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Admission Absolute Eosinophil Count can Discriminate Influenza from Other Respiratory Pathogens in Hospitalized Children with Lower Respiratory Tract Infection

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Abstract

Background: Given that influenza is frequently diagnosed late in children when nucleic acid testing is unavailable, a low-cost indicator obtained from routine blood counts would be clinically useful. Therefore, we evaluated the absolute eosinophil count (EOS) in children with and without influenza.

Methods: This retrospective cohort study enrolled 252 hospitalized children with lower respiratory tract infections (122 with influenza and 130 without influenza). A multivariable linear regression was fitted with ln(EOS) as the dependent variable and influenza status as the exposure variable, adjusted for age, sex, and glucocorticoid exposure. Discriminant performance was assessed against routine hematological indices, high-sensitivity C-reactive protein (hs-CRP), and interleukin-6, using analyses including the area under the receiver operating characteristic curve (AUC). A paired subgroup of 92 children underwent repeat blood counts before discharge.

Results: Admission EOS in the influenza group (0.0175×10^9/L) was significantly lower than that in the non-influenza group (0.1565×10^9/L; $P < 0.001$). EOS below the reportable limit was detected in 76.2% of cases (adjusted odds ratio (OR) 6.61, 95% confidence interval (CI) 3.54–12.34), and median EOS was lower than that in all other groups (all $P < 0.001$). In the paired subgroup (44 influenza, 48 non-influenza), EOS increased from 0.0215 to 0.0745 $\times10^9$/L in children with influenza ($P < 0.001$) and from 0.0869 to 0.1363 $\times10^9$/L in children without influenza (P=0.087); the subgroup was underpowered to compare the magnitude of change between groups.

Conclusions: Influenza was associated with markedly lower admission EOS, which increased during recovery. EOS added discriminative information beyond routine hematological indices and hs-CRP, and its high negative predictive value supports EOS as a low-cost adjunct for frontline influenza recognition but not as a standalone trigger for antiviral therapy.

Keywords: Child; Diagnosis, Differential; Eosinopenia; Influenza, Human; Leukocyte Count; Retrospective Studies

1. Introduction

Influenza can progress to viral pneumonia or acute necrotizing encephalopathy in children [1,2]. In primary care, nucleic acid confirmation is often unavailable, delaying antiviral initiation [3,4]. In contrast, routine blood counts are available within minutes, among which the peripheral eosinophil count reduces early during acute viral infections, particularly influenza [5,6]. However, whether this drop in eosinophil count differs between influenza and other common respiratory pathogens in hospitalized children remains unclear. Although high-sensitivity C-reactive protein and interleukin-6 levels are also widely available, their discriminatory value in children remains uncertain.

Eosinopenia is not specific to influenza, as it also occurs with glucocorticoid use and in severe systemic inflammation [7–10]. In acute infection, this condition appears to reflect rapid margination of circulating eosinophils onto vascular endothelium driven by complement C5a and type I interferons rather than suppressed marrow output [11–13]. Subsequently, an influenza infection may further suppress T helper 2-dependent eosinophil recruitment through an interferon-γ-mediated T helper 1 shift [14,15]. Davido et al. found that absolute eosinopenia independently predicts influenza in outpatients [6], while pediatric studies have reported lower eosinophil counts in patients with influenza A/B than in those with coronavirus disease 2019 [16–18]. However, most of these comparisons involved patients with coronavirus disease 2019 or healthy controls, and only a few have compared influenza head-to-head with respiratory syncytial virus (RSV), rhinovirus, adenovirus, or viral-negative children in a single hospitalized cohort. Notably, none of the previous studies have quantified the incremental discriminant value of admission EOS over routine hematological indices or established inflammatory markers at this

stage of the illness. Recently, Kawasaki et al. compared eosinophil counts across respiratory syncytial virus, adenoviral, and influenza infections in 80 children in the acute and recovery phases and reported a recovery-phase increase confined to the RSV group [19].

Therefore, we aimed to (i) compare admission absolute eosinophil count (EOS) between children with and without influenza; (ii) compare EOS across five pathogen-defined groups, including a viral-negative group; (iii) describe the change in EOS from admission to pre-discharge in children with paired counts; and (iv) quantify the incremental discriminant value of EOS over routine hematological indices, high-sensitivity C-reactive protein (hs-CRP), and interleukin-6 (IL-6).

2. Methods

2.1 Study design and setting

This single-center retrospective cohort study was conducted at the Department of Pediatrics, Zunyi Maternal and Child Health Hospital, Guizhou, China, and included children with lower respiratory tract infections hospitalized between November 1, 2025, and February 28, 2026. This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [20], and the completed STROBE checklist is provided in Additional file 1.

2.2 Study population

We consecutively enrolled children aged ≤ 14 years who were hospitalized for lower respiratory tract infections at our department between November 2025 and February 2026 and presented with the same illness episode. Lower respiratory tract infection was defined by acute respiratory symptoms (cough, tachypnea, or dyspnea) and chest imaging findings on radiography or computed tomography (CT).

The inclusion criteria were age ≤ 14 years, hospitalization for lower respiratory tract infection, influenza A/B nucleic acid testing at admission with a complete baseline blood count, including EOS, and complete baseline demographic data. The exclusion criteria were antiviral therapy

before admission and missing core demographic or key hematological data. Pre-admission antiviral exposure was ascertained from the first progress note recorded on admission, in which the referral history, prior treatment, and current medication were documented. Children documented as having received a neuraminidase inhibitor or a cap-dependent endonuclease inhibitor were excluded. Antiviral, antibiotic, and glucocorticoid agents administered after admission were recorded as clinical variables. All baseline blood samples were obtained before the first in-hospital dose of any of these agents. Pre-admission medications other than antivirals were not abstracted (see limitations).

Of the 253 children screened, one was excluded due to incomplete demographics, leaving 252 for analysis **(Fig. 1).** These children were divided, according to the result of influenza A/B nucleic acid testing at admission, into an influenza group (n=122) and a non-influenza group (n=130). Among them, 92 children underwent repeat blood counts within 5 days before discharge, forming a paired subgroup (44 children with influenza and 48 children without influenza).

2.3 Data collection

The following data were extracted from the electronic medical record: demographics (age, sex, comorbidities); pathogens (influenza A/B nucleic acid testing in all children, and, when clinically requested, testing for respiratory syncytial virus, rhinovirus, adenovirus and *Mycoplasma pneumoniae*); hematology and inflammatory markers (EOS, eosinophil percentage, white blood cell count (WBC), neutrophil count, lymphocyte count (LYM) and monocyte count, hs-CRP and IL-6); co-infection and medications (sputum and blood cultures; antiviral [oseltamivir or baloxavir], antibiotic and glucocorticoid use); and outcomes (length of stay, nasal oxygen and respiratory support, maximum temperature, fever duration). Sputum culture was performed at the discretion of the treating physician and was unavailable for 43 of the 252 children (17.1%; 35/122 influenza vs 8/130 non-influenza). Recovery EOS was the value measured within five days before discharge, including the day of discharge. IL-6 levels were measured by chemiluminescence

immunoassay on a UniCel DxI 800 Access Immunoassay System (Beckman Coulter, Brea, CA, USA) with the manufacturer's reagents, on the same admission sample as the blood count. hs-CRP was measured by a latex-enhanced immunoturbidimetric assay on a Beckman Coulter AU480 chemistry analyzer (Beckman Coulter, Brea, CA, USA) with the manufacturer's high-sensitivity CRP reagent.

2.4 Definitions

Comorbidity was defined as a chronic condition documented before admission that was expected to affect the course or management of the current illness, including congenital heart disease, diaphragmatic eventration, and febrile seizures. Laryngitis was not considered a comorbidity because it was regarded as a manifestation of the current respiratory infection rather than a pre-existing condition. The viral-negative group comprised children who tested negative for influenza A/B, respiratory syncytial virus, rhinovirus and adenovirus but whose sputum culture was positive; the term denotes the absence of a detectable respiratory virus and does not imply the absence of bacterial pathogens. EOS below the reportable limit was defined as a value reported by the analyzer as 0 (true value below 0.05 $\times 10^9$/L), a threshold reflecting analytical precision rather than a clinical decision limit. Influenza-only infection was defined as a positive influenza A/B test without co-detection of respiratory syncytial virus, rhinovirus, or adenovirus. The five pathogen-defined groups used in this report comprise the influenza group and four comparator groups defined by the pathogens detected at admission: respiratory syncytial virus, rhinovirus, adenovirus, and viral-negative infection. Because a child could test positive for more than one pathogen, these groups overlap and their counts are not additive.

