PHC Europe B.V.

PATHFAST

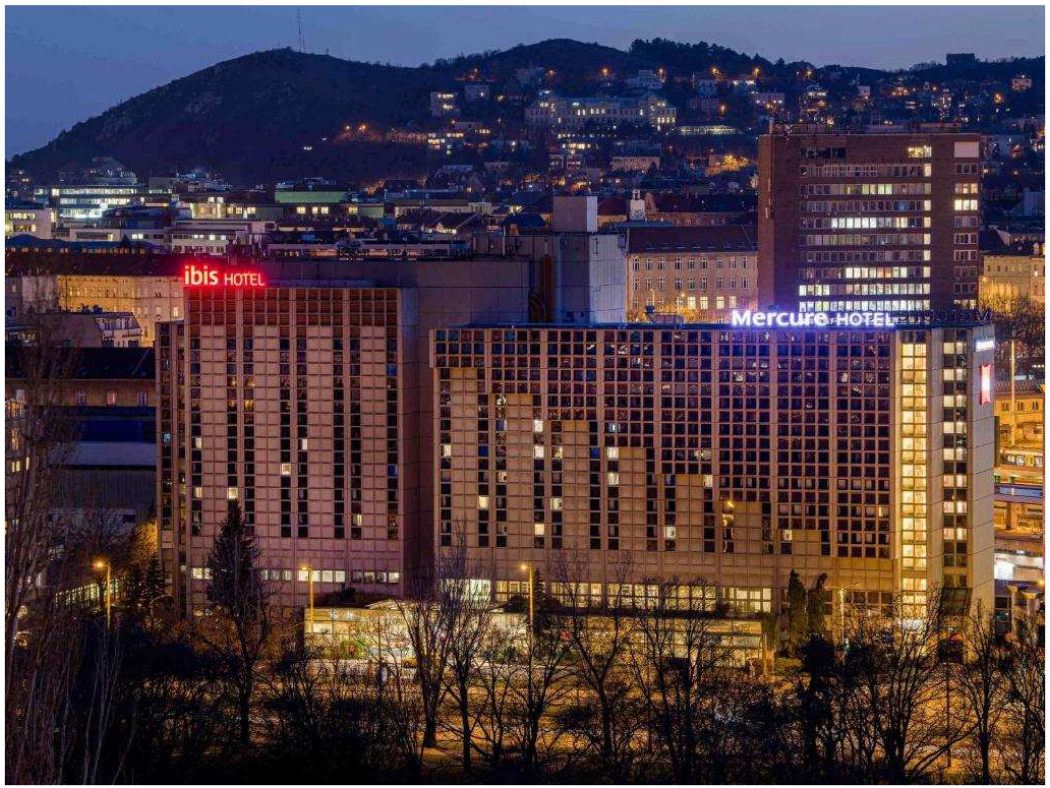
Product Management

Dr. Frank Ocklenburg

Healthcare with Precision

High precision clinical diagnostics and prognostics with PATHFAST™ POCT

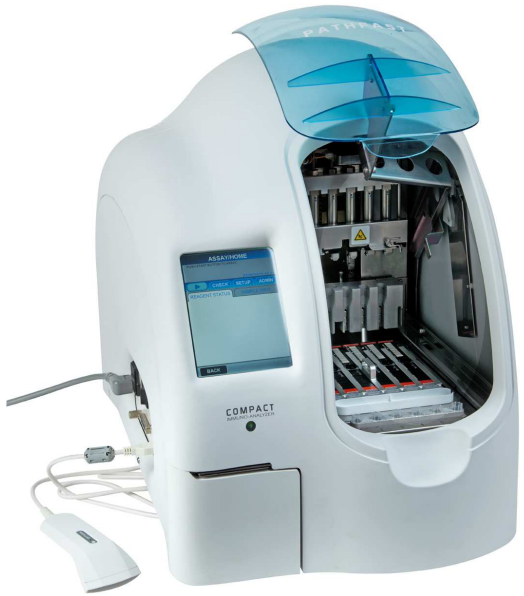
Medi-lab year-end party 2023



Thank you for having me here….

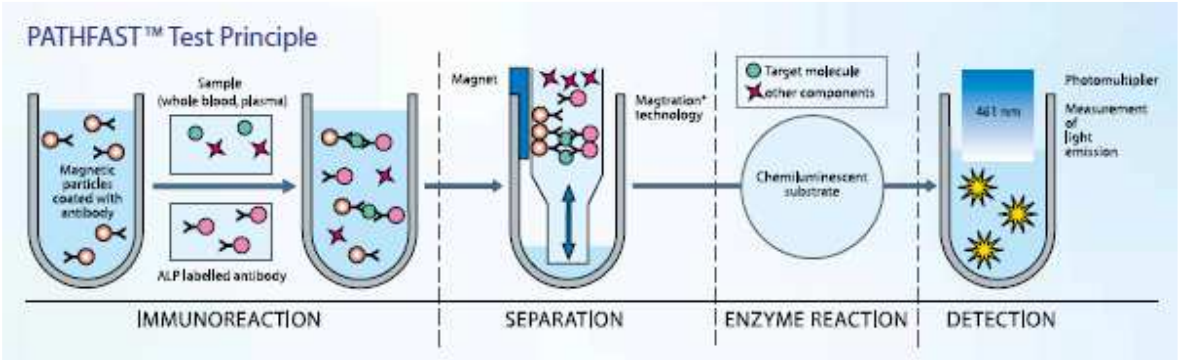
PHC Group Business Domains

What is the PATHFAST™ principle?



W = 343 mm
D = 569 mm
H = 475 mm

Weight
28kg



Assy procedere PATHFAST™

1

Collect

whole blood, serum or plasma samples, using heparin-NA, heparin-Li or EDTA collection tubes.

2

Transfer

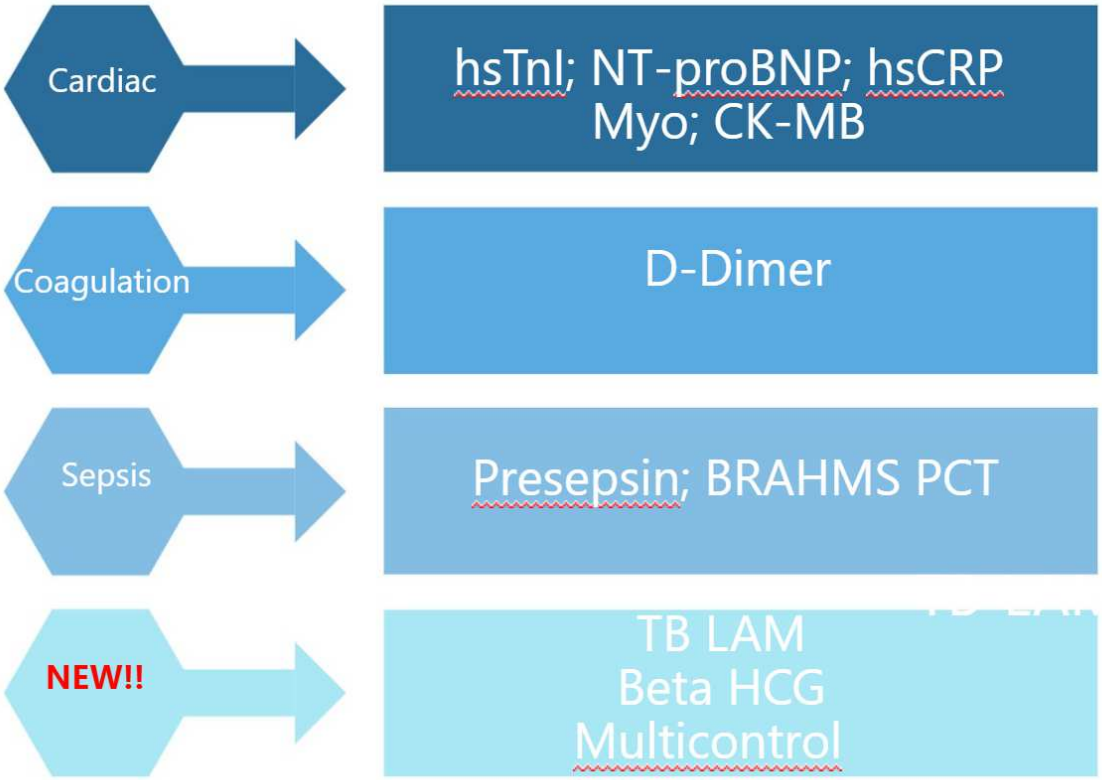
100 µL sample into each sample well of the reagent cartridges.

3

Place

the loaded reagent rack into the instrument and start the assay. Get **results in <17 minutes.**

