Mobilizing Computable Biomedical Knowledge
Welcome and Opening

Charles P. Friedman, PhD
Rachel Richesson, PhD
MCBK Co-Chairs

2nd Annual Public Meeting
July 18, 2019
NIH Natcher Conference Center
Outline

• Foundations for MCBK
• Why We’re All Here
• MCBK Community & Workgroups
• Goals and Plans for This Meeting
MCBK is Anchored in the “Learning Health System” Concept of Continuous Cycles of Improvement

Health Problem of Interest

D2K: Data to Knowledge

K2P: Knowledge to Performance

P2D: Performance to Data
Better Health Requires This

- D2K: Data to Knowledge
- K2P: Knowledge to Performance
- P2D: Performance to Data

Health Problem of Interest
Not Just This

Journals

Health Problem of Interest

D2K: Data to Knowledge

K2P: Knowledge to Performance

P2D: Performance to Data
Knowledge is the “Keystone” that Holds the Cycle Together

Health Problem of Interest

D2K: Data to Knowledge

K2P: Knowledge to Performance

P2D: Performance to Data
A Way to Think About Knowledge

The result of an analytical and/or deliberative process that holds significance for an identified community.
Examples of Biomedical Knowledge

From primarily analytical to primarily deliberative:

• Predictive/explanatory models
• Computable phenotypes
• Causal/propositional networks
• Best practices (guidelines)
• Decision Trees
• Policies
Two Complementary Ways to Represent Knowledge

Human readable in words, pictures, equations

Computable (machine-executable) in code

Library Holdings: Books & Journals

Library Holdings: Will add Digital Knowledge Objects
Selection Criteria for Lung-Cancer Screening


ABSTRACT

BACKGROUND

The National Lung Screening Trial (NLST) used risk factors for lung cancer (e.g., >30 pack-years of smoking and <15 years since quitting) as selection criteria for lung-cancer screening. Use of an accurate model that incorporates additional risk factors to select persons for screening may identify more persons who have lung cancer or in whom lung cancer will develop.

METHODS

We modified the 2011 lung-cancer risk-prediction model from our Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial to ensure applicability to NLST data; risk was the probability of a diagnosis of lung cancer during the 6-year study period. We developed and validated the model (PLCO_{M2012}) with data from the 80,375 persons in the PLCO control and intervention groups who had ever smoked. Discrimination (area under the receiver-operating-characteristic curve [AUC]) and calibration were assessed. In the validation data set, 14,144 of 37,332 persons (37.9%) met NLST criteria. For comparison, 14,144 highest-risk persons were considered positive (eligible for screening) according to PLCO_{M2012} criteria. We compared the accuracy of PLCO_{M2012} criteria with NLST criteria to detect lung cancer. Cox models were used to evaluate whether the reduction in mortality among 53,202 persons undergoing low-dose computed tomographic screening in the NLST differed according to risk.
The New Knowledge is Expressed in a Model

### Table 2. Modified Logistic-Regression Prediction Model (PLCO<sub>2012</sub>) of Cancer Risk for 36,286 Control Participants Who Had Ever Smoked.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
<th>Beta Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per 1-yr increase†</td>
<td>1.081 (1.057–1.105)</td>
<td>&lt;0.001</td>
<td>0.0778868</td>
</tr>
<tr>
<td>Race or ethnic group‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1.000</td>
<td>Reference group</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1.484 (1.083–2.033)</td>
<td>0.01</td>
<td>0.3944778</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.475 (0.195–1.160)</td>
<td>0.10</td>
<td>−0.7434744</td>
</tr>
<tr>
<td>Asian</td>
<td>0.627 (0.332–1.185)</td>
<td>0.15</td>
<td>−0.466585</td>
</tr>
<tr>
<td>American Indian or Alaskan Native</td>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Native Hawaiian or Pacific Islander</td>
<td>2.793 (0.992–7.862)</td>
<td>0.05</td>
<td>1.027152</td>
</tr>
<tr>
<td>Education, per increase of 1 level†§</td>
<td>0.922 (0.874–0.972)</td>
<td>0.003</td>
<td>−0.0812744</td>
</tr>
<tr>
<td>Body-mass index, per 1-unit increase†</td>
<td>0.973 (0.955–0.991)</td>
<td>0.003</td>
<td>−0.0274194</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease (yes vs. no)</td>
<td>1.427 (1.162–1.751)</td>
<td>0.001</td>
<td>0.3553063</td>
</tr>
<tr>
<td>Personal history of cancer (yes vs. no)</td>
<td>1.582 (1.172–2.128)</td>
<td>0.003</td>
<td>0.4589971</td>
</tr>
<tr>
<td>Family history of lung cancer (yes vs. no)</td>
<td>1.799 (1.471–2.200)</td>
<td>&lt;0.001</td>
<td>0.587185</td>
</tr>
<tr>
<td>Smoking status (current vs. former)</td>
<td>1.297 (1.047–1.605)</td>
<td>0.02</td>
<td>0.2597431</td>
</tr>
<tr>
<td>Smoking intensity¶</td>
<td></td>
<td></td>
<td>−1.822606</td>
</tr>
<tr>
<td>Duration of smoking, per 1-yr increase†</td>
<td>1.032 (1.014–1.051)</td>
<td>0.001</td>
<td>0.0317321</td>
</tr>
<tr>
<td>Smoking quit time, per 1-yr increase†</td>
<td>0.970 (0.950–0.990)</td>
<td>0.003</td>
<td>−0.0308572</td>
</tr>
<tr>
<td>Model constant</td>
<td></td>
<td></td>
<td>−4.532506</td>
</tr>
</tbody>
</table>

