

Speed is Safety – And You Can Save Money Too!

Rapid Identification of Positive Blood Cultures

April 23, 2014

Raymond P. Podzorski, Ph.D., D(ABMM)

Clinical Microbiologist

ProHealth Care Laboratories





Disclosure

Raymond P. Podzorski, Ph.D., D(ABMM)

April 23, 2014

No relevant financial relationships do disclose.



CASE PRESENTATION

- **39 y/o male admitted after experiencing fevers, chills, and hypotension**
- **Tachycardia also noted on examination**
- **Three sets of blood cultures were obtained on admission**
- **The blood cultures started signaling positive 13 hours after collection**



CASE OUTCOME

Hospital A

- Hospital LOS 11.9 days
- ICU LOS 7.3 days
- Pharmacy costs \$3,371
- Hospital costs \$45,000

Hospital B

- Hospital LOS 9.3 days
- ICU LOS 6.3 days
- Pharmacy costs \$2,386
- Hospital Costs \$26,000

Perez, et. al. 2012. Arch. Pathol. Lab. Med. 10.5858/arpa.2012-0651OA



What makes the difference?

CASE OUTCOME

Hospital A

- Hospital LOS 11.9 days
- ICU LOS 7.3 days
- Pharmacy costs \$3,371
- Hospital costs \$45,000

Hospital B

- Hospital LOS 9.3 days
- ICU LOS 6.3 days
- Pharmacy costs \$2,386
- Hospital Costs \$26,000

Perez, et. al. 2012. Arch. Pathol. Lab. Med. 10.5858/arpa.2012-0651OA



CASE OUTCOME

Hospital A

- Hospital LOS 11.9 days
- ICU LOS 7.3 days
- Pharmacy costs \$3,371
- Hospital costs \$45,000

Hospital B

- Hospital LOS 9.3 days
- ICU LOS 6.3 days
- Pharmacy costs \$2,386
- Hospital Costs \$26,000

Perez, et. al. 2012. Arch. Pathol. Lab. Med. 10.5858/arpa.2012-0651OA



Objectives

- Demonstrate how rapid microbiology diagnostics impacts patient outcome
- Demonstrate some of the systems available for rapid identification of positive blood cultures
- Illustrate the importance of taking action on a rapid ID result in a timely fashion



Hospital A - BC Time Line

13 hr incubation
Bottle positive



13 hr + 1 hour
1. Gram stain/Reported to floor
2. Subculture bottle



13 hr + 1 hr + 14 hr
Colonies growth on
Agar plate



1. Setup ID +
Susceptibility Test
2. Perform Presumptive ID



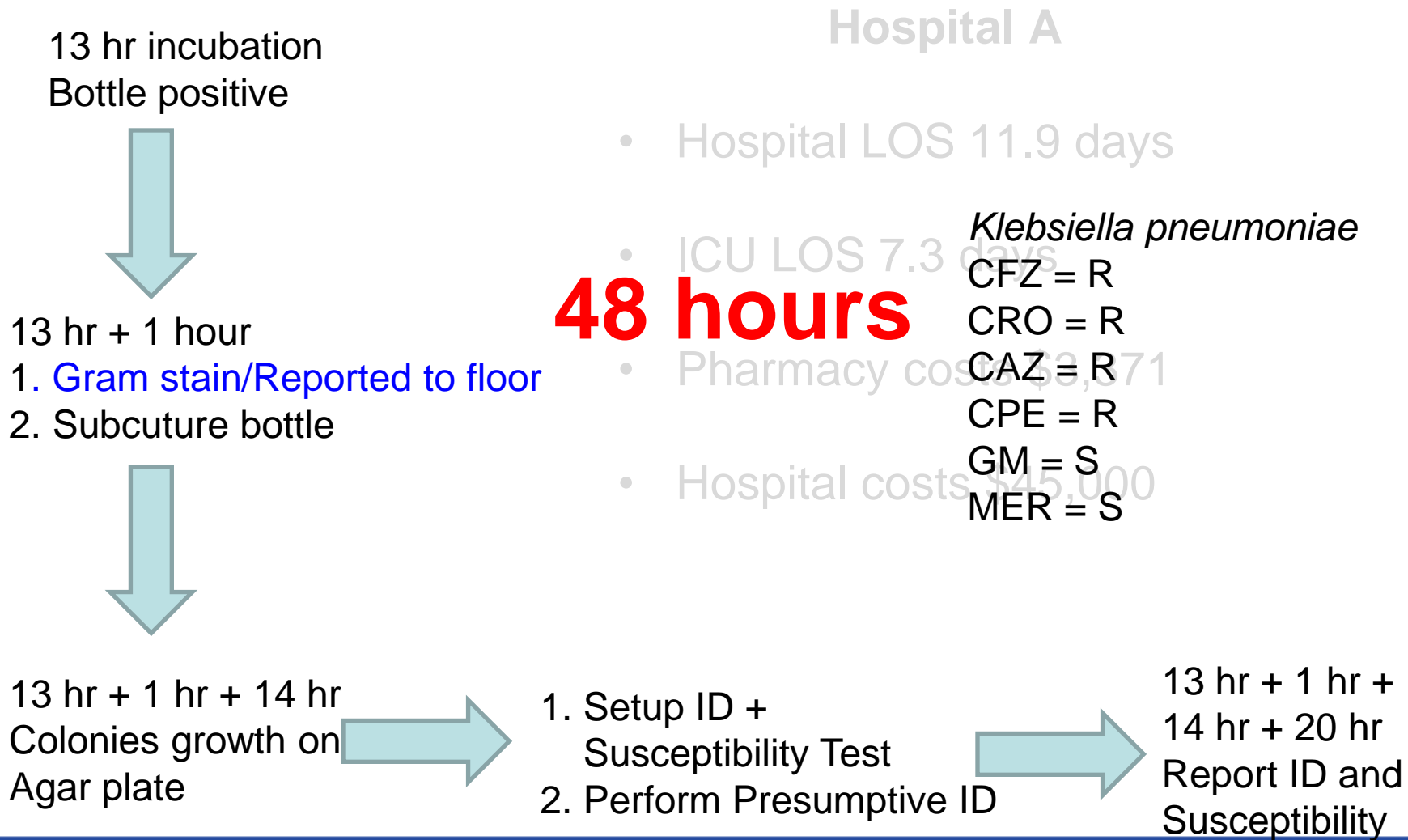
13 hr + 1 hr +
14 hr + 20 hr
Report ID and
Susceptibility

Hospital A

- Hospital LOS 11.9 days
- ICU LOS 7.3 days
- Pharmacy costs \$3,371
- Hospital costs \$45,000



Hospital A - BC Time Line



Hospital B - BC Time Line

13 hr incubation
Bottle positive



13 hr + 3 hour

1. Gram stain/Reported
2. Definitive ID done/Reported to floor + Pharmacy
3. Select Resistance markers/Reported

Hospital B

- Hospital LOS 9.3 days
- ICU LOS 6.3 days
- Pharmacy costs \$2,386
- Hospital Costs \$26,000



Hospital B - BC Time Line

13 hr incubation
Bottle positive



13 hr + 3 hour

1. Gram stain/Reported
2. Definitive ID done/Reported to floor + Pharmacy
3. Select Resistance markers/Reported

16 hours

Klebsiella pneumoniae
CTX-M detected

Hospital B

- Hospital LOS 9.3 days
- ICU LOS 6.3 days
- Pharmacy costs \$2,386
- Hospital Costs \$26,000



CASE OUTCOME

Hospital A

- Hospital LOS 11.9 days
- ICU LOS 7.3 days
- Pharmacy costs \$3,371
- Hospital costs \$45,000

48 hours

Hospital B

- Hospital LOS 9.3 days
- ICU LOS 6.3 days
- Pharmacy costs \$2,386
- Hospital Costs \$26,000

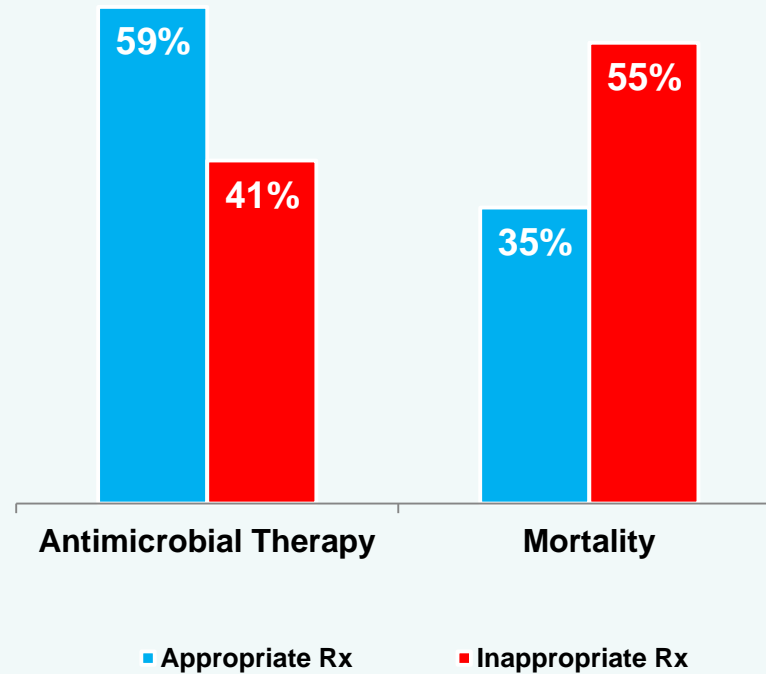
16 hours

Perez, et. al. 2012. Arch. Pathol. Lab. Med. 10.5858/arpa.2012-0651OA



Why is the timely selection of antibiotics important?

