Examples of how MDs can use informatics to improve clinical care.

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Using informatics tools:

1) Augment clinical decisions
2) Explore clinic-based hypotheses
3) Aid in Quality Assessment
Clinical Dilemma

Setting: Pediatric Intensive Care Unit

Patient: 13 year old female—malar rash, arthritis, nephritis, and auto-antibody profile consistent with systemic lupus.

- Pancreatitis
- Heavy proteinuria
- Anti-phospholipid antibodies
- Vasculitis
- High dose steroids
- Prolonged hospitalization
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- Pancreatitis in adults $\rightarrow$ predisposes to thrombosis
- Heavy proteinuria $\rightarrow$ loss of ATIII (anticoagulant)
- Anti-phospholipid antibodies $\rightarrow$ thrombosis
- Vasculitis $\rightarrow$ predisposes thrombosis
- High dose steroids $\rightarrow$ predisposes thrombosis
- Prolonged hospitalization $\rightarrow$ risk factor for thrombosis.
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Recalled similar patients with these risk factors who had life/organ threatening thrombosis.
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RECALL BIAS
Clinical Dilemma

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- Pancreatitis in adults predisposes to thrombosis
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- Anti-phospholipid antibodies - predisposes to thrombosis
- Vasculitis - predisposes to thrombosis
- High dose steroids - predisposes to thrombosis
- Prolonged hospitalization - risk factor for thrombosis.

Literature Review
- No published studies relevant to case
Clinical Dilemma

Setting: Pediatric Intensive Care Unit

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- Malar rash,
- Arthritis,
- Nephritis,
- Auto-antibody profile consistent with systemic lupus.

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- Anti-phospholipid antibodies → thrombosis
- Vasculitis → predisposes thrombosis
- High dose steroids → predisposes thrombosis
- Prolonged hospitalization → risk factor for thrombosis.

Stanford Pediatric Lupus Database.
- 98 Patients, consented
- IRB → risk factors for morbidity
- Loaded on the STRIDE Data Review Tool
Navigational search methods
Cohort 98 pediatric patients with Lupus: Electronic Search of Patient Medical Records Focused on Risk Factors for Thrombosis Relevant to Our 13-Year-Old Patient with Lupus.

<table>
<thead>
<tr>
<th>Outcome or Risk Factor</th>
<th>Keywords</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome: thrombosis</strong></td>
<td>“Thrombus” “Thrombosis” “Blood clot”</td>
</tr>
<tr>
<td><strong>Thrombosis risk factor</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Heavy proteinuria (&gt;2.5 g per deciliter)</strong></td>
<td>“Nephrosis” “Nephrotic” “Proteinuria” “Urine protein”</td>
</tr>
<tr>
<td>Present anytime (n=36)</td>
<td></td>
</tr>
<tr>
<td>Present for &gt; 60 days (n=23)</td>
<td></td>
</tr>
<tr>
<td><strong>Pancreatitis (n=8)</strong></td>
<td>“Pancreatitis” “Lipase”</td>
</tr>
<tr>
<td><strong>Antiphospholipid antibodies (n=51)</strong></td>
<td>“Aspirin”</td>
</tr>
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Cohort 98 pediatric patients with Lupus: Electronic Search of Patient Medical Records Focused on Risk Factors for Thrombosis Relevant to Our 13-Year-Old Patient with Lupus.

