A Roadmap for Improving Epilepsy Therapy Through Integrated Advanced Technologies
(The Knowledge Project)

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Disclosure

Name of Commercial Interest
- Eisai, Questcor
- Supernus, Sunovion, Lundbeck, Upsher-Smith, GeneDx
- AssureRx

Type of Financial Relationship
- Consulting and Speaking
- Consulting
- Royalties

American Epilepsy Society | Annual Meeting
Learning Objectives

• To identify how advanced technologies will be helpful in improving epilepsy therapy

• To identify how advanced technologies will impact how epilepsy medications are selected
Overview

• Evolution of epilepsy therapy
• Knowledge paradigm
• Roadmap for improving epilepsy therapy
• The future is now!
Evolution of epilepsy therapy

- Observation + Serendipity
- Animal Models
- Randomized Controlled Trials
- Knowledge + Integrated Advanced Technologies

Phenobarbital
Epilepsy therapy has become increasingly complex.

**AED specific variables**
- Efficacy/effectiveness for seizure type or epilepsy syndrome
- Adverse events – all types
- Pharmacokinetics
- Risk for drug-drug interaction
- Formulations

**Patient specific variables**
- Age
- Gender
- Co-medications
- Co-morbidities (e.g. obesity)
- Genetic background
- Ability to swallow pills or tablets
- Insurance coverage

ILAE Guidelines, Epilepsia 2006
Addressing the complexity problem

“…to accommodate the reality that although professional judgment will always be vital to shaping care, the amount of information required for any given decision is moving beyond unassisted human capacity.”

Need for Human + Information Technology
- Clinical decision support systems
- Universal electronic health records
- Tools for database linkage, mining, and use

Knowledge Paradigm

• Discovery
  - extraction of implicit, previously unknown, and potentially useful information

• Creation
  - the process that results in new knowledge, or organizes current knowledge in new ways

• Engineering
  - planning, design, development, construction, and management of expert systems

• Extension/Dissemination
  - transfer of scientific knowledge towards practical and useful applications

Roadmap for Knowledge Project

Step 1: Conceptualize goals of project

- Develop a dynamic corpus of epilepsy knowledge
- Develop ability to capture and integrate knowledge
- Develop and implement decision support systems
- Link multiple medical centers together to
  - identify homogenous cohorts of patients for predictive therapy models and decision support systems
  - facilitate benchmarking of outcomes between centers
- Improve next generation RCT design/conduct
  - Predictive model(s) versus empiric therapy
Roadmap for Knowledge Project
Step 2: Apply knowledge paradigm

• Discovery
  - Continue research in factors affecting AED response

• Creation
  - Develop algorithms to capture data from EMR/patients using machine learning/natural language processing
  - Develop clinical decision support algorithms

• Engineering
  - Create single site epilepsy knowledge base
  - Create working clinical decision support program

• Extension/Dissemination
  - Create multisite epilepsy knowledge bases
  - Implement multisite clinical decision support effort
Roadmap for knowledge project
Step #3: Develop new philosophy of care/research

• Providers:
  - *every patient encounter can contribute to epilepsy research (Learning Laboratories - IOM)*

• Patient/family:
  - *using this approach we can help you learn how to better care for your (your child’s) disease*

• Society:
  - *Learn from our current patients to help the next generation of children/adults with epilepsy*
Roadmap for knowledge project
Step #4: Agree to some infrastructure standardization

- Determine outcomes to be measured
- Determine method of measurement

Streamline Your Neuroscience Clinical Research using these content standards that enable clinical investigators to systematically collect, analyze, and share data across the research community.

The NINDS strongly encourages researchers who receive funding from the Institute to ensure their data collection is compatible with the common data elements (CDEs).
Roadmap for implementation:
Step #5: Agree to develop integrated infrastructure

Using step #4:

i) Determine outcomes to be measured
ii) Determine method of measurement

Advanced Decision Support Software

Measure outcomes

Data Capture System

Test interventions to improve outcomes

Identify factors predictive of favorable outcomes
The future is now!
Knowledge Creation/Engineering – Data Capture

- Machine learning using natural language processing
- Steps involved
  - Collect information
  - Teach the machine (annotation)
  - Improve the machine’s learning through feedback

Alan Turing (1912-1954)

Watson (2005-present)
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Knowledge Creation/Engineering – Decision Support

- Epilepsy therapy knowledge algorithms
  - CHRISTINE system
  - Integrates
    - Patient specific factors (history, genetics, environment)
    - Drug specific factors
  - Initially based on 1 person, then expert consensus, then evidence based

- Epilepsy knowledge bases
  - Prognosis
  - Risk for co-morbidities
Knowledge Creation/Engineering - Avatars
Clinical Data Repository → Research data warehouse (i2b2) → Epilepsy Data mart for the site

MiPeds: Multi-Institution Pediatric Epilepsy Decision Support

Center 1 Shrine → De-identified Center 1 data
Center 2 Shrine → De-identified Center 2 data
Center 3 Shrine → De-identified Center 3 data

Center 1 data → De-identified Center 1 data
Center 2 data → De-identified Center 2 data
Center 3 data → De-identified Center 3 data
Summary

• Active progress
  - Develop dynamic corpus of epilepsy knowledge
  - Capturing and integrating knowledge
  - Developing/implementing decision support systems

• Just started
  - Linking multiple medical centers

• Next steps
  - Improve next generation RCT design/conduct

The Future is Now!