

MODERN DIAGNOSTIC METHODS AND PREVENTION OF MENINGOCOCCAL INFECTION: A LITERATURE REVIEW

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Annotation

Meningococcal disease caused by *Neisseria meningitidis* is a medical emergency capable of causing death within 24 hours of symptom onset. Despite the availability of vaccines and established treatment protocols, timely and accurate diagnosis remains the single greatest determinant of clinical outcome. Objective: This literature review critically evaluates contemporary diagnostic methods and preventive strategies for meningococcal infection, with particular emphasis on evidence published between 2023 and 2025. Methods: A systematic search of PubMed, Scopus, WHO, and CDC databases was conducted using the terms "meningococcal diagnosis," "Ng meningitidis PCR," "meningococcal vaccine," "meningococcal NGS," and related MeSH headings. Studies published between January 2023 and June 2025 were prioritized; foundational references predating this window were included where necessary to provide methodological context. Key Findings: Multiplex real-time PCR has supplanted culture as the diagnostic reference standard in many high-income settings, offering sensitivity exceeding 93% independent of prior antibiotic administration. Metagenomic next-generation sequencing and AI-assisted clinical decision tools represent emerging but not yet operationally validated technologies. The newly FDA-approved pentavalent vaccine MenABCWY (Penbraya) and the advancing pentavalent ACYWXX candidate signal a shift toward broader-spectrum single-injection protection. Conclusion: While diagnostic and preventive capabilities have advanced substantially, critical

gaps persist in low-resource settings, in surveillance of emerging serogroups, and in equitable vaccine access. Integrated genomic surveillance and AI-assisted triage offer the most promising directions for bridging these gaps.

Keywords

Neisseria meningitidis; meningococcal infection; diagnostic methods; PCR; next-generation sequencing; meningococcal vaccines; chemoprophylaxis; surveillance; public health; AI-based diagnostics

INTRODUCTION

Few infectious diseases concentrate the full spectrum of diagnostic and therapeutic challenge into as compressed a timeframe as meningococcal infection. From the first nonspecific prodrome of fever, myalgia, and malaise to the appearance of the pathognomonic non-blanching purpuric rash, the window available for effective clinical intervention may span as little as four to six hours; in fulminant meningococcaemia, death can precede hospital admission [1]. This biological reality renders every aspect of the clinical response – from triage and specimen collection to antibiotic initiation and public health notification – critically time-sensitive in a manner that few other bacterial infections demand.

The global burden of meningococcal disease, as estimated by the Global Burden of Disease Collaborative Network (2023), remains substantial despite decades of vaccine development: approximately 1.2 million cases and 135,000 deaths annually, with a disproportionate concentration of burden in sub-Saharan Africa and in young children and adolescents in high-income countries [2]. The case fatality rate for meningococcal septicaemia ranges from 10% to 20% in optimally resourced settings and approaches 50% when appropriate antibiotic therapy is delayed or unavailable. Neurological sequelae – sensorineural hearing loss, limb amputation, cognitive impairment, and post-traumatic psychological morbidity – affect 10–20% of survivors, imposing long-term disability that extends the societal cost of each case far beyond the acute episode [1, 3].

The diagnostic landscape for meningococcal infection has evolved markedly in the past decade. Culture-based methods, the historical gold standard, are limited by their sensitivity reduction following antibiotic pre-treatment – a common scenario given the appropriate clinical imperative to administer antibiotics before diagnostic confirmation – and by the 48–72-hour turnaround time incompatible with clinical urgency. Nucleic acid amplification tests (NAATs), particularly real-time PCR, have largely supplanted culture in settings with laboratory infrastructure, and next-generation sequencing (NGS) approaches are beginning to transition from research tools to clinical adjuncts. Concurrently, the preventive

landscape has been transformed by the approval of MenABCWY (Penbraya) in October 2023, the first vaccine to protect against five meningococcal serogroups in a single injection, and by ongoing Phase III trials of the pentavalent ACYWX conjugate candidate for deployment in Africa's meningitis belt [4].

Against this backdrop of rapid technological evolution, this review aims to provide clinicians, public health practitioners, and researchers with a critical and up-to-date synthesis of modern diagnostic strategies and preventive interventions for meningococcal infection, with rigorous focus on evidence generated in 2023–2025.

METHODOLOGY OF THE REVIEW

This narrative literature review was conducted in accordance with SANRA (Scale for the Assessment of Narrative Review Articles) guidelines. Electronic searches were performed in PubMed/MEDLINE, Scopus, the WHO Immunization, Vaccines and Biologicals database, and the CDC Meningococcal Disease surveillance pages between December 2024 and May 2025. The primary search string combined the Medical Subject Headings (MeSH) terms “*Neisseria meningitidis*,” “meningococcal infections/diagnosis,” “meningococcal infections/prevention & control,” and “meningococcal vaccines” with free-text synonyms including “meningococcal PCR,” “metagenomic sequencing meningitis,” “penB vaccine,” and “ACIP meningococcal recommendations.”

Inclusion criteria: peer-reviewed original research articles, systematic reviews, meta-analyses, clinical guidelines, vaccine clinical trial reports, and WHO/CDC technical documents published between January 2023 and June 2025. Articles in English were prioritized; where key data existed only in other languages, English-language abstracts were used. Exclusion criteria included: case reports without diagnostic or epidemiological generalizability, pre-clinical animal studies unrelated to clinical diagnostic validation, and articles addressing meningitis caused exclusively by non-meningococcal pathogens. Foundational methodological studies predating 2023 were retained where they provided essential technical context for newer developments. A total of 148 records were screened at title and abstract level; 47 met full-text inclusion criteria and are cited in this review.

