Optimal Strategies for Clinical Decision Support for Geriatrics

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Agenda

• What is Clinical Decision Support (CDS)
• Principles of CDS and how to use
• Examples of different types of CDS in Epic
  – Orders Alerts
  – Order sets
  – Other CDS structures
  – Remote Monitoring
• Interactive quiz on CDS
• Genetic examples
• Presidential Precision Medicine Initiative
Motivation for Health IT

Medicine used to be simple, ineffective, & relatively safe.
Now it is complex, effective & potentially dangerous.

Sir Cyril Chantler
The IOM planted the idea of “learning health care systems” to solve the quality crisis.
Still more than a decade later…

• We are still struggling to achieve the IOM “triple aim”:
  – Improving patient experience (quality & satisfaction)
  – Improving the health of populations
  – Reducing per capita cost
What is a learning health care system?

• The IOM’s vision:
  – Research happens closer to clinical practice than in traditional university settings.
  – Scientists, clinicians, and administrators work together.
  – Studies occur in everyday practice settings.
  – Electronic medical records are linked and mined for research.

• Evidence informs practice and practice informs evidence.
Questions

• How do we make medicine safer for geriatric patients?
• What is Clinical Decision Support (CDS)?
• How can we integrate CDS to support more effective care of Geriatric patients?
Multiple definitions in the literature distills down to
- Patient specific assessments and/or recommendations

The act of providing clinicians, patients, and other healthcare stakeholders with pertinent knowledge and/or person-specific information, intelligently filtered or presented at appropriate times, to enhance health and health care.

(Osheroff, J. AM Med Inform Assoc, 2007)
The three pillars for realizing the promise of CDS.

## Examples of CDS Interventions

<table>
<thead>
<tr>
<th>Area of Care</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preventive care</td>
<td>Immunizations, screening</td>
</tr>
<tr>
<td>Treatment</td>
<td>• Treatment guidelines</td>
</tr>
<tr>
<td></td>
<td>• Drug dosages checking</td>
</tr>
<tr>
<td></td>
<td>• Warnings for drug interactions</td>
</tr>
<tr>
<td>Hospital, provider</td>
<td>Care plans to decrease LOS, order sets</td>
</tr>
<tr>
<td>Follow-up management</td>
<td>Reminders for drug adverse event monitoring</td>
</tr>
</tbody>
</table>
The Main Goal of CDS

- Provide the **right** information
- To the **right** person
- In the **right** manner
- Through the **right** format
- At the **right** point in clinical workflow

With the goal to improve healthcare decisions and health outcomes.

Osheroff, Improving med use and outcomes, HIMSS, 2009
Larger Organizational Goals of CDS

• Detect and prevent safety and quality problems
• Use of evidence-based medicine principles and guidelines
• Operationalize plans of care
• Ensure best clinical knowledge utilized to improve health care decisions

SPECIAL ARTICLE

PROTOCOL-BASED COMPUTER REMINDERS, THE QUALITY OF CARE AND THE NON-PERFECTABILITY OF MAN

Clement J. McDonald, M.D.

Abstract  To determine whether clinical errors can be reduced by prospective computer suggestions about the management of simple clinical events, I studied the responses of nine physicians to computer suggestions generated by 390 protocols in a controlled crossover design. These protocols dealt primarily with conditions managed (e.g., elevated blood pressure) or caused (e.g., liver toxicity) by drugs. Physicians responded to 51 per cent of 327 events when given, and 22 per cent of 385 events when not given computer suggestions. Neither level of postgraduate training (first-year postgraduate or third-year postgraduate) nor the order in which physicians served as study and control subjects had statistically significant overall effect on the results. It appears that the prospective reminders do reduce errors, and that many of these errors are probably due to man’s limitations as a data processor rather than to correctable human deficiencies. (N Engl J Med 295:1351-1355, 1976)

• Controlled crossover design study
• Reduction in clinical errors by computer suggestions
• Nine physicians – served as own controls
• Responded to 51% of CDS messages (327 events) study arm vs. 22% (385 events) in control arm
Evidence of CDS Effectiveness

- Evidence from systematic reviews
  - **Computer-generated** CDS as part of clinician workflow provided automatically at the **point-of-care** with **recommendations** significantly improved care quality in 94% of systems having these qualities *(Kawamoto, BMJ, 2005)*
  
  - **CDS improved health care process measures in prevention services** (OR= 1.42), ordering clinical studies (OR=1.72), and prescribing therapies (OR=1.57) *(Bright, Annals of Internal Medicine, 2012)*
10 Commandments For Effective CDS

1. Speed is everything
2. Deliver information when needed
3. Fit into user’s workflow
4. Improve usability
5. Offer alternatives rather than stopping an action
6. Changing defaults such as dose, route, or frequency can change behavior
7. Fit guidelines to one page
8. Request additional info carefully, less asked, better results
9. Monitor impact – if some reminders never followed, eliminate
10. Maintain knowledge base – update as needed

Characterizing Clinical Decision-Support Systems

• The mode for giving advice
  – *Passive role* - physician uses the system when advice needed
  – *Active role* - the system gives advice automatically under certain conditions
Passive CDS

• The user has total control:
  – Reminds user of potentially clinically active issue with advice in a non action mode
  – User may or may not analyze the advice
  – Users chooses to Accept/Reject the advice
Example of Passive CDS

**VTE Prophylaxis — Required**

- ACCP Guideline | Prevention of VTE in Nonsurgical Patients
- Padua VTE Risk Assessment Model
- Clinical Quality Measures

**VTE Prophylaxis — Required**

- **Patient has either active inpatient order or home medication for an anticoagulant**
- **Please review existing orders and home medications carefully before making selection**
  - Pharmacologic VTE Prophylaxis or Therapeutic Anticoagulation already being provided

- VTE Prophylaxis not clinically indicated as patient is low risk
  - Enoxaparin 30mg SQ daily [Weight 50-150kg + CrCl>30] 30 mg, Subcutaneous, PO
  - Enoxaparin 40mg SQ daily [Weight 50-150kg + CrCl≤30] 40 mg, Subcutaneous, PO
  - Heparin 5000units SQ q8h [Weight 50-150kg] 5,000 Units, Subcutaneous
  - Sequential Compression Device (SCD’s) in lieu of Pharmacologic VTE Prophylaxis
  - Pharmacologic and Mechanical VTE Prophylaxis Both Contraindicated

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RN Flowsheet Captures Discrete Data that Drives BPA

<table>
<thead>
<tr>
<th>Influenza Vaccine Screen - October through March</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you had an influenza vaccine this season?</td>
</tr>
<tr>
<td>[ ] Yes</td>
</tr>
</tbody>
</table>

If YES, verify that Influenza Vaccine has been added in the Immunization Activity.

CONTRAINDICATIONS

1. Previous anaphylaxis or hypersensitivity to eggs
   Verify Egg allergy is added to the Allergy Activity

2. Previous Adverse Reaction to Influenza Vaccine Component
   Verify that Influenza Vaccine Allergy has been added to the Allergy Activity.

