Clinical impact of a direct Rapid Antimicrobial Susceptibility Testing (dRAST™) in administration of optimal therapy in patients with bloodstream infection

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Symposium on Diagnostic and surveillance of infectious diseases – Sciensano

16th May 2024

Plan

1. Introduction
2. Materials and methods
3. Results and discussion
4. Conclusion

1. Introduction – Bloodstream infection

- Sepsis
  - Increased mortality
  - Increased morbidity
  - Prolonged hospitalizations
  - High costs for healthcare systems

Rapid administration of an effective antimicrobial therapy

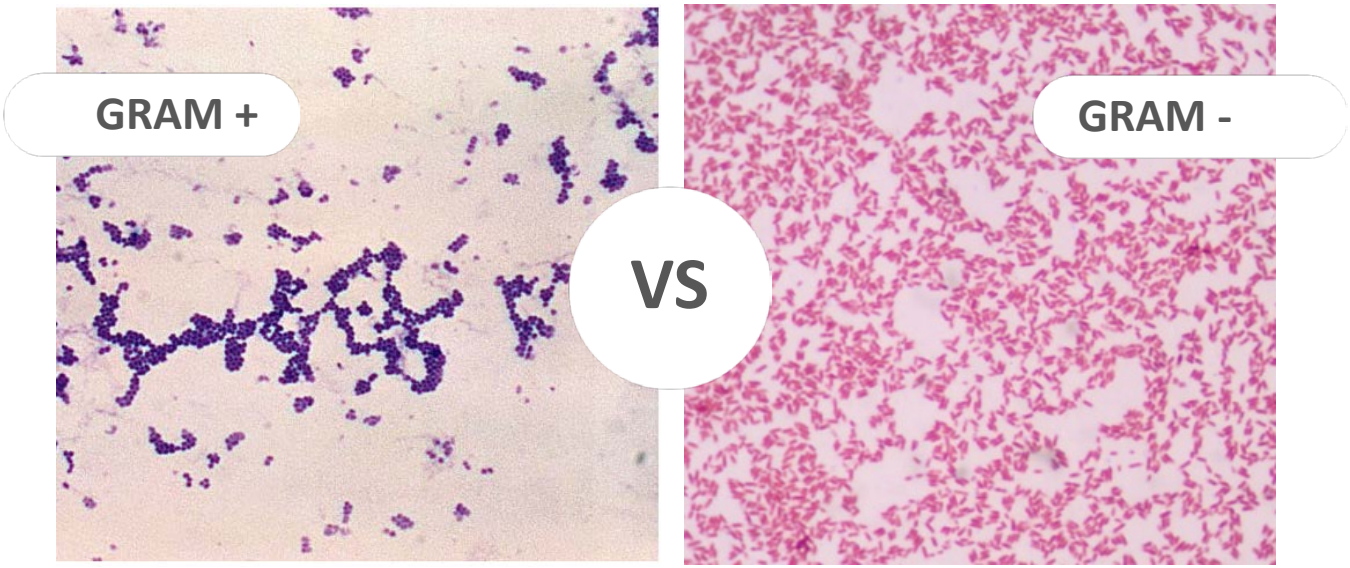
- ± 30% ineffecive empiric antimicrobial therapy :
  ↑ if MDR

Narrow spectrum

Adaptation of empirical therapy = to ensure the most effective treatment with the narrowest spectrum

Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. ICM. 2021;47:1181–1247.
Paul M, et al. Systematic review and meta-analysis of the efficacy of appropriate empiric antibiotic therapy for sepsis. Antimicrob Agents Chemother. 2010;54:4851–4863.
Singer M, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). JAMA; 2016. 801–810.
Goto M, et al. Overall burden of bloodstream infection and nosocomial bloodstream infection in North America and Europe. CMI. 2013;19:501–509. .
Retamar P, et al. Impact of inadequate empirical therapy on the mortality of patients with bloodstream infections: A propensity score-based analysis. AAC. 2012;56:472–478.

