Approaches to Laboratory Test Utilization: The St. Louis Children’s Hospital Experience

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Outline

• Define Laboratory Test Utilization and why it is important
• Review laboratory test utilization efforts at other institutions
• Review laboratory test utilization at St. Louis Children’s Hospital
• Open Discussion
“The potential number and cost of laboratory examinations in clinical medicine are enormous. Accordingly, it is a considerable responsibility of the physician to choose wisely the laboratory procedures that are to be performed.”

A. 1949

Thomas Hale Ham, MD

B. 1989

NEJM

C. 1999

September 29, 1949

D. 2009
Overutilization is gaining increased attention....

www.preventingoverdiagnosis.net

www.choosingwisely.org
It’s All About the Money

- Healthcare costs in the United States are thought to approach $2.5 trillion per year
- Laboratory and pathology testing accounts for $60 billion (4%) of total healthcare costs
- Experts estimate laboratory costs increasing at a 15% to 25% annual increase.
- Molecular and genetic assays are driving this escalation

All Healthcare
$413.92 pmpm spend
4-5% trend

Outpatient Clinical Lab
$19.80 pmpm spend
8-10% trend

Molecular/Genetic
$3.69 pmpm spend
15-20% Trend
[15% of all Lab]
Changes in Reimbursement

• Length of Stay and Outpatient Testing
  – Incentive: keep the patient in-house

• DRG models (with and without complications) and Outpatient Testing
  – Incentive: decrease LOS and increase outpatient visits

• Value-Based Care Models/Pay-for-Performance
  – Incentive: keep patients healthy
    • Take unnecessary costs out of the system
It’s [not] All About the Money

Patient Safety and Quality!

Overutilization ➔

• Increase chance of irrelevant abnormal, spurious result, preanalytical error
• Over-phlebotomization
• Getting results you don’t know what to do with
Irrelevant ‘abnormals’

- Virtually all quantitative laboratory test ‘normal ranges’ are based on the mean +/- 2 SD (95% confidence interval) for a subject population.

- 5% of normal patients will have values that lie outside this range (magnified for ill patients).
Irrelevant ‘abnormals’

- If a patient has 10 tests ordered, each with a 5% chance that the test may have a result outside the normal range. Then there is a 50% chance that at least one test will have an ‘abnormal’ result.
- This is especially true with ordering chemistry ‘panels’.
Iatrogenic anemia

General Wards: 175 ml/admin

ICU: 762 ml/admin

ICU w/ art line: 944 ml/admin

Smoller et al NEJM 314, 1986
Low et al Chest 108(1) Jul, 1995
Impacts of iatrogenic anemia

• Critically ill patients may not have the bone marrow reserve or erythropoietin drive to compensate for iatrogenic blood loss.

• Transfusion to correct for this anemia has been shown to negatively impact long term survival

• Other risks of phlebotomy:
  – Nerve damage, arterial damage, venous sclerosis, infection
# Confusing Results

The Case of the Over-Screened Baby

<table>
<thead>
<tr>
<th>Newborn Screen Date</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/27</td>
<td>Poor Quality Specimen</td>
</tr>
<tr>
<td>4/29</td>
<td>Abnormal CAH</td>
</tr>
<tr>
<td>5/11</td>
<td>Abnormal fatty acids and organic acids</td>
</tr>
<tr>
<td>5/27</td>
<td>Abnormal PTSH</td>
</tr>
<tr>
<td></td>
<td>Abnormal fatty acids and organic acids</td>
</tr>
<tr>
<td></td>
<td>Abnormal CF screen</td>
</tr>
</tbody>
</table>
Laboratory Test Utilization

• **Good Medicine**

• Strategy for performing appropriate laboratory and pathology testing with the goal of providing **high-quality, cost-effective patient care**

*Lab Medicine Taking an Active Role in Patient Care.*
Reasons for disagreeing (n=4):
- No motivation (25%)
- Test utilization not a role for pathologists (25%)
- Tried but resistance from clinicians so discontinued (50%)
Test Utilization Strategies