3. History of Guillain-Barre Syndrome within 6 weeks after prior flu vaccine

4. Bone Marrow Transplant within the past 6 months

5. Anaphylactic latex allergy
   Verify that Latex allergy had been added to the Allergy Activity.

6. Organ Transplant this hospitalization

7. Patient or agent declines/ refuses vaccine

8. Influenza Vaccine is Out of Stock

Influenza Vaccine Indications

- Age 6 months or older: RN to order vaccine
- Unable to determine contraindications: Needs provider review

This section does not need to be completed if patient had contraindication(s) noted above.

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Passive BPA for VTE prophylaxis and Immunizations

- All patients should have (1) venous thromboembolism (VTE) prophylaxis ordered, or (2) a reason documented why VTE prophylaxis was not given. Either order VTE prophylaxis or document the contraindication by selecting the appropriate order below.
  - Open Order Set: VTE Prophylaxis preview
  - Venous Thromboembolism Prophylaxis

- Nurse has indicated that a provider should decide whether to give pneumococcal vaccine to this patient.
  - Add to unsigned orders: Reason for not ordering pneumococcal vaccine
  - Add to unsigned orders: pneumococcal (PNEUMOVAX-23) vaccine
  - Indications for pneumococcal vaccination (UpToDate)

- Nurse has indicated that a provider should decide whether to give influenza vaccine to this patient.
  - Add to unsigned orders: flu vaccine 2014-15 injection
  - Add to unsigned orders: Reason for not ordering influenza vaccine

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Active CDS

• The user has partial control
  – System gives advice in an interactive manner
  – User evaluates the advice
  – The user required to either accept or reject the advice
    • Options of
      – Soft stop
      – Hard stop
## Anticoagulation for VTE example

<table>
<thead>
<tr>
<th>Weight</th>
<th>CrCl&lt;30</th>
<th>CrCl&gt;30</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50kg</td>
<td>Heparin 5000 q12h</td>
<td>Heparin 5000 q12h</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enoxaparin 30mg daily</td>
</tr>
<tr>
<td>50-150kg</td>
<td>Heparin 5000 q8h</td>
<td>Heparin 5000 q8h</td>
</tr>
<tr>
<td></td>
<td>Enoxaparin 30mg daily</td>
<td>Enoxaparin 40mg daily</td>
</tr>
<tr>
<td>&gt;150kg</td>
<td>Heparin 5000 q8h</td>
<td>Heparin 7500 q8h</td>
</tr>
<tr>
<td></td>
<td>Enoxaparin 40mg daily</td>
<td>Enoxaparin 40mg q12h</td>
</tr>
</tbody>
</table>
**Base Appearance**

Pt without weight/renal function

<table>
<thead>
<tr>
<th>VTE Prophylaxis — <em>Required</em></th>
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<tr>
<td>**ACCP Guideline</td>
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<tr>
<td><strong>Padua VTE Risk Assessment Model</strong></td>
</tr>
<tr>
<td><strong>Clinical Quality Measures</strong></td>
</tr>
<tr>
<td><strong>VTE Prophylaxis — <em>Required</em></strong></td>
</tr>
<tr>
<td>- VTE Prophylaxis not clinically indicated as patient is low Risk</td>
</tr>
<tr>
<td>- Enoxaparin 30mg SQ daily [Weight 50-150kg + CrCl&lt;30 OR Weight &lt; 50kg + CrCl&gt;=30]</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
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<tr>
<td>- Pharmacologic and Mechanical VTE Prophylaxis Both Contraindicated</td>
</tr>
</tbody>
</table>

Same Pharmacologic Agents that were in our prior clinical content
Dynamic Order Set for Weight < 50kg, Normal Renal Function on Warfarin

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<td>**VTE Prophylaxis — <strong>Required</strong></td>
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</table>
| **Patient has either active inpatient order or home medication for an anticoagulant** **
| **Please review existing orders and home medications carefully before making selection** **|
| | Pharmacologic VTE Prophylaxis or Therapeutic Anticoagulation already being provided |
| | VTE Prophylaxis not clinically indicated as patient is low Risk |
| **Enoxaparin 30mg SQ daily [Weight 50-150kg + CrCl<30 OR Weight < 50kg + CrCl><=30]** |
| 30 mg, Subcutaneous, Daily |
| **Heparin 5000units SQ q12h [Weight <50kg]** |
| 5,000 Units, Subcutaneous, Every 12 hours |
| Sequential Compression Device (SCD's) in lieu of Pharmacologic VTE Prophylaxis |
| Pharmacologic and Mechanical VTE Prophylaxis Both Contraindicated |

Heparin 5000 q12h
Dynamic VTE Order set for Weight >150kg + CrCl>30

Higher Dose Heparin 7500 q8h
Enoxaparin 40mg twice a day
Potential Benefits of CDS

- Improved patient safety
  - Reduction in medication errors
  - Enhancing prescribing behaviors
- Improved quality of care
  - Increased application of clinical guidelines
- Improved efficiency in healthcare delivery
  - Reduction in test duplication
  - Using cheaper generic brands of drugs

Coiera, 2003
<table>
<thead>
<tr>
<th>Goal</th>
<th>CDS Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Order VTE prophylaxis</td>
<td>Mandatory that physicians order something</td>
</tr>
<tr>
<td>Order correct antibiotics for pneumonia</td>
<td>Recommended orders with text guidance</td>
</tr>
<tr>
<td>More accurately describe severity of illness</td>
<td>Disease-specific note templates for assessment &amp; plan</td>
</tr>
<tr>
<td>Improve safety of anti-diabetic drugs related to npo status</td>
<td>Standardized, defaulted comments</td>
</tr>
<tr>
<td>Restrict usage of highly-concentrated insulin to specially-trained providers</td>
<td>Hard stop with descriptive text</td>
</tr>
<tr>
<td>Remove bladder catheter sooner</td>
<td>Default settings in order (next slide)</td>
</tr>
<tr>
<td>Improve selection of correct “step” of alcohol withdrawal pathway</td>
<td>Move guidance text out of hyperlinked reference into order set (in 2 slides)</td>
</tr>
<tr>
<td>Encourage prescribers to check NC narcotic-prescription database</td>
<td>Insert hyperlink into pain control meds &amp; order sets (being considered)</td>
</tr>
</tbody>
</table>
# Types of CDS

<table>
<thead>
<tr>
<th>Warnings Or Recommendations at Order Level</th>
<th>Order Sets/Smart Sets</th>
<th>Other Structures Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best Practice Alerts (BPA) Pop Up</td>
<td>Required Orders</td>
<td>Questions/Indications</td>
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<td>• Order Validation Alert</td>
<td>Hyperlinks</td>
<td>Available Frequencies</td>
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<tr>
<td>• Alternative Alerts</td>
<td>Design/Architecture</td>
<td>Order Panels</td>
</tr>
<tr>
<td>BPA In Line / Banner</td>
<td>Suggestion or Recommend an Order Set</td>
<td>Process Instructions</td>
</tr>
<tr>
<td>BPA Silent Alerts</td>
<td></td>
<td>Care Plans</td>
</tr>
<tr>
<td>Health Maintenance Alert</td>
<td></td>
<td>Reporting</td>
</tr>
<tr>
<td>Asynchronous Alert</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CDS with CPOE Medication Ordering

- Drug Allergy Checking
- Basic dosing guidance for medications
- Formulary decision support
- Duplicate therapy checking
- Drug-drug interaction checking
- Advanced guidance with laboratory testing
- Drug-disease interactions and contraindications
- Advanced drug-pregnancy alerting

(Kuperman, et al, 2007, JAMIA)
Medication CDS – Alerts and Reminders

- Allergy/Contraindication: amoxicillin
  - Reactions: Angioedema. No reaction type specified. User documented allergy severity: High. DRUG CLASS MATCH with PENICILLINS.
  - Details
  - Override Reason...

