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Diagnostic Stewardship and WHO AWaRe Antibiotic Exposure in Intracranial Suppurative Infections: A 10-Year Cohort from West Africa

Dr. Landry Teti[1]; Dr. Yao Bernard Fionko[2]; Dr. Konan Serge Yao[3]; Dr. Adama Kouadio[4]; Dr. Adama Simaga[5]; Adéréhime Haidara[6]

[1;2;3;6]MD, Department of Neurosurgery, Bouaké Teaching Hospital, Bouaké, Côte d'Ivoire.
[4;5]Interneship, Department of Neurosurgery, Bouaké Teaching Hospital, Bouaké, Côte d'Ivoire.

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Abstract

- *Background:*

In sub-Saharan Africa, where mortality attributable to antimicrobial resistance is the highest worldwide and only 1% of laboratories perform bacteriology, the quality of antibiotic therapy for intracranial suppurative infections has never been described. We hypothesised that the principal stewardship failure in such settings lies not in antibiotic choice but in the production of the microbiological information required to adapt it.

- *Methods:*

Single-centre observational study of 150 consecutive admissions (148 patients) managed between 2016 and 2026 at Bouaké Teaching Hospital, Côte d'Ivoire. We built a five-step microbiological cascade of care, classified every regimen by WHO AWaRe category and by a declared spectral coverage index, and analysed spectrum-pathogen concordance in both directions. Determinants were modelled with Firth penalised logistic regression using profile-likelihood intervals, bootstrap internal validation, and eleven sensitivity analyses.

- *Findings:*

Sampling occurred in 77.3% of admissions, culture was positive in 33.3%, and documented adaptation in 22.7% (95% CI 16.7-30.0). At least one Watch antibiotic featured in 92.7% of regimens; no Reserve antibiotic was used. Vancomycin was prescribed three times, and antipseudomonal coverage nineteen times, as often as the corresponding pathogens were isolated; conversely only 9 of 17 documented *S. aureus* were covered, all eight failures occurring in community-acquired disease. Access to sampling depended almost exclusively on surgery (OR 5.61; 2.22-14.56). No trend emerged over ten years, and unsampled patients received the longest courses (7.15 vs 6.35 weeks; p = 0.005, Kruskal-Wallis across the three groups).

- *Interpretation:*

Spectrum breadth appeared to reflect clinical uncertainty rather than documented ecology, and did so asymmetrically. Our findings support the hypothesis that strengthening diagnostic stewardship may represent a foundational component of antimicrobial stewardship in neurosurgical infections in resource-limited settings. The analytical framework we propose requires multicentre validation.

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Keywords: *Diagnostic Stewardship; Antimicrobial Stewardship; Brain Abscess; Subdural Empyema; WHO AWaRe; Antimicrobial Resistance; Neurosurgery; Sub-Saharan Africa.*

I. INTRODUCTION

Intracranial suppurative infections (brain abscess, subdural or extradural empyema, ventriculitis) are neurosurgical emergencies. Treatment combines evacuation of the focus with four to eight weeks of parenteral antibiotics. In Europe, mortality has fallen by more than half over three decades. This is attributed to imaging, standardisation of the surgical procedure and the precision of microbiology, which allows the spectrum to be narrowed and the duration adjusted [1,14–17]. The 2024 ESCMID guideline formalises this logic: it differentiates empirical regimens according to the mechanism of infection and expects the organism to guide what follows [1].

This model assumes that an organism will be identified. In sub-Saharan Africa, this is rarely the case. Of 53,770 laboratories recorded in fourteen countries, only 675 (1%) were responsible for bacteriology, and at least 14% of them could not perform antibiotic susceptibility testing [2]. The cost of blood culture, often paid by the patient, adds to the obstacles [18]. In West Africa, mortality attributable to resistance is the highest in the world: 27.3 deaths per 100,000 population [19–20]. The African Union places access to diagnosis among its priorities [21]. Point-prevalence surveys there describe empirical prescribing in more than 95% of cases, and up to half of antibiotics belong to the Watch category [3–8].

Intracranial suppuration poses a particular problem. Pus is accessible only at the time of surgery, and only once. Prior antibiotic therapy compromises culture, and a good part of the flora involved (anaerobes, fastidious bacteria) escapes conventional aerobic culture [22–23]. In pneumonia or bacteraemia, a new sample can be taken. Here, the microbiological quality of the record is determined on a single occasion, and that occasion itself depends on a surgical decision. This condition therefore illustrates well diagnostic stewardship: the set of decisions that determine whether microbiological information will or will not be produced, and not only how it is used [9–13].

➢ *Scientific Gap*

The WHO AWaRe classification [24–28] has been applied in internal medicine, paediatrics and general surgery. Regional surveys describe antibiotic exposure at the scale of entire hospitals. To our knowledge, no study has followed the complete chain from sampling to treatment adaptation in a neurosurgical infection in Africa, or compared, molecule by molecule, the prescribed spectrum with the documented ecology in the same patients.

➢ *Hypothesis*

Where resources are lacking, the main failing of stewardship lies not in the choice of molecules but in the production of the microbiological information that would allow them to be adapted. Without this information, the breadth of the spectrum would reflect clinical uncertainty more than documented ecology.

➢ *Objectives*

The primary objective was to quantify each step of the chain, from sampling to treatment adaptation, and to identify the step where information is lost. The secondary objectives were: (i) to describe antibiotic exposure according to AWaRe and to spectrum breadth; (ii) to compare, in both directions, the prescribed coverage and the documented ecology; (iii) to look for determinants of access to microbiology and for change over ten years. The relationship between microbiological status and clinical outcomes, and avoidable exposure, are presented as exploratory analyses.

II. METHODS

➢ *Setting and Population*

The study was conducted in the neurosurgery department of Bouaké Teaching Hospital, a tertiary hospital for central and northern Côte d'Ivoire. The laboratory performs aerobic culture on standard media and agar diffusion susceptibility testing. It has no anaerobic culture, mass spectrometry, nucleic acid amplification or automated blood culture system. During the study period, there was no antibiotic stewardship programme, no written protocol for empirical antibiotic therapy and no antibiotic committee.

We included all consecutive admissions for intracranial suppuration from January 2016 to January 2026: brain abscess, subdural or extradural empyema, ventriculitis, pre-suppurative cerebritis, and scalp suppuration with skull involvement or continuity. Admissions were identified from the department register, operative reports and hospitalisation records. Diagnosis was based on a compatible clinical picture and cross-sectional imaging. No exclusion criteria were applied. Patient flow is presented at the start of the results.

The unit of analysis is the admission. Two pairs of admissions involved the same patients, admitted for distinct episodes. We kept them separate; a sensitivity analysis excludes them.

The data come from a structured database of 117 variables, built from primary sources. Microbiological and therapeutic coding was checked admission by admission against the verbatim fields kept in the database. The variable dictionary (definition, coding, source, possible values, handling of missing data) and the versioned correction log form supplement S2.

➢ *Microbiological Cascade*

We drew inspiration from the care cascades used in public health, notably for HIV [29]. Our microbiological cascade has five steps: (1) admission included; (2) pus

sample taken, by whatever means; (3) positive culture; (4) susceptibility test performed; (5) antibiotic therapy documented as adapted to the susceptibility test. Each step is expressed as a proportion of the entire cohort, which makes the cumulative loss visible, then as a proportion of the previous step, which identifies the failing step. The 95% confidence intervals are Wilson intervals [30]. Figure 1 links this cascade to antibiotic exposure and to selection pressure.

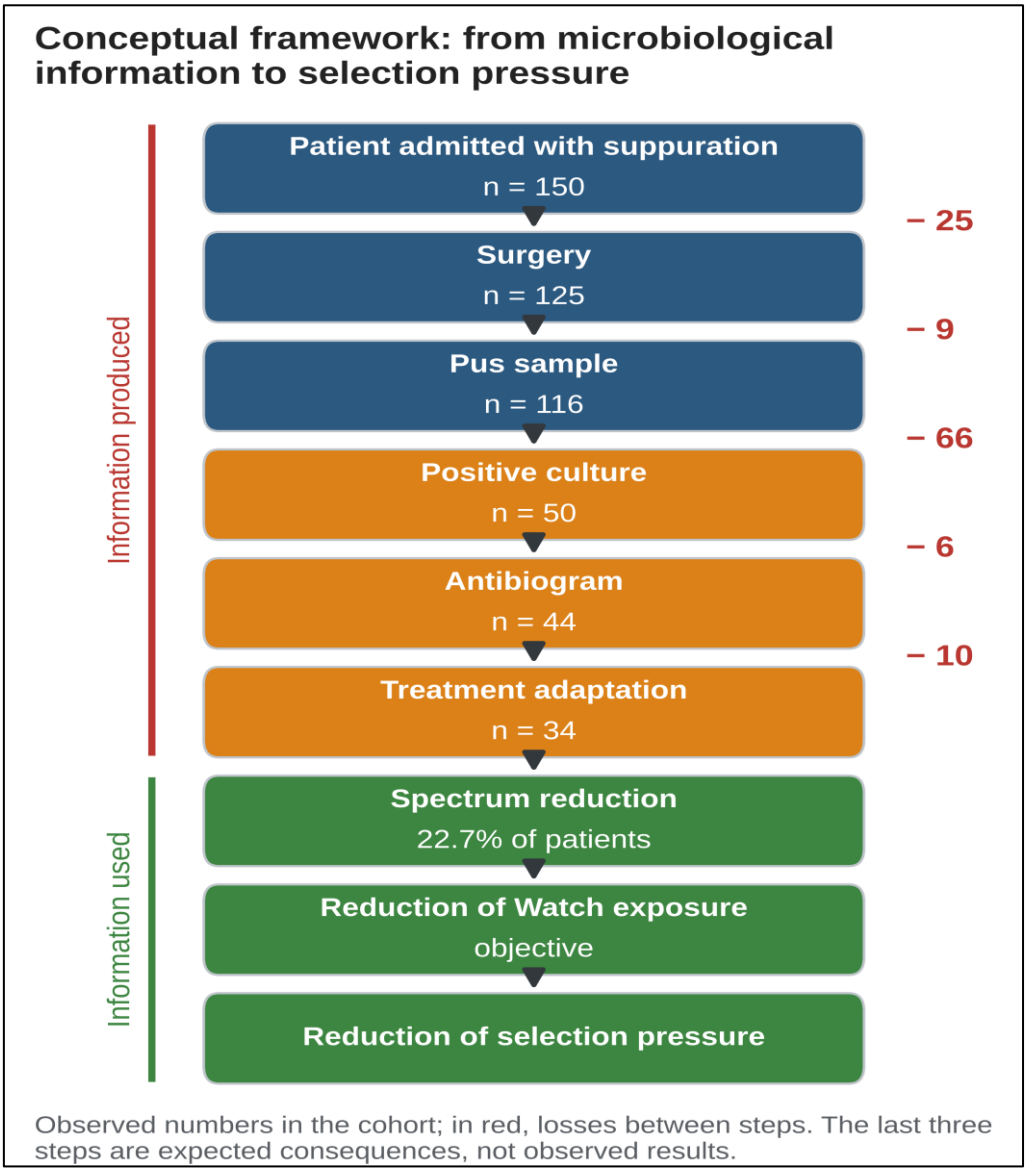


Fig 1 Conceptual Framework: From Microbiological Information to Selection Pressure

Linear chain running from admission to reduction of selection pressure, with the numbers observed at each step and the corresponding losses. The first six steps are observed in the cohort; the last three are expected consequences and not results. The side bar distinguishes the steps that produce information from those that use it.

