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REVIEW ARTICLE

Diagnosis, Prevention, Management, and Prognostication of Delirium in Acute-Care Neurosurgical Patients: A Systematic Scoping Review

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Abstract

Delirium represents a frequent and serious complication in neurosurgical patients, contributing to worse clinical outcomes and increased healthcare burden, yet evidence specific to this population remains fragmented. This scoping review systematically mapped literature on diagnosis, prevention, management, and prognostication of delirium in adult neurosurgical patients, including both surgical and nonsurgical settings, to identify knowledge gaps and inform future research and practice. Following JBI methodology and PRISMA-ScR guidelines, PubMed, MEDLINE, Scopus, and Web of Science were searched for studies published between January 2000 and November 2024. Of 4519 records screened, 102 studies met inclusion criteria. Reported delirium incidence varied widely (0.47–85%), with higher rates in cranial compared with spinal populations. Diagnosis relied mainly on validated screening tools such as the Confusion Assessment Method, while emerging approaches—including structured fluctuation-based assessments, electroencephalography, and pupillometry—showed potential for improved detection. Preventive evidence was limited; dexmedetomidine use, goal-directed fluid therapy, and early frailty-focused rehabilitation were associated with reduced incidence. Management data were scarce, with only two small randomized trials suggesting benefit from nonpharmacological family–environmental interventions and dexmedetomidine compared with haloperidol. Most studies focused on prognostication, identifying consistent risk factors such as preoperative cognitive impairment, frailty, sleep disruption, intraoperative hemodynamic instability, transfusion, and inflammatory or neuronal biomarkers. Across settings, delirium was associated with prolonged hospitalization, long-term cognitive decline, increased mortality, and greater influence on end-of-life decision-making. Overall, current evidence emphasizes risk identification rather than intervention. Significant gaps persist in neurosurgery-specific diagnostic tools, validated preventive bundles, and effective treatment strategies. Future research should prioritize the development and validation of tailored, multimodal approaches to enable personalized delirium care in neurosurgical populations.

Keywords: Delirium, Neurosurgery, Postoperative complication, Critical care, Risk factors, Review

Introduction

Delirium is an acute, fluctuating disturbance of cognition and attention that poses a serious clinical and economic challenge in hospitalized patients [1]. Postoperative and elderly patients are at highest risk, facing prolonged stays, higher costs, and increased mortality [2, 3]. With an aging population, delirium is increasingly burdensome,

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with US hospitalizations costing $16,303–$64,421 per patient and requiring substantial resources [4–6]. For these reasons, early detection and appropriate management are essential.

Neurosurgical patients are particularly vulnerable owing to neurological comorbidities, surgical invasiveness, and other procedure-related risks [7]. Postoperative delirium rates reach 22% after intracranial surgery (exceeding 40% in some cranial populations), and 17% after spinal surgery [8–10].

Despite this, a comprehensive mapping of the evidence across the entire continuum of care—including diagnosis, prevention, management, and prognosis—remains absent for the heterogeneous neurosurgical population. Indeed, existing studies focus on isolated aspects or only surgical patients, and a broader view is lacking [7–9]. This scoping review aims to comprehensively map the existing literature on delirium in adult neurosurgical patients—both surgical and nonsurgical—highlighting knowledge gaps and informing clinical practice and future research.

On the basis of the gathered data, to synthesize these priorities and guide subsequent investigations, we propose a conceptual framework (Fig. 1) that maps the critical research domains (diagnosis and assessment,