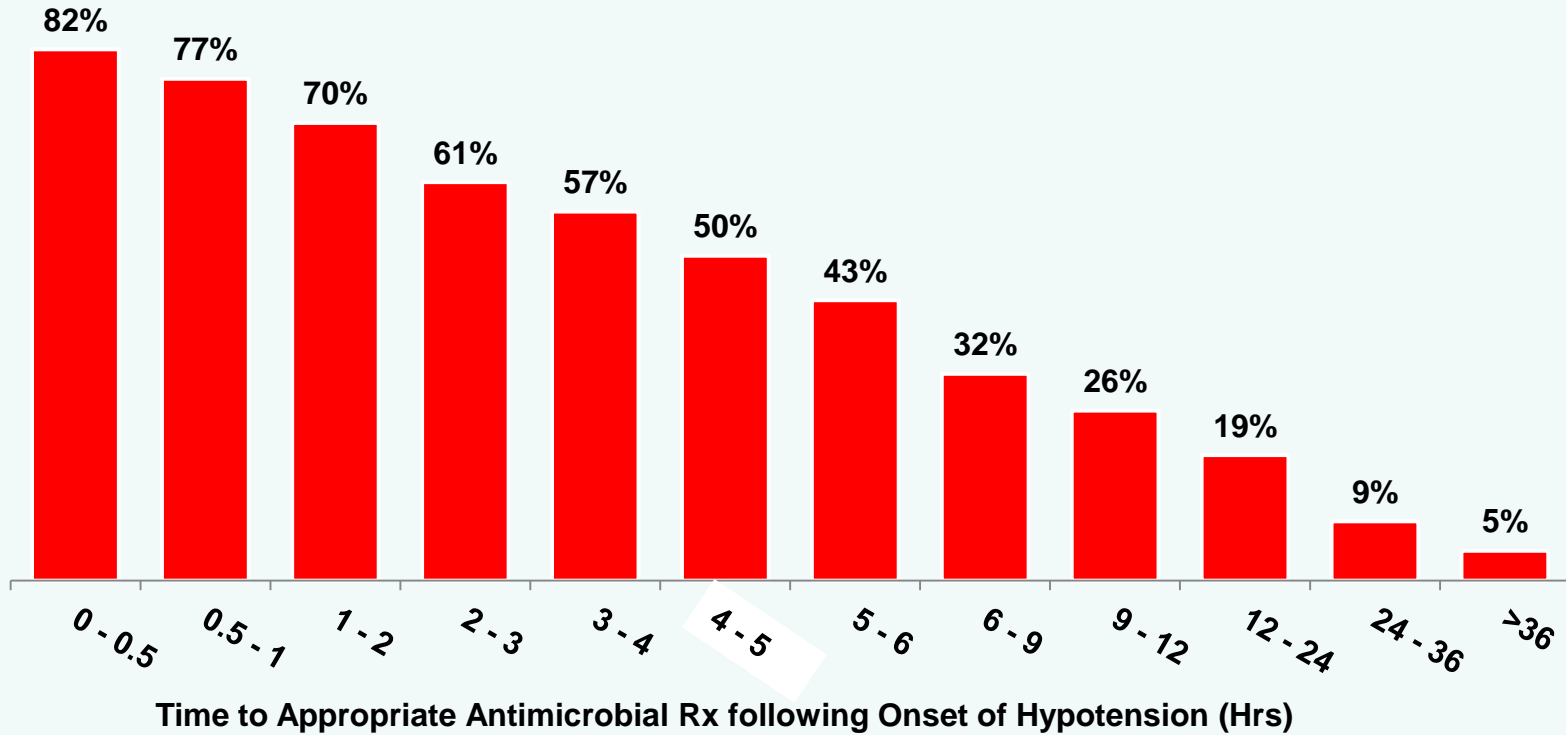
Appropriateness of Rx within
12 Hrs of BC+ and Mortality
(Severe Sepsis)



Golan et al. Candidal vs. Bacterial Severe Sepsis in the ICU: The Number-Needed-to-Treat (NNT). Poster # 631. IDSA 2010. Vancouver, BC, Canada.

Why is the timely selection of antibiotics important?

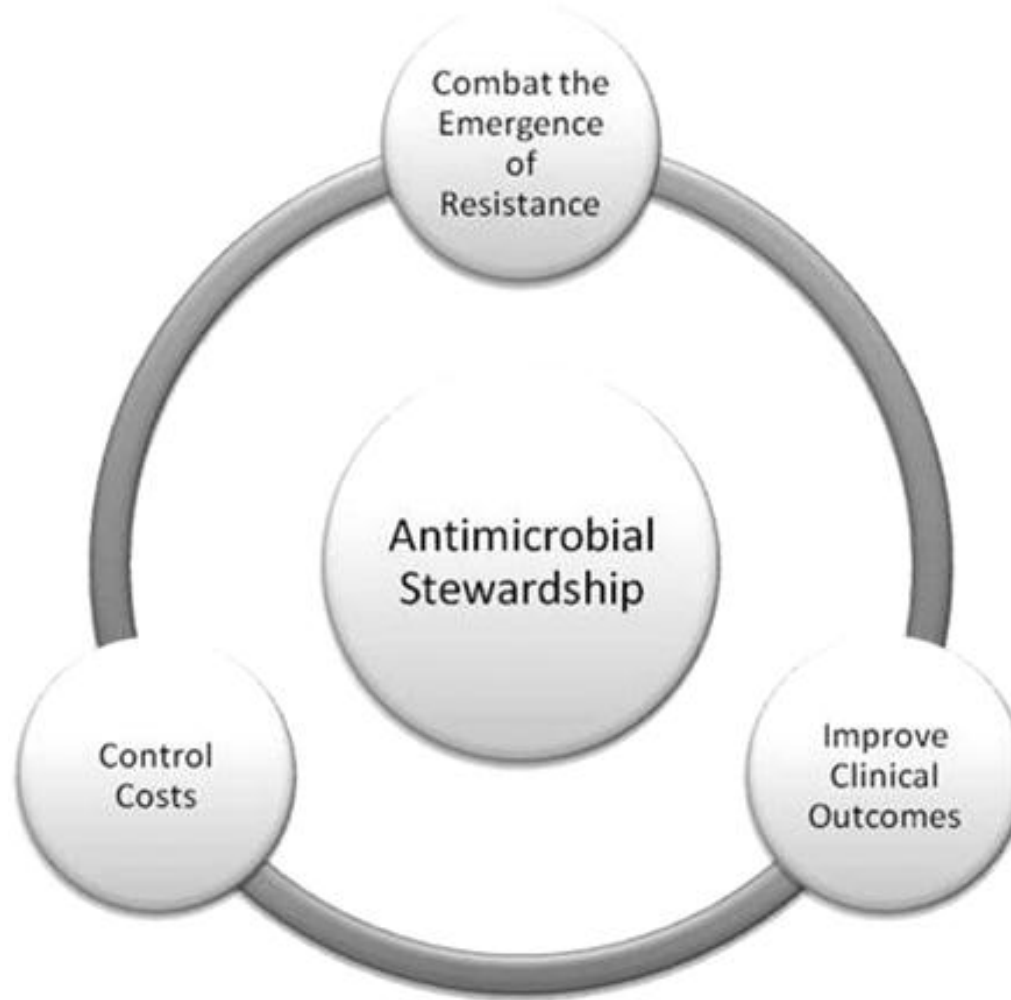
Survival – Patients with Septic Shock



Kumar et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006 Jun;34(6):1589-96.



HOW CAN WE DO THIS?



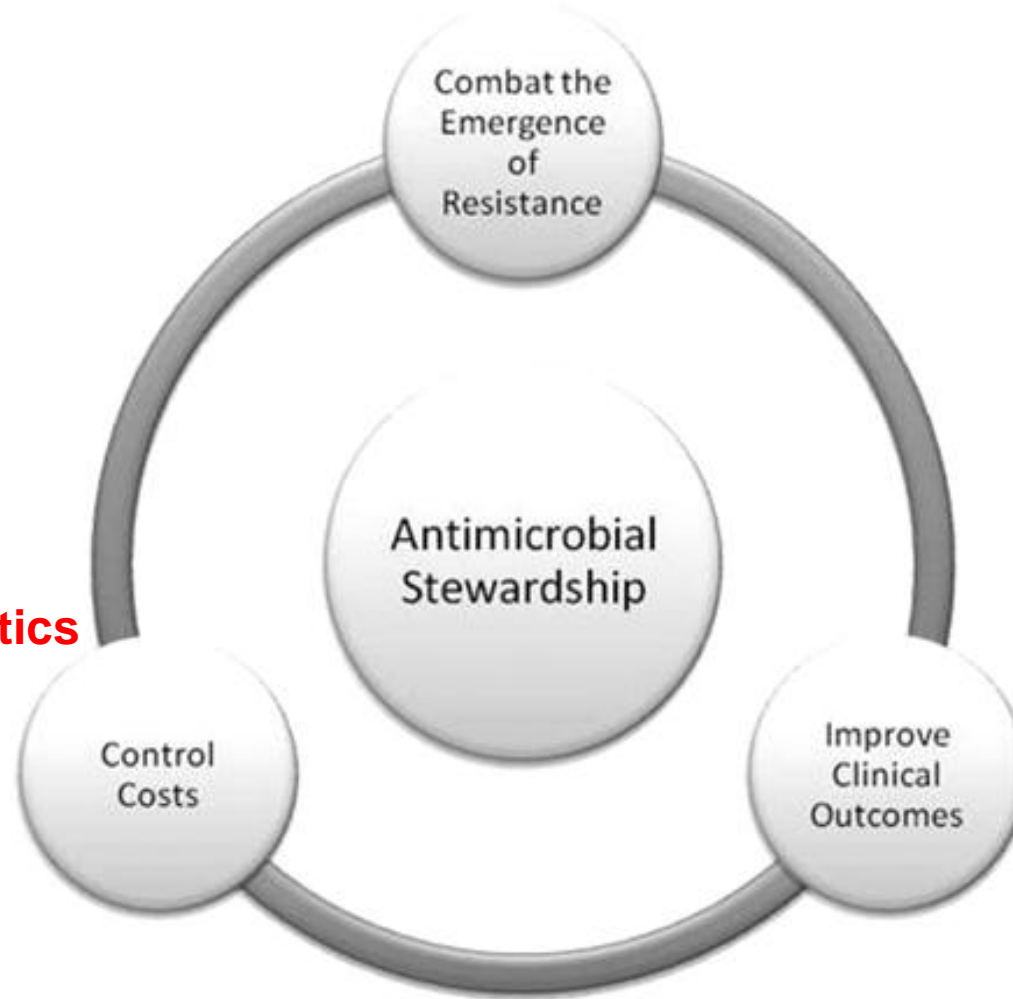
Antimicrobial Stewardship in the Intensive Care Unit
Advances and Obstacles

Am J Respir Crit Care Med Vol 179. pp 434–438, 2009



HOW CAN WE DO THIS?

