



Review Article

SAFETY AND CLINICAL OUTCOMES OF INTRAVENOUS-TO-ORAL ANTIBIOTIC THERAPY FOR BRAIN ABSCESS: A SYSTEMATIC REVIEW

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ABSTRACT

Introduction: Brain abscess requires prolonged intravenous (IV) antibiotics, but early transition-to-oral-switch (IVOS) therapy may reduce hospital stay and healthcare burden. Evidence on safety, efficacy, and timing remains limited.

Methods: A systematic search of PubMed, Cochrane Central, ScienceDirect, and Taylor & Francis identified 67 records; four met inclusion criteria, including 428 patients. Data on demographics, IV and oral antibiotic regimens, therapy duration, clinical outcomes, and adverse events were extracted.

Results: Patients were predominantly male (63–83.5%). IV antibiotics included β -lactams, metronidazole, thiopenicol, aminoglycosides, and penicillin derivatives, lasting 5–28 days. Oral regimens included fluoroquinolones, amoxicillin, rifampicin, clindamycin, cotrimoxazole, and nitroimidazoles. Total antibiotic duration ranged 36–140 days. IVOS was performed early (≤ 10 days) in 57% of patients in one study and after stabilization in others. Favorable outcomes (GOS 4–5) occurred in 61–82%. Mortality ranged 12–18.1%, mainly in severe cases. No abscess recurrence was reported at six months. Adverse events, mostly mild cytopenias, occurred in 25–76%; few required therapy modification. Early IVOS was associated with shorter hospitalization and fewer surgical revisions but was not an independent predictor of outcome.

Discussion: IVOS can be safely implemented in selected patients with brain abscess, potentially reducing hospital stay and healthcare costs. However, heterogeneity in timing and patient selection highlights the need for standardized protocol. GCS at admission and comorbidities remain the most important prognostic factors.

Conclusion: IVOS appears safe and effective, with potential additional benefits from early switch. Further research is needed to determine optimal timing and patient selection.

Keywords: Antibiotics; Brain abscess; Intravenous-to-oral switch; Systematic review; Treatment outcomes

INTRODUCTION

Brain abscess is defined as an encapsulated collection of pus within the brain parenchyma and remains one of the most severe infections of the central nervous system.¹ Although advances in antimicrobial therapy, neuroimaging, and neurosurgical techniques have substantially improved outcomes since the pre-antibiotic era, morbidity and mortality remain considerable.² Contemporary incidence estimates range from 0.4 to 0.9 cases per 100,000 persons annually in Northern Europe, with some evidence suggesting an increasing trend in recent decades.^{3–5} Reported mortality rates range from 7% to 20%, and may reach up to 50% in vulnerable populations such as immunocompromised patients, while approximately 30% of survivors experience persistent neurological deficits or epilepsy.^{1,4}

Brain abscess can result from contiguous spread of ear, nose, and throat or dental infections, hematogenous dissemination from distant foci, or complications of neurosurgery and cranial trauma. The

microbiological spectrum is heterogeneous and includes streptococci, staphylococci, Gram-negative bacilli, mycobacteria, fungi, and parasitic organisms, depending on the underlying source and host factors. Advanced age, immunocompromise, and significant comorbidities have been identified as important predictors of unfavorable outcome.^{4,6,7}

Standard treatment generally consists of neurosurgical aspiration or drainage combined with prolonged high-dose intravenous (IV) antimicrobial therapy, typically for 6–8 weeks. Empiric regimens generally include broad-spectrum β -lactams in combination with agents targeting anaerobic organisms, followed by pathogen-directed therapy when microbiological data are available. The rationale for extended IV therapy is to ensure adequate antibiotic penetration across the blood–brain barrier and into the abscess cavity, particularly during the encapsulated stage. However, prolonged IV treatment is associated with several challenges, including extended hospitalization,

catheter-related complications (infection, thrombosis, malfunction), risk of hospital-acquired infections, patient discomfort, and substantial healthcare costs.^{1,8,9}