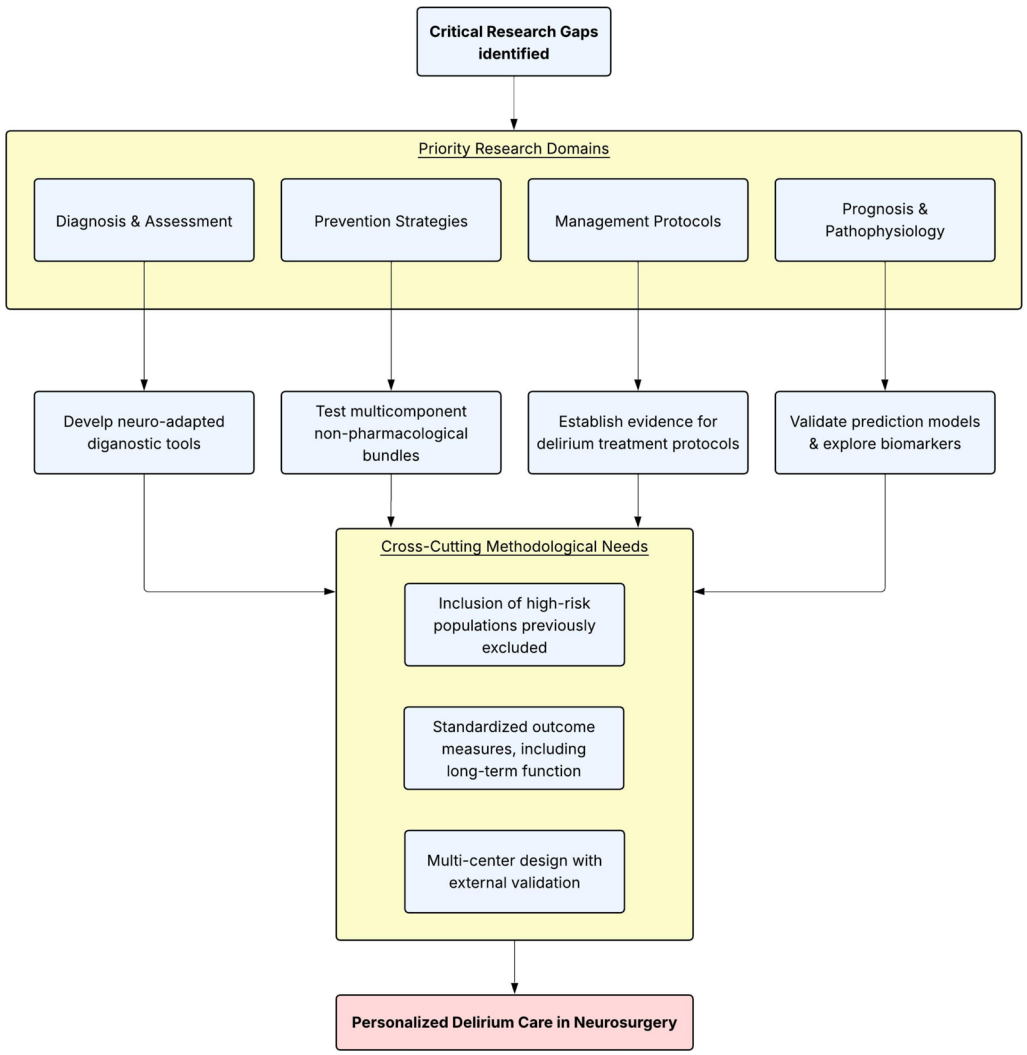

Fig. 1 Conceptual framework for prioritizing research to achieve personalized delirium care in the neurosurgical population. The framework identifies four primary research domains (diagnosis and assessment, prevention strategies, management protocols, and prognosis and pathophysiology), each with a critical research gap and a defined research objective. These domains are unified by three cross-cutting methodological necessities essential for rigorous and generalizable research. Progress across these interconnected areas is directed toward the central goal of delivering personalized delirium care in neurosurgery

prevention strategies, management protocols, prognosis, and pathophysiology), identifies the specific gaps, and outlines the necessary methodological approaches required to achieve personalized delirium care for this vulnerable population.

Methods

Study Design and Reporting Standards

We conducted this scoping review following JBI and PRISMA-ScR guidelines [11, 12]. The two primary authors (NM and FP) defined the review question, search strategy, and outcomes of interest.

Research Question

This research question guided the search strategy, data extraction, and thematic analysis to ensure comprehensive coverage of the topic and identification of knowledge gaps:

> *"What is the current evidence on the diagnosis, prevention, management, and prognostication of delirium in adult neurosurgical patients?"*

Eligibility Criteria

The review followed the population–concept–context (PCC) framework recommended for scoping reviews:

The population was adult neurosurgical patients with brain or spinal diseases (e.g., brain tumors, traumatic brain injury—TBI, subarachnoid hemorrhage) as primary reason for admission, regardless of whether they underwent a surgical procedure during their hospitalization. The decision to include both surgical and nonsurgical patients reflects the clinical reality of neurosurgical units, where the primary neurological insult (e.g., intracranial hemorrhage or traumatic injury) represents a major risk factor for delirium, independent of surgical intervention. A "neurosurgical patient" was defined as any adult patient requiring the care of a neurosurgical team for cranial or spinal pathologies, including those managed conservatively in a neuro-intensive care unit (ICU) or specialized ward.

The concept was defined a priori across four pillars by the main authors (NM, FP) and based on a preliminary literature scan and clinical relevance to delirium care:

Diagnosis: methods, tools, or criteria used to identify delirium once occurred, including their effectiveness
Prevention: strategies to reduce delirium incidence, including interventions, protocols, or practices implemented during hospitalization
Management: pharmacological and non-pharmacological treatments.
Prognostication: risk factors, clinical features, or biomarkers predicting delirium occurrence, early identification, or related outcomes such as symptom resolution, long-term cognitive impairment, length of hospital stay or mortality.

The context included perioperative or acute care settings. Exclusions were:

Pediatric populations (< 18 years of age) without subgroup analysis. Studies that did not explicitly report a minimum age of ≥ 18 years were included if the reported mean and standard deviation were consistent with an adult population.
Non-neurosurgical patient groups without neurosurgical subgroup analysis.
No delirium-specific data. Delirium-specific data refers to any reported outcomes concerning delirium incidence, duration, severity, or subtypes, identified via validated screening tools or clinical diagnosis.
Outcomes beyond the post-acute phase (generally 30 days post-admission).
Surgery for chronic neurological conditions (e.g., deep brain stimulation for Parkinson's disease), as these populations have distinct management protocols.
Emergence delirium, a separate clinical entity, defined as a state of acute agitation and confusion occurring immediately upon emergence from general anesthesia, typically within the recovery room setting.

Search Strategy

The search strategy included MeSH terms, subject headings, and synonyms related to the diagnosis, prevention, management, and prognostication of delirium in neurosurgical patients. Searches were conducted by one author (NM) and cross-checked by a second author (FP). Searched databases were: PubMed, Scopus, and Web of Science. The search was restricted to published English language from January 2000 up to and including 13 November 2024 (Supplement 1). The initial search employed a high-sensitivity approach using broad free-text terms to ensure comprehensive literature coverage on delirium in neurosurgical populations. The time limit was chosen to ensure the retrieval of contemporary data. We excluded animal studies, conference abstracts, case reports, theses, and book chapters. Guidelines and reviews were used for reference mining but not for analysis unless containing original data.

Study Selection

Search results were uploaded into the free platform "Rayyan" for screening, and duplicates were manually removed. Title and abstract screening was conducted

independently by NM and FP. After screening, eligible full texts were independently reviewed by NM and FP. Discrepancies at any stage were resolved by consensus. Reference lists of included studies were manually screened for additional relevant publications.

Data Extraction

Data were extracted using a standardized form piloted on five studies. The form captured study characteristics, interventions, outcomes, and key findings. Extraction was performed independently by two authors (NM, FP) with cross-checking.

Data Synthesis

Data were synthesized thematically into four predefined categories: (a) diagnosis, (b) prevention, (c) management, and (d) prognostication.

Reporting

The selection process was recorded in sufficient detail to complete a PRISMA flow diagram and a list of excluded full-text studies with reasons for exclusion. Studies were summarized in tables and narratively.

Bias Assessment

As the goal was to provide a comprehensive scoping review of the available evidence, conducting a formal bias analysis was not necessary.

Statistical Analysis

Given the purposes of the review, a formal meta-analysis was not performed.

Ethics and Dissemination

No ethical approval was required, as this review is based on already published data and did not involve interaction with human subjects.

Results

Overview of Included Studies

From 4519 identified records and after duplicate removal, 102 studies were included (Fig. 2, PRISMA flowchart), and on the basis of the synthesis of the included studies, we developed a conceptual framework to categorize the existing evidence and identify future research priorities (Fig. 1).