1. Introduction – Which microbiological information is usefull ?

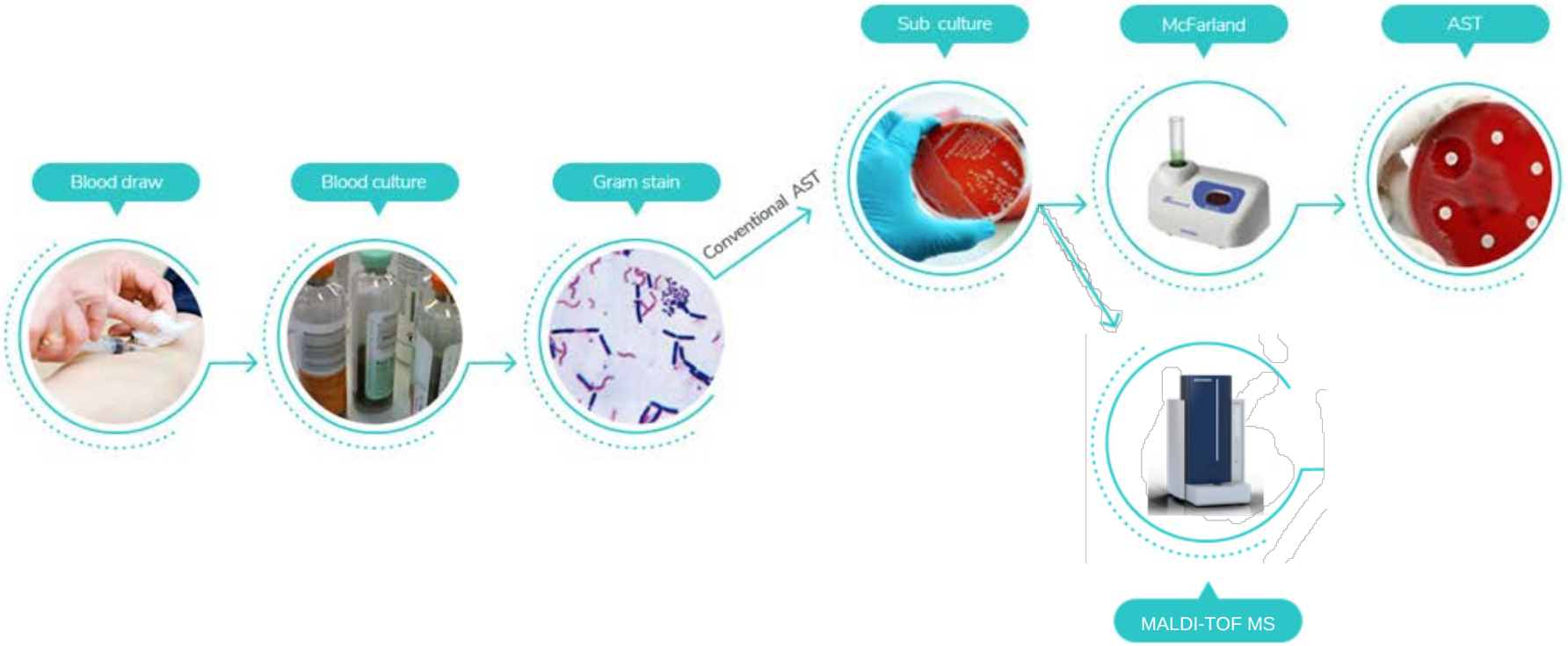


Gram stain
Identification by MALDI-TOF MS
(Rapid detection of resistance markers as bpb2a)

Antimicrobial Susceptibility Testing (AST)

Meda M, Clayton J, Varghese R, et al. What are the critical steps in processing blood cultures? A prospective audit evaluating current practice of reporting blood cultures in a centralised laboratory serving secondary care hospitals. J Clin Pathol. 2017;70:361–366.

1. Introduction – TAT



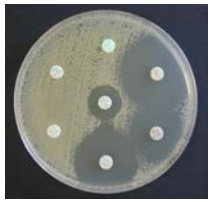
BC+ < 12am	± 1h	± 5h	± 24h
BC+ > 12am	± 1h	The next day	± 48h

1. Introduction – Rapid AST

- Phenotypic AST
  = Bacterial growth in presence of an antibiotic

  Expression of resistance mechanism in vitro
  Speed limited by bacterial growth

  Exact resistance phenotype
  MIC



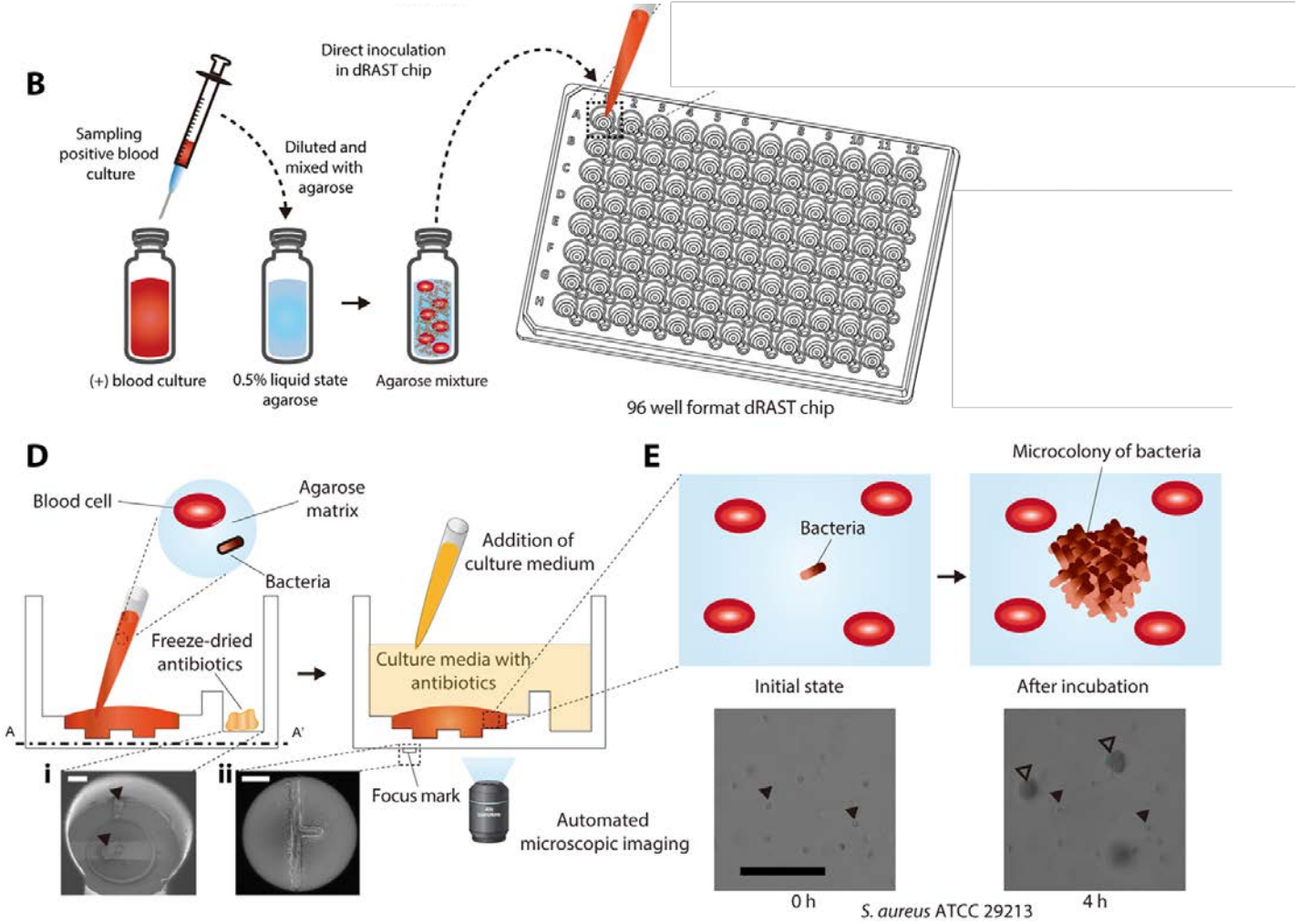
- Genotypic AST
  = Detection of a gene, or its product, linked to a resistance mechanism