These five steps are not merely administrative. Each corresponds to a biologically identified point of loss. Access to pus depends on a procedure. Culture yield suffers from prior antibiotic therapy and from the absence of anaerobic culture. The susceptibility test requires an exploitable identification. Adaptation requires that the result return to the record in time. The cascade therefore reads distinct mechanisms, each of which calls for a different intervention.

We present it as a methodological proposal, not as a validated instrument: it rests on a single centre and on our own data, and its transposition requires multicentre validation. We deliberately gave it neither an acronym nor a brand name.

➢ *AWaRe Classification and Spectrum Measurement*

Each molecule was classified according to the 2023 WHO AWaRe classification [24]; no Reserve molecule was found. Exposure is described as the proportion of patients exposed to each molecule, as the proportion of molecule-prescriptions by category, and as Watch exposure intensity per regimen.

To measure spectrum breadth independently of the AWaRe category, we defined a spectrum coverage index (SCI). It counts, from 0 to 6, the pathogen classes that a regimen theoretically covers: streptococci, methicillin-

susceptible *Staphylococcus aureus*, methicillin-resistant staphylococci, Enterobacterales, *Pseudomonas aeruginosa* and anaerobes. The assignment matrix is given in supplement S3; the molecules and their classes are recalled in the results. The index is inspired by published spectrum indices [31], but its rules were fixed a priori. It does not measure local resistance ecology, for which we have no data, and will need to be validated before any comparative use.

➢ *Spectrum–Pathogen Concordance*

We compared coverage and ecology in both directions. For excess coverage, we related, for each pathogen class, the frequency of patients receiving active coverage to the frequency of patients in whom the corresponding pathogen had been isolated. This ratio calls for caution: its denominator is underestimated because of the documentation deficit, and it has no meaning for anaerobes, whose culture is impossible here. For missing coverage, we checked, for each of the 50 isolates, whether the prescribed regimen theoretically covered the isolated organism. Excess spectrum was measured by the number of classes covered but not needed.

➢ *Antibiotic Exposure and Avoidable Exposure*

We approximated the exposure burden by the product of the prescribed duration (in weeks), of seven (days per week) and of the number of molecules. It is expressed as cumulative molecule-days, an approximation of days of therapy [32]. We did not use defined daily doses: they lose validity when dosing departs from standard doses, which is the rule in neuro-infectiology, and they require knowing the quantities dispensed, which we do not.

We defined three scenarios of avoidable exposure post hoc, presented as illustrative and not as effect estimates: (1) de-escalation to targeted monotherapy on day seven in documented patients; (2) alignment of the duration in patients not sampled with the mean duration in culture-negative patients; (3) replacement of ceftazidime with a non-antipseudomonal third-generation cephalosporin in community-acquired forms. Cost is given in parametric form, in the absence of hospital accounting data.

➢ *Statistical Analysis*

Categorical variables are described as numbers and percentages, with the Wilson interval; quantitative variables as median and interquartile range. We examined the shape of distributions on plots. The variables of interest departed from normality or rested on small numbers: we therefore used non-parametric tests systematically. Proportions are compared by the chi-square or Fisher exact test (with Cramér's V), and distributions by Kruskal-Wallis or Mann-Whitney (with epsilon squared).

For multivariable models, we used Firth penalised logistic regression [33], which corrects separation bias and small-sample bias [34]. Intervals come from the profile penalised likelihood, and p-values from the penalised likelihood ratio test.

Two models were specified a priori: whether a sample was taken in the whole cohort, and culture positivity in sampled patients only. Variables were chosen on clinical grounds, without automatic selection. To avoid overfitting and collinearity, we excluded: therapeutic strategy (redundant with surgery), type of suppuration and topography (linked to size and origin), and duration of antibiotic therapy (subsequent to the exposure studied). There were 19.3 events per variable in the first model and 7.8 in the second, which we therefore present as exploratory. Figure 2 shows, as a directed acyclic graph, the assumptions that guided these choices. It serves to make them transparent; it is not a causal identification graph, as we estimate no causal effect.

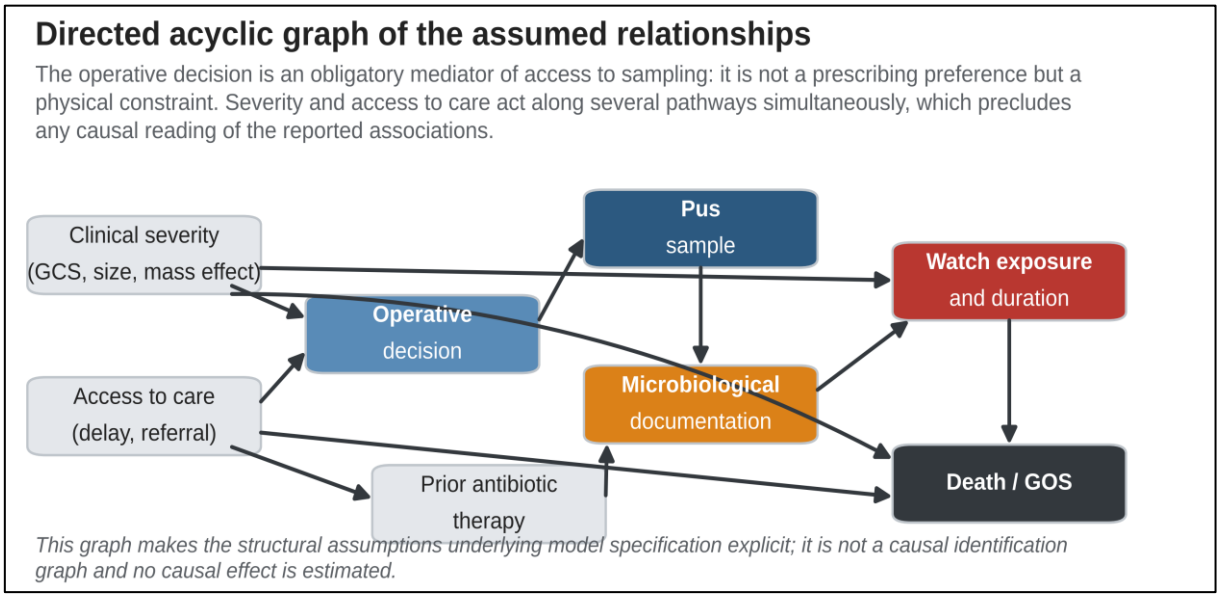


Fig 2 Directed Acyclic Graph of the Assumed Relationships.

The graph makes explicit the structural assumptions used to specify the models: the operative decision is an obligatory mediator of access to sampling, whereas severity and access to care act simultaneously along several paths. It is a tool for transparency of assumptions and not a causal identification graph; no causal effect is estimated in this work.

We internally validated both models by non-parametric bootstrap (2,000 resamples). We report the percentile intervals of the odds ratios, the stability of the sign of each coefficient and the frequency with which each variable had the largest effect. We report neither calibration slope nor intercept, nor Brier score, nor optimism correction: the models serve to estimate descriptive associations and propose no prognostic or predictive tool. These indicators would therefore be meaningless.

We assessed the trend over time by Firth regression on the year of admission (continuous variable), by the Cochran-Armitage trend test and, for the spectrum coverage index, by Spearman correlation. We carried out a post hoc power analysis for mortality, the study being exhaustive over the period.

We imputed no data; missing proportions are reported in the results. Four microbiological variables are missing by construction, downstream of a step not passed. Their absence is structural and informative, which excludes imputation.

The significance threshold is 0.05 (two-sided), without correction for multiplicity. The analyses are descriptive and exploratory, and an overall correction across analyses of different natures would have made illegible estimates whose interest lies in magnitude and precision. We give priority to effect sizes and confidence intervals, and flag isolated associations as hypothesis-generating.

Analyses were performed with Python 3.12.3 (NumPy 2.4.4, SciPy 1.17.1, pandas 3.0.2, statsmodels 0.14.6, Matplotlib 3.10.8). The code is given in supplement S7 and in the associated repository. No analysis protocol had been registered before the analyses, which is a limitation in transparency. The analysis plan was nevertheless frozen before the figures were produced.

We carried out eleven sensitivity analyses (supplementary table S6-1): restriction to operated patients; exclusion of scalp suppurations; exclusion of duplicate admissions; prospective-retrospective comparison; extreme assumption of a positive culture in all non-sampled patients; restriction to adults; restriction to post-operative forms; bootstrap of the terminal step; recalculation of the SCI without gentamicin; recalculation of concordance considering every *S. aureus* as methicillin-resistant; recalculation of AWaRe proportions in molecule-prescriptions.

- *Ethical Considerations, Public Involvement and Transparency*

The study was conducted in accordance with the Declaration of Helsinki. The protocol was approved by the Institutional Ethics Committee of Bouaké Teaching Hospital (opinion no. CEI/CHU-BKE/139/2026), which granted a waiver of individual consent (retrospective study, routine records anonymised before analysis). No patient or member of the public took part in the design of the study, owing to the retrospective data collection. The results will be fed back to the department and to the hospital management.

The report follows the STROBE checklist [35], supplemented by the RECORD items [36] applicable to routinely collected health data (supplement S1). The anonymised individual data, the complete analysis code, the dependency file and a description file allowing reproduction will be deposited in a public repository with a persistent identifier: code under MIT licence, data under CC BY 4.0 licence [repository and DOI to be created before submission].