2.5 Outcome definitions

The primary laboratory endpoint was admission EOS, derived using a Sysmex XN-L automated hematology analyzer (Sysmex Corporation, Kobe, Japan) with the manufacturer’s original reagents as WBC × eosinophil percentage / 100. The analyzer reports WBC and eosinophil

percentage to two decimal places but rounds EOS to one decimal place and reports values below 0.05 $\times 10^9$/L as 0. Therefore, 126 of 252 children (50.0%) had an EOS reported as 0. Reconstructing EOS from WBC and the eosinophil percentage recovers finer resolution in the low range (minimum non-zero value 0.0037 $\times 10^9$/L, two orders of magnitude finer than the reporting interval). This reconstruction was validated internally; among the 126 children with a non-zero reported value, the reconstructed value rounded to one decimal place matched the reported value in all 126 cases (100%). Of the 126 children with a reported value of 0, the reconstructed value was positive in 90 and remained 0 in 36 (14.3% of the cohort; reconstructed zero group). The reported zero definition and reconstructed threshold identified exactly the same children; therefore, reconstruction changed the resolution without altering the classification. Because ln(EOS) requires a positive value, the midpoint of the zero interval (0.025 $\times 10^9$/L) was substituted for the 36 reconstructed-zero observations. Sensitivity analyses excluded these children or used reported values without reconstruction. EOS was compared with the laboratory reference interval in use at our institution (0–0.5 $\times 10^9$/L); age-specific intervals were not applied. For inflammatory markers reported below the limit (e.g., hs-CRP), the reported limit value was used in all comparisons.

2.6 Statistical analysis

Continuous variables are summarized as median and interquartile range (IQR) and were compared using the Mann–Whitney U test or the Kruskal–Wallis H test, with Holm-corrected post hoc comparisons across groups. The five pathogen-defined groups were additionally compared by analysis of covariance of ln(EOS), with age as a covariate. Categorical variables were compared using Fisher's exact test. Odds ratios (ORs) for below-limit analyses were calculated using the Woolf (unconditional log-odds) method without continuity correction; no cells contained zero.

The primary analysis was a multivariable linear regression of ln(EOS) on influenza status adjusted for age, sex and glucocorticoid exposure, reporting median ratios with 95% confidence intervals (CIs); hs-CRP and IL-6 were added in secondary models, and an interaction term tested for effect modification by age. Logistic regression for influenza status used a base model of age, sex, WBC and LYM, and discrimination was compared before and after adding ln(EOS), ln(hs-CRP), ln(IL-6), eosinophil percentage or the neutrophil-to-lymphocyte ratio using the area under the receiver operating characteristic curve (AUC) with bootstrap 95% confidence intervals for differences (2,000 resamples), the integrated discrimination improvement (IDI) and the continuous net reclassification improvement (NRI). Decision-curve analysis was then performed to compare the net benefit across threshold probabilities of 0.05 to 0.80, and 10-fold cross-validation (calibration intercept, slope and Brier score) was performed to assess calibration. Discrimination was evaluated using the same data used for model fitting without external validation, and model development and reporting followed the TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) recommendations (checklist in Additional file 2).

Sensitivity analyses comprised restriction to children aged ≥ 2 or ≥ 3 years, 1:1 age matching (nearest neighbor, caliper 0.25 years), inverse probability weighting with age, sex and glucocorticoid as covariates, exclusion of reconstructed-zero observations, and analysis using reported EOS values. Paired comparisons were performed using the Wilcoxon signed-rank test with exact P values, and status transitions were performed using McNemar's exact test. The paired subgroup was underpowered for between-group comparisons (minimum detectable difference reported in the results). The subgroup analyses were exploratory without multiplicity correction. Two-sided $P < 0.05$ denoted significance. All analyses were performed using Python 3.13 (Python Software Foundation, Beaverton, OR, USA) with NumPy 2.5, pandas 3.0, SciPy 1.18, statsmodels 0.14 and scikit-learn 1.9.

2.7 Ethical statement

This retrospective observational study was approved by the Ethics Committee of Zunyi Maternal and Child Health Hospital (approval number: 2026-032). The requirement for written informed consent was waived by the Ethics Committee because the data were collected during routine clinical care and de-identified before analysis. This study was conducted in accordance with the principles of the Declaration of Helsinki.

2.8 Use of artificial intelligence

During the preparation of this manuscript, the authors used an AI-assisted language-editing tool (DeepSeek-V4.1) for language polishing and reference formatting. The study concept, figures, and original draft were developed by the authors, who reviewed and edited all AI-assisted output and take full responsibility for the content of this manuscript.

3. Results

3.1 Baseline characteristics

Of the 252 children, 122 had influenza (83 type A and 39 type B) and 130 did not. Children with influenza were older (median 4.0 [IQR 2.0–7.0] vs 1.5 [0.6–3.0] years, $P < 0.001$), included fewer boys (50.8% vs 65.4%, $P=0.022$), and more often underwent chest CT (68.9% vs 36.2%, $P < 0.001$). Compared to children without influenza, those with influenza more often had fever (maximum temperature ≥ 38.0 °C: 82.8% vs 38.5%, $P < 0.001$), a longer fever duration (median 3 [IQR 1–4] vs 0 [0–1] days, $P < 0.001$) and reached a higher maximum temperature (median 39.0 [38.5–39.6] vs 37.1 [36.8–38.8] °C, $P < 0.001$). Comorbidities were present in 2 of 122 children with influenza and 2 of 130 children without influenza (1.6% vs 1.5%). The baseline characteristics are shown in **Table 1.**

Antiviral therapy was given to all (100%; 122/122) children with influenza compared to only 1.5% (2/130) of children without influenza ($P < 0.001$). Glucocorticoid exposure was 4.1% (5/122) in the influenza group compared to 19.2% (25/130) in the non-influenza group (OR 0.18, 95% CI 0.07–0.49, $P < 0.001$). The length of hospital stay (median, 6 days in both groups), nasal

oxygen (7.5%, 19/252), and respiratory support (3.2%, 8/252) did not differ significantly between the two groups. Sputum cultures were not performed in 43 children (17.1%), most often for influenza (35/122 vs 8/130).

At admission, the influenza group had lower WBC (6.81 [5.21–8.62] vs 9.32 [7.37–11.76] $\times 10^9$/L) and LYM (1.60 [1.10–2.77] vs 4.20 [2.60–5.90] $\times 10^9$/L) than the non-influenza group (both $P < 0.001$). Neutrophil counts were comparable between the influenza and non-influenza groups (3.90 vs 3.45 $\times 10^9$/L, P=0.871), whereas hs-CRP (3.06 vs 1.81 mg/L, P=0.024) and IL-6 were higher in the influenza group than those in the non-influenza group (median 14.60 [IQR 8.45–36.50] vs 8.87 [5.72–26.57] pg/mL, P<0.001).

3.2 Intergroup comparison of admission eosinophils

Median reconstructed admission EOS was 0.0175 (IQR 0.0046–0.0453) in the influenza group compared to 0.1565 (0.0499–0.2825) $\times 10^9$/L in the non-influenza group. The Hodges–Lehmann median difference was -0.114 $\times 10^9$/L (95% CI -0.144 to -0.080; Mann–Whitney U=2947.5, z=-8.63, $P < 0.001$), with concordant results using reported values (0.00 vs 0.20 $\times 10^9$/L, U=3351.0, z=-8.52, $P < 0.001$) **(Fig. 2).** This difference persisted even after multivariable adjustment (Section 3.6).

