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ORIGINAL CONTRIBUTION

# The Influence of Age on the Diagnostic Performance of White Blood Cell Count and Absolute Neutrophil Count in Suspected Pediatric Appendicitis

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## Abstract

***Objective:*** White blood cell (WBC) count and absolute neutrophil count (ANC) are a standard part of the evaluation of suspected appendicitis. Specific threshold values are utilized in clinical pathways, but the discriminatory value of WBC count and ANC may vary by age. The objective of this study was to investigate whether the diagnostic value of WBC count and ANC varies across age groups and whether diagnostic thresholds should be age-adjusted.

***Methods:*** This is a multicenter prospective observational study of patients aged 3–18 years who were evaluated for appendicitis. Receiver operator characteristic curves were developed to assess overall discriminative power of WBC count and ANC across three age groups: <5, 5–11, and 12–18 years of age. Diagnostic performance of WBC count and ANC was then assessed at specific cut-points.

***Results:*** A total of 2,133 patients with a median age of 10.9 years (interquartile range = 8.0–13.9 years) were studied. Forty-one percent had appendicitis. The area under the curve (AUC) for WBC count was 0.69 (95% confidence interval [CI] = 0.61 to 0.77) for patients < 5 years of age, 0.76 (95% CI = 0.73 to 0.79) for 5–11 years of age, and 0.83 (95% CI = 0.81 to 0.86) for 12–18 years of age. The AUCs for ANC across age groups mirrored WBC performance. At a commonly utilized WBC cut-point of 10,000/mm$^3$, the sensitivity decreased with increasing age: 95% (<5 years), 91% (5–11 years), and 89% (12–18 years) whereas specificity increased by age: 36% (<5 years), 49% (5–12 years), and 64% (12–18 years).

***Conclusion:*** WBC count and ANC had better diagnostic performance with increasing age. Age-adjusted values of WBC count or ANC should be considered in diagnostic strategies for suspected pediatric appendicitis.

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The diagnostic evaluation of children and adolescents for possible appendicitis is common in outpatient settings such as primary care clinics and emergency departments (EDs). The presentation of appendicitis is known to vary by the duration of symptoms, the age of the patient, and specific location of the appendix. Prior to the past 20 years, the preoperative diagnosis was based on history and physical examination alone; recent advances to improve outcomes have included clinical decision algorithms and scores,[1–9] advanced diagnostic imaging,[10–15] and the pursuit of new biomarkers[16–20] to help clinicians discriminate appendicitis from other causes of abdominal pain.

Nearly all clinical scores and diagnostic algorithms utilize the white blood cell (WBC) count and associated WBC differential (as the proportion of neutrophils or absolute neutrophil count [ANC]) to guide care.[2,3,7,9,21] Previous investigations have shown the diagnostic importance of WBC and neutrophil predominance[22–29] in the evaluation of possible appendicitis. Furthermore, prior studies have demonstrated that the WBC count and ANC have the best test performance of currently available laboratory tests to predict appendicitis.[18,20] The two most utilized diagnostic scoring systems, the Alvarado Score[3] and Pediatric Appendicitis Score,[7] include an elevated WBC and neutrophil predominance as predictive factors. Previous investigations focused specifically on WBC have been limited by sample size,[28] investigated in a selective population of those undergoing surgery,[30–34] or included broader abdominal pain populations[26] rather than focusing the investigation to those being considered for appendicitis. Although many current algorithms employ the WBC count and ANC (or neutrophil predominance) in decision-making, specific diagnostic thresholds are not adjusted based on age. In this study we aimed to determine whether the discriminative performance of the WBC count and ANC vary by age and if the diagnostic thresholds should be adjusted by age for guiding care in the evaluation of possible pediatric appendicitis.

## METHODS

### Study Design and Setting

We conducted a secondary analysis of a prospective multicenter observational study whose primary objective was to refine a clinical prediction rule for appendicitis.[35] The original study enrolled children with suspected appendicitis at nine pediatric EDs who were members of the Pediatric Emergency Medicine Clinical Research Committee of the American Academy of Pediatrics. Subjects were enrolled from March 2009 through April 2010. The study was approved by each site's institutional review board (IRB). Seven IRBs granted a waiver of written consent/assent and obtained verbal consent. At the two remaining sites, written consent was obtained from the guardians and assent from children 7 years of age and older.

