

Unlocking the Complete Blood Count: Derivation of a Single-Panel Laboratory Test that includes Monocyte Distribution Width to Create a Universal Sepsis Screening Tool

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Background | Sepsis & CBC

Sepsis

3 million cases annually; 15-30% mortality

Timely initiation of simple measures is **life-saving**

Septic patients presenting **without obvious signs** have reported delays to treatment and increased risk of mortality.

Complete Blood Count (CBC)

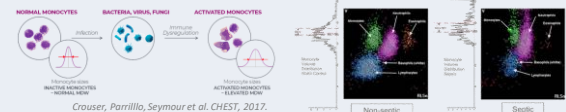
Unlocking the CBC for early detection of sepsis in the Emergency Department (ED) may have enormous impact, due to it's routine (and early) availability.

Monocyte Distribution Width (MDW) is a morphometric parameter that reflects variability in monocyte cell volume. It has emerged as a useful biomarker for early sepsis detection.



Background | Monocyte Distribution Width

Monocyte morphology changes in response to pathogens



Crouser, Parrillo, Seymour et al. CHEST, 2017.

MDW as a Diagnostic Marker for Sepsis

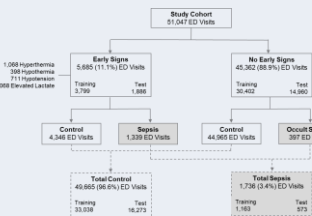
Study	Sample Size	MDW Cutoff	Sensitivity (95%CI)	Specificity (95%CI)
Summary	20		0.81 (0.79-0.83)	0.56 (0.43-0.68)
Summary	22.6		0.81 (0.78-0.83)	0.73 (0.67-0.78)

Malinovska, Hinson, Levin et al. CHEST, 2023.

Methods | Study Flow Diagram

Study Cohort

Adult (> 18yrs) ED visits with a CBC differential collected within 6-hours of ED arrival.



Early Signs Group

The presence of any early vital sign indicator:

- Abnormal temperature $> 38^{\circ}\text{C}$ or $< 36^{\circ}\text{C}$ at triage]
- Hypotension [< 90 mmHg at triage]
- Elevated lactate (> 2 mmol/L) known prior to the CBC result.

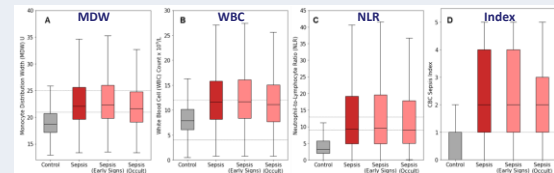
No Early Signs ("Occult")

No early vital sign at triage and no elevated lactate prior to the CBC result.

Results | CBC Index Performance

Leukocyte Parameters and the CBC Index by Sepsis Group

Sepsis sub-groups for patients with "Early Signs" or "Occult" displayed in light red.



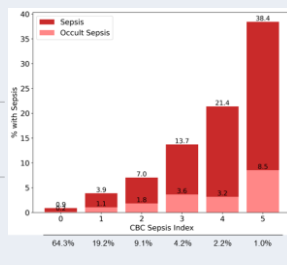
CBC Index Diagnostic Performance Metrics

Cohort stratified by patients presenting with "Early Signs" or "No Early Signs (Occult)".

