AACC Better health through laboratory medicine.

Effective POCT Utilization: The Key to Improved Outcomes

John Petersen, PhD, DABCC, FACB, NRCC(CC)
University of Texas Medical Branch (Galveston, TX)
Oscar W. Brown, MD, FAAP
The University of Texas Medical Branch (Galveston, TX)

April 28, 2016

Disclosures

John Petersen: Financial Disclosures

Alere Stock

Research funding from Roche Diagnostics

Oscar (Skip) Brown

None

utmb Health

Objectives

1. Gain insight into POCT testing from the early 80's to the present time.
2. Understand (Gain insight into) the various factors affecting the value of POCT in the clinic setting.
3. Explain why you do not screen for a low prevalence disease using rapid antigen tests.
4. Understand the use of POCT to improve the health of individuals.
5. Understand the goals of POCT program.

utmb Health

UTMB Health System Hospitals

Jennie Sealy Hospital and Children's Hospital

Angleton Danbury Campus

TX Dept. Corrections Hospital

John Sealy Hospital

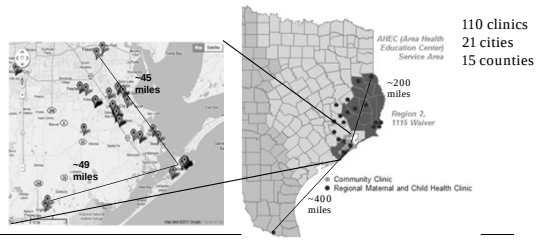
utmb Health

Surrounded by Galveston Bay or Gulf of Mexico
Views from 11th floor Jennie Sealy Hospital

utmb Health

UTMB Health
"small world network"

Statewide Health Care Resource



110 clinics
21 cities
15 counties

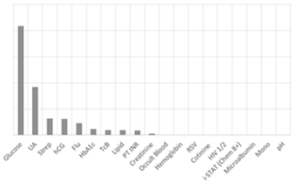
utmb Health

UTMB Health
"small world network"

Moderate Complex Testing

- PPM's
  - UA Microscopic
  - Wet Mount
  - KOH Prep
  - Pin Worm
  - Fern
  - Post-Cotial
- ACT
- AVOX
- VerifyNow (P2Y12)
- Thromboelastograph
- CBC

Waived Testing



POCT oversees 42 CLIA Certificates

- CAP 2
- CLIA 1
- PPMP 26 (TJC)
- Waived 13 (TJC)

utmb Health

POCT Testing Perspectives and Updates

utmb Health

Early POCT Testing & Patient Care

Show your age time--

a. Do you know what a Benedict's Test was used for?

b. Do you own a hemocytometer?

c. Do you actually know how to use a hemocytometer?

utmb Health

Value of the POCT in Practice

- POCT exams have been employed in practice situations for as long as clinical practice has existed. They provide rapid information not obtainable from a clinical exam alone.
- They can vary from highly accurate with excellent reproducibility to others that have been fraught with issues that make them easily suspect.

utmb Health

Modern Era of POCT's

- In the middle 1930's bioassay for pregnancy was developed – not exactly POCT but close
- By the 1960 an HI test for pregnancy was produced and became much more of a POCT. In1966 the first RIA for hCG was developed.
- 1976 saw the E.P.T. (ept) first home pregnancy test- many improvements and increases in sensitivity over ensuing 25 years.

utmb Health

Modern Era POCT's cont'd

- In the early 1980's the appearance of the first commercial Rapid Antigen Detection tests (RADT's) were developed to detect GABHS from throat swabs.
- Almost instant information had a great impact on practice. A. rapid identification and treatment of GABHS reduces spread to others.
- Treatment allows return to school and work and reduces morbidity.

utmb Health

Modern Era POCT's cont'd

- RADT's initially used LA technique, subsequently EIA and OIA techniques have evolved.
- Latest RADT's have progressed to molecular methods – Chemiluminescent ss-DNA probe detecting rRNA sequences unique to GABHS.
- Most recent is one-rapid-cycle, real-time PCR. (not a true POCT)
- Both tests take between 1-2 hours to complete.
- Still some variety of skill issues required for both

utmb Health

Standards

- Standard of Care for GABHS remains the BAP according to many professional best practices.
- Confirmation of the rapid test still needed at this point.
- How much longer will this continue?
- BAP + Rapid test utilization add to the cost of management of a disease that uses otherwise very inexpensive medication/interventions to effect cure.
- Where else does this occur?
- What opportunities exist with newer technology to decrease cost and improve quality of care for patients? Challenge!!

