4ème Journée Antibio-Résistance et Infection (JARI)
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Quelles méthodes diagnostiques rapides pour réduire et mieux cibler les choix antibiotiques ?

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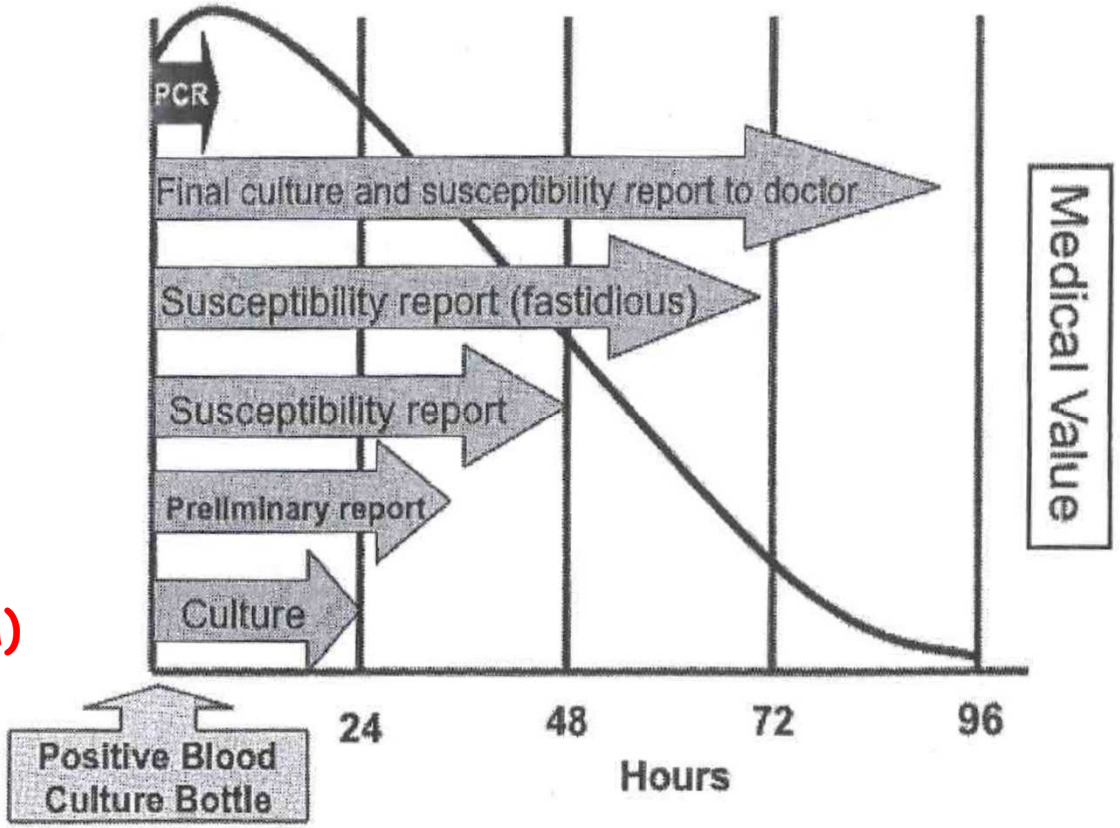
Méthodes conventionnelles

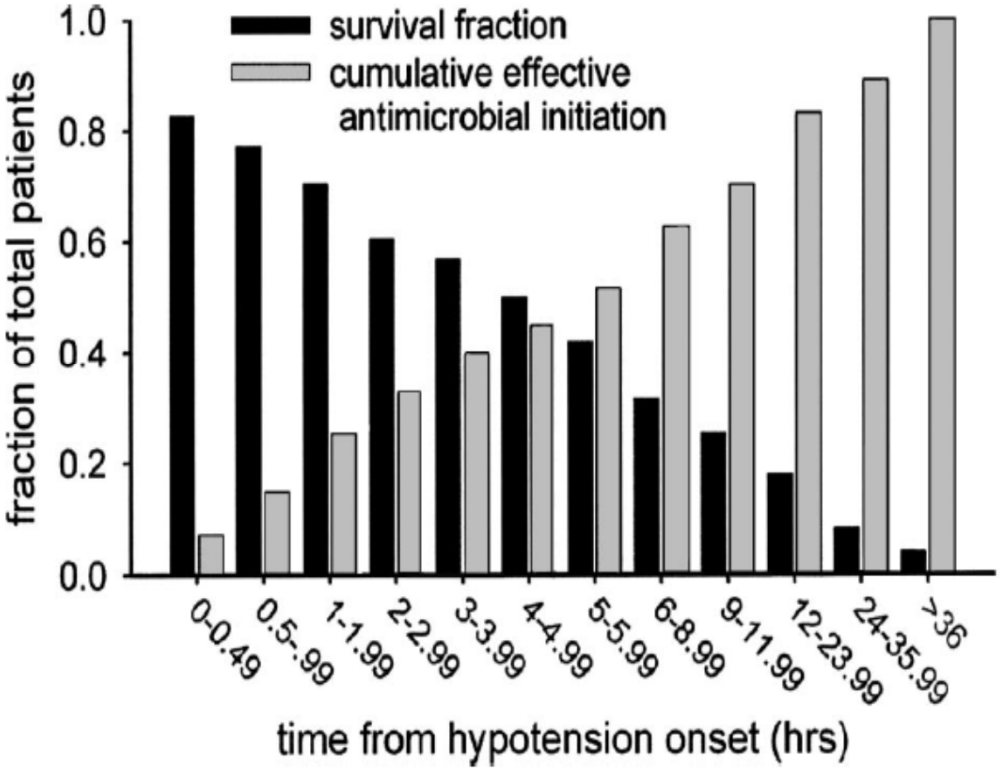


Positivité (12-48 h)

