

## Appendix 4 (as submitted by the authors): Sensitivity analyses

### Sensitivity Analyses – Classification Accuracy

Table A4-1: Contrasting diagnostic classification accuracy of paramedic approaches to sepsis identification between cohort including patients with missing measures and cohort excluding patients with missing measures

Missing Value Cohort	Sensitivity 95% CI			Specificity 95% CI			PPV †	NPV
	Included	Excluded		Included	Excluded		Excluded	
Sepsis Alert	0.07	0.06 (0.05-0.07)		0.99	0.99 (0.99-0.99)		0.68	0.80
qSOFA(2)	0.40	0.42 (0.4-0.43)		0.94	0.94 (0.94-0.95)		0.66	0.85
PITSTOP	0.02	0.02 (0.02-0.03)		1.00	1.00 (1-1)		0.65	0.79
qSOFA+EtCo2	0.44	0.71 (0.68-0.74)		0.92	0.65 (0.62-0.68)		0.59	0.76
PRESS(2)	0.11	0.10 (0.09-0.11)		0.98	0.98 (0.98-0.98)		0.56	0.80
SEPSIS Score (5)	0.26	0.27 (0.25-0.29)		0.94	0.94 (0.93-0.94)		0.55	0.82
BAS	0.26	0.58 (0.56-0.6)		0.94	0.79 (0.78-0.8)		0.43	0.87
<i>Borrelli(3)</i>	0.49	0.50 (0.48-0.52)		0.86	0.86 (0.85-0.87)		0.50	0.86
SIRS+EtCO2	0.74	0.93 (0.91-0.95)		0.40	0.09 (0.07-0.1)		0.41	0.64
MEWS(4)	0.57	0.54 (0.52-0.56)		0.79	0.77 (0.76-0.78)		0.35	0.85
PRESEP(4)	0.49	0.50 (0.48-0.52)		0.76	0.75 (0.74-0.76)		0.34	0.83
MBIS(2)	0.44	0.44 (0.42-0.46)		0.77	0.77 (0.76-0.77)		0.33	0.83
PSP(2)	0.42	0.43 (0.41-0.45)		0.77	0.76 (0.75-0.77)		0.32	0.83
PHANTASi	0.20	0.20 (0.19-0.22)		0.88	0.88 (0.87-0.89)		0.31	0.88
Robson(2)	0.75	0.79 (0.78-0.81)		0.54	0.46 (0.45-0.47)		0.31	0.84
PreSAT(2)	0.49	0.50 (0.48-0.52)		0.71	0.70 (0.69-0.71)		0.31	0.83
SIRS(2)	0.45	0.46 (0.44-0.48)		0.72	0.71 (0.7-0.72)		0.28	0.91
HEWS(2)	0.85	0.86 (0.84-0.87)		0.41	0.41 (0.4-0.42)		0.68	0.80
Suffoletto	0.70	0.74 (0.72-0.76)		0.38	0.33 (0.32-0.34)		0.66	0.85

PPV = positive predictive value, NPV = negative predictive value, qSOFA = Quick Sepsis-related Organ Failure; PITSTOP = Paramedic Initiated Treatment of Sepsis Targeting Out-of-hospital Patients clinical trial; PRESS = Prehospital Severe Sepsis, SEPSIS = Screening to Enhance Prehospital Identification of Sepsis, BAS = Blood Pressure "Andningsfrekvens" (respiratory rate in Swedish) Saturation, MEWS = Modified Early Warning Score, EtCO2 = end-tidal carbon dioxide, PRESEP = Prehospital Early Sepsis Detection, MBIS = Mecklenburg Bacterial Infection Scale, PSP = Prehospital Sepsis Project, PHANTASi = Prehospital ANTibiotics Against Sepsis, PreSAT = Prehospital Sepsis Assessment Tool, SIRS = Systemic Inflammatory Response Syndrome, HEWS = Hamilton Early Warning Score, N.B. No studies reporting thresholds of the CIP or NEWS score for the identification of sepsis were identified and as such these scores are not included in this table.