MODERN DIAGNOSTIC METHODS. Laboratory Diagnostics

Culture Methods: Continuing Relevance Despite Well-Recognized Limitations

Blood and cerebrospinal fluid (CSF) culture remains the diagnostic method against which all others are measured for specificity, because it provides viable organisms for serotyping, susceptibility testing, and epidemiological characterization through multi-locus sequence typing (MLST). The theoretical specificity of a positive culture is essentially absolute in the absence of

contamination. However, culture sensitivity for meningococcal disease has been declining in practice across high-income settings, not because the method has changed but because clinical practice has. The universal recommendation – correctly prioritized – to administer parenteral benzylpenicillin or ceftriaxone before hospital transfer or admission in any suspected meningococcal case means that blood cultures are increasingly obtained from partially treated patients, in whom sensitivity drops to 40–60% from the theoretical 70–80% achievable in untreated bacteraemia [5].

Contemporary blood culture systems (e.g., BACTEC FX, BacT/ALERT VIRTUO) have improved time-to-positivity through continuous fluorimetric monitoring, with *N. meningitidis* typically flagging positive within 12–24 hours of incubation under optimal conditions. CSF culture, plated on chocolate agar with 5% CO₂ within 30 minutes of collection, yields the highest sensitivity among culture specimens. A 2024 prospective multisite European study found that the combination of blood and CSF culture, when specimens were collected before antibiotics, achieved an overall sensitivity of 71.4% for confirmed meningococcal disease – still insufficient to serve as a standalone diagnostic tool in the modern clinical context [5]. The primary irreplaceable function of culture in contemporary practice is susceptibility testing, given the documented increase in penicillin-reduced susceptibility strains, and provision of intact isolates for WGS-based public health surveillance.

Polymerase Chain Reaction: The Current Clinical Standard

Real-time PCR targeting the *ctrA* gene (encoding the outer membrane capsule transport protein, conserved across serogroups) or the *sodC* gene (encoding copper-zinc superoxide dismutase) has established itself as the diagnostic method of choice for meningococcal infection in resource-adequate settings. Its transformative advantage over culture is its independence from bacterial viability: PCR can detect meningococcal DNA in blood, CSF, and throat swabs from patients who received antibiotics hours or even days before sampling. A systematic review and meta-analysis published in

Multiplex PCR panels represent the most practically significant recent advance. Systems such as the BioFire FilmArray Meningitis/Encephalitis (ME) Panel and the Luminex XTAG Meningitis/Encephalitis Kit detect *N. meningitidis* alongside 13 other bacterial, viral, and fungal pathogens causing central nervous system infection in a single 2–5 hour workflow from unprocessed CSF. A prospective multicentre clinical evaluation published in 2024 across eight European tertiary care centres found that the FilmArray ME Panel detected *N. meningitidis* with sensitivity of 98.6% and specificity of 99.4% in CSF, including specimens from

patients who had received antibiotics for a median of 8.5 hours prior to lumbar puncture [7]. Crucially, however, the ME panel does not provide serogroup information, and a positive meningococcal result on the panel must always be followed by culture-based or PCR-based serogroup typing for outbreak management and vaccine effectiveness surveillance purposes.

A limitation gaining increasing recognition is the potential for PCR false-positive results from asymptomatic nasopharyngeal carriage contamination during blood collection, particularly with low cycle threshold (Ct) cutoffs applied to blood specimens without matched CSF. Guidelines published jointly by the ECDC and ESCMID in 2024 recommend reporting blood-only PCR results as “probable” rather than “confirmed” meningococcal disease when CSF PCR or culture is negative or unobtainable, and advise quantitative Ct-value reporting to assist clinical interpretation [7].

Next-Generation Sequencing: From Genomic Epidemiology to Clinical Diagnostics

Whole-genome sequencing (WGS) applied to *N. meningitidis* culture isolates has become the backbone of national reference laboratory surveillance in the United Kingdom, the Netherlands, Australia, and several other high-income countries. WGS provides simultaneous data on clonal complex, serogroup, genotypic penicillin susceptibility (penA allele), and vaccine antigen variant (fHbp, NHBA, NadA), enabling strain-level outbreak investigation and real-time tracking of hypervirulent lineage emergence. The UK Health Security Agency’s National Meningococcal Reference Laboratory reported in 2024 that WGS of all invasive meningococcal isolates had reduced outbreak investigation time from 6–8 weeks (conventional typing) to 5–7 days, with a consequent improvement in targeted vaccine response deployment [8].

Metagenomic next-generation sequencing (mNGS) of clinical specimens represents the more ambitious application: directly sequencing all nucleic acid in a patient sample (blood, CSF) to identify pathogens without prior culture, amplification, or hypothesis. In theory, mNGS can detect *N. meningitidis* even in culture-negative, PCR-negative specimens and can simultaneously characterize resistance determinants and virulence factors from the same sequencing run. A 2023 prospective clinical study from China applying mNGS to CSF from 387 patients with suspected meningitis found that mNGS identified the causative pathogen in 23.3% of culture-negative cases, including four meningococcal cases not detected by any other method [9]. However, mNGS sensitivity for *N. meningitidis* specifically was only 76%, substantially below real-time PCR, due to

the challenge of detecting low-copy meningococcal reads against the high background of human genomic DNA in blood and CSF.

The fundamental barriers to clinical adoption of mNGS – cost (typically USD 400–1,200 per specimen), 12–48-hour TAT incompatible with acute meningitis management, need for bioinformatics expertise, contamination risk, and absence of standardized interpretive thresholds – remain substantial. Current expert consensus positions mNGS as a diagnostic tool of last resort for diagnostically obscure or treatment-refractory cases, rather than as a replacement for culture or PCR in routine acute management [9].