- Allergy/Contraindication: flu vaccine tri 2015-16 (PF) (4yr+)
  - Reactions: Anaphylaxis. No reaction type specified. User documented allergy severity: High. DRUG CLASS MATCH with INFLUENZA VIRUS VACCINES.
  - Details
  - Override Reason...

- High Dose: insulin LISPRO, 1,000 Units, Subcutaneous, Daily with breakfast
  - Single dose of 1,000 Units exceeds recommended maximum of 87.5 Units, over by 1043%.
  - Daily dose of 1,000 Units exceeds recommended maximum of 175 Units, over by 472%.
  - Details
  - Override Reason...

Immediately override all warnings:
- Clinician Reviewed
- Dose Appropriate
- Benefit Outweighs Risk
- Previously Tolerated
- Override All Warnings...
- Override and Accept
- Cancel

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This patient meets the criteria for lung cancer screening. An InBasket message can be sent directly to our Lung Cancer Screening group. Enter additional details as needed. Call 970-XXXX with any further questions.

The following actions were applied automatically:

- Message sent. This advisory has been sent via In Basket
In the Patient Header
<table>
<thead>
<tr>
<th>Warnings Order Level</th>
<th>Order Sets/Smart Sets</th>
<th>Other Structures and Reporting</th>
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<td>• Medication Duplicate Alert</td>
<td>Banners/Instructions Hyperlinks</td>
<td>Diagnosis Association</td>
</tr>
<tr>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
### Order Set CDS

#### Before

**IP Alcohol Withdrawal DUH Pathway**

**General**

- Select most appropriate option:
  - See knowledge base link for navigation between steps

**Alcohol Withdrawal Knowledgebase [DUH]**

- Prophylaxis P.O. (Symptoms/Signs Absent, PMHx or CAGE Positive)
- Prophylaxis I.V. (Symptoms/Signs Absent, PMHx or CAGE Positive)
- STEP 1: P.O. (Symptoms/Signs Stable-Moderate, PMHx or CAGE Positive)
- STEP 1: I.V. (Symptoms/Signs Stable-Moderate, PMHx or CAGE Positive)
- STEP 2: P.O. (Symptoms/Signs Moderate-Severe, PMHx or CAGE Positive)
- STEP 2: I.V. (Symptoms/Signs Moderate-Severe, PMHx or CAGE Positive)
- DTs / Withdrawal Delirium: P.O. (Symptoms/Signs Severe or Acute Confusion/Delirium)
- DTs / Withdrawal Delirium: I.V. (Symptoms/Signs Severe or Acute Confusion/Delirium)

**Labs**

- Baseline Studies (if not already done):
  - Hepatic function panel:
    - Once, Starting 9/4/14
  - Prolactin-INR:
    - Once, Starting 9/4/14
  - Magnesium:
    - Once, Starting 9/4/14

**Medications**

- Additional Medications
  - thiamine (5 days IV followed by PO)
  - Nicotine Patch
  - nicotine polacrilex (NICORETTE) gum

- 2 mg, Oral, Every 1 hour PRN, Smoking cessation

#### After

**Alcohol Withdrawal Pathway (DUH)**

**General**

**Prophylaxis step**

- PMHx or nursing screen positive BUT
- VS normal AND
- No current symptoms (no anxiety, tremor, diaphoresis, etc)

- Prophylaxis (at risk but no signs/symptoms): PO
- Prophylaxis (at risk but no signs/symptoms): IV

**Step 1: Mild withdrawal**

- PMHx or nursing screen positive AND
- VS mildly abnormal (T normal and SBP 140-160 or DBP 90-110 or HR 80-120) AND
  - 2 or more mild symptoms (anxiety, tremor, diaphoresis, nausea)

- Step 1 (mild withdrawal): PO
- Step 1 (mild withdrawal): IV

**Step 2: Moderate withdrawal**

- PMHx or nursing screen positive AND
- VS moderately abnormal (T > 38.3 or SBP > 160 or DBP > 110) AND
  - 2 or more moderate symptoms (anxiety, tremor, diaphoresis, nausea)

- Step 2 (moderate withdrawal): PO
- Step 2 (moderate withdrawal): IV

**DTs / withdrawal delirium**

- PMHx or nursing screen positive AND
- 2 or more VS moderately abnormal (SBP > 160, DBP > 110, HR > 120, T > 38.3) AND
- 2 or more moderate-to-severe symptoms (anxiety, tremor, diaphoresis, nausea) AND
- Confusion, disorientation, hallucination, altered mental status or sensorium, or seizure

- DTs / withdrawal delirium: PO
- DTs / withdrawal delirium: IV
# Padua Score SmartForm

## Padua VTE Risk Assessment Model

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Cancer (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous VTE (3)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Reduced Mobility (3)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Known thrombophillic condition (3)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Trauma or Surgery in last month (2)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Heart or Respiratory Failure (1)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Acute MI or Ischemic Stroke (1)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Acute Infection or Rheumatologic Disorder (1)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Ongoing Hormonal Therapy (1)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Obesity (BMI &gt;= 30) (1)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Elderly (Age &gt;= 70) (1)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Mark Remainder of Above Risk Factors as No

## Risk Assessment

**Padua Risk Score**

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Coming Full Circle to the OrderSet
Restrict / Promote Low Risk Selection

- Preselect LOW RISK if Risk Score Completed and is 0-3
- Restrict LOW RISK if Risk Score Completed and is >=4
- Keep option available if Risk Score Not completed
<table>
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</tbody>
</table>
## Diagnostic Support for Sepsis

![Image of diagnostic support interface for sepsis]

### Vital Signs (Click Report for complete view)

<table>
<thead>
<tr>
<th>Metric</th>
<th>06/08 0700</th>
<th>06/09 0659</th>
<th>06/09 0700</th>
<th>06/09 0953</th>
<th>Most Recent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temp (°C)</td>
<td>37.1 36.6</td>
<td>36.6–37.1</td>
<td>36.6–37.1</td>
<td>37.1 (98.8)</td>
<td></td>
</tr>
<tr>
<td>Pulse</td>
<td>150 78</td>
<td>78–150</td>
<td>98</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>Resp</td>
<td>24 15</td>
<td>15–24</td>
<td>22</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>BP</td>
<td>121 114</td>
<td>114/51–121/63</td>
<td>115/56</td>
<td>115/56</td>
<td></td>
</tr>
<tr>
<td>SpO2 (%)</td>
<td>99 93</td>
<td>95–99</td>
<td>99</td>
<td>99</td>
<td></td>
</tr>
<tr>
<td>NEWS Score</td>
<td>4 0</td>
<td>0–4</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>NEWS Score Change</td>
<td>0</td>
<td>-3</td>
<td>-3</td>
<td>-3</td>
<td></td>
</tr>
<tr>
<td>SIRS Score</td>
<td>2</td>
<td>0–2</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

