Diabetes Prevention: Research to Reality

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The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the CDC.

SAFER • HEALTHIER • PEOPLE™
Prevention of Type 2 Diabetes
The Community – Clinic Partnership Model

**Community**
- Insurers
- Employers
- Informed Population
- Strong Community Organizations
- Healthy Public Policy
- Supportive Environments

**Clinic**
- Proactive Practice Team
- Decision Support
- Information Systems
- Informed, Activated Patients

**Partnership Zone**
- Reimbursement
- Screening for High Risk
- Diagnosis of Pre-diabetes
- Structured Lifestyle Programs
- Regular Glucose Monitoring

**Total Population**
- Pre-diabetes
- Diabetes
- Complications

**DIVISION OF DIABETES TRANSLATION • WWW.CDC.GOV/DIABETES**
Diabetes Prevention in High Risk Persons:

WHAT IS KNOWN
What Are Our Chances of Developing Diabetes?

- **Lifetime – from birth till death**
  - 33% (male), 39% (female)
    (Narayan KMV, et al. JAMA 2003;290:1884-1890.)

- **Annual – adults**
  - ~ 1%
Current Definitions of Pre-Diabetes

- **A1C**
  - 5.7%-6.4%

- **Impaired Fasting Glucose (IFG)**
  - Fasting Blood Glucose Test (FBG)
    - Blood is tested after 8-hr fast.
    - 100 - <126 mg/dl (110 - <126 in rest of the world)

- **Impaired Glucose Tolerance (IGT)**
  - Oral Glucose Tolerance Test (OGTT)
    - Following the FBG patient is given 75 gm glucose solution.
    - 2 hrs later blood is tested again.
    - Fasting <100 and 2-hr = 140 - <200 mg/dl

- **Combined IFG and IGT (CIFGT)**
  - Fasting 100- <126 mg/dl and 2-hr = 140 - <200 mg/dl
For Illustrative Purposes Only:

Diabetes Risk is Heterogeneous, Therefore - EFFICIENCY or EQUITY or Both?

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>NHANES 2005-6 Prevalence (%)</th>
<th>Annual Incidence Rate (%)</th>
<th>Annual Number of New Cases</th>
<th>Percent of All New Cases</th>
<th>Number Needed to Treat: To prevent 1 new case* (NNT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NG</td>
<td>71</td>
<td>0.3</td>
<td>459,630</td>
<td>22</td>
<td>313</td>
</tr>
<tr>
<td>IFG</td>
<td>24</td>
<td>2.9</td>
<td>1,406,662</td>
<td>68</td>
<td>35</td>
</tr>
<tr>
<td>IGT</td>
<td>14</td>
<td>2.7</td>
<td>756,943</td>
<td>37</td>
<td>37</td>
</tr>
<tr>
<td>C-IFGT</td>
<td>8</td>
<td>3.9</td>
<td>638,983</td>
<td>31</td>
<td>26</td>
</tr>
<tr>
<td>BMI ≥35</td>
<td>13</td>
<td>2.6</td>
<td>731,691</td>
<td>35</td>
<td>38</td>
</tr>
<tr>
<td>BMI ≥29</td>
<td>40</td>
<td>1.7</td>
<td>1,477,769</td>
<td>71</td>
<td>59</td>
</tr>
<tr>
<td>Total Pop.</td>
<td>100</td>
<td>1.0</td>
<td>2,070,681</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

*Assumes intervention is 100% effective.

\[ NNT = \left( \frac{\text{Incidence}_{UT} - \text{Incidence}_T}{\text{Incidence}_T} \right)^{-1} \]
Diabetes Prevention in Normoglycemic Persons

XENDOS Study of weight loss drug Orlistat:

• Mean BMI = 37

• Weight loss for those with IGT and NGT was almost identical: 5.7 vs. 5.8 kg.

• In IGT participants, Orlistat significantly decreased the 4-year risk of diabetes by 45%, from 29% to 19%.

• In NGT participants, there was no impact on diabetes risk: 2.7% vs. 2.6%.