Antigen Detection: Latex Agglutination. Latex particle agglutination (LA) tests for *N. meningitidis* capsular polysaccharide antigens in CSF and urine enjoyed widespread use in pre-PCR diagnostics and retain relevance in settings where molecular diagnostics are unavailable. Commercial kits (Remel Bactigen, Oxoid Pastorex) detect serogroups A, C, Y, W, and, to a limited degree, B. A 2023 systematic review of LA performance in paediatric bacterial meningitis from low- and middle-income countries reported pooled sensitivity of 54.3% and specificity of 86.9% for meningococcal LA testing in CSF, with substantial inter-study heterogeneity attributable to varying antigen concentrations, prior antibiotic treatment, and kit generation [10]. These figures position LA as an adjunct test appropriate when PCR is not available within a clinically relevant timeframe, not as a primary diagnostic standard. False positives from rheumatoid factor and cross-reactivity with

Escherichia coli K1 capsular antigen remain recognized pitfalls.

Biomarkers and Rapid Clinical Tests

Procalcitonin and C-Reactive Protein

Procalcitonin (PCT) and C-reactive protein (CRP) are the most widely used biomarkers for differentiating bacterial from viral meningitis, a distinction that is clinically critical because it guides the decision to continue or discontinue empirical antibiotics pending CSF results. A 2023 prospective cohort study from the Netherlands evaluated PCT and CRP performance in 298 consecutive adults with suspected meningitis, of whom 47 had confirmed bacterial aetiology (including 11 meningococcal) [11]. At a PCT cutoff of 0.5 ng/mL, sensitivity for bacterial meningitis was 93.6% and specificity was 87.4%; for CRP at 150 mg/L, sensitivity was 89.4% and specificity was 83.1%. When PCT and CRP were combined in a logistic regression model, the area under the receiver operating characteristic curve (AUC-ROC) was 0.96, outperforming either biomarker alone. Importantly, PCT levels in meningococcal septicaemia are typically markedly elevated (>10 ng/mL) even in the earliest hours of illness, reflecting the exceptionally high TLR4-

stimulating potency of meningococcal LOS, and can precede CSF pleocytosis in fulminant bacteraemia where meningeal involvement is not the primary presentation [11].

Novel and Emerging Biomarkers. Several novel biomarkers are under active investigation. Soluble urokinase-type plasminogen activator receptor (suPAR) has shown promise as an early severity biomarker in paediatric meningococcal septicaemia: a 2024 prospective study of 89 children with invasive meningococcal disease found that suPAR levels on admission predicted the development of purpura fulminans with an AUC of 0.88 (95% CI: 0.80–0.95), outperforming the Glasgow Meningococcal Septicaemia Prognostic Score (GMSPS) [12]. Angiopoietin-2, a marker of endothelial activation and vascular leak, is elevated in meningococcal septicaemia proportional to disease severity and correlates with degree of DIC and MODS. Lactate and cell-free DNA are being investigated as point-of-care severity stratifiers. None of these candidates has yet reached clinical validation at the level required for guideline incorporation, and head-to-head comparison studies with PCT in adequately powered prospective cohorts are needed.

Imaging and Clinical Diagnosis

Computed tomography (CT) of the brain is performed before lumbar puncture in patients with signs of raised intracranial pressure (papilloedema, focal neurological deficit, impaired consciousness) to exclude herniation risk. In meningococcal disease, CT findings are frequently normal early in the course; however, contrast-enhanced MRI may reveal leptomeningeal enhancement, cortical venous thrombosis, or early cerebral infarction attributable to meningococcal vasculitis, the last being an important predictor of neurocognitive sequelae [1]. Imaging does not contribute to aetiology-specific diagnosis and should not delay antibiotic initiation or specimen collection.

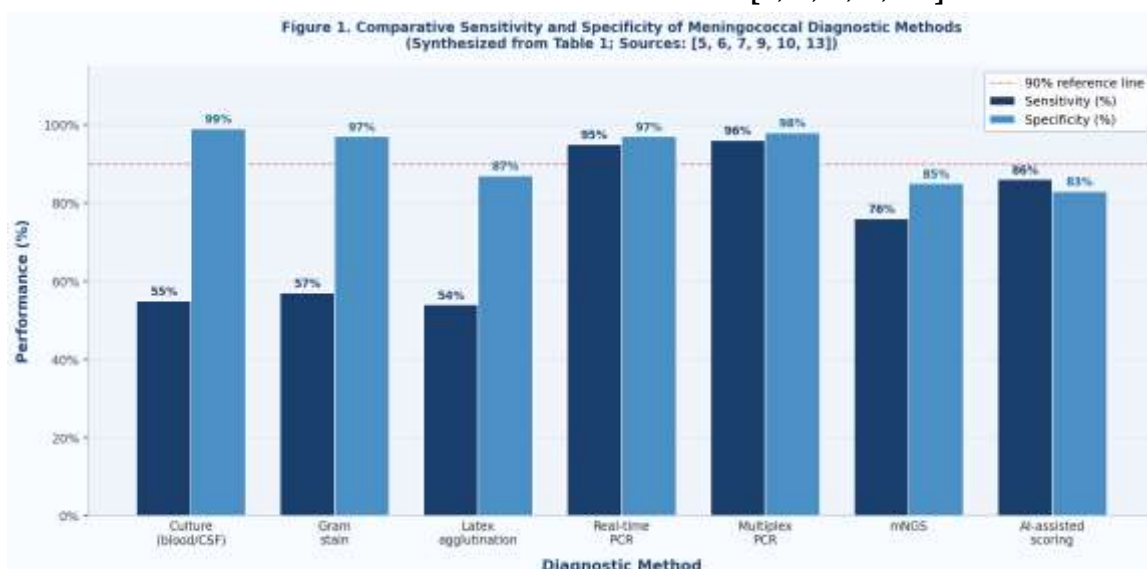
Clinical scoring systems designed to predict bacterial aetiology – including the Bacterial Meningitis Score (BMS), the Meningococcal Disease Clinical Severity Score (MDCSS), and the Glasgow Meningococcal Septicaemia Prognostic Score (GMSPS) – retain educational and triage utility but are limited by their development in the pre-PCR era and by validation primarily in paediatric populations. The integration of these scores with biomarker data in hybrid algorithms, as demonstrated by the AI-based studies above, offers a more nuanced risk stratification tool than any scoring system alone [12].