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Reducing excess days for bladder catheters

<table>
<thead>
<tr>
<th>Prompt</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Indications:</td>
<td>Perioperative, Immobility due to, Urinary retention, Monitoring, Incontinence &amp; Stage 3-4 ulcer, Chronic indwelling (PTA), Comfort care / End of life</td>
</tr>
<tr>
<td>A. Perioperative indications:</td>
<td>Routine- remove by POD 1, Routine- remove by POD 2, s/p urologic procedure, Other procedure (specify)</td>
</tr>
<tr>
<td>Size</td>
<td>Other (specify)</td>
</tr>
<tr>
<td>Collect Sterile Specimen For Lab</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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Pop Up with Required Clinical Action

New Flag
Flag type:

Single Ventricle

BestPractice Advisory - Clindoc_Julie

Cardiac Shunt FYI

Cardiac Shunt FYI
This patient is cardiac shunt dependent. They are fragile and at high risk for Sudden Death. Alert cardiology for all patient encounters. (919) 970-2916. Changes in volume status caused by poor intake or excessive losses can lead to rapid decompensation. Maintain hydration at all times. Rehydrate using enfalyte by NG tube. Review hospital protocols. Any patient who has undergone placement of a Blalock Taussig shunt or Norwood procedure is cardiac shunt-dependent. Please assure this clinical best practice advisory is applicable to this patient at this time.

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Example of Simple to Integrated CDS: Current ASCVD Recommendations

<table>
<thead>
<tr>
<th>Clinical ASCVD (Atherosclerotic Cardiovascular Disease)</th>
<th>Moderate-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-Intensity Statin Therapy</td>
<td>Daily dose lowers LDL-C by approximately 30% to &lt;50%</td>
</tr>
<tr>
<td>Atorvastatin (40 mg)</td>
<td>Atorvastatin 10 (20) mg</td>
</tr>
<tr>
<td>Rosuvastatin 20 (40)</td>
<td>Rosuvastatin (5) 10 mg</td>
</tr>
<tr>
<td></td>
<td>Simvastatin 20–40 mg</td>
</tr>
<tr>
<td></td>
<td>Pravastatin 40 (80) mg</td>
</tr>
<tr>
<td></td>
<td>Lovastatin 40 mg</td>
</tr>
<tr>
<td></td>
<td>80 mg</td>
</tr>
<tr>
<td></td>
<td>40 mg bid</td>
</tr>
<tr>
<td></td>
<td>Fluvastatin 20–40 mg</td>
</tr>
<tr>
<td></td>
<td>Pitavastatin 1 mg</td>
</tr>
</tbody>
</table>

*Note:* Includes Angina, Ischemic Ears, Other Structures and Reporting.
Current Process for Clinicians

1. Does my patient need a statin?
2. Look up all criteria for 10-year ASCVD risk in EHR
3. Go to AHA Site ASCVD calculator
4. Input each criteria
5. Get risk score, read guideline recommendation
6. Go back into EHR, find correct statin and place order
Risk Score Not calculated for AFib - requires provider to determine the risk themselves

The patient is identified with Atrial Fibr or Flutter
This is a required field. You must select an action taken or acknowledge that no action was taken. Click the Accept button to save your acknowledgement.

Acknowledge reason: □ Pt on anticoagulation
□ Not indicated given low stroke risk
□ High bleeding risk/prior severe bleed
□ Contraindicated secondary to falls, frailty risk
□ Contraindicated secondary to comorbid disease (e.g. thrombocytopenia)
□ Patient declines/refuses
□ Other (see progress note)
☞ Clinical Decision Support guidelines
☞ CHADS VASC2 Calculator
☞ Medical History

Other (1 Advisory)

The patient is due for Health Maintenance. Order the needed immunizations or tests from the SmartSet.

☐ Open SmartSet: Health Maintenance due preview

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The Analytic ASCVD Risk Score requires multiple discrete data components in the EHR.
Using Remote monitoring in tandem with Care Coordination to Improve post discharge CHF management and decrease 30 day readmissions.
Zubin Eapen MD Medical Director
Remote monitoring needs to be coupled with a care delivery model.

**PATIENT DISCHARGE**

**DAY 2**
Patient receives remote monitoring devices

**DAYS 0-30**
Nurses engage patients upon return home. Patients treated in the Same Day Access clinic as needed.

**LONG-TERM ENGAGEMENT**
Remote Monitoring integrated within EHR via Patient Portal

Figure 1. Data Flow.

A) Patient is seen by health provider and consents to study. B) Patient provided with JawboneUp24, Withings wireless scale, iHealth BP cuff, and iPod with Health App. C) The patient selects each health monitor(s) that they would like to allow for integration into HealthKit where through the Health App, they can organize data under one dashboard. D) The provider places a request in EPIC for patient to share their data; the patient, through Health App selects any Health data they would like to share with their physician and sends data to MyChart. This data will then be automatically uploaded to the Duke Epic EMR (Maestro Care). Provider is alerted that data is shared upon opening patient's chart.
Same Day Access Model

- Stable patient
  - Patient decompensates
    - Lack of availability with primary cardiologist
      - Appointment with SDA provider scheduled
        - IV Lasix and electrolyte supplementation
          - Returns to SDA as scheduled in 3 days
            - Primary cardiologist notified
              - Medication regimen adjusted
- Return care to primary provider
Initial 1 month and 1 year Outcomes for CHF readmission

- 115 Patients
- 3 30-day ED visits
- 4 30-day rehospitalizations

(15%) HF readmission rate declined 15% in first year
## Overview of CDS

<table>
<thead>
<tr>
<th>Warnings Or Recommendations at Order Level</th>
<th>Order Sets/Smart Sets</th>
<th>Other Structures Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best Practice Alerts (BPA) Pop Up</td>
<td>Required Orders</td>
<td>Questions/Indications</td>
</tr>
<tr>
<td>• Procedure Duplicate Alert</td>
<td>Conditional Orders</td>
<td>Preference List</td>
</tr>
<tr>
<td>• Medication Duplicate Alert</td>
<td>Banners/Instructions</td>
<td>Diagnosis Association</td>
</tr>
<tr>
<td>• Order Validation Alert</td>
<td>Hyperlinks</td>
<td>Available Frequencies</td>
</tr>
<tr>
<td>• Alternative Alerts</td>
<td>Design/Architecture</td>
<td>Order Panels</td>
</tr>
<tr>
<td>BPA In Line / Banner</td>
<td>Suggestion or Recommend</td>
<td>Process Instructions</td>
</tr>
<tr>
<td>BPA Silent Alerts</td>
<td>an Order Set</td>
<td>Care Plans</td>
</tr>
<tr>
<td>Health Maintenance Alert</td>
<td></td>
<td>Reporting</td>
</tr>
<tr>
<td>Asynchronous Alert</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Duke Geriatrics