- Removing antiquated tests from menus: 83% currently use, 3% used in past but discontinued, 8% never used - not considering, 6% never used - considering using in future.
- Canceling duplicate tests and/or tests ordered within certain time period: 78% currently use, 8% used in past but discontinued, 7% never used - not considering, 8% never used - considering using in future.
- Actively reviewing & requiring pathologist and/or specialist approval for esoteric, expensive and/or other lab tests that are often misused: 59% currently use, 5% used in past but discontinued, 16% never used - not considering, 21% never used - considering using in future.
- Providing guidelines or suggestions for appropriate testing on ordering menus, requisitions or info. systems: 56% currently use, 1% used in past but discontinued, 15% never used - not considering, 28% never used - considering using in future.
- Restricting type of tests offered or displayed in test order menus, requisitions and/or info. systems: 52% currently use, 3% used in past but discontinued, 24% never used - not considering, 21% never used - considering using in future.
- Utilizing diagnostic testing algorithms: 47% currently use, 2% used in past but discontinued, 22% never used - not considering, 29% never used - considering using in future.
- Providing feedback to providers regarding their test utilization practices: 36% currently use, 1% used in past but discontinued, 24% never used - not considering, 39% never used - considering using in future.
- Restricting certain tests to specialists only: 23% currently use, 5% used in past but discontinued, 38% never used - not considering, 34% never used - considering using in future.
- Profiling and comparing providers based on volume and/or types of tests ordered: 17% currently use, 6% used in past but discontinued, 32% never used - not considering, 45% never used - considering using in future.
- Providing cost info. on test ordering menus, requisitions or info. systems: 11% currently use, 3% used in past but discontinued, 46% never used - not considering, 41% never used - considering using in future.
Laboratory Test Utilization at St. Louis Children’s Hospital
Approaches to Lab Utilization

Gentle Guidance

If you could not order that test, that’d be great

M’KAY?

Strong Guidance

No test for you!!
SLCH Hospital Laboratory Utilization Committee (2012)

Proposal: Create a sub-committee of Pharmacy, Diagnostics and Therapeutics Committee for review of lab test utilization

Purpose: Provide physician oversight into laboratory test utilization in order to ensure a quality clinical and diagnostic capability and ensures appropriate utilization of resources

Objectives:

- Ensure appropriate test selection to meet desired clinical data need requirements
- Ensure clinically appropriate utilization (selection and frequency) for clinical laboratory testing
- Identify reference lab testing locations and drive compliance to those laboratories
- Increase use of clinical decision support systems to drive appropriate test selection and utilization to improve resource utilization
- Review new or expanded clinical testing requests
SLCH Laboratory Utilization Committee

Standing Members:
• Laboratory Medical Directors
• Laboratory Administrators
• Finance partner
• SLCH VP of Laboratories
• Chief Resident
• Faculty from GI, Neurology and Genetics

Others invited on ad hoc basis

2012 Deliverable:
• Develop formulary for send out tests
• Develop on-going monitor system for utilization of these tests
SLCH Utilization Management: Send Out Testing

Send out testing is increasing by 1000 tests/year (2009-2011)

2012 budget: $4.4 million

Jan-July 2013: Billed 9.8 million
Utilization Management: Miscellaneous Send Out Testing

• 1/10\textsuperscript{th} of total reference lab volume.
• Represents 2/3 of the total cost of send out testing.
• Average cost/test: $1,421.27 (SD $1,596)

57 Different reference labs were used in 2012
SLCH Laboratory Utilization Committee Meetings

• Introduce the issue
  – How test is currently being utilized

• Provider “homework”
  – What testing is really necessary?
  – What are criteria for the testing?

• Establish a policy

• Once a policy has been established, it is distributed by email and newsletter, and posted on the lab test guidebook online.
Three Core Questions

1) What will you do with the result?
   ➢ If the answer is the same whether the test is normal/abnormal, then the test has little utility.