<table>
<thead>
<tr>
<th>Outcome or Risk Factor</th>
<th>Keywords</th>
<th>Prevalence of Thrombosis</th>
<th>Relative Risk (95% CI)</th>
</tr>
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<tr>
<td><strong>Outcome: thrombosis</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>“Thrombus”</td>
<td>10/98 (10%)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>“Thrombosis”</td>
<td></td>
<td></td>
</tr>
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</tr>
<tr>
<td>Present anytime (n=36)</td>
<td>“Proteinuria”</td>
<td>8/36 (22%)</td>
<td>7.8 (1.7–50)</td>
</tr>
<tr>
<td>Present for &gt; 60 days (n=23)</td>
<td>“Urine protein”</td>
<td>7/23 (30%)</td>
<td>14.7 (3.3–96)</td>
</tr>
<tr>
<td><strong>Pancreatitis (n= 8)</strong></td>
<td>“Pancreatitis” “Lipase”</td>
<td>5/8 (63%)</td>
<td>11.8 (3.8–27)</td>
</tr>
<tr>
<td><strong>Antiphospholipid antibodies (n= 51)</strong></td>
<td>“Aspirin”</td>
<td>6/51 (12%)</td>
<td>1.0 (0.3–3.7)</td>
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</tbody>
</table>
Many physicians take great pride in the practice of evidence-based medicine. Modern medical education emphasizes the value of the randomized, controlled trial, and we learn early on not to rely on anecdotal evidence. But the application of such superior evidence, however admirable the ambition, can be constrained by trials’ strict inclusion and exclusion criteria — or the complete absence of a relevant trial. For those of us practicing pediatric medicine, this reality is all too familiar. In such situations, we are used to relying on evidence at Levels III through V — expert opinion — or resorting to anecdotal evidence. What should we do, though, when there aren’t even meager data available and we don’t have a single anecdote on which to draw?

We recently found ourselves in such a situation as we admitted to our service a 13-year-old girl with systemic lupus erythematosus (SLE). Our patient’s presentation was complicated by nephrotic-range proteinuria, antiphospholipid antibodies, and pancreatitis. Although anticoagulation is not standard practice for children with SLE even when they’re critically ill, these additional factors put our patient at potential risk for thrombosis, and we considered anticoagulation. However, we were
EMR Data - Use in Clinical Decisions

WARNINGS:
1) Selected cohorts must be rigorously established.
2) Risk factors & outcome variables must be verified by reading the context in the EMR.
3) The patient’s case and the data must be reviewed and debated by a team of doctors who have insight into the case, potential confounders, & limitations of the database & EMR data.
Perspective

Evidence-Based Medicine in the Era of Post-Stride

Jennifer Frankovich, M.D., Christopher A. Longhurst, M.D., and Scott M. Mehlman

Many physicians take great pride in the precision and value of the randomized, controlled trial, and we are taught that such evidence, however admirable the ambition, can be misleading in the complete absence of a relevant trial. For those of us practitioners of evidence-based medicine, this is familiar. In such situations, we are used to relying on evidence at Levels III through V when we can find it. But what do we do when there isn't even meager evidence on which to draw?

We recently found ourselves in such a situation as we admitted to our service a 13-year-old girl with systemic lupus erythematosus (SLE). Our patient’s presentation was complicated by nephrotic-range proteinuria, antiphospholipid antibodies, and pancreatitis. Although anticoagulation is not standard practice for children with SLE even when they're critically ill, these additional factors put our patient at potential risk for thrombosis, and we considered anticoagulation. However, we were

WARNING: Never use STRIDE based research to make clinical decisions.
Radiological Finding-
Incidental or Meaningful?

Term newborn, hypotonia, feeding difficulties, movement disorder and seizures.

– “Lenticulostriate Vasculopathy” on the head ultrasound (considered an incidental finding).
The lenticulostriate arteries
→ supply basal ganglia, thalamus, germinal matrix

Indistinct from brain parenchyma head ultrasound, in most infants.
→ Why is it visualized in 3%-5% of head ultrasounds?
Lenticulostriate Vasculopathy
Incidental or meaningful?

