Thank you for joining The Guideline Advantage this afternoon!

To access the audio portion:
Dial: (866) 832-6378
Conference ID: 91889463

We will be starting the presentation shortly.
Vision & Goal

**Vision**
To improve the health of all patients through widespread application of primary and secondary prevention guidelines in the United States through data collection, analysis, feedback and quality improvement in the ambulatory setting.

**Goal**
To improve the long-term compliance with the ACS, ADA and AHA/ACC guidelines, which in turn supports our shared organizational mission to prevent chronic diseases and to improve the lives of those living with the nation’s most prevalent chronic diseases.

The Guideline Advantage is based on the success of nearly 10 years experience in inpatient quality improvement and over 2 millions lives touched.
Providers can use several different technology platforms. Practices submit collective clinical data to Forward Health Group for The Guideline Advantage. Data are processed, analyzed and provided back to the practice via a practice portal. Performance is measured, professionals can set measurable goals and chart improvements in performance.
Advantages to Practices & Physicians

- On-demand access to quality improvement data using a web-based tool
- Available physician-level reporting
- Clinic and system aggregation
- Tools for creating action lists
- Alignment with key national initiatives
- National and State Benchmarking
- Practice Network opportunities including virtual workshops and national recognition
Alignment with National Programs

Million Hearts Initiative

The Guideline Advantage reports on the “ABCS” measures of interest to Million Hearts

Uniform Data System (UDS)

The program reports all adult UDS measures of interest to Community Health Centers and Federally Qualified Health Centers
Program Platform

One-click access to patient lists

Measure Performance

Populations
Action Lists

Filters to create action lists

Filtered By > Population: Diabetes, Payer: Medicare, Measure: HbA1c Poor Control, Category: A1c > 0

Action items
**Program Models**

**Basic Model**
- ✓ Common Measure Set & Reporting Measure Set, with clinic & provider views and one-click access to patient lists
- ✓ Patient Lists with filtering options and action list functionality
- ✓ Demographic Information & detail patient views
- ✓ Comparison, Benchmarking & Historical Trending by clinic and provider
- ✓ **No Cost** program implementation

**Premium Model**
- ✓ An Additional Measure Set available as defined by the customer
- ✓ Views & filtering options for Teams
- ✓ Customer Driven Functionality, including demographic information displays, incentive program tracking, & non-clinical custom groupings
- ✓ Complete data advisory service, including comprehensive consultations and guidance in identifying data sources, mapping, data cleansing and alignment
- ✓ Fixed implementation fee and annual licenses
The Legacy Effects of Intensive Glucose Control
The Guideline Advantage 2013

JAY SHUBROOK DO FACOFP, FAAFP
DIABETOLOGIST
THE DIABETES INSTITUTE AT OHIO UNIVERSITY
Objectives

• Glucose control does not reduce macrovascular events

• Glucose control reduces microvascular event

• Glucose control reduces macrovascular events BUT in time
# Major diabetes CV clinical trials

<table>
<thead>
<tr>
<th>Clinical trial</th>
<th>Years</th>
<th>Diabetes</th>
<th>Sponsor</th>
<th>Patient number</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCCT</td>
<td>1983 – 93</td>
<td>T1D</td>
<td>NIH (NIDDK)</td>
<td>1,441</td>
</tr>
<tr>
<td>UKPDS</td>
<td>1977 – 97</td>
<td>T2D</td>
<td>UK</td>
<td>&gt;5,000</td>
</tr>
<tr>
<td>ADVANCE</td>
<td>2001 – 08</td>
<td>T2D</td>
<td>International (20 countries)</td>
<td>&gt;11,140</td>
</tr>
<tr>
<td>ACCORD</td>
<td>1999 - 2010</td>
<td>T2D</td>
<td>NIH</td>
<td>10,251</td>
</tr>
<tr>
<td>VADT</td>
<td>2000 - 2008</td>
<td>T2D</td>
<td>VA</td>
<td>1,791</td>
</tr>
<tr>
<td>Steno-2</td>
<td>1992 - 2000</td>
<td>T2D</td>
<td>Steno Diabetes Center (Denmark)</td>
<td>160</td>
</tr>
</tbody>
</table>
Diabetes Complications and Control Trial/Epidemiology Diabetes Interventions and Complications

- Type 1 DM
  - Intensive glucose control
  - MDI or pump vs routine care
  - 6 year intervention
- EDIC- 11 year epidemiologic follow up

DCCT/EDIC: Intensive Treatment Is Associated With Reduction in Risk of CVD in Type 1 Diabetes

