Improving Diabetes Prevention
Based on Predicted Benefits of Treatment

David Kent, MD, MS
Director, Predictive Analytics and Comparative Effectiveness (PACE) Center, Tufts Medical Center – @Tufts_PACE

John Cuddeback, MD, PhD
Chief Medical Informatics Officer, AMGA (American Medical Group Association) – @theAMGA
David Kent, MD, MS, and John Cuddeback, MD, PhD

• Nothing to disclose.
Overview

• Why a predictive model for people with prediabetes?

• Reanalysis of a landmark clinical trial
  – Estimate risk for each individual, rather than an overall average
  – Adapt for clinical use

• Results from initial use for shared decision-making
AMGA Foundation: National Diabetes Campaign

Together2Goal®

Improve care for 1 million people with type 2 diabetes by 2021
Screening Is a Key Strategy

1 out of 4 people with type 2 diabetes don’t know they have it!

*Early treatment is important, to minimize future complications*
Together 2 Goal Member Survey

Which strategies will you adopt?

31% said they wouldn’t focus on screening.

They are already overwhelmed by the number of people with type 2 diabetes ...let alone prediabetes!
What Is Prediabetes?

Elevated blood sugar, but not high enough to indicate diabetes
Elevated risk of developing type 2 diabetes over 3 years—about 29%

84 million Americans have prediabetes—1 out of 3 adults

Is there an effective way to prevent progression to diabetes?
Is there a way to prioritize—identify those at highest risk?
Diabetes Prevention Program (DPP) Study: Randomized Controlled Trial

- Participants: 3,060 non-diabetic adults with impaired glucose metabolism
- Main outcome measure: Development of diabetes over 3 years
- Conducted 1996–2001, stopped early because interventions were so effective
- Three arms: Intensive lifestyle-modification program ("DPP program")
  - Taking metformin
  - No intervention (placebo)
Diabetes Prevention Program (DPP) Study: Randomized Controlled Trial

Overall risk of developing type 2 diabetes, over 3 years

- No intervention (placebo) 29%
- Intensive lifestyle intervention absolute risk reduction: 14%
- Taking metformin absolute risk reduction: 7%

AMGA members participating in Together 2 Goal still felt overwhelmed— for every person with a screening result in the diabetes range, 6 people are identified who have prediabetes
Assessing and Reporting Heterogeneity of Treatment Effect in Randomized Clinical Trials

Patient Centered Outcomes Research Institute (PCORI) Methods Pilot Project: 1IP2PI000722

7/2012–7/2014

David M Kent, MD, MS, Principal Investigator
Predicted Risk Distributions in 36 Clinical Trials
Predicted Risk Distribution in DPP Study

Includes all participants in the DPP Study—placebo arm, plus both intervention arms.
Absolute Risk Reduction across Risk Quartiles

- Substantial differences in absolute treatment effects were common.
- Displaying results across subgroups defined by risk is feasible and can lead to clinically important findings.
Absolute Risk Reduction Seen in DPP Study

Intensive Lifestyle Intervention

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Lowest</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Highest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute Risk Reduction (Percent)</td>
<td>4.9</td>
<td>9.2</td>
<td>13.6</td>
<td>28.3</td>
<td></td>
</tr>
</tbody>
</table>

Average: 14.2

Metformin

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Lowest</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Highest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute Risk Reduction (Percent)</td>
<td>-1.3</td>
<td>2.9</td>
<td>4.7</td>
<td>21.4</td>
<td></td>
</tr>
</tbody>
</table>

Average: 7.1

http://www.pcori.org/research-in-action/moving-beyond-averages
Improving Diabetes Prevention with Benefit-Based Tailored Treatment: Disseminating Patient-Centered Estimates of Benefit

Patient Centered Outcomes Research Institute (PCORI) D&I Project: DI-1604-35234

7/2017–7/2020

David M Kent, MD, MS, Principal Investigator
Re-develop Risk Model using Typical EHR Data

Step 1

• Re-develop basic risk model, using variables typically available in EHRs
Re-develop Risk Model using Typical EHR Data

<table>
<thead>
<tr>
<th>Model from DPP Study Data</th>
<th>Adapted Model for Use in EHR</th>
</tr>
</thead>
<tbody>
<tr>
<td>• HbA1c</td>
<td>• HbA1c</td>
</tr>
<tr>
<td>• Fasting glucose</td>
<td>• Fasting glucose</td>
</tr>
<tr>
<td>• Triglycerides</td>
<td>• Triglycerides</td>
</tr>
<tr>
<td>• History of elevated glucose</td>
<td>• Age</td>
</tr>
<tr>
<td>• Height</td>
<td>• Gender</td>
</tr>
<tr>
<td>• Waist circumference</td>
<td>• Race</td>
</tr>
<tr>
<td>• Waist:hip ratio</td>
<td>• BMI</td>
</tr>
<tr>
<td></td>
<td>• Smoking status</td>
</tr>
<tr>
<td></td>
<td>• Systolic blood pressure</td>
</tr>
<tr>
<td></td>
<td>• Hypertension diagnosis</td>
</tr>
<tr>
<td></td>
<td>• HDL cholesterol (‘‘good cholesterol’’)</td>
</tr>
</tbody>
</table>

Model from DPP Study Data

Adapted Model for Use in EHR

- HbA1c
- Fasting glucose
- Triglycerides
- History of elevated glucose
- Height
- Waist circumference
- Waist:hip ratio