A summary table of included studies is provided in Supplement 2, detailing study characteristics and key findings. At the title and abstract screening stage, records

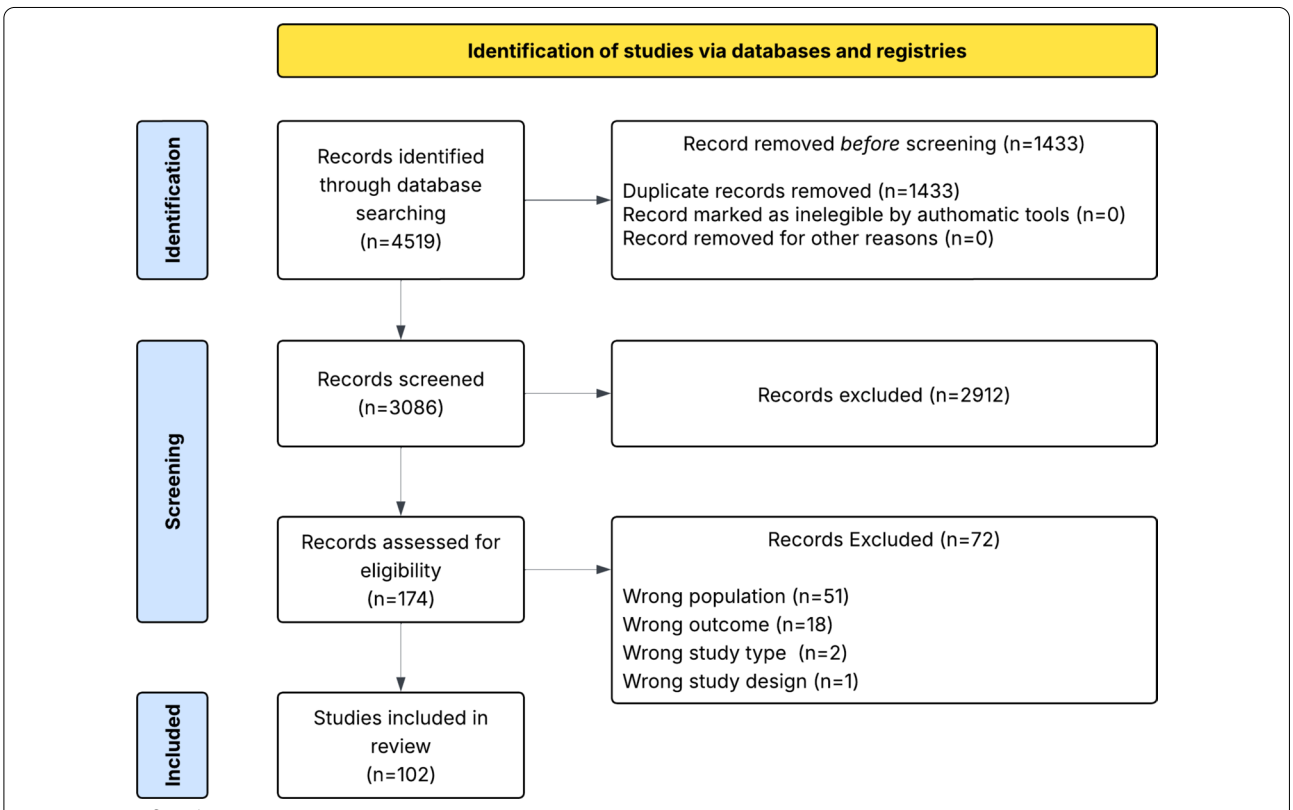

Fig. 2 PRISMA flowchart

were primarily excluded for not meeting the inclusion criteria, specifically targeting populations outside the neurosurgical scope (e.g., general surgical or pediatric cohorts), being nonclinical study designs (e.g., animal models, bench research), or being document types without primary data (e.g., editorials, letters, or case reports). Reasons for exclusion at full-text screening are listed in Supplement 3.

Geographically, most studies originated from the USA (30.4%), China (23.5%), and Korea (14.7%), with no representation from Latin America, Africa, or Oceania.

Most studies (68.6%) were published from 2020 onward, distributed across 63 journals.

Study designs were predominantly retrospective (52%), followed by prospective cohorts (31.4%) and randomized controlled trials (RCTs) (14.7%).

Population, Neurosurgical Conditions and Incidence

Sample sizes ranged from 25 to 493,431 patients (median 224). Most studies focused on brain diseases (56.9%), with one study (1%) including both brain and spinal disorders.

Among brain studies, common diseases were brain tumors (22.8%), TBI (19.3%), and subdural hematoma (10.5%). Spine studies predominantly addressed degenerative conditions (60.5%), with few focusing on spinal trauma (7%).

Most studies (71.3%) included only surgical patients, while only one study (1%) focused exclusively on nonsurgical patients with TBI [13].

Overall, reported delirium incidence ranged from 0.47 to 85% (mean 22.37%). In brain studies, delirium incidence ranged from 0.47 to 85% (mean 27.5%), while it occurred from 1.07 to 43.2% (mean 15.7%) in spinal studies.

Nearly half of the studies (48%) excluded patients with preexisting cognitive, behavioral, or psychiatric conditions that may be related to increased delirium incidence.

Diagnosis of Delirium

Most studies (91.3%) used validated delirium assessment tools. Half (51%) used a single screening instrument, while the remaining combined multiple tools or additional criteria. The Confusion Assessment Method (CAM) and its derivatives were most frequent (58.8%). Key features of assessment instruments are summarized in Table 1.

Most studies (79.4%) did not report delirium motor subtypes (hyperactive, hypoactive, mixed). When reported, hyperactive (10.0%) and mixed hyper/hypoactive forms (16.2%) were more frequently described.

Screening personnel varied and 13 studies did not specify assessors. Timing/frequency also differed widely, with 25.7% not reporting a clear schedule.

Delirium duration was not reported in most studies (77.5%). When reported, it typically lasted less than 1 week.

A total of five studies (4.9%) primarily focused on diagnosis and assessed the diagnostic performance of clinical tools or physiological measures [14–18]. Two studies on patients with intracerebral hemorrhage compared delirium screening tools: the Intensive Care Delirium Screening Checklist (ICDSC) showed superior diagnostic accuracy over CAM-ICU [14], and a newly developed Fluctuating Mental Status Evaluation (FMSE) demonstrated good sensitivity/specificity compared with the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 [15]. Three studies investigated novel physiological measures. A pilot electroencephalography (EEG)-based assessment identified characteristic high-frequency activation patterns in patients with delirium after spine surgery [16]. In traumatic brain injury, impaired pupillary light reflex was associated with delirium, supporting automated pupillometry as a potential bedside biomarker [17]. In subdural hematoma patients, variability in arousal [Richmond Agitation and Sedation Scale (RASS) dispersion] was linked to delirium and worse discharge outcomes [18].