Table A4-2: Diagnostic classification accuracy of paramedic approaches to sepsis identification in entire population (n = 131,745) using published thresholds

Strategy (Score Threshold)	Sensitivity (95% CI)	Specificity (95% CI)	PPV †	NPV
PITSTOP	0.02 (0.02-0.03)	1.00 (1-1)	0.41	0.98
SEPSIS(5)	0.26 (0.24-0.27)	0.98 (0.98-0.98)	0.24	0.98
Sepsis Alert	0.07 (0.06-0.08)	0.99 (0.99-1)	0.22	0.98
PRESS(2)	0.11 (0.1-0.12)	0.99 (0.99-0.99)	0.19	0.98
qSOFA(2)	0.40 (0.38-0.42)	0.95 (0.95-0.95)	0.15	0.99
Borrelli(3)	0.49 (0.47-0.51)	0.93 (0.93-0.93)	0.13	0.99
qSOFA+EtCO2(2)	0.44 (0.42-0.46)	0.94 (0.94-0.94)	0.13	0.99
PRESEP	0.49 (0.47-0.51)	0.91 (0.91-0.92)	0.11	0.99
BAS(1)	0.57 (0.55-0.59)	0.89 (0.89-0.89)	0.10	0.99
MBIS(2)	0.44 (0.42-0.46)	0.89 (0.89-0.89)	0.08	0.99
PSP(2)	0.42 (0.4-0.44)	0.89 (0.89-0.89)	0.08	0.99
PHANTASi	0.20 (0.19-0.22)	0.94 (0.94-0.95)	0.07	0.98
MEWS(4)	0.53 (0.51-0.55)	0.85 (0.85-0.85)	0.07	0.99
PreSAT(2)	0.49 (0.47-0.5)	0.83 (0.83-0.83)	0.06	0.99
SIRS(2)	0.45 (0.43-0.47)	0.84 (0.84-0.84)	0.06	0.99
Robson	0.75 (0.73-0.76)	0.66 (0.66-0.66)	0.04	0.99
HEWS(2)	0.85 (0.84-0.86)	0.51 (0.51-0.51)	0.04	0.99
Suffoletto	0.70 (0.68-0.71)	0.57 (0.56-0.57)	0.03	0.99
SIRS+EtCO2(2)	0.74 (0.73-0.76)	0.50 (0.49-0.5)	0.03	0.99

† Results ordered by decreasing positive predictive value

\*Authors include “nursing home transport” in score calculation. This variable was not available in our dataset

PPV = positive predictive value, NPV = negative predictive value, PITSTOP = Paramedic Initiated Treatment of Sepsis Targeting Out-of-hospital Patients clinical trial, SEPSIS = Screening to Enhance Prehospital Identification of Sepsis, PRESS = Prehospital Severe Sepsis, qSOFA = Quick Sepsis-related Organ Failure, EtCO2 = end-tidal carbon dioxide, PRESEP = Prehospital Early Sepsis Detection, BAS = Blood Pressure "Andningsfrekvens" (respiratory rate in Swedish) Saturation, MBIS = Mecklenburg Bacterial Infection Scale, PSP = Prehospital Sepsis Project, PHANTASi = Prehospital ANTibiotics Against Sepsis, MEWS = Modified Early Warning Score, PreSAT = Prehospital Sepsis Assessment Tool, SIRS, Systemic Inflammatory Response Syndrome, HEWS = Hamilton Early Warning Score,  
N.B. No studies reporting thresholds of the CIP or NEWS score for the identification of sepsis were identified and as such these scores are not included in this table.