Rapid Diagnostics



Rapid Diagnostics

Rapid Diagnostics

Antimicrobial Stewardship in the Intensive Care Unit
Advances and Obstacles

Am J Respir Crit Care Med Vol 179. pp 434–438, 2009



PROHEALTH CARE

MALDI-TOF Mass Spectrometry

Nanosphere BC-GP

AdvanDx QuickFISH Gram-Negative BC

Cepheid Xpert MRSA/SA BC

Biofire FilmArray BC Identification Panel

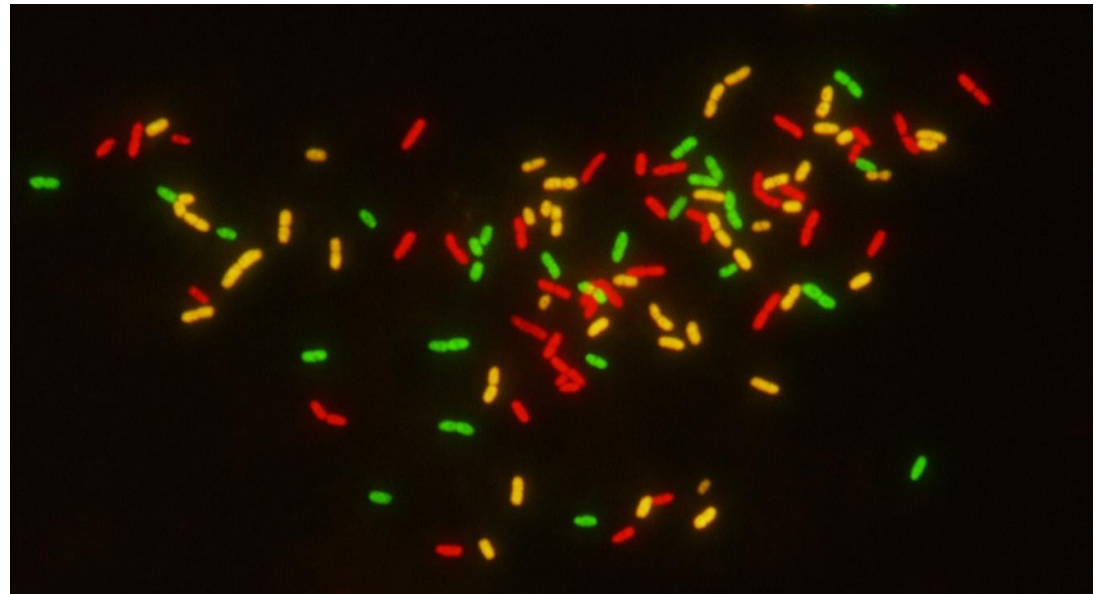
BD GeneOhm StaphSR

FDA cleared/approved



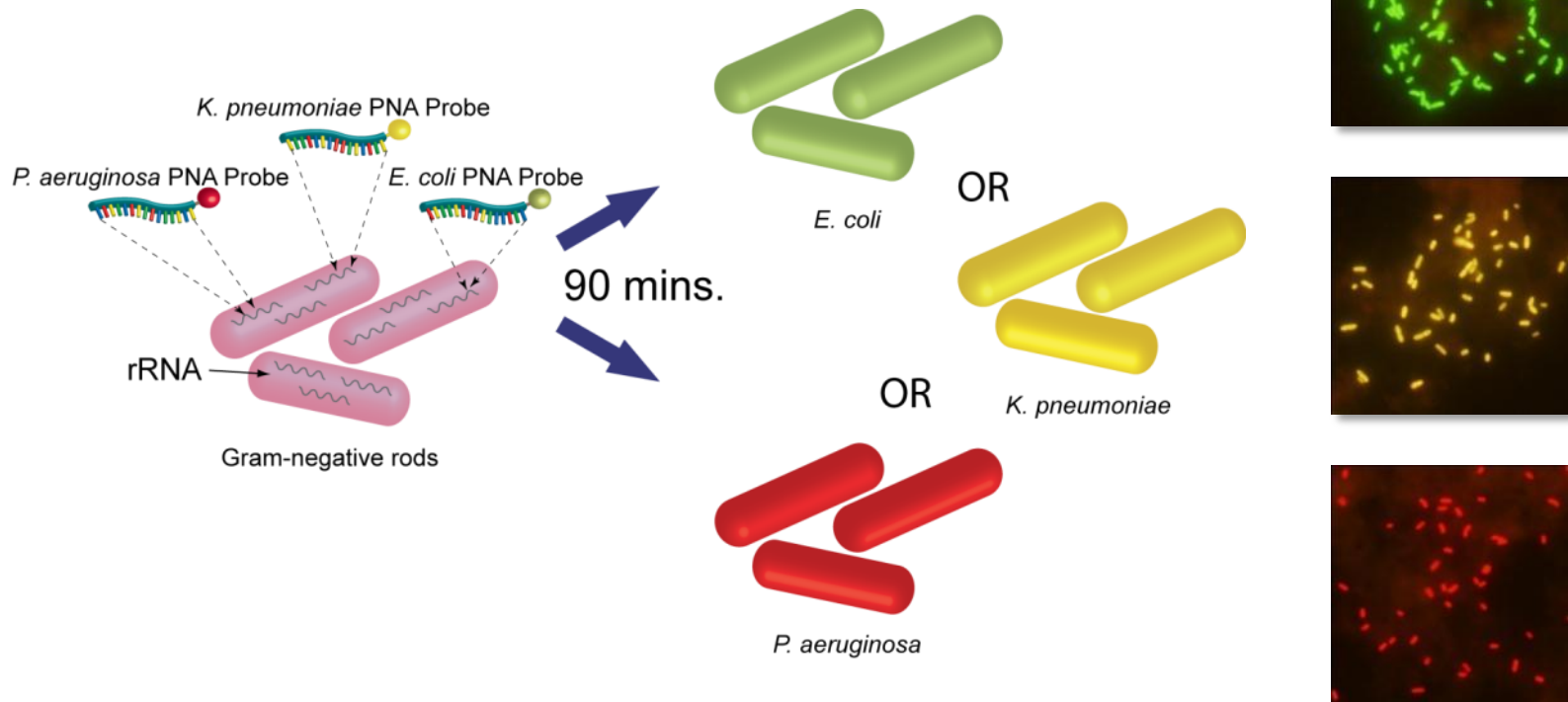
Gram-Negative QuickFISH™ BC

- Rapid Identification of *E. coli*, *K. pneumoniae* and *P. aeruginosa* from Positive Blood Cultures



PNA probes target ribosomal RNA inside cells

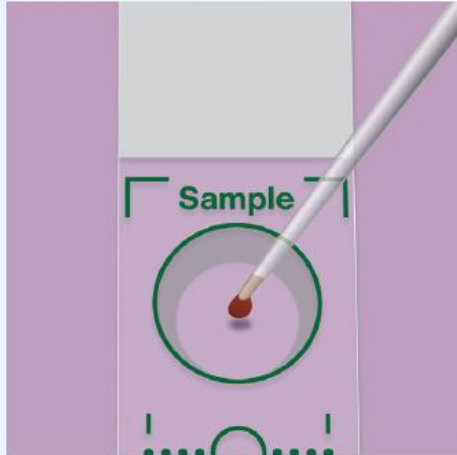
Peptide **N**ucleic **A**cid **F**luorescence **I**n **S**itu **H**ybridization



AdvanDx

3 Easy Steps: Fix Sample, Hybridize Probes and View Results.
5 Min. Hands-on Time. 20 Min. Turn-around Time.

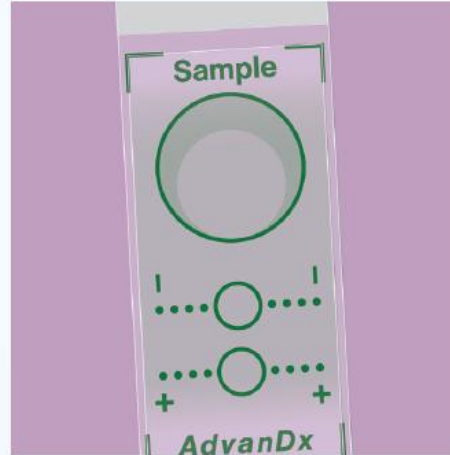
Fix



5 Min.

Fix 10 μ L of Blood Culture Sample to QuickFISH Slide.

Hybridize



15 Min.

Add PNA Reagents. Hybridize for 15 Min. at 55°C.

Examine



View Results

Examine on Fluorescence Microscope (60x or 100x Oil Objective).



Does Anybody Hear?



PNA FISH *Staphylococcus aureus*

AdvanDx

Batch testing, once per day, no specific notification of result.

TABLE 1. LOS and duration of vancomycin use for pre- and post-PNA FISH groups

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

Carol Holtzman, Dana Whitney, Tamar Barlam and Nancy S. Miller

J. Clin. Microbiol. 2011, 49(4):1581. DOI:



PNA FISH *Staphylococcus aureus*

AdvanDx

Batch testing, once per day, no specific notification of result.

TABLE 1. LOS and duration of vancomycin use for pre- and post-PNA FISH groups

Group (<i>n</i>)	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)
<i>P</i> value	0.35	0.49

Our study demonstrated that the *S. aureus* PNA FISH assay for the rapid detection of presumptive CoNS pseudobacteremia, when implemented without active reporting of results or additional support from an AST, did not reduce LOS or vancomycin use. In published studies, utilization of the PNA FISH

Carol Holtzman, Dana Whitney, Tamar Barlam and Nancy S. Miller

***J. Clin. Microbiol.* 2011, 49(4):1581. DOI:**



We may need to get someone's attention in addition to the nurse on the floor!



Who you gonna call?



PROHEALTH CARE

Who you gonna call?