“... the timeframe over which glucose values rose suddenly was estimated, having a median time to onset of <4.5 years from the time at which the exponential effect had contributed a modest increase of 10 mg/dl to the initial linear trend.”

“...we show changes in glucose concentrations, insulin sensitivity, and insulin secretion as much as 3–6 years before diagnosis of diabetes.”

Tabak et al. Lancet. Published Online June 8, 2009 DOI:10.1016/S0140-6736(09)60619-X
Other “Complications” of Pre-diabetes

- 5-year risk of total mortality increased 50-60%
- 5-year risk of CVD mortality increased 150%
  (Barr et al. Circulation 2007;116: July 18 online)
- Prevalent retinopathy about 8%
### Lifestyle Intervention Trials

(All participants had pre-diabetes)

Table 1 Randomized, clinical trials that aimed to prevent diabetes by lifestyle modification.

<table>
<thead>
<tr>
<th>Study^a</th>
<th>Number of patients by treatment group</th>
<th>BMI of participants (kg/m²)</th>
<th>Duration of intervention (years)</th>
<th>Lifestyle goals</th>
<th>Weight loss achieved at 1 year (kg)</th>
<th>Cumulative incidence of T2DM in controls</th>
<th>Risk reduction (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pan et al. (1997)^13</td>
<td>130 diet\  141 exercise\  126 diet and exercise\  133 control</td>
<td>26</td>
<td>6</td>
<td>Weight loss + maintenance of a healthy diet± exercise</td>
<td>NR</td>
<td>68% (15.7% per year)</td>
<td>Diet 31% (NR)\  Exercise 46% (NR)\  Both 42% (NR)</td>
</tr>
<tr>
<td>Tuomilehto et al. (2001)^14</td>
<td>265 active\  257 control</td>
<td>31</td>
<td>4</td>
<td>5% weight loss on low-fat, high-fiber diet +30 min exercise per day</td>
<td>4.2</td>
<td>23% (6% per year)</td>
<td>58% (30–70%)</td>
</tr>
<tr>
<td>DPP Research Group (2002)^19</td>
<td>1,079 active\  1,082 control</td>
<td>34</td>
<td>2.8</td>
<td>7% weight loss + 150 min exercise per week</td>
<td>7</td>
<td>28.9% at 3 years</td>
<td>58% (48–66%)</td>
</tr>
<tr>
<td>Kosaka et al. (2005)^22b</td>
<td>356 active\  102 control</td>
<td>24</td>
<td>4</td>
<td>Reduction in BMI to ≤22 kg/m² by 30–40 min exercise per day</td>
<td>2.5</td>
<td>9.3% (assessed by FPG &gt;7.8 mmol/l)</td>
<td>67.4% (NR)</td>
</tr>
<tr>
<td>Ramachandran et al. (2006)^23</td>
<td>133 active\  136 control</td>
<td>26</td>
<td>3</td>
<td>Weight maintenance by diet low in refined carbohydrates and fat +30 min exercise per day</td>
<td>0</td>
<td>55%</td>
<td>28.5% (20–37%)</td>
</tr>
</tbody>
</table>

## Effect of Treatment on Incidence of Diabetes in the DPP
*(All participants had IGT)*

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Metformin</th>
<th>Lifestyle</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Annual Incidence of diabetes</strong></td>
<td>11.0%</td>
<td>7.8%</td>
<td>4.8%</td>
</tr>
<tr>
<td><strong>Relative reduction</strong></td>
<td>----</td>
<td>31%</td>
<td>58%</td>
</tr>
<tr>
<td><em>(compared with placebo)</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Number needed to treat</strong></td>
<td>----</td>
<td>13.9</td>
<td>6.9</td>
</tr>
<tr>
<td><em>(to prevent 1 case in 3 years)</em></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The DPP Research Group, *NEJM* 346:393-403, 2002
Intervention Impact by Ethnicity

The DPP Research Group, *NEJM* 346:393-403, 2002

Division of Diabetes Translation • www.cdc.gov/diabetes
Further Benefits of Lifestyle Intervention: 
*Other CVD risk factors are also improved*

- Hypertension was present in 30% of participants at study entry - then increased in the placebo and metformin groups, but significantly decreased with intensive lifestyle intervention.