### Selection of Participants

ED patients who were 3 to 18 years of age presenting with acute abdominal pain and had suspected appendicitis were enrolled. Suspected appendicitis was defined by the clinical team's evaluation for appendicitis by obtaining blood tests, advanced radiologic studies, or surgical consultation. Patients with any of the following conditions were excluded: pregnancy, prior abdominal surgery, chronic gastrointestinal condition, or severe developmental delay (that might interfere with an accurate clinical assessment). For this secondary analysis, we included only those patients who had acute abdominal pain for less than 72 hours and had a WBC count and WBC differential obtained as part of the evaluation.

### Data Collection

Site primary investigators received a manual of operations and were instructed on proper completion of case report forms. A pediatric emergency medicine physician completed a standardized case report form with regard to symptoms and signs prior to any advanced imaging or operative care. Research assistants entered data from the medical record, including all laboratory values, for electronic transfer to a central data center.

### Outcome Measures

The primary outcome was the presence or absence of appendicitis. For those patients who had operative care, the presence of appendicitis was determined from the pathologist's final report. Presence or absence of perforation was determined from the attending surgeon's operative report. For patients discharged without surgery, telephone follow-up was performed between 1 and 2 weeks to determine resolution of signs and symptoms, visits to other sites of care, and need for any surgery. If we were unable to contact the guardian, research coordinators reviewed the medical record for the 90 days after the ED visit to determine if the patient underwent an operation at the index facility.

### Data Analysis

Descriptive statistics of patients' demographic and clinical characteristics were calculated using frequencies and proportions for categorical variables and medians with interquartile ranges (IQRs) for continuous variables. For our primary analysis, we determined the diagnostic performance (sensitivity, specificity, positive predictive value [PPV], negative predictive value [NPV], and positive likelihood ratio) of WBC count and ANC (using 1000/$mm^3$ increments from 5,000 to 15,000/$mm^3$ as cut-points), stratified across three age groups: preschool (<5 years), school age (5–11 years), and adolescents (12–18 years). Before conducting data analyses, the WBC count and ANC data were checked for the presence of outliers. To assess overall discriminative value, receiver operator characteristic curves (ROC) and the area under the curve (AUC) were determined and compared between age groups using a nonparametric test as described by DeLong et al.[36] The presence of influential data points was determined using the Delta-Beta influence statistic, a standardized measure of the difference in the coefficient vector (in this case, either WBC count or ANC) that is due to deletion of observations with the identical covariate pattern.[37] For illustrative purposes, the test characteristics corresponding to the commonly used WBC cutoff of 10,000/mm$^3$ were highlighted and presented.

We also considered the possibility that WBC count and ANC are affected by the duration of symptoms prior to the ED evaluation. To test if symptom duration contributed any predictive information to appendicitis status beyond that already provided by WBC count, we estimated a logistic regression model for each age subgroup with appendicitis as the outcome and WBC count as the independent variable. We then estimated a second logistic model with both WBC count and symptom duration as the independent variables. We then tested the null hypothesis that the AUCs from both models were equal. An identical assessment was made for ANC. All analyses were conducted using Stata 13.1.

## RESULTS

### Study Group

A total of 2,624 patients were enrolled in the parent study of which 2,133 (81%) patients had pain less than 72 hours and had a WBC count and WBC differential as part of their ED evaluation. Details of patient characteristics are presented in Table 1. The median age was 10.9 years (IQR = 8.0–13.9 years) and 48% were female. Forty-one percent of patients had appendicitis of which 219 (10%) were perforated. A total of 163 (8%) children were less than 5 years of age, 1,107 (52%) were 5–11 years of age, and 863 (40%) were 12–18 years of age. Of those patients not classified as appendicitis cases ($n$ = 1,236), the most common diagnosis was nonspecific abdominal pain, followed by gastroenteritis and constipation. This pattern was similar within each age group (Table 2).