2) Will the results be available before the patient is discharged?
   ➢ If not, consider ordering as an outpatient

3) Are you chasing diagnostic certainty?
   ➢ How much information do you really need before a treatment is initiated or withheld?
Genetic Testing for Cystic Fibrosis

The problem: different orders going to different reference labs, depending on service

– Full gene sequencing range $1200 to 5000 depending on reference lab
– Mutation panel coverage varies from 27-106 mutations detected
– Mutation panel charges vary from $102-1500

• With new policy:
  1) Mayo 106 Mutation Panel, $102
  2) Full gene sequencing if necessary, $1200
Evaluation of CFTR Algorithm

987 total sweat chloride tests

Positive
(>60mmol/L)
n= 25 (2.5%)

Mutation panel (5/5)

Full gene analysis (3/3)

Mutation panel and full gene (7/9)

redundant result
n= 7

new mutation*
n= 2$

*only listed if pathogenic/potentially pathogenic
$I1618T$ (likely clinically significant) and $E1371X$ (likely clinically significant)
Indeterminate (30-60 mmol/L)  
n= 115 (11.7%)  

- Mutation panel  
n= (7/12)  

- Full gene analysis  
n= (10/12)  

- Mutation panel and full gene  
n= (2/9)  
  - Redundant result  
n= 9  
  - New mutation*  
n= 0  

*only listed if pathogenic/potentially pathogenic  

Full gene sequencing does not provide clinical information  

$25,000
The Exome Challenge

• Expense
  • $7000 to $16000

• Quality
  • Coverage varies by reference lab
  • At least one reference lab includes mitochondrial DNA

• Utility
  • How useful are they, really, for diagnosis and medical decision making?
    • Especially for inpatients
The Exome Challenge: SLCH

• Expense
  • Insurance preauthorization only sought in a fraction of cases
    • Primarily outpatient
  • No preferred lab = no client pricing

• Quality
  • Multiple reference labs being used; selection criteria for reference lab variable

• Utility
  • Unclear in some cases. Sometimes ordered with additional genetic testing
  • Inpatient cases when TAT is 4-6 weeks?
The Exome Problem: SLCH

• Time spent in counseling/consenting patients and families extremely variable
  • Families unaware of the limitations of the test, or of possible unwanted discoveries
  • Families unaware of the cost of the testing

~2%
SLCH: Whole Exome Sequencing

- Selected one reference lab
- All orders through Genetics
- Order genetics consult, provide history and any previous genetic testing for review by genetics counselor
- Insurance pre-authorization/financial plan obtained
- **BEST PRACTICE: Appointment made with patient for counseling, consent, and follow-up. **
  - This is a 45 minute appointment specifically just to counsel the patient and family with what to expect from WES results. They also discuss the cost of the test and what the patient might be responsible for.
- Monthly “Exome Clinic” to accommodate these patients and families
REFERRAL FORM FOR WHOLE EXOME SEQUENCING

Child’s Name: ___________________________ Date of Birth: ___________________________

Parents/Guardians’ Names: ___________________________________________________________

Contact Phone Number(s): ___________________________________________________________

Referring MD: ___________________________ Primary Care Physician: _______________________

Phone: ______________________ Fax: ______________________

To refer a patient for whole exome sequencing, please complete the following:

- Complete this 2 page form in its entirety
- Provide printed copies of the patient’s pertinent medical records:
  - Most recent clinic note from any specialists
  - Radiology reports
  - Previous laboratory studies (e.g. metabolic and biochemical testing, CSF studies)
    - Note: please do not send copies of routine labs such as CBCs and CMPs unless you believe
      they are relevant to the patient’s underlying diagnosis.
  - Other diagnostic studies (e.g. EMG, EEG, muscle biopsy, pathology)
  - Copies of all previous genetic testing reports
- A copy (front and back) of the patient’s current insurance card(s)

Please note that we are unable to schedule the patient for whole exome sequencing until we have received all of
the above in addition to this form. These may be faxed to our office at (314) 454-2075. Attn: Genetic
Counselors, or delivered to our office by hand or campus mail (Marina Vineyard, Campus Box 5116).