utmb Health

Challenges with evolving POCT

1. Ensuring sensitivity and specificity are adequate to support clinical decisions that produce better outcomes.
2. Encouraging development and utilization of POCT testing so that it does not simply add to cost.
3. Seeking better ways to integrate new technology into the flow of patients in clinical settings. (what works?)
4. Identifying areas of research and development that will substantively add to quality of care with better information to guide intervention(early) and avoid more costly interventions (later) where possible.

utmb HealthHealth

Clinical Opportunities on the Horizon

- Utilization for diagnosis in evolving infectious diseases. (value for obvious public and individual health reasons)
- Application to manage costs(admissions vs observation in O.P. environment)
- Rapid interventions for a variety of diseases increases ability of community health centers to contribute to overall public well-being.
- Potential to contain costly interventions

utmb Health

Clinical Setting Challenges with POCT

- In previous slide notation of patient "through-put" or flow was recognized as a concern with upcoming POCT's - though the information may be superior.
- Challenge: if a POCT becomes available that requires 1 hour or more and has a frequent application of use then patient flow is likely to be sacrificed at times—what is a viable work-around for this? Is this POCT study likely to be widely applied?

utmb Health

Clinical Settings-Challenges cont'd

- Prime feature of any POCT must be rapidity of results along with Specificity and Sensitivity.
- Cost challenge- as practices/systems are more tightly managed for costs simply having results available are not acceptable.
- How the POCT contributes to productivity, efficiency, quality, and patient flow are all of significant value.

utmb Health

The Behind Scenes of POCT?

utmb Health

Things to Consider
(Physician/Provider/Laboratory View Point)

- Pre-preanalytic: What the Provider/Physician/Laboratory must consider:
  - What POCT is available?
  - What POCT will best serve the patient?
  - Will an immediate answer improve or affect the patient's outcome?
- Post-postanalytic: Is the Provider/Physician receptive to using an immediate POCT result?
  - Able to interpret result in the patient's context
  - Amenable to initiating an immediate response
  - Documentation in the patients chart (EMR)

POCT should only be performed if there is a demonstrable benefit (i.e. better outcome)

utmb Health 20

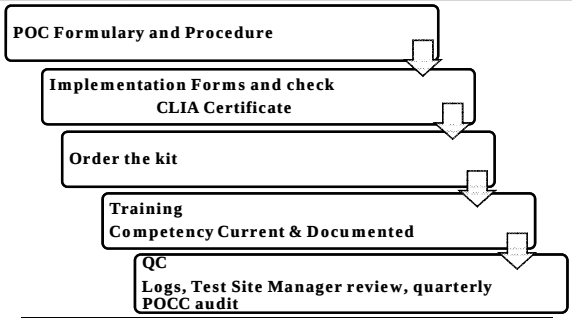
Formulary

Why is a formulary important?

- Regulatory (TJC)
- Identifies what POCT is acceptable in the clinics.
- Standardize
  - Even if you have a lot of tests keep the number of companies per test type to a minimum (one if possible).
  - Training

utmb Health

Implementation Scenario:
You are asked to buy a new POC test...



POCT Management is Complex

- Central Laboratory (one site)
  - Limited instrumentation to perform bulk of testing
  - Limited staff, focused on same equipment
  - Staff trained in laboratory skills
- POCT has dozens of sites, multiple test types, hundreds of devices and a lot (thousands) of operators
  - Regulatory requirements may come from CAP (moderate complexity testing) or TJC (waived testing/PPM).
  - Staff are clinically focused on the patient not on equipment
  - Staff do not have a laboratory training background

POC TEST SITE MANAGERS?

Test Site Manager (TSM):

"Person responsible for oversight of compliance at her/his test site, and to take leadership of operators at that site as well as be the enforcer of QC guidelines. A Test Site Manager is appointed by the Nurse Manager or similar authority, to oversee one or more sites, but less than four."