PATHFAST™ portfolio



PATHFAST™ Marketing Activities

PATHFAST Marketing Actions_23

Digital Marketing - SEO, Content Creation

Digital Marketing - Social Media LinkedIn

Digital Marketing - Webpage and leads

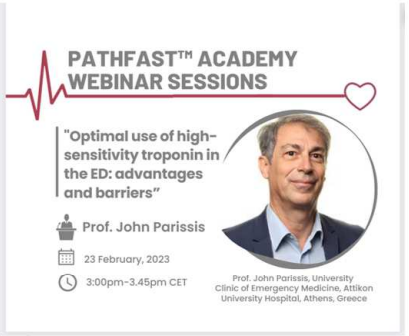
Digital Marketing – Newsletter

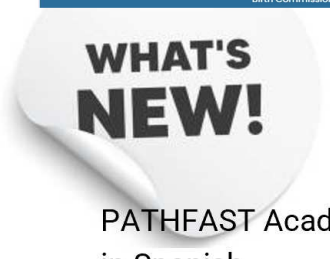
Digital Marketing - Academy

PATHFAST™ Marketing activities: Scientific Webinars

Digital Marketing _ Webinars

PATHFAST Academy Sessions





PATHFAST Academy Sessions in Spanish

PATHFAST™ Marketing activities: Product Manager Meetings

Product management meetings on a regular base

- ✓ New publications
- ✓ Studies review
- ✓ Recent scientific topics
- ✓ KOL´s

PATHFAST™ Marketing activities: Testimonials

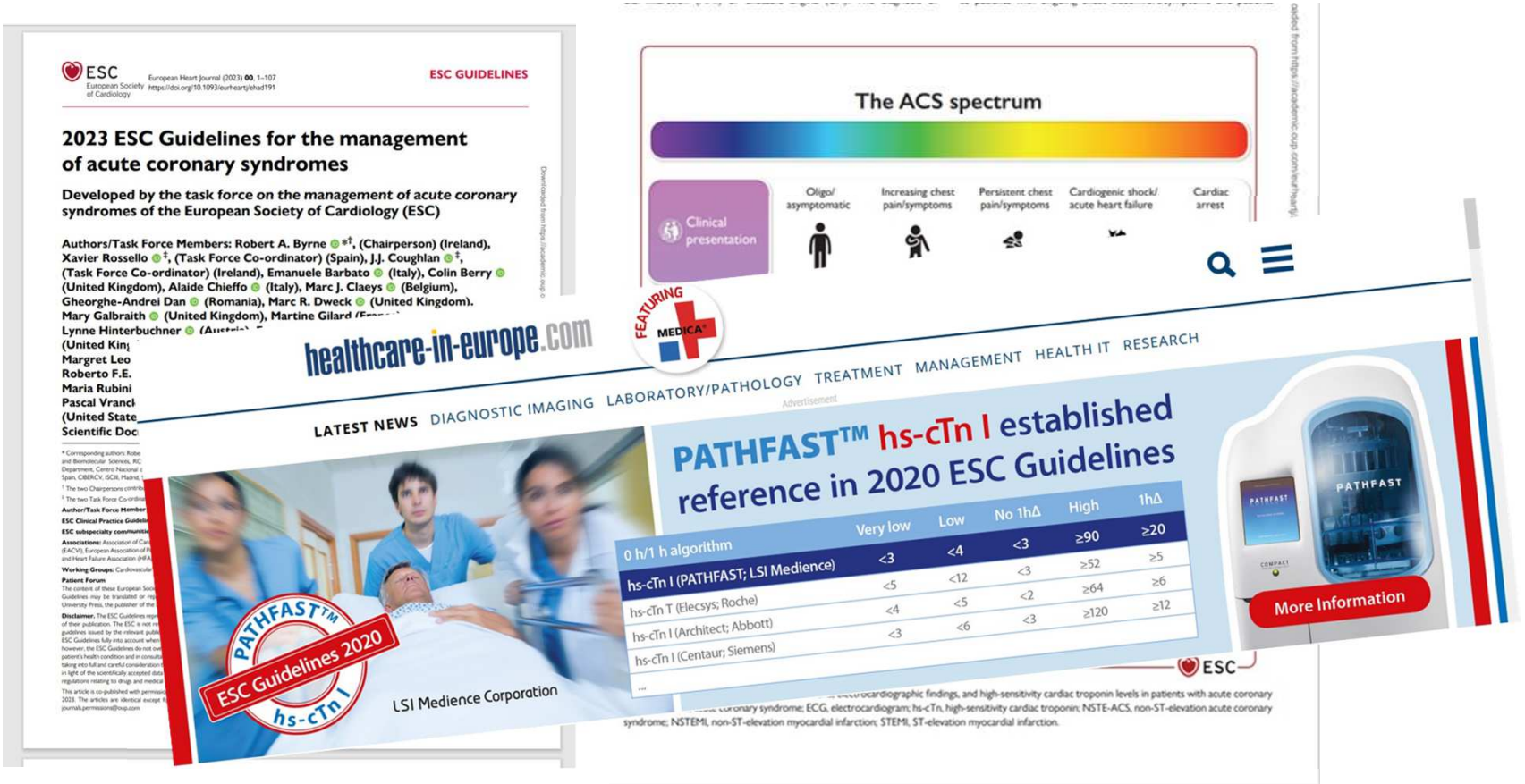
Testimonials

PATHFAST VOC´s

Perú
Nicaragua
Colombia
Costa Rica
Romania
Germany
Russia
Saudi Arabia

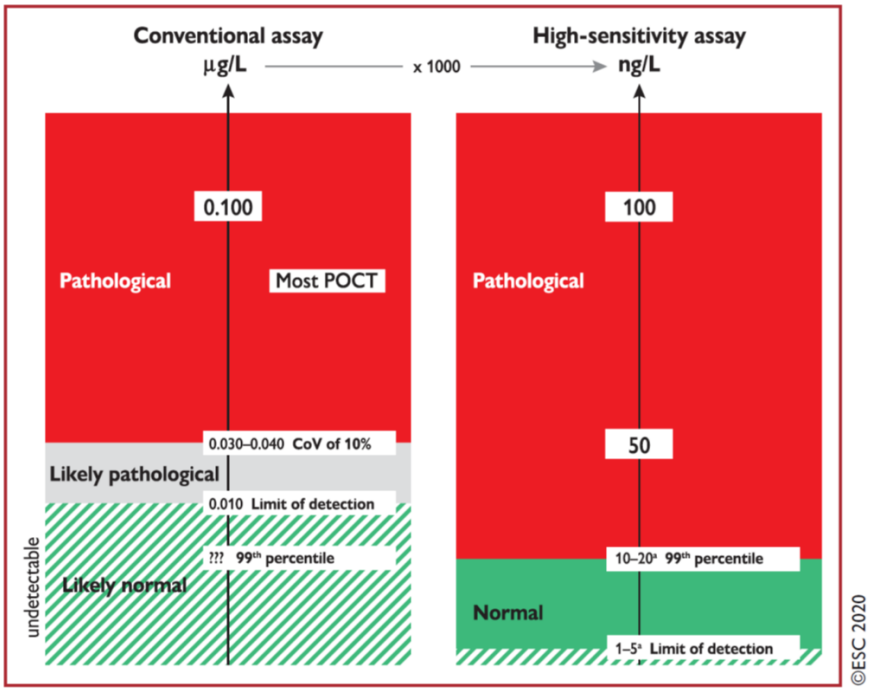
Kuwait
Egypt
Bahrain
Nicaragua
Guatemala
Panamá
Italy
Czech Republic
Lithuania
Belarus
Slovenia
Hungary
UK…

PATHFAST hs-troponin in ESC guidelines



Why chosing a hs-troponin?

High sensitivity cTnI assays can detect cTNI levels in patients with normal levels



PATHFAST hs-troponin in ESC guidelines: The cut off values

Table 5 Assay specific cut-off levels in ng/l within the 0 h/1 h and 0 h/2 h algorithms

0 h/1 h algorithm	Very low	Low	No 1hΔ	High	1hΔ
hs-cTn T (Elecsys; Roche)	<5	<12	<3	≥52	≥5
hs-cTn I (Architect; Abbott)	<4	<5	<2	≥64	≥6
hs-cTn I (Centaur; Siemens)	<3	<6	<3	≥120	≥12
hs-cTn I (Access; Beckman Coulter)	<4	<5	<4	≥50	≥15
hs-cTn I (Clarity; Singulex)	<1	<2	<1	≥30	≥6
hs-cTn I (Vitros; Clinical Diagnostics)	<1	<2	<1	≥40	≥4
hs-cTn I (Pathfast; LSI Medience)	<3	<4	<3	≥90	≥20
hs-cTn I (TriageTrue; Quidel)	<4	<5	<3	≥60	≥8
0 h/2 h algorithm	**Very low**	**Low**	**No 2hΔ**	**High**	**2hΔ**
hs-cTn T (Elecsys; Roche)	<5	<14	<4	≥52	≥10
hs-cTn I (Architect; Abbott)	<4	<6	<2	≥64	≥15
hs-cTn I (Centaur; Siemens)	<3	<8	<7	≥120	≥20
hs-cTn I (Access; Beckman Coulter)	<4	<5	<5	≥50	≥20
hs-cTn I (Clarity; Singulex)	<1	TBD	TBD	≥30	TBD
hs-cTn I (Vitros; Clinical Diagnostics)	<1	TBD	TBD	≥40	TBD
hs-cTn I (Pathfast; LSI Medience)	<3	TBD	TBD	≥90	TBD
hs-cTn I (TriageTrue; Quidel)	<4	TBD	TBD	≥60	TBD

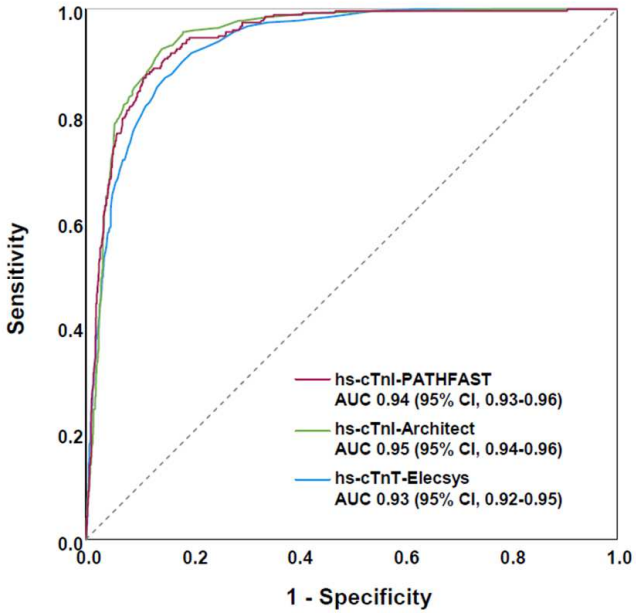
Assay-specific cutoffs are needed

PATHFAST hs-troponin is also evaluated for 0/2 hour algorithm

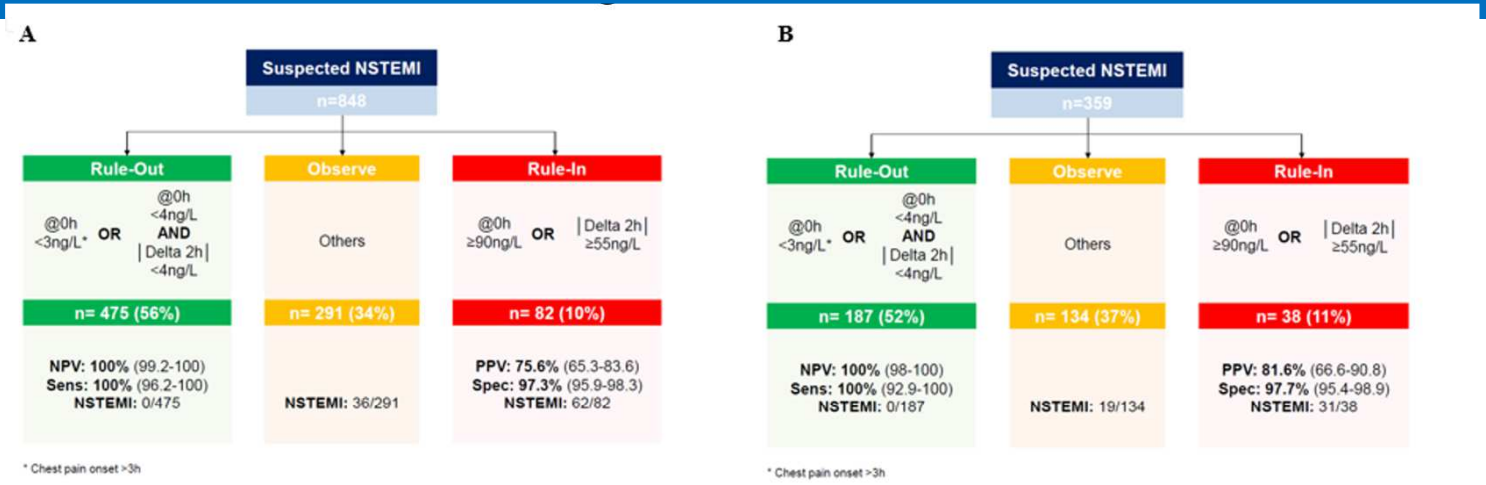
External Validation of the 0/1h-Algorithm and Derivation of a 0/2h-Algorithm using a New Point-of-Care Hs-cTnI Assay

Luca Koechlin[1,2,3*], Jasper Boeddinghaus[1,3,4*]; Pedro Lopez-Ayala[1,3]; Karin Wildi[1,3,5]; Thomas Nestelberger[1,3]; Desiree Wussler[1,3]; Caroline A. Guzman Tacla[1,3]; Timothy Holder[1]; Tamar Muench-Gerber[1,3]; Jonas Glaeser;[1,3] Ana Yufera Sanchez[1,3]; Òscar Miró[3,6]; F. Javier Martin-Sanchez[3,7]; Damian Kawecki[3,8]; Franz Buergler[9]; Andreas Buser[10]; Gabrielle Huré[1,3]; Maria Rubini Giménez[1,11]; Dagmar I. Keller[12]; Michael Christ[13]; and Christian Mueller[1,3] for the APACE investigators[#]

Department of Cardiac Surgery
University Hospital Basel
CH- 4031 Basel



PATHFAST hs-troponin is also evaluated for 0/2 hour: The alorithm found



NSTEMI - non-ST-elevation myocardial infarction

NPV - negative predictive value

Sens. – sensitivity

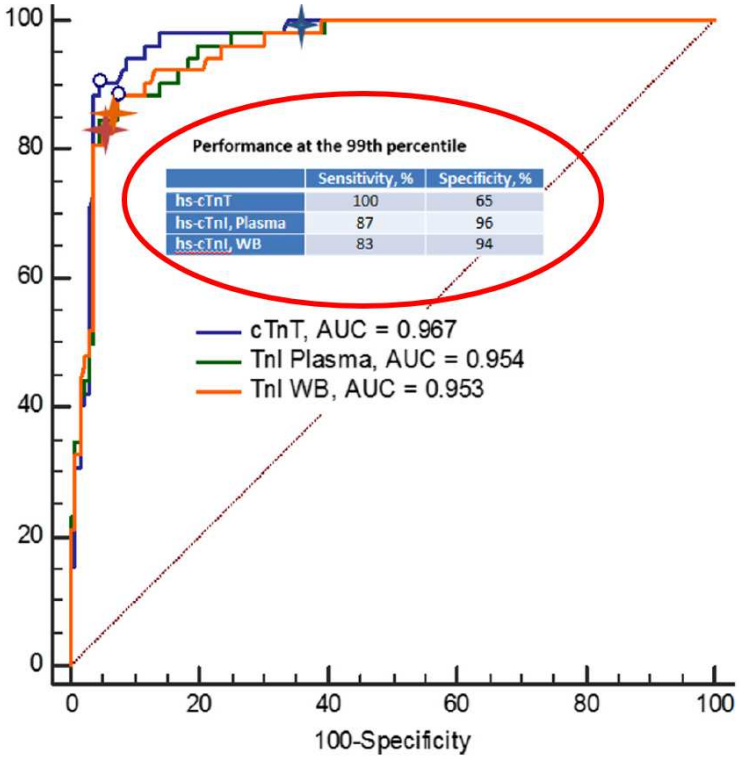
PPV - positive predictive value

Spec. - specificity

A) Derivation cohorte (n= 848)

B) Validation cohorte (n= 395)

PATHFAST troponin I measured from Whole blood or plasma show similar performance to Elecsys troponin T in terms of accuracy



DE GRUYTER Clin Chem Lab Med 2021; 59(9): 1579–1584

Vinajak Gopi, Barbara Milles, Eberhard Spanuth, Matthias Müller-Hennessen, Moritz Biener, Kiril Stoyanov, Norbert Frey and Evangelos Giannitsis*

Comparison of the analytical performance of the PATHFAST high sensitivity cardiac troponin I using fresh whole blood vs. fresh plasma samples

https://doi.org/10.1515/cclm-2021-0354
Received March 24, 2021; accepted May 25, 2021;
published online June 7, 2021

Abstract

Objectives: The PATHFAST hs-cTnI (high-sensitivity cardiac troponin) assay is the first point-of-care assay with a high-sensitivity designation that received FDA approval for diagnosis of myocardial infarction (MI). Testing from whole blood does not need centrifugation and therefore is faster and more convenient in the emergency room instead of plasma. However, there is sparse evidence whether point-of-care testing of Tn from whole blood is as reliable as from plasma samples.