**Someone who will review the case and
take action in a timely fashion.**



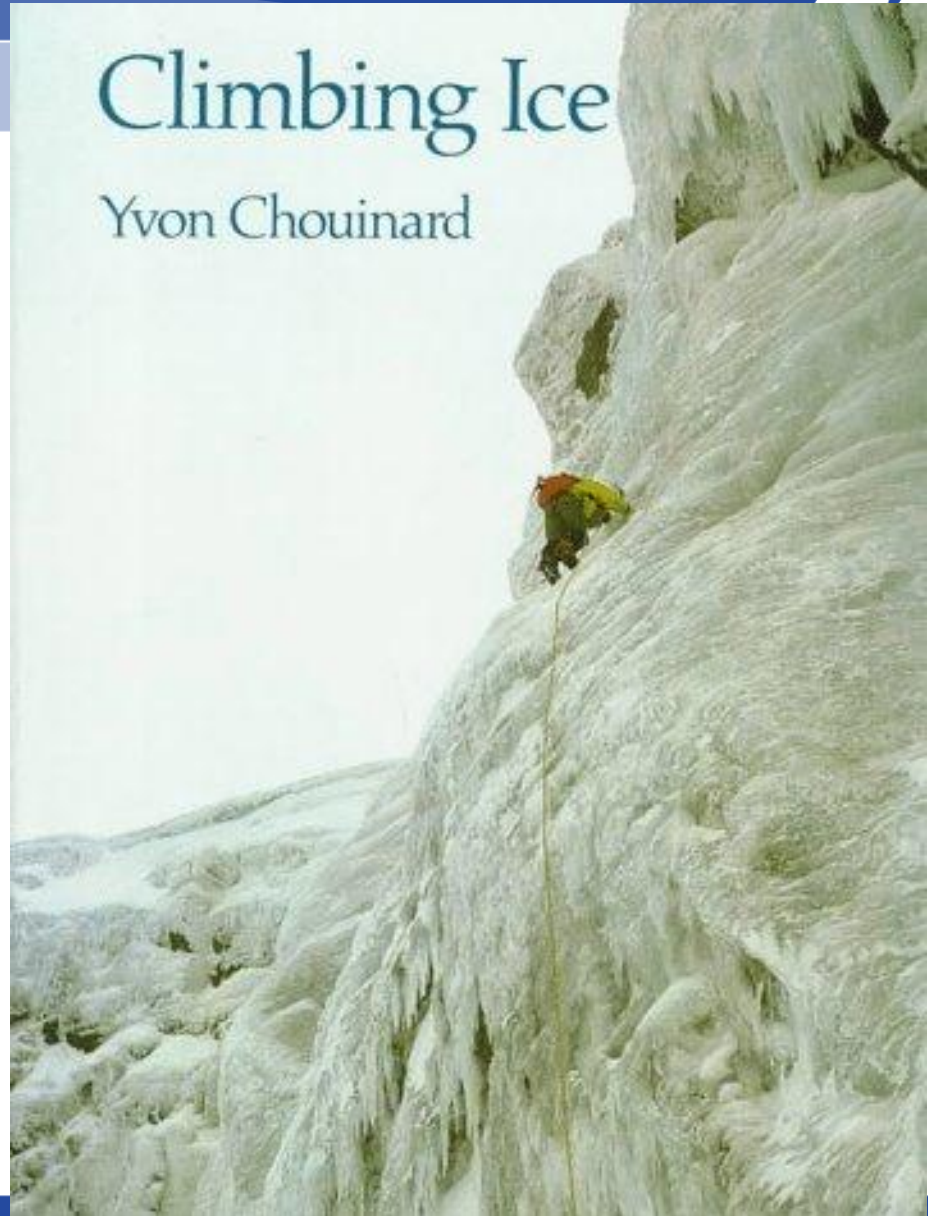
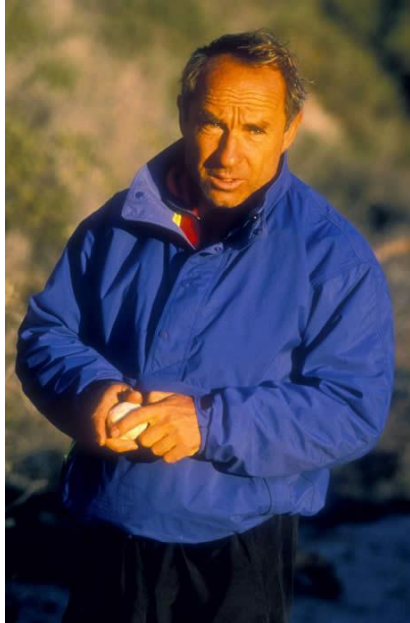
Who you gonna call?



For ProHealth Care it is the on-call Pharmacist.



Mountaineering Lore



“Speed is safety!”