In light of these limitations, early transition to oral antimicrobial therapy has been proposed as a potential strategy to reduce treatment burden while maintaining clinical efficacy. Oral step-down therapy may facilitate earlier hospital discharge, improve patient comfort, and reduce healthcare resource utilization. Nevertheless, uncertainties remain regarding its safety, optimal timing, antibiotic selection, and appropriate patient selection criteria in the management of brain abscess. The current evidence base is limited and predominantly observational. A comprehensive synthesis of the available evidence is therefore needed to clarify the safety and clinical outcomes associated with IVOS therapy in adults with brain abscess. This review provides a focused synthesis of IVOS safety and clinical outcomes, including treatment timing, antimicrobial regimens, adverse events, and factors

associated with clinical outcomes. This systematic review aims to evaluate the safety and clinical outcomes of IVOS therapy in adult patients with brain abscess.

MATERIALS AND METHODS

This study was registered with the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD420261325129 and followed the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹⁰

Data source and search strategy

A systematic literature search was conducted from database inception to February 2026 across four electronic databases: PubMed, ScienceDirect, CENTRAL (Cochrane Central Register of Controlled Trials), and Taylor & Francis Online. The search strategy combined controlled vocabulary and free-text terms related to “brain abscess,” “intracranial abscess,” and “cerebral abscess,” together with terms describing antibiotic strategies, including “oral antibiotic,”

“intravenous-to-oral switch,” “oral step-down therapy,” “oral relay,” “intravenous antibiotic,” and “parenteral antibiotic.” The search strategy was adapted appropriately for each database.

Eligibility criteria

Studies were considered eligible if they met the following criteria: (1) adult patients aged ≥ 18 years; (2) diagnosis of brain abscess confirmed clinically and/or radiologically (CT or MRI), with or without microbiological confirmation; (3) treatment with intravenous antibiotics followed by transition to oral therapy (intravenous-to-oral switch, IVOS); and (4) observational study designs, including prospective or retrospective cohort studies, case series, or comparative or single-arm. Studies were excluded if they were reviews, conference proceedings, book chapters, commentaries, editorials, letters, abstract-only publications, or experimental studies (in vitro or in silico).

Study selection and data extraction

All records identified through the search strategy were imported into

Zotero for reference management and removal of duplicate citations. Following deduplication, two reviewers (S. and T.V.) independently screened titles and abstracts against the predefined eligibility criteria. Studies deemed potentially eligible were retrieved for full-text assessment. The same reviewers independently evaluated full-text articles to determine final inclusion. Any disagreements at any stage of the selection process were resolved through discussion, and when necessary, consultation with a third reviewer (K.E.). Data extraction was performed using a standardized, pilot-tested data extraction form developed prior to the review. One reviewer (S.) extracted data from all included studies. To ensure accuracy and completeness, a second reviewer (T.V.) independently verified the extracted data by reviewing half of the included studies. Any discrepancies were resolved through discussion and consensus. The following data items were extracted: first author, year of publication, country of study, study design, sample size, patient characteristics (mean age and sex distribution),

details of intravenous and oral antibiotic regimens, timing of transition from intravenous to oral therapy, duration of intravenous therapy, total duration of antibiotic treatment, and reported clinical outcomes.

Risk of bias assessment

The risk of bias of eligible cohort studies was assessed using the Newcastle-Ottawa Scale (NOS). Risk of bias was assessed independently by two reviewers (S. and T.V.), with disagreements resolved through discussion and consultation with a third reviewer (K.E.). The NOS evaluates observational cohort studies across three domains: selection of study groups, comparability of groups, and ascertainment of exposure or outcomes, as appropriate to the study design. The case series was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Series.

Outcome measures

The primary outcomes were functional outcome, mortality, abscess recurrence, and

antibiotic-related adverse events. Functional outcome was defined as a favorable neurological status corresponding to a Glasgow Outcome Scale (GOS) score of 4–5 or as defined by individual studies. Mortality was defined as all-cause death during hospitalization or at the longest reported follow-up. Abscess recurrence was defined as clinically or radiologically confirmed reappearance of infection during follow-up. Antibiotic-related adverse events included complications attributed to antimicrobial therapy that required monitoring, treatment modification, or discontinuation. Secondary outcomes included duration of hospitalization, total antibiotic treatment duration (including intravenous and oral phases), timing of intravenous-to-oral switch (early versus delayed, as defined by each study), need for surgical revision, and treatment modification due to adverse events.