DCCT/EDIC: Mean 17 Years of Follow-up

- Conventional treatment (1-2 insulin injections/d during DCCT)
- Intensive treatment (≥3 insulin injections/d or treatment with external insulin pump, and glucose goals 70-120 mg/dL before meals and peaks after meals <180 mg/dL, during DCCT)

Cumulative Incidence of Any Predefined Cardiovascular Outcome

No. at risk

Years Since Entry

Years

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

Intensive treatment: 705, 683, 629, 113
Conventional treatment: 714, 688, 618, 92

42% risk reduction in any CVD event

CVD=cardiovascular disease; EDIC=Epidemiology of Diabetes Interventions and Complications.
DCCT-EDIC: Long-term Risk of Macrovascular Complications

Any Cardiovascular Outcome

42% risk reduction
\( P = 0.02 \)

*Diabetes Control and Complications Trial (DCCT) ended and Epidemiology of Diabetes Interventions and Complications (EDIC) began in year 10 (1993). Mean follow-up: 17 years.*

United Kingdom Prospective Diabetes Study

• Type 2 study
• Intensive glucose control
  – Fasting < 108 mg/dl
  – Median 10 year Intervention
  – 10 year Epidemiologic follow up

• Also BP arm-not shown

UK Prospective Diabetes Study

20-year Interventional Trial from 1977 to 1997
- 5,102 patients with newly-diagnosed type 2 diabetes recruited between 1977 and 1991
- Median follow-up 10.0 years, range 6 to 20 years
- Results presented at the 1998 EASD Barcelona meeting

# UKPDS Endpoints: Intensive Glucose control

<table>
<thead>
<tr>
<th>Complication</th>
<th>Reduction in Risk</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All microvascular</td>
<td>25%</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>– Retinopathy progression</td>
<td>21%</td>
<td>P&lt;0.02</td>
</tr>
<tr>
<td>– Microalbuminuria</td>
<td>33%</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>16%</td>
<td>P=0.052</td>
</tr>
<tr>
<td>All diabetes-related endpoints studied</td>
<td>12%</td>
<td>P&lt;0.03</td>
</tr>
</tbody>
</table>
ACCORD/ADVANCE/VADT

• Prospective randomized controlled trials to determine the benefit of intensive glucose control

• ACCORD- planned 5 years-terminated early at 3.4 years
• ADVANCE – 5 years
• VADT- 6.3 years
The ADVANCE Trial: Combined Major Macrovascular and Microvascular Events

Hazard ratio for intensive control vs standard control was 0.90 (95% CI: 0.82 to 0.98)

VADT: Time to First Occurrence of Major Cardiovascular Event (Primary Outcome)


![Graph showing the probability of survival over years for Standard therapy and Intensive therapy, with the probability of survival ranging from 1.0 to 0.0 and years ranging from 0 to 8. The graph indicates that the probability of survival is slightly higher for Standard therapy compared to Intensive therapy over the 8-year period. The number at risk for each therapy at each year is provided in the table below.

### No. at Risk

<table>
<thead>
<tr>
<th>Years</th>
<th>Standard therapy</th>
<th>Intensive therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>899</td>
<td>892</td>
</tr>
<tr>
<td>2</td>
<td>770</td>
<td>774</td>
</tr>
<tr>
<td>4</td>
<td>693</td>
<td>707</td>
</tr>
<tr>
<td>6</td>
<td>637</td>
<td>639</td>
</tr>
<tr>
<td>8</td>
<td>570</td>
<td>582</td>
</tr>
</tbody>
</table>

*P=0.14*
UKPDS Epidemiologic Follow up

- 10-year Post-Trial Monitoring from 1997 to 2007
- Annual follow-up of the survivor cohort
- Clinic-based for first five years
- Questionnaire-based for last five years
- Median overall follow-up 17.0 years, range 16 to 30 years

NEJM 2008;359:1577-1589
UKPDS: 10 yr Follow up

HbA1c difference disappeared

• Outcome reduction with intensive control
  – Any DM end point 9% p= 0.04
  – Myocardial infarction 15% p=0.01
  – Death overall 13% p=0.005