**Discrete Data Collection prototype**

#### Cognition
- **History of Cognitive Impairment**
  - Options: Yes, No
- **Severity of Cognitive Impairment**
  - Options: Mild, Moderate, Severe
- **Onset of Cognitive Impairment**
  - Options: Gradual, Sudden
- **Areas of Concern**
  - Options: Memory, Judgment, Concentration, Word Finding, Comprehension, Mood, Behaviors, Function, Medication Management

#### History of Delirium
- **Yes** No

#### Other Risk Factors for Delirium
- Options: Age > 70, Visual Impairment, Hearing Impairment, Polypharmacy, Use of Opioids, Use of Benzodiazepines, Depression, Alcohol Abuse

#### Pain
- **History of Chronic Pain**
  - Options: Yes, No

#### Constipation
- **Last BM Date**
- **History of Constipation**
  - Options: Yes, No

#### Urinary
- **History of Urinary Retention**
  - Options: Yes, No
- **Change in Urine Output**
  - Options: Yes, No
- **History of UTIs**
  - Options: Yes, No
- **History of Abdominal Pain and Distension**
  - Options: Yes, No

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Principles of Design

• Keep it short
  – Minimum needed for clarity
• Avoid clicks
• Beware of hard stops & pop up alerts
  – Constant struggle to figure out what technology can & can’t do
• Workflow Integration otherwise known at Timing
  – “Do CDS with users not to them” – Osheroff
  – Variability among user workflow
  – Configure system to meet users needs
Design Cycle for the development of a CDS

- Planning Phase
- Research Phase
- System Analysis and conceptual phase
- Design Phase
- Construction phase
- Further Development phase
- Maintenance, documentation and adaptation
Five Rights of Clinical Decision Support

• Right information
• To the right person
• In the right manner
• Through the right channel
• At the right time

http://healthit.ahrq.gov/images/mar09_cds_book_chapter/CDS_MedMgmt_ch_1_sec_2_five_rights.htm
Types of decision support and where you implement it

A. Order sets
B. Dynamic choice alteration
C. Chronic disease monitoring / Surveillance
D. Interruptive decision support (Best Practice Alert)
E. Passive decision support (information, information bars)
What is the best type of decision support for Hip fractures?

A. Order sets
B. Dynamic choice alteration
C. Chronic disease monitoring / Surveillance
D. Interruptive decision support (Best Practice Alert)
E. Passive decision support (information, information bars)
What is the best type of decision support for Proper medication dosing for geriatrics?

A. Order sets
B. Dynamic choice alteration
C. Chronic disease monitoring / Surveillance
D.Interruptive decision support (Best Practice Alert)
E. Passive decision support (information, information bars)
What is the best type of decision support for Avoiding Beer’s list medications?

A. Order sets
B. Dynamic choice alteration
C. Chronic disease monitoring / Surveillance
D. Interruptive decision support (Best Practice Alert)
E. Passive decision support (information, information bars)
What is the best type of decision support for Indwelling catheters?

A. Order sets
B. Dynamic choice alteration
C. Chronic disease monitoring / Surveillance
D. Interruptive decision support (Best Practice Alert)
E. Passive decision support (information, information bars)
Han et al.

Pediatrics

2005

ABSTRACT. Objective. In response to the landmark 1999 report by the Institute of Medicine and safety initiatives promoted by the Leapfrog Group, our institution implemented a commercially sold computerized physician order entry (CPOE) system in an effort to reduce medical errors and mortality. We sought to test the hypothesis that CPOE implementation results in reduced mortality among children who are transported for specialized care.

• Before CPOE: 39/1394 died (2.80%)
• After CPOE: 75/1942 children died (3.86%)
• CPOE independently associated with increased odds of mortality (odds ratio: 3.28; 95% confidence interval: 1.94 – 5.55)

ABBREVIATIONS. CPOE, computerized physician order entry; CHP, Children’s Hospital of Pittsburgh; ADE, adverse drug event; PRISM, Pediatric Risk of Mortality; OR, odds ratio; CI, confidence interval.
What is a Geriatric Dose?

- Dose reduced for
  - Expected higher serum concentrations
  - Increased patient susceptibility
- “Start low and go slow”
- Food and Drug Administration (FDA) requires drug manufacturers to recommend a geriatric dose if significant numbers of patients 65 and older are studied
Motivation

- Dosing errors are common
- Potentially inappropriate drug use is common
- Benzodiazepine use has dose-related risk of falls and hip fractures
- Reducing use and dose of sedatives and anticholinergic drugs likely prevents delirium
Implementation at Partners, early 2000s

- Overall agreement with recommendations:
  - 19% during control
  - 29% during intervention
- Less extreme dosing (10x recommended dose) – 5% -> 2.8%
- 50% reduction in falls (3.4 per 1000 patient-days to 1.7 per 1000 patient days)
Condition

Vital signs
  vital signs as dir "q2h x 2; q4h x 48h; then q shift if stable & afebrile"

Activity/limitations
  activity: "per protocol" » Oct 2 12:00...

Allergies

Nursing instructions
  in and out cath q6h prn "for inability to void after foley d/c'd" » Oct 2
  intake and output "until drains/tubes/iv's d/c'd; notify if uop <50cc/2h"
  nursing: "complete environmental assessment -- ensure that: (1) ambu
  nursing: "identify fall risk patients: caution sign on door" » Oct 2 12:0
  ted hose - thigh high "rle: 2; lle: 23; keep snugly in place except may re

Diet

Medications

IV fluids

TPN orders

Respiratory therapy
  ventilator settings
    - Mode: a/c
    - Rate (bpm): 10
    - FiO2 (%): 21
    - Tidal volume (ml): 200
    - PEEP/CPAP (cm H2O): 5

8n common orders
  1. pathway orders (adult) »
  2. general medicine orders »
  3. 8N admission orders »
  4. pulmonary medicine/critical care orders »
  5. STAT labs / tests »
  6. next morning stat labs / tests »
  7. next morning ROUTINE labs / tests »
  8. medications »
  9. workups »
  10. « Return to previous list

Select an item from the list

or enter another order

gent 80 iv q12h
• Intervention customizes dose and frequency for 89 medications
• Message on how quickly to titrate drug
• List possible adverse events
• Display a “default” for dose and frequency
• High doses often truncated from list
<table>
<thead>
<tr>
<th></th>
<th>% Agreement</th>
<th>Prescribed / Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control</strong></td>
<td>24.1%</td>
<td>Median 3.0 IQR [1.5,5]</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>28.6%</td>
<td>Median 2.5 IQR [1,4]</td>
</tr>
</tbody>
</table>

*p<0.001*
Benzodiazepines
Control vs Intervention

![Box plot showing daily dose ratio comparison between Control and Intervention groups.](image)
Anti-Spasmodics
Control vs Intervention