In total, 76.2% (93/122) of children with influenza and 25.4% (33/130) of children without influenza were below the lower-limit cutoff (< 0.05 $\times 10^9$/L) (OR 9.43, 95% CI 5.31–16.74, $P <$ 0.001). At thresholds of 0.01, 0.02, 0.03 and 0.10, the proportions of children below the thresholds were 39.3% vs 6.9% (OR 8.72), 52.5% vs 13.8% (OR 6.87), 64.8% vs 20.0% (OR 7.35) and 88.5% vs 38.5% (OR 12.34) in the influenza vs non-influenza groups, respectively (all $P < 0.001$; Additional file 3). The percentage of eosinophils showed the same trend in the influenza and non-influenza groups (0.30% vs 1.60%, $P < 0.001$). Because the reported zero definition and reconstructed threshold identified the same 126 children, the threshold analysis was unaffected by the choice between the reported and reconstructed values.

In every age stratum, EOS in the influenza group was lower than that in the non-influenza group: < 1 year (17 vs 48) 0.0818 vs 0.1839 (P=0.006); 1–3 years (22 vs 44) 0.0246 vs 0.1331 (P < 0.001); 3–6 years (38 vs 27) 0.0176 vs 0.0704 (P=0.002); ≥ 6 years (45 vs 11) 0.0086 vs 0.1109 (P=0.002). The ORs for below-limit EOS were 4.90, 5.71, 5.45 and 17.94 for the < 1 year, 1–3, 3–6 and ≥ 6 year groups, respectively, all in the same direction. The overall below-limit proportion increased with age (20.0%, 40.9%, 63.1%, and 80.4%, respectively; Additional file 4). Within influenza, median EOS for type A (n=83) and B (n=39) were 0.0211 and 0.0122 $\times 10^9$/L (P=0.122), and the comparison was underpowered given the smaller type B group.

3.3 Eosinophils across pathogen subgroups

Among the 130 children without influenza, 46 had RSV, 37 had rhinovirus, 31 had adenovirus, and 37 had no detectable virus (viral-negative group); one child had no pathogen panel recorded. Of the 122 children with influenza, 91 (74.6%) had no RSV, rhinovirus, or adenovirus (influenza-only infection), 10 had RSV, 17 had rhinovirus, 9 had adenovirus co-infection, and 12 had *Mycoplasma pneumoniae* detected; because these categories overlap, the counts are not additive. The EOS did not differ significantly between children with influenza-only and children co-infected with influenza and other viruses (0.0170 vs 0.0244 $\times 10^9$/L, P=0.270); the 12 children with *Mycoplasma pneumoniae* were retained in the influenza group. Single detections of human metapneumovirus, human parainfluenza virus, coxsackievirus, Epstein-Barr virus, and cytomegalovirus were also recorded; because testing for these agents was not systematic, they were not analyzed separately. Analysis of covariance of ln(EOS) across the five groups with age as covariate showed a significant overall effect (P < 0.001); after Holm correction influenza was lower than all four comparator groups (age-adjusted P = 1.47×10^{-5} to 3.07×10^{-9}), which did not differ from one another (adjusted P = 1.000).

3.4 Longitudinal dynamics of eosinophils

Of the 252 children, 92 had a repeat blood count within five days before discharge (44 influenza, 48 non-influenza), and the median interval from admission to the repeat sample was 5 days (IQR 4–6). In the influenza group, EOS increased from a median of 0.0215 to 0.0745 $\times 10^9$/L, with a median change of +0.0399 (IQR 0.0009–0.0841) (Wilcoxon signed-rank $P < 0.001$; exact sign test 34 up, 9 down, 1 unchanged, $P < 0.001$); 18 children moved from below to above the reportable limit (McNemar P=0.011) (Fig. 3A). In the non-influenza group, EOS increased from 0.0869 to 0.1363 $\times 10^9$/L, with a median change of +0.0220 (IQR -0.0312 to 0.1257) (Wilcoxon P=0.087; exact sign test 31 up, 16 down, 1 unchanged, P=0.040); 11 children crossed the limit upwards and 3 downwards (McNemar P=0.057) (Fig. 3B). The paired subgroup was underpowered to compare the magnitude of change between groups: with the observed standard deviations (0.092 and 0.207 $\times 10^9$/L), the minimum detectable difference at 80% power was approximately 0.09 $\times 10^9$/L, which exceeds the median change in either group (0.040 and 0.022 $\times 10^9$/L). Therefore, the absence of a significant between-group difference is inconclusive, rather than evidence that recovery dynamics are equivalent. The paired and unpaired subgroups were comparable in age, sex, influenza proportion and admission EOS, but paired children had longer stays (6.5 vs 6.0 days) and higher admission WBC (10.80 vs 7.43 $\times 10^9$/L) (both $P < 0.001$).

3.5 Bacterial co-infection and eosinophils

Sputum culture was performed in 209 of the 252 children (83.0%) and was positive in 85 (40.7%) children. Positivity among tested children was higher in the influenza group (42/87, 48.3%) than that in the non-influenza group (43/122, 35.2%) (OR 1.71, 95% CI 0.98–3.01). However, the testing rates differed substantially (untested: 35/122 influenza vs 8/130 non-influenza, $P < 0.001$); therefore, this comparison should be interpreted with caution. These isolates predominantly comprised *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pneumoniae*. Blood cultures were obtained from 16 (6.3%) children, all of whom tested negative. The admission EOS did not differ between children with a positive sputum culture and those with a

negative or untested culture (0.0587 [0.0155–0.1770] vs 0.0425 [0.0107–0.1742] $\times 10^9$/L, P=0.352) or within the influenza group (0.0266 vs 0.0163 $\times 10^9$/L, P=0.087). The viral-negative group had the highest hs-CRP (median 6.99 [IQR 1.96–19.35] mg/L; Kruskal–Wallis H=34.80, $P < 0.001$) compared with influenza (3.06), adenovirus (3.22), rhinovirus (0.89) and respiratory syncytial virus (0.65) groups.

3.6 Multivariable analysis of admission EOS

The primary linear regression analysis of ln(EOS) on age, sex, and glucocorticoid exposure included 252 children (Table 2). The adjusted median ratios were 0.302 (95% CI 0.225–0.405, $P < 0.001$) for influenza and 0.914 per year of age (0.868–0.962, $P < 0.001$). Sex (P=0.181) and glucocorticoid exposure (P=0.321) were not significantly associated with ln(EOS). Adding log-hs-CRP in the 246 children with available values resulted in an essentially unchanged influenza effect (0.326, 95% CI: 0.243–0.437, $P < 0.001$; the corresponding estimate without log-hs-CRP in this subset was 0.318). Excluding the 126 EOS-zero cases, the influenza effect remained significant (0.614, 95% CI 0.460–0.820, P=0.001), but was reported only as a directional check, given the selection bias. Logistic sensitivity analysis of below-limit EOS yielded adjusted OR 6.61 (95% CI 3.54–12.34, $P < 0.001$) for influenza and 1.28 per year (1.13–1.45, $P < 0.001$) for age, whereas sex (OR 0.75) and glucocorticoid exposure (OR 1.83) were not significantly associated with the below-limit EOS. Inverse-probability weighting achieved balance, with standardized mean differences 0.027, 0.033 and 0.013 for age, sex and glucocorticoid (all < 0.1); weighted influenza EOS remained lower (median ratio 0.275, bootstrap 95% CI 0.201–0.404) with below-limit OR 8.73 (95% CI 4.90–15.53). Adding ln(IL-6) to the primary model did not change the influenza estimate (median ratio 0.301, 95% CI 0.223–0.406). In the logistic model of influenza status including age, sex, WBC, LYM and ln(IL-6), IL-6 was independently associated with influenza in the direction of higher values (adjusted OR 1.47, 95% CI 1.08–2.00, P=0.015), whereas EOS remained strongly associated in the opposite direction.

