally at, or one space below, this level (Grade B; Moderate Level of Certainty).*
- **Recommendation**: *The transforaminal approach to the epidural space with fluoroscopic guidance can be considered in cases of prior laminectomies near the site of dural puncture or after unsuccessful interlaminar EBP (Grade C; Moderate Level of Certainty).*

EBP volume

The optimal EBP volume in obstetric,[8 338 344–346] general[46 337 341] and chronic pain settings[412] has been investigated. Several RCTs support the use of a 15–20 mL volume at the level of suspected lumbar dural puncture or at a low lumbar vertebral level.[166 167 336–338] In two RCTs, EBP has been effective compared with conservative therapy, typically with volumes of 15–20 mL.[336 337] Other studies have found no correlation between EBP volume and success.[46 344 412] Lower EBP volumes seem to result in less discomfort or pain in the back, buttocks or legs,[166] but do not appear to affect need for repeat EBP.[344 345]

In a prospective study of 53 patients undergoing LP, injecting larger, height-adjusted volumes was no more effective than using 10 mL.[341] A retrospective study of 159 patients also reported satisfactory results with 10 mL[413] while another study of 43 patients reported higher success rates (94.7%) with a mean volume of 19 mL (range 10–34 mL)[46]; need for repeat EBP was not reported in either study. A total of 17 IDDS patients requiring EBP received a mean blood volume of 18.6 mL below the level of catheter insertion, with an 80% relief rate.[412]

In obstetric settings, 1 RCT[338] showed 121 patients receiving EBP with a volume of 15, 20 or 30 mL had a rate of permanent or partial relief of 61%, 73% and 67% and complete relief in 10%, 32% and 26%, respectively. A retrospective study of 466 EBP[345] designed with an initial target of 30 mL, with injection stopped in the presence of pain, reported a final mean volume of 21 mL. Higher volumes were not associated with higher success rates for headache relief. In an RCT (n=33), low (7.5 mL) volumes were similar to high (15 mL) volumes for efficacy but had fewer side effects or systemic complications.[346] However, the study was underpowered to detect a difference in headache outcome (power analysis required 20 patients in each arm) and did not report on the need for repeat EBP in low-volume groups. An observational study reported mean (SD) blood volume of 17.4 (3.5) mL—most cases received 15 mL (25.9%) and 20 mL (41.4%), with 95% experiencing complete or partial relief and 31% experiencing recurrence of moderate or severe PDPH. There was no association between the volume of blood and efficacy.[344] In summary, injecting >30 mL does not appear to increase EBP success rate.[307 338 414–420]

- **Statement**: *Optimal EBP volume is unknown and likely varies among patients due to patient factors such as size, age, degree of spondylotic spine changes and relative size of the dural hole (Low Level of Certainty).*
- **Statement**: *Despite lack of correlation between EBP volume and success rates, most recommended volumes are between 15–20 mL of blood (Low Level of Certainty).*
- **Statement**: *Injection of >30 mL blood does not appear to increase the success of EBP (Moderate Level of Certainty).*

Radiological guidance

Publications on image guidance during EBP have been limited to case reports and observational studies.[328 356 357 375 380 421] In one case report of a 40-year-old woman who received a series of three epidural steroid injections for axial neck pain from degenerative disc disease, fluoroscopically guided transforaminal EBP was more effective than blind intralaminar approach.[357] In another case report, site leakage identified in MRI-directed proceduralists to targeted interlaminar EBP at the level of site leakage, with successful resolution of symptoms.[411] In obstetric settings, one case report described two EBPs that failed to resolve symptoms of PDPH but was successfully treated with a third EBP performed under CT guidance, which revealed the specific area of the CSF leak.[375] Other case series and retrospective studies similarly describe successes using fluoroscopy during EBP in cases of PDPH after labor and delivery.[380 417 421] Three case reports described ultrasound-guided EBP for PDPH.[422–424] In these cases, ultrasound was used for landmark clarification and depth of the epidural space prior to the EBP procedure. Publications on ultrasound or radiological guidance for EBP are mostly of low-quality evidence, primarily describe successes with no publications describing failures or hazards, and are subject to publication bias.