PROHEALTH CARE



Nanosphere

BC-GP

BC-GN



PROHEALTH CARE



Nanosphere

BC-GP

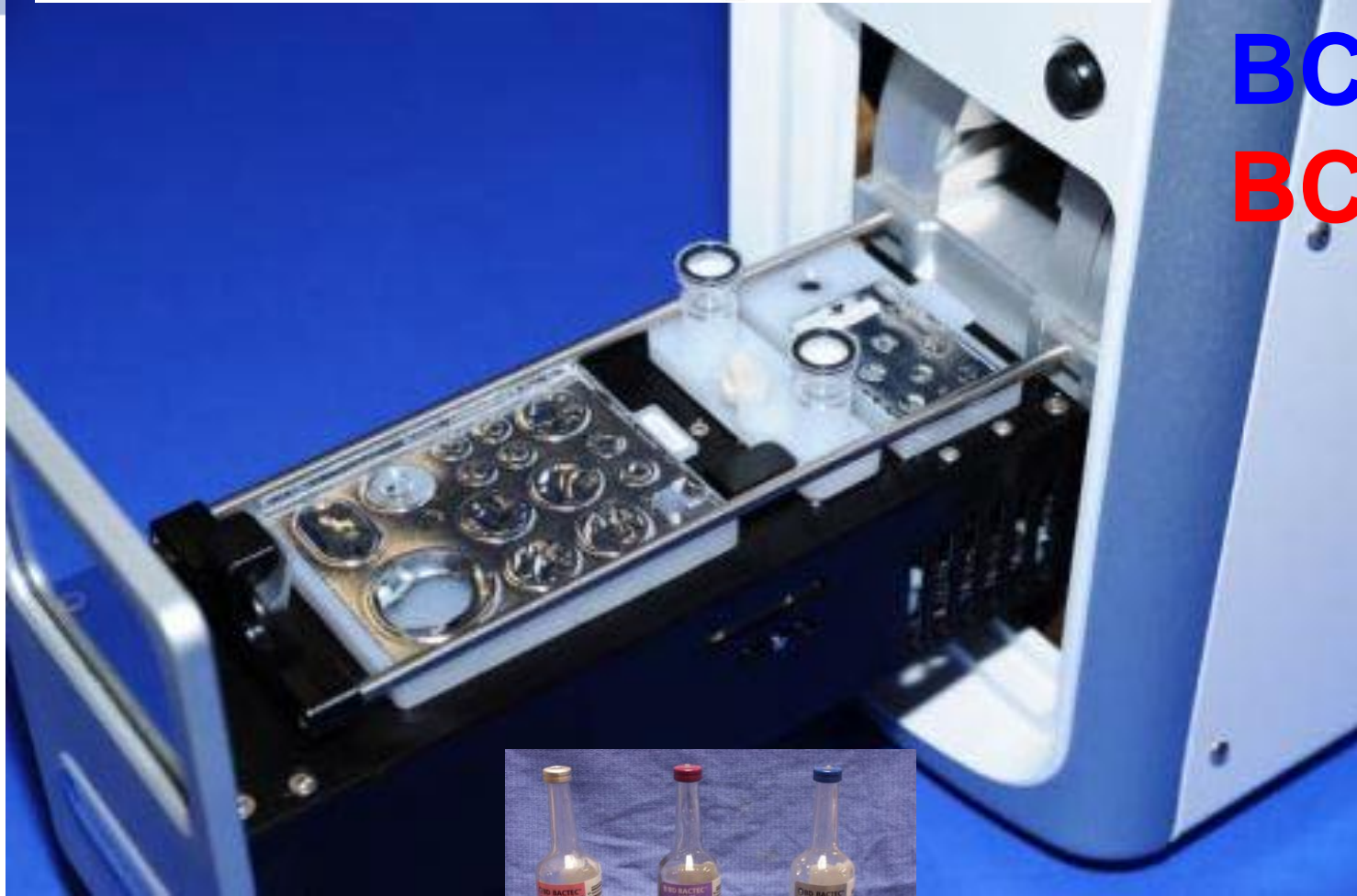
BC-GN





Nanosphere

BC-GP
BC-GN



3-4 minutes hands on



2 - 2.5 hour run time



PROHEALTH CARE

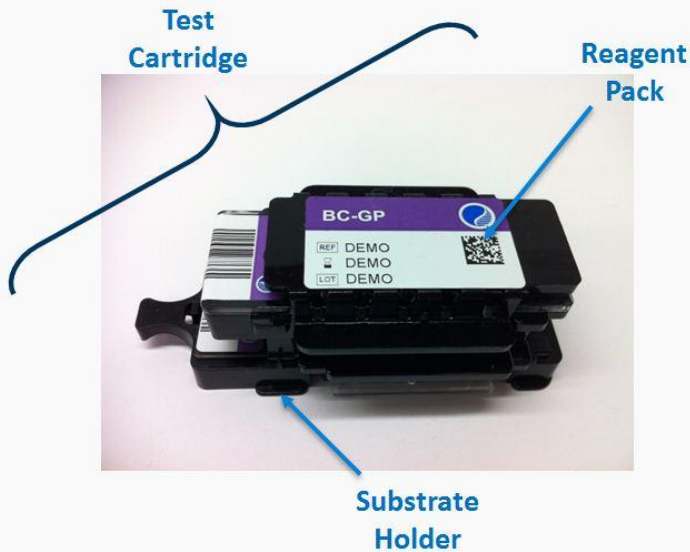


Nanosphere

BC-GP

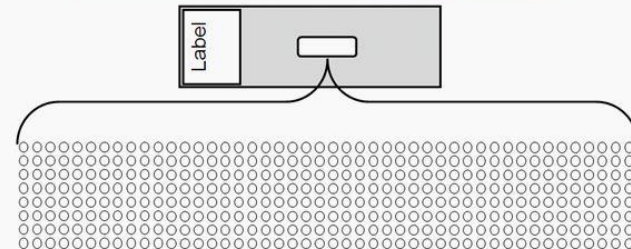
BC-GN

● Verigene Test Cartridge



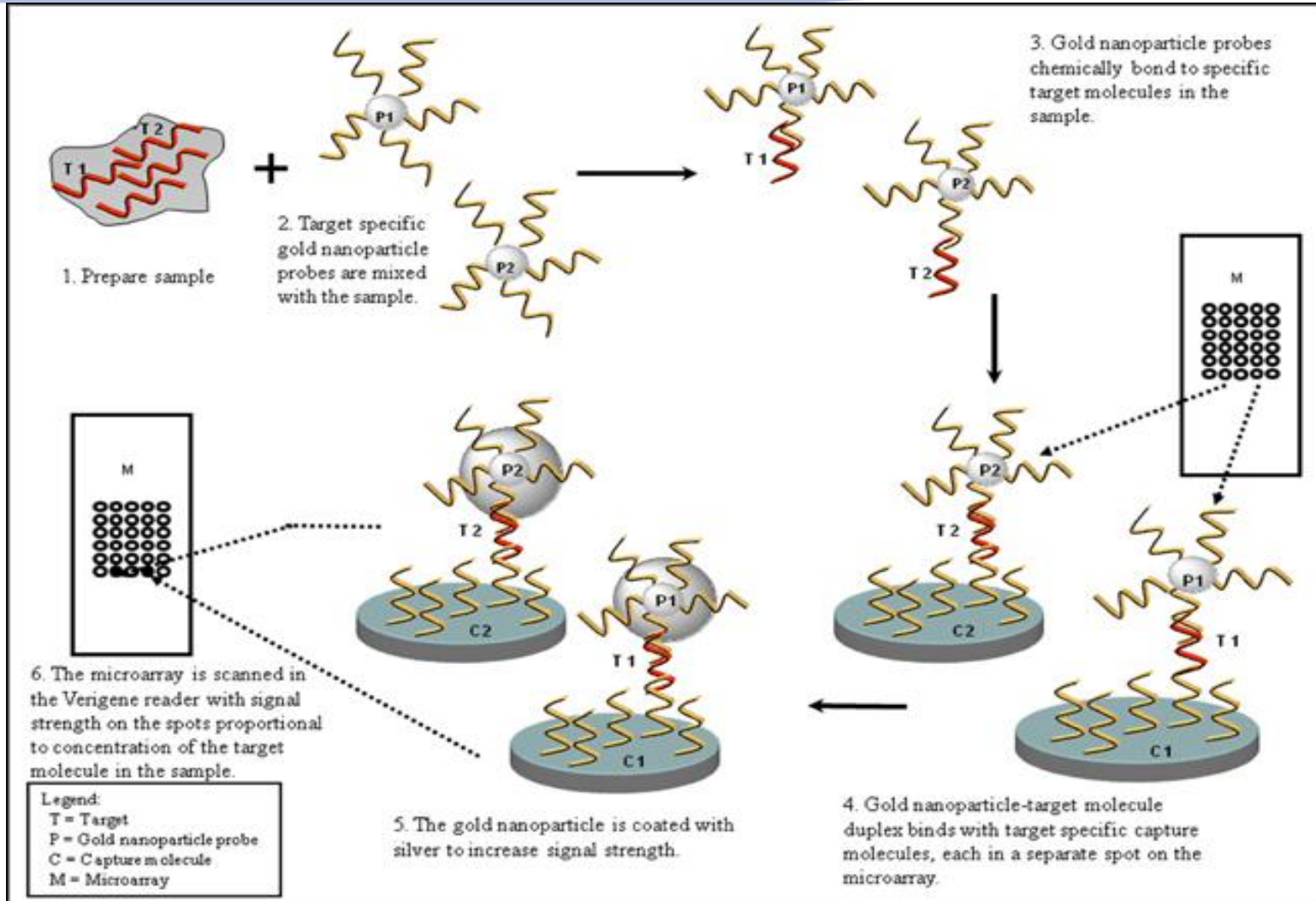
Substrate Holder

Reagent Pack





Nanosphere

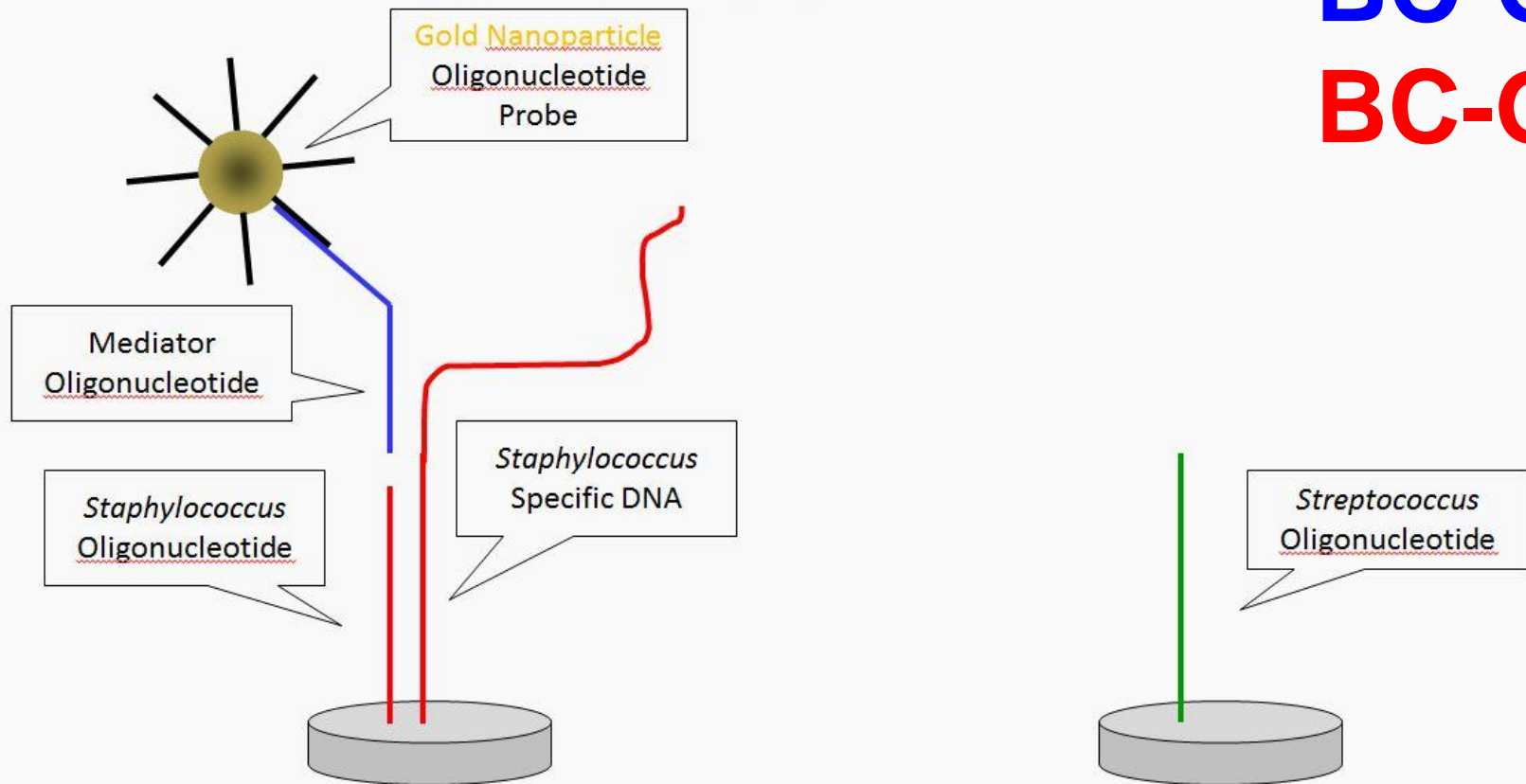




Nanosphere

- Bacterial DNA Detection – Secondary Hybridization

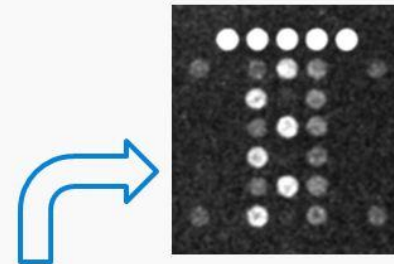
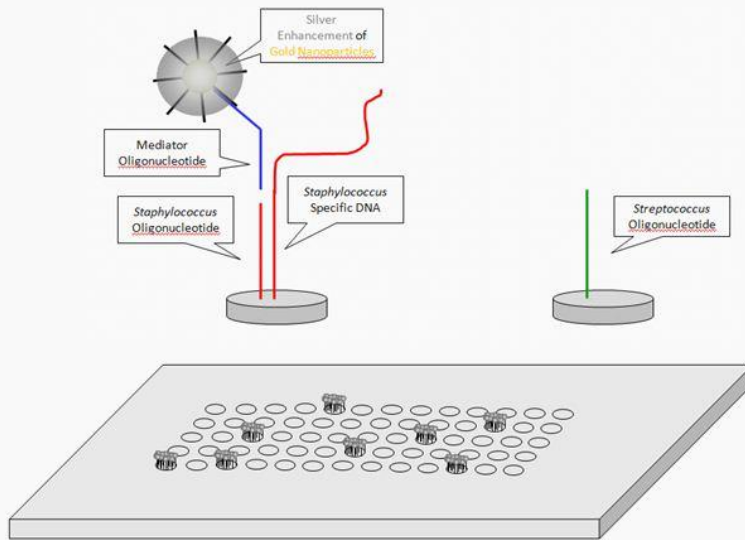
BC-GP
BC-GN





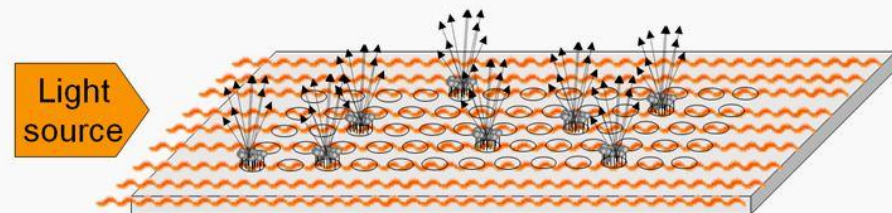
Nanosphere

- Bacterial DNA Detection – Signal Amplification by Silver Enhancement of Gold Nanoparticles



BC-GP
BC-GN

- Analysis of results via light-scattering (array scanning)





Nanosphere

BC-GP

Staphylococcus spp.