3.7 Incremental discriminant value and clinical utility of EOS over routine indices

Considering influenza status as the outcome and a base model of age, sex, WBC and LYM, the AUC was 0.790 (95% CI 0.734–0.847), which increased to 0.855 (0.807–0.903) after adding ln(EOS) (ΔAUC 0.066, bootstrap 95% CI 0.028–0.107; IDI 0.127; continuous NRI 41.3%) (Fig. 4A). Adding ln(hs-CRP) (AUC 0.788 to 0.791, ΔAUC 0.003, 95% CI -0.012 to 0.017, n = 246), and ln(IL-6) (AUC 0.795, ΔAUC 0.006, 95% CI -0.013 to 0.025) to the model did not improve discrimination. The base model was fitted in all 252 children (AUC, 0.790). Comparisons involving hs-CRP were restricted to 246 children with available hs-CRP values, in whom the base model AUC was 0.788. The model containing ln(EOS) and ln(hs-CRP) was not superior to that containing ln(EOS) alone (AUC 0.857, ΔAUC 0.002, 95% CI -0.003 to 0.009), and adding ln(IL-6) to ln(EOS) gave no further improvement (AUC 0.857, ΔAUC 0.002). The neutrophil-to-lymphocyte ratio added little (AUC 0.800, ΔAUC 0.010). Eosinophil percentage performed comparably to the absolute count (AUC 0.860), because EOS is calculated from WBC and the eosinophil percentage and WBC were already in the model; for laboratories reporting only the percentage, this marker is an equally usable proxy. The single-marker AUCs were as follows: EOS 0.812, LYM 0.797, eosinophil percentage 0.783, fever duration 0.763, age 0.747, maximum temperature 0.742, WBC 0.720, IL-6 0.628, hs-CRP 0.584, and lactate dehydrogenase (LDH) 0.555 (Fig. 4B). At the 0.05 $\times 10^9$/L cutoff, sensitivity was 76.2% and specificity 74.6% (Youden index 0.508); the cutoff with the maximum Youden index was approximately 0.047–0.049 $\times 10^9$/L. Because cohort prevalence (48.4%) exceeds that in primary care, predictive values at assumed prevalences of 10%, 20% and 30% were 25.0%/96.6%, 42.9%/92.6% and 56.3%/88.0% for positive/negative predictive value. Adding chest CT (versus radiography) or fever duration to the model containing ln(EOS) each increased the AUC to 0.873 and adding both increased it to 0.890.

In the decision curve analysis, the model containing ln(EOS) yielded a higher net benefit than the base model across threshold probabilities from 0.10 to 0.80, whereas the benefit of the model containing ln(hs-CRP) was indistinguishable from that of the base model. At a threshold of 0.25, the net benefit was 0.312 for the base model, 0.360 for ln(EOS), 0.318 for ln(hs-CRP), and 0.357 for both markers (Fig. 4C). Calibration of the model containing ln(EOS) was assessed by 10-fold cross-validation and was adequate (calibration intercept -0.017, calibration slope 0.901, Brier score 0.162; Fig. 4D).

3.8 Sensitivity analyses

The influenza association was consistent across sensitivity analyses, with no evidence of effect modification by age (influenza × age interaction β 0.021, 95% CI -0.088 to 0.130, *P*=0.709). The adjusted median ratio was 0.281 (95% CI 0.194–0.407) when restricted to children aged ≥ 2 years (n = 150), 0.293 (0.194–0.442) when restricted to those aged ≥ 3 years (n = 121), and 0.318 (0.220–0.461) in a 1:1 age-matched cohort (72 pairs; median age 2.54 years in both groups, *P*=0.990; below-limit proportion 69.4% vs 29.2%, OR 5.52), compared with 0.302 (0.225–0.405) for the full cohort. Excluding the 36 reconstructed-zero observations gave 0.285 (0.205–0.396); excluding the 126 children whose EOS was reported as 0 gave 0.614 (0.460–0.820); and using reported values without reconstruction gave 0.373 (0.289–0.482). Inverse probability weighting achieved balance (standardized mean differences 0.027, 0.033 and 0.013, all < 0.1) and gave a weighted median ratio of 0.275 (bootstrap 95% CI 0.201–0.404) with a below-limit OR of 8.73 (95% CI 4.90–15.53).

4. Discussion

In this study cohort, the admission EOS was approximately ninefold lower in the influenza group than that in the non-influenza group when the two group medians were compared directly (ratio of medians 0.112; adjusted median ratio 0.302, 95% CI 0.225–0.405; Hodges–Lehmann difference -0.114, 95% CI -0.144 to -0.080). Additionally, 76.2% of children with influenza were

below the reportable limit compared with 25.4% of children without influenza. This difference was observed across age strata and was not explained by greater inflammation because the viral-negative group had the highest hs-CRP (6.99 mg/L), and eosinophil counts were comparable to those of other non-influenza pathogens. Median counts among the four non-influenza subgroups clustered between 0.115 and 0.203 $\times 10^9$/L with no intergroup difference, consistent with Özaydın et al., who attributed inter-viral eosinophil variation to pathogen-specific host responses rather than age in a 1,143-child outpatient cohort [21]. The present study is complementary to these reports in that it addresses acute admission in a larger cohort (n = 252), adds rhinovirus and viral-negative comparators, and quantifies discriminant performance rather than group differences alone. The hs-CRP and IL-6 levels were higher in children with influenza, whereas EOS was lower, indicating that the eosinophil signal was not a proxy for the magnitude of the systemic inflammatory response. During recovery, both groups showed a predominantly upward trend in EOS, but the paired subgroup was too small to determine whether the magnitude of change differed between groups (minimum detectable difference approximately 0.09 $\times 10^9$/L at 80% power, exceeding the observed median changes). Therefore, the recovery data are descriptive; eosinophil counts increase as children improve, but we cannot conclude whether this increase is influenza-specific.

Our specificity of 74.6% at a cutoff of < 0.05 $\times 10^9$/L was lower than the 92% reported by Davido et al. for absolute eosinopenia, defined as an eosinophil count of 0 cells/mm³ [6]. However, the two thresholds are not equivalent. Additionally, that study enrolled an adult outpatient cohort (mean age 59 years) selected from patients presenting to an emergency department, in which 75.8% of viral detections were influenza and the adjusted odds ratio carried a wide confidence interval (6.16, 95% CI 1.14–33.24). Direct comparisons of the specificity across these populations are limited. In our cohort, adenovirus, another eosinopenia-inducing pathogen [22], was detected in 31 of the 130 children without influenza (23.8%), which probably contributed to the lower specificity. Mechanistically, murine data indicate that influenza A infection shifts the

airway cytokine milieu towards T helper 1 through interferon-γ and suppresses airway eosinophilia, although peripheral blood eosinophilia was not reduced in that model [14]; blood and airway compartments therefore do not behave identically, and our data pertain only to the circulation.

The clinical value lies mainly in primary care, where nucleic acid testing is constrained by equipment, reagent cost, and turnaround time [23,24], whereas blood count is universally available within minutes and eosinophil count is already a routine reporting field. At the 0.05 $\times 10^9$/L cutoff, sensitivity was 76.2% and specificity 74.6%. At primary care prevalence (10%–30%), the standalone positive predictive value was only 25%–56%, while the negative predictive value reached 88%–97%; therefore, the test is better framed as a rule-out adjunct combined with clinical judgment than as a standalone trigger for antivirals. For laboratories reporting only the eosinophil percentage, the percentage performed comparably to the absolute count (AUC 0.860) and was an equally usable proxy. Eosinopenia is not unique to influenza; bacterial infections, glucocorticoids, and severe systemic inflammation also cause it [25–27], and 25.4% of children in our non-influenza group were below this limit. Fever duration and maximum temperature discriminated influenza moderately (single-marker AUC 0.76 and 0.74), but both accumulate over the illness and are unavailable at presentation, whereas EOS is obtained within minutes from the blood count already drawn at triage. Therefore, the advantage of EOS at the point of care lies not in outperforming clinical variables but in being available at the moment the decision is made. In a model containing ln(EOS), chest CT findings, and fever duration, the discrimination reached an AUC of 0.890.