  Detection of only certain genes
  Resistance genes ≠ resistance phenotypes
  High cost
  Do not replace conventional AST for now (no MIC)

  Fast
  Can be performed on primary samples or cultures
  Take into acount the entire bacterial population

1. Introduction – dRAST™

1. Introduction – dRAST™



Choi J, Jeong HY, Lee GY, et al. Direct, rapid antimicrobial susceptibility test from positive blood cultures based on microscopic imaging analysis. Sci Rep. 2017;7:1–13.

1. Introduction – dRAST™

2 types of panels according to Gram result

- ☑ Molecules et MIC consistent with EUCAST

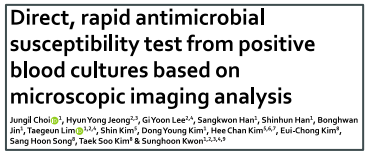
	Staphylococcus spp.	*Enterococcus* spp.
Ampicilline		✓
Céfoxitine	✓	
Clindamycine	✓	
Résistance Inductible à la Clindamycine	✓	
Daptomycine	✓	✓
Erythromycine	✓	✓
Acide Fusidique	✓	
Gentamicine	✓	
Gentamicine Haut-Niveau		✓
Lévofloxacine	✓	✓
Linézolide	✓	✓
Oxacilline	✓	
Pénicilline	✓	
Rifampicine	✓	
Streptomycine Haut-Niveau		✓
Téicoplanine	✓	✓
Tétracycline	✓	
Vancomycine	✓	✓

	Enterobacteriaceae	*Pseudomonas* spp.	*Acinetobacter* spp.	*Stenotrophomonas maltophilia*	*Burkholderia cepacia*	*Burkholderia pseudomallei*
Amikacine	✓	✓	✓			
Amoxicilline/Acide clavulanique	✓					✓
Ampicilline	✓					
Céfépime	✓	✓	✓	✓	✓	
Céfotaxime	✓		✓			
Céfotaxime/Acide clavulanique	✓					
Ceftazidime	✓	✓	✓	✓	✓	✓
Ceftazidime/Avibactam	✓	✓				
Ceftazidime/ Acide clavulanique	✓					
Ciprofloxacine	✓	✓	✓	✓		
Colistine	✓	✓	✓			
Gentamicine	✓	✓	✓			
Imipénème	✓	✓	✓		✓	✓
Lévofloxacine	✓	✓	✓	✓	✓	
Méropénème	✓	✓	✓		✓	✓
Pipéracilline	✓	✓	✓			
Pipéracilline/Tazobactam	✓	✓	✓			
Triméthoprime/Sulfaméthoxazole	✓		✓	✓	✓	✓

➔ « Final » AST

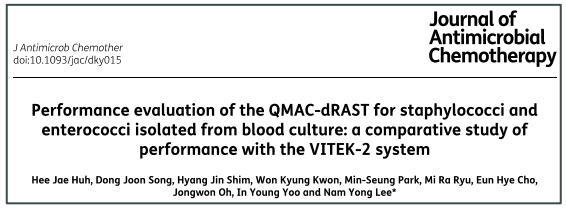
1. Introduction – Objectives

☑ Technical evaluation



Direct, rapid antimicrobial susceptibility test from positive blood cultures based on microscopic imaging analysis

Jungil Choi, Hyun Yong Jeong, Gi Yoon Lee, Sangkwon Han, Shinhun Han, Bonghwan Jin, Taegeun Lim, Shin Kim, Dong Young Kim, Hee Chan Kim, Eui-Chong Kim, Sang Hoon Song, Taek Soo Kim & Sunghoon Kwon

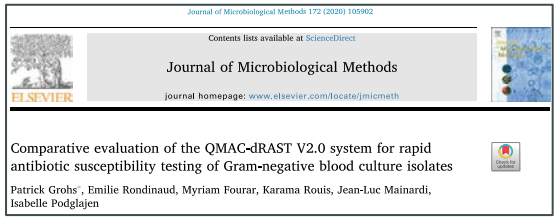


J Antimicrob Chemother
doi:10.1093/jac/dky015

Journal of Antimicrobial Chemotherapy

Performance evaluation of the QMAC-dRAST for staphylococci and enterococci isolated from blood culture: a comparative study of performance with the VITEK-2 system

Hee Jae Huh, Dong Joon Song, Hyang Jin Shim, Won Kyung Kwon, Min-Seung Park, Mi Ra Ryu, Eun Hye Cho, Jongwon Oh, In Young Yoo and Nam Yong Lee*



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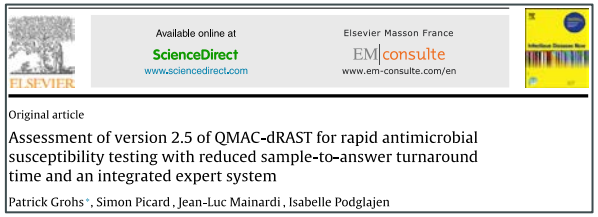
Comparative evaluation of the QMAC-dRAST V2.0 system for rapid antibiotic susceptibility testing of Gram-negative blood culture isolates

Patrick Grohs*, Emilie Rondinaud, Myriam Fourar, Karama Rouis, Jean-Luc Mainardi, Isabelle Podglajen