• If on metformin
  – MI 33% p=0.005
  – Death 27% p=0.002

Microvascular Disease Hazard Ratio

*(photocoagulation, vitreous haemorrhage, renal failure)*

Intensive (SU/Ins) vs. Conventional glucose control

- **Microvascular disease**
  - HR = 0.75
  - p = 0.0099

- HR = 0.76
  - p = 0.001

Hazard ratio

Number of events

<table>
<thead>
<tr>
<th>Year</th>
<th>Con:</th>
<th>Int:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>213</td>
<td>489</td>
</tr>
<tr>
<td>1999</td>
<td>267</td>
<td>610</td>
</tr>
<tr>
<td>2001</td>
<td>330</td>
<td>737</td>
</tr>
<tr>
<td>2003</td>
<td>400</td>
<td>868</td>
</tr>
<tr>
<td>2005</td>
<td>460</td>
<td>1028</td>
</tr>
<tr>
<td>2007</td>
<td>537</td>
<td>1162</td>
</tr>
</tbody>
</table>

*NEJM 2008;359:1577-1589*
Myocardial Infarction Hazard Ratio

(fatal or non-fatal myocardial infarction or sudden death)

Intensive (SU/Ins) vs. Conventional glucose control

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of events</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>186</td>
<td>0.84 (0.62, 1.14)</td>
</tr>
<tr>
<td>1999</td>
<td>212</td>
<td>0.85 (0.62, 1.14)</td>
</tr>
<tr>
<td>2001</td>
<td>239</td>
<td>0.85 (0.62, 1.14)</td>
</tr>
<tr>
<td>2003</td>
<td>271</td>
<td>0.85 (0.62, 1.14)</td>
</tr>
<tr>
<td>2005</td>
<td>296</td>
<td>0.85 (0.62, 1.14)</td>
</tr>
<tr>
<td>2007</td>
<td>319</td>
<td>0.85 (0.62, 1.14)</td>
</tr>
</tbody>
</table>

*NEJM 2008;359:1577-1589*
All-Cause Mortality Hazard Ratio

Intensive (SU/Ins) vs. Conventional glucose control

All-cause mortality
HR = 0.94
p = 0.44

HR = 0.87
p = 0.006

Hazard ratio

Con: 213 267 330 400 460 537
Int: 489 610 737 868 1028 1163

1997 1999 2001 2003 2005 2007

NEJM 2008;359:1577-1589
## Legacy Effect of Earlier Glucose Control

*After median 8.5 years post-trial follow-up*

<table>
<thead>
<tr>
<th>Aggregate Endpoint</th>
<th>1997</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any diabetes related endpoint</td>
<td>RRR: 12%</td>
<td>9%</td>
</tr>
<tr>
<td></td>
<td>(P): 0.029</td>
<td>0.040</td>
</tr>
<tr>
<td>Microvascular disease</td>
<td>RRR: 25%</td>
<td>24%</td>
</tr>
<tr>
<td></td>
<td>(P): 0.0099</td>
<td>0.001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>RRR: 16%</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td>(P): 0.052</td>
<td>0.014</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>RRR: 6%</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>(P): 0.44</td>
<td>0.007</td>
</tr>
</tbody>
</table>

**RRR** = Relative Risk Reduction, **\(P\)** = Log Rank
## Legacy Effect of Earlier Metformin Therapy

*After median 8.8 years post-trial follow-up*

<table>
<thead>
<tr>
<th>Aggregate Endpoint</th>
<th>1997</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any diabetes related endpoint</td>
<td>RRR: 32%</td>
<td>21%</td>
</tr>
<tr>
<td></td>
<td><em>P:</em> 0.0023</td>
<td>0.013</td>
</tr>
<tr>
<td>Microvascular disease</td>
<td>RRR: 29%</td>
<td>16%</td>
</tr>
<tr>
<td></td>
<td><em>P:</em> 0.19</td>
<td>0.31</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>RRR: 39%</td>
<td>33%</td>
</tr>
<tr>
<td></td>
<td><em>P:</em> 0.010</td>
<td>0.005</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>RRR: 36%</td>
<td>27%</td>
</tr>
<tr>
<td></td>
<td><em>P:</em> 0.011</td>
<td>0.002</td>
</tr>
</tbody>
</table>

*RRR = Relative Risk Reduction, P = Log Rank*
Probability of events of non-fatal myocardial infarction with intensive glucose-lowering vs. standard treatment