- Triglyceride levels fell in all treatment groups, but fell significantly more with intensive lifestyle intervention.

- Intensive lifestyle intervention significantly increased the HDL cholesterol level and reduced the cumulative incidence of the proatherogenic LDL phenotype B.

- At 3 years of follow-up, the use for pharmacologic therapy to achieve established goals in the intensive lifestyle group was 27–28% less for hypertension and 25% less for hyperlipidemia compared with placebo and metformin groups.

DPP. Diabetes Care 28:888–894, 2005
Longer-term impact?

- **Finnish Diabetes Prevention Study. Lancet 2006; 368: 1673–79.**
  - After 4 years active intervention was stopped.
  - During the total 7-year follow-up, the incidence of type 2 diabetes was still reduced by 43%.

- **China DaQing Diabetes Prevention Study. Lancet 2008; 371: 1783–89.**
  - After 6 years active intervention was stopped.
  - During the total 20-year follow-up, the incidence of type 2 diabetes was still reduced by 43%.

- **U.S. Diabetes Prevention Program Outcomes Study. Lancet 2009; Published Online October 29, 2009 DOI:10.1016/S0140-6736(09)61457-4.**
  - After 3 years a group version of the core lifestyle intervention was offered to the placebo and metformin groups, as well as the original lifestyle group, including 4 group “BOOST” sessions each year.
  - During the total 10-year follow-up, the incidences of type 2 diabetes was still reduced by 34% in the lifestyle group and by 18% in the metformin group.
### US Research Studies that have Translated the Diabetes Prevention Program (DPP) Trial Lifestyle Intervention