Statistical analyses

Given the heterogeneity in study designs, patient populations, antibiotic regimens, timing of IVOS,

and reported outcomes, a quantitative meta-analysis was not performed. Data were therefore synthesized narratively and summarized descriptively across included studies. Outcomes were extracted and reported as presented in the original studies without additional statistical recalculation or pooling.

DISCUSSION

Principal findings

The database search identified 67 records, of which 64 remained after removal of three duplicates. Following title and abstract screening, 13 reports were sought for retrieval; 10 full-text reports were assessed for eligibility, and four studies ultimately met the predefined

inclusion criteria (Figure 1). These four single-center observational studies comprised 428 adult patients with brain abscess or related intracranial bacterial suppurations and were conducted in France, South Africa, and Greece.^{2,11–13} The included studies consisted of three retrospective cohort studies and one case series, with sample sizes ranging from 8 to 190 patients. The proportion of patients undergoing IVOS ranged from 44.4% to 100%, while intravenous treatment before oral transition ranged from 5 to 28 days. Oral regimens included fluoroquinolones, amoxicillin, rifampicin, clindamycin, nitroimidazoles, cotrimoxazole, and quinolones.

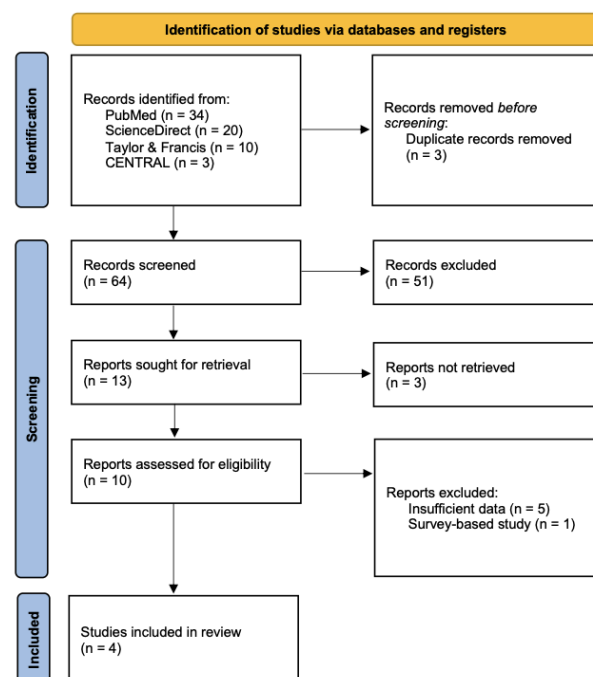


Figure 1. PRISMA flow diagram

The included populations were heterogeneous with respect to clinical presentation, underlying conditions, neurological status, and management. The South African cohort included 121 surgically treated patients, whereas the Greek case series included only eight highly selected patients with relatively small abscesses and preserved neurological status. The Nantes cohort included 109 patients, of whom 48 underwent oral antibiotic switch, while the Paris cohort included 190 patients, with 172 undergoing IVOS. Detailed characteristics of the included studies are presented in Table 1.

case series had generally adequate reporting but was limited by its very small sample size, non-comparative design, and highly selected patient population. Overall, the evidence base was limited by the observational nature of the included studies and the potential for selection and confounding biases. Detailed risk-of-bias assessments are presented in Supplementary Table 1 and 2.