Staphylococcus aureus +/- mecA

Staphylococcus epidermidis +/- mecA

Staphylococcus lugdunensis

Streptococcus spp.

Streptococcus pneumoniae

Streptococcus pyogenes

Streptococcus agalactiae

Streptococcus anginosus group

Enterococcus faecalis +/- vanA or vanB

Enterococcus faecium +/- vanA or vanB

Listeria spp.



PROHEALTH CARE



Nanosphere

BC- GN

Acinetobacter spp.

Proteus spp.

Citrobacter spp.

Enterobacter spp.

Escherichia coli

Klebsiella pneumonia

Klebsiella oxytoca

Pseudomonas aeruginosa

CTX-M (ESBL)

KPC

NDM – 37/11

VIM – 5/2

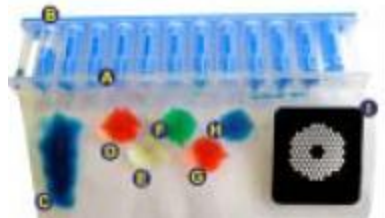
IMP – 3/1

OXA – 7/5



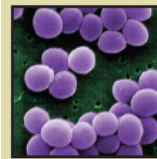
PROHEALTH CARE

FilmArray® Blood Culture ID Panel



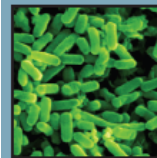
The FilmArray BCID Panel

Simultaneous detection of 27 targets:



Gram + Bacteria

- *Staphylococcus*
- *Staphylococcus aureus*
- *Streptococcus*
- *Streptococcus agalactiae*
- *Streptococcus pyogenes*
- *Streptococcus pneumoniae*
- *Enterococcus*
- *Listeria monocytogenes*



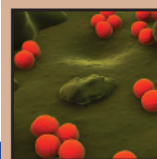
Gram - Bacteria

- *Klebsiella oxytoca*
- *Klebsiella pneumoniae*
- *Serratia*
- *Proteus*
- *Acinetobacter baumannii*
- *Haemophilus influenzae*
- *Neisseria meningitidis*
- *Pseudomonas aeruginosa*
- *Enterobacteriaceae*
- *Escherichia coli*
- *Enterobacter cloacae* complex



Fungi

- *Candida albicans*
- *Candida glabrata*
- *Candida krusei*
- *Candida parapsilosis*
- *Candida tropicalis*



Antibiotic Resistance

- *mecA*
- *vanA / vanB*
- KPC

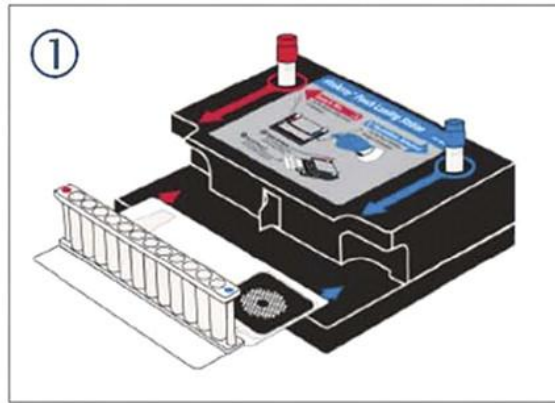
4-5 minutes hands on



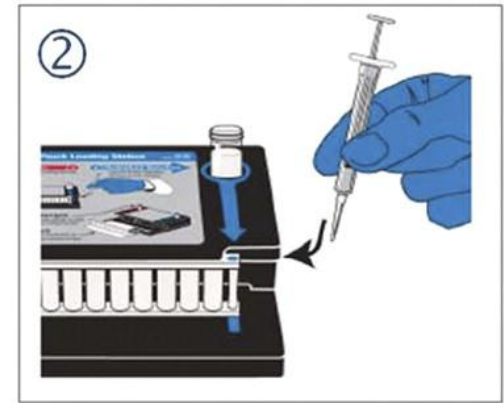
65 minutes



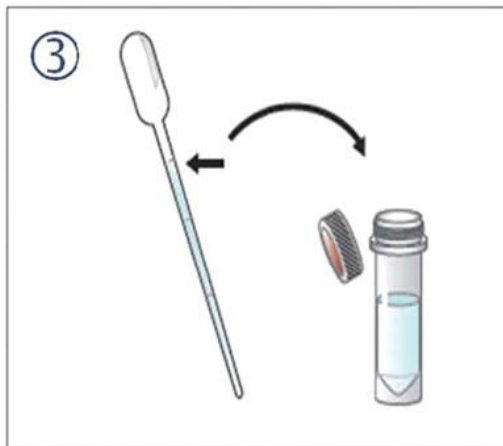
FilmArray RP Pouch



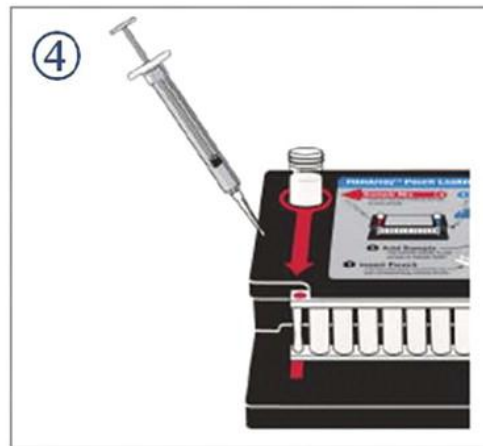
Load Pouch



Inject Hydration Solution



Add Sample to Buffer



Inject Sample



Load Pouch in FilmArray

Brought To You By?

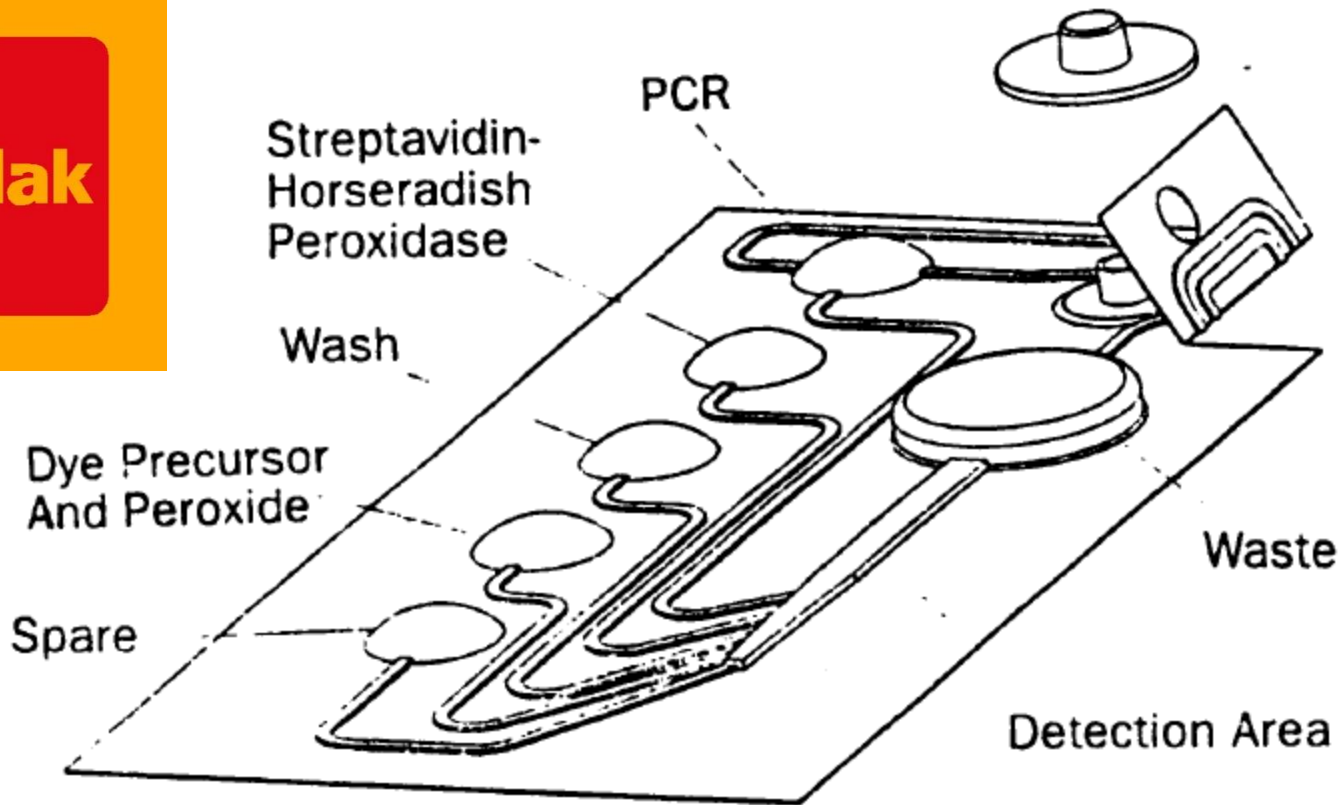
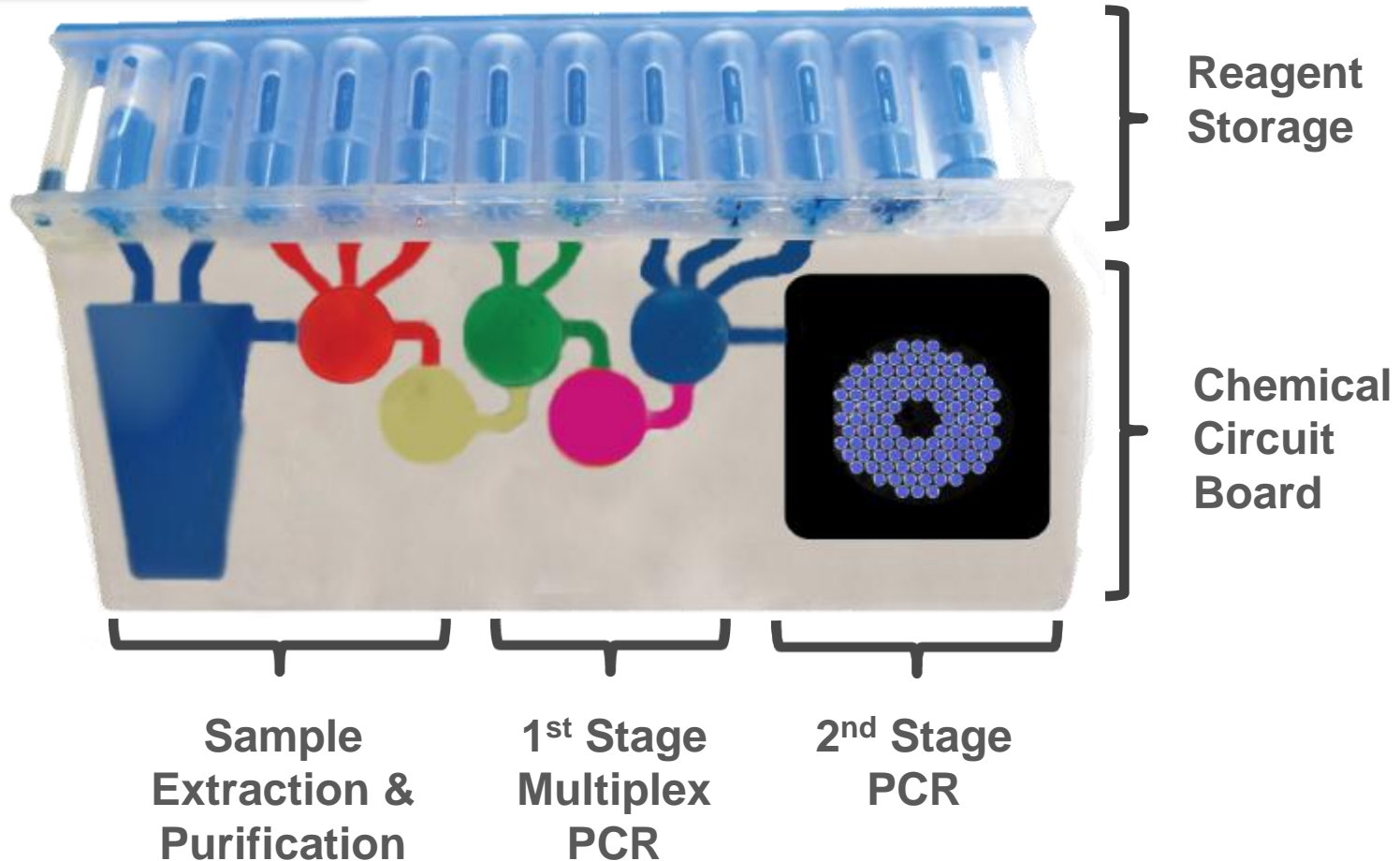