<table>
<thead>
<tr>
<th>First author, reference number</th>
<th>N* (% pre-diabetic)</th>
<th>Loss to Follow-up (%)</th>
<th>Age</th>
<th>Men (%)</th>
<th>Mean BMI</th>
<th># Core Sessions (wks)</th>
<th>During “Core” Intervention</th>
<th>Mean Sessions Attended (%)</th>
<th>Wt loss (kg)</th>
<th>Wt loss (%)</th>
<th>≥ 7% loss (%)</th>
<th>≥ 5% loss (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPP3</td>
<td>1079 (100)</td>
<td>6.5</td>
<td>50.6</td>
<td>32</td>
<td>33.9</td>
<td>16 (24)</td>
<td>15 (95%)</td>
<td>6.5</td>
<td>7</td>
<td>50</td>
<td>nr</td>
<td>nr</td>
</tr>
<tr>
<td>Ackermann13</td>
<td>46 (100)</td>
<td>15</td>
<td>56.5</td>
<td>50</td>
<td>32.0</td>
<td>16 (20)</td>
<td>9 (57)</td>
<td>5.5</td>
<td>6</td>
<td>36</td>
<td>36</td>
<td>59†</td>
</tr>
<tr>
<td>Amundson18</td>
<td>295 (52)</td>
<td>17</td>
<td>53.6</td>
<td>20</td>
<td>35.9</td>
<td>16 (16)</td>
<td>14 (91)</td>
<td>6.7</td>
<td>6.7</td>
<td>45</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>Aldana24</td>
<td>35 (89)</td>
<td>5</td>
<td>nr</td>
<td>34</td>
<td>32.0</td>
<td>16 (24)</td>
<td>11 (67)</td>
<td>2.9</td>
<td>3.3</td>
<td>nr</td>
<td>nr</td>
<td>nr</td>
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<tr>
<td>Pagoto25</td>
<td>118 (nr)</td>
<td>17</td>
<td>48.7</td>
<td>28</td>
<td>43.3</td>
<td>16 (16)</td>
<td>13 (81)</td>
<td>5.6</td>
<td>4.6</td>
<td>30</td>
<td>49</td>
<td></td>
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<tr>
<td>Boltri14</td>
<td>8 (100)</td>
<td>0</td>
<td>nr</td>
<td>nr</td>
<td>31.6</td>
<td>16 (24)</td>
<td>10 (65)</td>
<td>3.4</td>
<td>3.6</td>
<td>nr</td>
<td>nr</td>
<td></td>
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<tr>
<td>Seidel19</td>
<td>88 (42)</td>
<td>22</td>
<td>54</td>
<td>16</td>
<td>nr</td>
<td>12 (14)</td>
<td>9 (75)</td>
<td>nr</td>
<td>nr</td>
<td>26</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>Wolf15</td>
<td>73 (0)</td>
<td>26</td>
<td>53.4</td>
<td>38</td>
<td>37.6</td>
<td>12 (52)</td>
<td>7 (58)</td>
<td>2.4</td>
<td>4.9</td>
<td>nr</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Kramer20</td>
<td>93 (46)</td>
<td>22</td>
<td>54.8</td>
<td>19</td>
<td>35.7</td>
<td>12 (14)</td>
<td>8 (67)</td>
<td>3.4</td>
<td>3.5</td>
<td>24</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>McBride22</td>
<td>40 (70)</td>
<td>8</td>
<td>51.9</td>
<td>41</td>
<td>37.4</td>
<td>12 (12)</td>
<td>nr</td>
<td>5.0</td>
<td>4.6</td>
<td>nr</td>
<td>nr</td>
<td></td>
</tr>
<tr>
<td>McTigue23</td>
<td>72 (nr)</td>
<td>7</td>
<td>53</td>
<td>16</td>
<td>38.9</td>
<td>12 (52)</td>
<td>nr</td>
<td>5.2</td>
<td>nr</td>
<td>27</td>
<td>nr</td>
<td></td>
</tr>
<tr>
<td>Whittemore17</td>
<td>31 (nr)</td>
<td>22</td>
<td>48.2</td>
<td>10</td>
<td>40.0</td>
<td>11 (36)</td>
<td>8 (69)</td>
<td>nr</td>
<td>nr</td>
<td>nr</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Cramer21</td>
<td>27 (0)</td>
<td>nr</td>
<td>nr</td>
<td>nr</td>
<td>nr</td>
<td>7 (28)</td>
<td>nr</td>
<td>2.5</td>
<td>2.7</td>
<td>nr</td>
<td>nr</td>
<td></td>
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<tr>
<td>Davis-Smith16</td>
<td>10 (100)</td>
<td>10</td>
<td>nr</td>
<td>30</td>
<td>35.7</td>
<td>6 (6)</td>
<td>5 (78)</td>
<td>4.0</td>
<td>3.8</td>
<td>nr</td>
<td>nr</td>
<td></td>
</tr>
</tbody>
</table>

*In lifestyle arm of study.  nr = not reported.  †Personal communication with Dr. Ronald Ackermann.
Key Policy and Implementation Issues
Prevention of Type 2 Diabetes

Goal:

- Systematically scale the translated model of the Diabetes Prevention Program (DPP) for high risk persons in collaboration with community-based organizations that have necessary infrastructure, health payers, public health, academia, and others to reduce the incidence of type 2 diabetes in the United States.
Four Key Levers

(1) Training the work force that can implement the program cost effectively

(2) Implementing a recognition program that will contribute to assuring quality, lead to reimbursement, and allow CDC to develop a registry of programs for public reporting
Four Key Levers

(3) Implementing sites that will build the infrastructure and some will provide a “laboratory” for additional refinement of this prevention system

(4) Increasing referrals and utilization of the prevention system through health marketing and other strategies
Section 399V-3, page 310: National Diabetes Prevention Program

- Establishes a national Diabetes Prevention Program that includes grant program for model sites, recognition program for quality assurance and national registry, and applied research
- Lead agency = CDC
- Authorized appropriations = Such sums as may be necessary for each of fiscal years 2010-2014