- **Statement**: *Ultrasound-assisted EBP has the utility for landmark clarification before EBP or for image guidance in patients unable to receive fluoroscopy or CT (Low Level of Certainty).*
- **Recommendation**: *The decision to perform EBP under radiological guidance should be individualized based on patient factors, including age, BMI, degree of spondylotic change, context of dural puncture, and prior lumbar spine surgeries and, provider expertise (Grade I; Low Level of Certainty).*
- **Recommendation**: *Radiological guidance should consider risk-benefit analysis, available resources, and follow-up capabilities, and where the clinician determines that EBP cannot be safely performed with landmarks alone (Grade I; Low Level of Certainty).*

Blood cultures

Neuraxial infections may complicate an EBP with potential for significant morbidity.[322 383 425] The mechanism of infection can be related to contamination of the sterile field while collecting blood or during injection of blood into the epidural space or injection of already-infected blood.[383 425] When performing an EBP, strict aseptic precautions should therefore be observed by both the operator and venesector. One study involved immunocompromised patients with HIV infection who received an

autologous EBP. Patients did not appear to have CNS spread of HIV infection or secondary neuraxial bacterial infection.[319] To prevent neuraxial spread of disseminated coccidioidomycosis with autologous blood patch, one case report described allogeneic EBP with resolution of PDPH and no noted complications.[381] One case report involved neuraxial infection following EBP; blood cultures were taken simultaneously at the time of sterile autologous blood draw, with no growth of an organism.[381] When blood cultures were obtained to evaluate for infection, the probability of positive blood cultures was low (1.8%) when cultures were negative after 24 hours of collection.[426] If blood cultures are obtained prior to an EBP, they should be negative for at least 24 hours before proceeding.

- **Recommendation**: *Strict aseptic technique should be observed in both collection and injection of autologous blood (Grade A; Moderate Level of Certainty).*
- **Recommendation**: *Evidence does not support routine use of blood cultures before an EBP (Grade D; Low Level of Certainty).*

Mobilization

Although frequently advised following LP, bed rest has not been shown to be of benefit in reducing the incidence of PDPH when compared with immediate mobilization.[172] Evidence regarding the optimal time to mobilization following and EBP is lacking. Martin *et al* randomized 30 male and female patients with PDPH from various causes to remain flat for 30, 60 or 120 min after an EBP.[427] Mean VAS was similar between groups prior to EBP. On standing after the EBP and 24 hours later, scores were significantly lower in those who remained flat for 120 min compared with those who mobilized at 30 min. Patients are often advised to avoid twisting and straining for 1–2 weeks following an EBP to avoid disruption of the blood clot over the dural tear leading to recurrence of headache. While this advice may be sensible, it is unsupported by clinical studies.

- **Statement**: *Evidence is insufficient to recommend a specific duration of immobilization following EBP (Low Level of Evidence).*

Side effects and complications

EBPs have a long history of clinical use with a very low incidence of major complications.[347 379] The risk of new dural puncture during the performance of EBP is unknown[8] but may result in intrathecal blood injection. Some authors suggest using neuraxial imaging when repeat dural puncture occurs during an EBP.[8] Although low, the risk of repeat dural puncture should be discussed during the informed consent process.

In a prospective study of 81 patients,[341] EBP complications were mild and resolved in 4 weeks. By contrast, rare and more significant complications are described mostly in case reports. The complications associated with EBP can be divided in intrathecal and extrathecal (subdural and epidural) space origins.[417]

The most common extrathecal EBP complication is backache which has been reported in 37%–54% of patients during the procedure and in over 80% on the following day.[338] Backache during performance of an EBP mandates its interruption; it can also be experienced within the first month of EBP and up to 3 months after EBP.[338 341 344 347 350 398] In a 2-year follow-up after EBP, duration of backache was 3–100 days (average 28 days) with no sensory or motor deficits.[340] The mechanism behind backache is thought to be due to extensive subcutaneous hematoma,[401] hematoma calcification[8] or irritation of the nerve roots by hemolytic byproducts of injected blood.[428]