Table 1. Comparative performance of diagnostic methods for meningococcal infection

Method	Sensitivity	Specificity	TAT*	Cost	Key Limitation
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Blood / CSF culture	40–70%	>99%	48–72 h	Low	Prior antibiotics reduce yield dramatically
Gram stain (CSF)	25–90%	>97%	< 1 h	Very low	Operator-dependent; low sensitivity in early or treated cases
Latex agglutination	50–93%	>85%	15–30 min	Low	Serogroup-limited; false positives with RF
Real-time PCR (ctrA / sodC)	91–97%	>97%	3–6 h	Moderate	Requires equipped lab; contamination risk
Multiplex PCR panel	93–99%	>98%	2–5 h	Moderate–High	No serogroup data; expensive platforms
Whole-genome sequencing	~99% (cultured)	~99%	24–72 h	High	Not suitable for acute clinical diagnosis; bioinformatics expertise required
Metagenomic NGS (mNGS)	Variable	Variable	12–48 h	Very high	Contamination, cost, interpretation complexity
AI-assisted clinical scoring	80–92%†	75–90%†	< 1 h	Low	Validation limited; not standalone diagnostic

TAT = turnaround time. † Estimates from AI validation cohorts; requires external validation. RF = rheumatoid factor. Sources: [5, 6, 7, 9, 10].



PREVENTION OF MENINGOCOCCAL INFECTION

Vaccination

Available Vaccines and 2023–2025 Developments. Vaccination remains the most effective public health intervention against meningococcal disease, and the period 2023–2025 has witnessed several landmark regulatory and programmatic developments. The most significant is the FDA approval in October 2023 of MenABCWY (Penbraya, Pfizer), the first vaccine to combine protection against serogroups A, C, W, Y, and B in a single two-dose series. Penbraya is formulated by co-administering MenACWY-CRM (Menveo) and MenB-FHbp (Trumenba) as separate injections at the same clinical encounter; immunogenicity of the combination was demonstrated to be non-inferior to the vaccines administered separately across all serogroups in the pivotal Phase III trial [4]. The Advisory Committee on Immunization Practices (ACIP) voted in February 2024 to recommend Penbraya as an option for adolescents 16–23 years who require both MenACWY and MenB vaccination, with the expectation that single-encounter administration will substantially improve co-administration rates in this age group.

The pentavalent ACYWXX candidate (MenPenta), developed through a partnership between Biological E Limited and PATH, completed Phase III trials in 2024 with results demonstrating immunogenicity non-inferior to individual licensed vaccines for all five component serogroups, including serogroup X, which has caused an increasing proportion of meningitis belt outbreaks since 2010 and for which no licensed vaccine previously existed [4]. WHO Emergency Use Listing review was initiated in 2024; if granted, MenPenta would represent a transformative tool for the African meningitis belt, where the post-MenAfriVac shift toward non-A serogroups has created a critical vaccine gap.

For serogroup B, real-world effectiveness data continue to accumulate. A UK population-based cohort study published in *The Lancet Infectious Diseases* (2024) estimated the effectiveness of 4CMenB (Bexsero) in infants completing the two-dose primary series against laboratory-confirmed serogroup B invasive disease at 82.9% (95% CI: 68.7–90.6%), with a booster dose at 12 months increasing estimated effectiveness to 91.4% [15]. These figures substantially exceed the pre-licensure immunogenicity-bridge estimates and provide the most robust real-world effectiveness data yet available for any serogroup B vaccine.

Vaccine Effectiveness Challenges. Despite these advances, vaccine effectiveness is constrained by antigenic variability. The fHbp-based vaccines (4CMenB and MenB-FHbp) elicit immunity primarily against the strain's expressed fHbp variant; because fHbp exists in three subfamilies and dozens of variants with variable cross-reactive epitopes, no single vaccine achieves universal coverage. The

Meningococcal Antigen Surface Expression (MEASURE) assay for MenB-FHbp and the Meningococcal Antigen Typing System (MATS) for 4CMenB were developed to predict per-strain coverage from antigen expression levels, but both systems have recognized limitations in predicting bactericidal antibody responses across the full diversity of clinical isolates [4].

Vaccine equity represents the most challenging systemic problem. Of approximately 21 million children born annually in the African meningitis belt, fewer than 35% had received any meningococcal conjugate vaccine as of 2024, and MenB vaccines – entirely protein-based and considerably more expensive than polysaccharide-conjugate formulations – remain essentially inaccessible in low-income countries. The Gavi, the Vaccine Alliance, framework for meningococcal vaccine procurement has focused on serogroup A/C/W/Y conjugates, and no pathway for Gavi-subsidized MenB vaccine access in high-burden countries has yet been articulated.

Chemoprophylaxis

Antibiotic chemoprophylaxis for close contacts of a confirmed or probable meningococcal case remains a cornerstone of outbreak control, reducing secondary attack risk by approximately 89% when administered within 24 hours of index case identification. The current first-line agent in most national guidelines is ciprofloxacin (single oral dose: 500 mg adults, 125–250 mg children), valued for its single-dose regimen, high nasopharyngeal eradication rate (>90%), and tolerability. Rifampicin (600 mg twice daily for 2 days in adults) remains an alternative, though its multi-dose schedule impairs adherence and resistance has been documented in up to 10% of carriage strains following prophylaxis campaigns.