Prevention Strategies

In total, 16 studies (15.7%) evaluated prevention strategies before delirium onset and mostly were RCTs ($n=12$) (Table 2).

A total of four thematic groups were identified: pharmacological prophylaxis, anesthetic/physiological optimization, early mobilization and rehabilitation, and environmental/educational strategies.

In total, six RCTs tested pharmacological prophylaxis. Gabapentin showed no preventive effect after spine surgery [19], whereas dexmedetomidine in brain tumor and cranial surgery was associated with reduced postoperative delirium incidence and improved secondary outcomes [20, 21]. Preoperative oral saline was linked to decreased delirium and neuroinflammatory biomarkers in elderly patients with spinal disorders [22]. Methylphenidate after traumatic brain injury showed neuroprotective effects but no difference in delirium rates [13]. Aripiprazole reduced delirium in neurosurgical ICU patients [23].

Five studies focused on anesthetic/physiological intraoperative strategies. Goal-directed fluid therapy helped to reduce delirium in spinal stenosis surgery [24]. Lung-protective ventilation was associated with reduced delirium, inflammation, and cerebral desaturation in elderly

Table 1 Diagnostic tools and methods used for delirium assessment in the included studies

Diagnostic tool/method	Full name	Number of studies using tool	Key characteristics/notes
CAM/CAM-ICU	Confusion Assessment Method/for the ICU	60	Most frequently used tool. Designed for rapid, structured assessment. CAM-ICU validated for nonverbal/ventilated patients
DSM-IV/DSM-5	Diagnostic and Statistical Manual of Mental Disorders	27	Used as the diagnostic gold standard, often to confirm positive screens from other tools
Clinical Diagnosis (Symptoms)/Unspecified	–	12	Diagnosis based on chart documentation of specific symptoms (e.g., hallucinations, agitation)
ICDSC	Intensive Care Delirium Screening Checklist	9	Designed for the ICU setting; allows for assessment over a 24-h nursing shift
Nu-DESC	Nursing Delirium Screening Scale	8	A brief, nurse-friendly instrument suitable for busy clinical environments
RASS	Richmond Agitation–Sedation Scale	7	Primarily for assessing sedation level/arousal, often used in conjunction with CAM-ICU or ICDSC
ICD-9/10 codes	International Classification of Diseases	4	Used in large database studies; high specificity but low sensitivity for clinical delirium
DOSS	Delirium Observation Screening Scale	4	A 25-item scale based on nurses' observations during regular care
DRS/DRS-R-98	Delirium Rating Scale	3	Provides a measure of delirium severity
4AT	4 "A"s Test	2	Rapid assessment test (alertness, AMT, attention, acute change)
Korean-Nu-DESC	Korean Nursing Delirium Screening Scale	1	Culturally adapted version of the Nu-DESC

This table summarizes the variety of instruments and approaches employed to diagnose delirium across the reviewed literature, highlighting their frequency of use and key characteristics. The number of studies using tool reflects the count out of the 102 included studies

CAM, Confusion Assessment Method; CAM-ICU, Confusion Assessment Method for the Intensive Care Unit; DSM-IV/5, Diagnostic and Statistical Manual of Mental Disorders, Fourth/Fifth Edition; ICDSC, Intensive Care Delirium Screening Checklist; Nu-DESC, Nursing Delirium Screening Scale; RASS, Richmond Agitation–Sedation Scale; ICD-9/10, International Classification of Diseases, Ninth/Tenth Revision; DOSS, Delirium Observation Screening Scale; DRS/DRS-R-98, Delirium Rating Scale/Revised-98; 4AT, 4 "A"s Test

patients undergoing elective spinal surgery [25]. Target-controlled anesthesia was associated with reduced delirium in elective spinal patients [26]. Volatile agent choice (desflurane vs. isoflurane) did not influence delirium incidence after spinal surgery [27]. Transradial access for chronic subdural hematoma embolization, enabling earlier mobilization, was also linked to lower delirium rates [28]. Overall, physiological stability correlated with reduced risk.

A brain-tumor–specific frailty-centered rehabilitation protocol was associated with reduced delirium incidence, delayed onset, shortened duration, and improved functional outcomes up to 1 month postoperatively [29]. These findings highlight the importance of functional reserve and frailty modification.

Four studies focused on modifying the care environment. Family overnight presence after spine surgery showed a trend toward reduction in early postoperative delirium [30]. Enhanced anesthesia counseling helped to reduce delirium risk in the immediate post-extubation period [31]. Very frequent neurological examinations in traumatic brain injury patients were associated with increased delirium risk, likely linked to sleep disruption [32]. Perioperative music therapy in spinal surgery was linked to improved anxiety and pain control, without significant reduction in delirium incidence [33].

Most studies showed reduced delirium incidence, though evidence on long-term cognitive or healthcare outcomes remains limited.

Management

Only two RCT focused on delirium management. One enrolled patients with TBI. Only one specifically targeted the management of hyperactive delirium [34, 35].

These studies tested different interventional strategies. One investigated an environmental–familial approach, implementing a protocol of reassurance, emotional support, clear information, effective communication, and structured family visits twice a day for 45 min [34]. This intervention showed a not-negligible association with a reduction in delirium, with a recovery rate of 85% in the intervention group compared with 40% in the control group. The second study compared pharmacological solutions in mechanically ventilated traumatic brain injury patients in the ICU setting, administering intravenous dexmedetomidine at a dose of 0.5 µg/kg vs.

Table 2 Summary of studies evaluating delirium prevention strategies in neurosurgical patients. This table provides an overview of intervention studies aimed at preventing delirium, categorized by strategy type, and details study design, population, intervention specifics, and key outcomes