Fig. 5. PCR amplification and detection containment vessel prototype

Findlay, et. Al. 1993. Clin. Chem. 39:1927-1933



The FilmArray Pouch



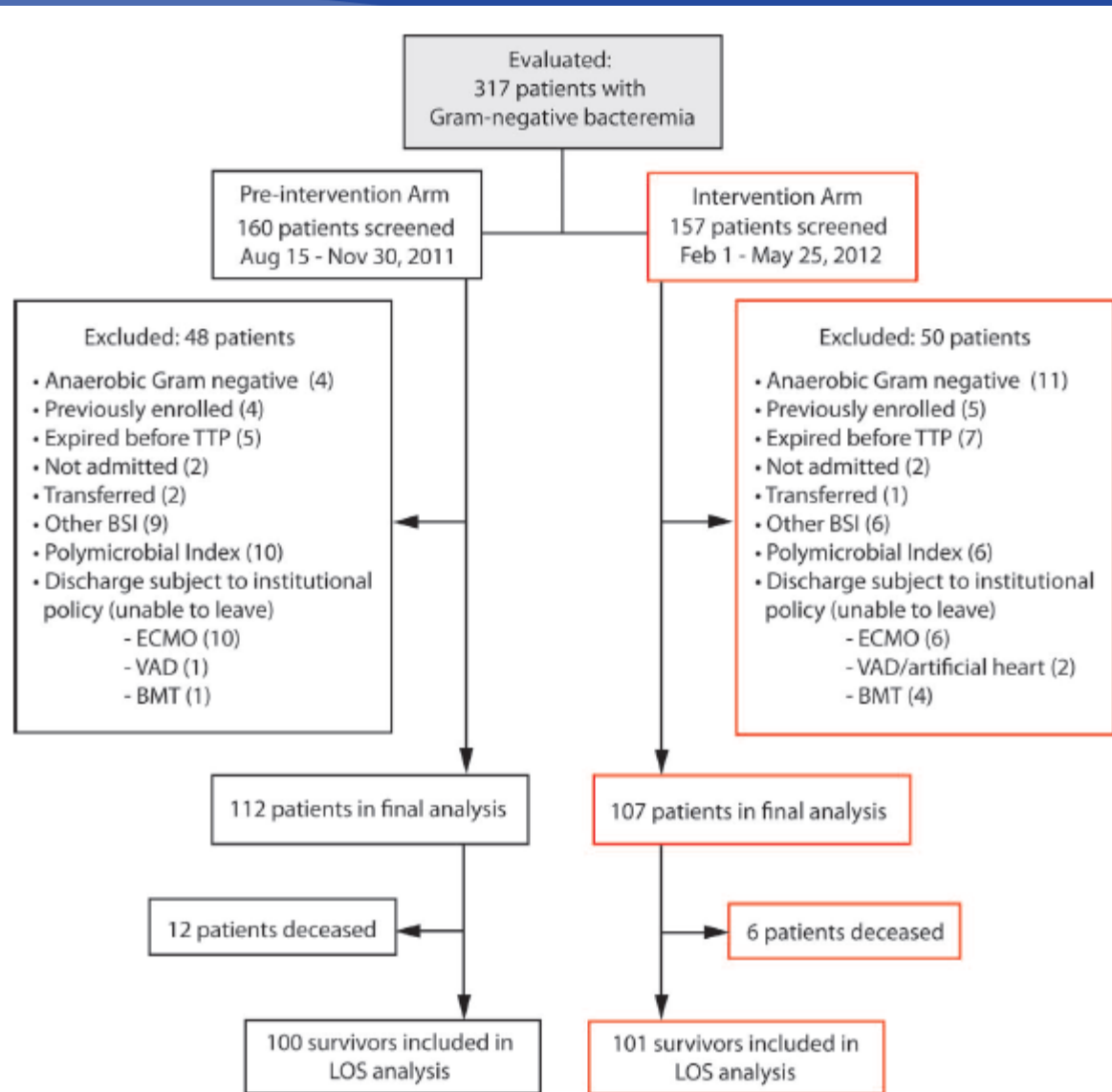


Figure 1. Eligibility and inclusion of the study participants. The most common reasons for ineligibility among patients were medical circumstances requiring prolonged hospitalization unrelated to the patient's bloodstream infection (BSI; 24.4%), including patients receiving extracorporeal membrane oxygenation (ECMO) for cardiorespiratory failure; advanced heart failure requiring ventricular assist devices (VADs) or an artificial heart; and elective admissions for bone marrow transplantation (BMT). Length of stay (LOS) and hospital cost analyses were conducted in those patients surviving to hospital discharge. Abbreviation: TTP, time-to-positivity of index blood culture.



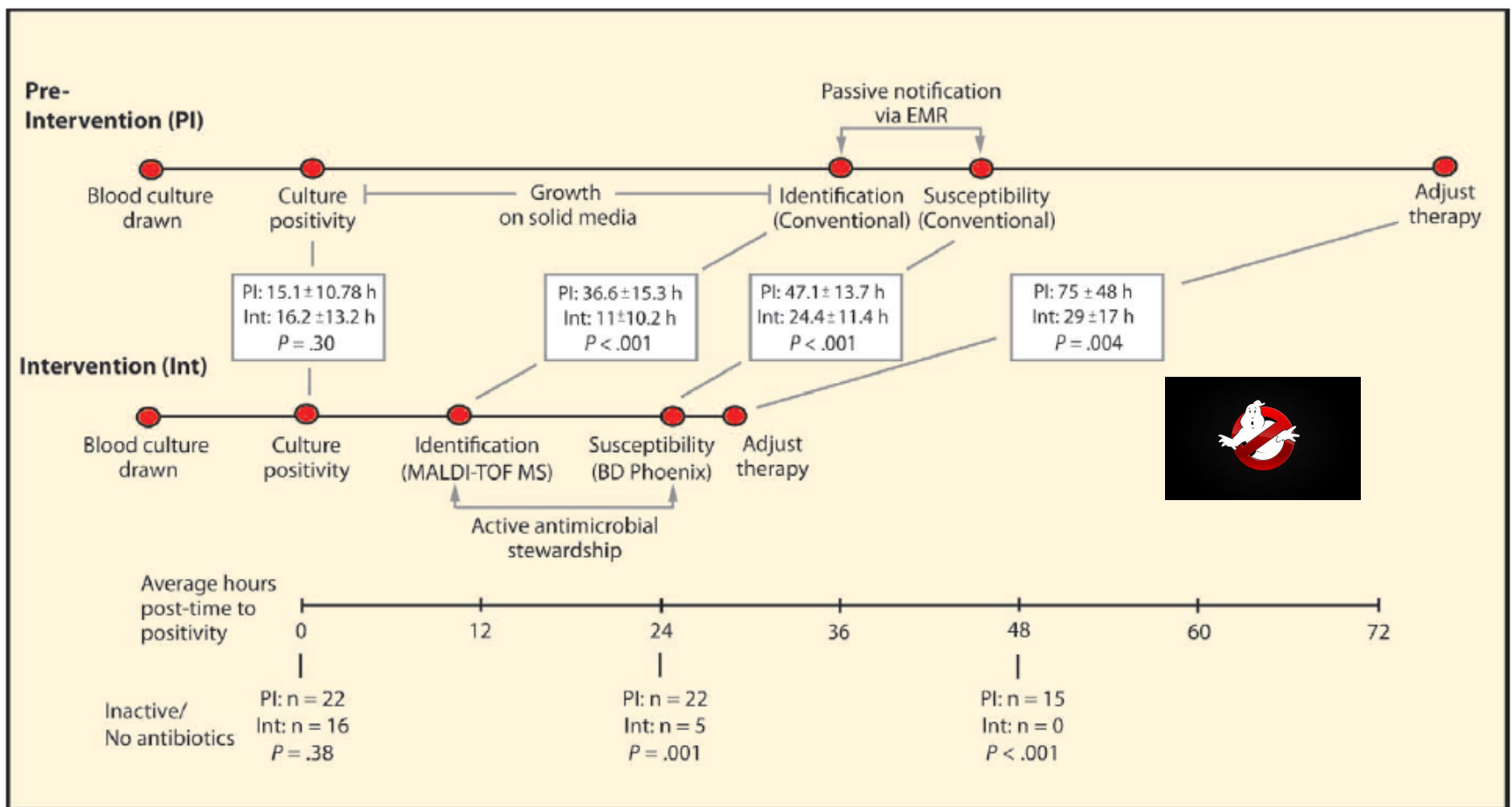


Figure 2. Timeline comparison of preintervention and intervention study periods depicting the differences in laboratory procedure and their respective impact on adjusted therapy. Adjusted therapy included, when clinically indicated, de-escalation/escalation of antibiotic therapy, dosing/route modifications, and/or discontinuation of unnecessary gram-positive coverage. White boxes denote the average times (hours) until the corresponding information was obtained or action implemented in the preintervention (PI) and intervention (Int) groups. The bottom horizontal line represents the global study/patient timeline (hours) and includes point measurements (below) for patients on inactive therapy at 0, 24, and 48 hours in both groups. Abbreviations: EMR, electronic medical record; MALDI-TOF MS, matrix-assisted laser desorption and ionization time-of-flight mass spectrometry.