![Box plot comparing control and intervention groups]
Proportion of Zolpidem (Ambien) Orders Among Patients > 65 yrs that were Consistent with Recommended Geriatric Dosing – by Week

Gradual Rollout of Dosing Decision Support
Proportion of Geriatric Inpatients
With Prescribed Meperidine:
Combined Effect of Educational Messages,
Substitution Prompt, Order Set Revision
Recommendations

• Implement geriatric dose support as a reference, but not as forcing function

• Implement geriatric dosing within specific contexts
  • Insomnia and sedation protocols
  • Peri-operative order sets

• If possible, identify frail elderly and target for potentially more intrusive decision support

• Dosing recommendations on POGOe:
  • https://www.pogoe.org/productid/19058
The PIMS (Potentially Inappropriate Medications) **Surveillance** Project

To Develop a Method to Identify Elderly, Hospitalized Patients at Imminent Risk of an Avoidable Adverse Drug Event in Real Time

The project will focus on known potentially inappropriate medications: Sedative/Hypnotics and Anticholinergic Medications
Brief Background

• PIMS lists are developed for geriatric outpatients but have been measured in most care settings
• Hospitalized elderly, receive brief, often intense exposure to PIMS medications
  • Many of these are indicated and have no safer alternative
• CDS can be effective, but for many drug decisions is a “blunt instrument”
• Education about geriatric drug selection and dosing should leverage a more holistic assessment of patient risk
Pharmacy Surveillance

Consultation

Providers → Data → EMR → Surveillance Tool → Pharmacists

EMR

CPOE/Decision Support

Design

Informatics Personnel
Putting information passively in front of providers: StarTracker

```
00000003 Ztrain SSS, Neal ( )
```

**Tracked Conditions/Status:** Diabetes Mellitus, Geriatrics

***Notation indicates test is due for repeat and value may be outdated.***

<table>
<thead>
<tr>
<th><strong>Diabetes</strong></th>
<th><strong>Geriatrics</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CE</strong></td>
<td><strong>HCT</strong></td>
</tr>
<tr>
<td><strong>A1C</strong></td>
<td><strong>Weight</strong></td>
</tr>
<tr>
<td><strong>LDL</strong></td>
<td><strong>eGFR</strong></td>
</tr>
<tr>
<td><strong>ACEI</strong></td>
<td><strong>PVAX</strong></td>
</tr>
<tr>
<td><strong>UrAlb</strong></td>
<td><strong>FLUVAZ</strong></td>
</tr>
<tr>
<td><strong>SMOKE</strong></td>
<td><strong>MedAlert</strong></td>
</tr>
<tr>
<td><strong>FOOT</strong></td>
<td><strong>ADLs</strong></td>
</tr>
<tr>
<td><strong>WEW</strong></td>
<td><strong>YN</strong></td>
</tr>
</tbody>
</table>

- **Diabetes:**
  - CE: 125/65
  - A1C: 9.5
  - LDL: 96
  - ACEI: NO
  - UrAlb: 5.2
  - SMOKE: NO
  - FOOT: YES
  - WEW: < 1 year

- **Geriatrics:**
  - HCT: 33
  - Weight: 124.74
  - eGFR: > 60
  - PVAX: YES
  - FLUVAZ: NONE
  - MedAlert: 1 meds
  - ADLs: YES

Updated 2004/05/26 10:09 by DUNA2E9Q for Jrij, Jim N.

Patient-specific guidelines

**Significant Medical Diagnoses and Conditions:**
- Hypercholesterolemia 272.2
- Migranes (sornal) 346.10
- Hypothyroidism 244.9
- CVA 999 (al MRA/MRI, TEE al except ascending aorta atherosclerotic)

**Adverse and Allergic Drug Reactions:**
- PCN
- Codeine
- Sulfa
- Lasuls - rash
Geriatrics Dashboard Usage

• Total active patients over age 65 (primary care)
  • 5,761 patients (22% of total in & out of primary care)
    • 807 patients in resident continuity clinics (10.4% of total in resident clinics)

• Visit-associated views of geriatric dashboard (approx.)
  • 2009 (Resident) 2,209 views (Attending) 16,000 views
  • 2010 (first half) 1,370 views 9,700 views
Geriatric Dashboard Summary Measures

- Smoking status assessment warning (incomplete)
  - 939 (42.9%) responded

- Warnings for patients reporting problems with ADL’s
  - 269 (12.3%) saw warning

- Warning to clinician re: chronic renal impairment
  - 769 (35.2%) of patients had a warning
Geriatric Dashboard Summary Measures

Change in documentation rates before/after – 1/1/2008

• Pneumococcal vaccination
  • Initial – 48.5%
  • Final – 69.4%

• Colorectal Cancer Screening
  • 378 new colonoscopies since 1/1/2008
  • 17% increase in compliance (approximate due to measuring changes/outside studies)
Geriatric Dashboard Summary Measures

Change in documentation rates before/after – 1/1/2008

- No change in # patients on high risk meds
  - 1513 (30%) → 1525 (31%)

- 291 patients had a net decrease in # risky meds
- 304 patients had a net increase in # risky meds
- 1590 patients were unchanged
Variable drug response is common; Genetics may predict this
Clopidogrel failure is predicted by CYP2C19*2

clopidogrel failure=MI, stroke, revascularization, death following MI or PCI
n=225 cases, 468 controls

WARNING: DIMINISHED EFFECTIVENESS IN POOR METABOLIZERS

See full prescribing information for complete boxed warning.

- Effectiveness of Plavix depends on activation to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. (5.1)
- Poor metabolizers treated with Plavix at recommended doses exhibit higher cardiovascular event rates following acute coronary syndrome (ACS) or percutaneous coronary intervention (PCI) than patients with normal CYP2C19 function. (12.5)
- Tests are available to identify a patient's CYP2C19 genotype and can be used as an aid in determining therapeutic strategy. (12.5)
- Consider alternative treatment or treatment strategies in patients identified as CYP2C19 poor metabolizers. (2.3, 5.1)
A Case for Prospective Genotyping

52,942 Vanderbilt “Medical Home” patients followed for up to 5 years....

How many patients received drug(s) that have a recognized pharmacogenetic story?

Estimated number of severe adverse events mitigated : 383
... or ~12-18 ADEs for the average PCP over 5 years

Schildcrout et al. *Curr Pharm Ther.* 2012
What is the role of known PGx meds in the geriatric population?

<table>
<thead>
<tr>
<th>&gt;=65yo analyzed with outpatient visit after 2007</th>
<th>44,960</th>
</tr>
</thead>
<tbody>
<tr>
<td>With exposure to:</td>
<td></td>
</tr>
<tr>
<td>clopidogrel</td>
<td>8040</td>
</tr>
<tr>
<td>warfarin</td>
<td>8720</td>
</tr>
<tr>
<td>simvastatin</td>
<td>16,050</td>
</tr>
<tr>
<td>tacrolimus</td>
<td>550</td>
</tr>
<tr>
<td>thiopurines (azathioprine, 6-MP)</td>
<td>800</td>
</tr>
<tr>
<td>Any of the above</td>
<td>23,160</td>
</tr>
</tbody>
</table>
"Here's my sequence..."