UTMB POINT OF CARE TESTING PROCEDURES
POLICY - Policy 5.0.87

POCT Quality Management: Implementation, Employee training and Test Site Accountability Effective: 05/00

UTMB POC TSM
Role & Responsibilities

Monthly

- QC LOGS & microscope log are reviewed for completeness, accuracy
- POC TSM sign off on each QC or maintenance log

Maintain 100% competency of staff ; current roster

Update *paper* copy procedures in site binders, or use those online

Document temperature, check proper storage and open/discard dating of reagents/controls

Instrument maintenance performed and documented per manufacturer

Maintain Test Site Manager status (yearly training and annual renewal)

utmb Health

POCT Impact on Patient Management—It's all about TAT! Especially with Diagnosis of Infectious Disease

- Children >2m of age with positive RIT (flu): **decreased additional testing** (CBC, blood cultures, urinalysis, urine culture, CXR), **fewer antibiotics**, **decreased LOS in ED (1)**.
- Infants with positive RIT (flu) had **fewer** blood **tests**, urinalysis, CXR, spinal tap, **shorter LOS in ED**, inpatient care, **antibiotic** treatment (2).
- Adults with positive RIT (flu) had **less antibiotic use**, greater antiviral use (3).

- It's all about sensitivity, since positive results impact management, and specificity.
- But what about false positives which is about specificity?

utmb Health

1. Pediatrics 2003; 112:363-7
2. Pedi Infect Dis J. 2006; 25:1153-7
3. Arch Intern Med. 2007;167:354-60

Sensitivity and Specificity of Rapid Influenza Tests

Specimen Type	Influenza Virus Type Detected	Population [a]	Sensitivity (95% CI) [c]	% Specificity (95% CI) [c]
Throat swab	Influenza A	Pediatric [b]	65 to 90	81 to 91
		Adult	24 to 91	69 to 94
Throat swab	Both Influenza A & B	Not specified	59 to 82	81 to 93
Nasopharyngeal wash/aspirate	Influenza A	Pediatric [b]	82 to 95	98 to 100
		Adult	53 to 87	90 to 100
Nasal wash	Influenza A	Pediatric [b]	36 to 88	92 to 99
		Adult	9 to 99	59 to 100
Nasal wash and aspirate	Influenza A	Not specified	65 to 84	95 to 99
Nasal swab	Both Influenza A & B	Not specified	65 to 87	87 to 97

a. From the U.S., Australia, or New Zealand during seasons where A/H3 and A/H1 were predominant circulating influenza A viruses (derived from WHO Flunet, http://gamapserver.who.int/GlobalAtlas/home.asp)
b. Age range not specified; majority are <10 years
c. 95% Confidence Interval

utmb Health

Source: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/TipsandArticlesonDeviceSafety/ucm109385.htm; Accessed 3/20/2016

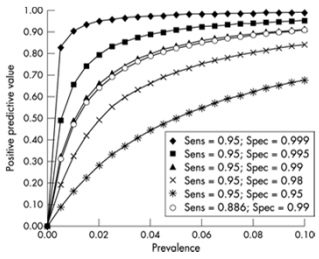
Why Clinical Microbiologists Love to Hate Rapid Influenza Antigen Tests

Poor analytical sensitivity = poor diagnostic sensitivity

- Inherent to assay design (visually reading)
- Influenza A subtype variability

Poor positive predictive value outside of "flu season"

With rare conditions (prevalence), the positive predictive value (PPV) is driven by specificity. This is shown in the attached figure where PPV is graphed vs. the prevalence for increasing specificity values.



utmb Health

Zenilman et al. Sex Transm Infect 2003;79:94-97

Cautions in Using Rapid Tests for Detecting Influenza Viruses

- "When influenza activity is low, (all) positive results should be confirmed…"
- "During peak activity when negative predictive values are lowest, false negatives are more likely…"
- "None of these tests provides any information about influenza A subtypes…"
- "The tests may have lower sensitivity for adults than for children…"

utmb Health

http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/TipsandArticlesonDeviceSafety/ucm109385.htm; Accessed 3/20/2016

Strep A – Why Test

- A sore throat can be mild to severe.
  - When is it "strep" throat?
  - How should you treat it?
  - Why treat?
    - rheumatic fever
    - acute glomerulonephritis
    - Strep toxic shock syndrome
    - Retropharyngeal abscess
  - Proper treatment can get you better faster and prevent spreading to others!
    - Before you treat you need to test.
    - Treatment with antibiotics is only recommended in those with a confirmed diagnosis (remember rapid antigen tests require culture confirmation of negative tests due to sensitivity issues). Those infected should stay away from other people for at least 24 hours after starting treatment.

utmb Health

Ann Intern Med. 2016 Mar 15;164(6):425-34

New Developments in POC Infectious Disease Testing

- Since 2012 two waived instrument-based readers/tests became available for Flu, Strep, and RSV
  - Why would you want to place an instrument in a clinic which takes up space and (potentially) requires maintenance?
    - The use of a reader to determine whether the test is positive or negative removes the user subjectivity and the use of majority rule of multiple nurses to determine whether the test was positive or negative.