III. RESULTS

- *Population*

The cohort comprised 150 admissions for 148 patients. Median age was 25.5 years (IQR 14.0-50.0), with a majority of men (69.3%). Patients lived in a rural area in 52.0% of cases and had been referred in 51.3%. The median time between first symptoms and admission was 19 days. Isolated brain abscess accounted for 48.0% of forms. The origin was community-acquired in 60.0% of cases, post-traumatic in 22.0% and post-operative in 18.0%. Surgery was performed in 125 patients (83.3%). In-hospital mortality was 10.7% (16 deaths). Table 1 gives the details; patient flow is shown in Figure 3.

Table 1 Characteristics of the Cohort (150 Admissions, 148 Patients)

Characteristic	Value
Age, median (IQR) — years	25.5 (14.0-50.0)
Male sex, n (%)	104 (69.3)
Rural residence, n (%)	78 (52.0)
Referred patient, n (%)	77 (51.3)
Symptom-to-admission delay, median (IQR) — days	19 (15.0-24.8)
Glasgow score at admission, median	13
Glasgow score < 9, n (%)	19 (12.7)
Documented immunosuppression, n (%)	13 (8.7)
Type of suppuration, n (%)	
Isolated brain abscess	72 (48.0)
Extradural empyema	20 (13.3)
Subdural empyema	17 (11.3)
Brain abscess + ventriculitis	12 (8.0)
Scalp suppuration	9 (6.0)
Isolated ventriculitis	4 (2.7)
Other associated forms	16 (10.7)
Origin, n (%)	
Community-acquired	90 (60.0)
Post-traumatic	33 (22.0)
Post-operative	27 (18.0)
Portal of entry, n (%)	
Post-traumatic	33 (22.0)
Sinus / ENT	30 (20.0)
Post-operative	26 (17.3)
Cryptogenic	21 (14.0)
Otogenic	12 (8.0)
Dental / stomatological	11 (7.3)
Cutaneous (scalp)	10 (6.7)
Haematogenous	7 (4.7)
Surgical treatment, n (%)	125 (83.3)
Admission-to-surgery delay, median — days	2
Corticosteroid therapy, n (%)	36 (24.0)
Infectious disease opinion requested, n (%)	25 (16.7)
Length of stay, median — days	11
In-hospital death, n (%)	16 (10.7)

- IQR: interquartile range. Post-operative origin: 27 admissions; post-operative portal of entry: 26 admissions, one case of post-operative origin having a portal of entry that was not formally documented.

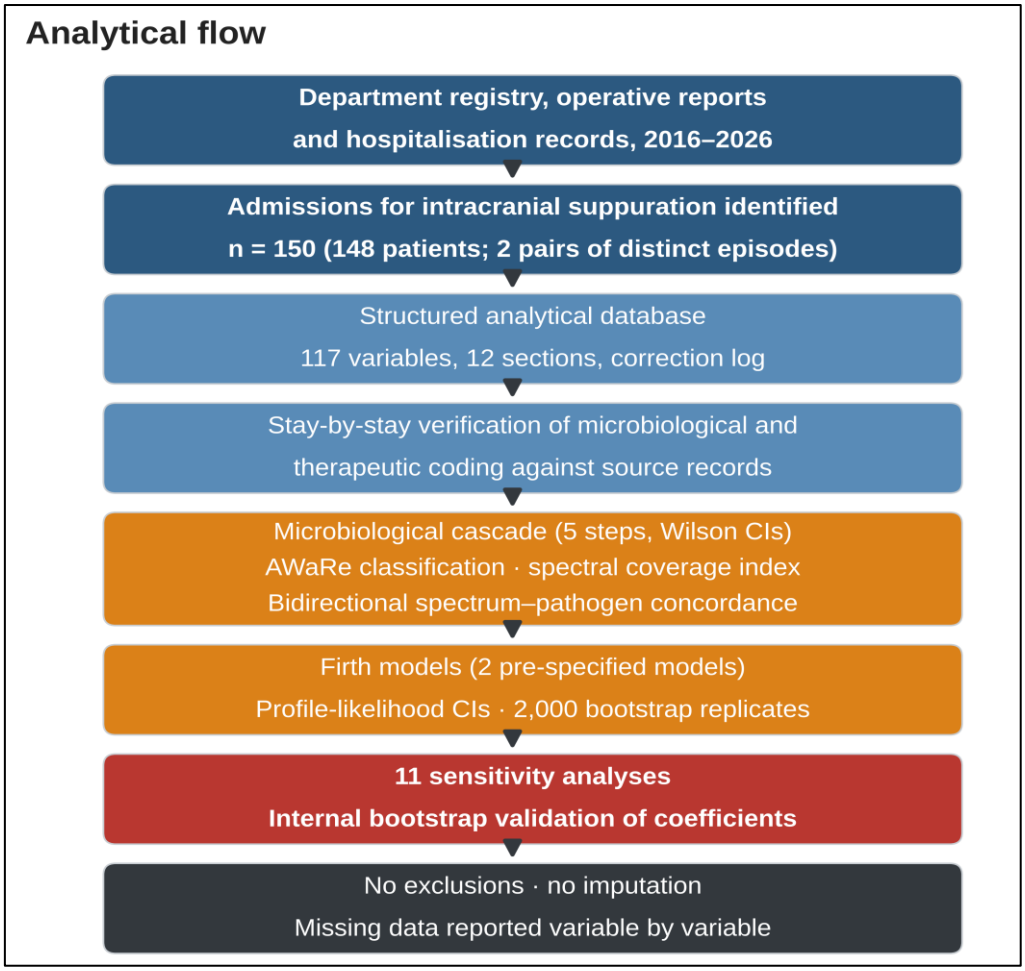


Fig 3 Analytical Flow

Sequence of steps, from identification of source records to internal validation, in the format recommended by STROBE. No exclusion or imputation was performed; missing data are reported variable by variable.

➢ *The Cascade Breaks Upstream of Prescription*

Of 150 admissions, a pus sample was taken in 116 (77.3%; 95% CI 70.0-83.3), a culture was positive in 50 (33.3%; 26.3-41.2), a susceptibility test was performed in 44 (29.3%; 22.6-37.1) and documented adaptation of treatment occurred in 34 (22.7%; 16.7-30.0). Fewer than one patient in four therefore received antibiotic therapy guided by a microbiological result (Table 2, Figure 4).

Table 2 Microbiological Cascade

Step	n	% of cohort (95% CI)	% of previous step (95% CI)
Admissions included	150	100	—
Pus sample taken	116	77.3 (70.0-83.3)	77.3 (70.0-83.3)
Positive culture	50	33.3 (26.3-41.2)	43.1 (34.5-52.2)
Susceptibility test performed	44	29.3 (22.6-37.1)	88.0 (76.2-94.4)
Documented adapted antibiotic therapy	34	22.7 (16.7-30.0)	77.3 (63.0-87.2)
Complementary investigations			
Blood culture performed (n recorded = 132)	39	29.5 (22.4-37.8)	—
Positive blood culture	4	10.3 (4.1-23.6) of blood cultures	—
Cerebrospinal fluid analysis	10	6.7 (3.7-11.8)	—
Yield by sampling method			
Intraoperative sample	44/105	41.9 (32.9-51.5)	—
Diagnostic puncture without drainage	5/9	55.6 (26.7-81.1)	—
Wound or scalp sample	1/2	50.0 (9.5-90.5)	—

Confidence intervals calculated by the Wilson method. The cascade is presented as a methodological proposal, built on a single centre and requiring multicentre validation before any comparative use.

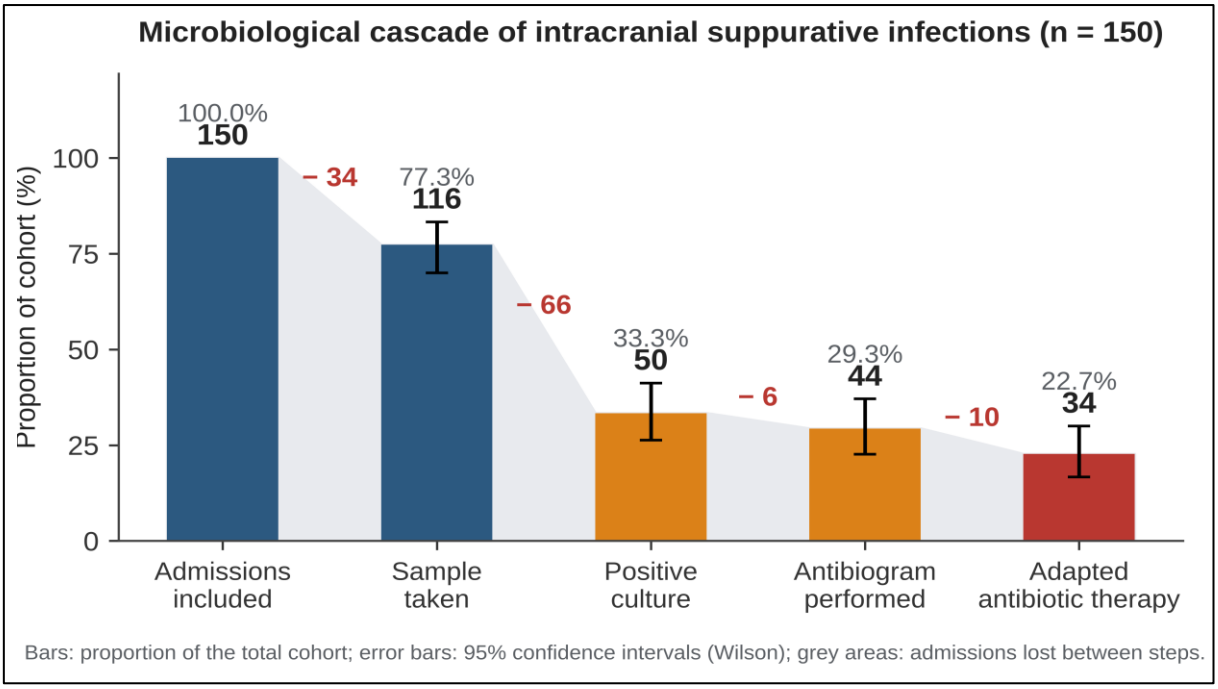


Fig 4 Microbiological Cascade of Intracranial Suppurative Infections (n = 150).

Each bar represents the proportion of the total cohort reaching the corresponding step; error bars show the 95% confidence interval (Wilson method) and grey areas the number lost between two consecutive steps. The loss is concentrated in the first two transitions.