Methods: We investigated the agreement between plasma and whole blood hs-cTnI by using the PATHFAST hs-cTnI assay. Hs-cTnT measured on Cobas 602 in the central laboratory and compared to a final diagnosis of NSTEMI using serial hs-cTnT served as reference. We assessed biases, limits of agreement (±1.96 SD) and coefficients of correlation, and tested the discriminatory ability of the baseline sample of plasma and whole blood hs-cTnI and plasma hs-cTnT to discriminate non-ST-segment elevation myocardial infarction (NSTEMI).

Results: A total of 224 paired fresh samples were collected simultaneously from 191 patients presenting with suspected acute coronary syndrome. There was an excellent correlation between plasma and whole blood hs-cTnI (r=0.99), and and normal plasma and whole blood results. Precision evaluation according to CLSI ep 15 revealed comparable coefficients of variation (CV) in whole blood and plasma. The discriminatory ability of baseline hs-cTnT, plasma and whole blood hs-cTnI was excellent (AUC 0.967, AUC 0.954 and AUC 0.953) without significant difference.

Conclusions: Whole blood can be used interchangeably with plasma for more convenient and less time and labor-consuming testing of hs-cTnI on the PATHFAST instrument.

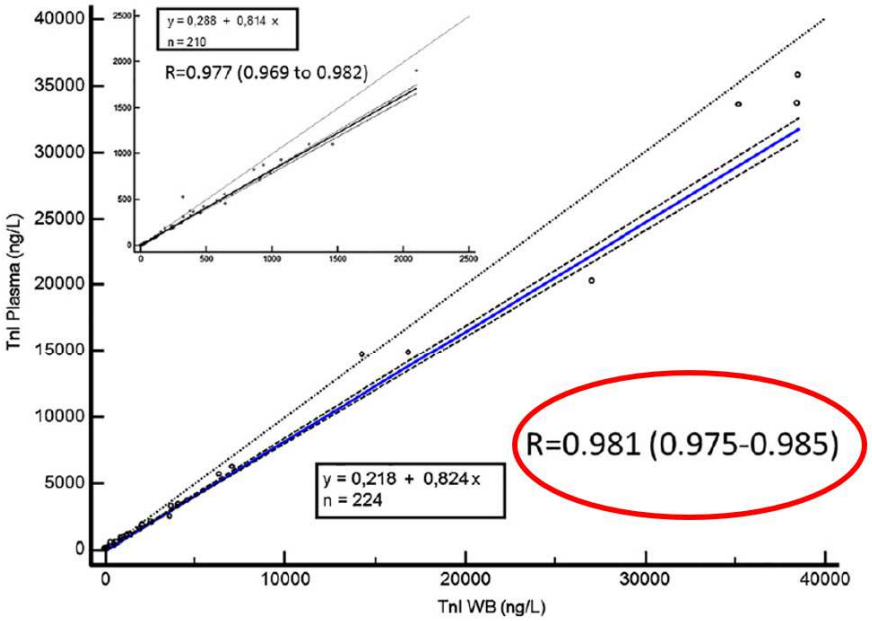
Keywords: high-sensitivity; method comparison; plasma; point-of-care; troponin; whole blood.

Introduction

Point-of-care (POC) cardiac troponin (cTn) assays are recommended when the central laboratory is unable to provide laboratory results timely to the emergency department (ED), or when central laboratory cTn measurements are temporarily or permanently not available [1]. The high number of patients admitted with unspecific chest pain or dyspnea of unknown etiology prompts the need to shorten the time to diagnosis, and the length of stay in order to decongest overcrowded EDs [2].

However, until recently POC cTn assays did not meet the International Federation of Clinical Chemistry and Laboratory Medicine Task Force on Clinical Applications of Bio-

PATHFAST troponin I measured from Whole blood or plasma show excellent correlation



Vinajak Gopi, Barbara Milles, Eberhard Spanuth, Matthias Müller-Hennessen, Moritz Biener, Kiril Stoyanov, Norbert Frey and Evangelos Giannitsis*

Comparison of the analytical performance of the PATHFAST high sensitivity cardiac troponin I using fresh whole blood vs. fresh plasma samples

Clin Chem Lab Med 2021; 59(9): 1579–1584

A new publication from 2023 for PATHFAST hs-cTnI

Key points:

- Use of unisex versus gender specific cut off values were investigated
- Manufacturer Devices implemented: Siemens, Abbott, Roche and PATHFAST
- Results show that application of sex specific 99th percentiles did neither affect diagnostic nor prognostic accuracy of PATHFAST hs-cTnI assay
- According to the latest ESC guideline from 2023 the 0/3 hour algorithm is still an alternative where the faster algorithms 0/1 abd 0/2 hour are not applicable
- Publication is freely available

[Diagnostic and prognostic value of the sex-specific 99th percentile of four high-sensitivity cardiac troponin assays in patients with suspected myocardial infarction - PubMed (nih.gov)]

Biomarkers for sepsis diagnostic and prognosis: Presepsin and PCT

Presepsin

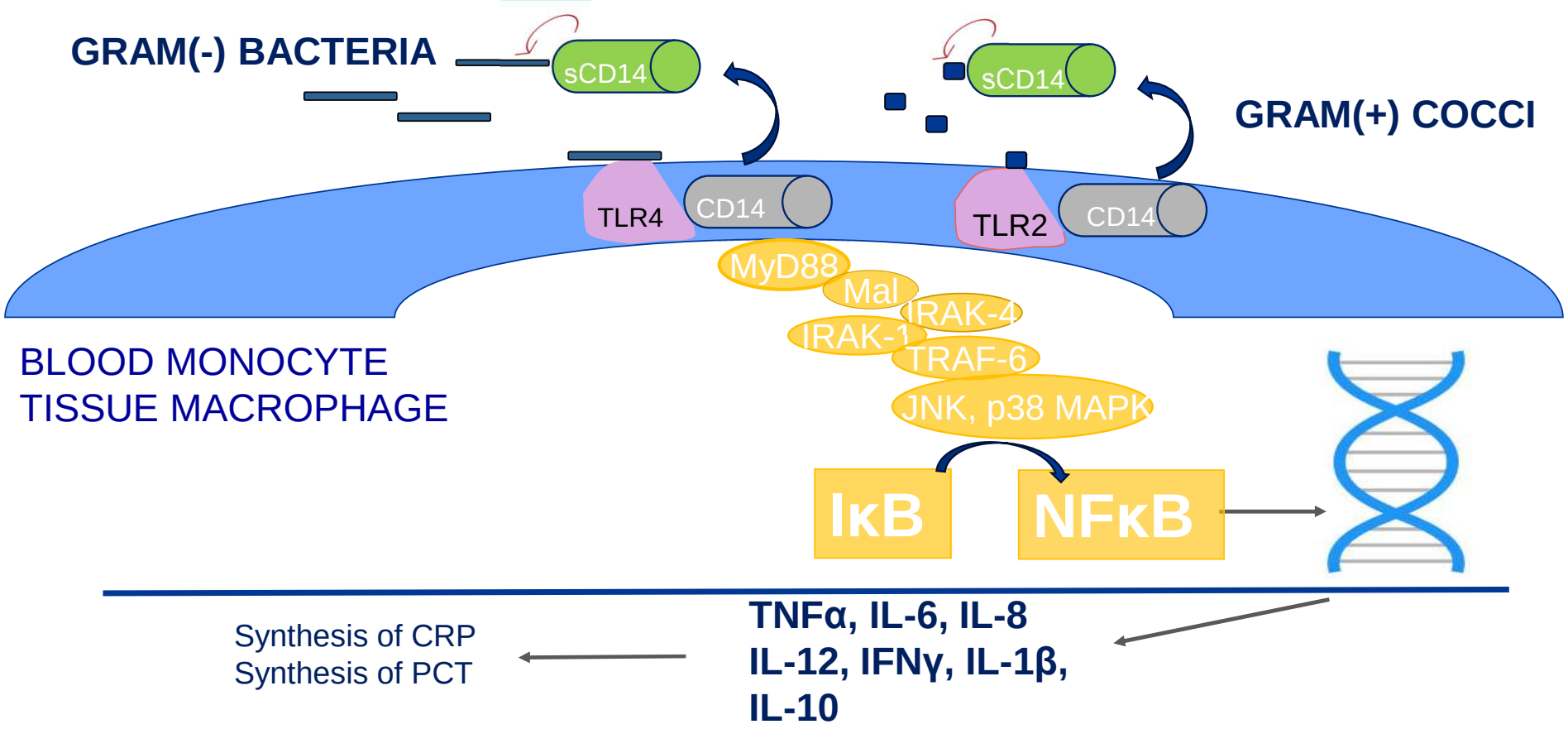
Early diagnosis and prognosis of sepsis in adults and neonates

PCT

Diagnosis and prognosis of sepsis

Antibiotic stewardship

What is our biomarker Presepsin?



Presepsin and Guidelines

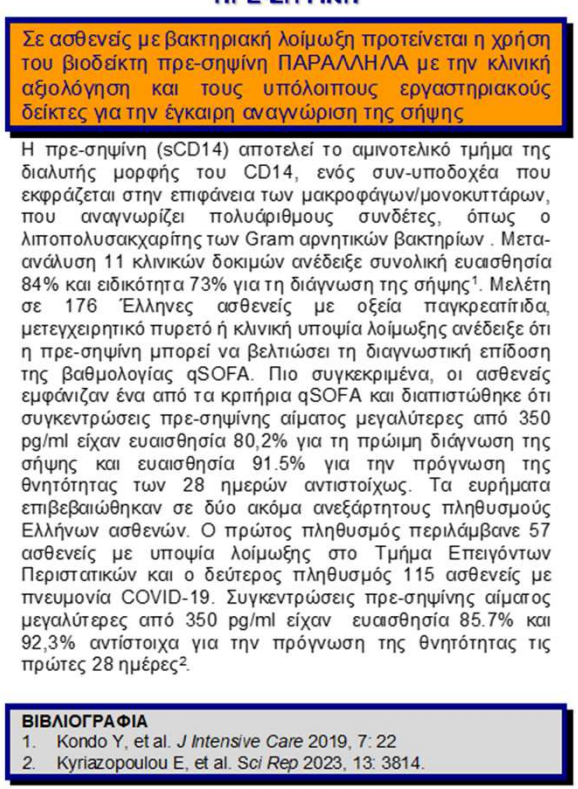
Presented in the conference of September 2023

In English accessible for free at www.sepsis.gr

Pocket book

One page devoted to presepsin

WE ARE IN GREEK SEPSIS GUIDELINES!!!



