Improving Chronic Disease Management with Pieces

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George (Holt) Oliver MD
(for ICD-Pieces Team)

Friday, September 23, 2016
ICD - Pieces: Pragmatic Clinical Trial in Patients with CKD, Diabetes and Hypertension
ICD- Pieces Overview

• CKD, Diabetes and Hypertension
  ◦ Clinical consequences
  ◦ Public health relevance

• Trial Design and Planning
  ◦ Background to clinical trial
  ◦ Challenges and protocol changes

• Early Implementation
  ◦ Trial conduct
  ◦ Milestones
  ◦ Lessons we are learning
Organization ICD - Pieces

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Parkland

Drs. Hedayati and Miller
THR

Drs. Velasco and Myers
VA

Dr. Meehan and K. Pasquale
ProHealth
Multiple Chronic Conditions

CKD

Diabetes

Hypertension

Excessive Cardiovascular morbidity/mortality
Progression to End Stage Renal Disease (ESRD)
Vulnerable populations
Gaps in clinical practice
Public health implications
ICD-Pieces Study Hypothesis

Patients who receive care with a collaborative model of primary care-subspecialty care enhanced by novel information technology (Pieces) and practice facilitators (PF) will have fewer hospitalizations, readmissions, ER visits, CV events and deaths than patients receiving standard medical care.
Specific Aims of ICD-Pieces Trial

- **UH2 – Planning Phase**
  - Establish a Health Care Systems (HCS) Collaboratory
  - Preparation for clinical trial

- **UH3 – Implementation Phase**
  - Conduct a randomized pragmatic clinical trial of management of patients with CKD, diabetes and hypertension
## Diverse Participatory Healthcare Systems and EHRs

<table>
<thead>
<tr>
<th>HCS</th>
<th>Description</th>
<th>Location</th>
<th>EHR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkland</td>
<td>Safety-net public</td>
<td>Dallas County</td>
<td>EPIC</td>
</tr>
<tr>
<td>Texas Health Resources</td>
<td>Private non-profit</td>
<td>North Texas</td>
<td>EPIC/All Scripts</td>
</tr>
<tr>
<td>ProHealth</td>
<td>Private non-profit</td>
<td>Connecticut</td>
<td>All Scripts</td>
</tr>
<tr>
<td>VA North Texas</td>
<td>Federal</td>
<td>North Texas</td>
<td>CPRS</td>
</tr>
</tbody>
</table>
Design ICD-Pieces

- Stratified Cluster Randomization
- Stratum: Healthcare System
- Randomization Unit: Clinical practice (practitioner/site)
- Sites randomized to either ICD-Pieces or standard care group.
- Every patient assigned to a practice receives the same intervention
Study Inclusion Criteria

Subject Inclusion Criteria
Patients 18-85 years of age with coexistent CKD, type 2 diabetes and hypertension.

CKD Inclusion Criteria (present at least \( \geq 3 \) months apart)
Two or more eGFRs less than 60ml/minute \( OR \) two or more positive tests for albuminuria and/or proteinuria
Study Inclusion Criteria

Diabetes Inclusion Criteria

Only patients with type 2 diabetes will be enrolled in this study.

1. Random blood glucose greater than 200mg/dL
2. Hemoglobin A1C greater than 7.5%
3. Use of hypoglycemic agents $OR$ Type 2 diabetes included in problem list

Hypertension Inclusion Criteria

1. SBP greater than 140mmHg on two occasions at least 1 week apart
2. DBP greater than 90mmHg on two occasions at least 1 week apart
3. Use of antihypertensive agents except thiazide diuretics $OR$ Hypertension included in problem list
Outcomes

• The primary outcome:

  1-year hospitalization rate for patients with a triad of CKD, diabetes and hypertension

• The secondary outcomes:

  1) 30-day readmissions
  2) Cardiovascular events
  3) Deaths
  4) Emergency room visits
  5) Disease-specific hospitalizations
  6) Safety events
# Sample Size (revised clusters)