### Diagnostic Performance of WBC Count and ANC

ROC analysis for WBC count and ANC by age group is shown in Figure 1. The AUC for WBC count was significantly greater in the 12- to 18-year-old group (0.83 [95% CI = 0.81 to 0.86]) compared to both the <5-year-old group (0.69 [95% CI = 0.61 to 0.77]; p = 0.001) and the 5- to 11-year-old group (0.76 [95% CI = 0.73 to 0.79]; p < 0.001). No difference was found between the WBC count AUC values of the <5- and 5- to 11-year-old groups (p = 0.11). Similarly, the AUC for ANC was significantly greater in the 12- to 18-year-old group (0.83 [95% CI = 0.80 to 0.86]) compared to both the <5-year-old group (0.68 [95% CI = 0.60 to 0.77]; p = 0.001) and the 5- to 11-year-old group (0.76 [95% CI = 0.73 to 0.78]; p < 0.001). No difference was found between the ANC AUC values of the <5- and 5- to 11-year-old groups (p = 0.11).

Evaluation of the Delta-Beta statistics revealed five WBC data points as influential (i.e., large Delta-Beta values outside the range of the rest of the distribution). However, repeating the analysis without these observations did not change the magnitude of the AUC values, their CIs, or the pattern of significance for the pairwise comparisons. No influential data points were detected in the analysis of ANC.

The detail of a range of cut-points is shown in Table 3 (WBC count) and Table 4 (ANC). The PPV and NPV are displayed across a range of WBC cut-points in Figures 2 and 3, respectively. The PPV and NPV are similarly graphed across a range of ANC cut-points in Data

Table 1
Clinical Characteristics of Study Sample ($N$ = 2,133)

| | No Appendicitis, $n$ = 1,263 | Appendicitis, $n$ = 870 | Nonperforated Appendicitis, $n$ = 651 | Perforated Appendicitis, $n$ = 219 |
|---|---|---|---|---|
| Age (y) | 11.0 (7.7–14.2) | 10.9 (8.3–13.3) | 11.3 (8.7–13.6) | 9.6 (7.1–12.4) |
| Age subgroups (y) | | | | |
| <5 | 125 (10) | 38 (4) | 21 (3) | 17 (8) |
| 5–11 | 609 (48) | 498 (57) | 363 (56) | 135 (62) |
| >12 | 529 (42) | 334 (38) | 267 (41) | 67 (31) |
| Female (%) | 683 (54) | 348 (40) | 252 (39) | 96 (44) |
| Duration of abdominal pain (h) | | | | |
| <12 | 416 (33) | 210 (17) | 193 (30) | 17 (8) |
| 12–24 | 400 (32) | 296 (34) | 244 (37) | 52 (24) |
| 25–48 | 312 (25) | 265 (30) | 176 (27) | 89 (41) |
| 49–72 | 135 (11) | 99 (11) | 38 (6) | 61 (28) |
| WBC count by age group ($\times$1,000/mm$^3$) | | | | |
| <5 y | 13.5 $\pm$ 6.7 | 17.1 $\pm$ 4.9 | 17.4 $\pm$ 3.1 | 16.7 $\pm$ 6.6 |
| 5–11 y | 11.5 $\pm$ 5.7 | 16.3 $\pm$ 5.0 | 15.6 $\pm$ 4.5 | 18.1 $\pm$ 5.7 |
| >12 y | 9.7 $\pm$ 4.0 | 15.3 $\pm$ 4.7 | 14.9 $\pm$ 4.4 | 16.6 $\pm$ 5.6 |
| ANC by age group ($\times$1,000/mm$^3$) | | | | |
| <5 y | 10.7 $\pm$ 6.2 | 13.9 $\pm$ 4.7 | 14.1 $\pm$ 3.3 | 13.7 $\pm$ 6.2 |
| 5–11 y | 8.7 $\pm$ 5.7 | 13.4 $\pm$ 4.9 | 12.7 $\pm$ 4.5 | 15.5 $\pm$ 5.3 |
| >12 y | 6.8 $\pm$ 4.2 | 12.5 $\pm$ 4.8 | 12.1 $\pm$ 4.5 | 14.1 $\pm$ 5.6 |

Categorical data are presented as $n$ (%); other data are reported as median (interquartile range) or mean $\pm$ SD.