Table A4-3: Probability of sepsis diagnosis among patients with emergency department diagnosed infection excluding patients with missing measures

		<b>Numeric score</b>					
<b>Strategy</b>	<b>C</b>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
qSOFA	0.77	0.07 (0.06-0.08)	0.25 (0.22-0.28)	0.60 (0.56-0.64)	0.87 (0.85-0.89)		
BAS	0.71	0.14 (0.11-0.16)	0.34 (0.31-0.38)	0.63 (0.6-0.67)	0.85 (0.82-0.87)		
Robson	0.72	0.07 (0.06-0.09)	0.13 (0.11-0.15)	0.23 (0.2-0.26)	0.36 (0.32-0.4)	0.52 (0.47-0.58)	0.68 (0.63-0.73)
PreSAT	0.65	0.12 (0.1-0.15)	0.20 (0.17-0.22)	0.29 (0.26-0.33)	0.42 (0.38-0.45)	0.55 (0.51-0.59)	
PSP	0.66	0.13 (0.11-0.16)	0.21 (0.18-0.24)	0.32 (0.28-0.35)	0.45 (0.41-0.49)		
SIRS	0.63	0.14 (0.12-0.16)	0.20 (0.18-0.23)	0.29 (0.25-0.32)	0.39 (0.35-0.43)		
MBIS	0.61	0.16 (0.13-0.19)	0.21 (0.18-0.24)	0.26 (0.23-0.29)	0.32 (0.29-0.35)		
		<b>Numeric score</b>					
<b>Strategy</b>	<b>C</b>	<b>2</b>	<b>4</b>	<b>6</b>	<b>8</b>	<b>10</b>	<b>11</b>
CIP	0.79	0.19 (0.17-0.22)	0.61 (0.58-0.63)	0.91 (0.9-0.92)	0.98 (0.98-0.99)		
Borrelli	0.78	0.23 (0.20-0.26)	0.63 (0.59-0.68)	0.91 (0.89-0.93)			
SEPSIS	0.73	0.16 (0.14-0.18)	0.36 (0.33-0.39)	0.63 (0.60-0.66)	0.84 (0.82-0.86)		
PRESEP	0.68	0.18 (0.16-0.21)	0.26 (0.23-0.29)	0.36 (0.32-0.4)	0.47 (0.43-0.51)	0.59 (0.54-0.63)	0.64 (0.38-0.45)
		<b>Numeric score</b>					
<b>Strategy</b>	<b>C</b>	<b>3</b>	<b>6</b>	<b>9</b>	<b>12</b>	<b>15</b>	<b>16</b>
NEWS	0.76	0.14 (0.12-0.17)	0.31 (0.28-0.35)	0.55 (0.52-0.58)	0.77 (0.74-0.79)	0.90 (0.88-0.91)	0.93 (0.91-0.94)
HEWS	0.73	0.20	0.39	0.62	0.81	0.92	

		(0.17- 0.23)	(0.36- 0.43)	(0.59- 0.66)	(0.78- 0.83)	(0.9- 0.93)
MEWS	0.74	0.21	0.50	0.78	0.93	
		(0.19- 0.24)	(0.46- 0.53)	(0.76- 0.81)	(0.92- 0.94)	
PRESS	0.64	0.16	0.25	0.37	0.51	0.64
		(0.14- 0.19)	(0.23- 0.28)	(0.34- 0.4)	(0.47- 0.55)	(0.59- 0.69)

C: C statistic, qSOFA = Quick Sepsis-related Organ Failure, BAS = Blood Pressure "Andningsfrekvens" (respiratory rate in Swedish) Saturation, PreSAT = Prehospital Sepsis Assessment Tool, PSP = Prehospital Sepsis Project, SIRS = Systemic Inflammatory Response Syndrome, CIP = Critical Illness Prediction, SEPSIS = Screening to Enhance Prehospital Identification of Sepsis, PRESEP = Prehospital Early Sepsis Detection, NEWS = National Early Warning Score, HEWS = Hamilton Early Warning Score, MEWS = Modified Early Warning Score, PRESS = Prehospital Severe Sepsis,