The conditional reading locates the loss precisely. Among samples, only 43.1% (34.5-52.2) yielded a positive culture. By contrast, 88.0% of positive cultures (76.2-94.4) were followed by a susceptibility test, and 77.3% of susceptibility tests (63.0-87.2) by documented adaptation. The two steps after the organism therefore work correctly. The loss is concentrated in access to sampling and in its yield.

Yield varied little by sampling method: 41.9% for intraoperative samples (32.9-51.5) and 55.6% for diagnostic punctures (26.7-81.1). Complementary investigations were little used: a blood culture in 29.5% of recorded cases, positive in 4 of 39, and cerebrospinal fluid analysis in 6.7% of admissions.

➢ *An Ecology Reduced to Two Genera*

The 50 isolates comprised 21 *Streptococcus* spp. (42.0%), 17 *Staphylococcus aureus* (34.0%), 4 Gram-negative bacilli not identified to species level, 3 coagulase-negative staphylococci, 3 *Pseudomonas aeruginosa* and 2 polymicrobial flora (Table 3). The distribution varied by origin. Streptococci dominated community-acquired and post-traumatic forms. All *P. aeruginosa* and all coagulase-negative staphylococci came from post-operative suppurations. *S. aureus* accounted for 41.7% of documented community-acquired isolates. Without anaerobic culture, we know nothing of the share of these organisms.

Table 3 Organisms Isolated by Origin of the Suppuration

Organism	**Total (n = 50)**	**Community-acquired (n = 24)**	**Post-traumatic (n = 13)**	**Post-operative (n = 13)**
Streptococcus spp.	21 (42.0%)	12	9	0
Staphylococcus aureus	17 (34.0%)	10	3	4
Gram-negative bacillus	4 (8.0%)	0	1	3
Coagulase-negative staphylococcus	3 (6.0%)	0	0	3
Pseudomonas aeruginosa	3 (6.0%)	0	0	3
Polymicrobial flora	2 (4.0%)	2	0	0

Percentages relate to the number of isolates. No anaerobic culture is available in the institution; the contribution of anaerobes is unknown and probably underestimated.

➢ *Watch Antibiotics Almost Everywhere, No Reserve*

Ten distinct antibiotic regimens were prescribed (Table 4, Figure 5 and supplementary table S3-1). Metronidazole featured in 92.7% of regimens, ceftriaxone in 52.7%, vancomycin in 40.7% and ceftazidime in 28.0%. Fifteen admissions (10.0%) included gentamicin, an aminoglycoside that penetrates poorly into the meninges [37] and whose therapeutic value here is doubtful.

Table 4 AWaRe category and Pathogen Classes Covered, by Molecule

Molecule	AWaRe	Pathogen classes covered	Patients exposed, n (%)
Metronidazole	Access	F	139 (92.7)
Ceftriaxone	Watch	A · D	79 (52.7)
Vancomycin	Watch	A · B · C	61 (40.7)
Ceftazidime	Watch	D · E	42 (28.0)
Cloxacillin	Access	B	16 (10.7)
Gentamicin	Access	D	15 (10.0)
Amoxicillin–clavulanic acid	Access	A · B · D · F	11 (7.3)
Meropenem	Watch	A · B · D · E · F	11 (7.3)
Cefotaxime	Watch	A · D	7 (4.7)
Ciprofloxacin	Watch	D · E	3 (2.0)

- Classes: A streptococci; B methicillin-susceptible *Staphylococcus aureus*; C methicillin-resistant staphylococci; D Enterobacterales; E *Pseudomonas aeruginosa*; F anaerobes. Matrix declared a priori, based on expected spectra; it takes account neither of meningeal penetration nor of local susceptibilities, which are unavailable. The spectrum coverage index of a regimen is the cardinality of the union of the classes covered by its molecules. The detail of the ten prescribed regimens is given in supplementary table S3-1.

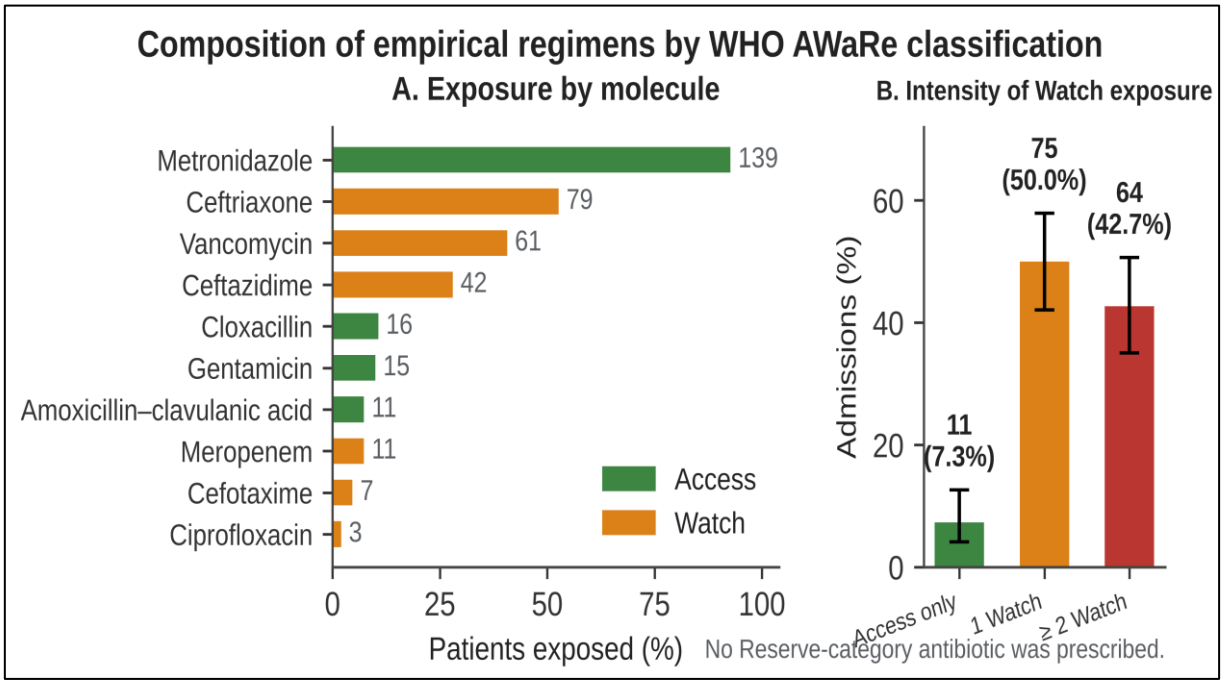


Fig 5 Composition of Empirical Regimens by AWaRe Classification. (A) Proportion of Patients Exposed to Each Molecule, Coloured by AWaRe Category. (B) Intensity of Watch Exposure by Regimen, with 95% Confidence Intervals. No Reserve-Category Antibiotic was Prescribed.

At least one Watch antibiotic featured in 139 regimens (92.7%; 87.4-95.9), and two or more in 64 (42.7%; 35.0-50.7). Eleven admissions (7.3%) received only Access molecules. No Reserve antibiotic was prescribed over the whole period. Of the 384 molecule-prescriptions, 52.9% belonged to the Watch category. The median spectrum coverage index was 4 out of 6 (IQR 3-6): a typical regimen therefore covered two thirds of the pathogen classes considered.

➢ *The Prescribed Spectrum Departs from Ecology in Both Directions*

This is the central result of this work (Figures 6 and 7, Table 5).

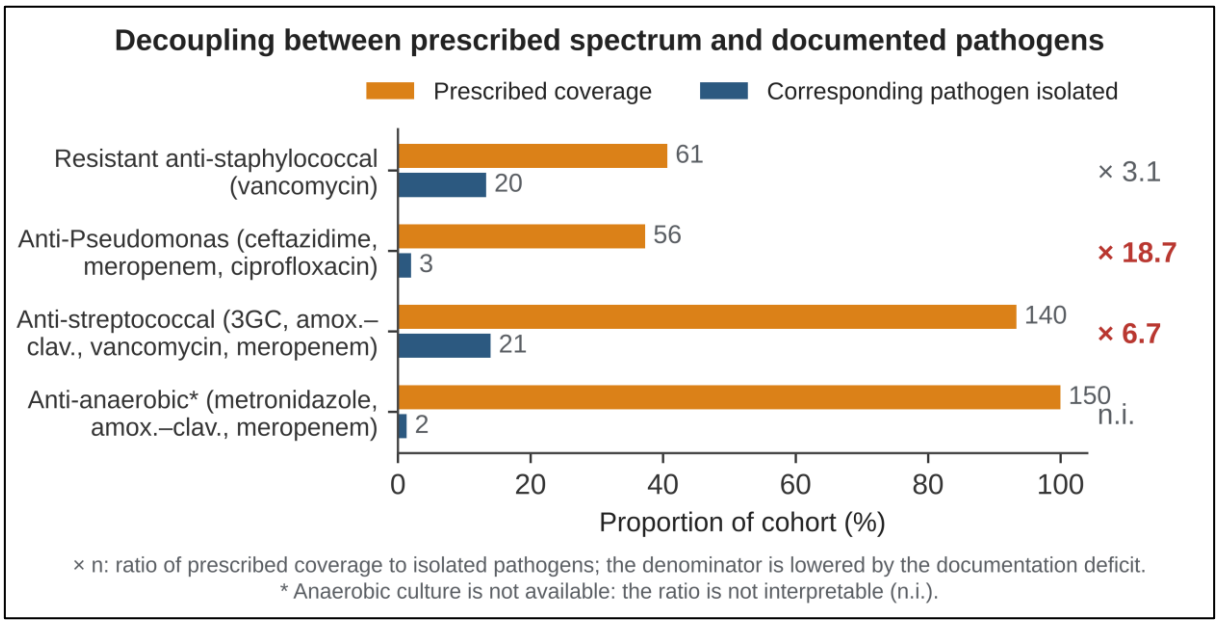


Fig 6 Decoupling Between the Prescribed Spectrum and the Documented Pathogens.

For each coverage class, the upper bar shows the proportion of patients treated with a molecule active against that class and the lower bar the proportion of patients in whom the corresponding pathogen was isolated; the ratio is shown on the right. The ratio cannot be interpreted for anaerobes, for which culture is not available.