<table>
<thead>
<tr>
<th>Healthcare System</th>
<th>Number of Practices</th>
<th>Number Patients to be Enrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkland Healthcare Systems</td>
<td>25</td>
<td>3,367</td>
</tr>
<tr>
<td>Texas Health Resources</td>
<td>40</td>
<td>3,610</td>
</tr>
<tr>
<td>ProHealth Connecticut</td>
<td>50</td>
<td>3,181</td>
</tr>
<tr>
<td>North Texas VA</td>
<td>9</td>
<td>833</td>
</tr>
<tr>
<td><strong>Total All Sites</strong></td>
<td><strong>124</strong></td>
<td><strong>10,991</strong></td>
</tr>
</tbody>
</table>
Sample size estimate under revised clusters

- Assumption of ICC=0.015 comparing event rate 11% vs. 14% for primary outcome
- Total number of patients to be recruited will be 10,991 patients of 14,425 available patients, which comprises 76.2% (=10,991/14,425)
- Challenges
  - Variations in primary event rates among different HCS
  - Heterogeneity in cluster size
  - Workflows and risks cross-contamination
Regulatory issues (IRBs and Consent)

- Waiver of informed consent obtained from IRB at all sites
- Opt-out option (for intervention and/or use of data) offered to patients in implementation and control groups
- Different methods of Opt-out offered to patients by participating HCS
- Several layers of approval required at some HCS
UH3-Implementation Phase
ICD- Pieces Study Implementation

• What happens in the study?

• How does it happen?

• What has been initial experience?

• What happens next?
What happens in the study?

1. Patients with triad identified
2. Clinicians notified
3. Clinical decision support implemented
4. Monitoring clinical measures → adjustment treatment
5. Electronic ascertainment outcomes
ICD-Pieces Patient Care Work Flow

- **Intervention Group**
  - BP control
  - ACEI/ARBs
  - Statins
  - Glucose control
  - Avoidance hypoglycemia
  - Avoidance NSAIDs
  - Education
  - Immunizations
  - Lifestyle modifications

- **Standard Care**

- **Reports**
  - Status clinical measures
  - Visits

- **Outcomes**
  - All-cause hospitalizations
  - Readmissions, Disease-specific hospitalizations, ER visits, CV events, Deaths

- **PCP**

- **Practice Facilitator**

- Order sets
- Patient reports

- **Pieces**
Study Sites

Pieces™ Connects with Implementation Sites

- ProHealth Physicians
- Parkland
- Department of Veterans Affairs
- Texas Health Resources
- Secure Database
- Southwestern Medical Center
Pieces<sup>TM</sup>

Transitional Care

- Cloud Decision support platform
- Standardizing patient selection with multiple clinical criteria including coded problems, medication and lab based criteria
- Helping identify the right interventions for the right people
ICD-Pieces

Standardized Patient Identification for DM, CKD, HTN

- Using Local Registry or database to store patients selected by centralized selection criteria
- Leverage in house solutions for distributing the candidate patient lists augmented by local source of truth labs/visit dates
- Copy database methods inside VA firewall
- Central study database to aggregated DSMB data and final outcomes
OVERVIEW

6/30/2016 visit with Idigo, Oliaku, RN for Patient Care

SmartSets

- CKD Collaboratory Diabetes Smart Set
- CKD Collaboratory HTN Smart Set

Right click on a SmartSet to add to favorites.

- Discuss best practices with the patient regarding home blood pressure monitoring.
- Ensure that they have a means to measure their blood pressures several times per month and know the appropriate instructions for HOW to measure (i.e. after resting for 5 minutes, legs uncrossed, arm resting on surface, not talking, not having recent caffeine or tobacco, etc...).

Link to CKD Hypertension Protocol

EDUCATION AND LIFESTYLE MODIFICATION REFERRALS

- Referrals

MEDICATIONS:

ACE inhibitors or ARB agents should be considered as first line agents for patients with hypertension and diabetes.

- ACEI/ARB
- Diuretics
Patient Education
Patient Education

For People with Diabetes or High Blood Pressure
Get Checked for Kidney Disease

How well are your kidneys working?