Table 2
Other diagnoses among patients without appendicitis, stratified by age group

| Other Diagnoses | < 5 years (*n* = 122) | 5-11 years (*n* = 597) | 12-18 years (*n* = 517) | Total (*n* = 1,236) |
|---|---|---|---|---|
| Non-specific abdominal pain | 42 (34) | 256 (43) | 222 (43) | 520 (42) |
| Gastroenteritis | 30 (25) | 103 (17) | 51 (10) | 184 (15) |
| Other, not classified | 21 (17) | 86 (14) | 69 (13) | 176 (14) |
| Constipation | 16 (13) | 73 (12) | 62 (12) | 151 (12) |
| Ovarian cyst | 0 (0) | 2 (<1) | 58 (11) | 60 (5) |
| Mesenteric adenitis | 3 (2) | 24 (4) | 15 (3) | 42 (3) |
| Pneumonia | 4 (3) | 19 (3) | 2 (<1) | 25 (2) |
| Urinary tract infection | 3 (2) | 12 (2) | 9 (2) | 24 (2) |
| Pyelonephritis | 2 (2) | 9 (2) | 5 (1) | 16 (1) |
| Renal stone | 0 (0) | 4 (1) | 10 (2) | 14 (1) |
| Gastritis | 1 (1) | 9 (2) | 3 (1) | 13 (1) |
| Pelvic inflammatory dIsease | 0 (0) | 0 (0) | 11 (2) | 11 (1) |

Values in table represent *frequency (percent)*

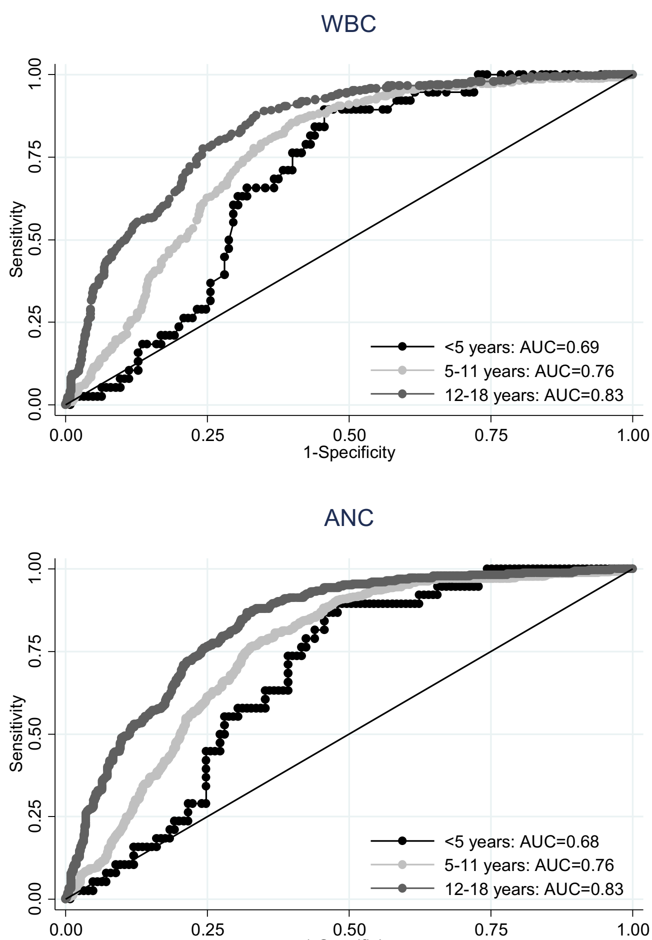


**Figure 1.** Receiver operator characteristic curves for WBC count and ANC across three age groups of children with suspected appendicitis. ANC = absolute neutrophil count; AUC = area under the curve; WBC = white blood cell.

Supplements S1 and S2 (available as supporting information in the online version of this paper). Within the three age subgroups, the AUCs of WBC count alone did not significantly differ from the AUCs of WBC count combined with symptom duration in classifying appendicitis (p-values = 0.79, 0.12, and 0.74 for the <5, 5–11, and 12–18 age groups, respectively). The same pattern of results was found for the AUCs of ANC with and without symptom duration in classifying appendicitis.

### Illustrative Example: WBC Count 10,000/mm$^3$ Threshold

At a WBC count cut-point of 10,000/mm$^3$, the sensitivity decreased with increasing age: <5 years, 95% (95% CI = 82% to 99%); 5–11 years, 91% (95% CI = 89% to 94%); and 12–18 years, 89% (95% CI = 85% to 92%). Specificity increased with increasing age (by group): 36% (95% CI = 28% to 45%), 49% (95% CI = 45% to 53%), and 64% (95% CI = 59% to 68%). The PPV increased with increasing age (by group) from 31% (95% CI = 23% to 40%) to 59% (95% CI = 56% to 63%) to 61% (95% CI = 56% to 65%), whereas the NPV was highest for children less than 5 years of age (96% [95% CI = 85% to 99%]) compared to the 5- to 11-year-old patients (87% [95% CI = 83% to 91%]) or those over 12 years of age [90% (95% CI 87 - 93%)].