Author	Design	Population	Intervention(s), if applicable	Intervention duration, if applicable	Comparison group(s), if applicable	Delirium incidence rate %	Key-findings
Pharmacological prophylaxis							
Leung, JM et al. [19]	RCT	Spine	-Gabapentin 900 mg preop + 300 mg TID for 3 days postop	Preoperatively and 3 days postoperatively	Perioperative gabapentin vs. placebo	Overall 26.6% (84/316; spine group); gabapentin 24.5% (38/155) vs. pacebo 28.6% (46/161); $p = 0.49$	-No ↓ in delirium with gabapentin (spine: 24.5% vs. 28.6% placebo, $P = 0.49$) -↓ POD1 opioid use ($P = 0.04$) -No LOS difference
Li, S et al. [20]	RCT	Brain	-Dexmedetomidine: 0.6 µg/kg load → 0.4 µg/kg/h until dural closure	Median 5 h	Dexmedetomidine vs. placebo (normal saline)	Dex 21.5% vs. placebo 46.2%	-Dexmedetomidine ↓ delirium by 50% ($P < 0.001$), ↓ pain, ↑ sleep quality without ↑adverse events
Chen, P–H et al. [21]	RCT	Brain	-Dexmedetomidine (0.5 µg/kg/h IV) + goal-directed hemodynamic therapy	Intraoperative (started preinduction, maintained throughout surgery)	Intraoperative dexmedetomidine versus saline placebo combined with goal-directed haemodynamic therapy	Dex 9.0% (ICDSC ≥ 4) vs. control 17.9% (ICDSC ≥ 4)	-↓ Delirium in dexmedetomidine group (9.0% vs. 17.9%; $P = 0.012$) -↓ Neurological complications (26.3% vs. 43.8%; $P = 0.031$) -↓ Serum HMGB1/GFAP (neuroinflammation biomarkers) in dex group -No hemodynamic compromise with goal-directed hemodynamic therapy
Chen, J et al. [22]	RCT	Spine	-Oral normal saline (5 mL/kg, max 400 mL) 2 h preop	Single dose preop	Oral normal saline vs. standard fasting (no liquids 8 h preop)	Control 27.8% vs. intervention: 8.3%	-↓ delirium incidence ($P = 0.033$), ↓ S100β/CRP ($P < 0.05$), ↑ MAP/HR at induction ($P < 0.01$), ↓ thirst ($P = 0.007$) in intervention group
Haddadi, K et al. [13]	RCT	Brain	-Methylphenidate 0.3 mg/kg/day (max 20 mg)	From day 2 until discharge	Methylphenidate vs. placebo	NR	-↑ GOS ($P = 0.013$), ↓ hospital stay ($P < 0.001$), ↓ ICU stay ($P = 0.014$) in methylphenidate group -No delirium difference

Table 2 (continued)

Author	Design	Population	Intervention(s), if applicable	Intervention duration, if applicable	Comparison group(s), if applicable	Delirium incidence rate %	Key-findings
Mokhtari, M et al. [23]	RCT	Brain	-Enteric aripiprazole (15 mg/day) vs. placebo for 7 days	Up to 7 days	Aripiprazole vs. placebo	Aripiprazole 20% vs. placebo: 55%	-Aripiprazole ↓ delirium incidence (20% vs. 55%, $P=0.022$) and prevalence during follow-up ($P=0.018$) -No significant difference in delirium-free days (5.6 vs. 4.3, $p=0.111$) or ICU stay -Safe
Anesthetic/physiological intraoperative strategies							
Wang, DD et al. [24]	RCT	Spine	-Goal-directed fluid therapy: fluid optimization via continuous noninvasive arterial pressure monitoring (PPV ≤ 14%); restricted fluid: fixed fluid protocol (5 mL/kg bolus + 5 mL/kg/h maintenance)	Intraoperative	Restricted fluid group vs. goal-directed fluid therapy group	Overall 8.2%; restricted fluid 12.4% vs. goal-directed fluid therapy 4.1%	-Goal-directed fluid therapy ↓ delirium incidence (12.4% vs. 4.1%, $P=0.035$), ↑ intraoperative fluids/urine output, improved hemodynamic stability, and shortened hospital stay (17 days vs. 14.5 days)
Wang, J et al. [25]	RCT	Spine	-LPV (tidal volume 6 mL/kg PBW, PEEP 5 cmH_2O, recruitment maneuvers)	Intraoperative	Conventional MV (tidal volume 8 mL/kg PBW, no PEEP) vs. lung-protective ventilation	MV 25% (8/32) vs. LPV 6% (2/32)	-LPV ↓ delirium ($P=0.039$), cerebral desaturation ($P=0.03$), and inflammation (↓IL-6/GFAP, ↑IL-10) -Improved cerebral oxygenation (rSO_2) in LPV group
Zhang, C H et al. [26]	Prospective cohort	Spine	-Blood trasfusion -Phenylephrine for hypotension	Not applicable	Target-controlled anesthesia (sevoflurane inhalation + sufentanil infusion) vs. manually controlled anesthesia	16.8% (81/480); S–S TCI 7.5% (18/240) vs. S–S MCI 26.2% (63/240)	-Target-controlled anesthesia ↓ POD incidence (7.5% vs. 26.2%), recovery time, and vasoactive drug use -Risk factors: manual anesthesia, ↑ blood loss
Joys, S et al. [27]	RCT	Spine	-Anesthesia with isoflurane vs. desflurane	Intraoperative	Isoflurane vs. desflurane groups	D1: 11.7% (7/60); D3: 3.3% (2/60) [Iso: D1 = 10%, D3 = 6.6%; Des: D1 = 13.3%, D3 = 0%]	-No significant difference in POD incidence/severity between isoflurane and desflurane -Median age of delirium patients ~ 36 years
Yamamoto et al. [28]	Retrospective cohort	Brain	-Transradial access vs. transfemoral access for middle meningeal artery embolization	Bilateral MMAE: transradial median 151 min; transfemoral median 174 min	Transradial vs. transfemoral	Transradial 16.7% (2/12) vs. transfemoral 46.2% (6/13)	-Transradial associated with ↓ delirium (16.7% vs. 46.2%) and ↓ procedure time (151 vs. 174 min)

Table 2 (continued)