ΠΡΕ-ΣΗΨΙΝΗ

Σε ασθενείς με βακτηριακή λοίμωξη προτείνεται η χρήση του βιοδείκτη πρε-σηψίνη ΠΑΡΑΛΛΗΛΑ με την κλινική αξιολόγηση και τους υπόλοιπους εργαστηριακούς δείκτες για την έγκαιρη αναγνώριση της σήψης

Η πρε-σηψίνη (sCD14) αποτελεί το αμινοτελικό τμήμα της διαλυτής μορφής του CD14, ενός συν-υποδοχέα που εκφράζεται στην επιφάνεια των μακροφάγων/μονοκυττάρων, που αναγνωρίζει πολυάριθμους συνδέτες, όπως ο λιποπολυσακχαρίτης των Gram αρνητικών βακτηρίων . Μετα-ανάλυση 11 κλινικών δοκιμών ανέδειξε συνολική ευαισθησία 84% και ειδικότητα 73% για τη διάγνωση της σήψης[1]. Μελέτη σε 176 Έλληνες ασθενείς με οξεία παγκρεατίτιδα, μετεγχειρητικό πυρετό ή κλινική υποψία λοίμωξης ανέδειξε ότι η πρε-σηψίνη μπορεί να βελτιώσει τη διαγνωστική επίδοση της βαθμολογίας qSOFA. Πιο συγκεκριμένα, οι ασθενείς εμφάνιζαν ένα από τα κριτήρια qSOFA και διαπιστώθηκε ότι συγκεντρώσεις πρε-σηψίνης αίματος μεγαλύτερες από 350 pg/ml είχαν ευαισθησία 80,2% για τη πρώιμη διάγνωση της σήψης και ευαισθησία 91.5% για την πρόγνωση της θνητότητας των 28 ημερών αντιστοίχως. Τα ευρήματα επιβεβαιώθηκαν σε δύο ακόμα ανεξάρτητους πληθυσμούς Ελλήνων ασθενών. Ο πρώτος πληθυσμός περιλάμβανε 57 ασθενείς με υποψία λοίμωξης στο Τμήμα Επειγόντων Περιστατικών και ο δεύτερος πληθυσμός 115 ασθενείς με πνευμονία COVID-19. Συγκεντρώσεις πρε-σηψίνης αίματος μεγαλύτερες από 350 pg/ml είχαν ευαισθησία 85.7% και 92,3% αντίστοιχα για την πρόγνωση της θνητότητας τις πρώτες 28 ημέρες[2].

ΒΙΒΛΙΟΓΡΑΦΙΑ

1. Kondo Y, et al. *J Intensive Care* 2019, 7: 22
2. Kyriazopoulou E, et al. *Sci Rep* 2023, 13: 3814.

Presepsin key studies

Presepsin is also established as sepsis biomarker for adults: Risk Stratification

Decision thresholds of PSEP for early risk stratification in patients with sepsis based on the study results.

PSEP, ng/l	<200	200–300	300–500	500–1000	>1000
Risk status	Very low	Low	Moderate	High	Very high
Sepsis; n, %	6, 8	7, 10	22, 30	21, 28	18, 24
Severe sepsis/sept. shock; n, %	1, 3	1, 3	2, 5	6, 15	30, 75
30-day death; n, %	1, 4	1, 4	3, 13	5, 21	14, 58
Combined endpoint; n, %	2, 6	1, 3	4, 11	9, 26	19, 54

Clinica Chimica Acta 450 (2015) 169–175

Tab. 3: Presepsin decision thresholds
based on presepsin determination at admission to the emergency department in patients with low grade sepsis (n=85), severe sepsis (N=40), sepstic shock (n=15), and 30-day death (n=23)

Risk stratification	Very low	Low	Moderate	High	Very high
Presepsin (ng/L)	< 200	200-300	300-500	500-1000	≥ 1000
Low grade sepsis, n (%)	3 (3.5)	9 (10.6)	18 (21.1)	29 (34.1)	26 (30.6)
Severe sepsis ,n (%)	0	0	5 (12.5)	11 (27.5)	24 (60.0)
Septic shock, n (%)	0	0	0	4 (26.7)	11 (73.3)
30-day death, n (%)	0	0	0	5 (21.7)	18 (78.3)

Data from Peru

Data from Germany

Fig.6: Decision thresholds of PSEP for early risk stratification in patients with sepsis

Presepsin (pg/ml)	Diagnosis
<200	Exclusion of sepsis
<300	Systemic infection not probable
<500	Systemic infection (sepsis) possible
<1000	Significant risk of the systemic infection progression (severe sepsis), increasing risk of unfavorable outcome
≥1000	High risk of the systemic infection progression (severe sepsis/septic shock). High risk for mortality after 30 day comparable with a SOFA score ≥8

Mod. from Carpio et al, 2015 and C. Chenevier-Gabeaux et al, 2015

21st International Congress of Clinical Chemistry and Laboratory Medicine, IFCC-WorldLab – EuroMedLab, Berlin, 15 -19 May 2011

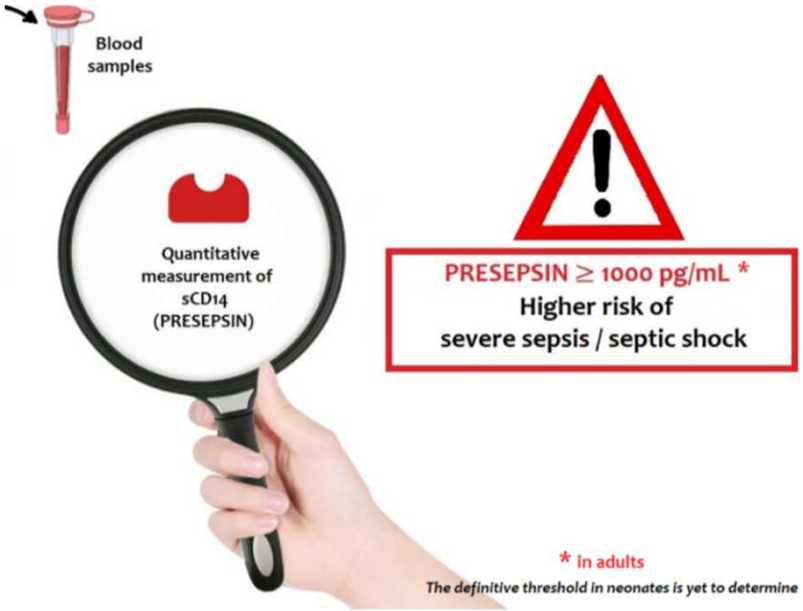
Review

The Emerging Role of Presepsin (P-SEP) in the Diagnosis of Sepsis in the Critically Ill Infant: A Literature Review

Review from Italy

Chiara Maddaloni [1], Domenico Umberto De Rose [1], Alessandra Santisi [1], Ludovica Martini [1], Stefano Caoci [1], Iliana Bersani [1], Maria Paola Ronchetti [1,2] and Cinzia Auriti [1,*,†]

Int. J. Mol. Sci. **2021**, *22*, 12154.



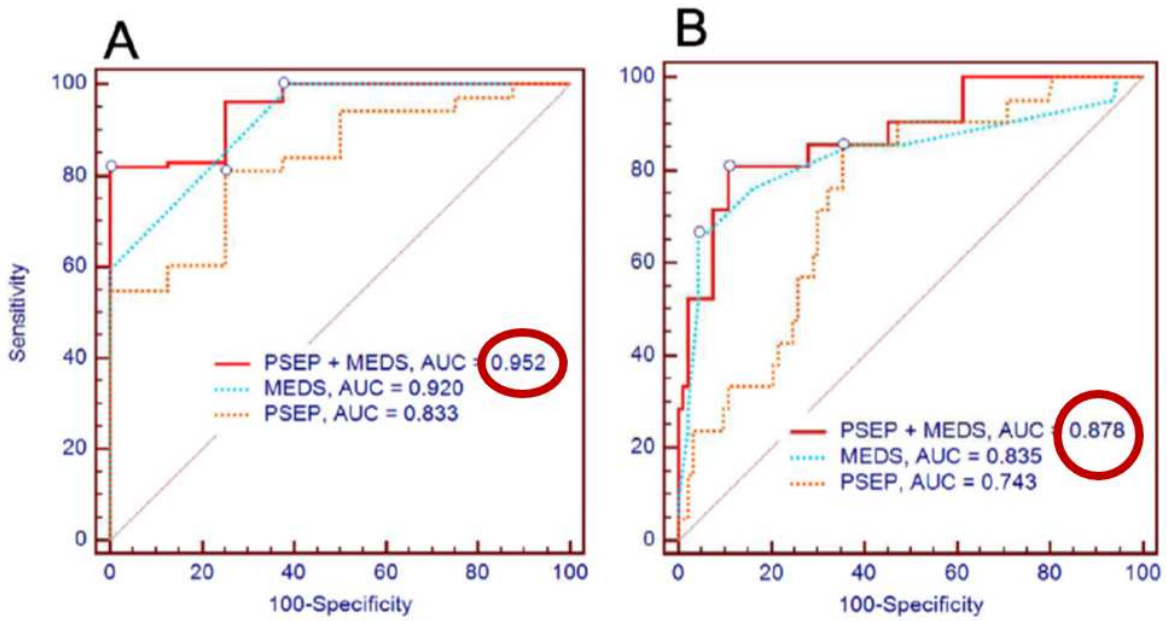
Review

Presepsin as Early Marker of Sepsis in Emergency Department: A Narrative Review

Presepsin in the Emergency Department (ER)

Utility of presepsin (sCD14-ST) as a diagnostic and prognostic marker of sepsis in the emergency department

Ricardo Carpio [a,b,*], Juan Zapata [a], Eberhard Spanuth [c], Georg Hess [d]



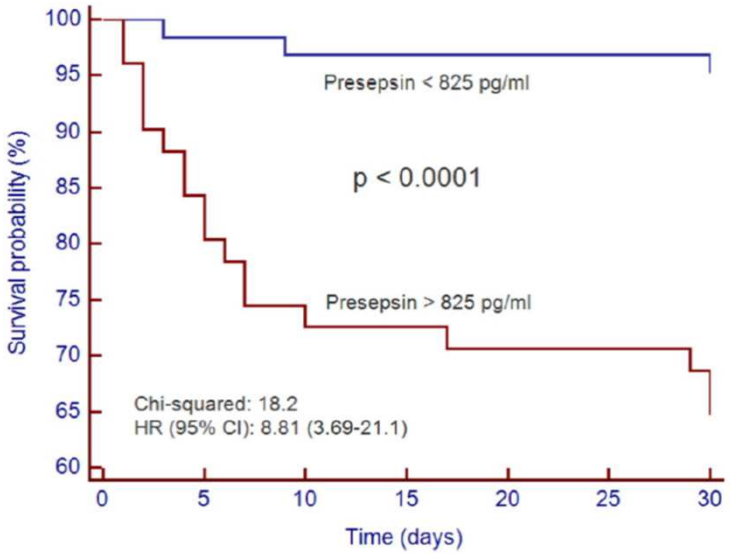


Fig. 3. Kaplan–Meier survival curve of 30-day death for PSEP at admission.

Fig. 2. Simultaneous assessment of PSEP and MEDS score at admission for mortality prediction and discrimination between SIRS and sepsis. A: ROC curves for discrimination between SIRS and sepsis; B: ROC curves for prediction of 30-day death.