This study has some limitations. First, this was a single-center retrospective cohort study from one winter season, and the paired subgroup was small and selected by clinical indication rather than at random. Inverse probability weighting balanced measured covariates but could not exclude unmeasured confounding. Second, the paired subgroup was underpowered to compare the magnitude of change in EOS between groups; therefore, the recovery analysis was

descriptive. Third, analytical precision (0.1 $\times 10^9$/L) left half of the reports at zero; reconstruction from WBC and the eosinophil percentage reduced this to 14.3%, but 36 children remained at zero with true values irrecoverable between 0 and 0.05 $\times 10^9$/L, and age-specific reference intervals were not applied. Fourth, we lacked data on atopy [28] and influenza vaccination status and did not record the interval from symptom onset to admission; therefore, eosinophil dynamics could not be standardized to the day of illness. Fifth, pre-admission medication data were limited to antiviral agents ascertained from the first progress note; pre-admission antibiotic and glucocorticoid exposures were not abstracted, and because glucocorticoids lower eosinophil counts independent of infection, residual confounding factors cannot be excluded. Sixth, sputum culture was performed at the discretion of the treating physician and was missing far more often in children with influenza than in those without (28.7% vs 6.2%); therefore, the comparison of bacterial co-infection is subject to differential testing bias, and the viral-negative group may include colonization [29] as well as undetected *Mycoplasma pneumoniae*. Seventh, testing for human metapneumovirus, human parainfluenza virus, and other agents was not systematic, and these detections were not analyzed separately. Eighth, the discriminant performance was evaluated using the same data used for model fitting without external validation, and the 48.4% influenza prevalence was far higher than that in primary care; therefore, predictive values should not be extrapolated. The core finding that influenza was associated with a lower admission EOS count, not explained by age, glucocorticoids, hs-CRP or IL-6, remained consistent across unadjusted, adjusted, weighted, age-restricted, age-matched, and reconstruction-independent analyses.

5. Conclusions

In hospitalized children, admission EOS was markedly lower in those with influenza than in those without, and lower than that in the respiratory syncytial virus, rhinovirus, adenovirus and viral-negative groups. The association persisted after adjusting for age, sex, and glucocorticoids in age-

matched and age-restricted analyses and after accounting for hs-CRP and IL-6 levels. EOS added discriminative information beyond routine hematological indices and the two inflammatory markers and improved the net benefit in the decision curve analysis. Derived from a blood count already part of routine care, EOS at the 0.05 $\times 10^9$/L cutoff carries a high negative predictive value and may serve as an adjunctive clue for frontline influenza recognition, though not as a standalone trigger for antivirals or a substitute for pathogen testing. Future larger prospective studies are required to determine the recovery trajectories.

List of abbreviations

AUC: area under the receiver operating characteristic curve; CI: confidence interval; CT: computed tomography; EOS: absolute eosinophil count; hs-CRP: high-sensitivity C-reactive protein; IDI: integrated discrimination improvement; IL-6: interleukin-6; IQR: interquartile range; LDH: lactate dehydrogenase; LYM: lymphocyte count; NRI: net reclassification improvement; OR: odds ratio; RSV: respiratory syncytial virus; STROBE: Strengthening the Reporting of Observational Studies in Epidemiology; TRIPOD: Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis; WBC: white blood cell count

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Zunyi Maternal and Child Health Hospital (approval number: 2026-032). The requirement for written informed consent was waived by the Ethics Committee because the data were collected during routine clinical care and were de-identified before analysis. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analyzed during the current study are not publicly available because they contain identifiable clinical information, but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Y.L. and W.H. contributed equally to this work and share first authorship. Conceptualization: Y.L. and R.C.; Methodology: Y.L., W.H., and R.C.; Investigation and data collection: Y.L., W.H., Z.W., and Y.S.; Formal analysis: Y.L. and W.H.; Writing – original draft: Y.L. and W.H.; Writing – review and editing: R.C., Y.L., W.H., and Z.W.; Supervision: R.C.; Funding acquisition: R.C. All authors read and approved the final manuscript.

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Additional files

Additional file 1. File format: Microsoft Word (.docx). Title of data: STROBE checklist. Description of data: Completed STROBE checklist mapping each item to the corresponding section of the manuscript.

Additional file 2. File format: Microsoft Word (.docx). Title of data: TRIPOD checklist. Description of data: Completed TRIPOD 2015 checklist for the prediction-model component of this study.

Additional file 3. File format: Microsoft Word (.docx). Title of data: Threshold sensitivity analysis of admission EOS. Description of data: Proportion of children with admission EOS below five prespecified thresholds, with odds ratios for influenza.

Additional file 4. File format: Microsoft Word (.docx). Title of data: Age-stratified analysis of admission EOS. Description of data: Admission EOS and below-limit proportions across four age strata.

References

1. Wolf RM, Antoon JW. Influenza in children and adolescents: epidemiology, management, and prevention. Pediatr Rev. 2023;44(11):605–617. https://doi.org/10.1542/pir.2023-005962.

2. Influenza-Associated Acute Necrotizing Encephalopathy (IA-ANE) Working Group. Influenza-associated acute necrotizing encephalopathy in US children. JAMA. 2025;334(8):692–701. https://doi.org/10.1001/jama.2025.11534.

3. Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2024–2025: technical report. Pediatrics. 2024;154(4):e2024068508. https://doi.org/10.1542/peds.2024-068508.

4. Chow EJ, Doyle JD, Uyeki TM. Influenza virus-related critical illness: prevention, diagnosis, treatment. Crit Care. 2019;23(1):214. https://doi.org/10.1186/s13054-019-2491-9.

5. Macchia I, La Sorsa V, Urbani F, et al. Eosinophils as potential biomarkers in respiratory viral infections. Front Immunol. 2023;14:1170035. https://doi.org/10.3389/fimmu.2023.1170035.

6. Davido B, Lemarie B, Gault E, et al. Interest of absolute eosinopenia as a marker of influenza in outpatients during the fall-winter seasons 2016–2018 in the Greater Paris area: the SUPERFLUOUS study. Diagnostics. 2023;13(12):2115. https://doi.org/10.3390/diagnostics13122115.

7. Bass DA. Behavior of eosinophil leukocytes in acute inflammation. I. Lack of dependence on adrenal function. J Clin Invest. 1975;55(6):1229–1236. https://doi.org/10.1172/jci108041.

8. Hong SG, Sato N, Legrand F, et al. Glucocorticoid-induced eosinopenia results from CXCR4-dependent bone marrow migration. Blood. 2020;136(23):2667–2678. https://doi.org/10.1182/blood.2020005161.

9. von Meijenfeldt GCI, Chary S, van der Laan MJ, et al. Eosinopenia and post-hospital outcomes in critically ill non-cardiac vascular surgery patients. Nutr Metab Cardiovasc Dis. 2019;29(8):847–855. https://doi.org/10.1016/j.numecd.2019.05.061.

10. Ravin KA, Loy M. The eosinophil in infection. Clin Rev Allergy Immunol. 2016;50(2):214–227. https://doi.org/10.1007/s12016-015-8525-4.

11. Bass DA, Gonwa TA, Szejda P, et al. Eosinopenia of acute infection: production of eosinopenia by chemotactic factors of acute inflammation. J Clin Invest. 1980;65(6):1265–1271. https://doi.org/10.1172/jci109789.

12. Sasaki H, Miyata J, Kawashima Y, et al. Distinct roles of types 1 and 2 interferons in human eosinophil regulation: a multi-omics analysis. Allergy. 2024;79(11):3141–3145. https://doi.org/10.1111/all.16215.
13. Kobayashi T, Takaku Y, Yokote A, et al. Interferon-β augments eosinophil adhesion-inducing activity of endothelial cells. Eur Respir J. 2008;32(6):1540–1547. https://doi.org/10.1183/09031936.00059507.
14. Wohlleben G, Muller J, Tatsch U, et al. Influenza A virus infection inhibits the efficient recruitment of Th2 cells into the airways and the development of airway eosinophilia. J Immunol. 2003;170(9):4601–4611. https://doi.org/10.4049/jimmunol.170.9.4601.
15. LeMessurier KS, Rooney R, Ghoneim HE, et al. Influenza A virus directly modulates mouse eosinophil responses. J Leukoc Biol. 2020;108(1):151–168. https://doi.org/10.1002/JLB.4MA0320-343R.
16. Temel H, Okur M, Gunduz M, et al. Clinical and laboratory comparison of COVID-19 and influenza A/B in children. Clin Lab. 2021;67(7):1655–1661. https://doi.org/10.7754/clin.lab.2020.201138.
17. Dulkadir R, Oztelcan Gunduz B. Differentiating COVID-19 and influenza in children: hemogram parameters as diagnostic tools. Front Public Health. 2024;12:1377785. https://doi.org/10.3389/fpubh.2024.1377785.
18. Tanni F, Akker E, Zaman MM, et al. Eosinopenia and COVID-19. J Am Osteopath Assoc. 2020;120(8):504–508. https://doi.org/10.7556/jaoa.2020.091.
19. Kawasaki Y, Hosoya M, Kanno H, et al. Serum regulated upon activation, normal T cell expressed and presumably secreted concentrations and eosinophils in respiratory syncytial virus infection. Pediatr Int. 2006;48(3):257–260. https://doi.org/10.1111/j.1442-200x.2006.02199.x.
20. von Elm E, Altman DG, Egger M, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ. 2007;335(7624):806–808. https://doi.org/10.1136/bmj.39335.541782.ad.
21. Özaydın E, Açar Bilge S, Özbilgiç Demiröz T, et al. Seasonal distribution, virus-specific hematologic profiles, and predictors of hospitalization in children with respiratory viral infections. Children (Basel). 2026;13(8):1040. https://doi.org/10.3390/children13081040.
22. Biserni GB, Scarpini S, Dondi A, et al. Potential diagnostic and prognostic biomarkers for adenovirus respiratory infection in children and young adults. Viruses. 2021;13(9):1885. https://doi.org/10.3390/v13091885.