Author	Design	Population	Intervention(s), if applicable	Intervention duration, if applicable	Comparison group(s), if applicable	Delirium incidence rate %	Key-findings
Early mobilization and rehabilitation							
Yuan, Y et al. [29]	RCT	Brain	-FORTITUDE program: early mobilization (day 0–5), daily living skills training, Bobath exercises, balance training	5 days postoperatively (60 min/day)	FORTITUDE vs. standard care (head elevation, multimodal analgesia, self-directed mobility)	FORTITUDE: 15.6% (22/141) vs. control 28.7% (43/150) ($P=0.007$)	-FORTITUDE ↓ delirium incidence, delayed onset (1.95 vs. 1.49 days, $P=0.035$), ↓ duration, improved ADL scores (1 week/month), ↓ frailty at discharge (19.9% vs. 30.7%, $P=0.034$), ↓ hospital stay
Environmental/educational strategies							
Kapoor, I et al. [31]	RCT	Spine	-Detailed preoperative anesthesia counseling	Preop (day before surgery + 15 min presurgery)	Detailed preoperative anesthesia counseling vs. standard care group (basic counseling)	Standard care 16% (4/25) vs. anesthesia counseling 0% (0/25)	-↓ Delirium in anesthesia counselling group (0% vs. 16% in standard care, not significant) -↑ Early cognitive function in anestheisa counselling (MMSE 29.52 vs. 27.56, $P=0.006$). No difference in emergence/extubation time or satisfaction
Chotai, S et al. [32]	Retrospective cohort	Brain	Not applicable	Not applicable	Neuro-check frequencies: Q1 (hourly) vs. Q2 (every 2 h) vs. Q4 (every 4 h)	Overall: 29.5% (Q1: 49.2%, Q2: 14.8%, Q4: 20.9%)	-Q1 neuro-checks ↑ delirium risk (HR = ref) -Q2 (HR = 0.44) and Q4 (HR = 0.48) protective -Dementia, tobacco use, IPH/contusion, tSAH, ↓GCS, ↑ISS also risk factors
Welsch, E et al. [30]	Prospective cohort	Spine	-Family presence during first night	One night (from surgery until next morning)	Family presence during first night vs. unaccompanied group (no family member)	Overall 13.3%; family: 6.3% vs. unaccompanied: 21.4%)	-Family presence associated with ↓ delirium rate (6.3% vs. 21.4%) but not significant ($P=0.23$) -In elderly subgroup, 0% vs. 25% ($P=0.097$)

Table 2 (continued)

Author	Design	Population	Intervention(s), if applicable	Intervention duration, if applicable	Comparison group(s), if applicable	Delirium incidence rate %	Key-findings
Kappen, PR et al. [33]	RCT	Brain	-Music before/during/after surgery until POD3	30 min preop, intraop, 30 min postop, then 30 min twice daily until POD3	Music vs. no music	DOSS: Control = 22.3%, Music = 11.6%, DSM-5: Control = 7.4%, Music = 4.2%	-Music ↓ DOSS-defined delirium (OR = 0.49, $P = 0.048$) but not DSM-5-confirmed delirium ($P = 0.342$) -Increased HRV (RMSSD, $P = 0.012$) -No difference in secondary outcomes (anxiety, LOS, complications)

RCT, randomized controlled trial; Preop, preoperative; Postop, postoperative; TID, three times a day; POD, postoperative delirium; LOS, length of stay; IV, intravenous; ICDSC, Intensive Care Delirium Screening Checklist; HMGB1, high-mobility group box 1; GFAP, glial fibrillary acidic protein; MAP, mean arterial pressure; HR, heart rate; NR, not reported; GOS, Glasgow Outcome Scale; ICU, intensive care unit; PPV, pulse pressure variation; LPV, lung-protective ventilation; PEEP, positive end-expiratory pressure; PBW, predicted body weight; MV, mechanical ventilation; IL-6, interleukin-6; IL-10, interleukin-10; rSO_2, regional cerebral oxygen saturation; S–S TCI, sevoflurane–sufentanil target-controlled infusion; S–S MCI, sevoflurane–sufentanil manually controlled infusion; MMAE, middle meningeal artery embolization; FORTITUDE, frailty-originated early rehabilitation program; ADL, activities of daily living; MMSE, Mini-Mental State Examination; HR, hazard ratio; IPH, intraparenchymal hemorrhage; tSAH, traumatic subarachnoid hemorrhage; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; DOSS, Delirium Observation Screening Scale; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; HRV, heart rate variability; RMSSD, root mean square of successive differences between heartbeats

intravenous haloperidol at a dose of 2.5 mg every 8 h [35]. The study reported a reduction in the incidence and severity of delirium in the dexmedetomidine group, with the haloperidol group showing a 40% incidence of delirium compared with 20% in the dexmedetomidine group.

The overall trend highlights a critical gap in literature: a striking lack of studies proposing or evaluating specific management protocols for delirium in the neurosurgical patient.

Prognostic Factors

Most studies (77.5%) focused on prognostication or identification of risk factors, predominantly using retrospective designs in acute/postoperative settings. Common outcomes were delirium incidence, length of stay (LOS), and mortality. Research covered three domains: patient vulnerability, perioperative/management factors, and physiological/radiological determinants (summarized in Table 3; references in Supplement 2).

About patient-related vulnerability factors, preoperative cognitive impairment and psychiatric comorbidities consistently emerged as major risk factors for postoperative delirium, particularly in spine surgery cohorts [36–38]. Frailty indices and poor nutritional status also demonstrated predictive associations in both brain and spine patients [39–41]. Other frequently identified vulnerabilities included advanced age (multiple studies), preoperative sleep disturbances [42, 43], and alcohol and other substance use [44]. About clinical management and perioperative variables, several modifiable risk factors were consistently associated with delirium: surgery duration and intraoperative blood pressure fluctuations [45], blood transfusions [46], early postoperative exposure to muscle relaxants or benzodiazepines [47], postoperative pain, and sleep disturbance management [48]. Conversely, several studies suggested protective associations with female sex and higher body mass index (BMI) [49, 50].

An increasing number of studies evaluated inflammatory, neuroendocrine, or neuronal biomarkers. Key findings included: elevated neutrophil–lymphocyte ratio (NLR), monocyte–lymphocyte ratio (MLR), C-reactive protein (CRP)-to-albumin, postoperative troponin, and S100β linked to delirium onset [51, 52]; cortisol, IGF-1, CRH, and glucose disturbances in pituitary tumor surgery [53]; biomarkers of neuroinflammation including sTREM2 and gasdermin D [54]; and preoperative resting-state EEG abnormalities predicting delirium and long-term cognitive decline [55]. Additionally, structural brain damage (e.g., frontal involvement, hematoma, and radiographic progression) increased delirium risk and mortality in brain injury and tumor cohorts [56–58].