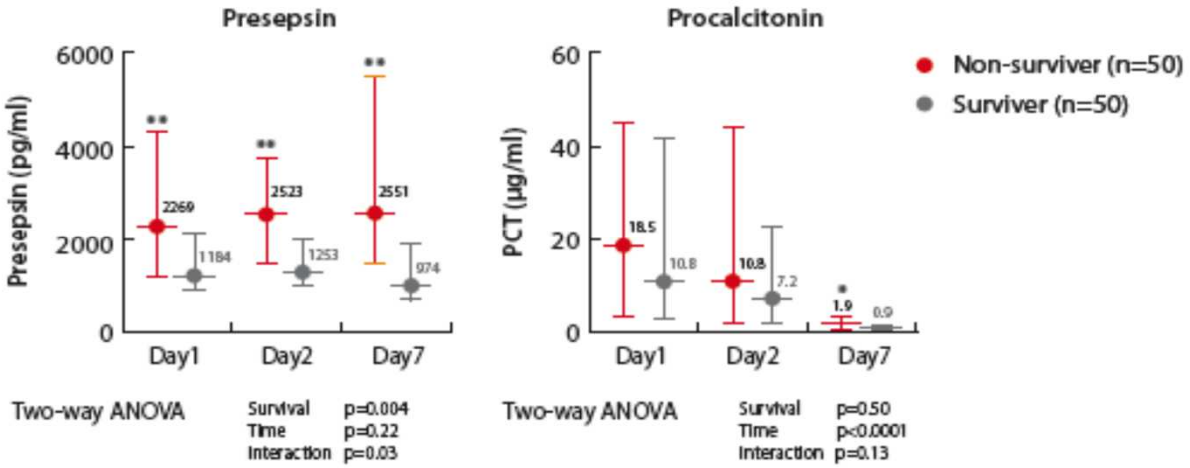
Clinica Chimica Acta 450 (2015) 169–175

Presepsin in the Intensive Care Unit (ICU)

Presepsin (soluble CD14 subtype) and procalcitonin levels for mortality prediction in sepsis: data from the Albumin Italian Outcome Sepsis trial

Serge Masson,[✉#1] Pietro Caironi,[#2,3] Eberhard Spanuth,[4] Ralf Thomae,[5] Mauro Panigada,[3] Gabriela Sangiorgi,[6] Roberto Fumagalli,[7] Tommaso Mauri,[8] Stefano Isgrò,[7] Caterina Fanizza,[9] Marilena Romero,[9] Gianni Tognoni,[9] Roberto Latini,[1] and Luciano Gattinoni[2,3], on behalf of the ALBIOS Study Investigators

Fig. 10: Time course of plasma concentrations of Presepsin and Procalcitonin during ICU stay by survival status



Adapted from Masson et al., 2014 (29)

Crit Care. 2014; 18(1): R6.
Published online 2014 Jan 7. doi: 10.1186/cc13183

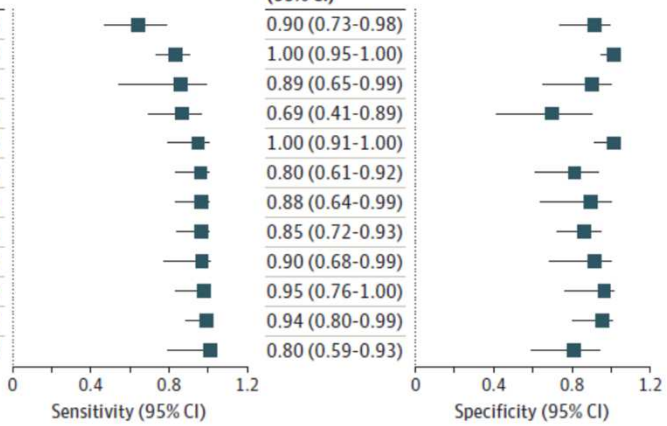
Presepsin for Early Onset Sepsis (EOS) in neonates

Presepsin for the Diagnosis of Neonatal Early-Onset Sepsis
A Systematic Review and Meta-analysis

Figure 2. Primary Analysis Presepsin Accuracy

A Forest plot

Source	True positive	False positive	False negative	True negative	Sensitivity (95% CI)	Specificity (95% CI)
Stojewska et al,[53] 2015	26	3	15	27	0.63 (0.47-0.78)	0.90 (0.73-0.98)
Rashwan et al,[47] 2019	84	0	18	66	0.82 (0.74-0.89)	1.00 (0.95-1.00)
Miyosawa et al,[49] 2018	11	2	2	16	0.85 (0.55-0.98)	0.89 (0.65-0.99)
Iskandar et al,[48] 2019	30	5	5	11	0.86 (0.70-0.95)	0.69 (0.41-0.89)
Montaldo et al,[51] 2017	30	0	2	38	0.94 (0.79-0.99)	1.00 (0.91-1.00)
Khater and Al-Hosiny,[44] 2020	38	6	2	24	0.95 (0.83-0.99)	0.80 (0.61-0.92)
Osman et al,[54] 2015	38	2	2	15	0.95 (0.83-0.99)	0.88 (0.64-0.99)
Xiao et al,[50] 2017	40	8	2	45	0.95 (0.84-0.99)	0.85 (0.72-0.93)
Tabl and Abed,[52] 2016	21	2	1	18	0.95 (0.77-1.00)	0.90 (0.68-0.99)
Gad et al,[45] 2020	30	1	1	20	0.97 (0.83-1.00)	0.95 (0.76-1.00)
Kamel et al,[46] 2019	45	2	1	32	0.98 (0.88-1.00)	0.94 (0.80-0.99)
Mussap et al,[5]2015	16	5	0	20	1.00 (0.79-1.00)	0.80 (0.59-0.93)



CONCLUSIONS AND RELEVANCE Results of this systematic review and meta-analysis suggest that **presepsin was an accurate biomarker of EOS**. **Clinical trials are warranted to assess its usefulness and safety to reduce early antibiotic exposure**, particularly in preterm newborns.

Presepsin accuracy for diagnosis of EOS: The largest systematic review and meta-analysis so far

OBJECTIVE To assess presepsin accuracy for the diagnosis of EOS.

RESULTS In the primary analysis, among 12 studies and 828 newborns of any gestational age, **pooled sensitivity and specificity were 0.93** (95%CI, 0.86-0.95) **and 0.91** (95%CI, 0.85-0.95), respectively; pooled diagnostic odds ratio was 131.69 (95%CI, 54.93-310.94).

- **Presepsin accuracy was not associated** with:
  - gestational age,
  - measurement with chemiluminescence enzyme immunoassay or ELISA testing,
  - country where the study was performed

Poggi C et al. JAMA 2022;176:250

Presepsin for Early Onset Sepsis (EOS) in neonates

Reference ranges of Presepsin in preterm infants in the first 48 h of life: A multicenter observational study

Table 4
Distribution of percentiles of P-SEP (ng/L) at T_0 for each week of gestational age.

GA (wks)	n	Percentiles				
		5th	25th	50th	75th	95th
23	11	321	554	760	1009	1464
24	12	302	529	728	971	1414
25	14	283	503	698	934	1365
26	14	264	479	668	897	1317
27	20	246	455	639	862	1270
28	20	229	432	611	829	1225
29	22	212	409	583	795	1181
30	21	195	387	557	762	1138
31	36	179	366	531	731	1096
32	13	163	345	505	700	1056

GA: gestational age; n: number of enrolled patients.

P-SEP levels at T0 are not influenced by perinatal factors, such as birth weight, WBC count, delivery mode, pPROM, IAP and antenatal steroids, in contrast to other sepsis biomarkers, such as CRP and PCT. In fact, CRP was found to increase by 2.4% for each increase of 100 g of birth weight, 0.4% for each hour of pPROM, 40% in case of antenatal steroids, and 28% in case of IAP and cesarean section in 200 uninfected preterm newborns during the first 4 days of life.
Moreover, PCT levels increased by 2.2% for each increase of 100 g of birth weight [13], in case of pPROM and clinical chorioamnionitis.
Thus, **P-SEP measured in the first 6 h of life would be a more reliable biomarker of EOS than CRP and PCT, as it is not affected by the most relevant perinatal factors**.

Poggi C et al., Clinica Chimica Acta 2020;508:191

Presepsin for Late Onset Sepsis (LOS) in neonates

Presepsin for the Detection of Late-Onset Sepsis in Preterm Newborns

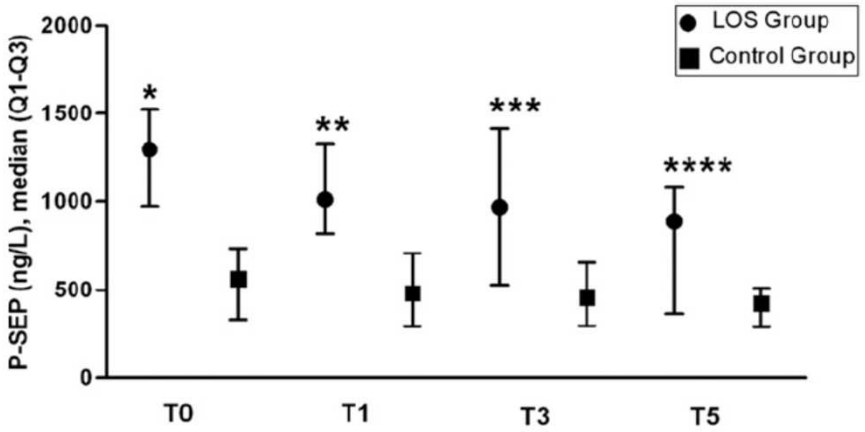


FIGURE 1
Changes and comparison of P-SEP values in infants in the LOS and Control groups. *P = .00001; **P = .00006; ***P = .004; and ****P = .01 LOS vs control group.

METHODS: We prospectively studied newborns ≤32 weeks' gestational age with LOS (n = 19) and noninfected controls (n = 21) at 4 to 60 days' postnatal age.
At enrollment, and 1, 3, and 5 days later, we ascertained the C-reactive protein, procalcitonin, and P-SEP in the LOS group, whereas P-SEP alone was ascertained in the control group.
RESULTS: **P-SEP at enrollment was higher in the LOS than the control group** (median 1295 vs 562 ng/L, P = .00001) **and remained higher throughout the study period**.

Poggi C et al., Pediatrics 2015;135:68

Presepsin for Late Onset Sepsis (LOS) in neonates

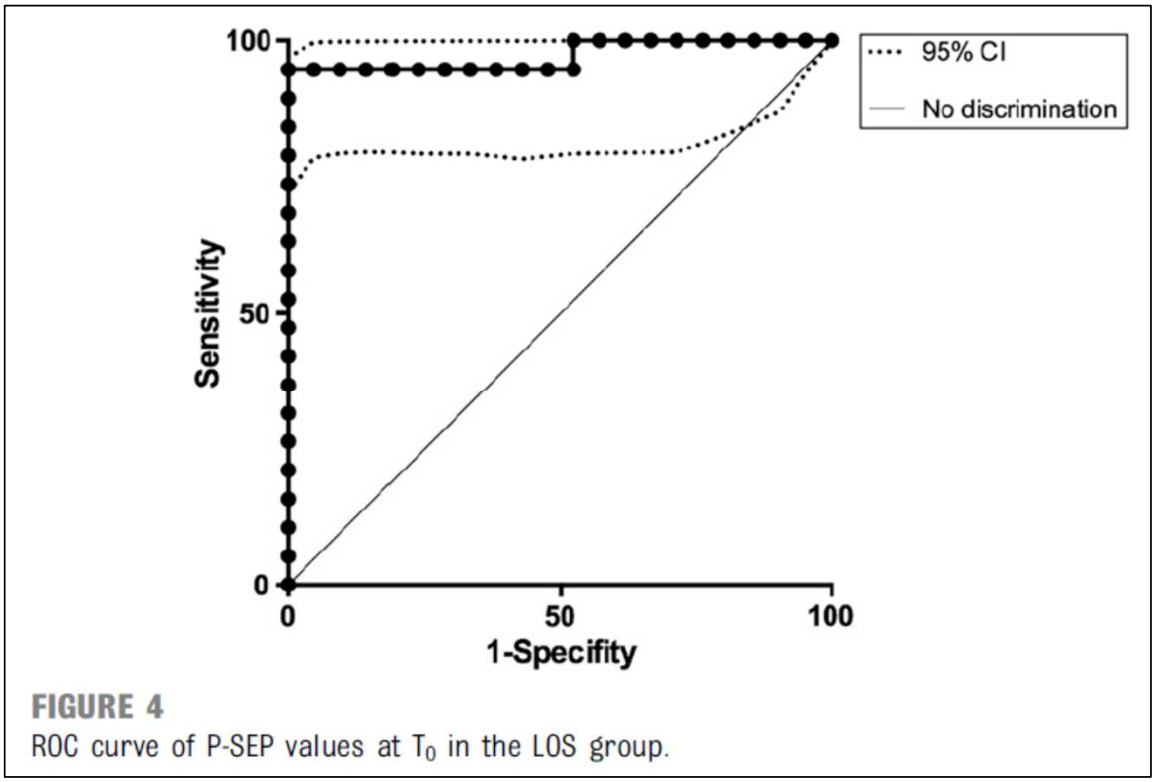


FIGURE 4
ROC curve of P-SEP values at T_0 in the LOS group.

The cutoff value of P-SEP with the best accuracy for diagnosis of probable LOS was 885 ng/L with a specificity of 100%, and sensitivity was 94%.