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

Abbreviations: BSI, bloodstream infection; ICU, intensive care unit; MS DRG, Medicare Diagnosis-Related Group.

^a Values for length of stay outcomes are given as days, mean ± SD. Costs are reported as cost per hospitalization, mean ± SD.



Perez, et.al. Arch. Pathol. Lab. Med. 2012. Dec. 6.

Xpert[®] MRSA/SA BC



GeneXpert I



GeneXpert II



GeneXpert IV



GeneXpert XVI



Cepheid Xpert MRSA/SA Blood Culture

1

Gently mix the sample by hand, transfer a 50 μ L aliquot to the elution reagent vial using the pipette provided



2

Vortex and transfer the sample into S chamber



3

Insert cartridge and start assay



(1-2 minutes hands on)

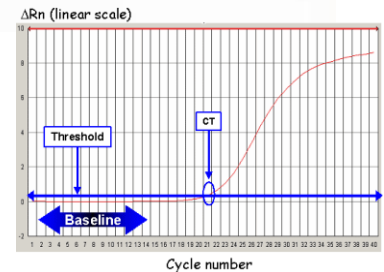


Table 2. Demographic and Clinical Characteristics of Patients in the Study Groups

Characteristic	Pre-rPCR period (n = 74)	Post-rPCR period (n = 82)	P ^a
Age, mean years ± SD	57 ± 16.7	56 ± 16.0	.51
Male sex	43 (58)	40 (49)	.26
Penicillin allergy	9 (12)	10 (12)	.60
Surgical service	24 (32)	10 (12)	.003
ICU ^b	49 (66)	55 (67)	>.99
MRSA infection	44 (59)	37 (45)	.08
ID consult	41 (55)	49 (60)	.63
Time to ID consult, mean days ± SD (n = 90)	9 ± 16.4	3 ± 2.4	.05
Hospital mortality	19 (26)	15 (18)	.33
Hospital costs by department			
Pharmacy, mean USD ± SD	10,375 ± 21,221	7457 ± 13,250	.08
Microbiology laboratory, mean USD ± SD	6806 ± 10,290	5081 ± 6677	.13
Room and board			
ICU, mean USD ± SD	27,667 ± 35,777	17,737 ± 21,464	.03
Non-ICU, mean USD ± SD	12,210 ± 13,741	10,117 ± 10,932	.32
Other, ^c mean USD ± SD	25,464 ± 36,633	16,400 ± 20,031	.02
Total hospital costs, mean USD ± SD (n = 154)	69,737 ± 96,050	48,350 ± 55,196	.03

NOTE.Data are no. (%) of patients, unless otherwise indicated. Reported hospital costs are representative of total pharmacy, microbiology laboratory, and room and board cost. ICU, intensive care unit; ID, infectious diseases; rPCR, methicillin-resistant *S. aureus*/*S. aureus* blood culture test; SD, standard deviation; USD, United States dollars.

^a P values were determined by Fisher's exact test or Wilcoxon rank-sum test as appropriate.

^b ICU stay at anytime during hospitalization.

^c Includes all hospital costs not previously described, including operating room services, imaging services, and medical and surgical supplies.



Cepheid Xpert MRSA/SA Blood Culture

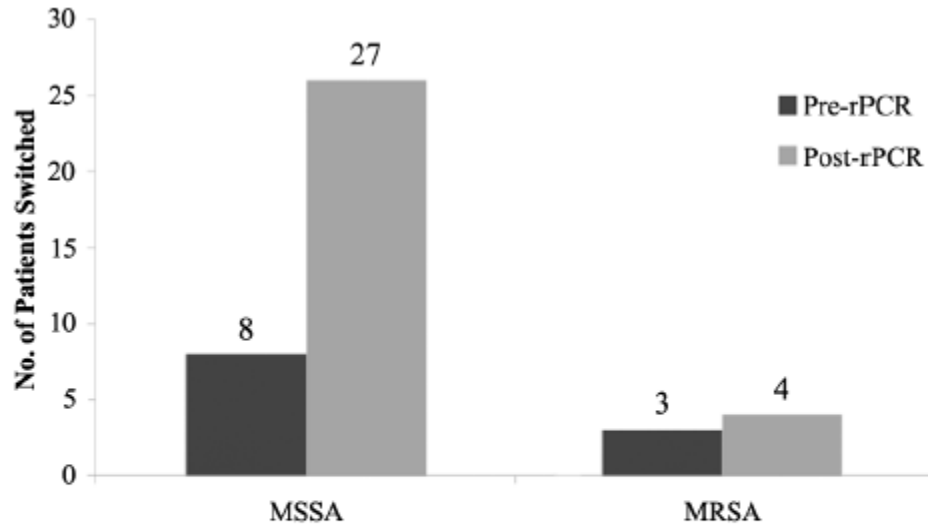


Figure 1. Number of infectious diseases pharmacist antibiotic changes from vancomycin to cefazolin or nafcillin for methicillin-susceptible *Staphylococcus aureus* (MSSA) bacteremia and vancomycin to daptomycin for methicillin-resistant *S. aureus* (MRSA) bacteremia. rPCR, rapid polymerase chain reaction MRSA/SA blood culture test.



Clinical Infectious Diseases 2010;51(9):1074-1080

Cepheid Xpert MRSA/SA Blood Culture

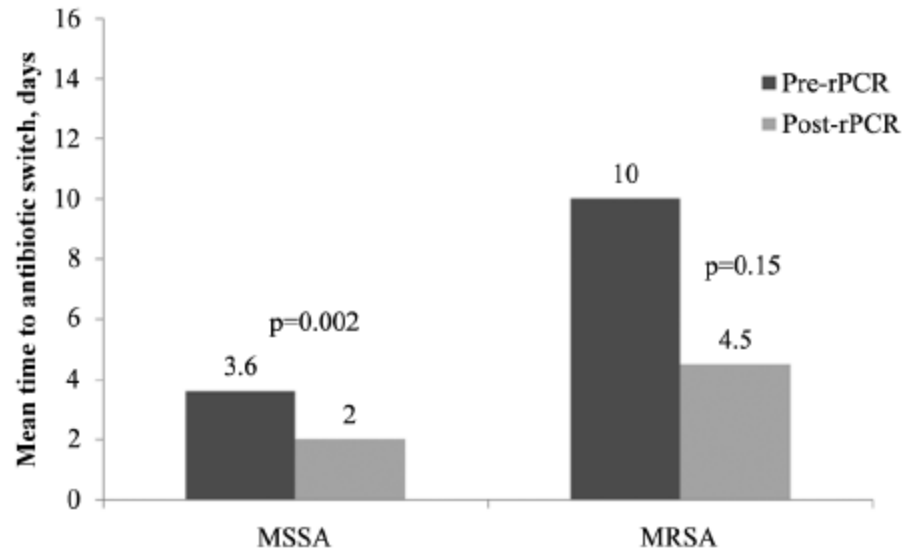


Figure 2. Mean time to antibiotic switch from vancomycin to cefazolin or nafcillin for methicillin-susceptible *Staphylococcus aureus* (MSSA) bacteremia and vancomycin to daptomycin for methicillin-resistant *S. aureus* (MRSA) bacteremia. rPCR, rapid polymerase chain reaction MRSA/SA blood culture test.



BD GeneOhm™ StaphSR

Assay Procedure Positive Blood Culture*



15 minutes hands on

70 minutes



PNAFish Yeast and *S. aureus*/CoNS

Table 2 Potential pharmaceutical cost savings with PNA-FISH

Case	Final Species ID	Initial Rx	Rx initiation until change (days)	Time to culture ID (days)	Time to PNA-FISH ID (days)	Potential time saved w/ PNA-FISH (days)	Potential cost saved w/PNA-FISH [†]
1	<i>C. albicans</i>	Caspofungin	6	3	0.3	2.7	\$1,093.50
2	<i>C. glabrata</i>	Fluconazole	2	5.4	0.6	4.8	Fluconazole changed to Caspofungin
3	<i>C. parapsilosis</i>	Caspofungin	5	3.6	0.7	2.9	\$1,174.50
1	CoNS	Vancomycin	3	3.7	0.8	2.9	\$58.00
2	CoNS	Vancomycin	4	2.1	0.2	1.9	\$38.00
3	CoNS	Vancomycin	5	3.2	0.3	2.9	\$58.00
4	CoNS	Vancomycin	2	0.8	0.7	0.1	\$2.00

[†] Potential time saved w/PNA-FISH X AWP = Potential cost saved w/PNA-FISH.

AWP:

Fluconazole 400mg po/day= \$27.26.

Caspofungin 50mg IV/day=\$405.00.

Vancomycin 2 g/day=\$20.00.



Annals of Clinical Microbiology and Antimicrobials 2013, **12**:2

Rapid Identification of Positive Blood Cultures

