CHANGE : OUTCOME

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A better way.

NICO ARNOLD

EXECUTIVE VICE PRESIDENT,
WORLDWIDE COMMERCIAL OPERATIONS,
CEPHEID

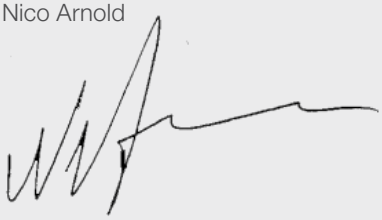
From the editor

Welcome to the third issue of IMPACT, a quarterly magazine published by Cepheid's Systems & Solutions Group.

In this issue we highlight the success that Dr. Najoua El Helali, a thought leader on the prevention of early onset neonatal infections, has had using Xpert® GBS to implement real-time PCR for intrapartum screening at the maternity ward at Paris-Saint-Joseph Hospital. In her informative feature article, Dr. El Helali outlines data on the cost and effectiveness of the intrapartum Xpert GBS strategy Paris-Saint-Joseph implemented. She also gives us insight into the analysis that led to placing a GeneXpert System in the delivery room — giving obstetricians and midwives 24/7 on-demand test results at the point of care.

In our last issue of IMPACT, we reported that *C. difficile* infections are at an all-time high and add over $1 billion in extra health care costs annually. In this issue's *C. difficile* Challenge article, we show how rapid, trusted test results can help your lab positively impact hospital workflow by identifying and treating CDI patients. We hope you will respond and show us how your organization is tackling the *C. difficile* challenge!

Enjoy reading this issue.
Nico Arnold



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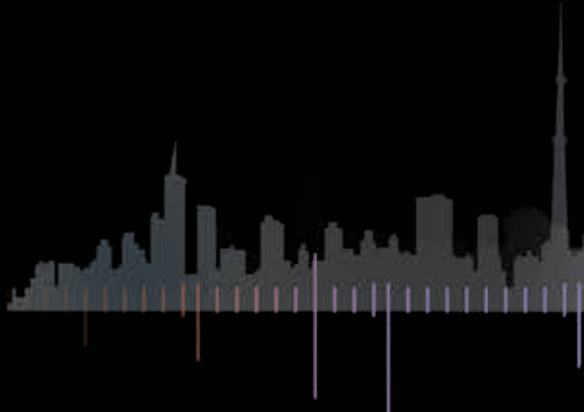
ON THE TABLE



FEATURE

Less Uncertainty — Better Safety — More Healthy Newborns

Paris-Saint-Joseph Hospital reduces GBS infection rate and improves patient management with Xpert® GBS and GeneXpert® System.

CONTRIBUTED BY
DR. NAJOUA EL HELALI

MICROBIOLOGISTE, HÔPITAL PARIS-SAINT-JOSEPH

Paris-Saint-Joseph Hospital is a consolidated private healthcare group of three hospitals: Saint-Joseph, Notre Dame de Bon Secours and Saint-Michel. The Paris-Saint-Joseph Hospital was certified in 2010 by the National Health Authority and its maternity unit has recognized as a reference for pathological pregnancies, childbirth, and postpartum disorders. The team at the hospital aims to improve the quality of life of the patient by investing in new technologies and advanced drugs.

In 2001 France introduced GBS vaginal screening for women at 35–37 weeks of pregnancy, with intrapartum antibiotic prophylaxis (IAP) being given to women who test antenatal positive. Women with unknown GBS status at the time of delivery received IAP if they presented risk factors (e.g., membrane rupture > 12 hours and/or fever > 38°C and/or delivery < 37 weeks).

At Paris-Saint-Joseph Hospital, these recommendations resulted in a reduction in the incidence of proven early onset GBS disease (EOGBSD) cases from 1.3 in the late 1990's to 0.7 per 1000 live births by 2009. During the same period, the global incidence of proven and probable[1] EOGBSD cases fell from 13.3 to 8.3 per 1000 live births. However, monitoring cases between April 2007 and December 2009 revealed that 65% of babies hospitalized for EOGBSD were born to mothers whose antenatal screening was negative.

Dr. Najoua El Helali : *A contemporary thought leader on the prevention of early onset neonatal infections. Based in Paris-Saint-Joseph Hospital she has been a member of the French health agency recommendations group for the prevention of early onset neonatal infections (2001–2002), and has been instrumental in the implementation of real-time PCR for intrapartum screening at the Point of Care in the maternity ward using Xpert GBS on the GeneXpert System.*

A further study[2] compared intrapartum with antenatal screening and showed that nearly half of the women who tested positive during labor were not detected by antenatal screening, and 42% who were positive at 35–37 weeks were actually intrapartum negative. The positive predictive value of antenatal screening for identifying colonization status at delivery was only 58.7%, whereas the negative predictive value was imperfect (92.1%), leading to inadequate prophylaxis for mothers and newborn babies still at risk for EOGBSD.