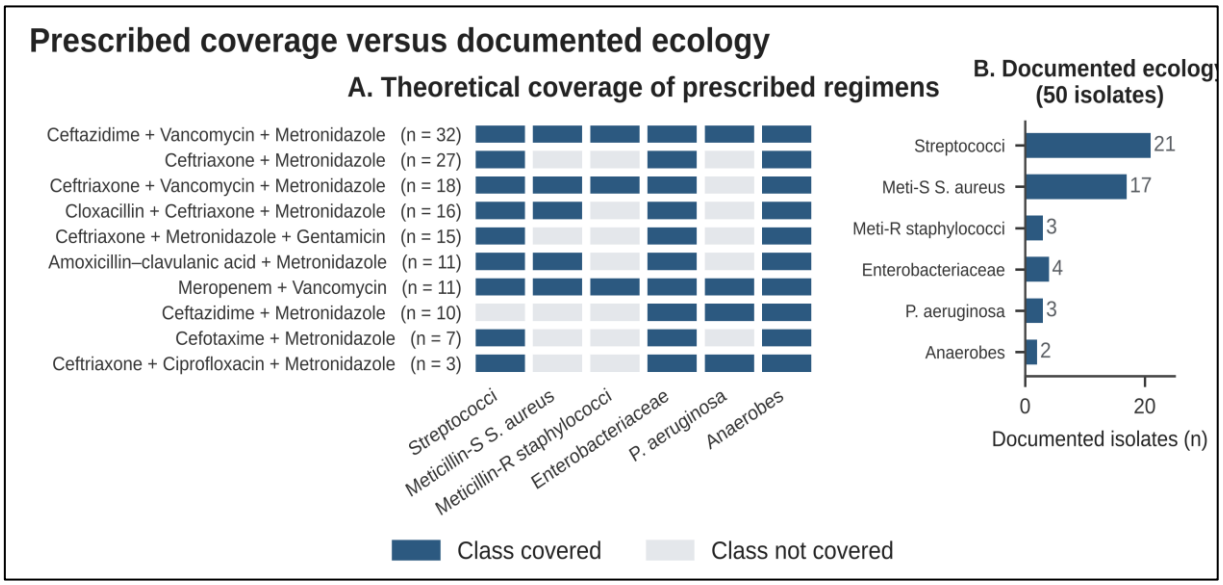


Fig 7 Comparison of Prescribed Coverage and Documented Ecology. (A) Theoretical coverage matrix of the ten prescribed regimens across the six pathogen classes considered, in solid fills. (B) Distribution of the 50 documented isolates. Comparison of the two panels highlights the excess coverage of P. aeruginosa and Enterobacterales and the deficit for resistant staphylococci.

Table 5 Concordance Between Prescribed Spectrum and Isolated Pathogen (50 Isolates)

Isolated organism	**n**	**Regimen covering the organism, n (%)**	**Classes covered in excess, median**
Streptococcus spp.	21	18 (85.7)	3
Staphylococcus aureus	17	9 (52.9)	4
Gram-negative bacillus	4	4 (100)	4
Coagulase-negative staphylococcus	3	3 (100)	5
Pseudomonas aeruginosa	3	2 (66.7)	5
Polymicrobial flora	2	2 (100)	1
Total	50	38 (76.0; 95% CI 62.6-85.7)	3 (IQR 3-5)

The eight uncovered *S. aureus* were all community-acquired; the three uncovered streptococci all received the combination ceftazidime + metronidazole.

In the direction of excess, anti-*Pseudomonas* coverage was prescribed to 37.3% of patients, whereas *P. aeruginosa* was isolated in only 2.0%, a ratio of 18.7. Vancomycin was prescribed to 40.7% of patients for 13.3% of staphylococci isolated, a ratio of 3.1 (61/20 = 3.05). The corresponding ratio for streptococci was 6.7 (140/21).

In the direction of deficit, 76.0% of regimens (62.6-85.7) covered the organism finally isolated. This overall adequacy masks marked inequalities. Streptococci were covered in 85.7% of cases and Gram-negative bacilli in 100%. By contrast, only 9 of the 17 documented *S. aureus* (52.9%) received appropriate anti-staphylococcal coverage. The eight coverage failures all concerned community-acquired infections; no coverage failure was observed among the four post-operative *S. aureus* isolates. The three uncovered streptococci all received the combination ceftazidime + metronidazole, prescribed to 28.0% of the cohort, whose anti-pseudomonal coverage comes at the price of lower activity against Gram-positive cocci.

The median number of classes covered in excess was 3 (IQR 3-5) per documented isolate.

➢ *Ten Years without Change*

None of the three dimensions changed over the period (Figure 8). The annual odds ratio was 0.93 (0.82-1.06; p = 0.28) for sampling, 1.00 (0.90-1.12; p = 0.96) for documentation and 0.98 (0.88-1.10; p = 0.75) for exposure to two or more Watch molecules. The Cochran-Armitage test and the Spearman correlation on the spectrum coverage index confirmed this stability. Comparison of the periods 2016-2020 and 2021-2026 showed no difference.

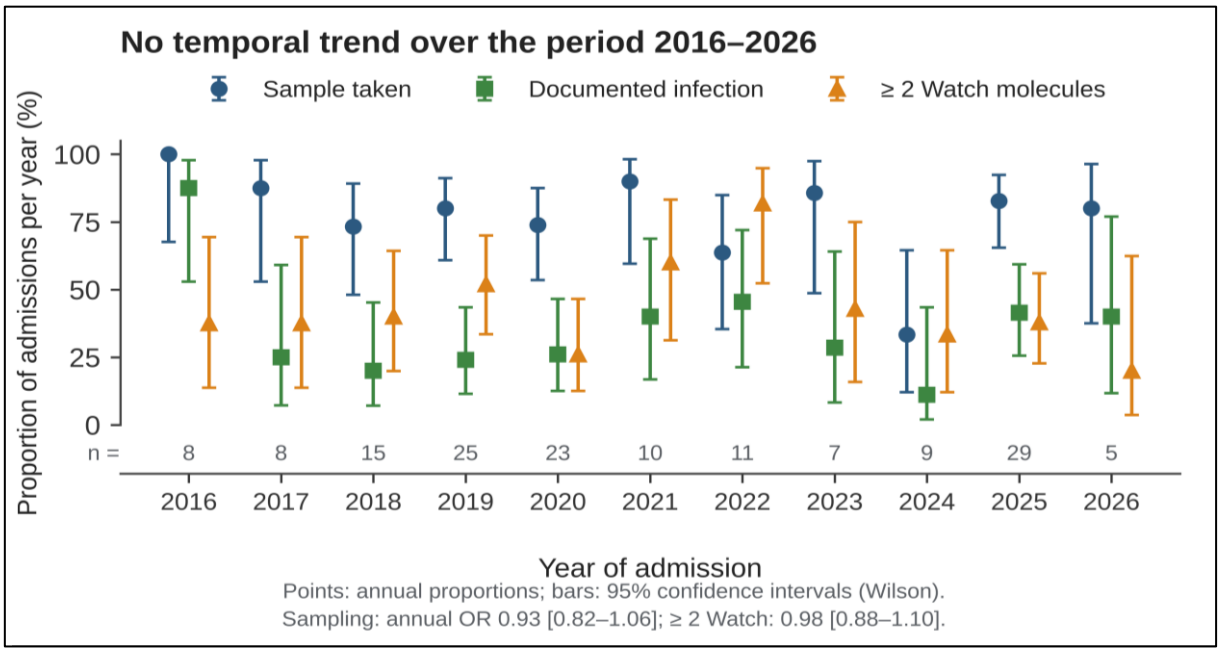


Fig 8 No Temporal Trend Over the Period 2016–2026.

Annual proportions of samples taken, documented infections and regimens containing at least two Watch molecules, shown as points with 95% Wilson confidence intervals; annual numbers are given below the axis.

➢ *Only Surgery Opens Access to Microbiology*

In the Firth model for whether a sample was taken (Figure 9, Table 6), a single determinant emerged: surgery (OR 5.61; 2.22-14.56; p < 0.001). Neither age, nor neurological severity, nor period, nor referral status, nor post-operative origin was associated with sampling. This association reflects a physical constraint on access to the focus (no procedure, no pus), not a prescribing preference.

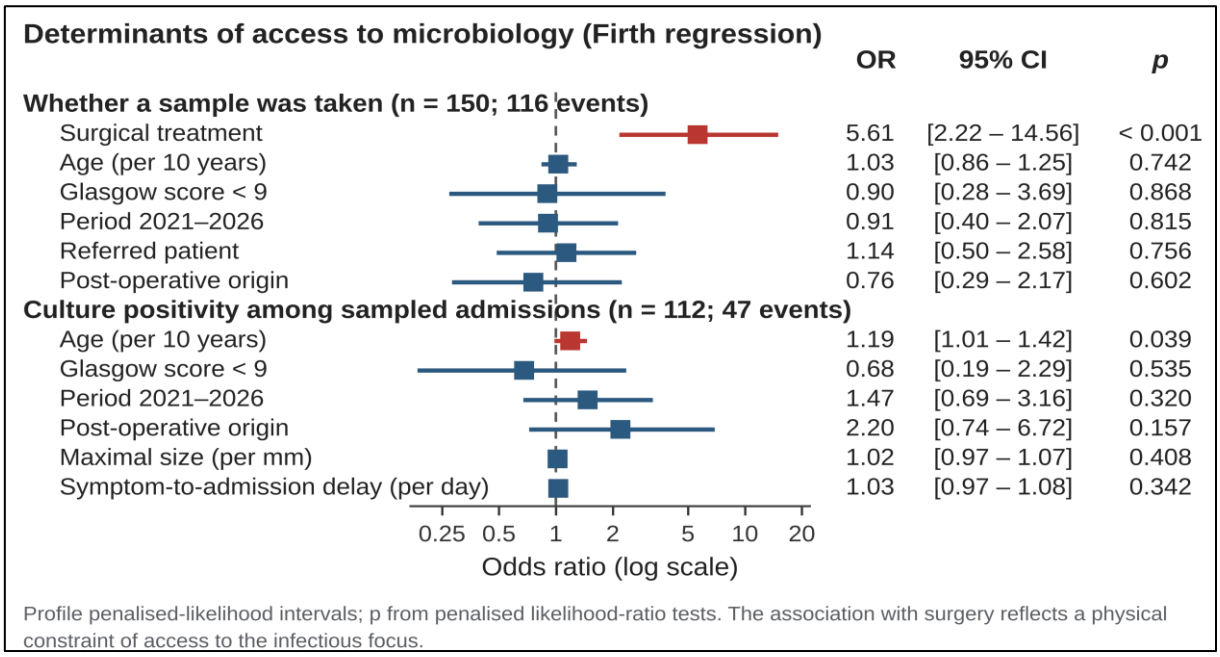


Fig 9 Determinants of Access to Microbiology (Firth Regression).

Odds ratios and 95% confidence intervals by profile penalised likelihood, for whether a sample was taken (whole cohort) and for culture positivity (sampled patients). The result reaching significance is highlighted.