Temps moyen pour résultats = 40 h

Goff et al. Pharmacother 2012
Kerremans et al., J Antimicrob Chemother 2008

Antibiothérapie adaptée



Etude de cohorte rétrospective multicentrique 1989-2004

2154 patients adultes avec **choc septique**

Dans les six 1ères heures : ↓ **survie 7,6 % par heure de retard**

Kumar et al., Crit Care Med 2006

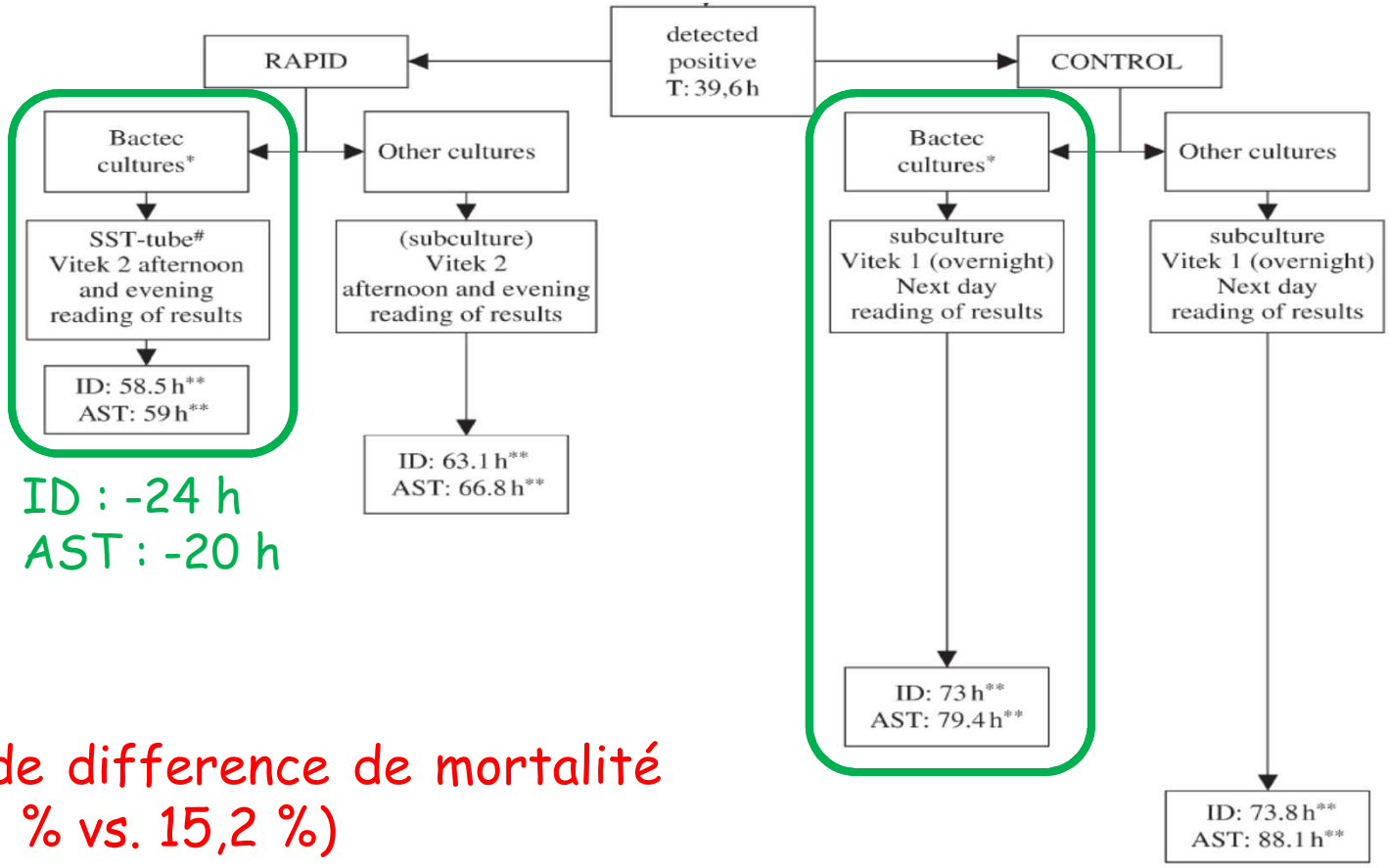
Tests phénotypiques optimisés

- ✓ Antibiogramme direct sur HC + (diffusion ou automate) :
  - Très bonne concordance (95-98 %)
  - Résultats 24-36 h plus tôt
  - Manque de standardisation
  - (Culture monomicrobienne)

- ✓ **Peu d'études** évaluant l'impact clinique

Mirrett et al. J Clin Microbiol 1979
Ling et al., J Clin Microbiol 2003

ATBG automatisé "même jour"



ID : -24 h
AST : -20 h

Pas de difference de mortalité
(17,6 % vs. 15,2 %)

Kerremans et al., J Antimicrob Chemother 2008

ATBG automatisé "même jour"

Etude espagnole comparant la stratégie classique (jour d'après) à une stratégie rapide (même jour) [Vitek 2 dans chaque bras]

Time to positivity	25.5 h	25.3 h	*P* = 0.3
ID result report	27.0 h	9.4 h	*P* < 0.001

Characteristic	Control group	Intervention group	*P*
Median length (days) of hospitalization in CHU[a]	10.1 ± 16.3	7.7 ± 14.6	0.003
Median length (days) of hospitalization in ICU[a]	1.7 ± 11.0	0.9 ± 25.0	0.1
Median total length (days) of hospitalization[a]	10.3 ± 20.9	8.0 ± 16.2	0.002
Median days of Endotracheal intubation[a]	3.9 ± 14.6	3.8 ± 4.5	0.5
Total no. patients (%) with Endotracheal intubation requirements[b]	41 (14.4)	23 (7.9)	0.017
Total no. (%) of patient deaths (until 3 months after discharge)[b]	24 (9.2)	23 (8.6)	0.9
Total no. (%) of patient deaths during hospitalization[b]	18 (6.3)	16 (5.5)	0.7
Total no. (%) of patient deaths attributable to infection[b]	12 (4.2)	6 (2.1)	0.2

NOTE. Data are mean ± standard deviation, unless otherwise indicated. CHU, conventional hospitalization unit; ICU, intensive care unit.

+ Réduction du nbre de tests microbiologiques (*P* = 0,038)
+ Réduction des coûts (16000 vs. 12400 €, *P* = 0,012)

Galar et al., J Infect 2012

ATBG direct

Etude prospective randomisée (Espagne) 2003-2005 comparant une méthode rapide (E-test OXA-TZP-FEP-IMP-CIP-AMI sur prél. resp.) vs. culture std dans PAVM

Outcome	E-test group (n = 167)	Control group (n = 83)	P
Fever, mean days ± SD	4.61 ± 5.06	7.84 ± 6.24	<.01
Antibiotic therapy, mean days ± SD	15.72 ± 9.47	18.92 ± 10.92	.02
Defined daily doses of antibiotic therapy, mean ± SD	31.43 ± 24.47	42.72 ± 34.13	.01
Median cost, in €, of antibiotic per episode (IQR)	666 (236–1360)	984 (437–1601)	.03
Percentage of adequate days of antibiotic therapy	95.22	76.26	<.01
Percentage of adequate defined daily doses of antibiotic therapy	91.28	68.26	<.01
Clostridium difficile–associated diarrhea, no. of patients (%)	3 (1.8)	8 (9.6)	<.01
Median no. of days on mechanical ventilation from VAP diagnosis (IQR)	8 (3–19)	12 (6–21)	.04

Pas de difference de mortalité au cours de l'épisode (32 % vs. 29 %, P = 0,07)

Bouza et al. Clin Infect Dis 2007

Impact PCR classique

Etude prospective monocentrique sur 3 ans (France) chez des patients d'USI comparant 2 groups : méthode rapide de PCR (6 h) vs. méthode classique (21 h)

Parameters (n.%)	PCR		Control		
	oxa-S 54	oxa-R 18	oxa-S 46	oxa-R 27	
Unfavourable outcome of infection	6 (11.1)	3 (16.7)	6 (13.0)	3 (11.1)	NS
Unfavourable general outcome	11 (20.4)	4 (22.2)	6 (13.0)	6 (22.2)	
Length of stay in ICU (days)	18±2	21±3	17±3	26±2	
Cost of antibiotics ($)	2105±303	6264±836	1882±290	4816±994	

➔ Pas d'impact clinique majeur

Allaouchiche et al. J Infect 1999

Impact PCR en temps réel

Etude prospective monocentrique sur 1 an (France) chez des patients avec HC+ à GPCC : qPCR vs. culture (250 épisodes)

- 97 épisodes de bactérimies

Characteristic	PCR testing group (n = 49)	Conventional testing group (n = 48)	OR (95% CI)	p value
Appropriate empirical antibiotic therapy, n (%)[a]	20 (40)	18 (37)	1.19 (0.52–2.70)	0.676
Time to initiation of appropriate therapy (h)[b]	1 (0–5)	3 (0–19)	0.99 (0.96–1.01)	0.443
Time to initiation of appropriate therapy after final identification of staphylococci (h)	4 (0–8)	27 (0–43)	0.96 (0.94–0.99)	0.012
Time to initiation of appropriate therapy after blood culture sampling, hours	25 (0–48)	26 (0–50)	0.99 (0.98–1.01)	0.814
Time between BC sampling and results reporting (h)	24 (24–48)	24 (24–24)	1.03 (1.01–1.06)	0.029
Optimal treatment, n (%)[c]	38 (78)	37 (77)	1.03 (0.36–2.94)	0.956
Duration of antibiotic treatment (days)	14 (11–26)	14 (9–19)	1.02 (0.99–1.05)	0.330

[a]Patients receiving antibiotic therapy that include a drug active against the isolated pathogen before reporting blood culture results.
[b]Delay between time of reporting blood culture results by the microbiological laboratory to the ward physician and the start of antibiotic therapy that include a drug active against the isolated pathogen.
[c]Patients receiving either methicillin for MSSA and MSCoNS, or vancomycin for MRSA and MRCoNS, on the day after reporting results.