*To calculate the 6-year probability of lung cancer in an individual person with the use of categorical variables, multiply the variable or the level beta coefficient of the variable by 1 if the factor is present and by 0 if it is absent. For continuous variables other than smoking intensity, subtract the centering value from the person’s value and multiply the difference by the beta coefficient of the variable. For smoking intensity, calculate the contribution of the variable to the model by dividing by 10, exponentiating by the power −1, centering by subtracting 0.4021541613, and multiplying this number by the beta coefficient of the variable. Add together all the previously calculated beta-coefficient products and the model constant. This sum is called the model logit. To obtain the person’s 6-year lung-cancer probability, calculate e<sup>logit</sup>/(1+e<sup>logit</sup>). CI denotes confidence interval.
And the Knowledge Can be Made Computable by Representing It as Coded “Knowledge Objects”

Example: A computer program that takes in characteristics of a person and computes a risk score for that person
Envisioning An Extended Publication Pipeline

Human Readable: Article

Extraction

Encoding: Model

Computable: Code

Library

Expanded Library
Computable Knowledge Enables a Continuous Connection Between Discovery and Improvement (and Further Discovery)

- **Discovery Systems**
  - D2K: Data to Knowledge
  - P2D: Performance to Data
  - K2P: Knowledge to Performance

- **Journals** (Human-Readable)

- **Learning Systems**
  - D2K: Data to Knowledge
  - P2D: Performance to Data
  - K2P: Knowledge to Performance

- **Knowledge Objects** (Machine readable)
Serial Discovery Systems Require Only Mass Access to Knowledge

To enable **mass access**, persistent human-readable knowledge is sufficient.
Learning Systems Operate in Parallel, Requiring Mass Action

To enable mass action, persistent computable knowledge is essential.
Outline

• Foundations for MCBK
• Why We’re All Here
• MCBK Community & Workgroups
• Goals and Plans for This Meeting
Better Health…

This is why we’re all here today
Life Expectancies in U.S. and Other Countries

Source: https://www.apha.org/topics-and-issues/health-rankings
Inequalities in Life Expectancy Among US Counties, 1980 to 2014

Many “Use Cases”

- **Clinical**: Applying pharmacogenomics to health care (making precision health actually work)
- **Public Health**: Detecting and automatically reporting notifiable diseases
- **Translational (“T1+”) Research**: Using computable phenotypes to identify study-eligible persons
- **Policy**: Identifying non-compliant documents
- **Education**: Early detection of and remediation for students who will encounter difficulties
Mobilizing Computable Biomedical Knowledge (CBK): A Manifesto

Preamble

Knowledge has the potential to improve health care, the health of individuals, and the health of populations. Every decision affecting health should be informed by the best available knowledge. For moral and ethical reasons, it is imperative that each and every member of society has access to what is known at the time they are making health-related choices and decisions.

It is no longer sufficient to represent knowledge in the form of printed words and static pictures. The increasingly rapid rate of scientific discovery needs knowledge representations that are more agile and amenable to scalability and mass action. This in turn can enable the continuous cycles of discovery and improvement envisioned as Learning Health Systems.

Contemporary digital technology enables knowledge to be represented in computable forms expressed in machine-executable code. Computable knowledge unleashes the potential of information technology to generate and deliver useful information—and particularly, decision-specific advice—to individuals and organizations with great speed on a world-wide scale. It is essential to take full advantage of these capabilities, while continuing established practices that validate knowledge, preserve it, and ensure that it can be trusted.

There is work to do to mobilize best available health knowledge for the greater good. To begin, biomedical knowledge in computable form must be made interoperable using open standards, and widely available so that it can be used to immediately impact health.

It is time for action on a global scale.

Computable Biomedical Knowledge

Computable Biomedical Knowledge is the result of an analytic and/or deliberative process about human health, or affecting human health, that is explicit, and therefore can be represented and reasoned upon using logic, formal standards, and mathematical approaches.

Vision

We are dedicated to:

Mobilizing biomedical knowledge that can support action toward improving human health. This should be done using computable formats that can be shared and integrated into health information systems and applications.