Risk of bias was assessed using the Newcastle–Ottawa Scale for the three cohort studies and the Joanna Briggs Institute Critical Appraisal Checklist for Case Series for the Greek study. The three cohort studies demonstrated moderate-to-high methodological quality, with the two French cohorts showing higher methodological quality than the South African cohort. The Greek

Table 1. Characteristics of Included Studies

Author (year), Country	Design	Sample characteristics				IV antibiotics		Oral antibiotics		Total Therapy Duration (days)	Key Findings
		Male (n [%])	Age	IV (n)	Switch to oral (n)	Types	Duration (days)	Types	Duration (days)		
Skoutelis et al. (2000), Greece	Case series	6 [75%]	N/A	8	8	Ceftriaxone Penicillin G Metronidazole	6–12	Ciprofloxacin Amoxicillin Metronidazole	N/A	112–140	All patients cured; no severe adverse events; feasibility of early switch in carefully selected mild cases
Sichizya et al. (2005), South Africa	Retrospective cohort	101 [83.5%]	Mean 33	121	121	Benzylpenicillin Chloramphenicol Ceftriaxone Cloxacillin Metronidazole	15–19	Flucloxacillin Cotrimoxazole	28–42	36–40	Mortality 13%; GCS at admission strongest prognostic factor; oral continuation after IV was standard practice
Asquier-Khati et al. (2020), Nantes, France	Retrospective cohort	80 [74.1%]	N/A	109	48	β -lactams Nitroimidazoles Thiophenicol Aminoglycosides	12–28	Fluoroquinolones Rifampicin Clindamycin Nitroimidazoles Cotrimoxazole	N/A	45–95	Oral switch independently associated with favorable neurological outcome; no increased risk in patients without initial neurological severity
Besnard et al. (2025), Paris, France	Retrospective cohort	120 [63%]	Median 51	190	172	β -lactams Thiophenicol Amoxicillin Rifampicin Fluoroquinolones	5–15	Amoxicillin Rifampicin Thiophenicol Quinolone	N/A	60–88	Early IVOS not associated with worse neurological outcome; no recurrence at 6 months; GCS strongest prognostic factor

Timing of IVOS and patient selection

The timing of IVOS varied considerably across the included studies, reflecting differences in patient selection and clinical management. In the Nantes cohort, oral therapy was initiated after a median of 19 days of intravenous treatment, whereas in the Paris cohort, IVOS occurred earlier, after a median of 9 days; early IVOS was defined as a transition within 10 days. In the South African cohort, transition to oral therapy was performed after clinical and biochemical stabilization and satisfactory radiological findings. The Greek case series reported the shortest intravenous courses, ranging from 6 to 12 days, followed by prolonged oral therapy. These findings demonstrate that IVOS has been implemented across a broad range of treatment durations rather than according to a uniform time threshold.

Importantly, the apparent association between earlier IVOS and favorable outcomes should be interpreted cautiously. In the Paris cohort, early IVOS (≤ 10 days) was associated with favorable outcomes in univariate analysis ($p = 0.002$), but this association was no longer significant after multivariable adjustment ($p = 0.564$). Similarly, in the Nantes cohort, oral antibiotic therapy was associated with a more favorable neurological outcome (OR 0.3; 95% CI 0.1–0.7; $p = 0.008$); however, baseline GCS and comorbidities were also important prognostic factors. Oral switch was not associated with unfavorable evolution among patients without initial neurological severity, suggesting that patient selection may have contributed to the observed outcomes.^{2,11} Thus, the favorable outcomes observed with earlier IVOS should not be interpreted as evidence that earlier transition itself improves neurological prognosis.

These observations are consistent with previous literature suggesting that IVOS is generally considered in clinically stable patients with adequate source control and without major contraindications to oral therapy. Lauda-Maillen et al. reported the feasibility of early oral antibiotic transition in patients with brain abscesses and empyema, while the 2023 narrative review by Bodilsen and Nielsen emphasized that early transition has primarily been considered for patients with mild or uncomplicated disease and that its overall benefit–risk balance remained unresolved.^{14,1} The 2024 ESCMID guideline similarly recommended 6–8 weeks of antimicrobial therapy but did not provide a recommendation for early transition to oral antimicrobials because of insufficient evidence.¹⁵ These recommendations provide important context for interpreting the observational findings in the present review.