☐ Please check this box to indicate that you are requesting a consultation for whole exome sequencing for
this patient and sign below.

Referring physician signature ___________________________ Date ______________________

For Genetics office use only:
☐ Form completed
☐ Printed records received
☐ Insurance card
☐ Other: ___________________________

☐ Insurance approval received
☐ Family notified of out of pocket
☐ Applied for financial assistance program
☐ Appointment scheduled

Basic Information

Have you already discussed whole exome sequencing with the family? ☐ Yes ☐ No

Will both biological parents be available to give blood samples? ☐ Yes ☐ No

If not, please explain: ____________________________________________________________

If not, does the patient have any full siblings or other family members who might be available to
provide a sample? ☐ Yes ☐ No If yes, please list: __________________________________________

Clinical Information

Please list your patient’s main features and most pertinent clinical history, including a summary of any
relevant test results:

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

Do you have any specific genetic diagnoses or genes in mind for this patient? ☐ Yes ☐ No

If yes, please list: _____________________________________________________________

Prior Genetic Testing – Please provide copies of all genetic test reports

Has the patient had chromosome microarray (CMA)? This is required prior to exome sequencing, except in
exceptional circumstances.

☐ Yes, and the results were normal. Please list the year CMA was performed: _______________

☐ Yes, but the findings did not explain the patient’s phenotype.

☐ No, I do not feel it is indicated. Please state reason: _____________________________

☐ No, the patient’s insurance would not cover CMA.

For each genetic test below, please check the box if the test was completed and list the results, if abnormal.

Test
☐ Chromosome/Chromosomes
☐ Fragile X
☐ Epilepsy panel
☐ Prader-Willi/Angelman syndrome
☐ Rett atypical Rett testing
☐ X-linked intellectual disability panel
☐ Other genetic tests:

Abnormal results, including variants of uncertain significance

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________
WES Results

• > 90% compliance with referral form

• Diagnostic hit rate = 40.7%
  – Based on review of first 150 cases sent from WU/SLCH.
  – Calculated by looking at who has a “definitive” mutation that explains the clinical phenotype, according to the interpretation of the results by the reference lab.

• Other published hit rates of 20-25%

Drs. Dustin Baldridge and Marwan Shinawi, manuscript submitted
Genetic Testing in Epilepsy

- Our diagnostic yield for epilepsy was low
- We were sending unnecessary tests
- We were using the wrong panel sent to the wrong lab
- Need a new approach to the “million dollar workup”
CMA Data

• 2900 CMA’s from past 5 years
• Phenotypes of all patients were standardized based on indications on the CMA paperwork
• Manual chart review performed on patients with epilepsy and cardiac problems to further refine phenotypes
SLCH Results – CMA

• 406 patients with epilepsy
  – Diagnostic yield with developmental delay – 27%
  – Diagnostic yield with congenital anomalies – 41%
  – Diagnostic yield with both of the above – 64%

• 102 with isolated epilepsy
  – Diagnostic yield of CMA - 0%
Results – Single Gene Testing

- 32 tests sent for SCN1A, SCN1B, and GABRG2
- Diagnostic Tests: 0
- VUS: 4
- VUS Rate: 12.5%
- Diagnostic Yield: 0%
- Discovered a 3 gene panel was commonly being sent at a cost of greater than $6000.00. This is higher than the cost of any of the larger panels available.
Results - WES

- 62 tests on patients with epilepsy
- Diagnostic Tests: 22
- VUS: 30
- VUS Rate: 48%
- Diagnostic Yield: 35%
- Our diagnostic yield on exome results was near reported ranges from 30 to 40%*