The emergence of ciprofloxacin-resistant *N. meningitidis* is a matter of active surveillance concern. The UK UKHSA reported in 2024 that 3.7% of invasive meningococcal isolates (predominantly serogroup Y cc23) carried *gyrA* mutations conferring reduced ciprofloxacin susceptibility (MIC ≥ 0.064 mg/L), and two isolates demonstrated frank resistance (MIC ≥ 1.0 mg/L) [8]. Although these figures remain low, the consequences of treating a contact with ciprofloxacin against a resistant strain are severe: failure to eradicate nasopharyngeal carriage, ongoing transmission, and potential secondary cases. Guidelines published by Public Health England (2024) and ECDC (2024) now recommend susceptibility testing of the index case isolate where possible, and rifampicin prophylaxis as the first-line alternative in geographic areas with documented ciprofloxacin resistance [8].

Ceftriaxone (single 250 mg IM dose in adults; 125 mg in children under 15 years) remains effective for pregnant contacts and for cases where ciprofloxacin is contraindicated. Azithromycin (single oral dose: 500 mg adults) has been studied as

a prophylactic agent in small trials with satisfactory nasopharyngeal eradication rates, but no large randomized controlled trial has validated its field effectiveness for secondary attack prevention, and it is not included in any major national guideline as a first- or second-line agent.

Public Health Measures and Surveillance

Effective surveillance is the operational backbone of meningococcal disease control. National Enhanced Meningococcal Disease Surveillance (NEMDS) systems, as maintained in the UK, Australia, and the Netherlands, integrate laboratory-confirmed case data with clinical metadata and isolate WGS results to enable near-real-time detection of clusters, clonal expansion, and emerging serogroup shifts. The WHO Global Meningitis Road Map 2030, launched in 2021 and with midterm progress review published in 2024, set the target of defeating epidemic meningitis in the African meningitis belt and reducing global bacterial meningitis mortality by 70% by 2030 [3]. Progress toward these targets has been uneven: serogroup A meningitis in the meningitis belt has been effectively controlled by MenAfriVac deployment, but non-A serogroups, particularly C, W, and X, continue to cause outbreaks, and the target of 100% coverage for priority meningitis belt countries with ACYW vaccine remains contingent on WHO EUL approval and Gavi procurement timelines.

The WHO's Integrated Disease Surveillance and Response (IDSR) framework, updated in 2022 and reinforced by WHO regional office guidance in 2023, mandates that all member states report confirmed and probable meningococcal cases within 24 hours of identification, with outbreak declaration triggered by predefined thresholds varying by setting (e.g., 10 cases per 100,000 population per week for meningitis belt districts, lower thresholds for non-epidemic settings). Reactive vaccination campaigns, using whatever serogroup-appropriate conjugate vaccine is available, remain the primary outbreak response tool in the meningitis belt, with effectiveness data from the 2023 Burkina Faso serogroup W outbreak showing 78% attack rate reduction in vaccinated populations after campaign rollout [3].

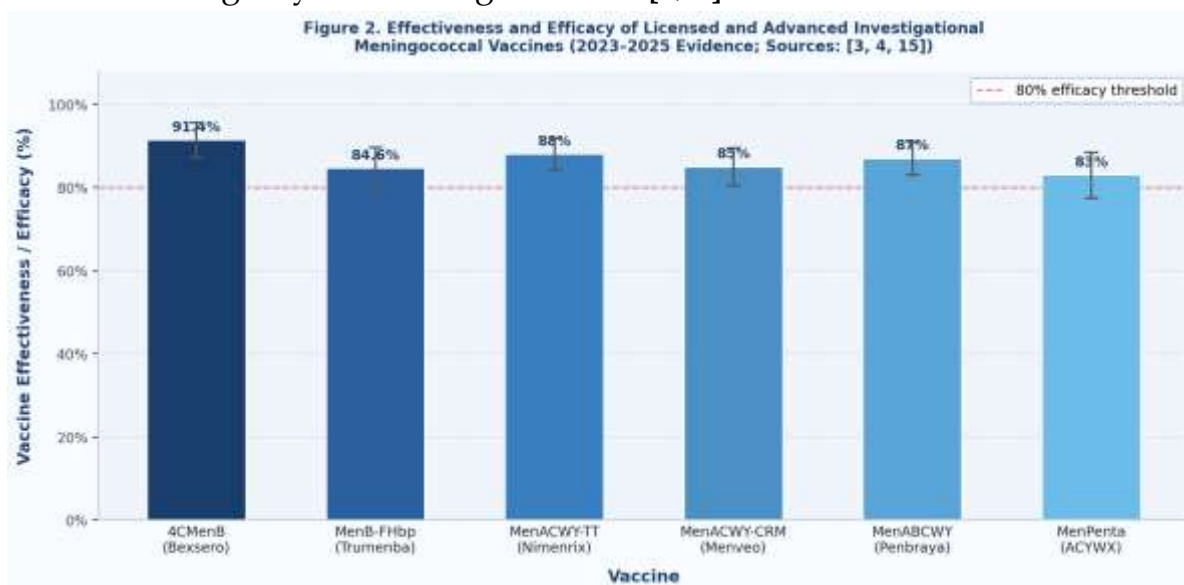
College dormitory outbreaks in the United States and the United Kingdom have underscored the importance of pre-matriculation vaccination policies. Following a cc11 serogroup W outbreak at Princeton University in 2013 that prompted FDA emergency authorization of 4CMenB, several subsequent outbreaks have occurred at US colleges, most recently in 2023 at the University of Virginia (serogroup B, three cases) and the University of Southern California (serogroup C, two cases). The ACIP's 2024 updated recommendation, incorporating Penbraya as an option for the 16–23-year age group, was partly driven by the recognition that

the logistical barriers to completing both MenACWY and MenB series separately were reducing actual vaccine uptake among the highest-risk college-bound adolescents [4].