Efficiently and equitably serving the learning and knowledge needs of all participants, as well as the public good. This will work to significantly reduce health disparities.

Ensuring that the knowledge properly reflects the best and most current evidence and science. This will ensure that knowledge can be trusted for use to improve health and health care.

Achieving this through evolution of an open Computable Biomedical Knowledge ecosystem dedicated to achieving the FAIR principles: making Computable Biomedical Knowledge easily findable, universally accessible, highly interoperable, and readily reusable. * The current interest in making data “FAIR” should be matched by equally intense interest in making knowledge “FAIR”.

Mechanisms of Activity

We believe that all of the following are important:

- The CBK Concept
  - Sustain the Computable Biomedical Knowledge ecosystem through public-private partnerships.
  - Establish broadly-based participatory governance of the ecosystem.
  - Make the ecosystem diverse and inclusive.
  - Explore sciences of Computable Biomedical Knowledge collaboratively.
  - Be agile to reflect the increasingly rapid changes in knowledge.

- The CBK Technical System
  - Enable the ecosystem with open standards.
  - Build and uphold trust in Computable Biomedical Knowledge through the ecosystem.
  - Ensure robust and unbiased methods to support transparency and expose the currency, validity and provenance of Computable Biomedical Knowledge.
  - Implement the highest standards of privacy and security for all stakeholders.
  - Enable a pipeline that transitions knowledge from human-readable to fully computable through successive stages.

- The CBK Use/User System
  - Ensure the safe and effective use of Computable Biomedical Knowledge through the ecosystem.
  - Generate value for the creators of the knowledge, the users of the knowledge, and the general public.
  - Engender equity in health and in knowledge accessibility

Making Knowledge FAIR

- **Findable**
- **Accessible**
- **Interoperable**
- **Reusable**

FAIR: https://www.force11.org/group/fairgroup/fairprinciples
Access Fuels Innovation

Data

Knowledge

Research, discovery, generation of evidence

Applications/Action

-- targeted, personalized, useful, usable, ...
Outline

• Foundations for MCBK
• Opportunities for Action
• MCBK Community & Workgroups
• Goals and Plans for This Meeting
Standards for MCBK

Bob Greenes
Co-Chair
Arizona State University

Bruce Bray
Co-Chair
University of UT
Technical Infrastructure for MCBK

Chris Shaffer
Co-Chair
University of California San Francisco

Leslie McIntosh
Co-Chair
Research Data Alliance
Policy and Coordination to Ensure Quality and Trust

Blackford Middleton
Co-Chair
Apervita, Inc.

Jody Platt
Co-Chair and MCBK Liaison
University of Michigan
Sustainability for Mobilization and Inclusion

Jerry Perry
Co-Chair
University of Arizona

Chris Dymek
Co-Chair
AHRQ
Outline

• Foundations for MCBK
• Why We’re All Here
• MCBK Community & Workgroups
• Goals and Plans for This Meeting
Who is here?
Meeting highlights

• 190+ participants (!)
• 24 posters (!)
• 17 technical demos (!)
• 4 working groups – action sessions
• Remarks and perspectives from national and international leaders
• Presentations and discussions
  • Use cases, critical stakeholders
Meeting Goals

• **Strengthen** foundation of shared recognition of values and principles for mobilizing CBK

• **Frame** and address important dimensions for mobilizing CBK

• **Advance** workgroups action plans

• **Identify** priorities

• **Plan** next steps

• **Grow** the MCBK community
Today’s Plan - Success Depends on You

• Remarks - Dr. Patricia Brennan (NLM)
• Panel - MCBK Use Cases
• Lunch & Technical Demonstrations & Posters
• Panel - Engaging Critical Stakeholders

[Highlight]
• Breakout Sessions – Workgroup Action Sessions

• “Open Mic”
• Reception at Rock Bottom Brewery
Plan for Tomorrow

- Workgroup Updates and Charge for Day 2
- Remarks - Dr. Don Rucker (ONC)
  - Dr. Dipak Kalra (i~HD)
- Lunch & Technical Demonstrations
  - Workgroup Action Sessions
- Panel - Meeting Reflections
- Closing
Steering Committee

- Julia Adler-Milstein
- Bruce Bray
- Milton Corn
- Chris Dymek
- Peter Embi
- Charles Friedman
- Bob Greenes
- Stan Huff
- Dipak Kalra
- Nancy Lorenzi
- Leslie McIntosh
- Blackford Middleton
- Mark Musen
- Jody Platt
- Jerry Perry
- Rachel Richesson
- Chris Shaffer
- Umberto Tachinardi
- John Wilbanks
1. Register for workgroups
2. Sign-up to view Technical demos
3. #MobilizeMCBK tag @DLHSumich
4. Restrooms location
5. Additional information
Onward!

Health Problem of Interest

D2K: Data to Knowledge

K2P: Knowledge to Performance

P2D: Performance to Data