Your GFR result on __________ was __________.
☐ A GFR of 60 or higher is in the normal range.
☐ A GFR below 60 may mean kidney disease.
☐ A GFR of 15 or lower may mean kidney failure.

What is GFR?
GFR stands for glomerular filtration rate. GFR is a measure of how well your kidneys filter blood.

Your urine albumin result on __________ was __________.
☐ A urine albumin result below 30 is normal.
☐ A urine albumin result above 30 may mean kidney disease.

What is urine albumin?
Albumin is a protein found in the blood. A healthy kidney does not let albumin pass into the urine. A damaged kidney lets some albumin pass into the urine. The less albumin in your urine, the better.

Inside a healthy kidney
Inside a damaged kidney

Your blood pressure result on __________ was __________.
Keeping your blood pressure below 130/80 may help to protect your kidneys.
Trust but verify.  
(at least with go live)

Lab based criteria to flag included to build trust

---

Flag Pharma Consult for Jake Smith –

<table>
<thead>
<tr>
<th>Patient</th>
<th>MRN</th>
<th>Confirmed Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith, Joe</td>
<td>M</td>
<td>9/1/2016</td>
</tr>
<tr>
<td>Smith, Jill</td>
<td>L</td>
<td>9/1/2016</td>
</tr>
<tr>
<td>Smith, Jake</td>
<td>H</td>
<td>9/1/2016</td>
</tr>
<tr>
<td>Smith, Jon</td>
<td>L</td>
<td>9/1/2016</td>
</tr>
<tr>
<td>Smith, John</td>
<td>M</td>
<td>9/1/2016</td>
</tr>
<tr>
<td>Smith, Jon</td>
<td>L</td>
<td>9/1/2016</td>
</tr>
<tr>
<td>Smith, Jarred</td>
<td>L</td>
<td>9/1/2016</td>
</tr>
<tr>
<td>Smith, Joel</td>
<td>M</td>
<td></td>
</tr>
<tr>
<td>Smith, Jane</td>
<td>L</td>
<td>9/1/2016</td>
</tr>
<tr>
<td>Smith, Jo</td>
<td>L</td>
<td>9/1/2016</td>
</tr>
</tbody>
</table>
# Use of EHR Data to Generate Safety Reports

<table>
<thead>
<tr>
<th>ICD9 CM</th>
<th>Text Description</th>
<th>ICD10 crosswalk</th>
</tr>
</thead>
<tbody>
<tr>
<td>276.7</td>
<td>hyperkalemia</td>
<td>E87.5</td>
</tr>
<tr>
<td>276.1</td>
<td>hyponatremia</td>
<td>E87.1</td>
</tr>
<tr>
<td>780.2</td>
<td>syncope</td>
<td>R55</td>
</tr>
<tr>
<td>458.0, 458.9</td>
<td>hypotension</td>
<td>I95.*</td>
</tr>
<tr>
<td>995.1</td>
<td>drug toxicity, ANGIOEDEMA</td>
<td>T78.3</td>
</tr>
<tr>
<td>584.9</td>
<td>acute kidney injury</td>
<td>N17.*</td>
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<tr>
<td>251.0-251.2</td>
<td>hypoglycemia</td>
<td>E16.0,E16.1,E16.2,</td>
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<tr>
<td>728.88</td>
<td>rhabdomyolysis</td>
<td>M62.82</td>
</tr>
<tr>
<td>729.1</td>
<td>myositis</td>
<td>M60.9, M60.8*</td>
</tr>
<tr>
<td>276.69</td>
<td>fluid overload</td>
<td>E87.7*</td>
</tr>
</tbody>
</table>
IT Security

Necessary evils: 2Factor authentication, SFTP protocols, VPN

Be kind to in kind partners
Enrollment Status - HCS with active sites

• **Texas Health Resources**
  ◦ Patient registries and alerts operational
  ◦ Active and PF working as member health care delivery team

• **Parkland Health and Hospital Systems**
  ◦ PF: Population Nurse and Nurse Practitioner
  ◦ Registries, alerts and smart sets operational
Enrollment Status - HCS to be active soon