Poggi C et al., Pediatrics 2015;135:68

Presepsin for Late Onset Sepsis (LOS) in neonates

International Journal of *Molecular Sciences*

Type of Study	Authors, Year	Country	Population	Cut-Off Value of P-SEP (pg/mL)	AUC	Type of Sample	Assay	Conclusions
LOS								
Prospective	Poggi et al., 2015 [1]	Italy	19 LOS 21 healthy (GA < 32 w)	885	0.97	Whole blood	CLEIA	P-SEP is an accurate marker for the diagnosis of LOS in preterm infants
Case-control	Sabry et al., 2016 [19]	Egypt	80 LOS 40 healthy	722	0.99	Serum	ELISA	P-SEP is an accurate marker for the diagnosis of LOS
Prospective	Topcuoglu et al., 2016 [20]	Turkey	42 LOS (GA < 34 w)	800.5	0.86	Plasma	CLEIA	P-SEP can used as a reliable biomarker for the diagnosis of and response to treatment in LOS
Prospective	Astrawinata et al., 2017 [21]	Indonesia	40 LOS in preterm 40 healthy	406 ?	0.89	Whole blood	CLEIA	P-SEP is the earliest and best-performing marker of LOS for the prognosis of preterm neonatal mortality when compared to CRP and PCT

Maddaloni C et al., Int J Mol Sci 2021;22:12154

Presepsin measurement in Cord Blood

Cord blood presepsin as a predictor of early-onset neonatal sepsis in term and preterm newborns

Italian Journal of Pediatrics

Table 3 Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in predicting clinical sepsis when 50th centile, 75th centile, and 90th centile are used

	Cord P-SEP value higher than 50th *centile*	*95% CI*	*Cord* P-SEP value higher than 75th *centile*	*95% CI*	*Cord* P-SEP value higher than 90th *centile*	*95% CI*
Sensitivity	62.5%	24.5–91.5%	50.0%	15.7–84.3%	50.0%	15.7–84.3%
Specificity	74.1%	63.5–83.0%	83.5%	73.9–90.7%	88.2%	79.4–94.2%
Positive Predictive Value	18.5%	10.6–30.3%	22.2%	11.0–39.9%	28.6%	13.9–49.7%
Negative Predictive Value	95.5%	89.5–98.1%	94.7%	89.8–97.3%	94.9%	90.3–97.4%
Accuracy	73.1%	62.9–81.8%	80.7%	71.2–88.1%	85.0%	76.0–91.5%

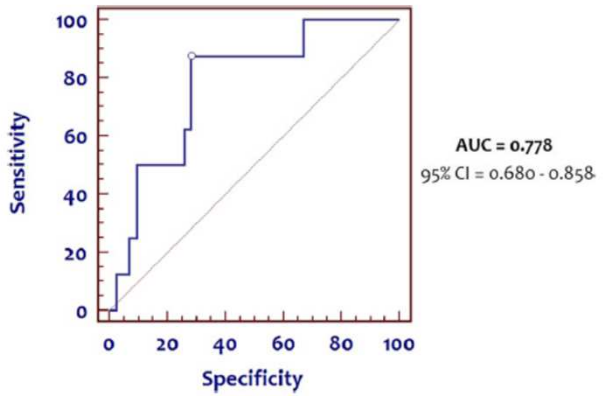


Fig. 1 ROC curve of cord P-SEP values for clinical EOS in all infants

Maximum Youden's index was 579 pg/ml for clinical EOS using cord P-SEP values

Conclusions

For the first time, we reported a cut-off of presepsin in the cord blood of term and preterm infants to predict clinical EOS. The use of biomarkers to decrease antibiotics administration in EOS should be one of the antibiotic stewardship targets in every neonatology unit [28]. Presepsin seems to be a promising candidate and our data could be the starting point to realize multicenter studies, confirming its feasibility in the management of antibiotic therapy in neonates with risk factors for EOS.

Priolo F. et al. It J Pediatr 2023;49:35

Presepsin: future studies
Italy: The PROPOSE study

ClinicalTrials.gov Identifier: NCT05796115

STUDY PROTOCOL: PROcalcitonin and Presepsin-guided decision for antibiotic prophylaxis of early-Onset SEpsis in preterm infants: a multicentre, randomised controlled trial (PROPOSE STUDY)

Study design and setting: **Multicenter randomized controlled study** in level three neonatal intensive care units.
Methods: Infants of 25^{+0}-31^{+6} weeks of gestational age without risk factors for EOS will be enrolled in the study. They will be electronically **randomized into two groups**:

- infants who will receive standard antibiotic prophylaxis for EOS (standard group)
- infants who will receive PCT/P-SEP-guided antibiotic prophylaxis for EOS (intervention group).

P-SEP values will be considered pathological when they exceed 800, 812, and 825 ng/L within 3 h of life, and at 12 and 24 h of life, respectively (these values correspond to the 75° percentile of reference range by Poggi et al. Clin Chim Acta 2020).
PCT values will be considered pathological when they exceed 0.6, 26, and 48 ng/L within 3 h of life, and at 12 and 24 h of life, respectively (these values correspond to the 97,5° percentile of reference ranges and to the upper limit of 95% C.I. reported by Chiesa et al. Clin Chim Acta 2011)

Presepsin: future studies
Italy: Presepsin measurement from unconventional biological fluids (urine)

STEP 1 (sample size: 80 preterm and 80 term newborns)

The samples in the different biological liquids will be collected as follows:

- Cord blood within 6-h of life: standard laboratory tests: ph, pO2, pCO2, EB, HCO3, hemoglobinemia, hematocrit, P-SEP;
- Urine and saliva within 6-h of life for P-SEP.

P-SEP will be measured using the Path-Fast method.

STEP 2 (sample size 800 newborns: 400 preterm/400 term newborns)

- Reference curves of P-SEP values in the urine and saliva of preterm and term infants;

P-SEP saliva and urine time points: T1 24h, T2 48h, T3 72h, T4 120h, T5 7 d

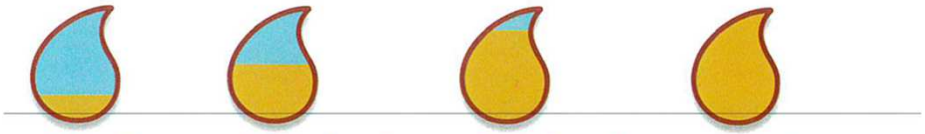
EXPECTED RESULTS

- Validation of the PATHFAST tool for the analysis of Presepsin in non-conventional biological liquids;
- Creation of reference curves for presepsin values in urine and saliva in preterm and full-term infants;
- Promote the standard of care assesment of Presepsin levels in urine and saliva for preterm and full-term infants.

PATHFAST BRAHMS PCT completes our portfolio for sepsis Antibiotic Stewardship (ABS) and sepsis thresholds

By severity

PCT levels rise with increasing severity of infection[2]

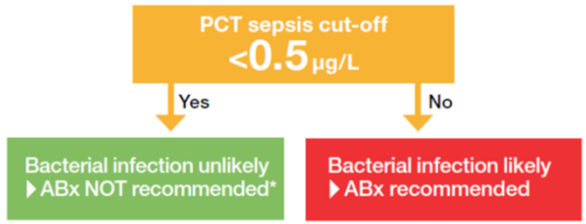


<0.5 µg/L	≥0.5 – <2 µg/L	≥2 – <10 µg/L	≥10 µg/L
Systemic infection not likely	Significant, but moderate systemic inflammatory response, sepsis likely	Severe sepsis: Severe systemic inflammatory response (SIRS), most likely due to infection (sepsis), high risk of developing organ dysfunction	Important systemic inflammatory response almost exclusively due to severe bacterial sepsis or septic shock

PCT (ng/mL)	Interpretation
< 0.5	Low risk for systemic bacterial infection, but local infection possible
≧ 0.5 – < 2.0	Moderate risk for the development of severe systemic infection (severe sepsis or septic shock)
≧ 2.0 – ≦ 10	High risk for the development of severe systemic infection (severe sepsis or septic shock)
> 10	Important systemic inflammatory response with very high risk of severe sepsis and septic shock

By indication

When to START antibiotics?



PCT_{Peak}: Highest observed PCT concentration
$PCT_{Current}$: Most recent PCT concentration
ΔPCT: Caluculate by the following equation:

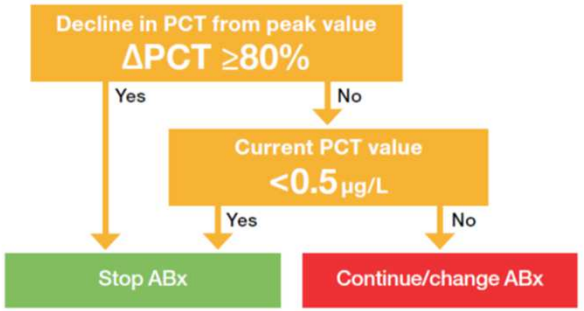
$$\Delta PCT = (PCT_{Peak} - PCT_{Current})/PCT_{Peak} \times 100\ \%$$

Antibiotic therapy may be discontinued if the ΔPCT is > 80%, or if the $PCT_{Current}$ is

- < 0.25 ng/mL for LRTI patients
- < 0.5 ng/mL for suspected or confirmed septic patients.

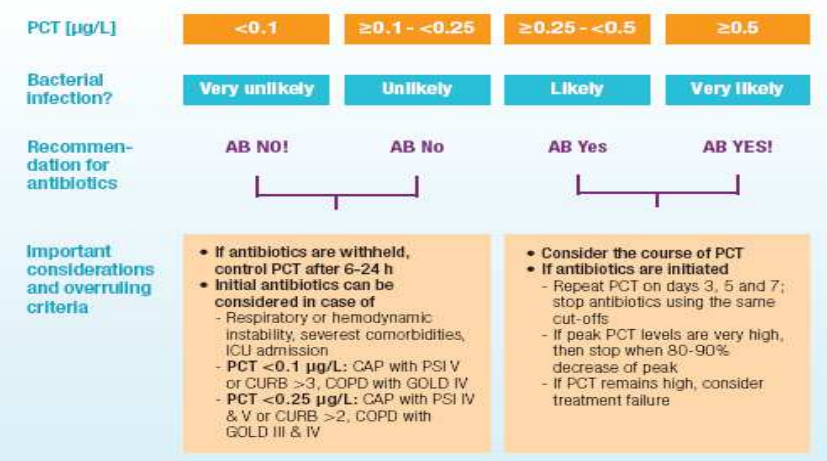
When to STOP antibiotics?[1]

Daily measurement of PCT is advised



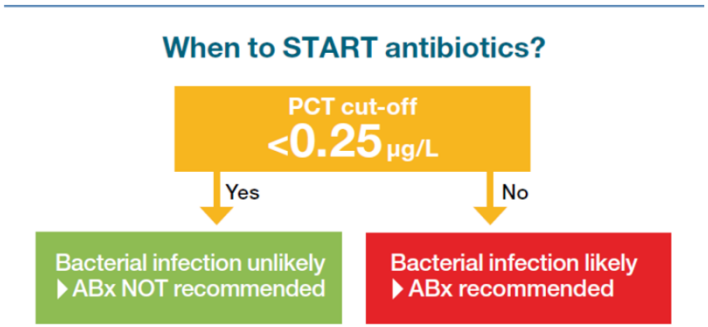
PATHFAST BRAHMS PCT completes our portfolio for sepsis Antibiotic Stewardship (ABS) and LRTI thresholds

By severity



PCT (ng/mL)	Interpretation
< 0.1	Indicate absence of bacterial infection. Use of antibiotics strongly discouraged, also in the presence of impaired pulmonary reserve in acute exacerbation of chronic obstructive pulmonary disease (COPD).
≧ 0.1 – < 0.25	Bacterial infection is unlikely. The use of antibiotics is discouraged.
≧ 0.25 – < 0.5	Bacterial infection is possible. Advice to initiate antimicrobial therapy.
≧ 0.5	Suggestive of the presence of bacterial infection. Antibiotic treatment strongly recommended.