The rationale for patient selection is further supported by studies of brain abscess prognosis. Baseline neurological status, particularly the admission GCS, has been associated with clinical outcomes in several cohorts, including the South African and Nantes studies.^{2,12} Accordingly, the decision to transition from intravenous to oral therapy should be considered in the context of clinical stability, neurological status, radiological response, microbiological information, source control, and the suitability of the selected oral regimen rather than on the basis of treatment duration alone. Overall, the available evidence supports the feasibility of IVOS in carefully selected patients, but does not establish an optimal time point for transition or demonstrate that earlier switching independently improves outcomes.

Clinical outcomes and mortality

Follow-up duration varied across the included studies. Asquier-Khati et al. assessed neurological outcomes primarily at 3 months, with extended follow-up at 12 months, reporting mortality rates of 12% and 18.1%,

respectively.² Besnard et al. performed structured follow-up for up to 6 months using the Extended Glasgow Outcome Scale (GOSE) and reported a 6-month mortality of 4%.¹¹ The South African cohort reported outpatient follow-up extending to at least 24 months, while the Greek case series documented follow-up periods ranging from 4 to 48 months.^{12,13}

Across the included cohorts, most survivors achieved favorable functional outcomes. In the Nantes cohort, 82.1% of patients had favorable neurological outcomes at 3 months, while in the South African cohort, 61% achieved GOS 5 and 23% achieved GOS 4.^{2,12} Poorer outcomes were associated with greater disease severity at presentation, particularly lower admission GCS scores. In the South African cohort, admission GCS was identified as the strongest prognostic factor, with most deaths occurring among patients presenting with severe neurological impairment.¹² These findings emphasize the importance of baseline neurological

status when interpreting outcomes following IVOS.

Mortality varied across the included studies, ranging from 4% to 18.1% depending on the study population and follow-up period. The Nantes cohort reported mortality of 12% at 3 months and 18.1% at 12 months, while the South African cohort reported 13% mortality during long-term follow-up.^{2,12} The Paris cohort reported a lower 6-month mortality of 4%.¹¹ Differences in mortality should be interpreted in the context of variations in baseline disease severity, patient selection, management strategies, and follow-up duration rather than being attributed directly to the route or timing of antibiotic therapy.

The association between IVOS and neurological outcomes was also inconsistent after adjustment for potential confounders. In the Nantes cohort, oral antibiotic therapy was associated with a favorable neurological outcome (OR 0.3; 95% CI 0.1–0.7; $p = 0.008$).² In the Paris cohort, patients with favorable outcomes underwent IVOS earlier

than those with unfavorable outcomes (median 8 vs. 13 days; $p = 0.035$), and early IVOS (≤ 10 days) was associated with favorable outcomes in univariate analysis ($p = 0.002$). However, this association was no longer significant after multivariable adjustment ($p = 0.564$).¹¹ These findings suggest that the observed relationship between earlier IVOS and favorable neurological outcomes may be influenced by baseline patient characteristics and clinical selection rather than representing an independent treatment effect.

Hospitalization outcomes also appeared to be related to the timing and duration of antibiotic therapy. In the Nantes cohort, longer total antibiotic duration, prolonged intravenous therapy, and delayed oral switch were associated with longer hospitalization, with total treatment duration remaining significant in multivariable analysis (adjusted OR 4.2; 95% CI 1.3–14.3; $p = 0.017$).² Although these findings suggest that earlier transition may facilitate shorter hospitalization, the

observational design precludes establishing a causal relationship.

Overall, the available evidence suggests that favorable neurological recovery is achievable following IVOS in appropriately selected patients, but baseline disease severity appears to be a more consistent determinant of outcome than the timing of oral transition itself. The available studies therefore support IVOS as a potentially feasible treatment strategy in selected patients, while the optimal timing and its independent effect on neurological outcomes remain uncertain.

Recurrence, hospitalization, and safety

Recurrence was infrequently reported. No recurrence was documented during 6 months of follow-up in the Paris cohort, while the Greek case series reported complete clinical and radiological resolution without relapse.^{11,13} The South African study provided long-term follow-up but did not report recurrence as a specific outcome.¹² Given the limited and

inconsistent reporting of recurrence across studies, the available evidence is insufficient to determine whether IVOS influences the risk of relapse.