Total Cohort							
Index Score	Sensitivity	Specificity	PPV	NPV	LR+	LR-	
≥ 1	82.9 (79.8-86.0)	65.9 (62.5-69.7)	7.9 (7.1-8.8)	99.1 (98.9-99.3)	2.43	0.26	
≥ 2	61.1 (57.1-65.1)	85.0 (84.5-85.5)	12.1 (11.3-13.0)	98.6 (98.2-98.8)	4.07	0.46	
≥ 3	42.2 (38.2-46.3)	93.8 (93.4-94.1)	18.1 (17.1-21.4)	97.9 (97.7-98.1)	6.76	0.62	
≥ 4	25.1 (21.6-28.7)	97.5 (97.3-97.8)	26.5 (22.8-30.0)	97.4 (97.1-97.6)	10.25	0.77	
5	11.0 (8.4-13.6)	99.4 (99.3-99.5)	38.4 (31.6-45.5)	96.9 (96.7-97.1)	17.7	0.9	
Early Signs							
Index Score	Sensitivity	Specificity	PPV	NPV	LR+	LR-	
≥ 1	81.9 (78.3-85.5)	41.9 (39.3-44.4)	30.1 (27.5-32.7)	88.3 (85.9-90.7)	1.41	0.43	
≥ 2	61.2 (56.7-65.8)	66.2 (63.7-68.6)	35.6 (32.2-39.5)	84.8 (82.7-86.9)	1.81	0.59	
≥ 3	45.1 (38.5-47.7)	83.8 (81.7-85.5)	44.1 (39.4-49.2)	82.0 (80.0-84.7)	2.63	0.68	
≥ 4	26.8 (22.6-30.9)	93.4 (92.1-94.6)	55.1 (48.5-61.4)	80.7 (78.8-82.4)	4.03	0.78	
5	11.1 (8.2-14.0)	98.2 (97.5-98.9)	65.3 (54.6-76.1)	78.4 (76.5-80.3)	6.18	0.91	
Occult							
Index Score	Sensitivity	Specificity	PPV	NPV	LR+	LR-	
≥ 1	86.4 (80.5-92.2)	68.3 (67.5-69.0)	2.4 (1.9-2.8)	99.8 (99.7-99.9)	2.72	0.2	
≥ 2	60.6 (52.2-68.8)	86.8 (86.2-87.4)	3.9 (3.1-4.8)	99.9 (99.9-100.0)	4.6	0.45	
≥ 3	39.4 (31.1-47.7)	94.7 (94.5-95.1)	6.3 (4.6-7.9)	99.4 (99.3-99.6)	7.5	0.64	
≥ 4	19.7 (12.9-26.5)	98.0 (97.7-98.2)	7.9 (5.0-10.8)	99.3 (99.1-99.4)	9.64	0.82	
5	10.6 (6.4-15.9)	99.3 (99.4-99.6)	15.1 (8.2-23.3)	99.1 (99.1-99.3)	20.97	0.9	

Results | CBC Index

Proportion of ED patients with Sepsis by CBC Index on Test Set



CBC Index Point System Derived by Logistic Regression on Training Set

Measure	Total	Control	Sepsis	Odds Ratio	CBC Sepsis Index Points
MDW [Reference + 21]	5098 (26.7)	5937 (16.1)	879 (22.4)	4.79 (3.39-6.82)	1
NLR [Reference + 6]	2271 (8.6)	3593 (9.3)	316 (27.2)	4.47 (3.79-5.28)	2
WBC [Reference + 12]	2212 (8.2)	1967 (6.0)	144 (13.2)	2.30 (1.89-2.80)	0
MDW + NLR + WBC	7980 (37.6)	7116 (16.4)	462 (39.2)	4.43 (3.12-6.14)	2
MDW + NLR	1642 (8.0)	1627 (4.9)	93 (5.0)	8.81 (6.57-11.84)	0
MDW + WBC	1013 (4.8)	4489 (13.6)	562 (48.3)	2.46 (1.32-4.50)	1

*NLR = Neutrophil to Lymphocyte Ratio

Conclusions

A CBC-based index that includes MDW was effective in early sepsis detection. Previous research found that MDW, WBC, and NLR in combination showed superior diagnostic performance than single parameters. In this study, a composite CBC Index was derived and tested. Diagnostic performance was strongest in the "occult" sepsis subgroup, representing the patients that are most often missed and suffer delays in care and are at increased risk of mortality.

Malinovska, Hinson, Levin et al. J Am Coll Emerg Physicians Open, 2022. Wayne et al. JAMA Netw Open, 2021. Filbin et al. Crit Care Med, 2018. Comanelli et al. BMJ Infect Dis. 2022.

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