Results:
4770 infants with head ultrasound of which 95 terms relating to Lenticulostriate Vasculopathy

**LSV was associated with the following outcomes:**

- “Congenital Hypotonia” or “Persistent Hypotonia”  **RR 2.4 (1.03-5.5)**
- “Truncal Hypotonia”  **RR 3.6 (1.5-8.1)**
- “Uncoordinated Suck” “Abnormal Suck” or “Swallow Dysfunction”  **RR 3.0 (1.3-6.8)**
- Abnormal Involuntary Movements & Movement Disorders (ICD 9 codes)  **RR 2.8 (1.2-6.3)**
- Newborn Convulsions/Seizures  **RR not signif**
Parents/patients can solve medical mysteries too!
Can we use informatics tools to answer parent/patient questions?

Patient = 8 yo boy with arthritis, flare in his uveitis when nasal allergies worsen
Parents/patients solve medical mysteries too!
Can we use informatics tools to answer parent/patients questions?

Patient= 8 yo boy with arthritis, flare in his uveitis, when nasal allergies worsen

Cohort= Juvenile arthritis (ICD 9 codes)
Outcome= Uveitis (ICD 9 codes)
Primary predictor= nasal allergy medications
Parents solve medical mysteries too!
Can we use informatics tools to answer parent questions?

Patient = 8 yo boy with arthritis, who has a flare in his uveitis every time his nasal allergies worsen

Cohort = Juvenile arthritis (ICD 9 codes)
Outcome = Uveitis (ICD 9 codes)
Primary predictor = nasal allergy medications

<table>
<thead>
<tr>
<th>Age 0-18yo</th>
<th>Total number</th>
<th>Relative risk of chronic uveitis</th>
<th>Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall JIA</td>
<td>1120</td>
<td>1.804</td>
<td>1.007-3.205</td>
</tr>
<tr>
<td>Pauciarticular &amp; monoarticular JIA</td>
<td>520</td>
<td>1.2</td>
<td>0.615-2.286</td>
</tr>
<tr>
<td>Polyarticular JIA</td>
<td>735</td>
<td>2.245</td>
<td>1.219-4.105</td>
</tr>
<tr>
<td>Spondyloarthropathy &amp; psoriatic arthritis</td>
<td>405</td>
<td>4.786</td>
<td>1.508-15.169</td>
</tr>
</tbody>
</table>
Select patients with juvenile idiopathic arthritis (JIA) ICD-9 codes (N = 834)

Clinical Data Warehouse

Select patients with chronic uveitis ICD-9 codes (N = 105)

A priori restrictions include age <= 18 years and year of diagnosis after or including 2000

Has a mention of juvenile arthritis terms in clinical notes?

Yes (N = 610)

JIA patients (N = 568)

JIA patients with uveitis (N = 42)

Uveitis patients (N = 34)

No

Exclude

No

Has a mention of uveitis terms in clinical notes?

Yes (N = 76)

Not considered in analysis

1:5 match of JIA + uveitis patients (N = 42) to JIA patients without uveitis (N = 210)

Mine clinical notes annotated with text analysis pipeline for hypothesized association

Clinical Data Warehouse

Nigam Shah &
Tyler Cole 2012
Matched on Demographics & clinical notes

Nigam Shah & Tyler Cole 2012
| **Primary Cohort**  
(Juvenile Idiopathic Arthritis) | **Outcome of interest**  
(Chronic Uveitis)* | **Reported & hypothesized patient factors associated with uveitis** |
|-------------------------------------------------|-------------------|---------------------------------------------------------------|
| **Juvenile Arthritis ICD 9 codes**  
696.0, 714.0, 714.2, 714.3, 714.9, 720.2, 720.9 | **Uveitis ICD 9 codes**  
364.00 (acute)*  
364.10 (chronic)* | **Medical status terms in dictated records:**  
ANA positive, positive ANA, psoriasis, allergic, allergy, oligoarticular, oligo-onset, pauciarticular, pauci-onset, monoarthritis, monoarticular, rheumatoid factor positive, rf positive |
| **Terms in dictated reports used to confirm diagnosis of juvenile arthritis:**  
juvenile idiopathic arthritis, jia,  
juvenile rheumatoid arthritis, jra, psoriatic arthritis,  
juvenile spondyloarthropathy,  
enthesitis related arthritis,  
sacroiliitis, reactive arthritis and derivatives | **Terms in dictated reports used to confirm the diagnosis of uveitis:**  
uveitis, iridocyclitis, iritis, and derivatives | **Examples of allergy medications dictated in clinical records:**  
Nasal steroids: Flonase, Nasacort  
Oral Antihistamines: Allegra, Zyrtec, Claritin, Clarinex, Benadryl, Xyzal  
Nasal antihistamines: Astelin  
Leukotriene inhibitors: Singulair  
Decongestant: Sudafed |
Ferritin > 10,000 is 96% specific for the diagnosis of Hemophagocytic Lymphohistiocytosis (HLH). Are we overlooking this diagnosis in our critically ill patients?
Are we overlooking this diagnosis in our critically ill patients?