Several groups have studied the association between chronic backache or headache after EBP.[34 393 399 416] The results are conflicting, ranging from no association[396] to increased prevalence of low backache (defined as sustained, new-onset backache<6 months).[399] A prospective, matched, observational study in parturients[416] included four groups: no epidural (n=118) versus uncomplicated epidural (n=117) versus PDPH no EBP (n=56) versus PDPH with EBP (n=59). In the no-epidural group, there were no reports of chronic headache and 1.7% chronic backache; in the uncomplicated epidural group, no chronic headache was mentioned and 6.0% reported chronic backache (not significantly different among groups). In the PDPH no-EBP group, 16.1% reported chronic headache and 17.9% chronic backache. In the PDPH with EBP group, 20.3% had chronic headache and 23.7% had chronic backache. High disability was reported by 8.9% of women in the PDPH no-EBP group and by 8.4% in the PDPH with EBP group versus none in the no epidural and uncomplicated epidural groups. There were no significant differences in chronic pain development between conservatively treated and EBP-treated patients. An international cohort study[34] found statistically higher incidence of chronic headache (moderate to severe) and backache and an increased use of analgesics at 3 months in the EBP group compared with the no-EBP group. The possibility of selection bias exists in these studies: patients with severe CSF leaks requiring EBP may be at higher risk for chronic headache for different reasons; therefore, the risk for chronic headache may not be causally linked to the EBP per se.

The incidence of some complications seems to increase with higher blood volumes administered and the number of EBP performed.[380 384 429] Several case reports have been described transient bladder and fecal incontinence,[430] sacral radiculitis,[429] inadvertent subdural blood injection with severe lumbar back pain and radiculitis,[431 432] and permanent spastic paraparesis with cauda equina syndrome,[433] epidural scarring,[378] and Terson syndrome.[387] If backache persists, increases in severity over time, or evolves, other diagnoses should be investigated.

Subdural abscess and hematoma after EBP have also been described. Two case reports described infected EBP after labor analgesia, highlighting the need for strict aseptic technique.[322] One case report[434] described severe back pain with radicular shooting pain to legs associated with urinary retention and 38°C fever, occurring 5 days after an initially uncomplicated EBP (20 mL) for PDPH after labor analgesia. MRI of the spinal revealed a large SDH from T8 to L5 with medullary compression. Neurosurgical consultation resulted in a period of observation and full resolution of symptoms within 5 days without surgical intervention. The authors posit that if a dural hole is large enough, it can potentially introduce communication between the dura and arachnoid that permits blood from an EBP to move from the epidural into the subdural space.

Intrathecal complications of EBP include arachnoiditis,[420 429 435–438] meningitis,[383 439–441] subarachnoid hematoma,[370 384 398 417 433 437 438 442–447] and pneumocephalus.[368 448] One study[449] found a linear relationship between increasing EBP volumes and adverse neurological outcomes. Patients experiencing compressive syndromes had received higher EBP volumes (35.4 mL) than those experiencing non-compressive syndromes (17.5 mL; p=0.025).

As the outcome of EBP-associated serious neurologic symptoms (eg, cauda equina syndrome, myelopathy) is difficult to predict, a high level of suspicion should prompt investigation and early involvement of a multidisciplinary team (eg, neurology, neurosurgery and/or neuroradiology).

- **Recommendation**: *Informed consent for an EBP should include the potential for repeat dural puncture, backache, and neurological complications (Grade A, High Level of Certainty).*
- **Recommendation**: *To minimize complications, blood should be injected slowly and incrementally. If the patient develops significant backache or headache (eg, pressure paresthesia), injection of blood should be stopped and resumed based on the clinical judgement if symptoms resolve (Grade A; Moderate Level of Certainty).*
- **Recommendation**: *After an EBP, if backache persists, increases in severity, or changes in its nature, other diagnoses should be investigated (Grade C; Low Level of Certainty).*