• VA of North Texas
  ◦ Multiple levels approval (IRB, PO, SO)
  ◦ Identified data stays behind VA firewall
  ◦ ICD-Pieces workflow replicated Quality Personnel

• ProHealth
  ◦ New team and governance (acquisition by Optum)
  ◦ Transmission encrypted data
  ◦ Plans for de-identified dataset linked to outcomes
# Enrollment Status Implementation Arm

<table>
<thead>
<tr>
<th>Healthcare System</th>
<th>Target # of Practices/Providers to be Enrolled</th>
<th># of Practices Currently Enrolled</th>
<th>Target # of Patients to be enrolled</th>
<th># of Patients Currently enrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkland Health and Hospital System</td>
<td>13 (out of 25)</td>
<td>3</td>
<td>1684 (3,367)</td>
<td>21</td>
</tr>
<tr>
<td>Texas Health Resources</td>
<td>20 (out of 40)</td>
<td>2</td>
<td>1805 (3,610)</td>
<td>14</td>
</tr>
<tr>
<td>ProHealth of Connecticut</td>
<td>25 (out of 50)</td>
<td>0</td>
<td>1591 (3,181)</td>
<td>0</td>
</tr>
<tr>
<td>North Texas VA</td>
<td>5 (out of 9)</td>
<td>0</td>
<td>417 (833)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total Enrollment</strong></td>
<td><strong>63 (out of 124)</strong></td>
<td><strong>5</strong></td>
<td><strong>5,497 (10,991)</strong></td>
<td><strong>39</strong></td>
</tr>
</tbody>
</table>
Percent of Practices Implementation Group with Actively Enrolled Patients

- Parkland
- Texas Health Resources
- ProHealth
- VA of North Texas

![Bar chart showing the percentage of active and inactive practices across different health organizations.](chart.png)

Legend:
- Green: Active Practices/Total Practices
- Red: Inactive Practices/Total Practices
Progress Reports to NIH and DSMB

1. Primary outcome

2. Secondary outcomes

3. Safety events

4. Recruitment and targets

5. Primary event rates (at each HCS)
Milestones Update

• **Organizational**
  ◦ 2 out of 4 HCS active
  ◦ Steering Committee Sept 27, 2016
  ◦ Workflows with different types of visits

• **Study operation**
  ◦ Practice facilitators (different models) at 4 HCS
  ◦ Protocols developed at all sites

• **Informatics**
  ◦ Patient registries active
  ◦ Capture outcome data and safety events

• **Regulatory**
  ◦ Reports to NIH and DSMB—quarterly
  ◦ IRB updates and renewals
Early Lessons Learned

• Providers
  ◦ Inclusion and exclusion criteria
  ◦ Concerns burden of visits

• Operations
  ◦ Candidates vs confirmed patients
  ◦ Workflows with different types of visits

• Informatics
  ◦ Corrupt files—rapid turnaround and fix

• Regulatory
  ◦ Clarification waiver of consent and opt-out
ICD Pieces - Strengths

- Pragmatic design
- Use of novel technology and EHR
- Unique contribution Practice Facilitators
- Addresses complex chronic conditions
- Diversity health care systems
  - Safety net
  - Integrated
  - Regional providers
  - ACO
- Model for identification and ongoing care patients
- Applications model to other chronic conditions
Study Challenges

- Lengthy approval process protocols
- Multiple stakeholders at all sites
- Concerns about extra “burden” from study
- Ambitious recruitment goals
- Multiple interventions over extended period
- Personnel turnover
- Changing trends standard care
- Risks of cross-contamination control group
- Uncertainties event rates and heterogeneity clusters
- Success depends on collaboration HCS
Next steps

- Initiate recruitment 2 additional HCS
- Extend active study to all recruitment sites
- Review study procedures
- Reports to NIH and DSMB
- Review with CCC (Collaboratory) and Working groups
- Reassess sample size (based on event rates)-contingencies
- Prepare for capture PROs
- Prepare for sustainability interventions and future dissemination
Improving Chronic Disease Management with Pieces