23. de Lusignan S, Hoang U, Liyanage H, et al. Integrating molecular point-of-care testing for influenza into primary care: a mixed-methods feasibility study. Br J Gen Pract. 2020;70(697):e555-e562. https://doi.org/10.3399/bjgp20x710897.

24. Pinsky BA, Hayden RT. Cost-effective respiratory virus testing. J Clin Microbiol. 2019;57(9):e00373-19. https://doi.org/10.1128/JCM.00373-19.

25. Davido B, Makhloufi S, Matt M, et al. Changes in eosinophil count during bacterial infection: revisiting an old marker to assess the efficacy of antimicrobial therapy. Int J Infect Dis. 2017;61:62–66. https://doi.org/10.1016/j.ijid.2017.06.005.

26. Pinte L, Dumitru AC, Usurelu AC, et al. Low eosinophils and their dynamic as a predictor of death in patients with infections: a systematic review and meta-analysis of cohort studies. Ann Med. 2025;57(1):2541084. https://doi.org/10.1080/07853890.2025.2541084.

27. Gazzinelli-Guimaraes PH, Jones SM, Voehringer D, et al. Eosinophils as modulators of host defense during parasitic, fungal, bacterial, and viral infections. J Leukoc Biol. 2024;116(6):1301–1323. https://doi.org/10.1093/jleuko/qiae173.

28. Sonntag HJ, Filippi S, Pipis S, et al. Blood biomarkers of sensitization and asthma. Front Pediatr. 2019;7:251. https://doi.org/10.3389/fped.2019.00251.

29. Popova G, Boskovska K, Arnaudova-Danevska I, et al. Sputum quality assessment regarding sputum culture for diagnosing lower respiratory tract infections in children. Open Access Maced J Med Sci. 2019;7(12):1926–1930. https://doi.org/10.3889/oamjms.2019.551.

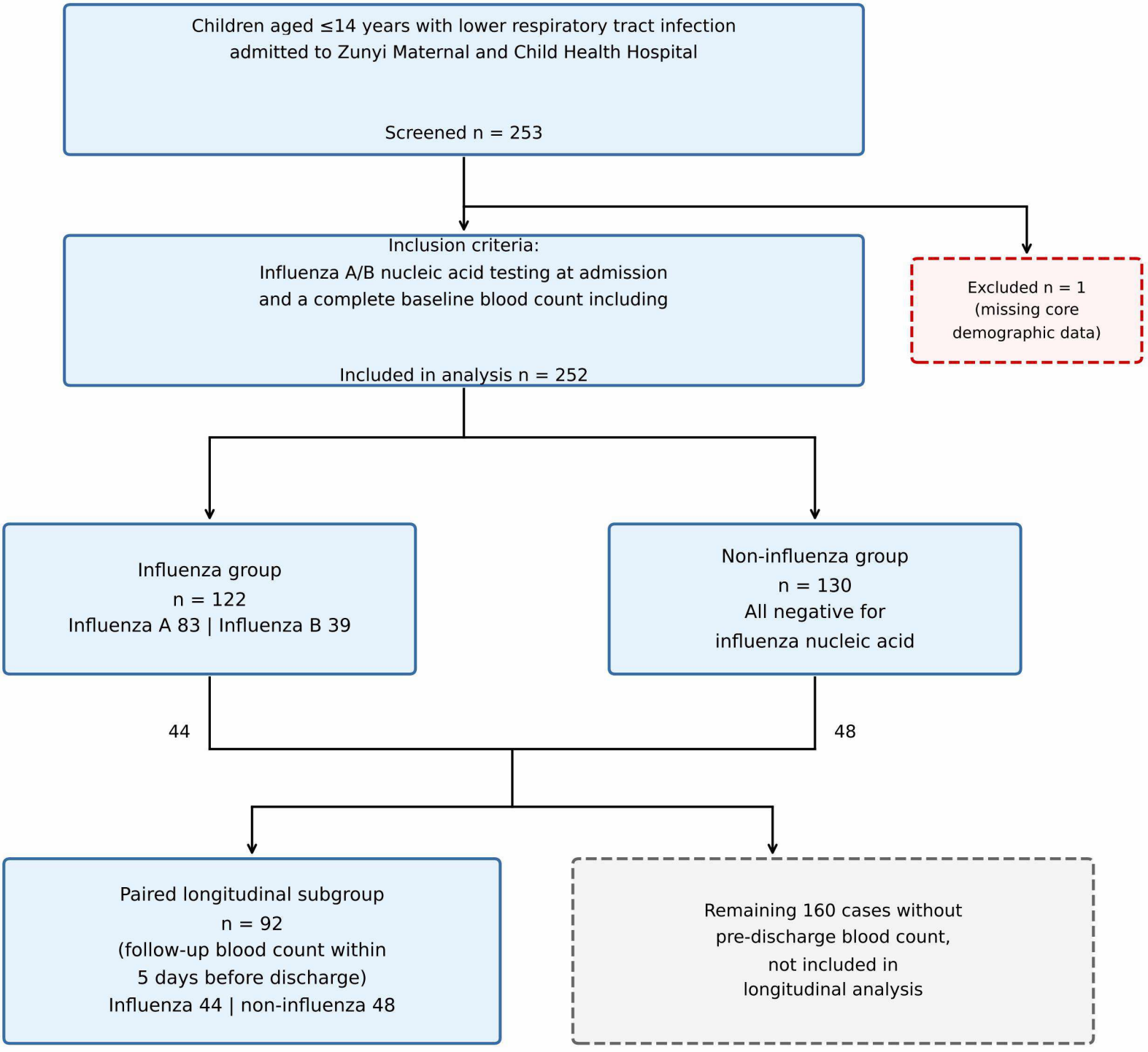
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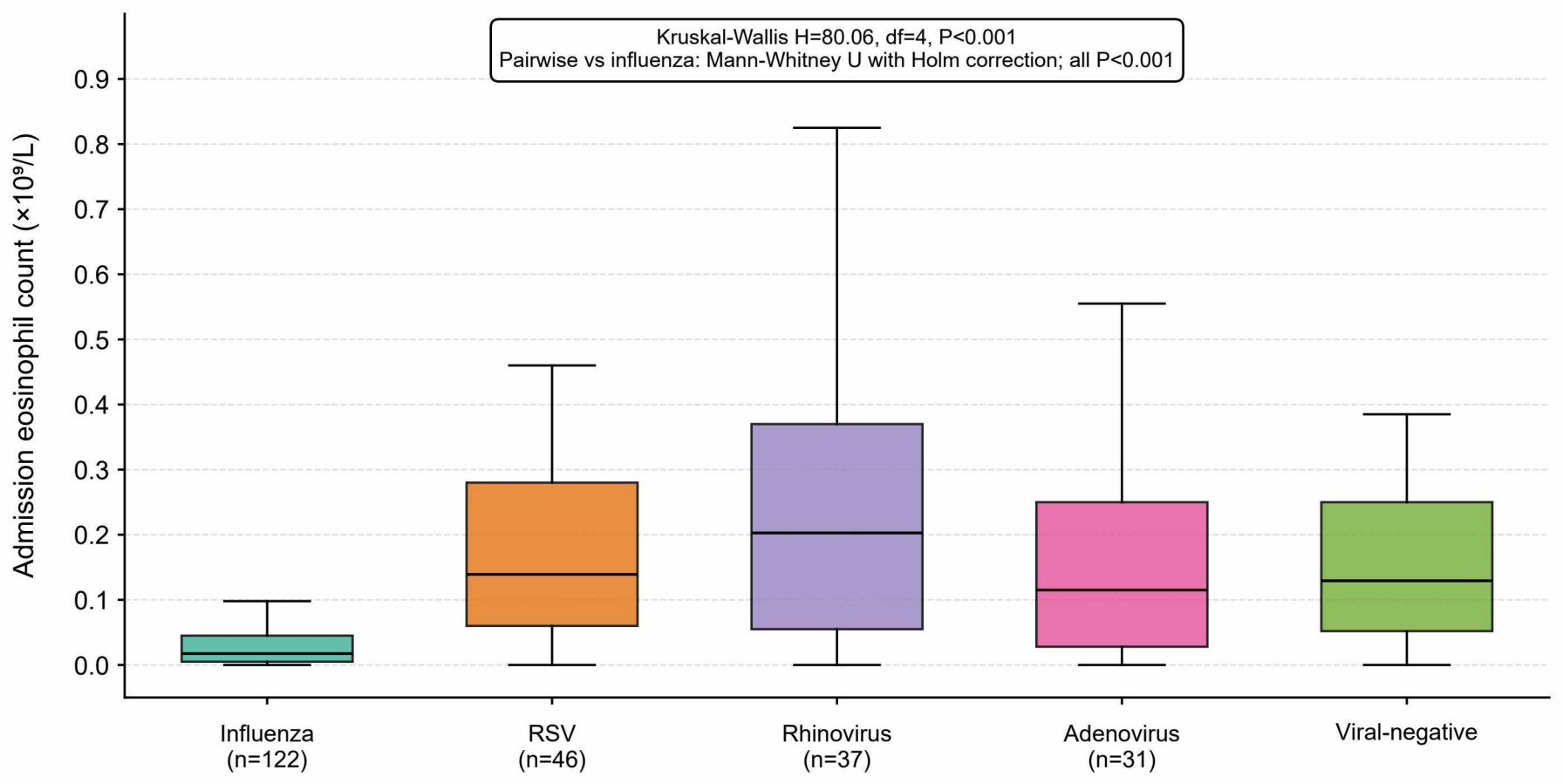
Fig. 1 Flowchart of participant enrollment. In total, 253 children were screened, of which one was excluded for incomplete demographic data. The remaining 252 children were divided into the influenza (n=122 [83 type A, 39 type B]) and non-influenza (n=130) groups. Children without influenza included 46, 37, 31, and 37 children with respiratory syncytial virus, rhinovirus, adenovirus, and no virus detected, respectively; one further child had no pathogen panel recorded. Counts are not additive because 22 children harboured two or more pathogens. A paired subgroup of 92 (44 influenza, 48 non-influenza) had a repeat count within 5 days before discharge.