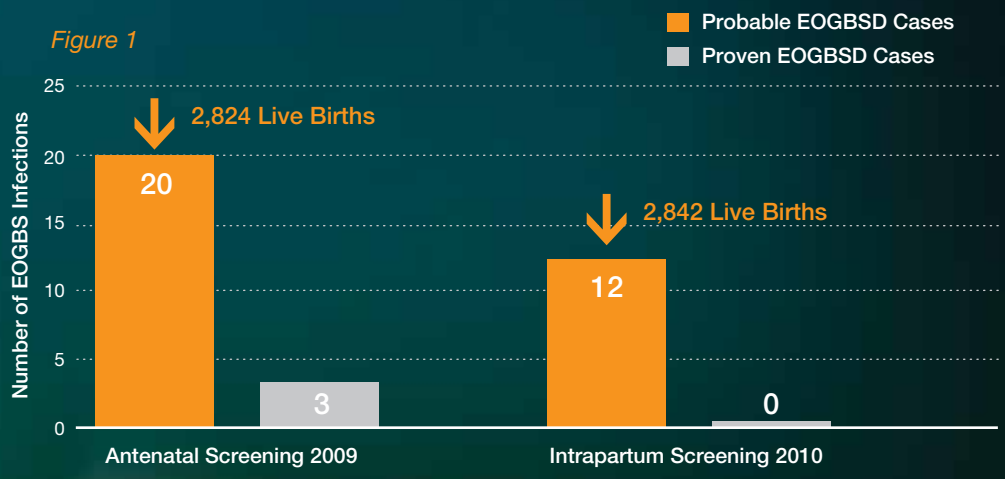
As a result, Paris-Saint-Joseph Hospital evaluated the performance and the feasibility of intrapartum testing with Xpert GBS. The test provided good performance comparable to culture methods (98.5% sensitivity, 99.6% specificity, 97.8% positive predictive value and 99.7% negative predictive value)[2], with actionable results made available in just 30–50 minutes. The test was simple and quick enough that it could be performed by midwives at the admission for delivery in order to target appropriate IAP to prevent EOGBSD.

In January 2010, intrapartum Xpert GBS screening was introduced for term deliveries in Paris-Saint-Joseph Hospital. During that first year, on-demand, intrapartum Xpert GBS screening was performed for 2,814 term deliveries. The GBS colonization rate increased from 11.7% in 2009 (previous antenatal screening rate) to 16.7% in 2010 and resulted in 436 women receiving appropriate IAP.

1 The Impact of the Intrapartum Xpert GBS screening[3]:

- From 2009 to 2010, the number of EOGBSD cases was decreased by nearly half. There were 8 fewer probable cases and no proven cases.

Figure 1



- There were no severe cases of EOGBSD using the intrapartum screening strategy in 2010.

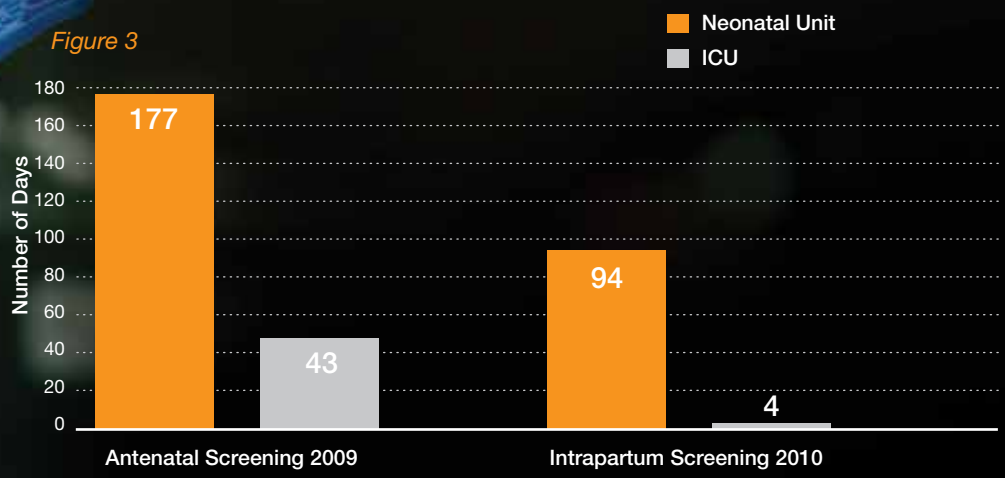
Characteristics of GBS-infected Newborns

Figure 2

	Antenatal Screening (2009)	Intrapartum Screening (2010)
Live Births	2,824	2,842
Total EOGBSD	23	12
Proven EOGBSD	3 Severe Cases — 1 Meningitis — 2 Bacteremia	0
Probable EOGBSD	20 — 4 Severe cases — 16 Mildly ill cases	12 — All mildly ill cases

- Length of Hospital Stay (LOS) nearly halved the neonatal bed days and even more significantly ICU bed days dropped from 43 to 4