Efficacy for neuraxial blocks after an EBP

After an EBP, there is the potential for diminished efficacy of neuraxial blocks related to restricted spread of injectate due to scarring and fibrosis from the blood.[360 378] The evidence regarding efficacy of neuraxial analgesia after EBP is limited, conflicting and derived from case reports and retrospective reviews. In a retrospective study,[450] 59% of patients had an uncomplicated successful second epidural anesthetic following a prior EBP compared with 88%–92% of patients without previous dural puncture or EBP. Another study[363] reported that epidural anesthesia and analgesia were not impaired in 96% of patients who had prior EBP compared with 95% of patients who had prior epidural anesthesia without reported dural puncture. The timing following EBP may affect neuraxial analgesia effectiveness, as case reports demonstrate successful epidural analgesia shortly after EBP before the development of scarring and fibrosis.[386 451 452] Impaired analgesia has been observed primarily in patients where the neuraxial analgesia was performed≥2 years after the EBP, although these studies are limited to case reports and retrospective reviews.[360 378 450] Factors that predispose to inadvertent dural puncture and the need for an EBP (eg, challenging anatomy) may be associated with ineffective analgesia.

- **Recommendation**: *Epidural analgesia and anesthesia can be effective following EBP and should not be withheld (Grade C; Low Level of Certainty).*

Question 10: what are the long-term complications of PDPH and how should patients be followed up?

PDPH is increasingly appreciated to be an independent predictor for severe subacute as well as chronic morbidity. Furthermore, the 2009–2012 Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK (MBRRACE-UK) report contained details of the deaths of two women who experienced dural puncture during epidural catheter insertion and subsequently developed PDPH that was not adequately followed-up after discharge from hospital.[453] One died from SDH, the other from CVST. The recent literature demonstrates associations between PDPH and subacute presentation of SDH, CVST and depression. PDPH is also strongly associated with cranial nerve dysfunction resulting in visual disturbances, facial nerve deficits or hearing impairment as well as chronic headache, backache and neckache.

With the length of hospital stay decreasing, symptoms resulting from dural puncture may develop after discharge. It is therefore important that information on postpartum headaches, such as that provided by the OAA,[454] is provided for patients following neuraxial procedures and LP.

Subdural hematoma and cerebral venous sinus thrombosis

Case reports have linked PDPH with SDH, likely caused by brain sagging due to CSF hypotension leading to traction on intracranial veins.[331 455–458] Two large database observational studies quantified this association. Moore *et al* performed an observational cohort study with over 22 million deliveries from the US Agency for Healthcare Research and Quality National Readmission Database. They identified 68 374 cases of PDPH and 342 cases of SDH. PDPH had an aOR for SDH of 199 (95% CI, 126 to 317; p<0.001) and an adjusted absolute risk increase of 130 per 100 000 deliveries.[24] Delayed treatment of PDPH was the strongest risk factor for SDH.[24] Guglielminotti *et al* similarly leveraged the New York State Hospital database for data on over one million obstetric patients who received neuraxial anesthesia or analgesia, including 4808 cases of PDPH. The incidence of SDH was 1.46 per 1000 neuraxial procedures complicated by PDPH versus 0.02 per 1000 in uncomplicated neuraxial procedures, yielding a crude OR of 77 (95% CI, 32 to 182, p<0.001).[30] Most SDH cases were identified during hospital readmission at a median of 5 days but with diagnosis occurring as late as 22 days.[30]

Case reports and a large cohort study also demonstrate an association between PDPH and CVST, which may present similarly to SDH, with worsening headache, loss of the postural component of PDPH and focal neurologic symptoms or seizures.[30 459–462] The suggested mechanism is that decreased intracranial pressure from PDPH results in compensatory cerebral venous dilation, which may lead to clot propensity when combined with the hypercoagulability of the postsurgical, pregnant or postpartum states. The absolute risk of CVST in postpartum patients was quantified using retrospective data at 1.66 per 1000 deliveries complicated by PDPH compared with 0.15 per 1000 after uncomplicated deliveries, yielding a crude OR of 11.48 (95% CI, 5.63 to 23.41; p<0.0001).[30]