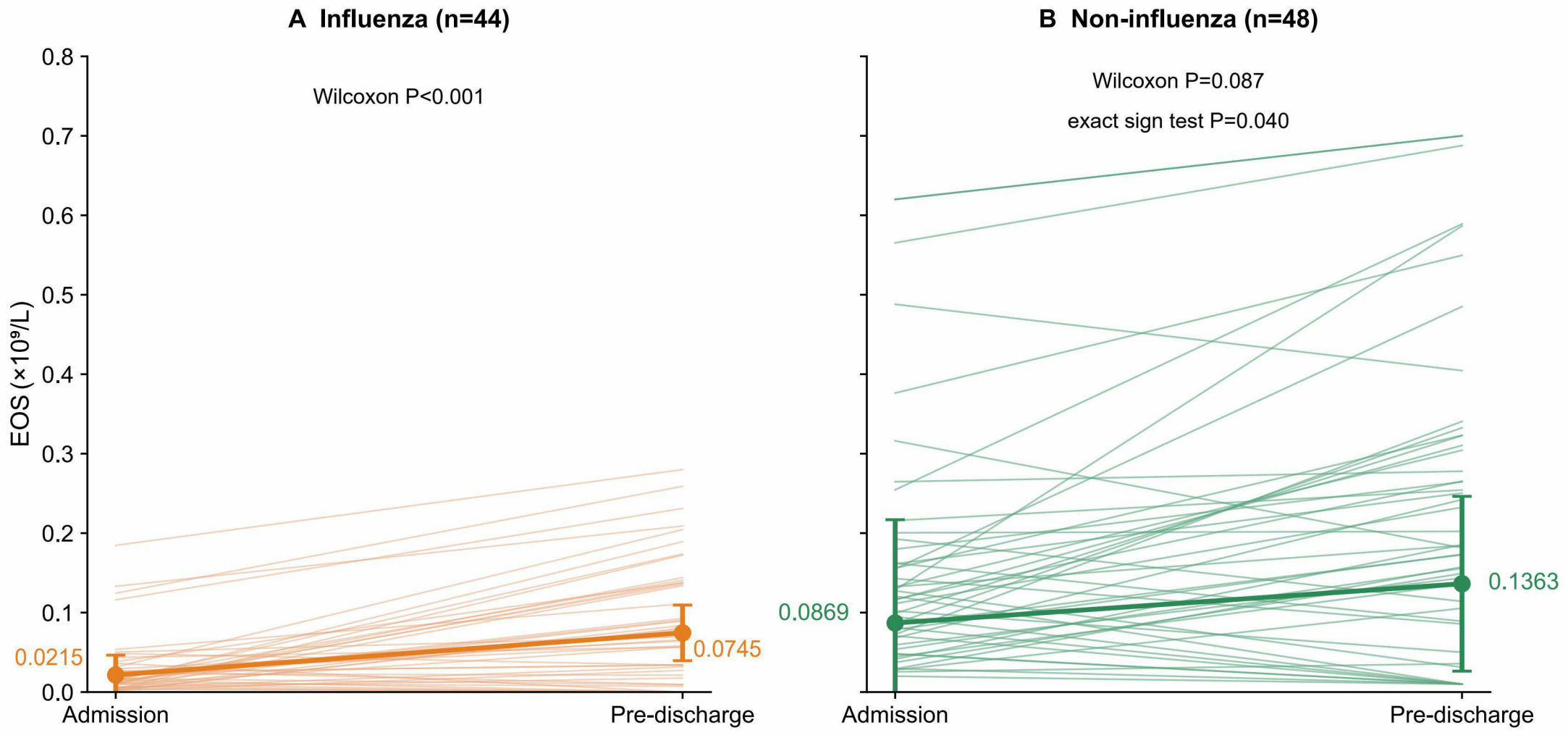
Fig. 2 Admission EOS by infecting pathogen. Groups (n): influenza (122), respiratory syncytial virus (46), rhinovirus (37), adenovirus (31), viral-negative (37). Boxes show interquartile ranges and horizontal lines medians; whiskers extend to 1.5 times the interquartile range. The dashed line marks the 0.05 $\times 10^9$/L reporting threshold. Medians ($\times 10^9$/L): 0.0175, 0.1391, 0.2028, 0.1151 and 0.1293; below-limit proportions: 76.2%, 21.7%, 24.3%, 32.3% and 27.0%. Kruskal–Wallis H = 80.06, df = 4, $P < 0.001$. After Holm correction, median EOS was lower in the influenza group than in every comparator group (adjusted $P = 4.25\times10^{-5}$ to 3.54×10^{-9}), and the comparators did not differ from one another (adjusted $P = 0.951$–1.000). Post hoc P values are Holm-adjusted but not age-adjusted.

