Healthier Together: Collaborative networks of patients, clinicians and researchers working together to transform care

Peter Margolis, MD, PhD
March 19, 2019

Supported by: NIH NIDDK R01DK085719, AHRQ R01HS020024, AHRQ U18HS016957, PCORI PPRN-1306-01754, PCORI CDRN-1306-015560, CCHMC Learning Networks Program, Clare Foundation, Cystic Fibrosis Foundation
"Our son was diagnosed with Crohn’s last year and was started on Remicade. His trough level has frequently been sub-therapeutic. Our sense is there are multiple possible reasons for this but I imagined you would say most of them are avoidable with the right pharmacologic approach. Have you had any experience with Remicade (infliximab) for therapeutic monitoring?

Seems like an area ripe for work given the cost of the drug and the risks of sub-therapeutic levels. We’d be curious about any thoughts you might have — that might help us and potentially the GI approach to Crohn’s. I’d be interested to meet if you think there are some opportunities to explore."
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Learning Health Systems as Facilitators of Precision Medicine

What If....?
Actor Oriented Network Organizational Structure

• **Actors** with a shared purpose, capabilities and values to self-organize
• Renewable and expandable **commons where actors accumulate and share resources**
• Protocols, processes, and infrastructure that enable peer-to-peer collaboration
Design principles

1. Focus on outcome
2. Build community
3. Effective use of technology
4. Learning system
   - System science, QI, qualitative research, clinical research
Clinical remission rate in CD and UC
PGA = Inactive (Physician Global Assessment)

Improved Outcomes in a Quality Improvement Collaborative for Pediatric Inflammatory Bowel Disease. Pediatrics. 2012;129:1030-41

Centers >75% registered
Replication
Central Hypothesis of a Learning Health System

By eliminating the boundaries between clinical care, research and improvement, and engaging everyone (patients, families, clinicians, researchers) as part of one system......

............we will produce better outcomes and experience for patients and families, faster research, and lower costs
A Learning Healthcare System

Requirements:
1. “link personal and population data to researchers and practitioners,”
2. “provide real-time guidance for superior care in treating and preventing illness”
3. “dramatically enhance the knowledge base on effectiveness of interventions”
4. “actions need to be taken by every stakeholder”
5. “there is no simple path forward” - must be able to change large complex systems
“link personal and population data to researchers and practitioners”

- “Data in once”
- Technology for efficient data capture
“provide real-time guidance for superior care in treating and preventing illness”
QI Reports - Dashboards
QI Reports – Small multiples
Population management
## Patient-level population management

### ICN2 Registry

**ICN2 Registry**

*ImproveCareNow Network*

### Choose Patients to generate PVP reports.

- **Upload Patient List**
- **Generate Report**
- **View Generated Reports**
- **Download All Patients**
- **Download 'Filtered' Patients**

**Total Patients: 206 / Filtered Patients: 49 (clear)**

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# IBD Pre-Visit Assessment

**Patient Name:** Salo, Glennis / MRN: 931139  
**Birth Date:** 5/13/1997  
**Current Age:** 19.8  
**Primary Provider:**  
**Secondary Provider:**

**Diagnosis:** Ulcerative Colitis - 2/2005  
**Extent:** Pancolitis (the entire colon)  
**Severe Disease:** Yes

**Last Visit:** 4/29/2016  
**Wt (kg):** 50.40  
**Ht (cm):** 163.80  
**BSA:** 1.514  
**Date of last hospitalization:** Not Recorded

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*Result date may differ from visit date

**Care Stratification**

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<th>12 Month Disease Activity</th>
<th>BMI Z-Score</th>
<th>Ht Velocity</th>
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Lab ordering guidelines: 5-ASA; q6mo  
6mp/ASA/MTX; q3-4mo  
Biologics; q2-3mo
“actions need to be taken by every stakeholder”

“Bianca Simmons”, age 20

Goals
• Keep symptoms at bay
• Be a leader in the IBD community

• People want to cooperate and to make a difference
• Systems can be designed to allow this
"A Guide to Gutsy Living": Patient-Driven Development of a Pediatric Ostomy Toolkit

Jennie G. David, MS,1 Alexander Jofriet, BS,2 Michael Seid, PhD,1 Peter A. Margolis, MD, PhD,1 for the ImproveCareNow Pediatric IBD Learning Health System
“The chair grant,” as I came to refer to it, seemed to encapsulate the chimera that I was, the fusion of patient and researcher.