*New Yorker, 2000*
PREDICT: Pharmacogenomic Resource for Enhanced Decisions In Care and Treatment

- Prospective identification of those at risk to receive candidate medications
- Coupled with EMR-based Decision Support
PREDICT: Genotype many variants at once

CYP2C19 clopidogrel poor metabolizer
CYP2C19 clopidogrel Rapid metabolizer
CYP2C9 warfarin dose/bleeds
CYP2C9 warfarin dose/bleeds
VKORC1 warfarin dose/bleeds
CYP2D6 tamoxifen, antidepressants, codeine poor metabolizer
SLCO1B1 simvastatin myopathy

PREDICT platform tests 184 variants in 34 drug-related genes
Testing for clopidogrel efficacy

Clopidogrel $\xrightarrow{CYP2C19}$ 2-oxoclopidogrel

- 2.7% homozygous
- 18.9% heterozygous
- 78.4% no common variant

Risk of MI
Multiplex testing for pharmacogenetic variants

- 0 variants: 17%
- 1 variant: 48%
- 2 variants: 29%
- 3 variants: 6%
- 4 variants: 0.3%

Risk variants for drugs:
- clopidogrel
- warfarin
- simvastatin
- azathioprine
- tacrolimus

83% carry a risk variant!

Total n>15,000

99.8% of African Americans had actionable variants
PREDICT Results Appear in Patient Summary

Drug Genome Interactions in the Patient Summary
Clinical Decision Support

“I don't want to interpret the pharmacogenomic data. I want to know how is metabolism for that particular patient... I don't need to know all the interesting academic details. I really want help...”

Survey: Please select the format for the genotype result that is most clear and useful to you as a clinician.
*1B No Call;*11/*13 No Call;*3 HET; *5 HET 3%
*1/*5 3%
1 copy of *5 risk allele (*1B No Call;*11/*13 No Call;*3 HET; *5 HET) 20%
1 copy of *5 risk allele 23%
No reporting of specific genotype result is necessary 50%

Survey: Please select the format for the genotype interpretation that is most clear and useful to you as a clinician.
Simvastatin sensitivity: intermediate metabolizer, increased myopathy risk 3%
Simvastatin sensitivity: intermediate metabolizer, increased myopathy risk, consider switching to alternate statin medication 73%
Simvastatin sensitivity: intermediate metabolizer, click here for full explanation and recommendations 20%
None of these formats are clear or useful 3%
Clinical Decision Support within E-Prescribing

Drug-Genome Advisor
Intermediate Metabolizer - clopidogrel (Plavix) - Rare Risk Allele
Substitution recommended due to increased cardiovascular risks

If not otherwise contraindicated:
- ☐ Prescribe prasugrel (Effient) 10 mg daily
  - **Prasugrel should not be given to patients:**
    - history of stroke or transient ischemic attack
    - >= 75 years of age [Current patient age: 51]
    - with body weight < 60 kg [Current patient weight: 59.0 kg as of 10/12/2012]
- ☐ Prescribe ticagrelor (Brilinta) 90 mg twice daily
  - **Ticagrelor should not be given to patients:**
    - history of severe hepatic impairment
    - intracranial bleed
- ☑ Continue with clopidogrel (Plavix) prescription
  - **Primary override reason:**
    - ☐ Contraindicated for prasugrel or ticagrelor
    - ☐ Potential side effects
    - ☐ Provider/Patient opts for clopidogrel
    - ☐ Cost

This patient has been tested for CYP2C19 variants which has identified the presence of one copy of a rare risk allele which is associated with intermediate metabolism of clopidogrel. Intermediate metabolizers treated with clopidogrel at normal doses are associated with higher rates of stent thrombosis and other cardiovascular events. The Vanderblit P&T Committee recommends that prasugrel or ticagrelor replace clopidogrel for poor metabolizers unless contraindicated. If not feasible, maintain standard dose of clopidogrel. The guidelines above were developed based on the outcome studies of patients who received a drug-eluting stent into a coronary artery. However, there is not a national consensus on drug/dose guidance particularly associated with the population possessing extremely rare genetic variants.

Evidence Link
Response to Genetic Risk Phenotypes

- Poor Metabolizer
- Intermediate Metabolizer
- Non-Actionable

Time to Antiplatelet Drug Change (Months)

- 46%
- 27%
- 6%

Log rank p < 0.001

2419 pts → 1121 pts
PREDICT helps match patient with proper drug
BY: KATHY WHITNEY

10/28/2010 - Had Scyble Van Cleve, a spry 83-year-old from Brentwood, had her heart procedure done a month ago instead of one week ago, she would have been prescribed the standard dose of clopidogrel, a blood thinner used to prevent blood clots from forming around her coronary stents.

Scyble Van Cleve, right, is the first patient at Vanderbilt to benefit from a new program that puts genetic information in the patient’s medical records to help physicians like John McPherson, M.D., choose the drug and dose that will benefit them the most. (photo by Susan Urmy)
Our case: What personalizing medicine really means

57yo with admitted for angina, receives stent

January

clopidogrel started

April

Recath, stent
"Plavix x 1 year minimum. ASA life long."

In-stent thrombosis, restent

In-stent thrombosis, restent

Cath, more stents

9th admission, 5th intervention, 9th stent

PREDICT: CYP2C19*2/*2

December

Switched to prasugrel
Personalized medicine – not a new idea

The good physician treats the disease; the great physician treats the patient who has the disease.

Sir William Osler
Seeking a new paradigm for 21st century medicine: The Precision Medicine Initiative

State of the Union Address, Jan. 20, 2015
Mission of the Precision Medicine Initiative

To enable a new era of medicine through research, technology, and polices that empower patients, researchers, and providers to work together toward development of individualized treatments.
PMI Proposed Support: FY16

<table>
<thead>
<tr>
<th>Agency</th>
<th>$ Million</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH</td>
<td>$200</td>
</tr>
<tr>
<td>• Cancer</td>
<td>$70</td>
</tr>
<tr>
<td>• Cohort</td>
<td>$130</td>
</tr>
<tr>
<td>FDA</td>
<td>$10</td>
</tr>
<tr>
<td>ONC</td>
<td>$5</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>$215</strong></td>
</tr>
</tbody>
</table>
PMI Working Group of the Advisory Committee to the NIH Director (ACD)

- Working Group Charge: develop a vision for the PMI Cohort Program (PMI-CP) and advise on the design of a longitudinal national research cohort of ≥1 million volunteers

- Leverage existing cohorts, start from scratch, or hybrid?
- Who to recruit?
- How to capture the rich diversity in the U.S. population?
- What data types should be included?
- What policies need to be in place for maximal benefit?
Inputs

- Workshops
  - April 28-29: Unique Scientific Opportunities for the National Research Cohort (NIH)
  - May 28-29: Digital Health Data in a Million-Person Precision Medicine Initiative (Vanderbilt University, Nashville, TN)
  - July 1-2: Participant Engagement and Health Equity (NIH, Bethesda, MD)
  - July 27-28: Mobile and Personal Technologies in Precision Medicine (Intel Corp., Santa Clara, CA)

- Requests for Information
  - Building the cohort
  - Strategies to address community engagement and health disparities

- FNIH Survey of public perceptions of precision medicine cohort
- White House Privacy and Trust Principles
Why?

