The FDA’s Mini-Sentinel Program and the Learning Health System

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Vision

“We seek the development of a learning health system that generates and applies the best evidence for the collaborative health care choices of each patient and provider; drives … discovery as a natural outgrowth of patient care; and ensures innovation, quality, safety, and value in health care.”

(Roundtable Charter)
Learning Healthcare System

“The increased complexity of health care requires a sustainable system that gets the right care to the right people when they need it, and then captures the results for improvement. The nation needs a healthcare system that learns.”

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES
Advising the nation / Improving health
Every day, patients and doctors face common questions for which we have no solid evidence

“For ‘short cervix’ does bed rest prevent early labor?”

“Should I take my daily blood pressure medicine in the morning or at night?”

“How can I help my 87 year old patient with multiple myeloma decide which chemotherapy option is best?”

“What are the benefits and risks of giving medication to my child with ADHD?”
Which Treatment is Best for Whom?
High-Quality Evidence is Scarce: < 15% of guideline recommendations are supported by high quality evidence

Scientific Evidence Underlying the ACC/AHA Clinical Practice Guidelines

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Context The joint cardiovascular practice guidelines of the American College of Cardiology (ACC) and the American Heart Association (AHA) have become important documents for guiding cardiology practice and establishing benchmarks for quality of care.

Objective To describe the evolution of recommendations in ACC/AHA cardiovascular guidelines and the distribution of recommendations across classes of recommendations and levels of evidence.

Data Sources and Study Selection Data from all ACC/AHA practice guidelines issued from 1984 to September 2008 were abstracted by personnel in the ACC Science and Quality Division. Fifty-three guidelines on 22 topics, including a total of 7196 recommendations, were abstracted.

pcornet
A Vision For A National Patient-Centered Research Network

Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health

National Workshop to Advance the Use of Electronic Data in Patient-Centered Outcomes Research

July 2, 2012

www.pcori.org/assets/2-Collins-Slides-Network.pdf
PUBLIC HEALTH

- Health Promotion
- Surveillance
- Research
- Risk
- Communication
- Disease Prevention
- Monitoring
- Analysis
- Outbreaks
- Epidemics
Influenza-like Illness
National Healthcare Safety Network (NHSN)

Tracking Infections in Acute Care Hospitals/Facilities

NHSN is the HAIs surveillance gold standard. The system (and its predecessors) started years ago helping a few hundred healthcare facilities; today, more than 11,000 healthcare facilities use NHSN as the cornerstone of their HAI elimination strategies. Specifically, facilities use NHSN to:

- Access NHSN enrollment requirements for CMS Hospital Inpatient Quality Reporting Program,
- Obtain baseline HAI rates,
- Compare rates to CDC’s national data,
- Participate in state or national HAI prevention collaboratives,
- Devise and implement HAI elimination strategies,
- Evaluate immediate and long-term results of elimination efforts,
- Refocus efforts as needed, or advance to different areas.

CLABS - Surveillance for Central Line-associated Bloodstream Infections
- Training
- Protocols
- Forms
- Support Materials
- Analysis Resources
- FAQs

CAUTI - Surveillance for Catheter-associated Urinary Tract Infections
- Training
- Protocols
- Forms
- Support Materials
- Analysis Resources
- FAQs

CLIP - Surveillance for Central Line Insertion Practices Adherence
- Training
- Protocols
- Forms
- Support Materials
- Analysis Resources
- FAQs

SSI - Surveillance for Surgical Site Infections
- Training
- Protocols
- Forms
- Support Materials
- Analysis Resources
- FAQs
When could we have suspected a link?
MedWatch: The FDA Safety Information and Adverse Event Reporting Program

Subscribe to MedWatch Safety Alerts

Safety Information

Reporting Serious Problems to FDA

Report a Serious Medical Product Problem Online

Resources for You

- Report a Serious Medical Product Problem Online

Your FDA gateway for clinically important safety information and reporting serious problems with human medical products.
Digital platform

Issues for further attention
• Functionality standards
• Governance and coordination
• The public case
FDA's Mini-Sentinel Program
Mini-Sentinel