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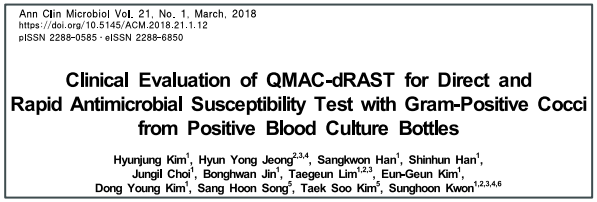
Original article

Assessment of version 2.5 of QMAC-dRAST for rapid antimicrobial susceptibility testing with reduced sample-to-answer turnaround time and an integrated expert system

Patrick Grohs*, Simon Picard, Jean-Luc Mainardi, Isabelle Podglajen



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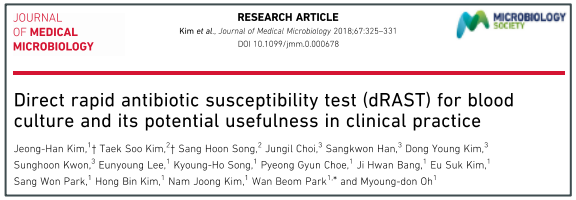
Clinical Evaluation of QMAC-dRAST for Direct and Rapid Antimicrobial Susceptibility Test with Gram-Positive Cocci from Positive Blood Culture Bottles

Hyunjung Kim, Hyun Yong Jeong, Sangkwon Han, Shinhun Han, Jungil Choi, Bonghwan Jin, Taegeun Lim, Eun-Geun Kim, Dong Young Kim, Sang Hoon Song, Taek Soo Kim, Sunghoon Kwon

☑ Retrospective evaluation of clinical impact



JOURNAL OF MEDICAL MICROBIOLOGY

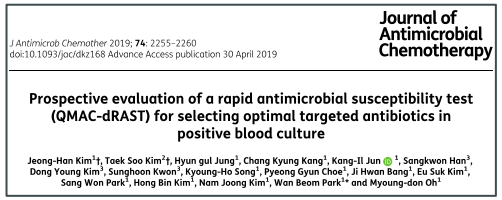
RESEARCH ARTICLE

Kim et al., Journal of Medical Microbiology 2018;67:325–331
DOI 10.1099/jmm.0.000678

MICROBIOLOGY SOCIETY

Direct rapid antibiotic susceptibility test (dRAST) for blood culture and its potential usefulness in clinical practice

Jeong-Han Kim, Taek Soo Kim, Sang Hoon Song, Jungil Choi, Sangkwon Han, Dong Young Kim, Sunghoon Kwon, Eunyoung Lee, Kyoung-Ho Song, Pyeong Gyun Choe, Ji Hwan Bang, Eu Suk Kim, Sang Won Park, Hong Bin Kim, Nam Joong Kim, Wan Beom Park* and Myoung-don Oh



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Journal of Antimicrobial Chemotherapy

Prospective evaluation of a rapid antimicrobial susceptibility test (QMAC-dRAST) for selecting optimal targeted antibiotics in positive blood culture

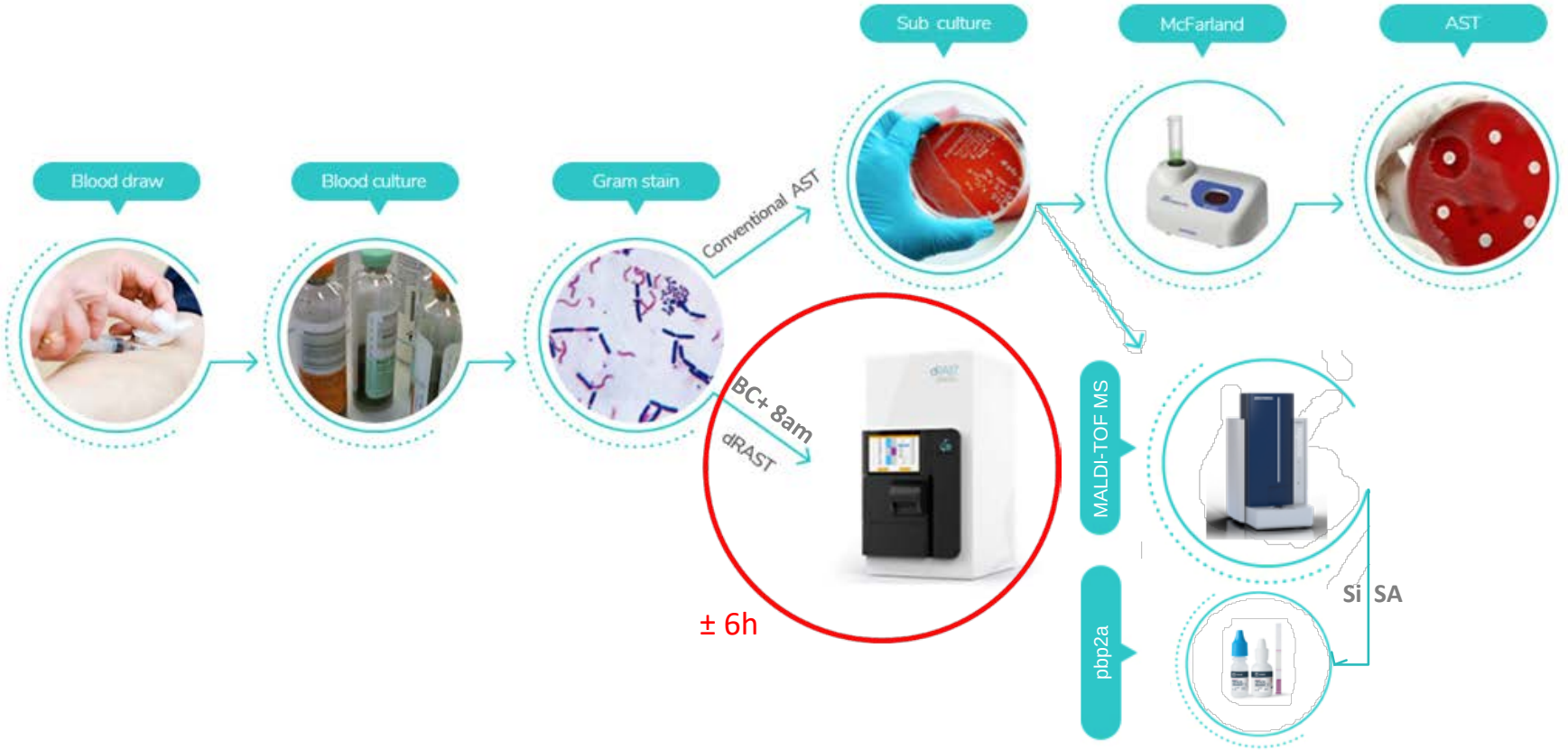
Jeong-Han Kim, Taek Soo Kim, Hyun gul Jung, Chang Kyung Kang, Kang-Il Jun, Sangkwon Han, Dong Young Kim, Sunghoon Kwon, Kyoung-Ho Song, Pyeong Gyun Choe, Ji Hwan Bang, Eu Suk Kim, Sang Won Park, Hong Bin Kim, Nam Joong Kim, Wan Beom Park* and Myoung-don Oh