*Helbig, Katherine L., et al. "Diagnostic exome sequencing provides a molecular diagnosis for a significant proportion of patients with epilepsy." Genetics in Medicine (2016).
Proposed Algorithm

Epilepsy

Has one of the following:
- Congenital Anomalies
- Dystrophic Features
- Developmental Delay/Autism
- Or is not old enough to determine if delay is present

YES

CMA

Negative Result

Positive Result

NO

Whole Exome Sequencing

Negative Result

Deletion Duplication
Summary

• Physicians remember the hits, not the losses. Data are convincing.
• Single gene testing has no place in epilepsy.
• CMA is not appropriate for first line testing in isolated epilepsy.
• Larger panels are better.
• The more atypical your phenotype the more likely your result will be found on exome and not on a panel.
Send Out Testing Utilization Management Pilot

• Would doctoral-level review of high-cost reference lab requests be useful at SLCH?

• 6 weeks, M-F

• All requests for miscellaneous reference lab testing reviewed by lab medical director
Most samples were sent within 24 hours
Physicians amenable and cooperative (very few exceptions)
Technicians were on-board and caught on quickly

Utilization Management Pilot Results

4 Weeks (20 Days)

Reviewed Tests
- Total Tests Reviewed = 65
  - Tests approved = 42 (65%)
  - Tests modified = 10 (15.4%)
  - Tests performed sequentially = 5 (7%)
  - Tests canceled = 8 (12%)

Cost Savings
- Total Savings = $20,176.32 (20% of total costs)
  - Cost savings of genetic tests = $16,703.00 (19% of total genetic referral test costs)
SLCH: Send Out Testing Policy

Purpose/Goals:
The goal of this policy is to provide high-quality, cost effective patient care.

Requests which meet the criteria defined below may be selected for utilization management review

Criteria:
1. Tests which cost >$1000
2. Multiple genetic tests on one requisition
3. Requests to send to non-preferred laboratories
4. Requests to send to international laboratories
5. Requests for alternate site testing when the requested test is performed in-house, or for tests ordered outside of LUC-approved algorithms
6. Tests which have limited clinical utility, as identified by the SLCH Laboratory Medical Directors of the Laboratory Utilization Committee. These are listed under the “Policies” tab in the Lab Test Guidebook.
Summary of Lab Utilization at SLCH

• Active Laboratory Utilization Committee in place
  – Recognized by the CMEC, and supported by the Hospital VP over Labs and the CMO
• Established preferred reference labs
  – 57 in 2012 → 24 in 2015
• Protocols and algorithms
  – Physician driven, evidence based
• Basis for a lab test formulary
### Future Tool?

#### LAB UTILIZATION ORDER REVIEW

<table>
<thead>
<tr>
<th>Test</th>
<th>Probability of Positive Test</th>
<th>Actionable</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroperoxidase Antibodies</td>
<td>12%</td>
<td>X</td>
<td>$230.00</td>
</tr>
<tr>
<td>Chromosomal Microarray</td>
<td>3%</td>
<td></td>
<td>$3300.00</td>
</tr>
<tr>
<td>Acylcarnitine Profile</td>
<td>1%</td>
<td>X</td>
<td>$450.00</td>
</tr>
<tr>
<td>NMDA Receptor Antibodies</td>
<td>0.02%</td>
<td></td>
<td>$29,000.00</td>
</tr>
<tr>
<td>GAD65</td>
<td>No Chance in Hell</td>
<td></td>
<td>$450.00</td>
</tr>
</tbody>
</table>

- REMOVE LABS THAT DONT MAKE SENSE
- ORDER
So What’s the Right Answer?

- Clinician Decision Support, Education?
- Limits and Hard Stops?
- Formularies?
- All of the above: lab test formulary, with CPOE tools and open communication with lab medicine partners
- Lab Medicine Involved in Clinical Decisions
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Dennis Dietzen

**The SLCH Lab Utilization Committee**

**PLUGS**
Pediatric Laboratory Utilization Guidance Services
Seattle Children’s Hospital