## DISCUSSION

Despite the near-universal use of WBC count and ANC as part of the diagnostic evaluation of suspected appendicitis in children, threshold values in published scores and decision algorithms have not been previously age-adjusted. We demonstrated that the predictive capability of WBC count and ANC varies by age. More importantly, at any specific cut-point, the predictive value varies significantly between age groups thereby arguing for age-adjusted WBC count or ANC thresholds. Furthermore, the diagnostic value of WBC count and ANC did not vary with duration of abdominal pain and is consistent with previous investigations;[22,23,28,38] specific to our investigation, this lack of association with pain duration remained true among the age subgroups.

Despite the ubiquity of patient presentations with abdominal pain and a concern for appendicitis, the diagnostic evaluation for appendicitis remains challenging especially in children. The diagnostic value of

Table 3
Diagnostic Performance of WBC Count Across Different Cut-points by Age of Patient

| WBC classification cut-point (×1000/mm³) | Age Group (y) <5 (*n* = 163) | | | | | 5–11 (*n* = 1,107) | | | | | 12–18 (*n* = 863) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sens | Spec | PPV | NPV | +LR | Sens | Spec | PPV | NPV | +LR | Sens | Spec | PPV | NPV | +LR |
| ≥5 | 100 | 5 | 24 | 100 | 1.05 | 99 | 7 | 46 | 88 | 1.06 | 100 | 5 | 40 | 100 | 1.05 |
| ≥6 | 100 | 10 | 25 | 100 | 1.12 | 99 | 14 | 48 | 93 | 1.15 | 99 | 13 | 42 | 97 | 1.15 |
| ≥7 | 100 | 14 | 26 | 100 | 1.16 | 98 | 23 | 51 | 92 | 1.27 | 98 | 27 | 46 | 95 | 1.33 |
| ≥8 | 100 | 20 | 28 | 100 | 1.25 | 97 | 33 | 54 | 92 | 1.43 | 97 | 41 | 51 | 95 | 1.64 |
| ≥9 | 97 | 28 | 29 | 97 | 1.35 | 95 | 41 | 57 | 91 | 1.6 | 94 | 52 | 55 | 93 | 1.96 |
| ≥10 | 95 | 36 | 31 | 96 | 1.48 | 91 | 49 | 59 | 87 | 1.78 | 89 | 64 | 61 | 90 | 2.46 |
| ≥11 | 92 | 42 | 32 | 95 | 1.58 | 87 | 58 | 63 | 85 | 2.06 | 81 | 71 | 64 | 86 | 2.81 |
| ≥12 | 89 | 50 | 35 | 94 | 1.78 | 82 | 63 | 64 | 81 | 2.19 | 73 | 77 | 67 | 82 | 3.15 |
| ≥13 | 84 | 56 | 37 | 92 | 1.91 | 76 | 67 | 66 | 77 | 2.33 | 62 | 82 | 68 | 77 | 3.4 |
| ≥14 | 76 | 60 | 37 | 89 | 1.91 | 67 | 72 | 66 | 72 | 2.35 | 55 | 87 | 73 | 76 | 4.37 |
| ≥15 | 68 | 63 | 36 | 87 | 1.86 | 60 | 76 | 67 | 70 | 2.5 | 48 | 91 | 77 | 73 | 5.25 |

Values for Sens, Spec, PPV, and NPV represent percentages;
+LR = positive likelihood ratio; NPV = negative predictive value; PPV = positive predictive value; Sens = sensitivity; Spec = specificity; WBC = white blood cell.