Figure 3



HÔPITAL
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PARIS, FRANCE

Costs of Prevention Strategies[2] Antenatal Culture vs. Intrapartum PCR

Figure 4

	2009: Antenatal Culture Screening Strategy	2010: Intrapartum PCR Screening Strategy
Costs of screening	€ 8,923 ≈ $ 11,295 (N=2372)	€ 91,432 ≈ $ 115,736 (N=2378)
Costs of prophylaxis	€ 491 ≈ $ 621 (N=311)	€ 685 ≈ $ 867 (N=436)
Costs of treating GBS infected newborns	€ 115,385 ≈ $ 146,057 (N=23)	€ 20,100 ≈ $ 25,433 (N=12)
Costs of deliveries for healthy newborns	€ 3,712,991 ≈ $ 4,698,626 (N=2738)	€ 3,787,987 ≈ $ 4,793,720 (N=2802)
Average cost per patient of prevention strategies	€ 1,390 +/- 955 ≈ $ 1,759 +/- 1,209	€ 1,386 +/- 665 ≈ $ 1,754 +/- 842

Cost and effectiveness of the intrapartum Xpert GBS strategy was estimated using direct costs, including screening costs, hospital costs for deliveries of healthy newborns, and costs of treating GBS infected newborns[3]. The average total cost per delivery was €1,386 ≈ $ 1,754 with Xpert GBS intrapartum screening in 2010 compared to €1,390 ≈ $ 1,759 when using antenatal screening in 2009.

2 Conclusion

The intrapartum screening is a very effective strategy for appropriately targeting IAP and prevent ing EOGBSD in newborns. The Xpert GBS test provides a highly accurate result for identifying GBS carriers at the onset of labor. The simplicity of the test means that it can easily be introduced at point of care and performed by midwives. In one year, the incidence of probable EOGBSD cases was reduced by nearly half and no proven cases were recorded. The impact was shown in the reduction in costs of treating GBS infected neonates in Paris-Saint-Joseph Hospital, and so the strategy was cost-neutral.

As a result of this success, in March 2011, the testing was transferred to the delivery room. Since then midwives have performed the test 24/7, on-demand, at the time of admission for delivery.

3 Intrapartum PCR is performed successfully by midwives at the point of care, in the delivery room, 24/7

4 Intrapartum Xpert GBS screening continues to help save babies' lives at risk of EOGBS disease at Paris-Saint-Joseph Hospital

Figure 5

	Risk Based Strategy End 1990's	Antenatal Screen Strategy End 2009's	Intrapartum Screening Strategy January 2010 — April 2012
	Per 1,000 live births		
Proven EOGBSD	1.3	0.7	0.2
Proven + Probable EOGBSD	13.3	8.3	2.8

Q&A with Dr. Najoua El Helali

CONTRIBUTED BY
DR. NAJOUA EL HELALI

MICROBIOLOGISTE, HÔPITAL PARIS-SAINT-JOSEPH

How have clinicians responded to the changes to intrapartum testing?

The midwives, obstetrician, and the neonatologist feel much more confident in the management of EOGBS disease. In the last 2.5 years they have been able to get results on GBS colonization status, on-demand while it is most clinically important.

How did you implement testing in the labor ward and how easily did midwives adapt?

The GeneXpert® System was transferred to the delivery room in March 2011. We trained our midwives to use the swabs and perform the tests. At first they were uncertain if they would be able to add testing to their busy workload, but now they are very happy. They can manage their own time and they find the test easy to perform. Now they know when the results will be available and they don't lose time taking samples to the lab and waiting for results.