Adapted Model for Use in EHR

- HbA1c
- Fasting glucose
- Triglycerides
- Age
- Gender
- Race
- BMI
- Smoking status
- Systolic blood pressure
- Hypertension diagnosis
- HDL cholesterol (‘‘good cholesterol’’)

OPTUM Labs
Re-develop Risk Model using Typical EHR Data

Step 1 (continued)

• Re-develop model using data from 1.08 million people with prediabetes from three regions: Northeast, South, and West
  – $c$-statistic = 0.735, indicating good discrimination

• Validate model using data on 1.08 million people from the Midwest
  – $c$-statistic = 0.763

• Discrimination is similar to original risk model from DPP Study data
  – $c$-statistic = 0.73
Step 2

- Obtain risk-specific estimates of the effects of the two interventions by applying this model to the DPP Study data
  - Intensive lifestyle program
  - Metformin
Re-develop Risk Model using Typical EHR Data

Then...

• For each person with prediabetes, estimate risk of developing diabetes over 3 years and benefit from interventions
  – Risk model using EHR data (from Step 1) – accommodate missing data elements
  – Apply risk-specific estimates of benefit (from Step 2)
AMGA Members

- Ambulatory practice in Monroeville, PA (southeastern Pittsburgh metro area)
- 100 providers
- 24 specialties

- Integrated health system based in St. Louis, spanning 4 states
- 45 hospitals
- 3,200 providers
Patient and Provider Focus Groups

People with prediabetes want a personalized estimate—*their* risk of diabetes

- Quoted ages when family members developed type 2 diabetes

Providers want guidance for shared decision-making

- Want to support and encourage patients—especially for lifestyle program
- Feel overwhelmed—need to prioritize
- Multivariable model is more informative than any single lab result
  - Highest-risk quartile: 25% had A1c < 6.0
  - Lowest-risk quartile: 15% had A1c ≥ 6.0

*Prediabetes: A1c 5.7 – 6.4*
### Predictive Model Results as Displayed in EHR

#### Interpretation: Low-Risk Patient

<table>
<thead>
<tr>
<th>Predicted Risk of Diabetes at 3 Years</th>
<th>Treatment</th>
<th>Relative Risk Reduction</th>
<th>Number Needed to Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.47%</td>
<td>Usual Care</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td>4.38%</td>
<td>Metformin</td>
<td>20%</td>
<td>91.4</td>
</tr>
<tr>
<td>2.30%</td>
<td>DPP Lifestyle</td>
<td>58%</td>
<td>31.5</td>
</tr>
</tbody>
</table>

#### Interpretation: High-Risk Patient

<table>
<thead>
<tr>
<th>Predicted Risk of Diabetes at 3 Years</th>
<th>Treatment</th>
<th>Relative Risk Reduction</th>
<th>Number Needed to Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>55.7%</td>
<td>Usual Care</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td>24.5%</td>
<td>Metformin</td>
<td>56%</td>
<td>4</td>
</tr>
<tr>
<td>23.4%</td>
<td>DPP Lifestyle</td>
<td>58%</td>
<td>4</td>
</tr>
</tbody>
</table>
Premier Medical Associates: May 2018 – Aug. 2019

Of the 901 high-risk patients...

41 were On Metformin before 5/1/2018 (5%)
150 were Started on Metformin after 5/1/2018 (16%)

0 were Referred to a DPP before 5/1/2018 (0%)
487 were Referred to a DPP after 5/1/2018 (54%)
## Premier Medical Associates: May 2018 – Aug. 2019

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Action Taken</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>75%</td>
</tr>
<tr>
<td>Moderate</td>
<td>21%</td>
</tr>
<tr>
<td>Low</td>
<td>7%</td>
</tr>
</tbody>
</table>

During the 15 months, 97 patients were identified as having diabetes, through timely screening.
Personalized Risk Estimates at the Point of Care

• Build model into EHR — Premier

• “Subscribe” to a cloud-hosted SMART app, using FHIR resources — Mercy
  – Emerging EHR standards – Office of the National Coordinator for Health IT (ONC)
  – EHR vendors are exposing data elements as “FHIR resources” and enabling integration of cloud-hosted apps
  – EHR vendors charge a small transaction fee, each time the model is used

EHR – Electronic health record (Premier uses Allscripts, with Galen eCalcs; Mercy uses Epic)
SMART – Substitutable Medical Apps and Reusable Technology
FHIR – Fast Healthcare Interoperability Resources, an HL7 standard
Potential for Cost Savings

• Intermountain insurance plan saves $3,500 per person per year that development of diabetes is averted or delayed

• CMS Office of the Actuary estimates a net savings of $2,650 over 15 months for Medicare beneficiaries participating in a DPP lifestyle program

• Cost of a DPP lifestyle program ~ $600


In 2018, John Schultz talked to his doctor, Frank Colangelo, at Premier Medical Associates.

John learned he had prediabetes, and *his personal risk for developing diabetes* was high. That got his attention.

He took the DPP Lifestyle program seriously—healthy eating, more exercise. He lost over 30 pounds.

“I’ve had more energy, and I’m doing more things,” Schultz said. “From that meeting with Frank, it was a snowball effect.”

https://www.pcori.org/research-results/pcori-stories/health-risks-each-individual-not-average-patient
Personalized Risk Estimates at the Point of Care

NIH

Diabetes Prevention Program Study (DPP)

Population Risk Stratification Model

Adapt for Use in Clinical Practice

PCORI

Personalized Risk Estimates at the Point of Care

Precision medicine without waiting for genomics