Table 4
Diagnostic Performance of ANC Across Different Cut-points by Age of Patient

| ANC classification cut-point (×1000/mm³) | Age Group (y) <5 (*n* = 163) | | | | | 5–11 (*n* = 1,107) | | | | | 12–18 (*n* = 863) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sens | Spec | PPV | NPV | +LR | Sens | Spec | PPV | NPV | +LR | Sens | Spec | PPV | NPV | +LR |
| ≥5 | 100 | 20 | 28 | 100 | 1.25 | 97 | 33 | 54 | 94 | 1.45 | 96 | 43 | 52 | 95 | 1.7 |
| ≥6 | 97 | 27 | 29 | 97 | 1.34 | 95 | 40 | 57 | 91 | 1.6 | 93 | 56 | 57 | 93 | 2.11 |
| ≥7 | 95 | 30 | 29 | 95 | 1.36 | 92 | 47 | 59 | 88 | 1.75 | 89 | 64 | 61 | 90 | 2.45 |
| ≥8 | 92 | 38 | 31 | 94 | 1.48 | 88 | 55 | 61 | 85 | 1.94 | 83 | 70 | 63 | 87 | 2.72 |
| ≥9 | 89 | 45 | 33 | 93 | 1.62 | 82 | 60 | 63 | 80 | 2.04 | 75 | 76 | 66 | 83 | 3.12 |
| ≥10 | 87 | 54 | 36 | 93 | 1.87 | 77 | 66 | 65 | 78 | 2.27 | 64 | 81 | 68 | 78 | 3.41 |
| ≥11 | 74 | 59 | 35 | 88 | 1.81 | 70 | 70 | 66 | 74 | 2.33 | 57 | 85 | 70 | 76 | 3.72 |
| ≥12 | 63 | 62 | 34 | 85 | 1.68 | 61 | 75 | 67 | 70 | 2.44 | 51 | 89 | 74 | 74 | 4.49 |
| ≥13 | 55 | 70 | 36 | 84 | 1.87 | 52 | 79 | 67 | 67 | 2.49 | 45 | 91 | 76 | 72 | 5.02 |
| ≥14 | 50 | 73 | 36 | 83 | 1.84 | 41 | 83 | 66 | 63 | 2.36 | 37 | 93 | 77 | 70 | 5.37 |
| ≥15 | 34 | 75 | 30 | 79 | 1.38 | 32 | 87 | 66 | 61 | 2.42 | 29 | 95 | 79 | 68 | 5.85 |

Values for Sens, Spec, PPV and NPV represent percentages.
ANC = absolute neutrophil count; +LR = positive likelihood ratio; NPV = negative predictive value; PPV = positive predictive value; Sens = sensitivity; Spec = specificity.

WBC count and ANC has been previously studied in adults[22,30,34,39,40] and children.[16,23,26,28,31,33,34,38,40,41] Even with limitations in the sample size or biases in the study population, the markers have consistently shown discriminatory value for appendicitis and complicated appendicitis. High-quality cohort studies inclusive of pediatric patients have reported overall diagnostic value of WBC count and ANC to have AUCs of 0.78–0.92 and 0.78–0.89 respectively.[28,39]

WBC count and ANC (or neutrophil predominance) are incorporated into nearly all diagnostic pathways for appendicitis. The two most referenced clinical scores are the Alvarado score[3] and the Pediatric Appendicitis Score.[7] Both scoring systems considered an elevated WBC count (>10,000/mm³) and neutrophil predominance (Alvarado score > 75% PMN; Pediatric Appendicitis Score includes "neutrophilia" without a definition) as predictors for appendicitis. Other guidelines for suspected appendicitis have assigned similar cutoffs[2,8,9] or performed an independent analysis of threshold values.[21,29] The exact cut-points incorporated into guidelines depended on the balance between sensitivity and specificity and whether the goal of the guideline was to identify high-risk or low-risk patients. None of the prior published guidelines or scoring systems has provided age-adjusted values for WBC count or ANC.

Outside of clinical score and decision pathways, we found two prior relevant investigations that considered age-adjusted values of WBCs. In a study of 200 children undergoing surgery for appendicitis, the AUC using ROC analysis was 0.46 for those < 6 years of age compared to 0.79 for those 6 to 19 years of age.[32] Unfortunately, the study population only included those with operative care and therefore does not reflect a standard sample of children with suspected appendicitis. Another