- 153 contaminations : pas de difference d'ATBT non justifiée (17 % vs. 10 %, P = 0,237)

Cattoir et al. Clin Microbiol Infect 2011

Impact PCR en temps réel

Pas de difference en termes de :

- Succès clinique : 61 % vs. 73 % (*P* = 0,221)
- Localisations secondaires : 10 % vs. 8 % (*P* = 0,726)
- Succès clinique à S12 : 58 % vs. 60 % (*P* = 0,68)

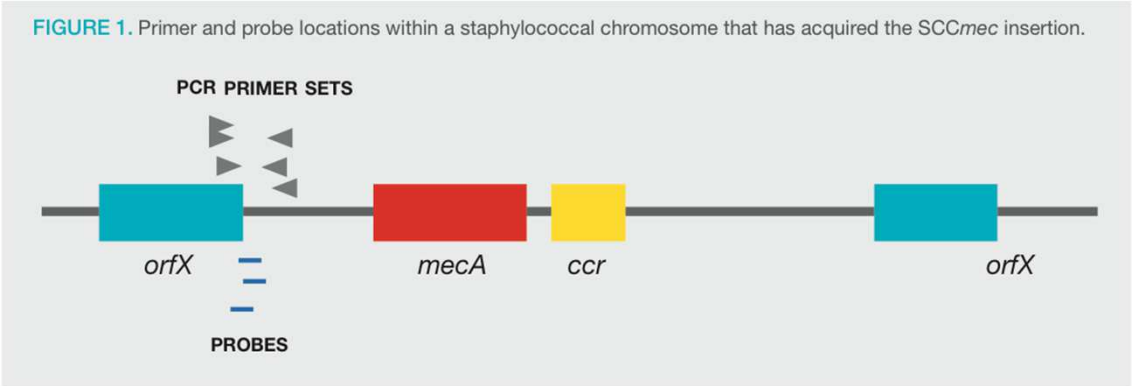
TABLE 4. Factors independently associated with a favorable outcome

Variable	Adjusted OR	95% CI	p value
Age	0.96	0.93–0.99	0.037
Absence of comorbidity	2.12	0.49–9.12	0.314
SOFA score	0.89	0.79–1.01	0.075
Methicillin-susceptible *Staphylococcus aureus*	3.11	1.12–8.65	0.029
Duration of antibiotic treatment	1.03	0.98–1.08	0.225
Metastatic complication	0.52	0.15–1.85	0.313
PCR testing	0.63	0.22–1.77	0.380

Cattoir et al. Clin Microbiol Infect 2011

Xpert MRSA/SA (Cepheid)

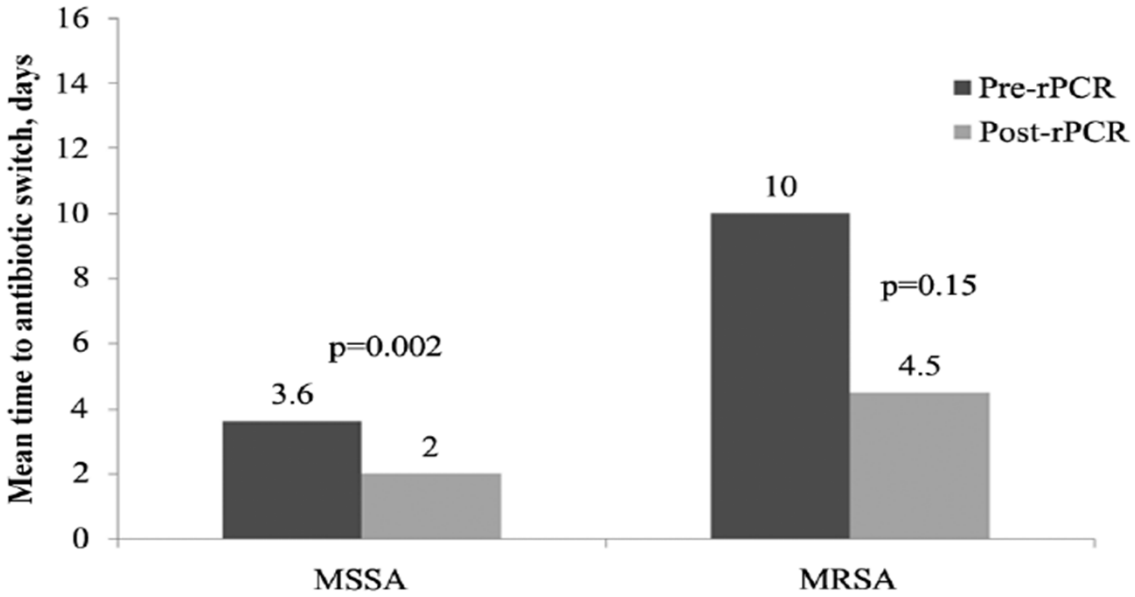
1 h



Target	PCR results:					
spa	+	+	+	+	-	-
mecA	+	-	-	+	+	-
SSC_{mec}-*orfX*	+	-	+	-	-	-
Internal control	+/-	+/-	+/-	+/-	+/-	+
Interpretation	**MRSA or MSSA drop out + MR-CoNS**	**MSSA**	**MSSA drop out**	**MSSA + MR-CoNS or MRSA (SCC_{mec} variant)**	**MR-CoNS**	**MS-CoNS or nothing**

Impact Xpert MRSA/SA

Etude monocentrique (US) comparant l'impact AST+PCR (Xpert, Cepheid) sur 2 périodes : pré-PCR (2008) et post-PCR (2009)



DMS plus courte de 6,2 j (P = 0,07)

Coûts moindres de 21400 $ (P = 0,03)

Mais pas de différence de mortalité (26 % vs. 18 %, *P* = 0,33)

Bauer et al., Clin Infect Dis 2010

Impact Xpert MRSA/SA

Etude américaine comparant patients avec HC+ à GPCC avec Xpert (groupe 1) vs. méthode std (groupe 2)

TABLE 2. Data on Drug Therapy for Patients with Bacteremia due to Methicillin-Susceptible *Staphylococcus aureus* at the Michael E. DeBakey Veterans Affairs Medical Center in Houston, Texas (2008–2009)

Variable	Group 1[a] ($n = 12$)	Group 2[b] ($n = 48$)	P[c]
Mean time to initiate MSS drug therapy, hours	5.2	49.8	.007
Median time to initiate MSS drug therapy, hours	0	48.5	.004
Mean duration of MRS drug therapy, hours	19.7	80.7	.003
No. (%) of patients not initially treated with MRS drug	3 (25.0)	5 (10.4)	
No. (%) of patients treated with MRS drug for unrelated condition	3 (25.0)	4 (8.3)	
No. (%) of patients treated with MRS drug for staphylococcal bacteremia	6 (50.0)	39 (81.3)	.025

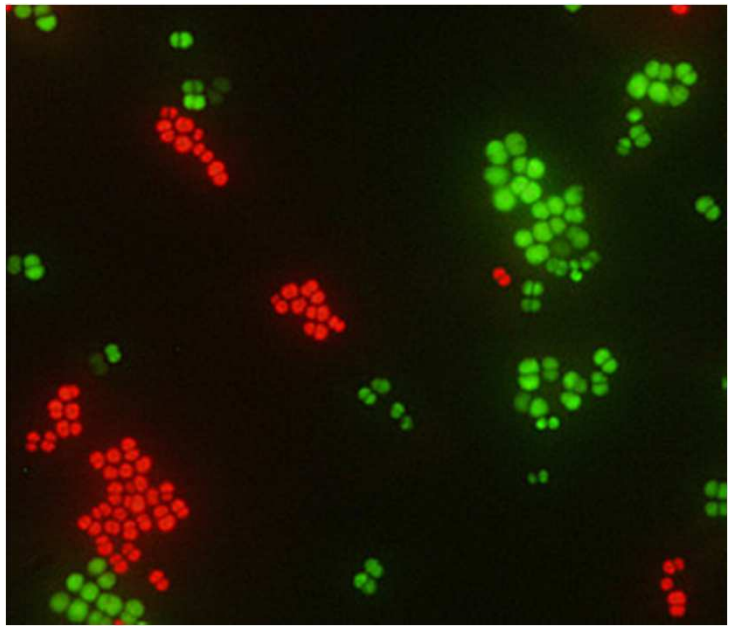
Pas de différence pour de délai d'initiation de TTT pour bactériémies à SARM (P = 0,33)

Parta et al., Int Control Hosp Infect 2010

PNA-FISH (AdvanDx)

Peptide Nucleic Acid-Fluorescence *In Situ* Hybridization
Sondes ARNr 16S spécifiques (90' → 20') – Fiabilité >98 %

SCN



S. aureus

Ne distingue pas SASM et SARM

Impact du PNA-FISH Staph

Etude rétrospective (US) sur 3 mois sur la différentiation *S. aureus*/SCN par PNA-FISH vs. culture std