Table 6 Determinants of Access to Microbiology and Internal Validation

Variable	OR	95% CI (profile likelihood)	p	Bootstrap CI (2,000)	Sign stability
Whether a sample was taken (n = 150; 116 events; EPV 19.3)					
Surgical treatment	5.61	2.22-14.56	< 0.001	2.32-18.52	100.0%
Age (per 10 years)	1.03	0.86-1.25	0.742	0.87-1.25	65.8%
Glasgow score < 9	0.90	0.28-3.69	0.868	0.28-6.38	56.1%
Period 2021-2026	0.91	0.40-2.07	0.815	0.37-2.37	58.4%
Referred patient	1.14	0.50-2.58	0.756	0.48-2.80	64.0%
Post-operative origin	0.76	0.29-2.17	0.602	0.27-2.48	68.0%
Culture positivity among sampled patients (n = 112; 47 events; EPV 7.8)					
Age (per 10 years)	1.19	1.01-1.42	0.039	1.00-1.46	97.5%
Glasgow score < 9	0.68	0.19-2.29	0.535	0.18-2.24	76.8%
Period 2021-2026	1.47	0.69-3.16	0.320	0.65-3.25	81.5%
Post-operative origin	2.20	0.74-6.72	0.157	0.72-7.36	92.1%
Maximum size (per mm)	1.02	0.97-1.07	0.408	0.97-1.07	80.5%
Symptom-to-admission delay (per day)	1.03	0.97-1.08	0.342	0.97-1.08	83.2%

- EPV: events per variable. Firth penalised logistic regression; p-values by penalised likelihood ratio test. Surgical treatment is the largest-magnitude effect of the first model in 94.0% of bootstrap resamples. The second model, whose events-per-variable ratio is below 10, is presented as exploratory.

In sampled patients, only age was associated with culture positivity (OR 1.19 per decade; 1.01-1.42; p = 0.039). We report this isolated association as hypothesis-generating. Neither the size of the collection, nor the time between symptoms and admission, nor severity modified the yield.

Bootstrap validation confirms the structure of the models (Table 6). The sign of the effect of surgery remains the same in 100% of resamples (percentile interval 2.32-18.52), and it is the largest effect in the model in 94.0% of them. For no other variable of the first model does the percentile interval exclude the null value. In the second model, age keeps its sign in 97.5% of resamples, but its percentile interval touches the null value (1.00-1.46): this single significant result calls for caution.

➢ *Missing Data*

The main clinical and therapeutic variables are complete (Table 7). Missing data concern the maximum

size of the collection (4.0%), the GOS outcome score (5.3%) and the performance of blood cultures (12.0%). Four microbiological variables (culture positivity, performance of a susceptibility test, documented adaptation, blood culture positivity) are missing in 22.7%, 22.7%, 70.7% and 74.0% of cases. The first two correspond to the 34 patients not sampled, the third to the 106 patients without a susceptibility test, and the last to the 111 patients without a blood culture. This absence is structural and informative: it constitutes the result itself, which justifies the complete-case analysis.

Table 7 Missing Data for the Variables Analysed

Variable	Missing, n (%)	Nature
Pus sample	0 (0.0)	—
Positive culture	34 (22.7)	Structural: patient not sampled
Susceptibility test performed	34 (22.7)	Structural: patient not sampled
Adaptation to susceptibility test	106 (70.7)	Structural: no susceptibility test
Blood culture performed	18 (12.0)	Not recorded in the file
Positive blood culture	111 (74.0)	Structural: test not performed
Antibiotic regimen	0 (0.0)	—
Duration of antibiotic therapy	0 (0.0)	—
Age, sex, Glasgow score, delay	0 (0.0)	—
Maximum size of the collection	6 (4.0)	Imaging not measurable or not available
Origin, referral, therapeutic strategy	0 (0.0)	—
Death, length of stay	0 (0.0)	—
GOS outcome score	8 (5.3)	Lost to follow-up at discharge

No imputation was performed. Structural missing data correspond to patients who did not reach the step that makes the variable definable (not sampled, no susceptibility test or no blood culture): their absence is the result and not a gap, which excludes any imputation.

➢ *No Link with Outcomes, But a Link with Duration*

Mortality was 11.8% in patients not sampled, 9.1% in those with a negative culture and 12.0% in documented patients (p = 0.86). Functional outcome (GOS ≤ 3: 31.0%, 42.9% and 42.0%; p = 0.53), reoperations, recurrences and length of stay did not differ either. After adjustment for severity and age, microbiological documentation was not associated with death (OR 1.34; 0.44-3.87; p = 0.60), unlike a Glasgow score below 9 (OR 3.92; 1.17-12.04; p = 0.028). Power is low: 30.7% to detect a doubling of the risk of death (supplementary table S5-1).

The duration of antibiotic therapy, however, differed by microbiological status, and in a direction contrary to de-escalation (Figure 10, Table 8). Patients not sampled received the longest treatments: 7.15 weeks on average, versus 6.35 in culture-negative patients and 6.68 in documented patients (p = 0.005; epsilon² = 0.059). The gap between non-sampled and culture-negative patients approaches six days per patient.

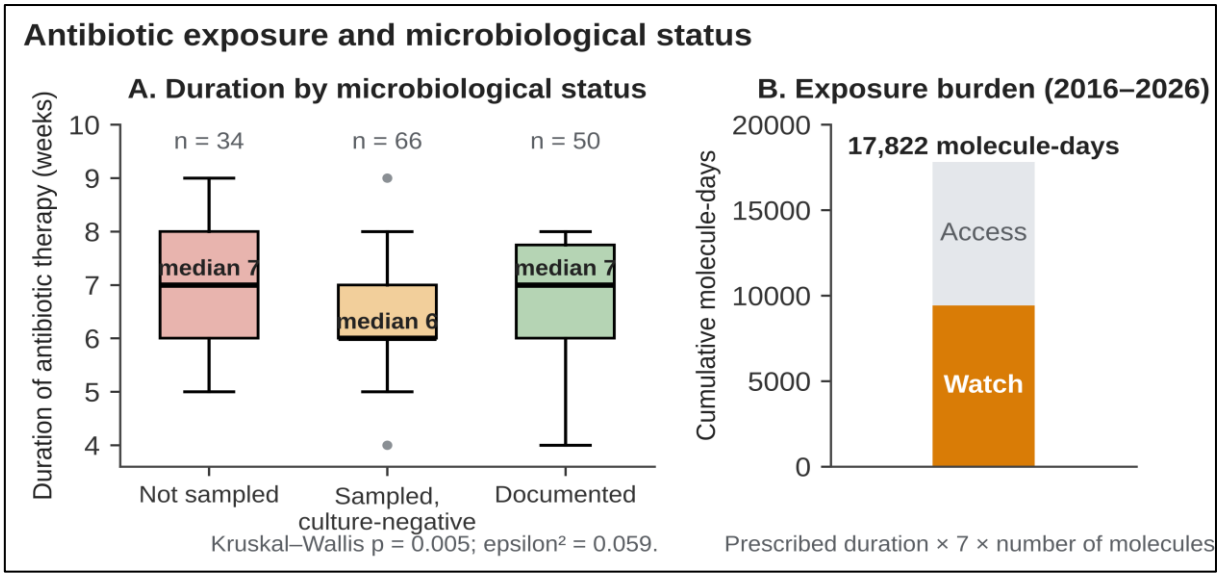


Fig 10 Antibiotic Exposure and Microbiological Status. (A) Distribution of Antibiotic Therapy Durations by Microbiological Status, Medians Annotated; Points Show Individual Observations. (B) Cumulative Exposure Burden in Molecule-Days, Watch-Category Share Highlighted.

Table 8 Microbiological Status, Antibiotic Exposure and Outcomes

	Not sampled (n = 34)	Culture-negative (n = 66)	Documented (n = 50)	p
Duration of antibiotic therapy, mean — weeks	7.15	6.35	6.68	0.005
Duration of antibiotic therapy, median — weeks	7	6	7	—
Watch molecules per regimen, mean	1.47	1.23	1.44	—
Spectrum coverage index, mean	4.56	4.09	4.40	0.201
Death, n (%)	4 (11.8)	6 (9.1)	6 (12.0)	0.857
GOS ≤ 3, n/N (%)	9/29 (31.0)	27/63 (42.9)	21/50 (42.0)	0.531
Reoperation, n	3	5	5	—
Recurrence, n	2	1	3	—
Length of stay, median — days	10	12	11	—

Kruskal-Wallis for continuous variables, chi-square for proportions. After adjustment (Firth) for Glasgow score < 9 and age, microbiological documentation was not associated with death (OR 1.34; 95% CI 0.44-3.87; p = 0.598) whereas Glasgow score < 9 was (OR 3.92; 1.17-12.04; p = 0.028). Power to detect a doubling of the risk of death: 30.7% (see supplementary table S5-1).

➢ *Avoidable Antibiotic Exposure: Three Illustrative Scenarios*

Over ten years, the cohort accumulated 17,822 molecule-days (118.8 per patient), of which 9,415 (52.8%) were of the Watch category. Three scenarios estimate the avoidable share (supplementary table S5-1). De-escalation to targeted monotherapy on day seven in the 50 documented patients would avoid 3,108 molecule-days, or 17.4% of total exposure. Aligning the duration of the 34 non-sampled patients with that of culture-negative patients would avoid a further 638. Together, these two scenarios represent 3,746 molecule-days over ten years: 21.0% of total exposure, 375 per year and 25.0 per patient. The third scenario does not reduce volume; it shifts the nature of exposure: the 19 community-acquired patients treated with ceftazidime totalled 861 days of anti-pseudomonal coverage, whereas no *P. aeruginosa* was isolated in a community-acquired form in this series.

These figures rest on de-escalation assumptions that were not observed, ignore implementation costs and incorporate no accounting data. They are orders of magnitude, not effect estimates.

➢ *Sensitivity Analyses*

The eleven sensitivity analyses (supplementary table S6-1) change no conclusion. In operated patients, the proportion sampled reaches 84.0%, documentation 35.2% and Watch exposure remains at 91.2%. Excluding scalp suppurations, duplicate admissions or paediatric patients changes the proportions very little. Even if all non-sampled patients had returned a positive culture, the theoretical maximum documentation would not exceed 56.0%: the deficit persists. Post-operative suppurations all received at least two Watch molecules. If every *S. aureus* is considered methicillin-resistant, adequacy falls from 76.0% to 74.0%.

