Priorities for Diabetes Research

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Obesity Trends in the United States
Adults 20-74 years of age

Source: Data from Centers for Disease Control and Prevention
Type 2 Diabetes Prevention
Where are we now?

Cost effectiveness
- More health benefits with lifestyle and nearly cost neutral
- Most cost saving with metformin

New Diabetes Cases (%)
- Placebo
- Metformin
- Lifestyle

Cumulative Incidence (%)
Type 2 Diabetes Prevention

What are the Challenges?

Population-wide Delivery of Effective Interventions

Translational research
- Practical and generalizable approaches to deliver a DPP-based lifestyle intervention to adults with prediabetes
- Dissemination potential
- Cost effectiveness
- Diverse populations
- Real world settings (communities, worksites, etc.)
New NIDDK Fact Sheet Explains A1C Test for Diabetes and Prediabetes

The A1C Test and Diabetes

What is the A1C test?
The A1C test is a blood test that provides information about a person’s average levels of blood glucose over the past 3 months. The A1C test is sometimes called the home glucose A1C, HbA1C, or glycated hemoglobin test. The A1C test is the primary test used for diabetes management and diabetes research.

How does the A1C test work?
The A1C test is based on the attachment of glucose to hemoglobin, the protein in red blood cells that carries oxygen. In the body, red blood cells are constantly forming and dying, but typically they live for about 3 months. Thus, the A1C test reflects the average of a person’s blood glucose levels over the past 3 months. The A1C test result is reported as a percentage. The higher the percentage, the higher a person’s blood glucose levels have been. A normal A1C level is below 5.7 percent.

Can the A1C test be used to diagnose type 2 diabetes and prediabetes?
Yes. In 2009, an international expert committee recommended the A1C test as one of the tests available to help diagnose type 2 diabetes and prediabetes. 

Why should a person be tested for diabetes?
Testing is especially important because early in the disease, diabetes has no symptoms. Although no test is perfect, the A1C and blood glucose tests are the best tools available to diagnose diabetes—a serious and life-threatening disease. Testing enables health care providers to find and treat diabetes before complications occur and to find and treat prediabetes, which can delay or prevent type 2 diabetes from developing.

www.diabetes.niddk.nih.gov/dm/pubs/A1CTest/
The A1C Test and Diabetes

National Diabetes Information Clearinghouse


A1c

Fasting plasma glucose
Primary Prevention

Secondary Prevention

Tertiary Prevention

*Includes type 1 (5-10%) and type 2 (90-95%) diabetes; diagnosed and undiagnosed cases.
Lifestyle Change and Mobility in Obese Adults with Type 2 Diabetes

W. Jack Rejeski, Ph.D., Edward H. Ip, Ph.D., Alain G. Bertoni, M.D., George A. Bray, M.D., Gina Evans, Ph.D., Edward W. Gregg, Ph.D., and Qiang Zhang, M.S., for the Look AHEAD Research Group*

“Participants in the lifestyle-intervention group had a 48% reduction in mobility-related disability, as compared with those in the support group.”
Bariatric Surgery for Type 2 Diabetes

- LABS 1—Short term safety in 4,776 adults (NEJM 2009)
- LABS 2—Longer-term safety and efficacy (enrollment completed 2009)
- LABS 3—Mechanistic studies in LABS subjects
- Teen-LABS
Bariatric Surgery for Type 2 Diabetes
Unanswered Questions

- Role is less obese subjects
- Mechanisms and durability of diabetes remission
- Timing relative to other interventions
- Predictors of success
- Comparative effectiveness
  - Among surgical procedures
  - Vs. Lifestyle
- Effect on clinical outcomes
Management of Diabetes
Where Are We Now?

Recent decades have brought about new or improved...

- Glucose monitoring technologies
- Insulin delivery systems
- Insulin formulations
- Drugs for type 2 diabetes and medications to treat CVD risk factors

Research has shown that...

- Good blood glucose control prevents complications in type 1 and type 2 diabetes
- Near normalization of glucose reduced early microvascular disease but increased mortality

Research Studies:
- ACCORD
- UKPDS
- DCCT/EDIC
- NIDDK

Good blood glucose control prevents complications in type 1 and type 2 diabetes
Near normalization of glucose reduced early microvascular disease but increased mortality
DCCT/EDIC Metabolic Control

Study begins 1983

Microalbuminuria 39% in intensive group 1993

Impaired GFR 50% in intensive group 2011

Conventional - DCCT mean 9.1%
Intensive - DCCT mean 7.2%

Conventional - EDIC mean
Intensive - EDIC mean 8.0%

Glycosylated hemoglobin (%)

Study Year
Management of Diabetes
Challenges of individualizing therapy...