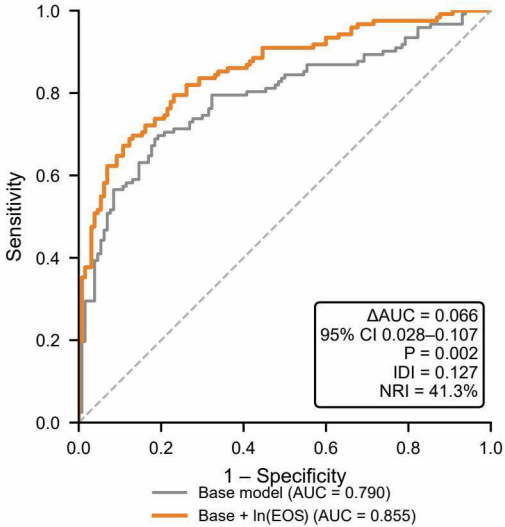
Fig. 3 Longitudinal EOS from admission to pre-discharge in children with paired counts. Thin lines represent individual children and thick lines group medians; both panels share the y-axis scale. (A) Influenza (n = 44): median 0.0215 to 0.0745 $\times 10^9$/L, median change +0.0399 (IQR 0.0009–0.0841); 34 increased, 9 decreased, 1 unchanged; Wilcoxon signed-rank $P < 0.001$. (B) Non-influenza (n = 48): median 0.0869 to 0.1363 $\times 10^9$/L, median change +0.0220 (IQR -0.0312

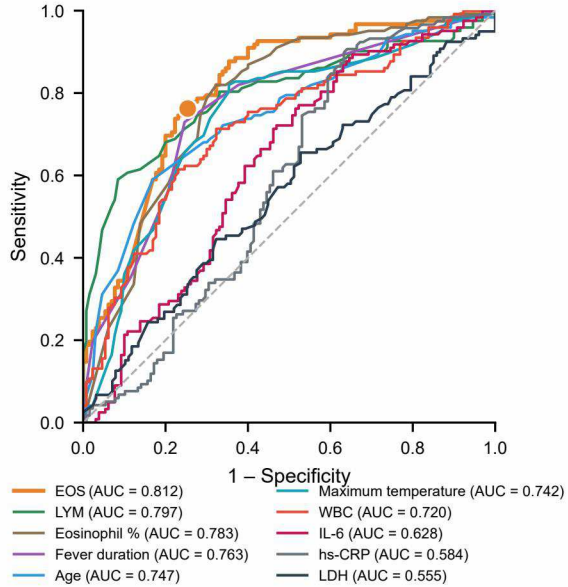
630 to 0.1257); 31 increased, 16 decreased, 1 unchanged; Wilcoxon $P = 0.087$. The subgroup was
631 underpowered for between-group comparison.
632
633 **Fig. 4 Discriminant performance of the absolute eosinophil count (EOS) for influenza in**
634 **hospitalized children.** (A) Receiver operating characteristic curves for all 252 children in the
635 base model (age, sex, WBC, LYM; grey) and with ln(EOS) added (orange). Inset: ΔAUC 0.066
636 (bootstrap 95% CI 0.028–0.107), $P = 0.002$, IDI 0.127, continuous NRI 41.3%. (B) Single-
637 marker curves, ordered by AUC: EOS 0.812, LYM 0.797, eosinophil percentage 0.783, fever
638 duration 0.763, age 0.747, maximum temperature 0.742, WBC 0.720, IL-6 0.628, hs-CRP 0.584
639 and LDH 0.555. The filled orange circle marks the prespecified 0.05 $\times 10^9$/L cutoff (sensitivity
640 76.2%, specificity 74.6%); curves for hs-CRP and LDH used the 246 children with an available
641 value. (C) Decision-curve analysis for the four nested models, as labeled (models containing hs-
642 CRP were fitted in the 246 children with an available value); the light dotted curve and the
643 horizontal line show treating all and treating none. Net benefit was higher with ln(EOS) over
644 most of the range examined and was not further increased by ln(hs-CRP). (D) Calibration of the
645 model containing ln(EOS) by 10-fold cross-validation; open circles show the observed proportion
646 of influenza per decile of predicted probability (Wilson 95% CI), the orange line is a loess fit and
647 the grey dashed line the line of identity. Inset: intercept -0.017, slope 0.901, Brier score 0.162.

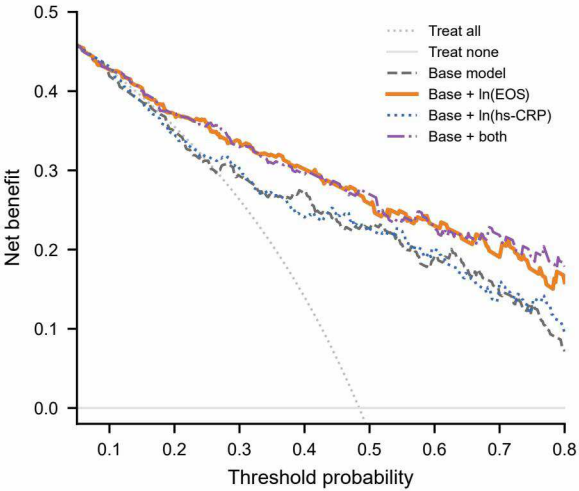

Children aged ≤14 years with lower respiratory tract infection
admitted to Zunyi Maternal and Child Health Hospital
Screened n = 253
Inclusion criteria:
Influenza A/B nucleic acid testing at admission
and a complete baseline blood count including
Included in analysis n = 252
Excluded n = 1
(missing core
demographic data)
Influenza group
n = 122
Influenza A 83 | Influenza B 39
Non-influenza group
n = 130
All negative for
influenza nucleic acid
44
48
Paired longitudinal subgroup
n = 92
(follow-up blood count within
5 days before discharge)
Influenza 44 | non-influenza 48
Remaining 160 cases without
pre-discharge blood count,
not included in
longitudinal analysis

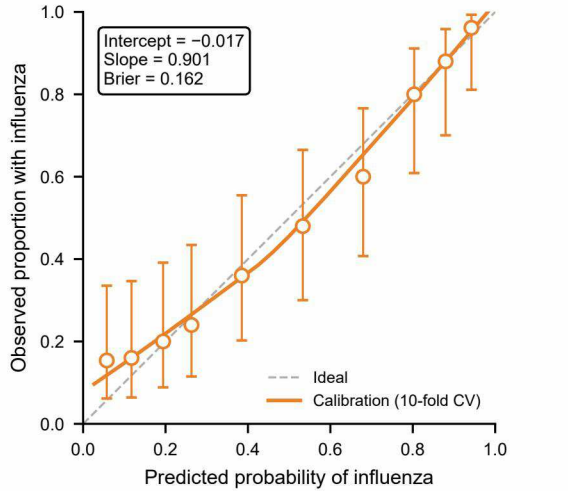

Kruskal-Wallis H=80.06, df=4, P<0.001
Pairwise vs influenza: Mann-Whitney U with Holm correction; all P<0.001
Admission eosinophil count (×10⁹/L)
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
Influenza (n=122)
RSV (n=46)
Rhinovirus (n=37)
Adenovirus (n=31)
Viral-negative


A Influenza (n=44)
Wilcoxon P<0.001
EOS (×10⁹/L)
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0.0215
0.0745
Admission
Pre-discharge
B Non-influenza (n=48)
Wilcoxon P=0.087
exact sign test P=0.040
0.0869
0.1363
Admission
Pre-discharge


Sensitivity
1 – Specificity
ΔAUC = 0.066
95% CI 0.028–0.107
P = 0.002
IDI = 0.127
NRI = 41.3%
Base model (AUC = 0.790)
Base + ln(EOS) (AUC = 0.855)


Sensitivity
1 – Specificity
EOS (AUC = 0.812)
LYM (AUC = 0.797)
Eosinophil % (AUC = 0.783)
Fever duration (AUC = 0.763)
Age (AUC = 0.747)
Maximum temperature (AUC = 0.742)
WBC (AUC = 0.720)
IL-6 (AUC = 0.628)
hs-CRP (AUC = 0.584)
LDH (AUC = 0.555)


Net benefit
Threshold probability
Treat all
Treat none
Base model
Base + ln(EOS)
Base + ln(hs-CRP)
Base + both


Observed proportion with influenza
Predicted probability of influenza
Intercept = −0.017
Slope = 0.901
Brier = 0.162
Ideal
Calibration (10-fold CV)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.docx
- Table2.docx
- Additionalfile1.docx
- Additionalfile2.docx
- Additionalfile4.docx
- Additionalfile3.docx