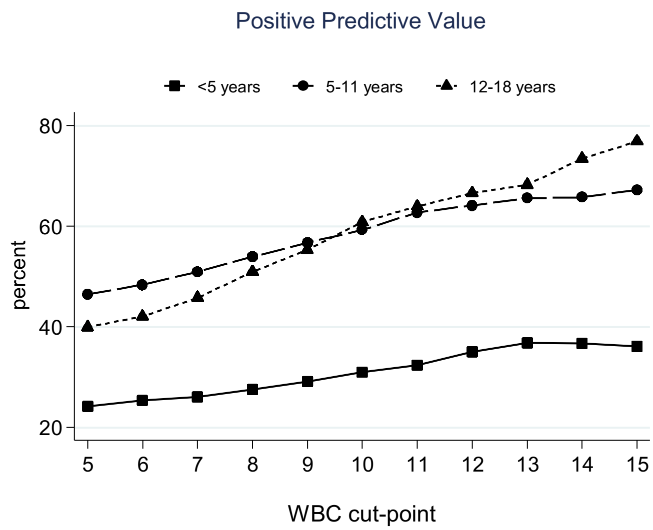


**Figure 2.** Positive predictive value of WBC count for appendicitis over a range of cut-points and stratified by age group. WBC = white blood cell.

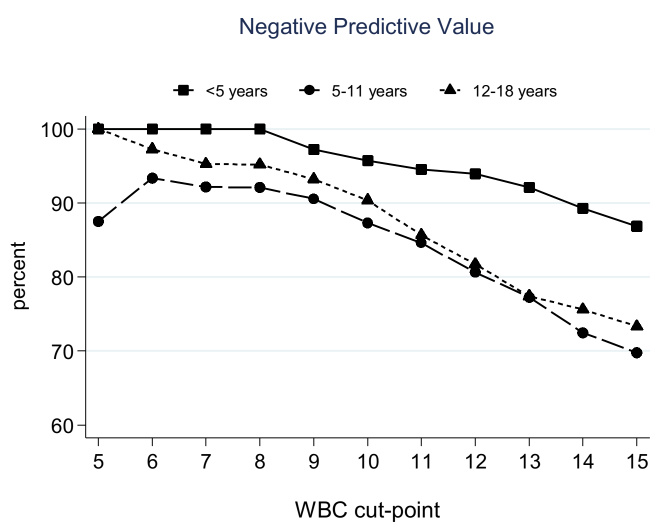


**Figure 3.** Negative predictive value of WBC count for appendicitis over a range of cut-points and stratified by age group. WBC = white blood cell.

study of nontraumatic acute abdominal pain used the laboratory-derived range of normal values for WBC that were age-adjusted; although this study was not focused on patients with suspected appendicitis (only 10.2% of sample had appendicitis), the age adjustment was integrated into the definition of an abnormal result as a predictor of appendicitis.[26]

## LIMITATIONS

Our study has some strengths and limitations that deserve discussion. The prospective enrollment of a study sample across multiple sites allows for greater generalizability to a population of patients with suspected appendicitis. However, each site represented an academic pediatric ED that may not mirror the population evaluated in other settings; accordingly, the relatively high prevalence of appendicitis in the study population influences the reported predictive values. We also acknowledge that we artificially dichotomized the patients into the outcomes of appendicitis and absence of appendicitis when in fact other diagnoses are important to consider and may explain some of the differences in discriminatory power of WBC count and ANC across age groups. Furthermore, we did not investigate the impact of race and sex on total WBC count and ANC, both of which have been previously shown to vary across populations of healthy adults. Finally, even with a cohort of over 2,000 patients, the sample size of children less than 5 years of age was relatively small and therefore estimates of diagnostic performance of the WBC count and ANC have less precision than the two other age groups.

## CONCLUSION

The diagnostic performance of white blood cell count and absolute neutrophil count improves with increasing age. Age-adjusted values of white blood cell count or absolute neutrophil count should be considered in diagnostic strategies for suspected pediatric appendicitis. In the short term, clinical decision pathways might include age-adjusted thresholds for age groups. Future applications of these findings might integrate age-based predictive values of white blood cell count and absolute neutrophil count into electronic medical record-based decision support algorithms.

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## Supporting Information

The following supporting information is available in the online version of this paper:

**Data Supplement S1.** Positive predictive value of absolute neutrophil count (ANC) for appendicitis over a range of cut-points and stratified by age group.

**Data Supplement S2.** Negative predictive value of absolute neutrophil count (ANC) for appendicitis over a range of cut-points and stratified by age group.