- Congress mandated FDA develop electronic record based safety surveillance system

- Mini-Sentinel:
  - Develops operational capacity for active medical product safety surveillance in existing automated healthcare data systems
  - Develops and evaluates scientific methods
  - Offers FDA the opportunity to evaluate safety issues
  - Assesses barriers and challenges
Mini-Sentinel Partner Organizations

Lead – HPHC Institute

Data and scientific partners

Scientific partners
Mini-Sentinel Distributed Database*

- Populations with well-defined person-time for which most medically-attended events are known
- 358 million person-years of observation time
- 48 million people currently accruing new data
- 4 billion dispensings
- 4.1 billion unique encounters
  - 42 million acute inpatient stays
- 30 million people with \( \geq 1 \) laboratory test result

*As of July 2014
Mini-Sentinel’s Data Sources

- **Administrative data**
  - Enrollment
  - Demographics
  - Outpatient pharmacy dispensing
  - Utilization (encounters, diagnoses, procedures)

- **EHR data**
  - Height, weight, blood pressure, temperature
  - Laboratory test results (selected tests)

- **Registries**
  - Immunization
  - Birth certificates

- **Full text records (small number to confirm selected exposures and outcomes)**
Mini-Sentinel’s Common Data Model

<table>
<thead>
<tr>
<th>Enrollment</th>
<th>Demographic</th>
<th>Dispensing</th>
<th>Encounter</th>
<th>Lab Result</th>
<th>Vital Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person ID</td>
<td>Person ID</td>
<td>Person ID</td>
<td>Person ID</td>
<td>Person ID</td>
<td>Person ID</td>
</tr>
<tr>
<td>Enrollment start &amp; end dates</td>
<td>Birth date</td>
<td>Dispensing date</td>
<td>Dates of service</td>
<td>Dates of order, collection &amp; result</td>
<td>Date &amp; time of measurement</td>
</tr>
<tr>
<td>Drug coverage</td>
<td>Sex</td>
<td>National drug code (NDC)</td>
<td>Provider seen</td>
<td>Test type, immediacy &amp; location</td>
<td>Height</td>
</tr>
<tr>
<td>Medical coverage</td>
<td>Race</td>
<td>Days supply</td>
<td>Type of encounter</td>
<td>Procedure code &amp; type</td>
<td>Weight</td>
</tr>
<tr>
<td>Etc.</td>
<td>Amount dispensed</td>
<td>Abnormal result indicator</td>
<td>Facility</td>
<td>Test result &amp; unit</td>
<td>Diastolic &amp; systolic BP</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Death</th>
<th>Cause of Death</th>
<th>Diagnosis</th>
<th>Procedure</th>
<th>Vital Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person ID</td>
<td>Person ID</td>
<td>Person ID</td>
<td>Person ID</td>
<td>Person ID</td>
</tr>
<tr>
<td>Date of death</td>
<td>Cause of death</td>
<td>Date</td>
<td>Dates of service</td>
<td>Date &amp; time of measurement</td>
</tr>
<tr>
<td>Source</td>
<td>Diagnosis code &amp; code type</td>
<td>Principal diagnosis flag</td>
<td>Procedure code &amp; type</td>
<td>Height</td>
</tr>
<tr>
<td>Confidence</td>
<td>Source</td>
<td>Encounter type &amp; provider</td>
<td>Encounter type &amp; provider</td>
<td>Weight</td>
</tr>
<tr>
<td>Etc.</td>
<td>Confidence</td>
<td>Diagnosis code &amp; type</td>
<td>Etc.</td>
<td>Diastolic &amp; systolic BP</td>
</tr>
<tr>
<td>Etc.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Also:
- Vaccine table
- Birth certificate table
- Blood components table

Common Data Model Standards

- The data set uses the data source’s original codes whenever possible.
- For each variable, the model captures both the value AND coding system, e.g., ICD-9-CM, SNOMED, CPT, HCPCS, LOINC.
Ensuring Data Privacy
Mini-Sentinel Distributed Analysis