	Control group	PNA FISH	*P* value
Total DDD of vancomycin/patient	6.78	4.9	NS
DDD of vancomycin/patient after GPCC result	4.8	2.55	0.06
Patients receiving no doses of vancomycin	3/34 (9%)	9/53 (17%)	0.06, NS
Patients receiving 1 or less doses of vancomycin	5/34 (15%)	23/53 (43%)	<0.005
Number of patients with LOS < 3 days after GPCC result	6/34 (18%)	20/53 (38%)	0.06, NS
Median LOS (days)	6	4	<0.05, CI 0.95–1.87

+ diminution du coût (~4000 $/patient)

Forrest et al., J Antimicrob Chemother 2006

Impact du PNA-FISH Staph

Etude prospective randomisée controlée (US) sur 7 mois sur la différentiation *S. aureus*/SCN par PNA-FISH vs. culture std

All hospital locations	All patients		
	Usual care	Notification	P
	(N = 101)	(N = 101)	
Hospital stay, median days	9	9	
Charges, median $	92,373.78	72,932.41	0.09
Antibiotics, median day	3	1	0.01
Deaths, No (%)	17 (16.8)	8 (7.9)	0.05

Ly et al., Ther Clin Risk Manag 2008

Rôle majeur de l'ETI

Etude rétrospective monocentrique (US) pré/post PNA-FISH **sans avis ETI**

Group (*n*)	Mean hospital LOS (days) ± SD (median; range)	Mean duration (days) of vancomycin treatment ± SD (median; range)
Pre-PNA FISH patients (100)	18.7 ± 16.5 (13.0; 2.0–83.3)	4.15 ± 4.03 (2.9; 0.3–19.2)
Post-PNA FISH patients (99)	20.9 ± 21.0 (13.7; 1.8–113.5)	3.51 ± 3.43 (1.8; 0.3–10.8)
P value	0.35	0.49

Holtzman et al., J Clin Microbiol 2011

Impact du PNA-FISH Entero

Etude quasi-expérimentale monocentrique (US) sur 2 ans sur la différentiation *E. faecalis/Enterococcus* spp. par PNA-FISH vs. culture std

Characteristic[a]	Value					
	E. faecalis			*E. faecium*		
	Pre-PNA FISH (n = 64)	PNA FISH (n = 48)	P	Pre-PNA FISH (n = 65)	PNA FISH (n = 47)	P
Ampicillin susceptible [no. (%)]	64 (100)	48 (100)	1	0 (0)	0 (0)	1
Vancomycin susceptible [no. (%)]	57 (89)	43 (90)	0.93	11 (17)	2 (4)	0.04[b]
Other bacteria in same BC draw [no. (%)]	41 (64)	30 (63)	0.87	22 (34)	15 (34)	0.9
Total time in days from BC drawn to PNA FISH report		1.1 (0.5–3.3)	<0.001[b]		1.1 (0.5–3.5)	<0.001[b]
Total time in days from BC drawn to appropriate therapy [median (range)]				3.1 (0–9)	1.3 (0–4.3)	<0.001[b]
Received appropriate therapy after final microbiological report [no. (%)]	64 (100)	48 (100)	1	56 (86)	46 (98)	0.04[b]
30 day mortality [no. (%)]				29 (45)	12 (26)	0.039[b]

Forrest et al., Antimicrob Agents Chemother 2008

Diagnostic rapide *C. difficile*

Etude prospective monocentrique (France) comparant 3 stratégies sur 3 périodes de 3 mois : **CTA + CT / Xpert C. diff / GDH + LAMP**

TABLE 3. Management of patient without *Clostridium difficile* infection

	Period 1 (CTA+TC) (*N* = 323)	Period 2 (Xpert) (*N* = 327)	Period 3 (GDH+Illu.) (*N* = 340)	p (P1 vs. P2)	p (P1 vs. P3)	p (P2 vs. P3)
Time for return of results						
Days, mean ± SD (median)	3.5 ± 0.95 (3)	0.55 ± 0.72 (0)	0.63 ± 0.96 (0)	<0.0001	<0.0001	0.57
Hours, mean ± SD (median)	84.9 ± 22.9 (75)	15.6 ± 16.8 (4)	17.3 ± 22.9 (6)	<0.0001	0.0001	0.15
Redundant stool samples (<7 days), *n* (%)	68 (21.1%)	43 (13.3%)	52 (15.3%)	0.007	0.05	0.42
Empiric treatment by VA or MTZ, *n* (%)	44 (13.6%)	21 (6.4%)	19 (5.6%)	0.002	0.0004	0.64
Time to stop an empiric treatment (days) mean ± SD (median)	5.5 ± 3.3 (4)	3.6 ± 4.2 (2)	3.8 ± 4.6 (2)	0.04	0.10	0.68
Number of unjustified treatment days	243	75	73			
Contact precautions, *n* (%)	18 (5.6%)	10 (3.1%)	15 (4.4%)	0.11	0.48	0.36
Length of contact precautions (days) mean ± SD (median)	4.5 ± 1.8 (4)	4.7 ± 6.8 (1.5)	3.7 ± 3.6 (2)	0.043	0.08	0.93
Number of unjustified contact precautions days	82	47	55			

Barbut et al., Clin Microbiol Infect 2014

Diagnostic rapide *C. difficile*

TABLE 4. Management of patients with *Clostridium difficile* infection

	Period 1 (CTA+TC) (n = 36)	Period 2 (Xpert) (n = 45)	Period 3 (GDH+Illumig.) (n = 45)	p (P1 vs. P2)	p (P1 vs. P3)	p (P2 vs. P3)
Clinical presentation						
Patients with ≥ 10 stools per day, *n* (%)	5 (14.7%)	6 (13.6%)	3 (6.7%)	0.57	0.23	0.31
Abdominal pain, *n* (%)	66 (72.2%)	29 (64.4%)	20 (44.4%)	0.45	0.01	0.06
Tenderness, *n* (%)	13 (36.1)	11 (24.4%)	7 (15.6%)	0.25	0.03	0.29
Time for return of results						
Days, mean ± SD (median)	3.1 + 2.58 (2)	0.53 + 0.66 (0)	1.20 + 1.64 (1)	<0.0001	0.00015	0.013
Hours, mean ± SD (median)	75.7 + 61.9 (51)	15.4 + 15.4 (5)	31.4 + 38.7 (27)	<0.0001	0.00017	0.004
Redundant stool samples (<7 days), *n* (%)	13 (36.1%)	8 (17.8%)	2 (4.4%)	0.06	0.00026	0.04
Specific treatment by VA or MTZ, *n* (%)	29 (80.6%)	42 (93.3%)	38 (84.4%)	0.08	0.64	0.18
Time (days) elapse between *C. difficile* testing and specific treatment mean ± SD (median)	2.00 + 1.68(2)	0.49 + 0.56 (0)	1.03 + 1.80 (0)	<0.0001	0.039	0.43
Contact precautions, *n* (%)	29 (80.6%)	42 (93.3%)	34 (77.3%)	0.08	0.72	0.03
Clinical outcome						
Clinical cure at day 10, *n* (%)	29 (85.3%)	43 (95.6%)	39 (90.7%)	0.11	0.46	0.36
Recurrence (within 30 days), *n* (%)	6 (17.6%)	6 (13.3%)	6 (14%)	0.59	0.65	0.93
Severity, *n* (%)	5 (14.7%)	2 (4.4%)	4 (9.3%)	0.11	0.46	0.37
Mortality at day 10, *n* (%)	5 (13.9%)	2 (4.4%)	5 (11.4%)	0.13	0.43	0.22
Mortality at day 30, *n* (%)	5 (13.9%)	5 (11.1%)	6 (13.3%)	0.70	0.59	0.74
LOS (days) mean ± SD (median)	30.3 ± 36.3 (19.5)	23.2 ± 25.4 (15)	26.9 ± 28.9 (20)	0.32	0.63	0.51
LOS after stool culture mean ± SD (median)	15.8 ± 14.0 (10.5)	12.3 ± 19.7 (8)	12.5 ± 12.5 (9)	0.05	0.27	0.51

Barbut et al., Clin Microbiol Infect 2014

Détection rapide SGB

Etude prospective monocentrique (France) comparant la qPCR (Xpert) à l'accouchement vs. culture classique à 34-38 SA