## Sensitivity Analysis – Paramedic Suspected Infection

Table A4-4: Contrasting diagnostic classification accuracy of paramedic approaches to sepsis identification among patients with paramedic suspected infection with patients with emergency department diagnosed infection

Infection Cohort	Sensitivity 95% CI			Specificity 95% CI		PPV †	NPV	
	ED	EMS		ED	EMS	EMS	EMS	
Sepsis Alert	0.07	0.13	(0.1-0.17)	0.99	0.99	(0.99-0.99)	0.59	0.91
PITSTOP	0.02	0.08	(0.05-0.11)	1.0	0.99	(0.99-0.99)	0.53	0.91
qSOFA(2)	0.40	0.55	(0.51-0.6)	0.94	0.92	(0.91-0.92)	0.43	0.95
SEPSIS(5)	0.26	0.43	(0.38-0.48)	0.94	0.93	(0.93-0.94)	0.41	0.93
qSOFA+EtCO2	0.44	0.58	(0.53-0.63)	0.92	0.90	(0.89-0.91)	0.40	0.95
PRESS(2)	0.11	0.16	(0.12-0.2)	0.98	0.97	(0.97-0.98)	0.38	0.91
Borrelli(3)	0.49	0.65	(0.60-0.69)	0.86	0.86	(0.84-0.87)	0.34	0.96
BAS(1)	0.57	0.63	(0.58-0.68)	0.79	0.82	(0.81-0.84)	0.29	0.95
MEWS(4)	0.53	0.69	(0.65-0.74)	0.77	0.77	(0.76-0.78)	0.25	0.96
PRESEP(4)	0.49	0.66	(0.62-0.71)	0.76	0.77	(0.76-0.78)	0.25	0.95
PHANTASi	0.20	0.41	(0.36-0.46)	0.88	0.85	(0.84-0.86)	0.24	0.93
MBIS(2)	0.44	0.75	(0.7-0.79)	0.77	0.72	(0.71-0.73)	0.23	0.96
PSP(2)	0.42	0.64	(0.59-0.69)	0.68	0.76	(0.74-0.77)	0.23	0.95
PreSAT(2)	0.49	0.69	(0.64-0.73)	0.77	0.71	(0.69-0.72)	0.21	0.95
SIRS(2)	0.45	0.64	(0.59-0.68)	0.72	0.72	(0.7-0.73)	0.20	0.95
Robson	0.75	0.84	(0.8-0.88)	0.54	0.57	(0.55-0.58)	0.18	0.97
HEWS(2)	0.85	0.91	(0.88-0.94)	0.41	0.45	(0.43-0.47)	0.16	0.98
SIRS+EtCO2	0.74	0.86	(0.83-0.89)	0.40	0.42	(0.4-0.43)	0.14	0.96
Suffoletto	0.70	0.82	(0.78-0.86)	0.38	0.38	(0.36-0.4)	0.13	0.95

† Results ordered by decreasing positive predictive value

\*Authors include “nursing home transport” in score calculation. This variable was not available in our dataset

PPV = positive predictive value, NPV = negative predictive value, PITSTOP = Paramedic Initiated Treatment of Sepsis Targeting Out-of-hospital Patients clinical trial, qSOFA = Quick Sepsis-related Organ Failure, SEPSIS = Screening to Enhance Prehospital Identification of Sepsis, EtCO2 = end-tidal carbon dioxide, PRESS = Prehospital Severe Sepsis, BAS = Blood Pressure "Andningsfrekvens" (respiratory rate in Swedish) Saturation, MEWS = Modified Early Warning Score, PRESEP = Prehospital Early Sepsis Detection, PHANTASi = Prehospital ANTibiotics Against Sepsis, MBIS = Mecklenburg Bacterial Infection Scale, PSP = Prehospital Sepsis Project, PreSAT = Prehospital Sepsis Assessment Tool, SIRS = Systemic Inflammatory Response Syndrome, HEWS = Hamilton Early Warning Score,