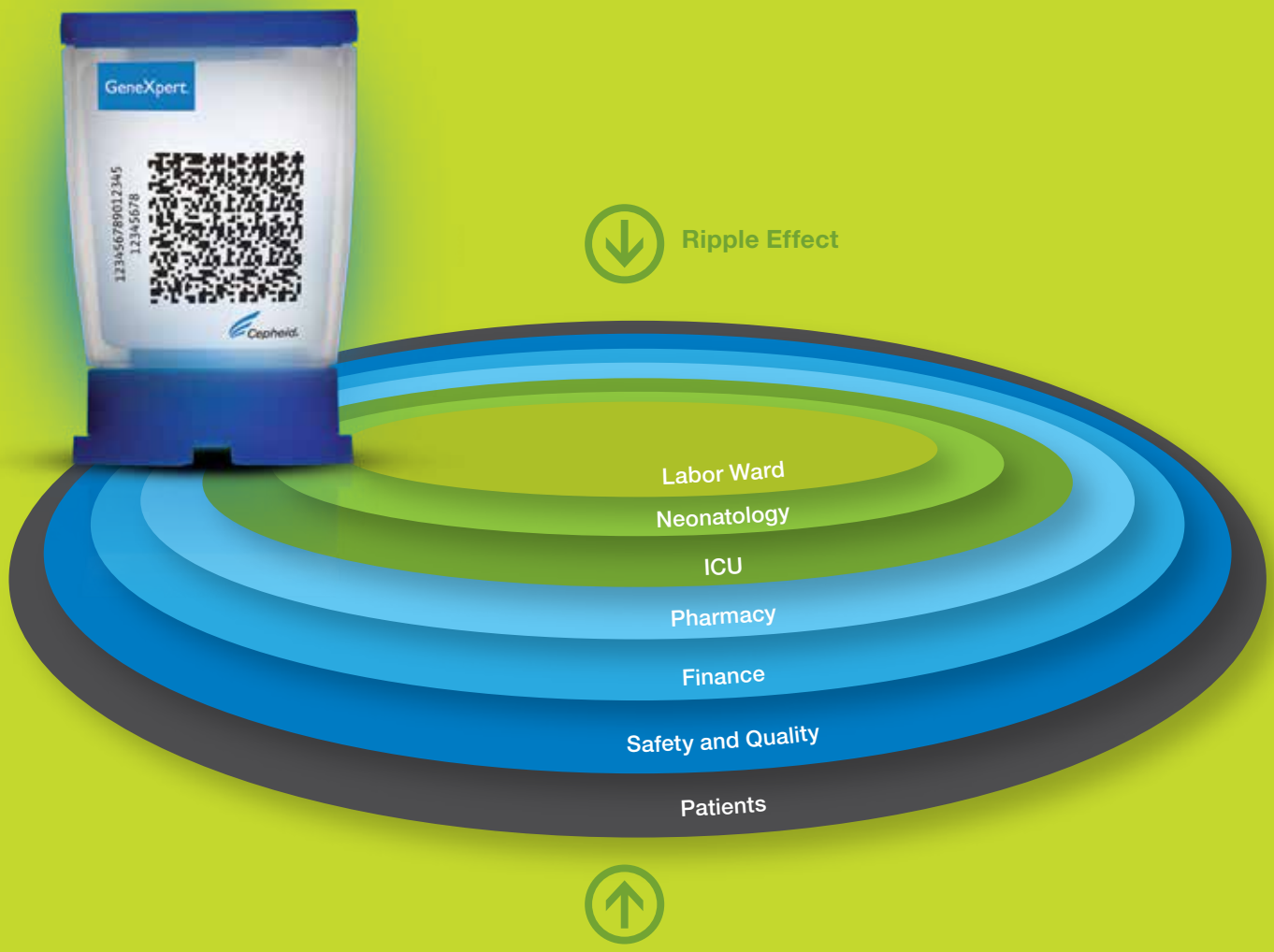
With the intrapartum strategy do you collect vaginal and rectal swabs to test?

We only collect lower vaginal swabs for Xpert GBS intrapartum testing. This is sufficient when a woman is about to deliver normally and it is not necessary to test the rectal swab. In antenatal screening both lower vaginal and rectal swabs are collected to increase the positive predictive value of GBS culture.

How did you convince the various stakeholders to adopt and comply with intrapartum screening?

All the obstetricians were convinced and enthusiastic about the need for intrapartum screening. The midwives were convinced by the results of false positive and false negatives they saw for antenatal screening. Now that our midwives have started using the Xpert GBS test they would be reluctant to go back to antenatal screening. They find it easier to manage patients. They go to the delivery room with the Xpert GBS cartridge in one pocket and a swab in the other ready to perform the test. All our delivery rooms have a chart with the PCR results and IAP status listed. Not only is this easier for the midwives, they feel empowered and confident that they are making the right choices for their patients and newborn babies.

VIEW WEBINAR: http://cepheidimpact.com/workshop-series.php



1 Agence Nationale d'Accréditation et d'Evaluation en Santé. Antenatal prevention of the risk of early neonatal bacterial infection. Clinical practice guidelines. September 2001:1–10.

2 Diagnostic Accuracy of a Rapid Real-Time Polymerase Chain Reaction Assay for Universal Intrapartum Group B *Streptococcus* Screening. *El Helali et al.*, CID 2009:49, 417-423.

3 Cost and Effectiveness of Intrapartum Group B *Streptococcus* Polymerase Chain Reaction Screening for Term Deliveries. *El Helali et al., Obstetrics and Gynecology* 2012:119 N°4, 822-829.

The *C. difficile* Challenge

A Typical Patient Pathway

CONTRIBUTED BY
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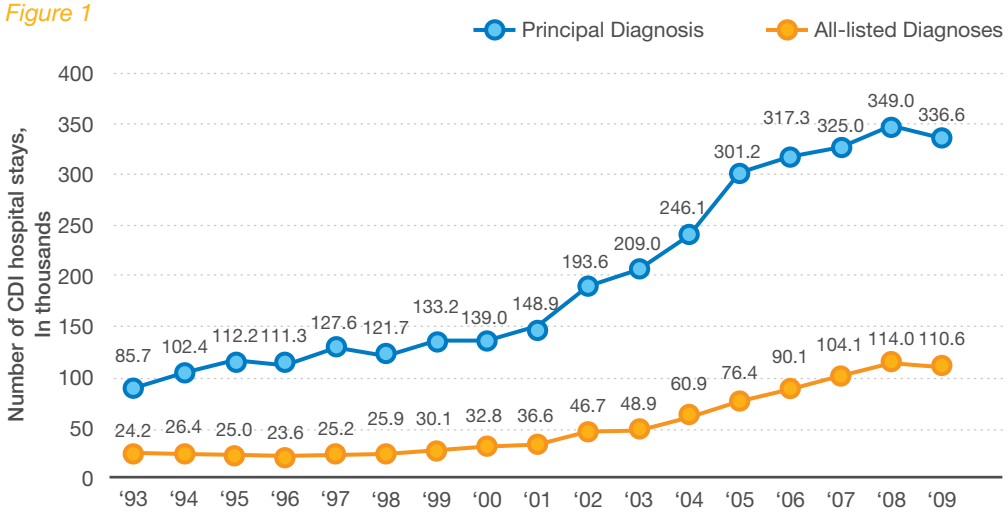
SYSTEMS AND SOLUTIONS MANAGER, CEPHEID