Postpartum depression

Orbach-Zinger *et al* performed a retrospective cohort study comparing 132 patients with PDPH to 276 controls and found an increased incidence of postpartum depression, 52% vs 11% (p<0.001); post-traumatic stress disorder, 13% vs 0.4%, p<0.001); and decreased breast feeding (55% vs 77%, p<0.001).[463] In a 2022 systematic review and meta-analysis of retrospective and prospective cohort studies in obstetric patients, Mims *et al* found that unintentional dural puncture and/or PDPH were associated with depression lasting more than 1 month (RR, 3.12; 95% CI, 1.44 to 6.77).[182]

Obstetricians and anesthesiologists should note the association between PDPH and postpartum depression. The US Preventive Services Task Force and the American College of Obstetricians and Gynecologists recommend universal screening for postpartum depression and anxiety with a validated instrument during the comprehensive postpartum visit, with higher vigilance for patients with risk factors for depression.[464 465] Additional studies are needed to determine whether interventions such as treatment of PDPH symptoms with an early EBP can decrease the incidence of depression.

Cranial nerve palsy

PDPH has been associated with acute and chronic abducens (cranial nerve VI) and facial (cranial nerve VII) palsies as well as auditory impairment (cranial nerve VIII). In a 2022 cohort study, patients who suffered unintentional dural puncture were more likely to report chronic hearing loss at least 6 months after

delivery than matched controls (14.3% vs 1.6%, p=0.01).[466] Darvish *et al* found statistically significant hearing loss on audiometry in patients with remote PDPH necessitating an EBP compared with controls. However, the effect size of this hearing loss is of unclear clinical significance.[335 467] Case series also demonstrate associations between PDPH and facial as well as abducens palsies sometimes resulting in permanent deficits necessitating surgical correction of diplopia.[36 335 468] Authors of some narrative reviews recommend considering an EBP within 24 hours of onset of PDPH symptoms to reduce traction on cranial nerves which may potentially reduce the risk of permanent injury.[36 468]

Chronic headache

Multiple retrospective[27–30 399 463 466] and prospective[31 416 469] cohort studies and reviews[470 471] have demonstrated an association between inadvertent puncture or PDPH and chronic headache. The long-term morbidity of chronic headache following dural puncture has been reviewed in a 2022 systematic review and meta-analysis of multiple studies.[28 31 182 416 469] In the meta-analysis, the RR of headache lasting≥12 months was 3.95 (95% CI: 2.13 to 7.34)[182]: EBP was not found to be associated with a significant reduction in the long-term risk for chronic headache.[182] Future studies are essential to determine whether early EBP or other interventions such as prophylactic EBP can decrease chronic headache sequelae of PDPH and the length of time required for follow-up.

Chronic backache or neckache

In 12 retrospective and prospective studies including over 6000 patients with PDPH versus over 1 million controls with uncomplicated neuraxial procedures in obstetric patients, PDPH was associated with increased incidence of backache (RR, 2.72; 95% CI, 2.04 to 3.62) and neckache (RR, 8.09; 95% CI, 1.03 to 63.35).[182] EBP was not associated with significant reduction in the risk for chronic backache or neckache.[182] Future studies are essential to determine whether early EBP or other interventions such as prophylactic EBP can decrease the risk for chronic backache and neckache and the length of time required for follow-up.