	Culture at 34–38 weeks of gestation	PCR at delivery	Statistical analysis*
Diagnostic performance (%):			
Sensitivity (95% CI)	55.6 (35.3–74.5)	66.7 (46.0–83.5)	
Specificity (95% CI)	84.5 (78.7–89.3)	94.9 (90.9–97.5)	
Positive predictive value (95% CI)	33.3 (20.0–48.9)	64.3 (44.1–81.4)	
Negative predictive value (95% CI)	93.2 (88.4–96.4)	95.4 (91.5–97.9)	
Women inadequately treated with prophylactic antimicrobial treatment (%)	13.6	4.5	$P < 0.001$
Women adequately treated with prophylactic antimicrobial treatment (%)	6.8	8.0	NS
Women inadequately not treated with prophylactic antimicrobial treatment (%)	5.4	4.0	NS
Women adequately not treated with prophylactic antimicrobial treatment (%)	74.2	83.5	$P < 0.05$
Technical performances (%):			
Sensitivity (95% CI)	58.3 (36.6–77.9)	76.9 (56.3–91.0)	
Specificity (95% CI)	92.7 (87.8–96.0)	95.4 (91.4–97.9)	
Positive predictive value (95% CI)	51.9 (31.9–71.3)	69.0 (49.2–84.7)	
Negative predictive value (95% CI)	94.3 (89.7–97.2)	96.9 (93.3–98.8)	

Poncelet-Jasserand et al., BJOG 2013

Nouvelles techniques

2 solutions automatisées à partir des HC+

Verigene Blood Culture Gram-Positive (BC-GP) and Gram-Negative (BC-GN) tests [Nanosphere]

FilmArray Blood Culture Identification Panel [BioFire → bioMérieux]

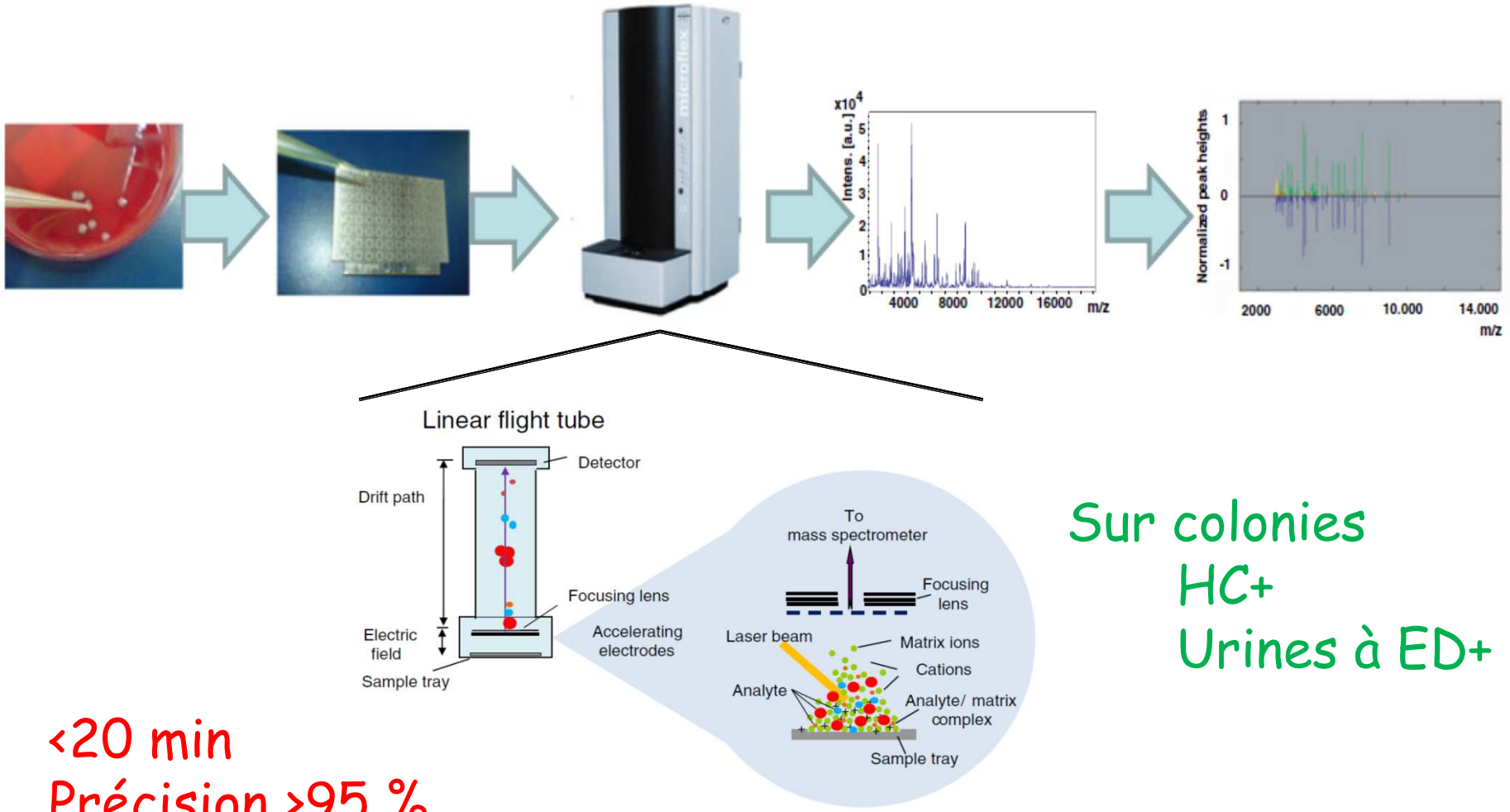
Table 1 Mean time in hours taken for species-level identification and antimicrobial sensitivity testing

Task	Conventional method (h)	Verigene® (h) Mean for BC-GP and BC-GN	FilmArray® (h)
Sample transportation	3.7	3.7	3.7
Bottle culture	27.91	27.91	27.91
Gram stain	7.5	7.5	7.5
Species identification*	18.18	2.3	1.07
Antimicrobial sensitivity testing*	30.28	2.3	1.07
Total time from sample collection to species-level identification	57.29	41.44	40.22
Total time from sample collection to antimicrobial sensitivity testing	69.39	41.44	40.22

Intérêt clinique ??

Ward et al., Eur J Clin Microbiol Infect Dis 2014

MALDI-TOF (ID)



Sur colonies
HC+
Urines à ED+

<20 min
Précision >95 %

Wieser et al., Appl Microbiol Biotechnol 2012

Impact du MALDI-TOF (ID)

Etude prospective monocentrique (Pays-Bas) comparant l'ID à partir des HC+ par MALDI-TOF vs. culture classique

	Direct MALDI-TOF MS (n = 89)	Standard care (n = 164)	p-value
Median identification time in hours (IQR)	16.4 (10.3–42.9) **-28,8 h**	45.2 (35.5–55.9)	<0.001

	Direct MALDI-TOF MS	Standard care
% (n) of episodes with appropriate therapy<24 h after positive BC[a]	75.3% (67)* **+11,3 %**	64.0% (105)*
% (n) of episodes with inappropriate therapy<24 h after positive BC[a]	4.5% (4)*	14.6% (24)*
% (n) of episodes without antibiotic therapy<24 h after positive BC[a]	20.2% (18) (6.7% (6) other interventions[b], 13.5% (12) contaminated BC)	21.4% (35) (4.3% (7) other interventions[b], 11.0% (18) contaminated BC, 6.1% (10) not applicable[c])

[a]blood culture, [b]removal of intravenous catheters, [c]palliative care or patient died shortly after blood culture was positive.
*p value 0.01.