This year the **"superbug"** that continues to challenge our health care systems across the country and around the world is *C. difficile*. The Healthcare Cost and Utilization Project (HCUP) has documented how the average cost to treat a *C. difficile* healthcare-associated infection (HAI) has jumped from approximately $3,600 (2001)[1] to $22,500 (2009)[2] per event, and length of stay (LOS) from 3 days to 11.5 days. This increase can be specifically correlated with the appearance and spread of a hyper-virulent strain (NAP1/027). At the same time, the rate of CDI stays has also increased, as shown in ***Figure 2***. Translated across the patient population, the number of CDI-related stays has increased four-fold[2].

Trends number of in hospital stays associated with *Clostridium difficile* infections (CDI), 1993–2009

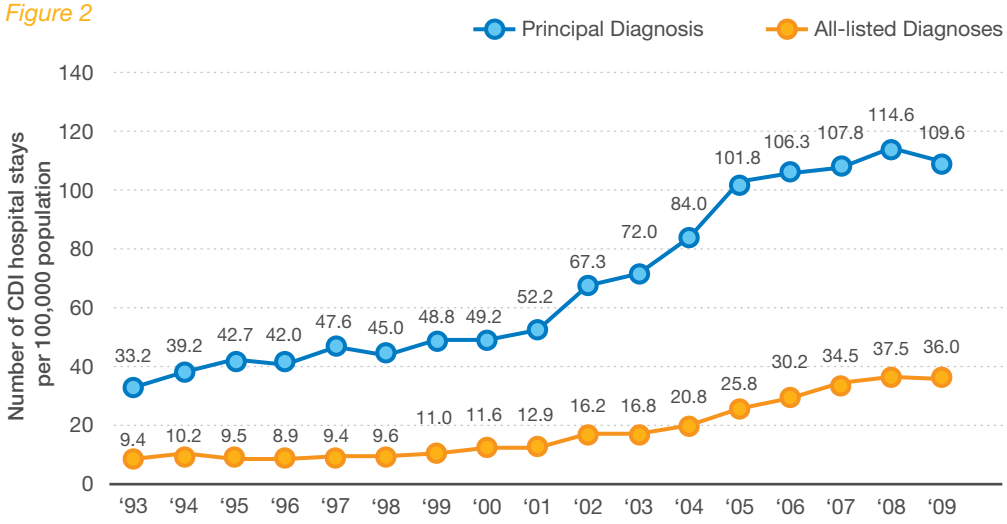
Figure 1



Source: *AHRQ, Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project, Nationwide Inpatient Sample, 1993–2009.*

Rate of hospital stays associated with *Clostridium difficile* infections (CDI), per 100,000 population, 1993–2009

Figure 2



Source: *AHRQ, Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project, Nationwide Inpatient Sample, 1993–2009.*

Committing to Containment/Control

At this year's APIC meeting, the Veterans Affairs (VA) healthcare system announced an increased focus on attaining a zero rate of *C. difficile* infections. The Centers for Medicare & Medicaid Services (CMS) is also targeting CDI as an HAI, and adding it to the list of reportable infections under the Inpatient Quality Reporting (IQR) Program effective January 1, 2013. Healthcare institutions with CDI HAI occurrences could face reimbursement penalties beginning in 2015. And, as those who participate in LinkedIn discussion groups or attend regional/national shows can attest, controlling *C. difficile* infections (CDI) is a constant topic of conversation.

Combatting and controlling the spread of *C. difficile* requires a coordinated effort by multiple departments in the healthcare organization. ***Figure 3*** (see p. 12) illustrates a typical pathway experienced by patient suspected of having *C. difficile*. Guidelines suggest this patient be admitted into a private* room and placed in isolation until his status can be determined. From the Bed Manager's perspective, coordinating this patient generally takes much longer than a non-isolation patient. This can back up the ED (Emergency Department) and slow the health system down.

* "*Private*," meaning either single-bed room or shared room turned private by blocking the additional beds.