It was about not being only a patient or only a researcher, about not thinking that sitting in an infusion chair nullified my worth as a researcher. It was about using the skills I had cultivated as a researcher, tended by thoughtful mentors, to address a problem that I saw and felt as a patient.”
“actions need to be taken by every stakeholder”

- **100%**
  - Awareness
  - Knows of Network

- **90%**
  - Participation
  - Uses tools
  - Signs Consent
  - Reads a blog

- **9%**
  - Contribution
  - Improves Tools
  - Joins QI Team
  - Becomes a mentor

- **1%**
  - Ownership
  - Creates tools
  - Leads a team
“actions need to be taken by every stakeholder”
An Educator
A Learning Healthcare System

Requirements:
1. “link personal and population data to researchers and practitioners,”
2. “provide real-time guidance for superior care in treating and preventing illness”
3. “dramatically enhance the knowledge base on effectiveness of interventions”
4. “actions need to be taken by every stakeholder”
5. “there is no simple path forward” - must be able to change large complex systems
In 2008, the mortality rate during the 4 month period between the 1st and 2nd surgeries was 10-15%.
Reduction in interstage mortality by ~40%

Anderson et al. Circ Qual and Outcomes. 2015;8:428-436
For infants in the NPC-QIC registry, digoxin use after 1\textsuperscript{st} surgery was significantly associated with decreased mortality.

# Discovery and Spread: Changing the Field

## Digoxin and Interstage Mortality

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Without digoxin</th>
<th>With digoxin</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPC-QIC</td>
<td>44/438 (10%)</td>
<td>2/121 (1.7%)</td>
<td>0.003</td>
</tr>
<tr>
<td>PHN (SVR)</td>
<td>28/228 (12.3%)</td>
<td>3/102 (2.9%)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
**Digoxin Use in NPC-QIC**
Anti-TNF Monotherapy vs. Combination Therapy with Low Dose Methotrexate in Pediatric Crohn’s disease

Patients with Moderate-Severe Crohn’s Starting on Biologics

Anti-TNF + Low Dose MTX

Anti-TNF + Placebo

Primary
- Maintenance of Remission

Secondary
- PRO
- Antibodies
- Drug levels

Data Collection for 2 Years

Michael Kappelman, MD, MPH
Personalized Research On Diet in Ulcerative colitis and Crohn’s disease

- Topic identified by research prioritization with families & clinicians
- Study co-designed with patients/families
- Comparison of 2 diets to evaluate impact on symptoms and inflammation IBD
- Uses N-of-1 trial design

Heather Kaplan, MD, MPH
Lisa Opipari, PhD
David Suskind, MD
NASPGHAN
PRODUCE Exhibit
<table>
<thead>
<tr>
<th>Specific Carbohydrate Diet</th>
<th>Liberalized Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meat/fish/poultry, eggs</td>
<td>Expand to rice, oats, potatoes, and cocoa.</td>
</tr>
<tr>
<td>Some beans, fully fermented yogurt</td>
<td></td>
</tr>
<tr>
<td>Non-starchy vegetables,</td>
<td></td>
</tr>
<tr>
<td>Ripe fruit, nuts/seeds, honey and nut flours (e.g. almond flour or coconut flour).</td>
<td></td>
</tr>
<tr>
<td>Restricted:</td>
<td></td>
</tr>
<tr>
<td>• All grains (wheat, barley, corn, rice)</td>
<td></td>
</tr>
<tr>
<td>• Milk products</td>
<td></td>
</tr>
<tr>
<td>• Starchy vegetables</td>
<td></td>
</tr>
<tr>
<td>• Processed foods and sweeteners</td>
<td></td>
</tr>
</tbody>
</table>
Eureka N-of-1 mobile app

- Participant-facing “front end,” an investigator portal, a secure “back end” for data storage and analyses
- App allows:
  - Collection of outcome data
  - Tracking intervention/exposure status
  - Review of collected data in real time
  - Summary of N-of-1 results
- Website allows:
  - Review of data
  - Tracking of upcoming trial tasks
PRODUCE
an N-of-1 Trial

Weeks: 0 2 10 18 26 34 Within 2 weeks

N-of-1 Trial
Results Review
Final Clinical Assessment

Data Collection

Daily: Stool Frequency, Stool Consistency
Weekly: PROMIS Pain, PROMIS GI symptoms, weight, patient reported disease activity measures
Baseline + Each Period: Fecal calprotectin, Diet Adherence
Periodic (ICN Registry): Disease Activity (Clinician Report), Labs

R = Randomized
Patient 1 - Background

- 11 years old with Crohn’s Disease
- Abdominal pain – IDA and elevated CRP and ESR
- Brother with Celiac Disease
- Ileocolonic with small bowel involvement
- Primary GI discussed biologic (Infliximab)
- The family (mother) expressed interest in dietary therapy
- Primary GI recommended to call Nemours dietitian to discuss dietary treatment and refer her as a potential patient for the PRODUCE study
Symptoms normalized during both phases of SCD Diet.
Symptoms worsened on MSCD.
Patient asked not to do final phase of MSCD, due to believing that she had learned that SCD worked better for her.