Vlek et al., PLoS One 2012

Impact du MALDI-TOF (ID)

Etude quasi-expérimentale monocentrique (US) comparant l'ID par MALDI-TOF vs. culture classique chez patients avec HC+ à SCN

TABLE 3 Antimicrobial use and outcomes for patients with CoNS contamination

Characteristic	Preintervention group ($n = 83$)	AST intervention group ($n = 85$)	P value
Duration of CoNS antibiotic therapy[a] (days)	4.4 ± 4.2	3.0 ± 1.6	0.015
Vancomycin utilization[a] (g)	4.8 ± 6.3	3.0 ± 3.9	0.038
Daptomycin utilization[a] (g)	2.88	0	0.243
No. of vancomycin serum assays obtained[a]	2.0 ± 2.2	0.9 ± 1.4	<0.001
No. (%) of patients with 30-day all-cause mortality	9 (10.8)	10 (11.8)	>0.99
Length of hospitalization[a] (days)	14.6 ± 22.9	15.8 ± 18.6	0.7
No. (%) of patients with recurrent bacteremia	3 (3.6)	2 (2.4)	0.68
No. (%) of patients with 30-day readmission with CoNS bacteremia	2 (2.4)	1 (1.2)	0.618
No. (%) of patients *Clostridium difficile* colitis	7 (8.4)	4 (4.7)	0.367

Nagel et al., J Clin Microbiol 2014

Impact du MALDI-TOF (ID)

Etude prospective monocentrique (US) comparant l'ID à partir des HC+ à BGN par MALDI-TOF vs. culture classique (ETI+++)

Outcome	Preintervention Cohort (n = 100)	Intervention Cohort (n = 101)	*P*
Hospital length of stay	11.9 ± 9.3	9.3 ± 7.6	.01
Hospital length of stay after BSI onset	9.9 ± 7.1	8.1 ± 6.4	.01
ICU length of stay	7.3 ± 8.5	6.3 ± 8.7	.05
ICU length of stay after BSI onset	6.1 ± 6	4.9 ± 6.7	.09
Total hospital costs	$45 709 ± $61 806	$26 162 ± $28 996	.009
MS DRG weight	2.7 ± 2.4	±1.9	54

Perez et al., Arch Pathol Lab Med 2013

Impact du MALDI-TOF (ID)

Table 3. Independent Factors Associated with Length of Stay[a]

Factor	Univariate			Multivariate[b]		
	HR	95% CI	*P*	HR	95% CI	*P*
Active antibiotic therapy at 48 h	2.24	1.23–4.08	.009	2.90	1.15–7.33	.02
MALDI-TOF MS antimicrobial stewardship intervention	1.40	1.06–1.85	.02	1.38	1.01–1.88	.04
APACHE II	0.96	0.93–0.99	.003	0.97	0.93–0.999	.05
Preinfection LOS	0.87	0.83–0.91	<.001	0.86	0.83–0.91	<.001
Preexisting lung disease	0.62	0.40–0.94	.02	0.54	0.35–0.84	.006

Perez et al., Arch Pathol Lab Med 2013

Impact du MALDI-TOF (ID)

Etude prospective monocentrique (US) comparant l'ID à partir des HC+ à BGN par MALDI-TOF vs. culture classique (ETI+++)

Outcome	Pre-intervention cohort (n = 157)	Intervention cohort (n = 112)	P value
30-Day all-cause mortality	33 (21)	10 (8.9)	0.01
60-Day all-cause mortality	48 (30.6)	14 (12.5)	0.001
Inpatient mortality	29 (18.5)	9 (8)	0.02

Table 4 Univariate and multivariate logistic regression– independent predictors of 30-day mortality.

Variable	Univariate analysis			Multivariate analysis[a]		
	OR	95% CI	P value	OR	95% CI	P value
Nosocomial acquisition	2.35	1.21–4.55	0.01	1.03	0.38–2.84	0.95
Pre-infection LOS	1.02	1.0–1.05	0.04	1.01	0.98–1.04	0.49
APACHE II	1.15	1.08–1.22	<0.001	1.18	1.10–1.27	<0.001
Respiratory source	2.13	1.08–4.23	0.03	0.82	0.35–1.96	0.66
Genitourinary source	0.31	0.1–0.7	0.003	0.37	0.17–1.12	0.07
MALDI-TOF MS + antimicrobial stewardship	0.37	0.17–0.78	0.009	0.28	0.12–0.71	0.008
Time to active therapy	1.00	1.00–1.01	0.02	1.00	1.00–1.01	0.007

Perez et al., J Infect 2014

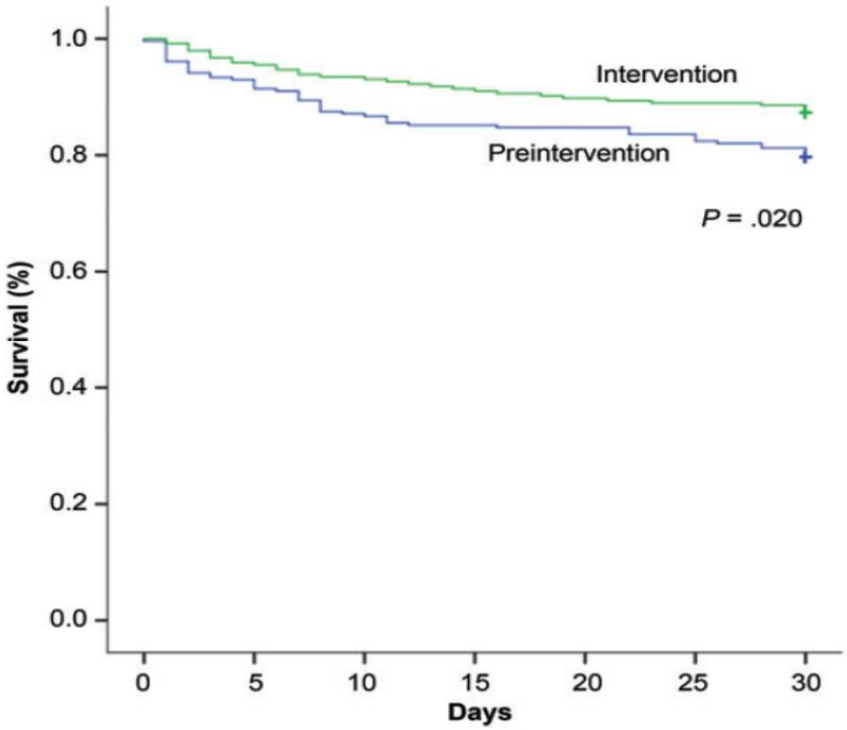
Impact du MALDI-TOF (ID)

Etude monocentrique (US) pré/post comparant l'ID par MALDI-TOF vs. culture classique dans bactériémies/candidémies

Table 3. Clinical and Treatment-Related Outcomes

Outcome	Total		
	Preintervention (n = 256)	Intervention (n = 245)	*P* Value
Clinical outcomes			
30-day all-cause mortality	52 (20.3)	31 (12.7)	.021
Time to microbiological clearance, d	3.3 ± 4.8	3.3 ± 5.7	.928
Length of hospitalization, d[a]	14.2 ± 20.6	11.4 ± 12.9	.066
Length of ICU stay, d[a]	14.9 ± 24.2	8.3 ± 9.0	.014
Recurrence of same BSI	15 (5.9)	5 (2.0)	.038
30-day readmission with same BSI	9 (3.5)	4 (1.6)	.262
Treatment-related outcomes			
Time to effective therapy, h	30.1 ± 67.7	20.4 ± 20.7	.021
Time to optimal therapy, h	90.3 ± 75.4	47.3 ± 121.5	<.001

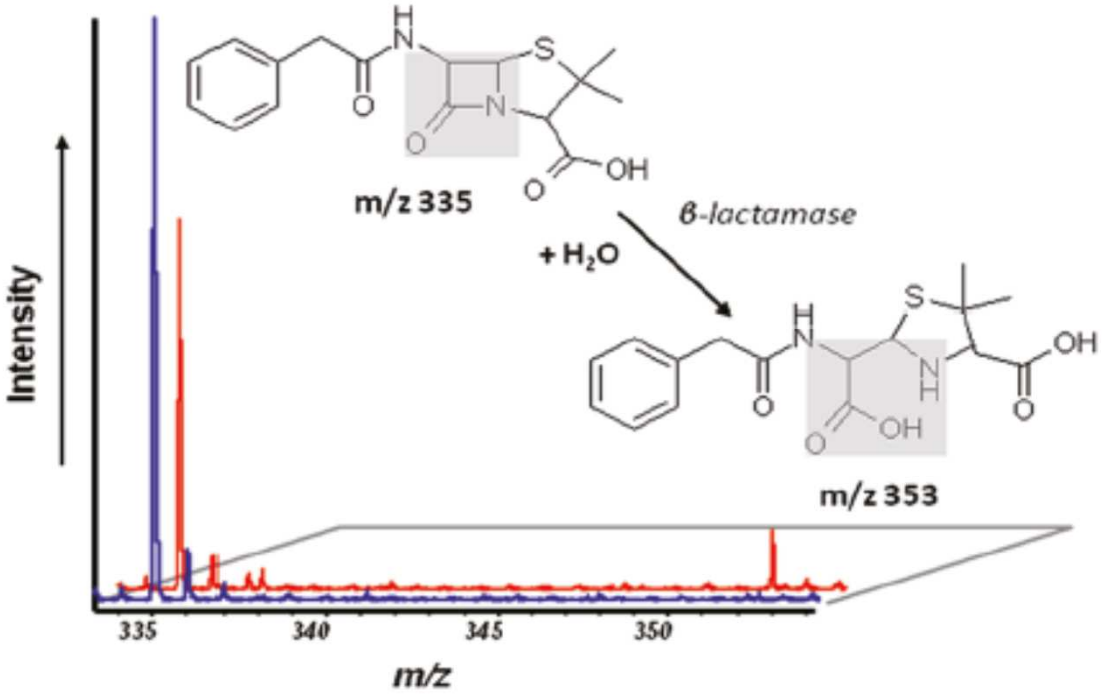
Data are No. (%) or mean ± standard deviation