<u>Aim of the study :</u> Retrospective and prospective evaluation of clinical impact of dRAST™

2. Materials and methods - Populations

Retrospective study	**Prospective study**
150 patients	15 patients
Gram -, *Staph. aureus, Enterococcus spp.*, or CNS for which an AB is pursued for at least 48h after ID	Gram -, *Staph. aureus, Enterococcus spp.*, or CNS judged clinically relevant by the « AMS team »
All wards	Intensive care units
dRAST™ and Vitek® performed on 150 BC+	dRAST™ et Vitek® perfomed on 15 BC+ and Vitek®performed on a control group of 15 patients

2. Materials and methods – Lab

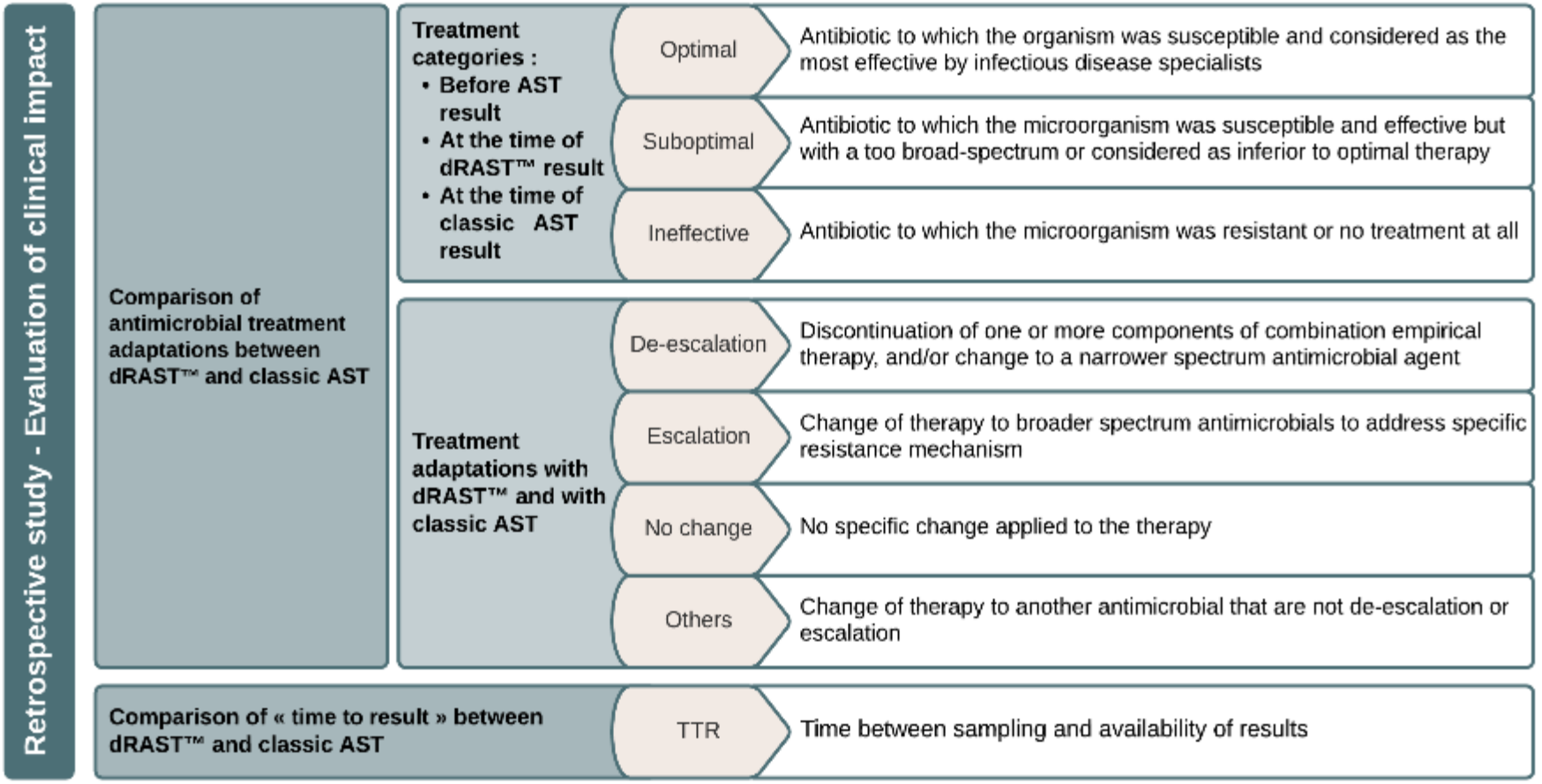


BC+ < 12h ± 1h ± 5h ± 24h

BC+ > 12h ± 1h The next day ± 48h

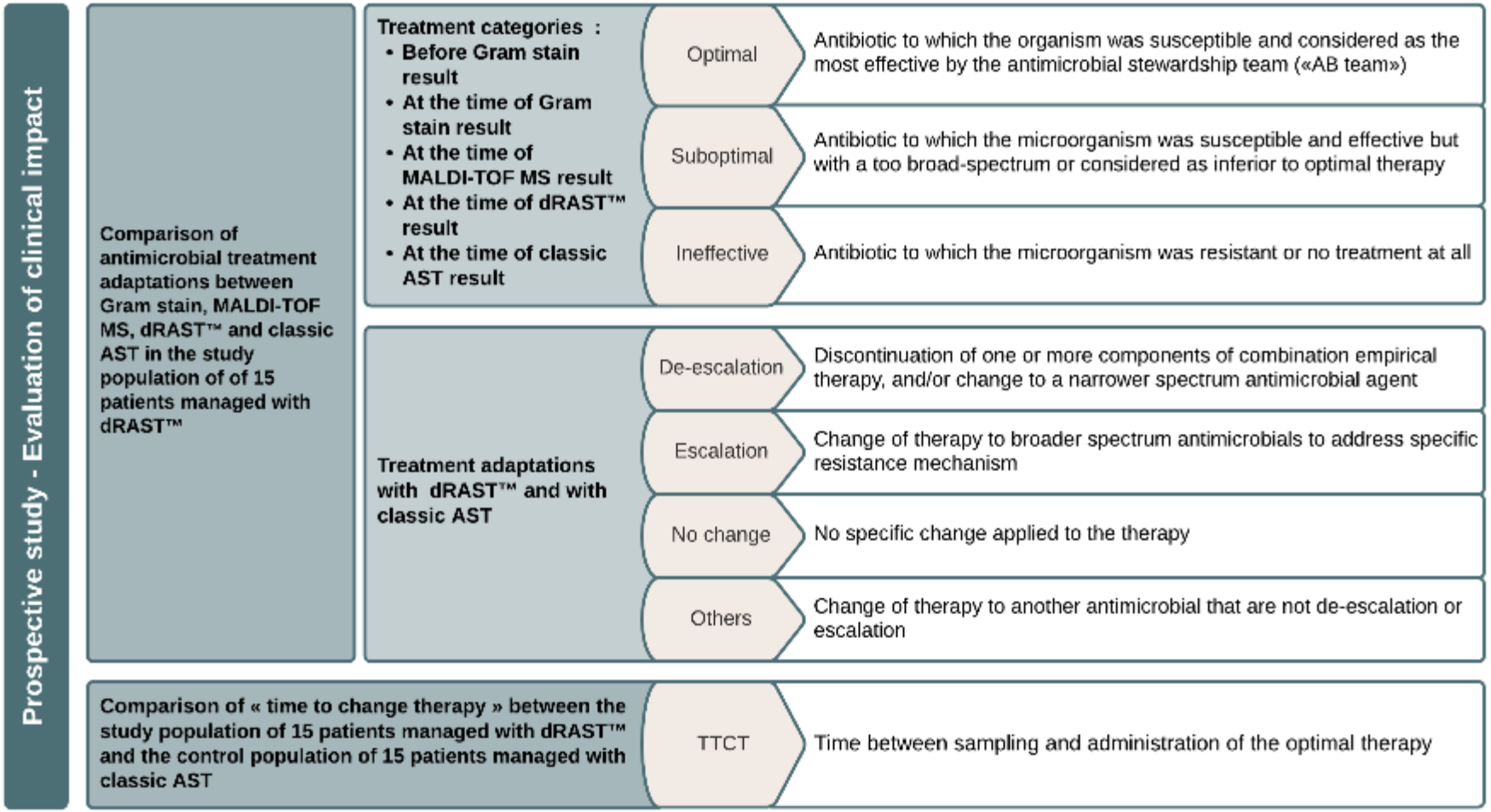
2. Materials and methods – Cinical impact

Retrospective study :

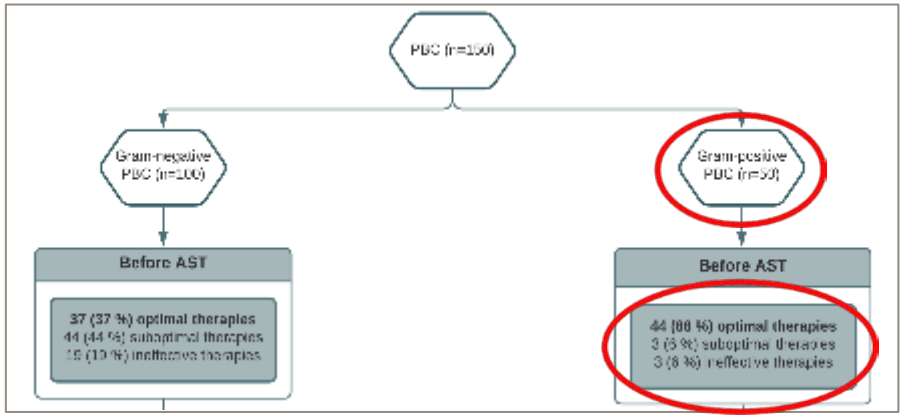


2. Materials and methods – Clinical impact (2)

Prospective study :

