

# Clinical impact of metagenomic next-generation sequencing testing on cerebrospinal fluid in a pediatric cohort with suspected central nervous system infections

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## Background

Clinical metagenomic next-generation sequencing (mNGS) testing of cerebrospinal fluid (CSF) has been shown to improve diagnostic yield in suspected central nervous system (CNS) infections. However, real-life impact on patient care and outcomes, especially for children, remains poorly understood.

## Methods

We retrospectively evaluated the clinical impact of mNGS testing in a cohort of 193 pediatric patients at University of California San Francisco, reviewing cases of suspected CNS infections who underwent CSF mNGS testing from 2016 to 2023.

## Results

Patients had a median age of 9 years [IQR 2 – 16], 43.0% females, 93.3% inpatient, 65.3% requiring an intensive care unit stay, and 31.6% immunocompromised. Mortality at day 60 post-mNGS testing was 8.3% (Table 1).

Criteria to assess clinical impact are listed in Figure 1A. Positive and negative clinical impact of CSF mNGS testing was observed in 38.4% and 0.5% of cases, respectively. Among the 74 positive clinical impact, concomitant CNS infection was ruled out in 17 cases (22.7%) and new infectious diagnoses were identified in 7 cases (9.3%). mNGS results led to a management change in 8 cases (10.7%), whereas the results from two additional cases prompted a public health investigation (Figure 1B).

Pediatric cohort characteristics (unique patient, n = 176)		Total (n=193)
Age	median [IQR]	9.0 [2.0,16.0]
Gender	Female, n (%)	83 (43.0)
Race	American Indian or Alaska Native, n (%)	5 (2.6)
	Asian, n (%)	31 (16.1)
	Black or African American, n (%)	13 (6.7)
	Native Hawaiian or Pacific Islander, n (%)	5 (2.6)
	White, n (%)	73 (37.8)
	Other, n (%)	80 (41.5)
Ethnicity	Latino/Hispanic, n (%)	80 (41.5)
	Other, n (%)	80 (41.5)
Main diagnostic category	AINI, n (%)	66 (34.2)
	Bacterial, n (%)	10 (5.2)
	DNA virus, n (%)	9 (4.7)
	Fungal, n (%)	5 (2.6)
	Parasitic, n (%)	3 (1.6)
	RNA virus, n (%)	6 (3.1)
	Unknown, n (%)	94 (48.7)
	Other, n (%)	42 (21.8)
Immunosuppression	No, n (%)	132 (68.4)
	HIV/AIDS, n (%)	1 (0.5)
	Bone-Marrow Transplant recipient, n (%)	19 (9.8)
	Chemotherapy, n (%)	3 (1.6)
	Immunomodulators, n (%)	11 (5.7)
	Congenital, n (%)	11 (5.7)
	Other, n (%)	16 (8.3)
	Not applicable (outpatient), n (%)	13 (6.7)
Clinical setting	Inpatient, n (%)	180 (93.3)
	Outpatient, n (%)	13 (6.7)
Patient in ICU	No, n (%)	54 (28.0)
	Yes, n (%)	126 (65.3)
	Not applicable (outpatient), n (%)	13 (6.7)
Presence of neurohardware	No, n (%)	178 (92.2)
	Yes, n (%)	15 (7.8)
Death within 60 days of mNGS testing	No, n (%)	177 (91.7)
	Yes, n (%)	16 (8.3)
Primary syndrome	None, n (%)	22 (11.4)
	Encephalitis, n (%)	50 (25.9)
	Meningitis, n (%)	49 (25.4)
	Myelitis, n (%)	9 (4.7)
	Meningoencephalitis, n (%)	21 (10.9)
Abnormalities found by brain biopsy	No, n (%)	1 (0.5)
	Yes, n (%)	7 (3.6)
	Not performed, n (%)	184 (95.8)