Huang et al., Clin Infect Dis 2013

MALDI-TOF (AST)

Détection activité β-lactamase



2,5 h à partir des HC+ (AMP, CTX)

Sens et Spé 100 %

Hoof et al., J Proteome Res 2012
Hrabak et al., Clin Microbiol Rev 2013
Jung et al., J Clin Microbiol 2014

Tests chromogéniques (E-BLSE)

- ✓ Détection de la résistance aux C3G (entérobactéries) :
  - Céphalosporine chromogènique HMRZ-86 (jaune → rouge si hydrolysée) [**β LACTA test, Bio-Rad**]
  - Céfotaxime ± tazobactam (virage du rouge phénol → jaune si hydrolyse) [**ESBL NDP test**]

- ✓ **Avantages :**
  - Sens et spé élevées (>90 %)
  - Rapides <15 min
  - Peu chers
  - Utilisables sur colonies, HC+ et urines à ED+

- ✓ **Limites :**
  - Pas d'étude clinique publiée

Renvoisé et al., J Clin Microbiol 2013
Morosini et al., J Clin Microbiol 2014
Nordmann et al., J Clin Microbiol 2012
Dortet et al., J Clin Microbiol 2014
Dortet et al., Emerg Infect Dis 2014

Impact du β LACTA test

Bactériémies

Temps moyen de rendu du résultat :
40,9 h vs. 24 h

Gain de temps pour :
. Adaptation TTT (38,1 h)
. Mise en place PCC (36 h)

Infections urinaires

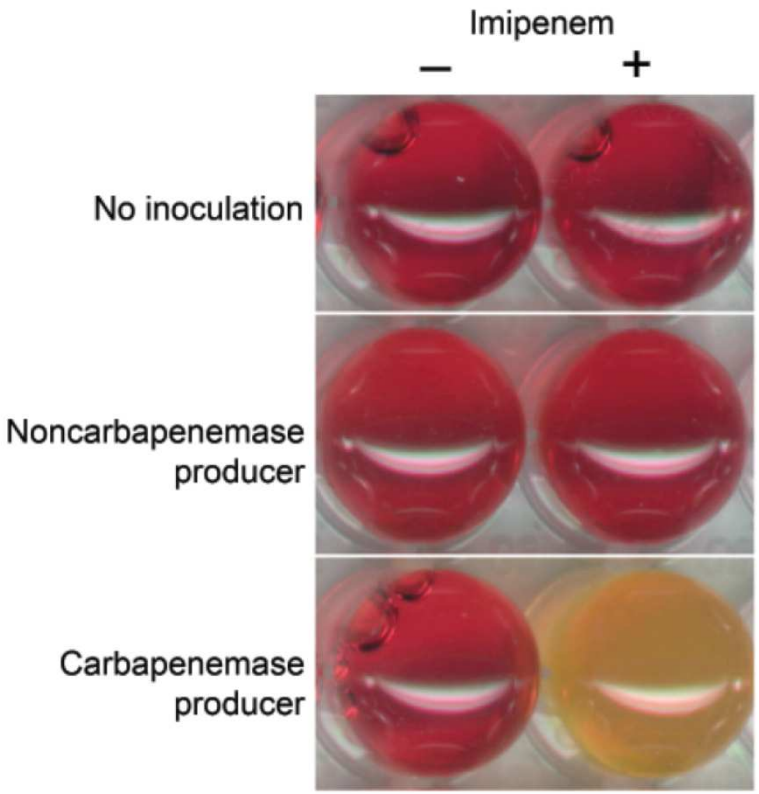
Temps moyen d'adaptation ATBT adéquate :
54 h vs. 2,7 h (P <0,0001)

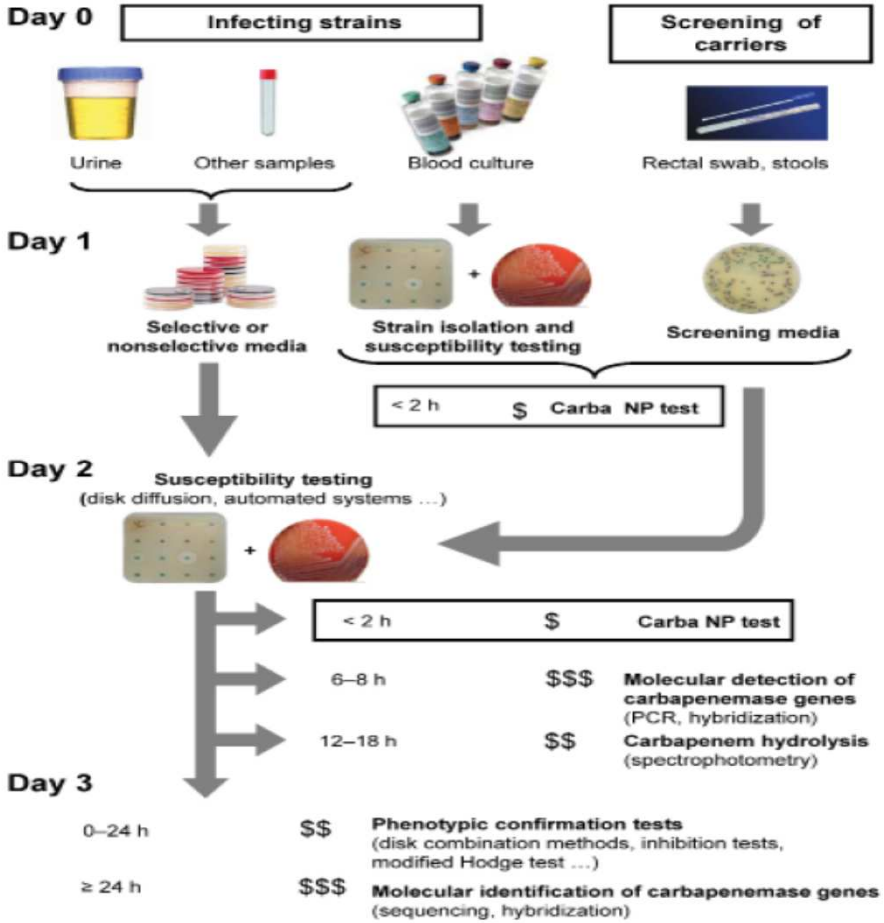
Délai moyen de mise en place des PCC :
55,2 h vs. 2,6 h (P<0,0001)

Amzalag et al., RICAI 2014
Naouri et al., RICAI 2014

Tests chromogéniques (EPC)

Carba NP test (15'-2h)





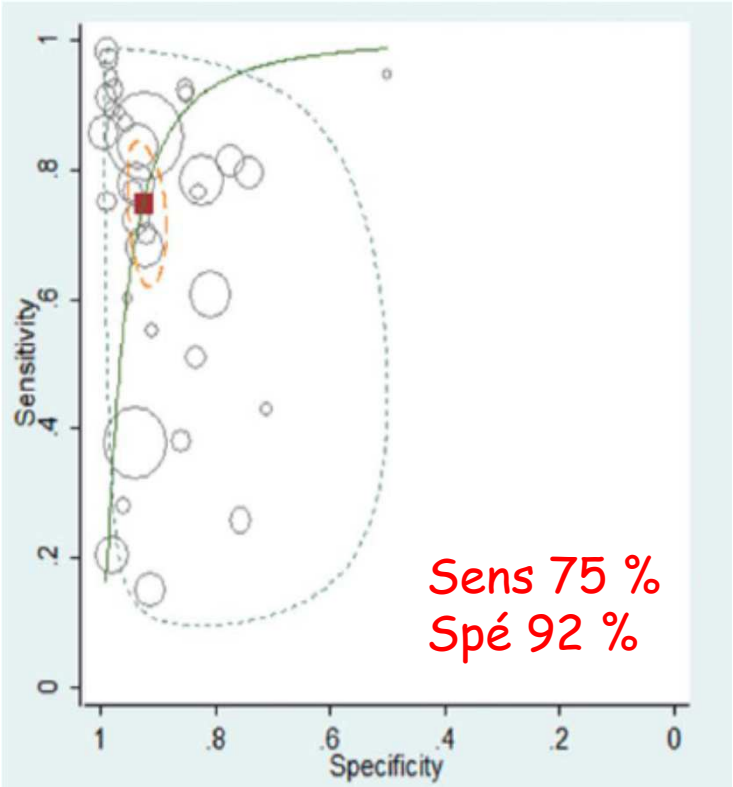
Nordmann et al., Emerg Infect Dis 2012

LC SeptiFast test (Roche)