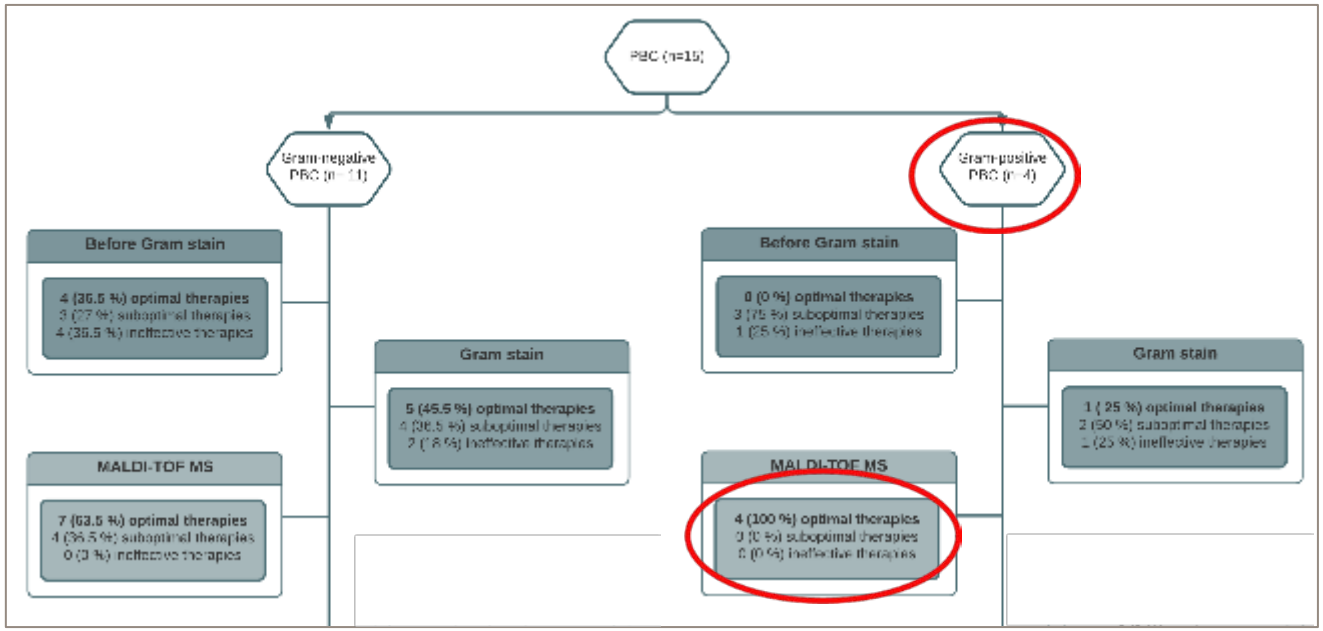


3. Results – Antimicrobial therapies before AST



Retrospective study :

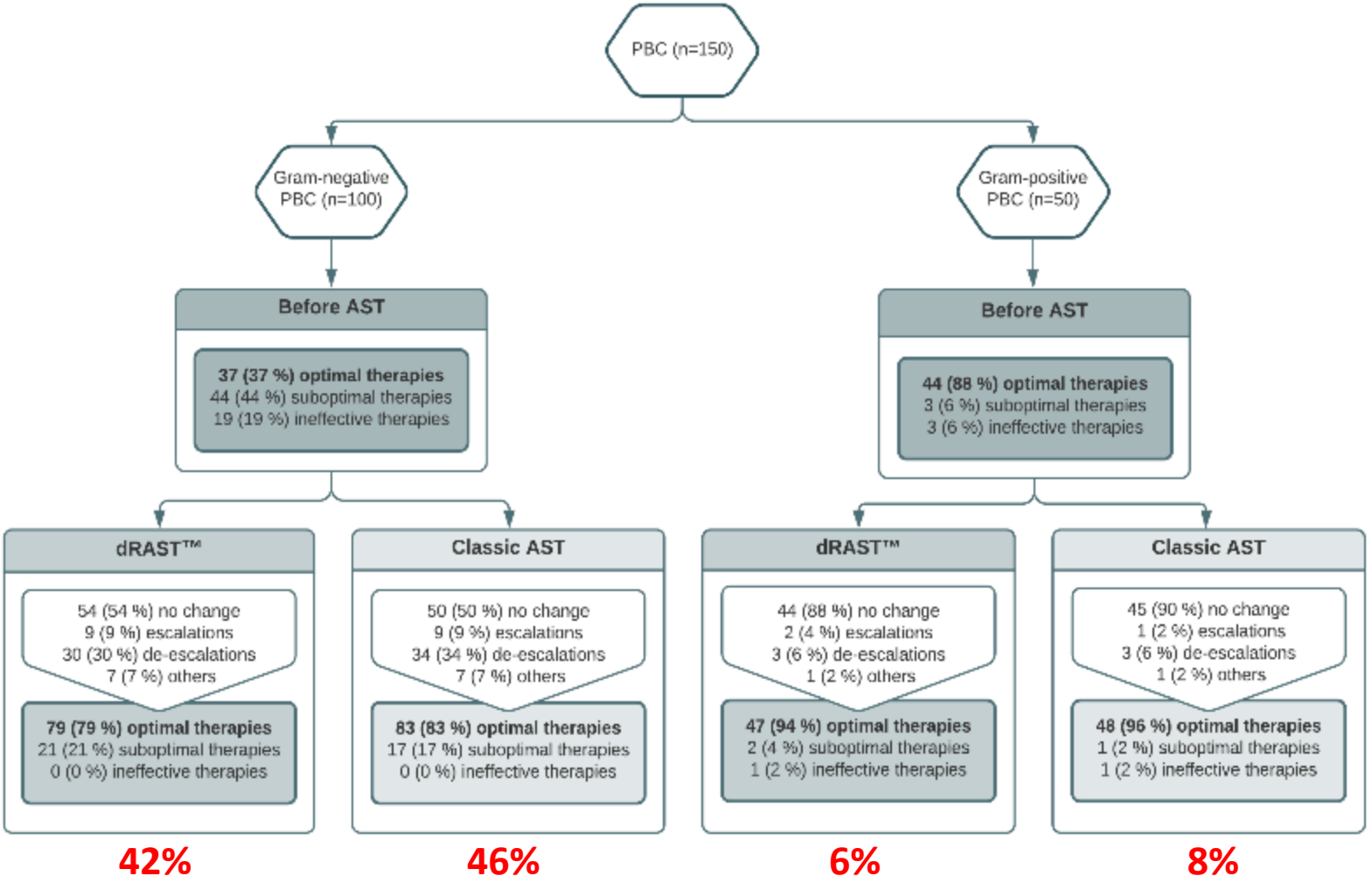
54% optimal therapies
31,3% Suboptimal therapies
14,7% Ineffective therapies