Table 1. UCSF Pediatric cohort characteristics

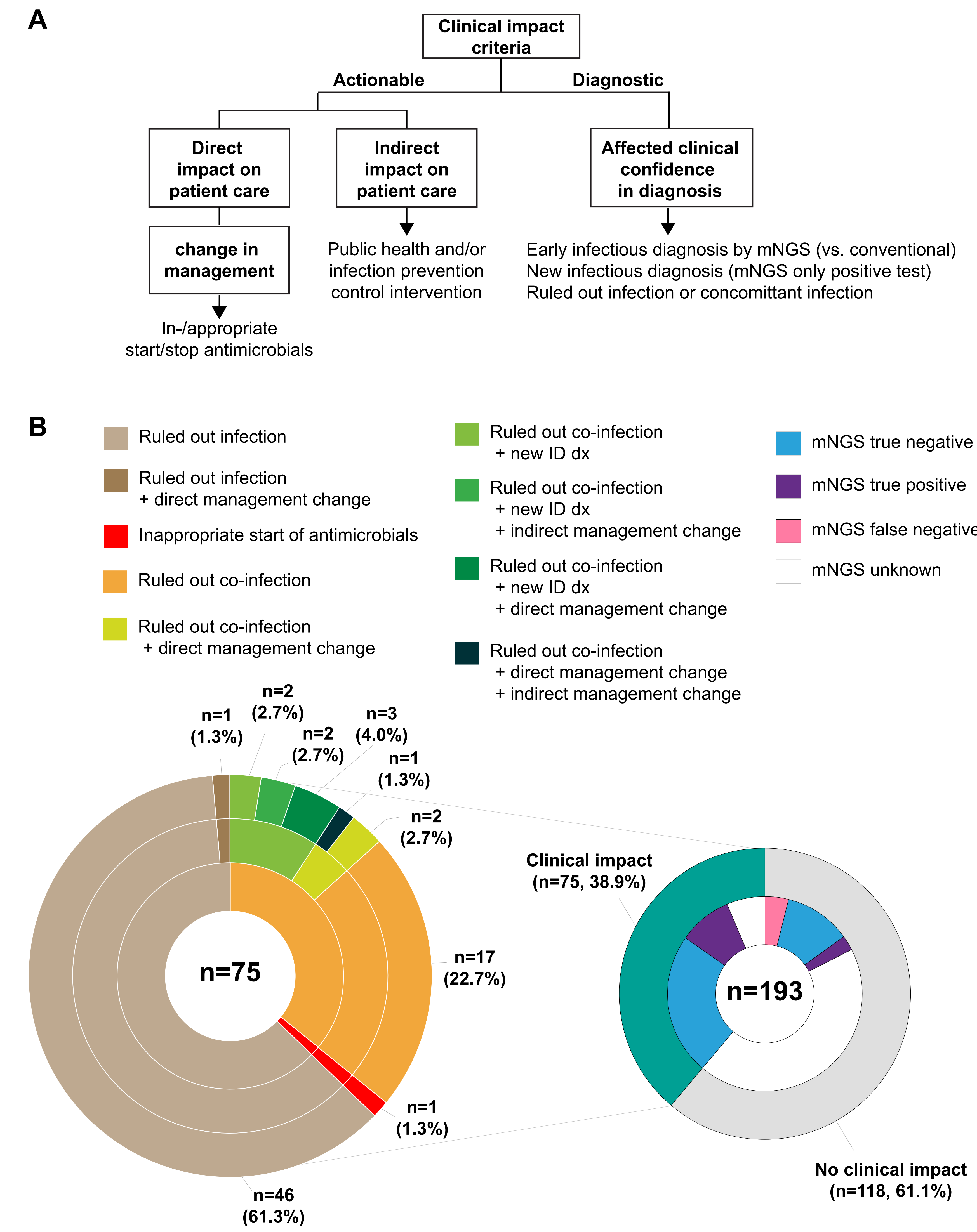


Figure 1. Clinical impact criteria (A) and results (B) based on clinical adjudication.

## Conclusion

CSF mNGS testing had a positive clinical impact in 38.9% of our pediatric cohort. Among the 61.1% of cases with no impact, more than half may have yielded actionable results with an 44.4% decrease in assay median turnaround time (from 9 to 4 days). Prioritizing strategies to reduce assay turnaround time would likely improve patient care management and enhance the clinical impact of CSF mNGS testing. In addition, our study shows that CSF mNGS is primarily used by clinicians as a rule-out test for CNS infections.