1- User creates and submits query (a computer program)
2- Data partners retrieve query
3- Data partners review and run query against their local data
4- Data partners review results
5- Data partners return results via secure network
6- Results are aggregated
Dabigatran vs warfarin and stroke / bleeding

- Goal: Compare ischemic and hemorrhagic stroke and gastrointestinal bleeding rates among new users of dabigatran or warfarin therapy who have atrial fibrillation/flutter
Start Date

Start of new treatment episode

End Date

• Look back XX days
• Inclusion/exclusion condition

Need all dispensings and days’ supply from any pharmacy to determine treatment duration

• Outcome(s)
• Optional: blackout days
• Optional: extension days

Need all diagnoses at any ED or hospital

Need all inpatient, ED, ambulatory diagnoses / procedures from every provider

Index Date

Time

Need all dispensings from any pharmacy in the prior X months
Dabigatran vs warfarin and stroke / bleeding

- **Analysis:** A standard, reusable, SAS program

- **Inputs:**
  - **Population:** Patients with pre-existing atrial fibrillation,
  - **Exposures:** New users of dabigatran or warfarin (no prior exposure to either in preceding 183 days).
  - **Outcomes:** First diagnoses of gastrointestinal (GI) or intracerebral hemorrhage in inpatient or ED settings. (No event in the 183 days prior to initiating therapy.)
  - **Period:** 10/19/2010 to 12/31/2011

- **Results:**
  - Counts of eligible patients and days under observation
  - Counts of new users of dabigatran and warfarin, dispensings, total days supplied, treatment episodes,
  - Counts of first GI or intracerebral hemorrhage diagnoses
Dabigatran vs warfarin: Data sources

- Administrative files:
  - Demographic data
  - Eligible person time (periods when both presence and absence of events is reliably known)

- Dispensing data:
  - Outpatient medications, including dosage form and days supply

- Claims:
  - Diagnoses, ambulatory and inpatient
  - Procedures, ambulatory and inpatient
Dabigatran vs Warfarin: Data sharing

- No person-level data is shared!
- Count data only is shared
GI bleeding after warfarin or dabigatran

Figure 1a. New Events of GIH per 100k Days at Risk in the MSDD between October 19, 2010 and December 31, 2011, by Drug, Incidence Criteria, and Washout Period for Individuals with a Pre-Existing Condition of Atrial Fibrillation

Rate per 100,000 days at risk
“Bleeding rates associated with new use of Pradaxa do not appear to be higher than bleeding rates associated with new use of warfarin.”
“we are now conducting two protocol-based assessments, using claims data from Mini-Sentinel and other claims databases, in which adjustments will be made for confounding factors”
PCORnet’s Goal

Improve the nation’s capacity to conduct rapid, efficient, and economical comparative effectiveness research
11 Clinical Data Research Networks and 18 Patient Powered Research Networks

Numbers indicate the number of networks active in each state.
18 Patient Powered Research Networks

The National Patient-Centered Clinical Research Network
Goals for Patient-Powered Research Networks (PPRNs)

- Enroll >0.5% of those with the condition in the U.S. (~50 to 50,000)
- Patient-reported data for ≥80% of cohort
- Patients involved in governance
- Standardized data able to respond to queries
Community Engaged Network for All

CENA announces that two of the nine disease advocacy organizations in the network launched research registries on September 15, 2014. Spotlight on the National Gaucher Foundation and Joubert Syndrome and Related Disorders Foundation. See press release.

What is the Community Engaged Network for All (CENA)?

What conditions are covered in CENA?

What organizations are involved in CENA?

What CENA means for individuals, families and communities?

What about individual preferences with regard to health information sharing?

What CENA means for Researchers?

How other organizations, institutions and groups can participate in CENA?

Information about the nine organizations involved in CENA.
The NIH Collaboratory: Complementary development of health care systems research capabilities

Millions of people. Strong collaborations. Privacy first.
Each organization can participate in multiple networks
Each network controls its governance and coordination
Networks share infrastructure, data curation, analytics, lessons, security, software development
Thank you!