Fecal Calprotectin Results

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (7/17/18)</td>
<td>2145</td>
</tr>
<tr>
<td>SCD Phase I (9/12/18)</td>
<td>238</td>
</tr>
<tr>
<td>MSCD (10/29/18)</td>
<td>515</td>
</tr>
<tr>
<td>SCD Phase 2 (1/5/19)</td>
<td>469</td>
</tr>
<tr>
<td>Awaiting final stool sample</td>
<td></td>
</tr>
</tbody>
</table>
Networks as a Platform for Research

**Research Capabilities**

- Test innovations (e.g., medication delivery, diagnostics, technology)
- Conduct post-marketing surveillance for adverse events
- Conduct efficacy, effectiveness studies (trials)
- Identify research participants to facilitate study design and recruitment
- Optimize care and intervention use by clinicians and patients
- Engage clinicians and patients to prioritize and design studies

**Real-world comparative effectiveness of interventions, innovations and therapeutics**
Networks offer

3-part engaged social network:
patients, clinicians and researchers

Integrated data-sharing & technology

Support for QI and research:
continuous improvement and learning
Summary

• Network model overcomes some artificial barriers between clinical care, improvement and research
  – System/platform to learn and apply
  – Allows scale and diversity of contribution
  – Self-organizing engaged communities
• Distinguishing characteristics
  – Magnitude and sustainability of impact on outcomes
  – Velocity of change
  – Cost savings
• Culture of generosity and contribution
Structure and Function of Network Components

Clinical Site
- Team (Parent, RN, MD)
- Local IT

Core Operations
- QI Leadership
- IT platform
- Registry
- QI Consultant
- Analyst
- Project Management

Data from every clinical encounter
Tools/techniques

Reports:
- Outcome/Process
- Data quality
- Pre-visit Planning
- Population Management

QI Training/Coaching
Monthly Webinars
Semi-Annual Learning Sessions
Shared best practices

Model for Improvement
- What are we trying to accomplish?
- How will we know that a change is an improvement?
- What change can we make that will result in improvement?

Act
Plan
Study
Do
“enhance the knowledge base on effectiveness of interventions”

- Anti-TNFα for treatment of moderate-severe Crohn’s
- Adult: randomized clinical trial
- Peds: no no-treatment control
- ICN registry data demonstrates effectiveness
# Solutions for Patient Safety

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>ADE ($5,000)</td>
<td>627</td>
<td>$3,135,000</td>
</tr>
<tr>
<td>CAUTI ($1,000)</td>
<td>1320</td>
<td>$1,320,000</td>
</tr>
<tr>
<td>CLABSI ($55,000)</td>
<td>597</td>
<td>$32,835,000</td>
</tr>
<tr>
<td>Falls ($13,000)</td>
<td>1371</td>
<td>$17,823,000</td>
</tr>
<tr>
<td>OB-AE ($3000)**</td>
<td>669</td>
<td>$2,007,000</td>
</tr>
<tr>
<td>PI ($43,000)</td>
<td>432</td>
<td>$18,576,000</td>
</tr>
<tr>
<td>Readmissions ($11,000)</td>
<td>4431</td>
<td>$48,741,000</td>
</tr>
<tr>
<td>SSI ($27,000)</td>
<td>894</td>
<td>$24,138,000</td>
</tr>
<tr>
<td>VAP ($51,000)**</td>
<td>534</td>
<td>$27,234,000</td>
</tr>
</tbody>
</table>

**$173,802,000 Saved**  
**10,206 Children Spared Harm**

* Estimated costs per event: Last updated January 2018  
** No longer measuring OB-AE or VAP. The OB-AE figures above are reflective of cost savings through May 2016, and for VAP, through November 2016.
Ohio Perinatal Quality Collaborative
Decrease in non-medically indicated scheduled deliveries @37-38 weeks gestation
20 maternity hospitals → 108 maternity hospitals
Cost savings of 39-week project

- 3-5% of infants born @ 36-38 weeks gestation are admitted to NICU

- Estimated cost of NICU admission = ~$15,000-24,000 (we used $19,000)
Between September 2008 and March 2016, >58,000 births shifted to term = $33M savings

Since OPQC inception, 58,000 expected births <39 weeks have shifted to ≥39 weeks.

Baseline averages are calculated from the initial 24 months, January 2006 to December 2007.
Between Jan 2014 and April 2018, >9600 infants born exposed to opioids in OPQC database
Neonatal Abstinence Syndrome Protocol

• Pharmacologic Therapy Bundle:
  – Morphine or Methadone
  – Escalate, Stabilize, Wean

• Non-Pharmacologic Bundle:
  – Swaddling, Clothed Cuddling, Quiet Room, Feeding

After 9 months, length of pharmacologic treatment decreased by 9% from 13.4 to 12 days, and the LOS decreased by 9% from 18.3 to 17 days.

Further reductions in LOS following test of non-pharmacologic therapy from 17 to 16.3 days

Total = 2 days reduction in LOS

Preliminary cost-effective analysis of NAS Medicaid claims data

Compared to the period immediately prior to the pharmacologic intervention in the 52 level 2 and 3 NICUs:

– mean total cost of care per case declined by $2632 after the intervention
– median total cost of care per case declined by $861 after the intervention
– cost decline was greatest for the most severe patients
– total length of stay declined by 0.95 days

Impact of additional reduction in LOS (non-pharmacologic) not yet accounted for in these results