What is the problem with these methods?

  - Being rapid antigen tests both still have issues with PPV (Positive Predicative Value) when the disease (flu) prevalence is low.
  - Because of sensitivity both still require culture confirmation for negative Strep A screens.

utmb Health

Newer Developments in POC Infectious Disease Testing

- More recently two waived molecular based tests (isothermal nucleic acid amplification and the other PCR) for Flu and Strep A have become available.
  - Negatives
    - Both are instruments with requires space and maintenance
    - Both are expensive (~ $40-50/test for flu, $20-30 for Strep A)
  - Positives
    - Being molecular assays they are more sensitive and specific for detecting influenza and Strep A than rapid antigen tests.
    - Because of specificity the likelihood of a false positive or false negative result is low which means they are less impacted by the disease prevalence in the community
    - Because of the sensitivity, both may eliminate the need to send negative Strep A tests to the main laboratory for confirmation.
    - Reimbursement is much higher than antigen tests Flu ($115.80) and Strep ($47.76)

utmb Health

Impact of POCT vs. Central Laboratory on Reduction of Mean HbA1c Results

	Time	# Patients	POCT	Central Lab	p-value
Retrospective cohort (1)		1000	7.79%	8.66%	<0.001
Retrospective review (2)	1 yr.	93	Reduction of 1.03% (0.33%)	Reduction of 0.33% (0.83%)	0.04
Retrospective review (3)	1 yr.	4538	7.75% to 7.41%	7.81 % to 7.69%	POCT – 0.001 Central Lab – N.S.
Retrospective Pilot study (4)		69	8.55% to 7.84%		0.004

While this appears that HbA1c is useful in monitoring the treatment of diabetics there are some issues.

1. Clinician must engage the patient at time of clinic visit to ensure that HbA1c results are discussed with patients when generated.
2. The analytical performance of the POCT system is critical.

utmb Health

1. Health Technol Assess 1999; 3:1–74
2. Endocr Pract 2001;7:85–8
3. Diabetes Care 2007;30:713–5
4. Int J Health Care Qual Assur 2008;21:325–35

Are all Waived HbA1c Methods the Same?

The simple answer is NO!

- In 2010 only two waived methods were shown to meet the criteria established by the National Glycohemoglobin Standardization Program (NGSP) acceptance criteria including having a total CV < 3% in the clinically relevant range.
- This was repeated by the same authors in 2014 and four methods were shown to meet the NGSP criteria (although only the two above have been cleared in the US by the FDA)

Can POCT methods be used for diagnosis?

At this time the answer is still NO!

- Proficiency testing is not mandated so consistent quality at the POC is still a question
- They are useful for monitoring

utmb Health

Clin Chem 2010; 56:44-52 Clin Chem. 2014;60:1062-72.

Transcutaneous Bilirubin

- Transcutaneous Bilirubin or TcB is noninvasive and measures the tissue bilirubin by measuring reflected light that has penetrated the skin and subcutaneous tissue. The reflected light corrected for the contribution of Hgb, melanin and dermal thickness, estimates the TcB concentration.
  - Not equivalent to a TSB but it is highly correlated and can be used to screen infants.
  - Useful for screening up to ~14 mg/dL.
  - AAP considers the use of TcB as an acceptable alternative to TSB
    - Why because TSB is an invasive, stressful, time-consuming procedure, and TAT can be from 1 hr. for inpatient to >1 day for out patients
- Studies have evaluated the use of TcB in post delivery hospital stays.
  - One showed that through use of TcB a 34% decrease in blood sampling occurred (1).
  - Another showed that there was a reduction of readmission rate for hyperbilirubinemia when babies are screened for elevated TcB prior to discharge. No difference was noted for TSB measurements, length of stay, nor days of phototherapy treatment (2).
- Universal pre-discharge neonatal screening with TcB measurements has become a common practice throughout the world.