<table>
<thead>
<tr>
<th>Patient age</th>
<th>Disease duration</th>
<th>Comorbidities</th>
<th>Hypoglycemia risk</th>
<th>Established Complications</th>
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- **Behavioral - Social - Economic**
  - Higher motivation, knowledge, ample resources
  - Greater self-care capacity, insight, support
  - Less motivated, non-adherent, few resources
  - Limited self-care capacity, insight, support

Average A1C Is Improving

National Health and Nutrition Examination Survey (NHANES)

Source: Diabetes Care 31: 81, 2008
"Good": age specific HbA1c, < 6 yr, <8.5%; 6-12 yr, <8.0%; 13-18 yr, <7.5%; 19+ yr, <7.0%
"Intermediate": HbA1c between “good” and “poor”
“Poor”: HbA1c ≥ 9.5%

J Peds 155: 668, 2009
SEARCH for Diabetes in Youth

- Over 150,000 U.S. youth with physician-diagnosed diabetes
- 15,000 youth are diagnosed annually with T1D
- 3,600 youth are diagnosed annually with T2D
- Rising incidence of both T1D and T2D
- Cohort followed longitudinally to understand clinical course, including complications, and quality of care/quality of life issues
Obesity Trends in the United States

![Graph showing obesity trends from 1970 to 2010 for adults and children/youth.]

**Adults**
- 20-74 years of age
- Obesity rates have increased significantly over the years.

**Children/Youth**
- 2-19 years of age
- Obesity rates have also increased, mirroring the trend in adults.

**Obesity-related diseases once seen only in adults are now being seen in children.**

*Source: Data from Centers for Disease Control and Prevention*
Preventing and Treating Type 2 Diabetes in Youth

Normal ↔ Pre-diabetes ↔ Type 2 Diabetes → Complications → Disability → Death

HEALTHY
Another reason to prevent and treat obesity in children...

\[ \frac{dBW}{dt} = ? \]
Healthy – Results

- Half of the students were overweight or obese at the beginning of the study.
- In this group of high risk students, those in intervention schools had significantly greater decreases in the prevalence of obesity.
- BMI z score, waist circumference, and insulin levels were significantly lowered in intervention schools.
- Overall, the combined rate of overweight and obesity fell by 4% in both intervention and control schools.
Resources to make “HEALTHY” changes in more schools

HEALTHY materials are available free online, to help staff at other schools implement changes to support healthy lifestyles among youth:

- physical education curriculum,
- student and teacher workbooks for behavior change curriculum,
- nutrition messaging,
- posters and social marketing materials

www.healthystudy.org
Early influences on childhood obesity – risks from maternal obesity or diabetes during pregnancy

- Pregnant woman with obesity or diabetes
- Young woman with obesity or diabetes
- Infant (daughter)
Raising Awareness of GDM

- DPP trial showed that diabetes can be prevented or delayed in women with a history of GDM

- NDEP has expanded the reach of *Small Steps. Big Rewards. Prevent type 2 Diabetes/It’s Never Too Early...To Prevent Diabetes*

- Outreach activities designed to raise awareness among women and health care providers of—
  - future health risks for women with a history of GDM and their children; and
  - steps they can take to prevent or delay the onset of diabetes.
LIFE-Moms Consortium
Lifestyle Interventions for Expectant Moms

To test lifestyle interventions for overweight/obese pregnant women, in order to improve weight and metabolic outcomes in both the pregnant women and their offspring.

Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) Study

To test long term consequences of maternal glycemia in mother and child.
TEDDY
The Environmental Determinants of Diabetes in the Young

**Primary Goal**
- To identify the triggers that cause children to get type 1 diabetes

**Secondary goal**
- Establish a central repository of data and biologic samples

> 8,000 children enrolled and being followed until age 15
The NIH Supports Research At Every Stage of Disease Progression

Genetic susceptibility | Inciting Event(s) | “Silent” β Cell Loss | Diabetes Onset | “Brittle” Diabetes

Islet Cell Mass

Time (years)

Prevent Disease

Delay Progression

Prevent and Treat Complications

Complications
TrialNet Prevention Trials

TrialNet Pathway to Prevention

TrialNet Oral Insulin

TrialNet Anti-CD3 Prevention
Prevalence* of Diabetes in 2011
Adults, Ages 20-79

*Comparative prevalence, percent