IV. DISCUSSION

➢ *Main Finding*

Over 150 admissions in ten years, the microbiological information needed to adapt antibiotic therapy was produced in only 22.7% of patients. The loss lies upstream of prescription: among patients in whom an organism was obtained, 88% had a susceptibility test and 77% of those a documented adaptation, whereas only 43% of samples yielded a positive culture and nearly one patient in four was not sampled at all. The deficit therefore does not stem from a poor therapeutic decision, but from a lack of information produced.

Three further observations emerge. The prescribed spectrum departed from the documented ecology in both directions at once. The absence of documentation was accompanied by longer, not shorter, treatments. Finally, none of this changed over ten years.

➢ *Locating the Failure Rather than Merely Noting it*

The value of the cascade is to distinguish a global deficit from a localised one: the final step measures system performance, while the conditional proportions point to the weak link. The practical consequence is direct. A programme centred on restricting prescriptions (validation by a designated expert, justification form, limitation of broad-spectrum molecules) would have little purchase here, because the problem is not that clinicians ignore available results: no result exists. The useful lever is upstream, in what the literature calls diagnostic stewardship, that is, the decisions that determine whether, when and how a specimen is collected, transported, processed and reported [9–13]. This distinction is considered central in resource-limited settings, where programmes modelled on those of wealthy countries often fail [38–39].

Our results invite us to think in three levels rather than two. Surgical stewardship decides whether the focus will be approached, and therefore whether sampling is physically possible; in this cohort, it alone governs access to microbiology. Diagnostic stewardship decides whether this opportunity will be seized, protected from contact with the antibiotic, transported and reported. Antibiotic stewardship, in the usual sense [40], operates only after the first two. This hierarchy could explain why restriction

programmes, which make up most of the methodological offer, would be of little effect here. This proposal remains to be demonstrated.

The proposed cascade is an analytical framework, not a validated instrument. Its steps come from our data, in a single centre. Its transposition to other centres, to other deep surgical conditions and to other laboratory systems is a hypothesis to be tested.

➢ *An Asymmetry of the Spectrum Rather than Simple Overprescription*

The most original result is not that the spectrum is broad, which was expected, but that it appears poorly oriented. Reading the two directions of concordance together reveals a structure that spectrum breadth alone would have masked.

Anti-*Pseudomonas* coverage, prescribed to 37.3% of the cohort for 2% of *P. aeruginosa* isolated, and vancomycin, prescribed to 40.7% for 13.3% of staphylococci isolated, reflect an insurance logic: without information, one covers what one fears. But this insurance was not taken out everywhere. Anti-staphylococcal regimens were used mainly in post-operative forms, which all received them and contained at least two Watch molecules, in line with European recommendations [1]. In a community-acquired abscess, the same organism did not lead to this treatment, although it accounted for 41.7% of documented community-acquired isolates. The most visible contextual signs (recent surgery, craniocerebral wound, hardware) therefore seem to weigh more than an estimate of the probability of the organism.

The example of ceftazidime illustrates this mismatch. Prescribed to 28.0% of patients, this anti-pseudomonal cephalosporin provides superfluous coverage of *Pseudomonas* while being less active than ceftriaxone against Gram-positive cocci. The only three uncovered streptococci in the series received precisely ceftazidime and metronidazole. A molecule chosen to broaden the spectrum in fact shifted it.

We present this interpretation as a hypothesis. Our study observes a link between clinical context and choice of molecule, but we have neither the recorded reasons for prescribing nor interviews with prescribers. A qualitative study of prescribing reasoning would be the natural complement [41].

➢ *The Paradox of Duration*

The logic of de-escalation would have the absence of documentation lead to treatment being reassessed more often. We observe the opposite. Patients not sampled received on average 7.15 weeks of treatment, versus 6.35 for those whose culture had remained negative: nearly six days more per patient ($p = 0.005$).

Two mechanisms, not mutually exclusive, may explain this. A negative culture, even without an organism, can reassure and allow discontinuation, whereas the absence of sampling leaves the doubt intact. Another possibility: patients not sampled are those who were not operated on, whose clinical response is harder to judge and whose focus is not evacuated. This confounding by indication cannot be excluded with our data. In both cases, the absence of information costs additional days of exposure. Two simple de-escalation scenarios would represent 21% of total exposure. We express the corresponding saving parametrically rather than in money: the unit cost is not documented and families bear most of it. The economic stake lies less in the price of the vials avoided than in the deferred costs of resistance [42].

➢ *Comparison with the Literature*

- Sub-Saharan Africa. The most comparable series is that of Kabré and colleagues: 112 brain abscesses collected over twelve years in Ouagadougou, with a bacterium isolated in 16.1% of cases and a mortality of 13.4% [43]. Our documentation rate, 33.3%, is twice as high. The difference probably does not stem from laboratory quality, which is comparable, but from the proportion of patients operated on (83.3% here), which governs access to pus: in our model, surgery is the only determinant of sampling. This interpretation predicts that a centre that operates more will document more, with equal technical facilities, and it is testable. Nigerian series report difficulties in transporting and preserving specimens [44–45]. This mechanism acts on yield, not on access, and could explain part of our 43% of positive cultures. The South African series of Nathoo and colleagues (699 subdural empyemas) shows that wide documentation was possible in Africa when the laboratory was integrated into the department [46]. The explanation there is organisational (proximity, circuit) rather than technical.

Our antibiotic exposure closely overlaps with regional surveys. The Global-PPS survey of Burkina Faso finds empirical prescribing in 98.5% of cases and an Access-Watch split of about 50-50, with no Reserve antibiotic [5]. Ghana, Benin, Zambia, Tanzania and Nigeria have the same profile [3–4,6–7], as does the international survey across 53 countries [8] and regional policy analyses [47]. The composition of exposure therefore seems to depend less on the disease treated than on the available formulary and the absence of microbiological information, two constraints common to all these centres. Our study adds the linkage, molecule by molecule, to the documented ecology of the same patient. It shows that the apparent uniformity hides an asymmetry.

- Other regions. European series report 50 to 80% documentation [14–17]. The gap with our 33.3% stems from three mechanisms that add up. First, anaerobic culture, which captures a flora that we do not see [22]. Second, molecular techniques, which increase yield further on the same specimen [23]. Finally, sampling more often performed before the antibiotic where the

surgical delay is short. Large Asian series show that a local ecology accumulated over long series allows empirical antibiotic therapy to be rationalised without waiting for each susceptibility test [48–50]. It is this mechanism that we lack, and it explains why the absence of documentation is self-perpetuating: without local ecology, no rational empirical protocol; without a protocol, no reduction in the heterogeneity of practice. North American work stresses the joint action of the infectious disease specialist and the neurosurgeon [51–52]. In our cohort, an infectious disease opinion was requested in only 16.7% of admissions: this is an immediate lever, requiring no material investment.

- *Why the Absence of Association with Mortality does not Weaken the Argument*

We report a negative result: microbiological status was associated neither with mortality, nor with functional prognosis, nor with reoperations. We place it at the centre of the discussion for three reasons.

First reason: power is insufficient. With sixteen deaths, it is 30.7% to detect a doubling of risk, and about 223 patients per group would be needed to reach 80%. Second reason: the comparison is confounded by construction, since patients sampled are patients operated on. Third reason, the most important: the stewardship argument does not rest on an immediate individual benefit. Broad empirical antibiotic therapy has, by construction, a good chance of being active, and 76% of regimens did cover the organism finally isolated. Its cost is paid collectively and later: selection of resistance, prolonged exposure, toxicity (vancomycin prescribed to 40.7% of patients for six to seven weeks without pharmacological monitoring, which is nevertheless recommended [53]), and the impossibility of building a local ecology. Here, the argument in favour of documentation therefore cannot be individual survival.

- *Scope Beyond Microbiology*

What the cascade measures goes beyond microbiology: the capacity of an organisation to circulate information within itself. No link (operative decision, transport, return of the result to the record, review at the right time) is technical in nature. The proportion of patients whose antibiotic therapy was adapted to a result is an outcome indicator, not a structure indicator [54]. It joins the idea that the quality of health systems, and not only access, determines outcomes in low- and middle-income countries [55].

These results lie at the crossroads of two global agendas that rarely meet: global neurosurgery, centred on access and operative capacity [56–58], and the fight against antimicrobial resistance, centred on surveillance and stewardship without regard to surgical disciplines [59–60]. The readiness of sub-Saharan African countries for this surveillance remains uneven [61–64]. Intracranial suppurations, treated by surgery then by long antibiotic therapy, are a sensitive indicator of the joint maturity of the two systems. They also touch on universal health coverage: a patient who reaches the operating theatre without their infection ever being identified has crossed the barrier of access without benefiting from quality [55].

One point deserves emphasis for the policy reading. The total absence of Reserve antibiotics can be read in two opposite ways. On the face of it, this is good news with regard to WHO targets. In reality, it is at least in part the reflection of unavailability: linezolid, daptomycin and ceftazidime-avibactam are not accessible in the institution. Apparently meeting an international target therefore does not mean doing stewardship well. This is the paradox of access and excess, now well described [65–68], which will become a major problem the day resistant strains emerge in a system incapable of detecting them.

- *Implications*

- Clinical implications. Each surgical procedure is the single diagnostic opportunity of the episode. Sampling must therefore be a full operative step, and not an optional test; aspiration-drainage, the dominant modality here as in the literature [69], offers it systematically. Sampling before the first dose of antibiotic, whenever the surgical delay allows, is the action with the highest expected yield: sterilisation by prior antibiotic therapy is the most likely explanation of our 43% yield. A documented reassessment at the 72nd hour (molecule, route, planned duration) is feasible without any additional resources.
- Microbiological implications. A written empirical protocol, differentiated by mechanism, should explicitly provide for anti-staphylococcal coverage in community-acquired forms. In our cohort, this would have corrected the eight coverage failures. Ceftazidime should be reserved for post-operative or post-traumatic situations. Producing a local ecological profile each year, even on small numbers, is the condition for any protocol based on local data.
- Organisational implications. The sampling circuit (transport, laboratory opening hours, return of the result to the record) is, at no step, technical in nature: it falls under clinical governance. A weekly antibiotic meeting bringing together neurosurgeon, microbiologist and infectious disease specialist, and traceability of the delay between sampling and start of culture, are the two simplest instruments.
- Implications for health policy. Neurosurgical infections are absent from national resistance surveillance systems, even though they combine long, parenteral and broad-spectrum exposure. Adding them to the syndromes monitored is a political decision that has no material cost. Table 9 classifies the proposed measures by level of actor and by implementation horizon.