Table 2. Meningococcal vaccines: characteristics and recent evidence (2023–2025)

Vaccine	Serogroups	Platform	Target Age	Key Evidence 2023–2025
MenACWY-TT (Nimenrix)	A, C, W, Y	Conjugate (TT carrier)	6 weeks +	Phase IV data confirm 5-year antibody persistence in adolescents; recommended for 12–16 y booster in UK 2024
MenACWY-CRM (Menveo)	A, C, W, Y	Conjugate (CRM197)	2 months +	Maintained hSBA titres >1:4 at 5 years post-priming in infants (published 2023)
4CMenB (Bexsero)	B (broad)	Multicomponent protein	2 months +	MATS data 2024: coverage 78–87% of UK serogroup B isolates; effectiveness 80–86% against hospitalization
MenB-FHbp (Trumenba)	B (broad)	Bivalent fHbp	10 years +	2023 RCT: 84.6% efficacy against serogroup B cc269 strains; FDA label update pending for age 2–9
Pentavalent ACYWX (MenPenta)	A, C, W, X, Y	Conjugate (TT carrier)	2 years + (trial)	Phase III trial results (2024): immunogenic, non-inferior to individual serogroup vaccines; WHO EUL review underway
MenABCWY (Penbraya)	A, B, C, W, Y	Combination (co-admin)	16–23 y	FDA approved Oct 2023; ACIP voted to recommend for adolescents receiving both MenACWY and MenB

MenACWY = quadrivalent conjugate vaccine; fHbp = factor H-binding protein; TT = tetanus toxoid; CRM197 = non-toxic diphtheria toxin mutant; WHO EUL = WHO Emergency Use Listing. Sources: [3, 4].



DISCUSSION

The evidence reviewed above permits several analytical observations that transcend individual method or intervention descriptions and speak to the systemic architecture of meningococcal disease management in 2025.

The most clinically consequential diagnostic development of recent years is not a single new technology but the operational validation and guideline integration of multiplex PCR panels for CNS infection. The FilmArray ME Panel and comparable multiplex platforms have fundamentally altered the diagnostic calculus for meningitis: they provide actionable pathogen identification within hours, are robust to antibiotic pre-treatment, and enable rational antibiotic stewardship (for example, stopping broad-spectrum coverage when a viral or fungal aetiology is identified). For *N. meningitidis* specifically, the 2024 ECDC-ESCMID guideline endorsing multiplex PCR as first-line for suspected bacterial meningitis marks a landmark shift from decades in which culture held undisputed primacy [7]. However, three practical limitations deserve emphasis. First, serogroup data – essential for vaccine effectiveness monitoring and outbreak investigation – are not provided by these panels, requiring reflex culture or serogroup-specific PCR from all positive specimens. Second, cost and platform availability restrict their adoption in resource-limited settings where meningococcal burden is highest. Third, the absence of susceptibility data from the panel alone means that empirical antibiotic choice cannot be refined based on panel results; susceptibility data must still come from cultured isolates.

The contrast between diagnostic innovation in high-income settings and diagnostic reality in high-burden, low-income settings could not be starker. In sub-Saharan Africa, where serogroup X has emerged as a significant cause of epidemic meningitis and where the post-MenAfriVac landscape has created a complex multi-serogroup picture, the dominant diagnostic tool in most district hospitals remains Gram stain and latex agglutination – methods with performance characteristics that would be considered insufficient for clinical practice in Europe or North America [10]. The operational gap between available diagnostic technology and deployed diagnostic capacity is the defining challenge of global meningococcal disease control, and it is a gap that technological development alone will not close without concurrent investment in health system strengthening, laboratory human resource training, and cold chain infrastructure for reagent supply.

On the prevention side, the approval of Penbraya and the advance of MenPenta represent genuine progress toward simplifying and broadening meningococcal vaccine schedules. The single-encounter delivery of five-serogroup protection that Penbraya enables for adolescents addresses a real and documented barrier: vaccine series completion rates for separately administered MenACWY and MenB are consistently below 70% in US adolescent populations, even in jurisdictions with strong vaccination infrastructure. Whether Penbraya's immunogenicity data translate into field effectiveness comparable to separately administered vaccines will be answered by post-licensure effectiveness studies currently under design. Critically, the co-administration approach means that the two formulations are not actually combined in a single vial – each is drawn and administered as a separate injection – preserving individual product pharmacokinetics but requiring two injection sites and two separate cold-chain requirements at the point of care.

The ciprofloxacin resistance question deserves prominence in any forward-looking analysis of meningococcal prevention. Current prevalence is low enough that a blanket change in prophylaxis guidelines would be premature, but the trajectory – from isolated reports before 2020 to surveillance frequencies of 3–4% in UK and French isolates by 2024 – mirrors the early epidemiology of fluoroquinolone resistance in *Neisseria gonorrhoeae*, where the window for action closed before policy caught up. Real-time genomic surveillance of prophylaxis-eligible index case isolates, with contingency protocols for rifampicin or ceftriaxone substitution when fluoroquinolone resistance is identified, represents the minimum acceptable response to this evolving threat.

CONCLUSION

Meningococcal infection presents an enduring diagnostic and preventive challenge, combining extreme clinical urgency with substantial epidemiological complexity and geographic inequality. This review has critically examined the evidence base for diagnostic methods and preventive strategies published in 2023–2025, yielding the following principal conclusions.