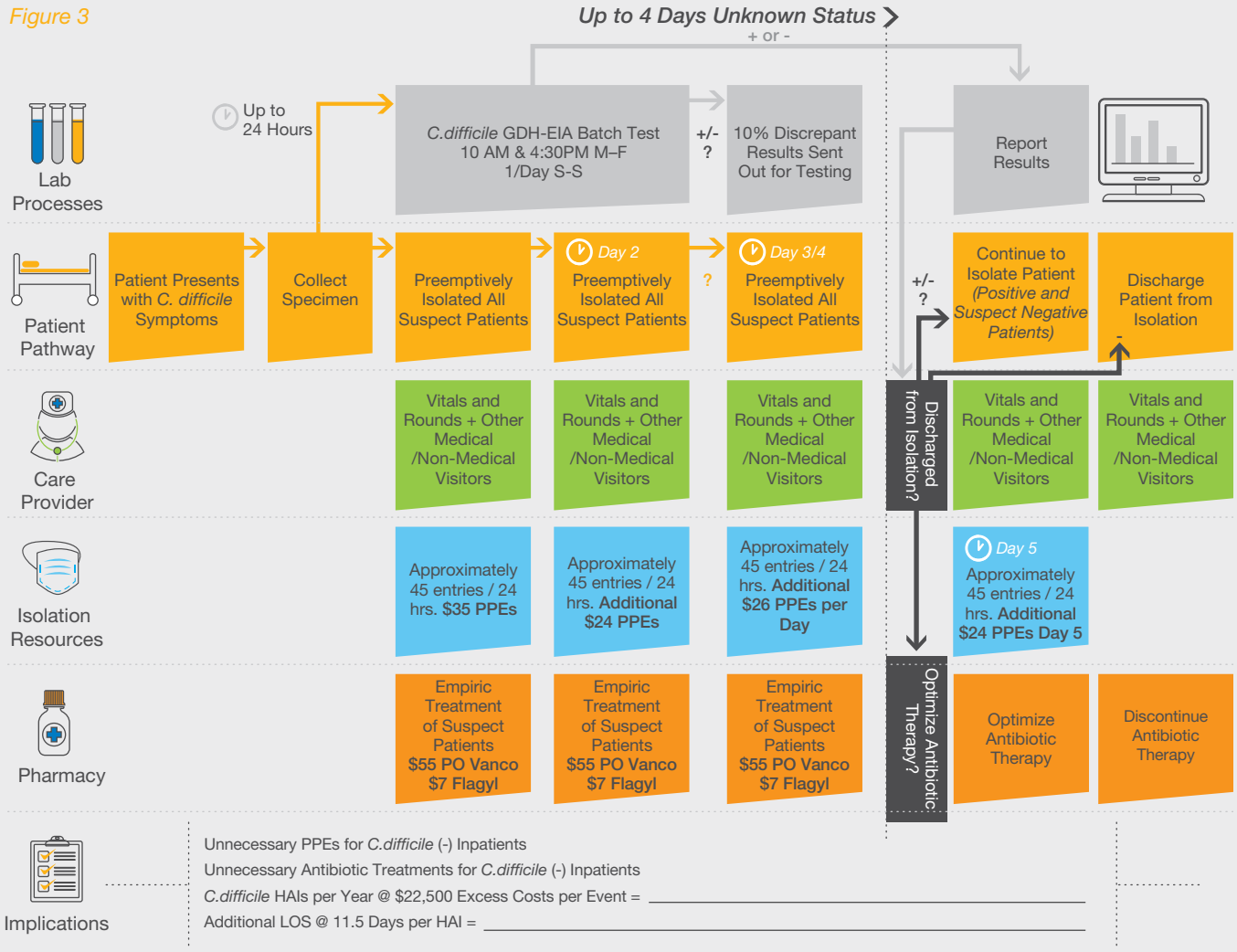
A Typical Patient Path

When the patient is placed in isolation, most hospitals also begin empiric treatment with either metronidazole or PO Vancomycin. Lab results for *C. difficile* tests may not be available for at least a day. Longer waits are possible, depending on the frequency of batch testing, lab not running 7 days per week, and/or sending out for confirmation.

Enzyme immunoassays (EIA) are the most commonly used tests for *C. difficile*. As recently as 2006, 95% of U.S. hospitals were using EIA for *C. difficile* testing. Unfortunately, EIA sensitivity is less than ideal (sensitivity 33%)[3]. The low level of sensitivity reduces the confidence physicians have in negative results, so patients remain in isolation and continue empiric treatment until their symptoms subside. They may also have repeat tests to confirm the presence of *C. difficile*. This not only takes additional time, but adds to the total cost of care.