Méta-analyse de 34 études (6012 patients)
Panel de 25 germes (6 h)

Gram-negative bacteria	Gram-positive bacteria	Fungal pathogens
Escherichia coli	Staphylococcus aureus	Candida albicans
Klebsiella pneumoniae	Coagulase-negative Staphylococci†	Candida tropicalis
Klebsiella oxytoca	Streptococcus pneumoniae	Candida parapsilosis
Serratia marcescens	Streptococcus spp.‡	Candida krusei
Enterobacter cloacae	Enterococcus faecium	Candida glabrata
Enterobacter aerogenes	Enterococcus faecalis	Aspergillus fumigatus
Proteus mirabilis		
Pseudomonas aeruginosa		
Acinetobacter baumannii		
Stenotrophomonas maltophilia		

+ mecA, vanA, vanB

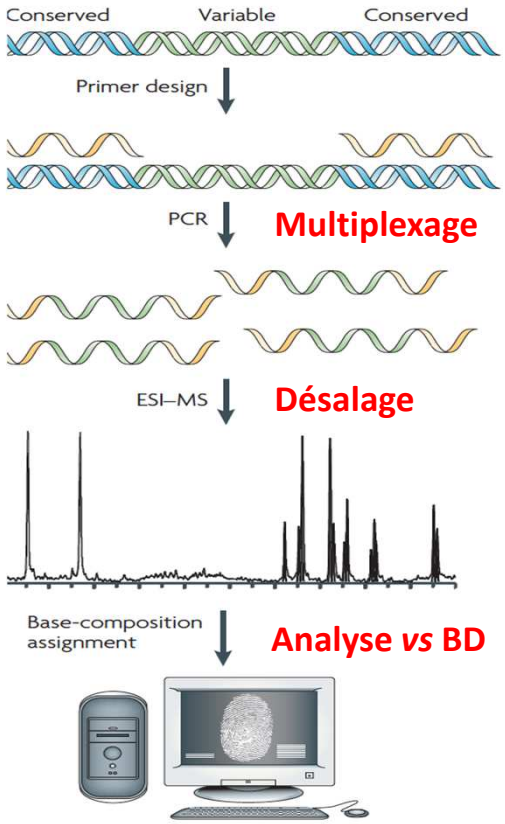


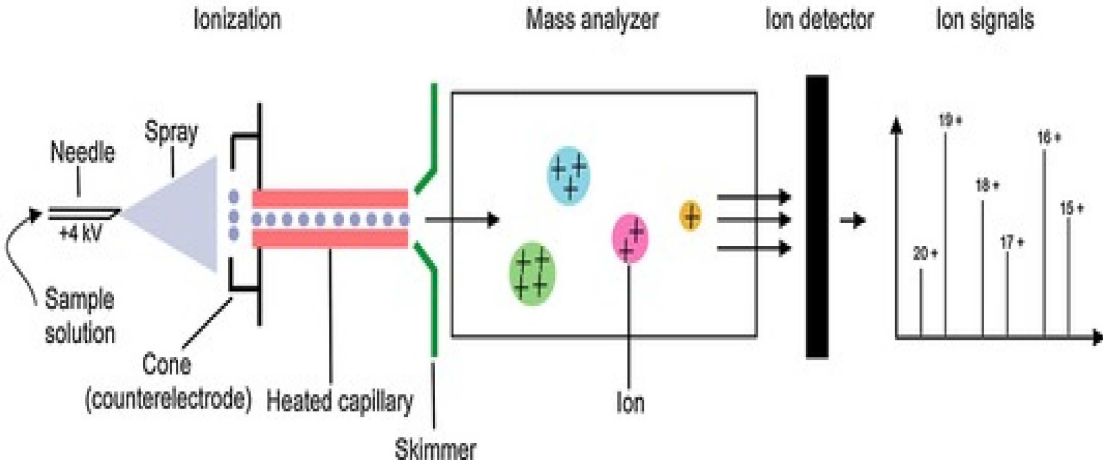
Pas d'étude sur l'impact clinique

Chang et al., PLoS One 2013

PCR-ESI-MS

PCR/electrospray ionization-mass spectrometry (**PCR/ESI-MS**) [PlexID™, Abbott] (6-8 h)





Bactériémies : Sens (96,8 %) et spé (98,5 %)

Possible aussi pour des mécanismes de résistance (ex. *mecA*, *erm*(A), *erm*(C), *vanA* et *vanB*, bla_{KPC})

Ecker et al., Nat Rev Microbiol 2008
Lavigne et al., Clin Chem Lab Med 2012
Jordana-Lluch et al., PLoS One 2013

Infections respiratoires

	Time to result	Type of technology	Targets	Sensitivity	Specificity
Cepheid Xpert MRSA/SA SSTI[62]	1 h	Automated sample preparation of respiratory specimen, real-time PCR and detection using molecular beacon technology	MSSA and MRSA	99·0% compared with quantitative culture of endotracheal aspirates	72·2% compared with quantitative culture of endotracheal aspirates
Curetis Unyvero Pneumonia P50 Test[63]	4 h	Multiplex endpoint PCR and amplicon detection by hybridisation to oligo probes spotted on membrane arrays direct from respiratory samples	Detection of 17 bacterial and fungal pathogens in addition to 22 antibiotic resistance genes	80·9% overall; target specific values 50–100%	99·0% overall, target specific values 72·3–100%
Biofire Filmarray Respiratory Panel[64,65]	1 h	Pouch format comprising nucleic acid extraction, and nested PCR from nasopharyngeal swabs	20 targets including respiratory viruses, *Bordetella pertussis*, *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*	84–100%	98–100%

MSSA=methicillin-sensitive *Staphylococcus aureus*. MRSA=methicillin-resistant *S aureus*. SSTI=skin and soft tissue infection.

Table 3: Rapid molecular platforms and tests available for the diagnosis of bacterial respiratory tract infections

Zumla et al., Lancet Infect Dis 2014

Conclusion (1)

- ✓ **ATBG direct** sur HC+ (RTI ?) + tests simples*
- ✓ PCR multiplex/PNA-FISH utile pour les infections à **coques à Gram positif** (BSI, SSTI)
- ✓ A évaluer cliniquement : Identification des **BGN** au MALDI-TOF ± test d'hydrolyse des β-lactamines (SM ou test colorimétrique) sur HC+ / urines à ED+
- ✓ qPCR utile pour ***C. difficile*** **et SGB**
- ✓ **PCR-ESI-MS** prometteuse mais chère

Conclusion (2)

Preimplementation
- Identify most useful RDT based on hospital pathogen prevalence
  - Example: Number of *Staphylococcus aureus* bacteremias, number of coagulase-negative staphylococci, number of *Pseudomonas aeruginosa*, number of *Candida* species
- Identify hospital cost of infection
  - Example:
    - Utilize information warehouse personnel to pull cost by *ICD-9* code mortality data
    - Obtain time to ID specialist consult
    - Length of stay
    - 30-day readmission
- Time to effective therapy

Implementation
- Microbiologist-validated RDT instrument
- Determine if test is done in real time 24/7 or batch
- Communication of RDT results from microbiologist to physician and ASP pharmacist is established
- ASP pharmacist-physician educates medical staff
- ASP documents interventions and acceptance rate

Postimplementation
- Time to effective therapy
- Time to discontinuation or de-escalation
- Time to ID consult
- Documented negative blood culture prior to hospital discharge
- 30-day readmission
- Mortality

Bauer et al., Clin Infect Dis 2014