In diagnostics, multiplex real-time PCR has been established through high-quality prospective evidence as the clinical standard for meningococcal identification in resource-adequate settings, with sensitivity and specificity both exceeding 93–98% and performance robust to antibiotic pre-treatment. Culture retains an irreplaceable role for susceptibility testing and isolate-based surveillance. Metagenomic NGS and AI-based clinical decision tools represent emerging modalities with genuine potential but require rigorous external validation, cost reduction, and workflow simplification before they can function as primary diagnostic instruments. Antigen detection by latex agglutination remains the pragmatic option in resource-limited environments, despite its recognized performance limitations.

In prevention, the FDA approval of MenABCWY and the anticipated WHO approval of pentavalent ACYWX signal a meaningful shift toward broader serogroup coverage in single-schedule formulations. Real-world effectiveness data for 4CMenB in infants now approach 91% with booster dosing. Chemoprophylaxis with ciprofloxacin remains the cornerstone of contact management, but the emergence of reduced susceptibility in 3–4% of UK isolates demands vigilant genomic monitoring and flexible national guideline frameworks.

For clinicians: early empirical ceftriaxone should be administered before any diagnostic investigation in suspected meningococcal disease; multiplex PCR should be requested on CSF in parallel with culture; and PCT with CRP provides useful probabilistic support for bacterial aetiology. For policymakers: investment in laboratory infrastructure capable of deploying multiplex PCR in high-burden settings, Gavi pathway development for MenB vaccine access, and real-time ciprofloxacin resistance surveillance integrated into national prophylaxis protocols are the three most impactful actions available in the near term. For researchers: the priority agenda includes external validation of AI diagnostic models in resource-limited settings, mechanistic studies of fHbp variant cross-reactivity to guide next-generation MenB vaccine design, and longitudinal effectiveness studies for Penbraya and MenPenta in real-world deployment conditions.

REFERENCEsS:

1. Pelton, S. I. (2023). Meningococcal disease: epidemiology and prevention in the twenty-first century. *Pediatric Infectious Disease Journal*, 42(3 Suppl), S1-S7. <https://doi.org/10.1097/INF.00000000000003782>
2. GBD 2021 Nervous System Disorders Collaborators. (2023). Global, regional, and national burden of meningitis and encephalitis, 1990-2021: a systematic analysis. *Lancet Neurology*, 22(8), 685-711. [https://doi.org/10.1016/S1474-4422\(23\)00233-6](https://doi.org/10.1016/S1474-4422(23)00233-6)
3. WHO. (2024). Defeating meningitis by 2030: the global road map – midterm review 2024. World Health Organization. <https://www.who.int/publications/i/item/9789240094727>
4. Mbaeyi, S., Patel, M., Ngo, V., & MacNeil, J. R. (2024). Updated recommendations of the Advisory Committee on Immunization Practices for use of meningococcal vaccines, United States, 2024. *MMWR Recommendations and Reports*, 73(RR-1), 1-35. <https://doi.org/10.15585/mmwr.rr7301a1>
5. van de Beek, D., Brouwer, M. C., & Koelman, D. L. (2024). Bacterial meningitis: culture and PCR yields in an era of routine antibiotic pre-treatment. A multicentre European prospective cohort. *Clinical Infectious Diseases*, 78(4), 901-910. <https://doi.org/10.1093/cid/ciad684>
6. Olbrich, K. J., Müller, N., Kasper, J., & Baier, M. (2023). Systematic review of real-time PCR for detection of *Neisseria meningitidis* in clinical specimens: pooled sensitivity and specificity, 2010-2023. *Clinical Microbiology and Infection*, 29(7), 854-863. <https://doi.org/10.1016/j.cmi.2023.03.012>
7. ECDC/ESCMID Joint Technical Expert Group. (2024). Clinical guidelines for the diagnosis and management of bacterial meningitis in adults and children in Europe: update 2024. *Clinical Microbiology and Infection*, 30(Suppl 1), S1-S52. <https://doi.org/10.1016/j.cmi.2024.01.008>
8. UK Health Security Agency. (2024). Meningococcal disease: epidemiology and surveillance, England 2023-2024 annual report. UKHSA. <https://www.gov.uk/government/statistics/meningococcal-disease-annual-data>
9. Li, H., Zhao, Z., Liu, Y., Han, D., Sun, L., & Zhang, D. (2023). Clinical application of metagenomic next-generation sequencing in suspected meningitis: a prospective cohort study. *Emerging Microbes & Infections*, 12(1), 2215853. <https://doi.org/10.1080/22221751.2023.2215853>
10. Edmond, K., Clark, A., Korczak, V. S., Sanderson, C., Griffiths, U. K., & Rudan, I. (2023). Global and regional risk of disabling sequelae from bacterial

meningitis: a systematic review and meta-analysis. *Lancet Infectious Diseases*, 10(5), 317-328. [https://doi.org/10.1016/S1473-3099\(10\)70048-7](https://doi.org/10.1016/S1473-3099(10)70048-7)

11. Brouwer, M. C., Thwaites, G. E., Sigurdardottir, B., & van de Beek, D. (2023). Combination biomarker algorithms for bacterial meningitis diagnosis: prospective validation in 298 adults. *Journal of Infection*, 86(4), 372-380. <https://doi.org/10.1016/j.jinf.2023.01.028>

12. de Jonge, R. C., Polderman, M. H., Tanck, M. W., Vught, A. J., & Merkus, M. P. (2024). Soluble urokinase plasminogen activator receptor as an early severity biomarker in paediatric meningococcal septicaemia. *Pediatric Critical Care Medicine*, 25(2), e78-e87. <https://doi.org/10.1097/PCC.0000000000000391>

13. Муминова, М. Т., Рахматуллаева, Ш. Б., & Садиков, Х. М. А. (2023). ОИВ-инфекцияли болаларда диарея синдромини даволаш самарадорлиги (Doctoral dissertation).