Table 9 Roadmap: Proposed Measures by Level of Actor and Horizon

Horizon	Level	Measure	Resource required	Monitoring indicator
Immediate	Department	Mandatory, documented intraoperative sample; any absence to be justified in writing in the operative report	None	% of procedures with documented sample
Immediate	Department	Sampling before the first dose of antibiotic whenever the surgical delay allows	None	% of samples taken before the first dose
3 months	Department	Documented reassessment at the 72nd hour (molecule, route, planned duration)	None	% of records with a documented reassessment
3 months	Hospital	Weekly antibiotic meeting (neurosurgery, microbiology, infectious diseases)	Medical time	Number of cases discussed per month
6 months	Department	Written empirical protocol differentiated by mechanism, including anti-staphylococcal coverage in community-acquired forms	Collective drafting	% of prescriptions compliant with the protocol
6 months	Hospital	Accelerated pus transport circuit, with traceability of the sampling-to-laboratory delay	Organisation	Median sampling-to-culture delay
1 an	Hospital	Annual local ecological profile, even on small numbers	Microbiologist time	Annual internal publication
2-3 years	National / regional	Inclusion of neurosurgical infections among the syndromes monitored by resistance surveillance	Public policy decision	Number of reporting centres

These measures are proposed and not evaluated; their effectiveness is a hypothesis to be tested (see Research agenda).

- *Box — Setting up Diagnostic Stewardship in Neurosurgery: Five Steps:*

✓ Standardise intraoperative sampling: mandatory, documented procedure; any absence is justified in writing in the operative report.
✓ Protect the yield: sample before the first dose of antibiotic whenever the surgical delay allows.
✓ Shorten the microbiological processing delay: identified transport circuit, with measurement of the delay between sampling and start of culture.
✓ Organise reassessment: documented review at the 72nd hour and weekly multidisciplinary antibiotic meeting.
✓ Monitor with standardised indicators: proportion of patients whose antibiotic therapy was adapted to a result, and AWaRe exposure (proportion of regimens containing at least one Watch antibiotic).

These measures are proposed, not evaluated. No data from this study demonstrate their effectiveness: they are testable intervention hypotheses, with an audit and feedback system whose effectiveness is established in other fields [70].

➢ *Strengths and Limitations*

The study rests on a consecutive ten-year cohort, with a homogeneous case definition and admission-by-admission verification of microbiological coding against primary sources. The analytical framework is explicit and reproducible thanks to the rules published in the supplement. The methods are adapted to the numbers: Firth penalised regression, profile likelihood intervals, Wilson intervals, systematic effect sizes, eleven sensitivity analyses and internal validation by bootstrap.

The limitations are important. The study is single-centre and without external validation. The agreement of our AWaRe proportions with regional multicentre surveys is reassuring, but does not replace replication. Data collection is mainly retrospective (127 of 150 admissions). We considered any absence of a trace as an absence of performance: this cautious choice may underestimate actual practice, and the prospective-retrospective comparison (87.0% versus 75.6%) suggests that part of the gap stems from traceability. The spectrum coverage index rests on a theoretical matrix. It takes account neither of meningeal penetration [37], nor of dosing, nor of adherence: it measures an intention to cover, not an efficacy, and it is not validated. The adaptation variable is declarative and does not distinguish de-escalation from escalation. Durations are prescribed and not administered; the exposure actually received may therefore be lower than the estimated exposure, which leads to interpreting molecule-days as upper bounds. Power is low for outcome endpoints. The absence of technical facilities limits the microbiological scope: no anaerobic culture, although anaerobes hold a major place in brain abscesses [22]; no nucleic acid amplification or metagenomics, which reveal a polymicrobial richness that conventional culture does not see [23]; no mass spectrometry, hence no species identification for Gram-negative bacilli. The ecology described is thus impoverished by its means of measurement. Finally, the analyses are multiple and uncorrected, and the unit of analysis is the admission.

What the study does not show must also be stated. It does not show that microbiological documentation improves survival. It does not show that the prescriptions observed are clinically inappropriate: without an organism, a broad regimen is often defensible. It does not show that the documentation deficit causes more resistance, for lack of local resistance data. It allows no

causal inference on the determinants of sampling, the association with surgery being a physical constraint.

The results seem transposable to neurosurgery departments in francophone West Africa whose laboratory is conventional, without anaerobic culture or an automated blood culture system, which corresponds to the majority of university centres in the subregion. They are less so to centres with a complete laboratory, where the lever would be prescribing rather than sampling, and not to high-income systems. The analytical framework, for its part, could in principle apply to other deep surgical infections (mediastinitis, spondylodiscitis, prosthetic infections), subject to the external validation already mentioned.

➢ *Research Agenda*

Six steps seem to us a priority. One: replicate the cascade in at least five West African centres, with a common data collection protocol, to know whether the failing step is the same everywhere; this is also the condition for validating the proposed framework. Two: conduct a qualitative study of the determinants of the decision to sample and of the choice of molecule, through interviews with neurosurgeons, anaesthetists and microbiologists [41]. Three: measure the transport delay of specimens and its relationship with yield, the most accessible mechanistic hypothesis to explain our 43%. Four: conduct a stepped-wedge trial [71] of a bundle of diagnostic stewardship interventions (mandatory documented sampling, sampling before antibiotics, reassessment at 72 hours, written empirical protocol), with the proportion of patients receiving documented antibiotic therapy as the primary endpoint. Five: build a regional ecological register, possibly supplemented by molecular approaches [23,72], a necessary condition for empirical recommendations based on African data. Six: evaluate, from a health-economic standpoint, the strengthening of dedicated microbiological capacity, relative to investments in imaging and operative capacity.

The proposed framework is refutable, and here is how. It predicts that better microbiological documentation, obtained through these measures and without changing the technical facilities, would increase the frequency of treatment reassessment and reduce unnecessary exposure to Watch antibiotics, without lengthening durations. If a multicentre trial showed that increased documentation changes neither the frequency of adaptations nor the AWaRe composition of regimens, the central hypothesis of this work would be refuted: the deficit would then indeed lie at prescription, and not upstream.

The absent techniques (mass spectrometry, nucleic acid amplification, metagenomics) will have their greatest value once the sampling circuit is secured, and little value as long as nearly one patient in four is not sampled. The literature moreover warns against technological solutions deployed without the foundation of conventional bacteriology that makes them interpretable [72]. The order of investments matters as much as their amount.

- *Key Messages*

✓ Fewer than one patient in four received antibiotic therapy guided by a microbiological result. The loss was upstream of prescription: in access to sampling and in its yield.
✓ Each surgical procedure is a unique diagnostic opportunity: in this condition, there will be no other.
✓ Without documentation, treatments were longer, not shorter: one cannot de-escalate without information.
✓ The prescribed coverage was asymmetric: excessive for *Pseudomonas*, insufficient for proven community-acquired staphylococcus. A simple measure of spectrum breadth would not have revealed it.
✓ The eight proposed measures require no additional equipment, only time, organisation and traceability. Their effectiveness remains to be demonstrated by an implementation trial.

V. CONCLUSION

In a teaching hospital in West Africa, more than three patients in four treated for an intracranial suppuration received six to seven weeks of antibiotics without any microbiological result guiding treatment. Nine regimens in ten contained a Watch antibiotic. Spectrum breadth appeared to reflect clinical uncertainty more than documented ecology, with a clear asymmetry: broadening towards rare pathogens, and insufficient coverage of proven community-acquired staphylococcus. Ten years did not change this profile.

This finding is not primarily one of poor prescribing, but of missing information. The response therefore lies upstream of prescription: protect the single sample that surgery makes possible, take it before the first dose, trace it, transport it quickly, reassess at 72 hours and write an empirical protocol based on mechanism. None of these measures requires new equipment. Our results support diagnostic stewardship as a foundational component of antibiotic stewardship in resource-limited neurosurgical infections. The proposed framework now requires multicentre validation, and it is formulated so that it can be refuted.

ABBREVIATIONS

- AWaRe: Access, Watch, Reserve (WHO classification); CHU: teaching hospital (centre hospitalier universitaire); CI: confidence interval; EPV: events per variable; ESCMID: European Society of Clinical Microbiology and Infectious Diseases; GOS: Glasgow Outcome Scale; IQR: interquartile range; OR: odds ratio; RECORD: REporting of studies Conducted using Observational Routinely-collected health Data; SCI: spectrum coverage index; STROBE: Strengthening the Reporting of Observational Studies in Epidemiology; WHO: World Health Organization.

DECLARATIONS

- Conflicts of interest: The authors declare no conflict of interest.
- Funding: No specific funding was received for this work.
- Ethical approval: Study conducted in accordance with the Declaration of Helsinki; protocol approved by the Institutional Ethics Committee of Bouaké Teaching Hospital (opinion no. CEI/CHU-BKE/139/2026), with waiver of individual consent (retrospective study, anonymised routine records).
- Data and code availability: The anonymised individual data and the complete analysis code will be deposited in a public repository.
- Author contributions: Faozo Stéphane Landry Teti: conceptualisation, methodology, data analysis, writing of the original draft and revision of the manuscript. Yao Bernard Fionko: data collection, investigation and validation. Konan Serge Yao: conceptualisation, methodology and supervision. Adama Kouadio: data collection and resources. Adama Simaga: investigation, data collection and validation. Aderehime Haidara: supervision, validation and critical revision of the manuscript. All authors have read and approved the final version of the manuscript.

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➢ *Supplementary Material*

The following supplements are to be provided separately:

- S1. Annotated STROBE checklist, supplemented with the RECORD items.
- S2. Dictionary of microbiological and therapeutic variables: definition, coding, source, possible values, rule for handling missing data; versioned correction log.
- S3. Complete molecule-class assignment matrix and justification of each assignment. Table S3-1: the ten prescribed regimens, numbers, Watch molecules and spectrum coverage index.
- S4. Detailed microbiological cascade by year, by origin and by type of suppuration.
- S5. Complete concordance tables, isolate by isolate. Table S5-1: post hoc power analysis for the mortality endpoint and detail of the three avoidable-exposure scenarios.
- S6. Table S6-1: detailed results of the eleven sensitivity analyses.
- S7. Statistical appendix: equations of Firth penalised regression, profile likelihood procedure, bootstrap procedure, pinned software versions, dependency file, pseudo-code.
- S8. Supplementary figures: cascade by subgroup, distribution of the spectrum coverage index, exposure by origin.
- S9. Complete analytical log: import, cleaning, descriptive analyses, models, bootstrap, figure generation, with a description file allowing full reproduction.

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