Hemophagocytic Lymphohistiocytosis (HLH)

AKA Macrophage Activation Syndrome (MAS)

• Multisystem inflammatory disease
• Primary disease or secondary to infection, malignancy, or rheumatic disease.
• Cytokine Storm ➔ hypotention, multi-organ failure
Are we overlooking this diagnosis in our critically ill patients?

Cohort:

age <21 years + ferritin level ≥ 10 K → 45 patients

Jan 2000-Sept 2009

Only 30% of the “Clinical Documents” had one of the following terms.

- Hemophagocytic Lymphohistiocytosis
- HLH
- Macrophage Activation
- MAS
40 patients had ferritin levels >10,000 μg/L + evidence of systemic inflammation + adequate records:

- 18 (45%) had malignancies
- 10 (25%) had rheumatologic diseases
- 5 (13%) had a primary infections/no underlying disease
- 4 (10%) had immunodeficiency
- 3 (7%) other

Only 13 patients (33%) had a documented diagnosis of HLH/MAS.

Are we overlooking this diagnosis in our critically ill patients?
Kaplan-Meier survival probability estimates for patients with ferritin > 10 K

Patients with “recognized” HLH or MAS

Patients with “unrecognized” HLH or MAS
Kaplan-Meier survival probability estimates for patients with ferritin > 10 K and systemic inflammatory diseases

Failure to diagnosis HLH in patients with Ferritin > 10K was a risk factor for death (RR=3.6  95% C.I. 1-13)
Take Home Points & Questions to Ponder

1) Should we analyze EMR data (in disease-specific cohorts) to assist with real-time decision making?
   – Established databases (not based on ICD-9 codes)
   – Verification of variables by reading text
   – Discussion/critique of results, data, and patient situation with a team of experts

• *simulate the review process that occurs with research publication*
2) Should we use EMR data to conduct rapid retrospective case control studies?

- Informatics tools make this form of research more feasible (time efficient) & more reliable (decreases bias) than manual review of charts.

- Hypotheses are often generated by clinicians & patients and this age-old approach may still be an important reservoir for discovery.
Take Home Points & Questions to Ponder

3) Can we use EMR data to uncover associations between an “incidental findings” and patient outcomes?
   - Can “incidental findings” be clues?

4) Should we use EMR data to conduct quality control research?
Strategies in using EMR Data

1) Use creative thinking get at data which may not be in charts
   Ex: Proxies for disease or disease complications can include: medications, procedures, or instruments dictated in surgical reports, etc.
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Proxy may be more reliable than disease itself
Ex: Allergy meds vs. rheumatologist dictating history of allergies
Strategies in using EMR Data

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   Ex: Proxies for disease or disease complications can include: medications, procedures, or instruments dictated in surgical reports, etc.

2) Create and study cohorts based on
   • Unusual pattern of patient symptoms
   • Imaging findings
   • Pathology findings
   • Extreme or unusual lab result
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3) Clinician ↔ Informatics Expert