C.difficile GDH-EIA Workflow

Figure 3

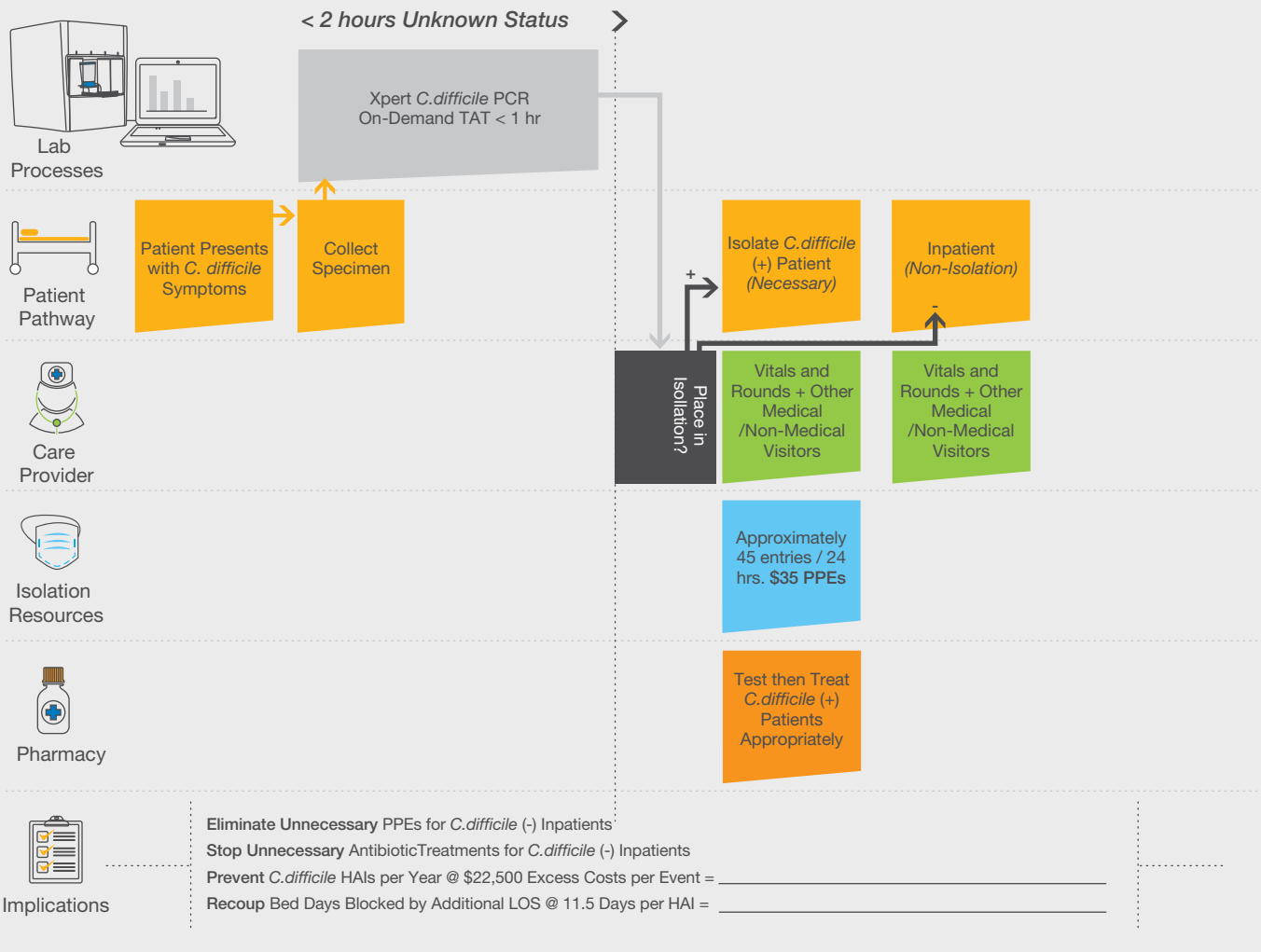


High Transmission Risk Points

Since a majority of patients with suspected CDI are actually negative, hospital staff and visitors are typically not fully compliant in using personal protection equipment. Even one missed case or false negative can ripple outward to other patients, causing comorbidity with new treatment workflow. Another transmission risk is found upon discharge. When patients treated for CDI are discharged, a special terminal clean is performed on the room. The question raised by the EIA sensitivity issue is: How do you clean a room where the patient tested negative for CDI? Was it a true negative? If it wasn't, the next patient will be at risk for contracting a *C. difficile* HAI.

Xpert® *C. difficile* GeneXpert One-and-Done Workflow:

Figure 4



What If You Had Rapid, *Trusted* Test Results?

In looking at how the lab can positively impact the workflow in identifying and treating CDI patients, the questions to ask are:

- What if you could know a patient's *C. difficile* status within 2 hours total TAT, with a highly sensitive and specific PCR assay?
- What if this capability was available 24 hours a day, 7 days a week?
- How would this improve the effectiveness of your treatment, efficiencies in your operations, and reduce unnecessary expense?

Figure 4 (see p. 13) maps out how patients who present at the Emergency Department with CDI symptoms can be immediately tested, with results returned from the lab in less than an hour. True positives (along with NAP1/027 callout) are admitted into isolation and treated as appropriate. Negatives are admitted, diagnosed, and treated as necessary.

For patients who test negative by PCR, unnecessary supplies are not wasted, ineffective antibiotics are not consumed, precious resources are conserved, and clinicians can focus on what is truly ailing the patient. There is a substantial additional benefit of treating the right patients at the right time with the right intervention — the reduction of CDI transmission to other patients. The result: fewer cases of CDI HAI. The costs and risks associated with CDI are increasing. Health professionals are asking what number of CDI HAI cases is realistic and optimal. According to both the CMS and VA, zero is the answer.