Follow-up statements and recommendations

- **Statement**: *Evidence shows an association between inadvertent dural puncture and/or PDPH with chronic headache, backache, neckache, depression, cranial nerve palsy, SDH or CVST (Moderate Level of Certainty).*
- **Statement**: *Evidence is insufficient to determine whether EBP mitigates, prevents, or treats these sequelae (Low Level of Certainty).*
- **Statement**: *PDPH is associated with the development of chronic headache (Moderate Level of Certainty).*
- **Recommendation**: *Before discharge, information regarding PDPH sequelae should be conveyed to patients with arrangements for appropriate follow-up and contact information with their anesthesia provider and other health care providers (Grade B, Moderate Level of Certainty).*
- **Recommendation**: *The person (or team member) responsible for dural puncture leading to PDPH should ensure that other specialties or primary care physicians are informed of PDPH management and potential for long-term symptoms (Grade B, Moderate Level of Certainty).*
- **Recommendation**: *Follow-up with patients who experience PDPH should be continued until headache resolves (Grade B; Moderate Level of Certainty).*
- **Recommendation**: *Following discharge from hospital, follow-up may be continued by the patient's primary care physician. Information regarding PDPH diagnosis and/or inadvertent dural puncture should also be communicated to the patient's primary care physician and other specialists with referrals to a pain or neurology specialist if indicated (Grade C; Low Level of Certainty).*
- **Recommendation**: *Urgent neuroimaging and referral to an appropriate specialist should be performed for any PDPH patient with worsening symptoms despite an EBP, new focal neurologic symptoms, or a change in the nature of headache (Grade B; Moderate Level of Certainty).*

DISCUSSION

The current guidelines provide structured and evidence-based recommendations on pertinent aspects of PDPH, including risk factors, diagnosis, preventative and prophylactic measures, and, finally, therapeutic options and their side effects. This systematic and evidence-based approach to PDPH diagnosis and management may reduce morbidity and mortality in patients with PDPH. In addition, this may reduce the economic impact on the healthcare system and society. The diagnostic criteria for PDPH have changed with subsequent iterations of IHS guidelines,[16] and while our understanding of the pathophysiology and clinical course of PDPH continues to evolve, diagnostic criteria may again change over time.

A crucial aspect highlighted in our guidelines is that it is essential to identify risk factors before performing an intentional dural puncture or a procedure that carries the potential risk of unintentional dural puncture to mitigate these risks. The clinician should assess the procedure's risk–benefit profile and consider if a dural puncture is justifiable. Salient risk factors delineated in our guidelines which showed association with a high level of certainty, such as needle size, type of needle and patient risk factors (younger age, female sex), need to be considered before offering neuraxial procedures.

Another vital aspect stressed in our guidelines is the need for an informed consent process to incorporate the possibility of PDPH before performing neuraxial procedures. Any center offering LP or neuraxial procedures should have a policy on postdischarge follow-up of patients. The policy should include (a) integrating inpatient and outpatient services for identifying and managing PDPH, (b) a plan to diagnose and manage PDPH until resolution and (c) a pathway to access care to identify and prevent complications of PDPH. As symptoms of PDPH are similar to other causes of headache, including those that can lead to intracranial hypertension (such as SDH and CVST), a high index of suspicion should exist when typical features of PDPH are not present or when therapies for PDPH remain ineffective.

Limitations

There are multiple challenges to developing evidence-based guidelines for PDPH, such as the wide variety of practice conditions and heterogeneity of the patient population. Our evidence review focused on adult patients, with most of the evidence emanating from publications on anesthesia, and lacks patient representation. The review may not have encompassed all clinical scenarios (eg, diagnostic dural punctures, intrathecal chemotherapy, chronic pain interventions) or special populations (eg, pediatric population or those with multiple comorbidities). Future studies on the effectiveness of diagnostic and therapeutic options and the prevention of serious complications of PDPH are needed. Investigators may consider novel study

methodologies such as registry trials and adaptive study designs as conventional study methods (eg, RCTs) may be impractical due to low event rates.

Despite advances in evaluation and management of PDPH over recent decades, we must acknowledge that several recommendations remain of moderate-to-low certainty because of small study sample size, suboptimal study design or, at times, out-of-date evidence. Another reason for moderate-to-low certainty of evidence was emerging therapies, notably with procedural options for PDPH management. Several interventional techniques, such as GONB or SPGBs, are novel therapies and need more robust evidence. A similar scenario exists with optimal imaging guidance for performance of a blood patch (fluoroscopic guidance vs landmark approach). Finally, we want to highlight that with the availability of better evidence, our confidence in the certainty of evidence for our recommendations may change.

Conclusion

Current approaches to the treatment of PDPH are far from uniform and hindered by the paucity of evidence. We hope these guidelines will provide a framework for individual clinicians to assess risk, confirm the diagnosis and provide a more systematic approach to its management.

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