utmb Health

1. Pediatrics 99:599–601; 1997 2. Clin Chem 51:540-44; 2005

Transcutaneous Bilirubin in Outpatient Setting

- Canadian study assessed the impact of universal screening combined with routine follow up in the home or clinic.
  - Used the existing single public health nurse program to insure that every infant born in one of 3 newborn nurseries in Calgary, Canada was assessed by TcB.
  - Using a nomogram that assessed the risk of hyperbilirubinemia vs. age in hrs. the nurses determined if a TcB should be repeated within 24 hrs.
  - Prior to use of TcB measurements visual inspection was used to determine if a TSB was needed.
- Outcome
  - 55% reduction of TSB values > 20 ng/dL.
  - Total number of TSB draws was reduced by 23%.
  - Phototherapy was reduced by 19%.
- While it will be difficult if not impossible to replicate in the US and other parts of the world the study can be used as an example to try and emulate.

utmb Health

Pediatrics 129:77–86; 2012

Impact of POCT PT-INR vs. Central Laboratory

- The use of POCT PT-INR to monitor patient anti-coagulation has been established by a number of studies (1,2) although there are some questions if POCT meters have adequate accuracy to monitor and regulate Coumadin dosages relative to a central laboratory.
- Multiple studies have shown that a systematic approach to anticoagulation management, focused at the point of care, may increase the time patients are in range and reduce the risk of adverse events (3,4).
- In particular, these studies have shown that point-of-care PT/INR testing and anticoagulation management can be more cost effective than traditional medical care. By putting patient, physician, and test results in the same place at the same time, prompt and proper patient evaluation and education can be facilitated (5).

utmb Health

1. J Thromb Haemost 10: 251–260;2012 2. Thromb Haemost 105:1103–05;2011 3. Dis Manage. 2006:4:201-203
4. Ann Pharmacother. 1997:31:604-615 5. Dis Manage Clin Out 2;2000

Oversite of the POCT Program

- Proficiency/Comparison studies in clinics
  - Compare samples sent to clinics (glucose, HbA1c, Hgb, hCG, UA, Creatinine)
  - Send samples to the lab for comparison (PT INR, TcB)
- With EMRs it may also be possible to search for specific POC tests, look at results, ordering physician and location (clinic/dept). This will allow the POCC to identify whether the physician is following protocol. i.e. strep A and whether a neg. rapid antigen test is followed up with culture in the lab.
  - Can determine whether a test such as flu is being run out of flu season. *Remember if there is low prevalence unless the test is 100% specific false positives can and do occur.*

utmb Health

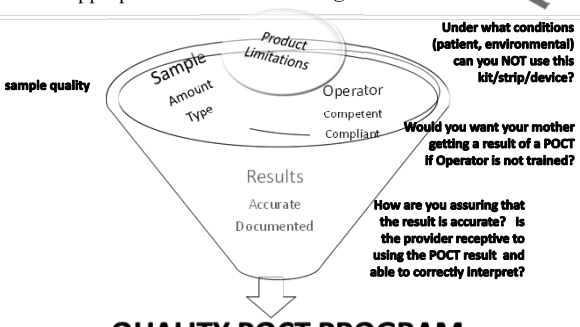
Oversite of the POCT Program

- Proficiency/Comparison studies in clinics
  - Compare samples sent to clinics (glucose, HbA1c, Hgb, hCG, UA, Creatinine)
  - Send samples to the lab for comparison (PT INR, TcB)
- With EMRs it may also be possible to search for specific POC tests, look at results, ordering physician and location (clinic/dept).
  - This will allow the POCC to identify whether the physician is following protocol. i.e. strep A and whether a neg. rapid antigen test is followed up with culture in the lab.
  - Can determine whether a test such as flu is being run out of flu season. *Remember if there is low prevalence unless the test is 100% specific false positives can and do occur.*

utmb Health

Aim of a Quality POC Program

Appropriate Patient Lab Testing & Outcomes



sample quality

Under what conditions (patient, environmental) can you NOT use this kit/strip/device?

Would you want your mother getting a result of a POCT if Operator is not trained?

How are you assuring that the result is accurate? Is the provider receptive to using the POCT result and able to correctly interpret?

QUALITY POCT PROGRAM

utmb Health

40

utmb Health

AACC Better health through laboratory medicine.

Thank you for attending!

Please join Drs. Petersen & Brown in the networking lounge for an online Q&A chat.

Visit the Resource Center to get the CE code for this session.