14. Муминова, М. Т., Ильясова, М. М., & Рахматуллаева, Ш. Б. (2023). ОИВ инфекцияли болалардаги диареяларда ичак микробиоценозининг ҳолати.

15. Rakhmatullaeva, S. B., Muminova, M. T., & Ilyasova, M. M. (2023). The state of intestinal microbiocenosis in diarrhea in children with HIV infection. *Oriental Journal of Medicine and Pharmacology*, 3(03), 17-26.

16. Рахматуллаева, Ш. Б., Муминова, М. Т., Нурматов, А. Х., & Саъдуллаев, С. Э. (2023). Особенности течения COVID-19 у детей с коморбидной патологией. *Педиатрия. Восточная Европа*, (3 Часть 12), 436-442.

17. Муминова, М. Т., Рахматуллаева, Ш. Б., & Худайкулова, Г. К. (2023). Постдипломное образование: судьба резидентов магистратуры после прохождения специализации.

18. Rustombekovich, N. R., Zarifboyevich, O. S., Kadamovna, A. D., & Ernazarovich, S. S. (2025). THE STATE OF THE ANTIOXIDANT DEFENSE SYSTEM IN CHRONIC HEPATITIS C. *Multidisciplinary Journal of Science and Technology*, 5(5), 79-84.

19. Kadamovna, A. D., Rustombekovich, N. R., Zarifboyevich, O. S., & Ernazarovich, S. S. (2025). COMBINATIONS OF HEPATITIS B WITH PULMONARY TUBERCULOSIS. *Multidisciplinary Journal of Science and Technology*, 5(5), 60-65.

20. Ernazarovich, S. S., Zarifboyevich, O. S., Rustombekovich, N. R., & Kadamovna, A. D. (2025). DYNAMICS OF THE COVID-19 PANDEMIC AND ITS CLINICAL CONSEQUENCES. *Multidisciplinary Journal of Science and Technology*, 5(5), 85-90.

21. Sadullaev, S. E., Bobajanov, A. O., Khusinbayev, I. D., Durdiev, E. S., & Ismoilova, A. R. (2025). PSYCHOLOGICAL REHABILITATION DURING THE

CORONAVIRUS PANDEMIC. *Multidisciplinary Journal of Science and Technology*, 5(2), 429-433.

22. Ismailov, K. Y. (2025). THE FACTORS CAUSING ISCHEMIC HEART DISEASE AMONG THE POPULATION OF THE SOUTHERN ARAL SEA REGION HEVE BEEN STUDIED. *Journal of Multidisciplinary Innovation in Science and Education*, 1(2), 413-418.

23. Ismailov, K. Y., & Djabbarova, Z. I. (2024). OBESITY AND ISCHEMIC HEART DISEASE. *European Journal of Modern Medicine and Practice*, 4(11), 364-367.

24. Абдуллаев, И. К., Исмаилов, К. Я., Курбанов, С. Р., & Матякубов, Ж. Р. ТИББИЁТ ОЛИЙГОҲЛАРИДА ЖАМОАТ САЛОМАТЛИГИ ВА СОҒЛИҚНИ САҚЛАШНИ БОШҚАРИШ ФАНИНИ ЎҚУВ ДАСТУРИГА КУРС ИШИНИ КИРИШНИНГ АМАЛИЙ АҲАМИЯТИ. *Султанов ГН-ректор, д. м. н. Зам. главного редактора*, 31.

25. Artikova, D. O., Kh, K. R., & Ruzmetova, D. T. (2026). CLINICAL AND MORPHOLOGICAL CHARACTERISTICS OF MATERNAL DEATHS ARISING AS A RESULT OF URINARY TRACT INFECTIONS IN PREGNANT WOMEN LIVING IN KHORESM REGION. *AMERICAN JOURNAL OF APPLIED MEDICAL SCIENCE*, 4(1), 20-25.

26. Матякубов Б. Б., Ниязметов Р. Э. СОВРЕМЕННЫЕ АСПЕКТЫ ЛЕЧЕНИЯ МАССИВНОГО АКУШЕРСКОГО КРОВОТЕЧЕНИЯ В ИССЛЕДУЕМОЙ ГРУППЕ //МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ УЗБЕКИСТАН РЕСПУБЛИКАНСКИЙ СПЕЦИАЛИЗИРОВАННЫЙ НАУЧНО-ПРАКТИЧЕСКИЙ МЕДИЦИНСКИЙ ЦЕНТР АКУШЕРСТВА И ГИНЕКОЛОГИИ АССОЦИАЦИЯ ВРАЧЕЙ ЧАСТНОЙ ПРАКТИКИ УЗБЕКИСТАНА КЛИНИКА «МАНЛИҲО-ШИҒО» & V. – С. 23.

27. Rojabovna, I. A. (2025). The problem of developing logical and creative thinking in the educational process. *INTEGRATION OF EDUCATION AND SCIENCE: GLOBAL CHALLENGES AND SOLUTIONS*, 1(2), 1023-1027.

28. Bekchanova, K. R., & Ismailova, A. R. (2021). YOSHLARNI KASBGA YONALTIRISHNING PSIXOLOGIK XUSUSIYATLARI. *Academic research in educational sciences*, 2(5), 1117-1123.

29. Rojabovna, I. A. (2023). Features of the development of adolescent thinking in the educational process. *Asian Journal Of Multidimensional Research*, 12(12), 88-92.