How is your organization tackling the *C. difficile* challenge? Let us know, at **cdiffchallenge@cepheid.com.**

> To prevent transmission of *C. difficile,* early detection and isolation of patients with CDI is essential.
>
> ***CDC'S MMWR: VITAL SIGNS: PREVENTING CLOSTRIDIUM DIFFICILE INFECTIONS. MARCH 9, 2012 / 61(09);157–162***

1 Kyne L, Hamel MB, Polavaram R, Kelly CP, Health care costs and mortality associated with nosocomial diarrhea due to *Clostridium difficile. Clin Infect Dis* 2002; 34:346-353.

2 *Clostridium difficile* Infections (CDI) in Hospital Stays, 2009. HCUP Statistical Brief #124, January 2012, p. 4.

3 Tenover, et al. *Journal of Clinical Microbiology*, October 2010, p. 3719-3724, Vol. 48. No. 10

Xperience Cepheid — Everywhere

WRITTEN BY
JARED TIPTON
SENIOR DIRECTOR OF CORPORATE COMMUNICATIONS, CEPHEID

Cepheid is talking mobile. Not the LOL, IMHO, and OMG kind of mobile talk. We're talking road trip here — and our incredible new Mobile Xperience Center. We've taken our entire family of industry-leading GeneXpert® Systems, from the portable GX-I to the high-throughput Infinity-80, and put them into a one-of-a-kind experience on wheels.

Beginning this year, we're bringing our unique story directly to you. Throughout the country, Xperience Center guests will now have the opportunity to interact with Cepheid's most innovative products — right at their institution doorstep.

> The Mobile Experience Center is a major new customer experience," said David Freestone, Executive Director of Systems Marketing. "With the ability to physically interact with our GeneXpert Systems first-hand, customers can see for themselves how our solutions are improving efficiencies and reducing overall costs in healthcare institutions worldwide.

Modern, sleek, and fun, Cepheid's Mobile Xperience Center officially kicked off its North American tour at the 2012 AACC/ASCLS show in Los Angeles this July 17–19. There, the Xperience Center was on full display within Cepheid's booth, where attendees were treated to more than Cepheid's newest GeneXpert Systems.

> For the first six months of our Xperience Center tour, the now-famous Cepheid chopper — designed and built by Paul Jr. Designs for Discovery Channel's American Chopper TV show — will also be on display within our Mobile Xperience Center," continued Freestone. "It will then make way for our new addition to the GeneXpert family, the Infinity-48s, and find a permanent home at our Customer Xperience in Sunnyvale, CA.

If you would like to have the Mobile Xperience Center visit your institution, email us today at: cepheidmxc@cepheid.com. And be sure to follow the Mobile Experience Center at www.cepheidinnovation.com and via Twitter at @CepheidNews.

JOHN BISHOP
CEO, CEPHEID

FACT.

Preventing further complications in patients who develop infections after surgery to replace a knee or hip could save the U.S. healthcare system as much as $65 million annually, according to an analysis presented at the APIC Annual meeting in June.*

FACT.

Rehospitalizations after treatment for Surgical Site Infections add $10–65 million to healthcare costs annually in the United States.*

FACT.

In the APIC study, subsequent rehospitalizations for Surgical Site Infections were associated with an average hospital stay of 8.6 days, costing on average $26,812.*

FACT.

According to the Centers for Disease Control and Prevention, infections develop in about 1 to 3 out of every 100 patients who have surgery.*

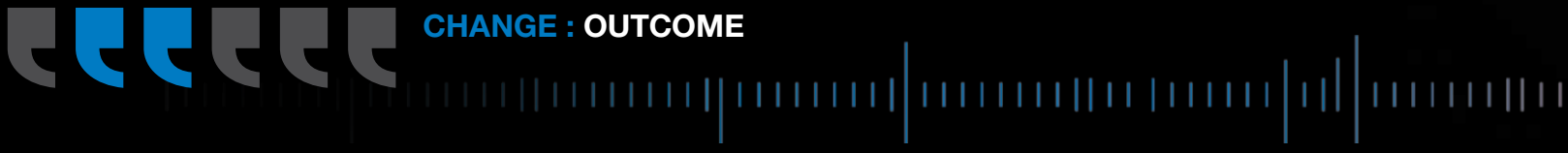
* All Facts from a June 4, 2012 Press Release titled "*Rehospitalizations after treatment for surgical site infections add $10–65 million to healthcare costs: new analysis*" by the Association for Professionals in Infection Control and Epidemiology (APIC)

Excellence in access to innovation and quality are what make the Clinique des Cèdres a pioneer in managing infectious disease risk. Our institution is owned by a group of physicians rather than a private health organization. This gives us the freedom to invest in medically innovative technology, such as our partnership with Cepheid to prevent healthcare-associated infections.

The GeneXpert® Infinity-80 will truly impact our institution by adding medical value. Obtaining rapid results will improve patient management, providing a better control of bacteria transmission and will decrease the patients' length of stay. More importantly, this innovation will enable us to improve the safety of our patients.

DR. GUILLAUME RICHALET

CEO OF THE CLINIQUE DES CÈDRES, ECHIROLLES, FRANCE



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