<table>
<thead>
<tr>
<th>Intensive treatment/standard treatment</th>
<th>Participants</th>
<th>Events</th>
<th>Weight of study size</th>
<th>Odds ratio (95% CI)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UKPDS(^4)</td>
<td>3071/1549</td>
<td>221/141</td>
<td>21.8%</td>
<td>0.78 (0.62–0.98)</td>
<td></td>
</tr>
<tr>
<td>PROactive(^1)(^8)(^–)(^2)(^0)</td>
<td>2605/2633</td>
<td>119/144</td>
<td>18.0%</td>
<td>0.83 (0.64–1.06)</td>
<td></td>
</tr>
<tr>
<td>ADVANCE(^5)</td>
<td>5571/5569</td>
<td>153/156</td>
<td>21.9%</td>
<td>0.98 (0.78–1.23)</td>
<td></td>
</tr>
<tr>
<td>VADT(^2)(^1)(^2)(^2)</td>
<td>892/899</td>
<td>64/78</td>
<td>9.4%</td>
<td>0.81 (0.58–1.15)</td>
<td></td>
</tr>
<tr>
<td>ACCORD(^8)</td>
<td>5128/5123</td>
<td>186/235</td>
<td>28.9%</td>
<td>0.78 (0.64–0.95)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>17267/15773</td>
<td>743/754</td>
<td>100%</td>
<td>0.83 (0.75–0.93)</td>
<td></td>
</tr>
</tbody>
</table>

Ray et al, Lancet 2009; 373: 1765–72
STENO-2 TRIAL
The effect of coordinated care for T2DM: STENO-2

- 80 pts/arm T2DM with microalbuminuria randomized to:
  - Control
    - Regular care
  - Intensive intervention
    - Step-wise introduction of lifestyle and pharmacological interventions aimed at keeping:
      - HgA1c <6.5%
      - blood pressure <130/80mmHg
      - total cholesterol <175mg/dl
      - and triglycerides <150mg/dl.
      - reduction in intake dietary fat regular exercise and smoking cessation.

Multi-modal intensive therapy: Steno 2

- Aggressive HTN, lipid, and glucose control
- Data at 7.8 yrs
  - Intensive therapy decreased
    - CV disease 53%
    - Nephropathy 61%
    - Retinopathy 58%
    - Autonomic neuropathy 63%
  - 1 Cardiovascular event prevented for every 5 patients treated
Multifactorial intervention and CVD in type 2 diabetes: STENO 2

**STENO 2 - Risk of Death from Any Cause**

Cumulative Incidence of death (%)

Follow-up time (years)

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intensive</strong></td>
<td>80</td>
<td>78</td>
<td>75</td>
<td>72</td>
<td>65</td>
<td>62</td>
<td>57</td>
<td>43</td>
<td>30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Conventional</strong></td>
<td>80</td>
<td>80</td>
<td>77</td>
<td>69</td>
<td>63</td>
<td>51</td>
<td>43</td>
<td>30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **p = 0.02**

# Impact of Intensive Therapy for Diabetes: Summary of Major Clinical Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Microvasc</th>
<th>CVD</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UKPDS</strong></td>
<td><img src="down.png" alt="down" /></td>
<td><img src="equivalent.png" alt="equivalent" /></td>
<td><img src="down.png" alt="down" /></td>
</tr>
<tr>
<td><strong>DCCT / EDIC</strong></td>
<td><img src="down.png" alt="down" /></td>
<td><img src="equivalent.png" alt="equivalent" /></td>
<td><img src="equivalent.png" alt="equivalent" /></td>
</tr>
<tr>
<td><strong>ACCORD</strong></td>
<td><img src="down.png" alt="down" /></td>
<td><img src="equivalent.png" alt="equivalent" /></td>
<td><img src="up.png" alt="up" /></td>
</tr>
<tr>
<td><strong>ADVANCE</strong></td>
<td><img src="down.png" alt="down" /></td>
<td><img src="equivalent.png" alt="equivalent" /></td>
<td><img src="equivalent.png" alt="equivalent" /></td>
</tr>
<tr>
<td><strong>VADT</strong></td>
<td><img src="down.png" alt="down" /></td>
<td><img src="equivalent.png" alt="equivalent" /></td>
<td><img src="equivalent.png" alt="equivalent" /></td>
</tr>
</tbody>
</table>

Kendall DM, Bergenstal RM. © International Diabetes Center 2009


* in T1DM
Closing Thoughts

• Intensive glucose control decreases microvascular risk but not macrovascular risk EARLY
  – Time is needed to gain CV benefit

• Benefit seen in repeated Epidemiologic follow up

• Why design short term study if time is needed?

• What will happen in 2018 when we follow up on ACCORD/ADVANCE/VADT??
REFERENCES


References


References


• Riddle MC, Karl DM. Individualizing target an Tactics for High Risk Patients with Type 2 DM. Practical lessons from ACCORD and other CV Trials. Diabetes Care 2012;35:2100-2107.
Questions?

Type question into the Q&A tab at the top of your screen.

Additional questions email laura.jansky@heart.org

Download this slide deck within 5-7 working days from:
GuidelineAdvantage.org