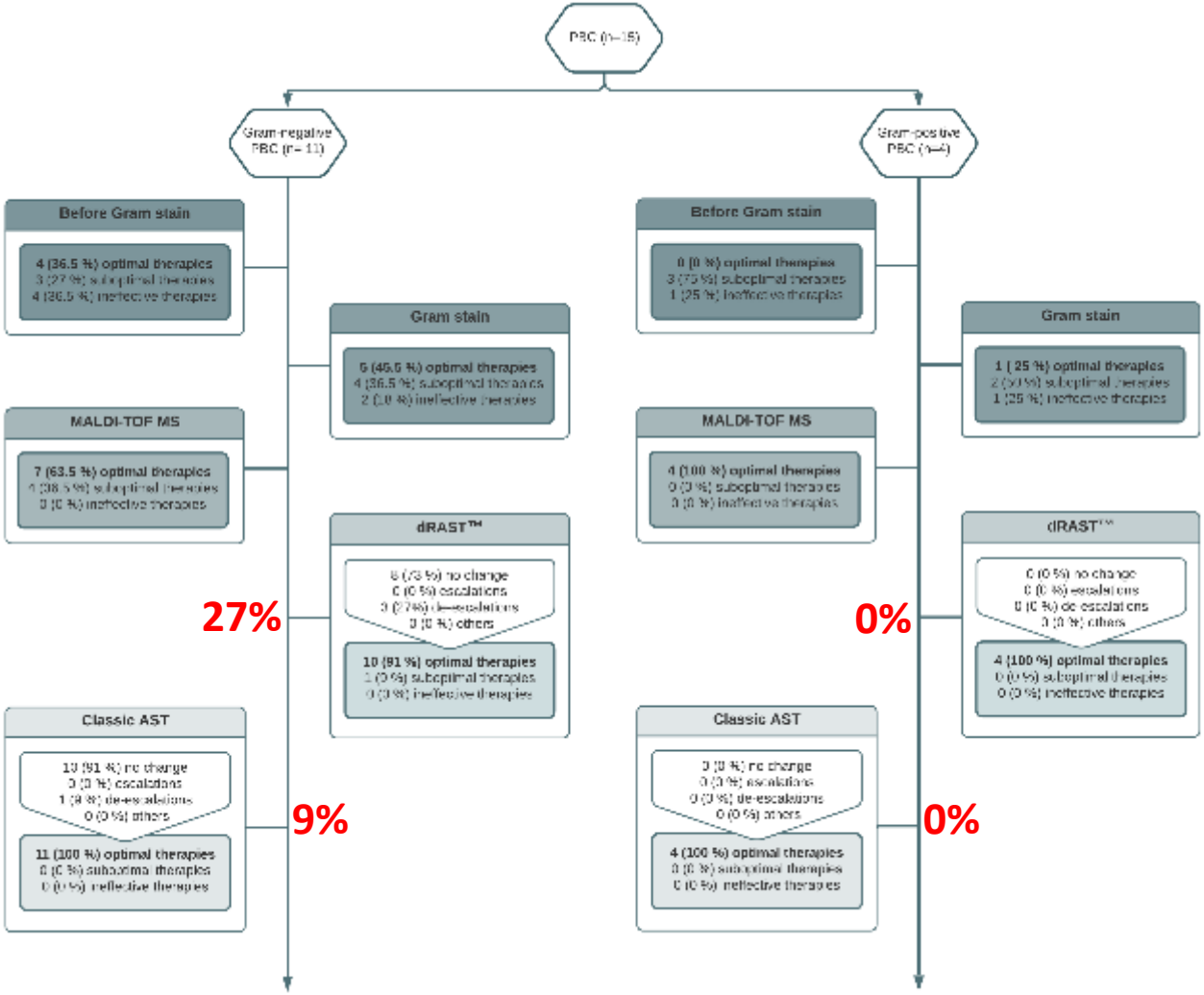
Prospective study :

73,3% optimal therapies
26,7% suboptimal therapies
0% ineffective therapies

3. Results – Clinical impact (retrospective study)



3. Results – Clinical impact (prospective study)



3. Results – Time saved

Retrospective study :

	Time to Result (hh:mm)			*p*-value
	dRAST™	Classic AST	Time saved (Classic AST - dRAST™)	
Gram-negative PBC (n=46)	29:33 (± 08:42)	50:43 (± 11:17)	18:13 (± 07:25)	< 0.001
Gram-positive PBC (n=4)	33:05 (± 11:11)	73:23 (± 22:20)	40:18 (± 12:33)	-
Total (n=50)	**29:35 (± 08:48)**	**50:55 (± 12:45)**	**18:15 (± 08:29)**	**< 0.001**

Prospective study :

No matching with a control population → no TTCT, but faster adaptation (the day before) thanks to dRAST

3. Results – Outstanding issues

- Need of an « antimicrobial stewardship » ?
  - Need for clinicians to receive information, interpret it, and adapt antimicrobial therapy if necessary
  - Independant impact on antibiotic therapy
- Need of lab technicians 24/7 ?
  - Technical handling and basic validation of AST
  - Above all, 24/7 management of PBC
- Need of MIC ?
  - Could less expensive rapid AST be sufficient (disk diffusion AST) ?
  - Easy to use and interpret dRAST™

4. Conclusion

- Limited usefulness for BC+ with Gram positive
- Greater usefulness for BC+ with Gram negative

- Significantly faster adaptation of antimicrobial therapy (if necessary) with dRAST ™

4. Conclusion – Perspectives

- Further studies
- Polymicrobial PBC ?
- Economic impact

4. Conclusion

For the fastest administration of optimal therapy in patient with BSI :

COMBINATION OF INTERVENTIONS AND METHODS.