In the Nantes cohort, longer total antibiotic duration, prolonged intravenous therapy, and delayed oral switch were associated with longer hospitalization, with total treatment duration remaining significant after multivariable adjustment (adjusted OR 4.2; 95% CI, 1.3–14.3; $p = 0.017$).² However, because treatment duration and timing of IVOS may themselves be influenced by disease severity and clinical decision-making, this association should not be interpreted as evidence that early IVOS directly reduces hospitalization.

Antimicrobial-related adverse events were reported in 25%–76% of patients in the larger cohorts, predominantly thiophenicol-associated reversible cytopenia. In the Nantes cohort, adverse drug reactions led to antibiotic discontinuation in 25% of patients, while in the Paris cohort, adverse effects were reported in 76%

and treatment modification was required in 53%.^{2,11} These findings suggest that adverse-event risk may be influenced substantially by the antimicrobial regimen itself rather than by the intravenous or oral route alone. However, the heterogeneity of antimicrobial regimens and the observational nature of the available evidence limit direct comparisons of safety between treatment strategies.

Strengths and limitations

This systematic review has several strengths. First, it specifically synthesized the available evidence on intravenous-to-oral antibiotic switch (IVOS) therapy in adult patients with brain abscess and related intracranial bacterial suppurations, with particular attention to treatment timing, antimicrobial regimens, clinical outcomes, recurrence, hospitalization, and adverse events. Second, a structured search strategy was conducted across multiple databases using predefined eligibility criteria, and study selection, data extraction, and risk-of-bias assessment followed prespecified methodological procedures. Third, the review provides a detailed

descriptive synthesis of the available evidence despite substantial variation in treatment strategies and outcome reporting.

Several limitations should be acknowledged. All included studies were non-randomized observational studies, comprising retrospective cohorts and one case series, which limits causal inference and increases the risk of confounding and selection bias. No randomized controlled trials were identified among the studies meeting the predefined eligibility criteria. Considerable heterogeneity was also observed in patient characteristics, underlying disease severity, antimicrobial regimens, duration of intravenous therapy, timing of IVOS, and outcome definitions. In addition, some studies included highly selected populations, limiting the generalizability of their findings. Because of this clinical and methodological heterogeneity and insufficient comparable data, quantitative meta-analysis was not feasible. Recurrence, long-term outcomes, and adverse events were also inconsistently reported across studies. Finally, the relatively small

number of included studies and patients limits the precision of the available estimates and precludes definitive conclusions regarding the optimal timing, comparative safety, or effectiveness of IVOS therapy.

CONCLUSION

This systematic review suggests that intravenous-to-oral antibiotic switch (IVOS) therapy may be a feasible treatment strategy for carefully selected, clinically stable adult patients with brain abscess. Across the included observational studies, IVOS was not associated with an apparent increase in mortality, and recurrence was infrequently reported; however, the limited and heterogeneous reporting of safety outcomes precludes definitive conclusions regarding comparative safety. Earlier IVOS was associated with shorter hospitalization and fewer surgical re-interventions in individual cohorts, but these associations were not consistently independent after adjustment and should not be interpreted as causal effects.

Nevertheless, the available evidence is limited by the absence of randomized controlled trials, substantial heterogeneity in treatment protocols and patient populations, and inconsistent reporting of outcomes. Current evidence supports consideration of IVOS in appropriately selected patients, but standardized criteria for patient selection and timing of transition remain undefined. Prospective studies and randomized controlled

trials are warranted to establish optimal IVOS protocols and clarify their effects on clinical outcomes and safety.

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Supplementary Table 1. Newcastle–Ottawa Scale (NOS) Assessment of Included Cohort Studies

	Selection	Comparability	Outcome	Overall Star Rating
Sichizya et al. (2005)	★★★★	★★	★★	8
Asquier-Khati et al. (2020)	★★★★	★★	★★	8
Besnard et al. (2025)	★★★	★	★★	6

Supplementary Table 2. JBI Critical Appraisal Checklist for Case Series

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Score
Skouelis et al. (2000)	Y	Y	Y	U	U	Y	Y	Y	Y	U	6/10