Table 3 Identified risk factors and prognostic determinants for delirium in neurosurgical patients, categorized by domain

Domain	Category	Specific risk factor
Patient-related vulnerability	Cognitive and psychiatric	Preoperative cognitive impairment
		Depression/anxiety
		Preexisting dementia/delirium history
	Frailty and nutrition	Frailty
		Poor nutritional status
	Demographics and comorbidities	Advanced age
		Preoperative sleep disturbances
		Alcohol/substance use
Clinical management and perioperative factors	Surgical and anesthetic	Longer surgery duration
		Intraoperative BP deviations
		Deep anesthesia/low BIS
	Medications	Benzodiazepines
		Muscle relaxants (postop)
		Ketamine (intraoperative)
	Procedural and supportive	Blood transfusions
		Incidental durotomy
		Postoperative pain
		Physical/restraint use
Injury and physiological determinants	Injury severity and location	Structural brain damage
		Lower GCS/neurological deficits
	Biomarkers	Systemic Inflammation
		Neuroinflammation and injury
		Endocrine/metabolic Stress
	Radiological and monitoring	Hematoma/mass Effect
		Hydrocephalus/IVH
		Impaired cerebral physiology

This table synthesizes the patient-related, clinical management, and physiological determinants associated with an increased risk of delirium, as identified across the included studies

BP, blood pressure; BIS, bispectral index

Multiple studies developed delirium prediction tools tailored to neurosurgical populations, including nomogram models in chronic subdural hematoma [59, 60] and delirium risk scoring systems in spinal trauma and fusion patients [61]. However, external validation is generally lacking, and calibration metrics vary substantially.

About the prognostic impact, delirium was consistently associated with increased length of stay, ICU admission, and healthcare costs [49, 50, 58]; higher mortality in brain-injured patients [56]; and long-term cognitive impairment following both cranial and spinal surgery [45, 55]. Notably, delirium influenced end-of-life decisions, including the withdrawal of life-sustaining treatment in intracerebral hemorrhage [62].

In summary, prognostic research provides strong evidence supporting multifactorial vulnerability encompassing premorbid frailty, modifiable perioperative elements, and brain injury severity and demonstrating clear associations between delirium and worse short- and long-term outcomes.

Discussion

This scoping review comprehensively maps the evidence on delirium in adult neurosurgical patients, with brain and spinal diseases, operated or not, encompassing diagnostic approaches, prevention, management, and prognostication. Across 102 studies, delirium was found to be a frequent and multifactorial occurrence in both cranial and spinal populations admitted in neurosurgical institutions. Despite increasing research, substantial gaps and heterogeneity persist in diagnostic criteria, assessment timing, and preventive or therapeutic strategies. Our findings identify critical gaps requiring targeted research to optimize care for this vulnerable population.

Diagnosis

The diagnostic assessment of delirium in neurosurgical patients remains challenging. Most of the analyzed studies relied on tools originally designed for general medical or ICU populations (CAM-ICU, ICDSC, or Nu-DESC), which may not optimally suit neurosurgical patients. Indeed, a major challenge identified in our review is the potential for "diagnostic overshadowing" in patients with acute neurological injuries. In the neurosurgical population, focal deficits resulting from the primary injury—such as aphasia, neglect, or motor impairment—can frequently mask or mimic the clinical features of delirium. This overlap makes it difficult to distinguish between the natural progression of a brain injury and the onset of delirium [8]. Furthermore, the fluctuating consciousness typical of patients with TBI or subarachnoid hemorrhage may be indistinguishable from the waxing and waning course of delirium using bedside scales alone. In these complex neurosurgical cases, a multimodal assessment is often required. This may include neurophysiological monitoring, such as continuous electroencephalography, to differentiate delirium from nonconvulsive status epilepticus, which can present with a nearly identical clinical phenotype.

Overall, our results mirror prior reviews reporting significant heterogeneity in delirium definition and measurement and the lack of a population-specific reference standard. Although 91% of articles used at least one validated tool, nearly 80% did not differentiate delirium subtypes, limiting the understanding of hyperactive, hypoactive, and mixed forms—particularly underrecognized in neurosurgical settings. This lack of granularity limits the understanding of pathophysiological differences between hyperactive, hypoactive, and mixed forms, the latter being particularly underrecognized in neurosurgical settings. Significant disparities were also found in personnel, timing and endpoint of delirium assessment, limiting comparison among studies. Recent pilot searches have proposed alternative or adjunctive approaches—such as the Fluctuating Mental Status Evaluation (FMSE), continuous EEG monitoring, and automated pupillometry—that appear to improve diagnostic accuracy in this population [15, 17]. However, the current evidence remains preliminary, as none of these methods have undergone rigorous external validation or been integrated into standardized clinical pathways, underscoring the gap identified in our framework.

Prevention

Preventive strategies before delirium onset in neurosurgical conditions are beginning to emerge but remain underinvestigated compared with other surgical specialties. For example, a large amount of high-quality studies focused on specific pharmacologic interventions (i.e., perioperative dexmedetomidine infusion) are available for the non-neurosurgical patient [63]. High-quality trials on perioperative dexmedetomidine in non-neurosurgical cohorts contrast with the neurosurgical context, where such approaches require further studies owing to safety concerns [64]. A large body of high-quality evidence from general and surgical inpatient populations supports multicomponent, nonpharmacological interventions to address modifiable risks such as immobility, sensory impairment, sleep deprivation, and dehydration. Several of these approaches have been shown to reduce delirium incidence, severity, and duration in hospitalized cohorts [65–67]. Furthermore, they have been found to be cost-effective across settings, decreasing length of stay and avoiding prolonged institutionalization [68]. Despite this, a full implementation in the neurosurgical patient faces specific challenges: altered level of consciousness, focal neurologic deficits, and language impairment can limit the feasibility of standard cognitive reorientation, early mobilization protocols, and sensory re-adaptation as implemented in geriatric wards. For these reasons, most studies on neurosurgical patients are still exploratory in nature [33]. Family-centered interventions are nonpharmacological strategies that have been shown to be effective in delirium prevention in other surgical populations [69]. Tailoring these approaches for the neurosurgical needs and implementing them in wards and intensive care units may contribute to building some evidence on their effectiveness in this population.

Taken together, the broader delirium literature argues strongly for testing adapted multicomponent, environmental and family-inclusive bundles in neurosurgical settings rather than pharmacologic monotherapy alone. Careful attention should be placed on safety, feasibility, and outcome definitions tailored to neurosurgical patients.

Management

Evidence on delirium management in neurosurgical patients remains limited and heterogeneous. While the two analyzed studies provide valuable insights, both had relatively small sample sizes and were single-center, allowing us to consider them as hypothesis-generating rather than practice-changing.