By indication



PCT_{Peak}: Highest observed PCT concentration
$PCT_{Current}$: Most recent PCT concentration
ΔPCT: Caluculate by the following equation:

$$\Delta PCT = (PCT_{Peak} - PCT_{Current})/PCT_{Peak} \times 100\ \%$$

Antibiotic therapy may be discontinued if the ΔPCT is > 80%, or if the $PCT_{Current}$ is

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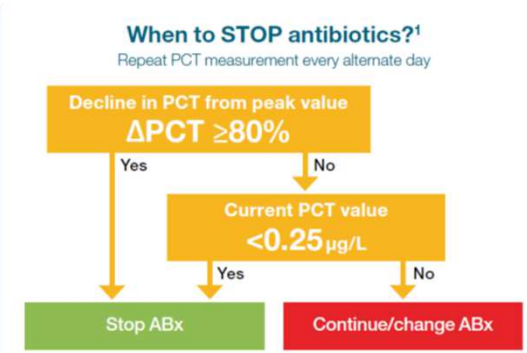
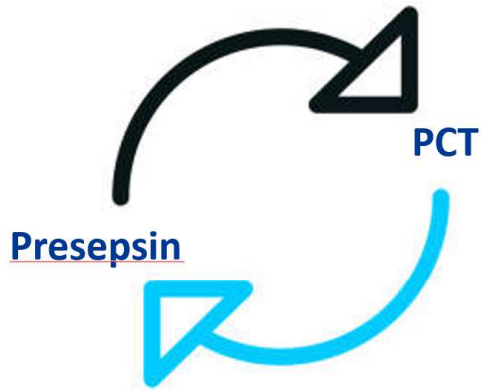
- < 0.5 ng/mL for suspected or confirmed septic patients.



The common use of Presepsin and PCT



Why Presepsin & PCT together?

The common use of Presepsin and PCT in combination with qSOFA

2020 AACC Annual Scientific Meeting & Clinical Lab Expo; December 13-17, Chicago, IL USA

Combined assessment of presepsin and procalcitonin in addition to the quickSOFA score improve the prediction of mortality, complicated sepsis, and septic shock in patients with early sepsis admitted to the emergency department

PCT & PSEP & qSOFA

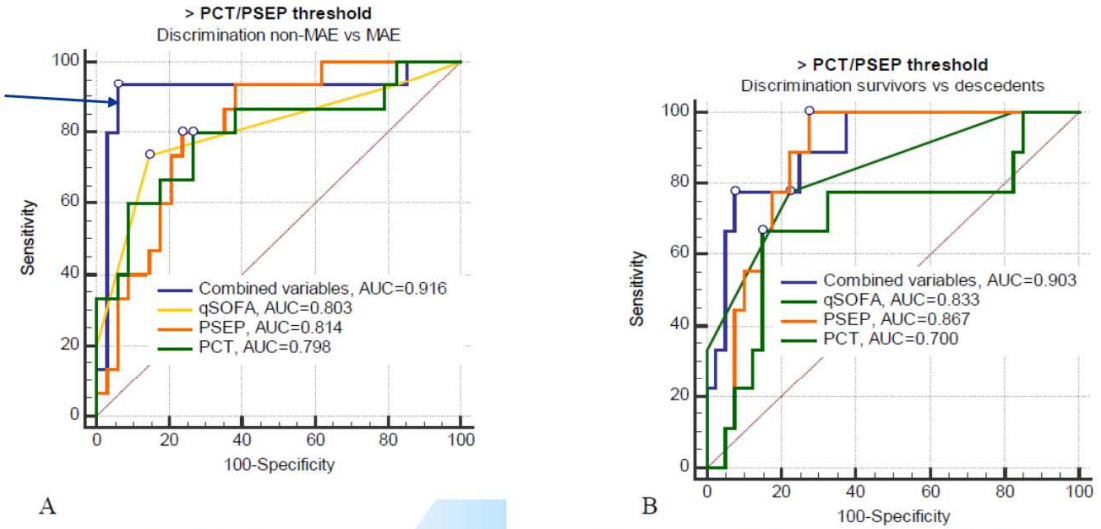
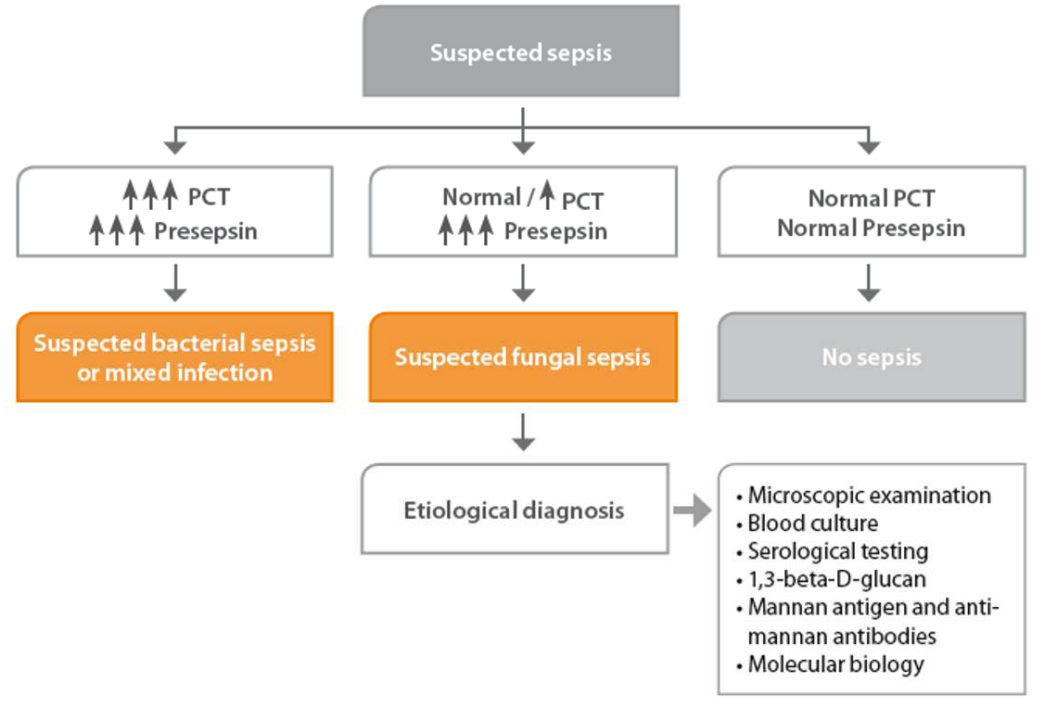


Fig. 1: Results of ROC analysis for discrimination non-MAE vs MAE and alive vs death

Combination of PSEP & PCT & qSOFA improves significantly discrimination of MAE from non MAE patients with sepsis

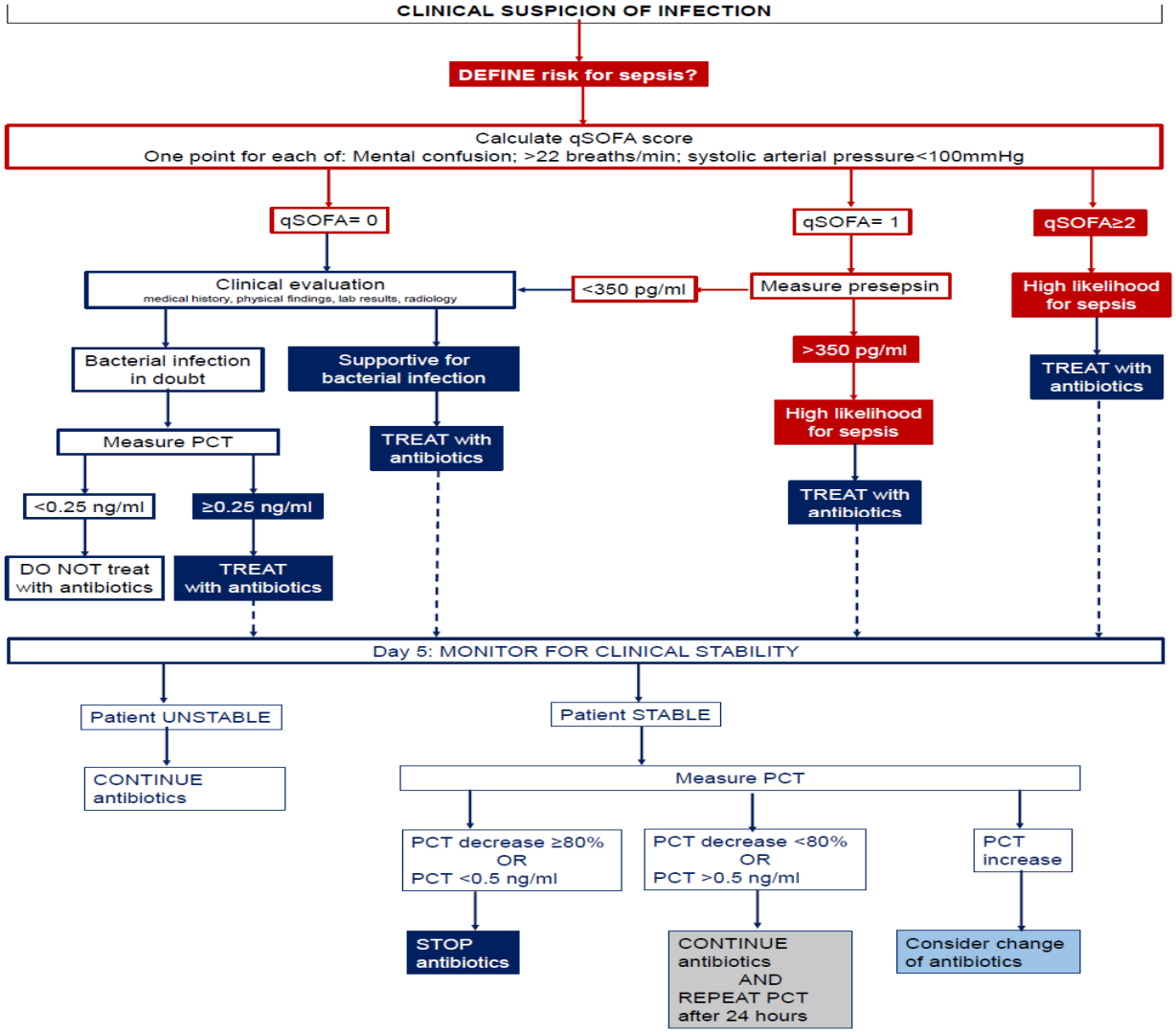
Tentative algorithm: Presepsin & PCT for the detection of invasive fungal infections

Fig. 15: Algorithm based on Procalcitonin (PCT) and Presepsin test results for screening invasive fungal infections



PCT: Procalcitonin; *Adapted from Lippi et al., 2019 (55)*

Proposal Prof. Giamarellos based on his clinical experience, preliminary INSPIRE data for PSEP and his BRAHMS PCT evaluations/ experiences:



PROCALCITONIN (PCT) AND PRESEPSIS FOR 2023

Use Presepsin to Evaluate the Patient

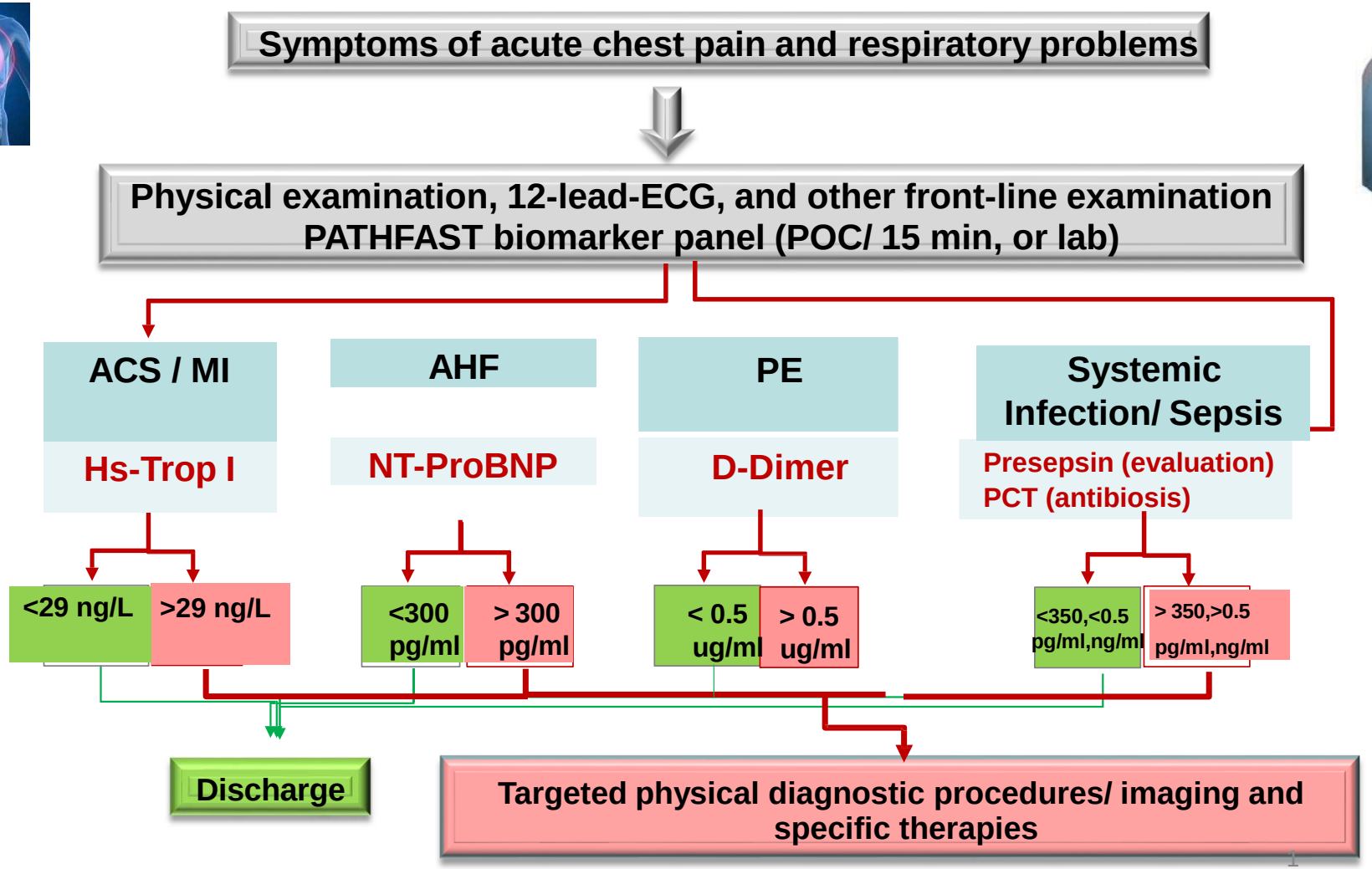
- Better kinetics than C-reactive protein and soluble cytokines
- >350 pg/ml sepsis diagnosis and risk for severe infection: Consider early antibiotics
- Low: consider discharge from the emergency department

Use Procalcitonin (PCT) to Guide Early Stop of Antibiotics

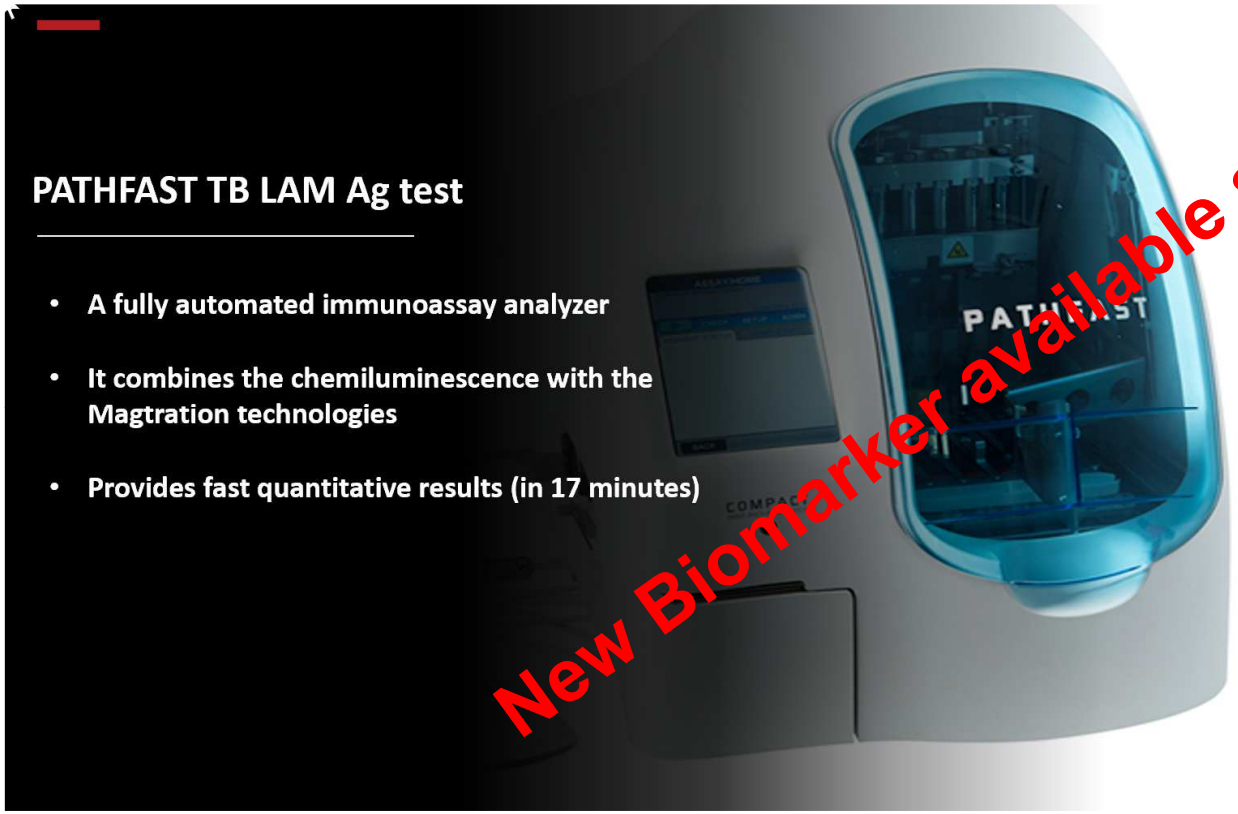
- When PCT decreases by at least 80% or when PCT is below 0.50 ng/ml
- ↓ infection-associated adverse events after 180 days
- ↓ 28-day mortality + antibiotic-associated adverse events
- Association with decrease of stool colonization by MDRO and *C. difficile*

MDRO: multidrug-resistant organisms

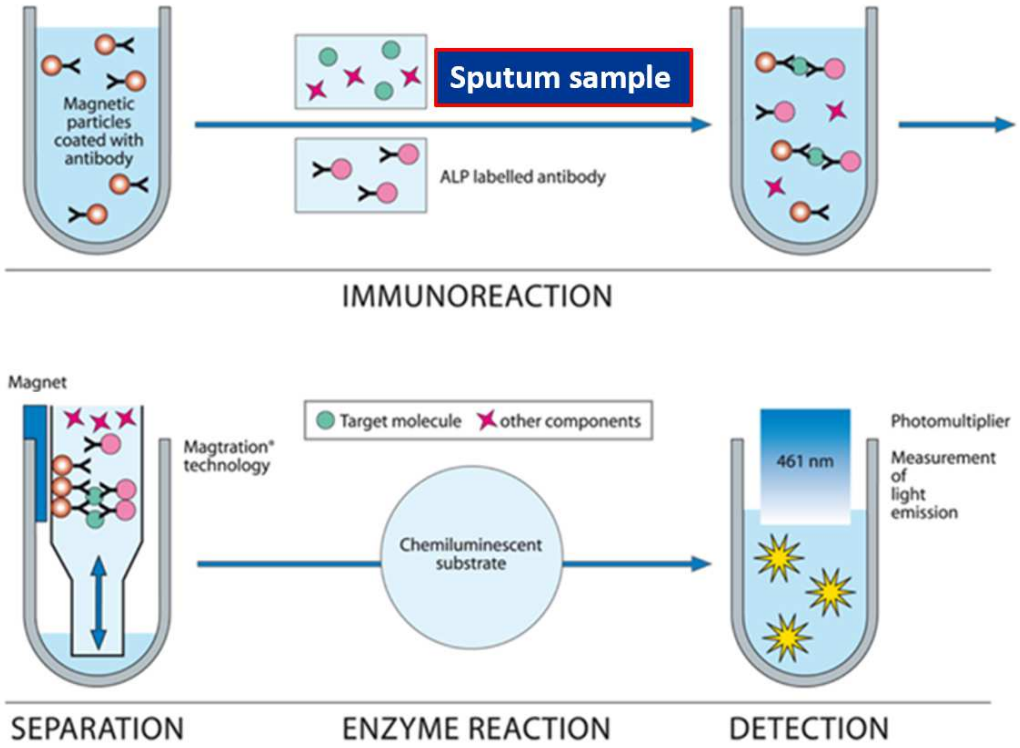
A potential algorithm for ER and chest pain units implementing biomarkers- multimarker panel



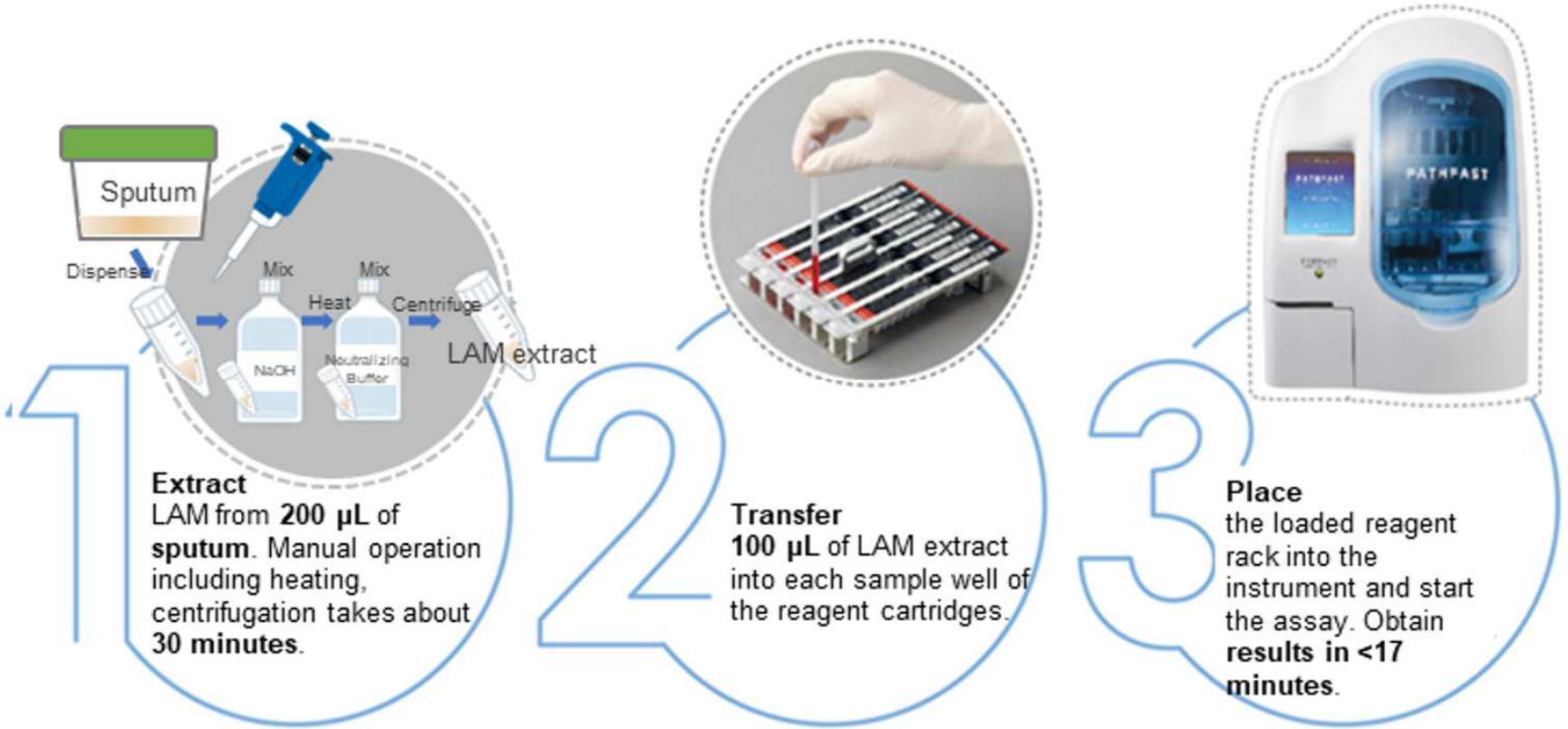
New Biomarker on PATHFAST for Infectious disease soon to come…. PATHFAST TB LAM Ag test



PATHFAST TB LAM Ag test: the principle



PATHFAST TB LAM Ag test: the principle




THANK
YOU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GROUP