- Discover new biomarkers predictive of individual risk of future disease for many common diseases
- Understand individual variation in response to therapies
- Study populations reflecting diversity of the US population
- Accelerate research across many areas of health and disease
- Participant engagement and ongoing contact allows follow-up studies to advance understanding of disease mechanisms and targeted clinical trials.
## Why now?

<table>
<thead>
<tr>
<th></th>
<th>Ten Years Ago</th>
<th>Now – 2014 (most recent data)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of sequencing a human genome</td>
<td>$22,000,000</td>
<td>$1,000 - $5,000</td>
</tr>
<tr>
<td>Amount of Time to Sequence a Human Genome</td>
<td>2 years</td>
<td>&lt;1 day</td>
</tr>
<tr>
<td>Number of smart phones in the United States</td>
<td>1 million (&lt;2%)</td>
<td>160 million (58%)</td>
</tr>
<tr>
<td>EHR Adoption (% hospitals)</td>
<td>20-30%</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>Computing Power</td>
<td>n</td>
<td>n x 16</td>
</tr>
</tbody>
</table>
## Estimated disease incidences and prevalences in one million people

<table>
<thead>
<tr>
<th>Disease</th>
<th>Expected prevalent cases</th>
<th>Incident cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>5 years</td>
</tr>
<tr>
<td>Type 2 Diabetes</td>
<td>135,658</td>
<td>40,411</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>78,272</td>
<td>35,047</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>73,723</td>
<td>21,315</td>
</tr>
<tr>
<td>COPD</td>
<td>48,728</td>
<td>15,396</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>39,273</td>
<td>14,981</td>
</tr>
<tr>
<td>Epilepsy and seizures</td>
<td>33,426</td>
<td>4,161</td>
</tr>
<tr>
<td>Sensorineural hearing loss</td>
<td>29,901</td>
<td>17,339</td>
</tr>
<tr>
<td>Breast cancer (female)</td>
<td>20,470</td>
<td>12,068</td>
</tr>
<tr>
<td>Stroke</td>
<td>16,016</td>
<td>8,969</td>
</tr>
<tr>
<td>Dementia</td>
<td>13,373</td>
<td>7,028</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>4,311</td>
<td>2,127</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>9,407</td>
<td>3,745</td>
</tr>
</tbody>
</table>
Assembling the PMI Cohort

- One million or more volunteers:
  - Be recontactable
  - Collect EHR data, provide biospecimen, survey, and complete a baseline exam
- Longitudinal cohort, with continuing interactions, recontactable for secondary studies
- Two methods of recruitment
  - Direct volunteers
    - Anyone can sign up
  - Healthcare provider organizations (incl. FQHCs)
    - Consider HPO diversity, robustness of EHR, patient follow-up
Assembling the PMI Cohort

Broadly reflect the diversity of the U.S.

- Groups that are underrepresented
- All states of health and disease
- All areas of the U.S.
- All ages and all life-stages
- Special policy considerations
  - enrolling children
  - enrolling decisionally impaired
  - participants who become incarcerated
PMI-CP Focus on Engagement

- Highly interactive and proactive participant model
  - Participant representation in governance, design, conduct, dissemination, evaluation
  - Build a strong foundation of trust
- Consent is with PMI Cohort Program
  - Basic consent to be part of the cohort
  - Broad consent for secondary use
  - Consent is adaptable over time for new components
  - Future option to join supplementary/complementary studies
- Single IRB for PMI-CP
## Expected data sources for the PMI Cohort

<table>
<thead>
<tr>
<th>Data Source</th>
<th>Example Data Provided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self report measures</td>
<td>Diet, substance use, self-report of disease and symptoms (e.g., cognitive or mood assessment)</td>
</tr>
<tr>
<td>Structured clinical data (EHR)</td>
<td>ICD and CPD codes, medication history, laboratory results, vitals, encounter records</td>
</tr>
<tr>
<td>Unstructured clinical data (EHR)</td>
<td>Narrative documents, images, EKG and EEG waveform data</td>
</tr>
<tr>
<td>Biospecimens</td>
<td>Blood sample, microbiome, nail and hair for environmental exposures over time</td>
</tr>
<tr>
<td>mHealth and sensor data</td>
<td>Passively-collected data (e.g., location, movement, social connections), wearable sensor data (activity, calories expended, hours and quality of sleep, time sedentary).</td>
</tr>
<tr>
<td>Healthcare claims data</td>
<td>Billing codes as received by public and private payors, outpatient pharmacy dispensing</td>
</tr>
<tr>
<td>Geospatial and environmental data</td>
<td>Weather, air quality, environmental pollutant levels, food deserts, walkability, population density, climate change</td>
</tr>
<tr>
<td>Other data</td>
<td>Social networking e.g., Twitter feeds, over-the-counter medication purchases</td>
</tr>
</tbody>
</table>
Information Flow In

Direct Volunteers → Self-report Measures → mHealth Data → Consent → EHR Data → Baseline Exam → Biological Samples → HPO Volunteers

HPO Volunteers → Biological Samples → Baseline Exam → EHR Data → Consent → mHealth Data → Self-report Measures → Direct Volunteers
Information Flow Out

Volunteers → Data → Public → Results → Researchers
Biospecimen Collections

- PMI-CP would collect new biospecimens
  - Anticipate what future uses may be
  - Collect initially from everyone and at subsequent intervals as determined by use cases
  - Start with blood, but should accommodate samples for exposure studies, metabolites, microbiome, etc.
- Quickly establish a central PMI-CP biobank
- Maintain CLIA-compliance in specimen collection and testing where possible
Next Steps

- Quickly build infrastructure to support enrollment
  - Communications & engagement
  - Single IRB and consent
  - Data storage & acquisition infrastructure
  - Biobank
- Begin enrollment
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• Bill Gregg
• Donna Rosenstiel

Duke
• Jeff Ferranti
• Eric Poon
• Ed Hammond
• Constance Johnson
• Clay Musser
• Karen Rourk
• Jeanette Jansen

Reynolds Foundation
Questions?
Provider perception of clinical evidence

**Evidence Types**

Survey: Which of the following would influence your use of pharmacogenomics information? (% who ranked as of “major importance”)

- Original research in peer-reviewed literature: 75%
- Systematic review of peer-reviewed literature: 85%
- Guidance from national standards-setting organizations: 87%
- Guidance from local institution: 63%
- Information in FDA-approved drug label: 44%

“Poor metabolizer is fine… I have a lot of difficulty with the intermediate category, particularly if the intermediate doesn’t associate with a substantial absolute risk increase for the outcome of interest, okay?”
Computing techniques used to create DSS

- Machine Learning and Adaptive Computing
  - Inductive Tree Methods
  - Case Based Reasoning
  - Artificial Neural Networks

- Expert Systems - Knowledge based Methods
  - Rule based Systems