For this reason, awaiting more definitive data from the neurosurgical field, several general principles from other surgical cohorts should be considered for the management of delirium. First, multicomponent, nonpharmacological interventions including orientation, sleep protection, early mobilization, sensory aids, and hydration could be adapted to neurosurgical wards with attention to neurological monitoring constraints. Indeed, they

have been shown to be linked to reduced delirium severity and consequences [65, 70]. Second, pharmacological therapy remains highly controversial. The benefits of routine use of antipsychotics should be carefully weighed against potential harms [71–73]. Conversely, α2-agonists, such as dexmedetomidine, have been shown to be effective in reducing delirium duration (and may reduce incidence in some acute care settings). However, their use in neurosurgical wards is generally not feasible, and potential risks (e.g., bradycardia, hypotension, oversedation) require careful balancing, especially in neurosurgical patients with intracranial pressure and cerebral perfusion pressure instability. Benzodiazepines remain generally discouraged outside alcohol-withdrawal delirium because of associations with delirium and sedation, especially in older or critically ill patients [74].

The management of pain is another issue in the neurosurgical patient, requiring a delicate balance: while uncontrolled pain is a powerful driver of delirium, the heavy use of opioid analgesics can equally contribute to cognitive clouding. Our review highlights that optimized, multimodal analgesia is a key, yet underinvestigated, prevention strategy in this population.

A further challenge unique to neurosurgical practice is the concern that pharmacological sedation may mask neurological deterioration, such as hematoma expansion or postoperative intracranial complications. This fear often leads to agitation undertreatment [74]. Balancing adequate symptom control with the need for frequent neurological assessment therefore remains a distinctive and unresolved dilemma in this setting.

Taken together, evidence supports a multimodal management strategy for delirium in neurosurgery that prioritizes (a) prevention and environment-oriented measures adapted to neurological monitoring, (b) avoidance of delirogenic medications where possible, and (c) selective use of pharmacologic agents (e.g., dexmedetomidine for agitated patients) within safety-driven protocols and trials.

Given neurosurgical-specific risks (focal deficits, variable arousal, intracranial dynamics), urgent needs are high-quality data that test tailored nonpharmacological bundles and evaluate the safety/efficacy of specific pharmacological interventions.

Prognostication and Risk Factors

Prognostic factors were the most studied domain, likely owing to feasibility in retrospective and database studies. The identified factors align with models describing the interplay between preexisting patient vulnerability and acute insult [67]. This is particularly relevant in the neurosurgical patient, in which diseases and interventions can become additional acute stressors on preexisting frail systems and brain networks, further compromising cerebral reserves. This is supported by the association of inflammatory and neuronal injury biomarkers (e.g., NLR, S100β) with delirium, suggesting that it manifests when a primed, vulnerable brain is subjected to a significant neuroinflammatory and metabolic hit (surgery, anesthesia, or the underlying disease process) [51, 52]. However, modifiable factors represent the most critical target for clinical intervention. Exposure to benzodiazepines, blood pressure instability, sleep disorders and poorly managed pain are iatrogenic stressors that may be mitigated through protocolized care and offer clear and actionable pathways for quality improvement. The development of population-specific tools, such as nomograms for chronic subdural hematoma and risk scores for spinal surgery, are examples of such frameworks [59, 61]. Despite the focus of this review being on the acute phase, several articles highlighted that the prognostic impact of delirium in neurosurgical patients extends far beyond, including a higher likelihood of discharge to an institutional care facility, long-term cognitive dysfunction, and reduced survival in specific populations [45, 57, 75]. The influence of delirium on end-of-life decisions in devastating brain injuries adds another layer of ethical complexity [62]. In summary, the identified risk factors for delirium provide a model for targeted prevention, while consistent links with long-term functional and cognitive outcomes convincingly support the integration of delirium prevention and management as a central component of neurocritical care and recovery pathways.

Gaps in Knowledge/Research Priorities

The gaps identified from our review are synthesized in a conceptual framework that includes a clear set of research priorities (Fig. 1). This framework delineates four primary domains, each with a critical gap and a defined research objective. In summary:

1. Diagnosis and assessment: current delirium tools are not optimized for neurosurgical patients with neurological deficits (e.g., aphasia, baseline cognitive impairment). The priority is develop and validate neuro-adapted diagnostic tools, potentially incorporating objective biomarkers.
2. Prevention: the efficacy of multicomponent, nonpharmacological prevention bundles—a cornerstone in other medical fields—remains largely unproven in neurosurgical settings. The priority is to design and test tailored prevention protocols that are feasible in neurosurgical units, accounting for neurological monitoring constraints and leveraging family involvement.

3. Management: a critical evidence gap exists for managing established delirium. The priority is to establish safe, effective treatment protocols that balance agitation control with neurological monitoring, comparing both nonpharmacological strategies and pharmacological strategies.
4. Prognosis and pathophysiology: risk factor identification has not yet translated into clinically robust prediction models, and the unique pathophysiology of delirium in the neurosurgical patient is poorly understood. The priority is to externally validate prediction models and explore biomarkers to elucidate mechanisms and enable personalized prognostication.

Strengths and Limitations

Main strengths of this study include being the first review to encompass the entire adult neurosurgical population (brain/spine, surgical/nonsurgical), enhancing real-world generalizability, and employing rigorous methodology.

Several limitations must be acknowledged. Nearly half of studies excluded patients with preexisting cognitive or psychiatric disorders, likely underestimating true delirium incidence and limiting applicability to vulnerable patients.

The significant heterogeneity in delirium assessment tools, diagnostic criteria, timing, and frequency across the included studies poses a fundamental challenge to evidence synthesis. This variability limits the comparability of incidence rates and outcomes between studies, and precludes any meaningful meta-analysis, reflecting a fundamental methodological issue that future research must address through standardization.

While the broad scope of this review across heterogeneous neurosurgical conditions may limit the depth of analysis for specific subgroups, it serves to map the current landscape and identify key research gaps, providing a foundational framework for future, more focused systematic reviews.

Furthermore, study categorization was interpretive, though unlikely to alter conclusions. Finally, limited studies from low- and middle-income countries underscores a geographic gap, highlighting the need for resource-sensitive research in high-burden regions.

Conclusions

Delirium represents a frequent and clinically relevant occurrence among adult neurosurgical patients, affecting both cranial and spinal populations. Despite an expanding evidence base, research remains fragmented and predominantly focused on risk factors rather than practical interventions. Diagnostic tools are largely nonspecific, preventive strategies are underexplored, and management protocols are lacking. Future studies should move beyond descriptive analyses to rigorously test neuro-adapted diagnostic methods, tailored prevention bundles, and standardized management frameworks.

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