Number (in Millions) of Civilian, Non-Institutionalized Persons with Diagnosed Diabetes, United States, 1980-2014

Diabetes is becoming more common in the United States. From 1980 through 2014, the number of Americans with diagnosed diabetes has increased fourfold (from 5.5 million to 22.0 million).

April 7 is WHO’s annual World Health Day, which celebrates WHO’s founding in 1948

• In 2014, 422 million adults (8.5% of the population) had diabetes, compared with 108 million (4.7%) in 1980.

• Many diabetes related deaths (43%) occur prematurely, before age 70 years, and are largely preventable through adoption of policies to create supportive environments for healthy lifestyles and better detection and treatment of the disease.
Long-term Complications of Diabetes
Consequences of Sustained Hyperglycemia

Diabetic Retinopathy
Leading cause of blindness in working age adults

Diabetic Nephropathy
Leading cause of end-stage renal disease

Stroke
2- to 4-fold increase in cardiovascular events and mortality

Cardiovascular Disease

Diabetic Neuropathy
Leading cause of nontraumatic lower extremity amputations


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Overview of the Diabetes Epidemic in the United States

- ~9-11% of the population have diabetes
- 7 million are undiagnosed
- Centers for Disease Control and Prevention estimates that 1 in 3 adult Americans will have diabetes by 2050
- Type 2 diabetes
  - Associated with obesity, older age, decreased physical activity, and race/ethnicity
  - Incidence in children and adolescents is increasing

Glimmer of Hope

- After more than doubling from 1990 to 2008, age-adjusted diabetes incidence among adults aged 18 to 79 years dropped between 2008 and 2014, from 8.5 to 6.6 per 1000.

- But according to IDF atlas, United States still has highest prevalence of diabetes among developed nations: 11% of population aged 20 to 79 years.

IDF Atlas, 7th edition 2015
Cost of Diabetes, 2012

Estimated national cost of diabetes in 2012
$245 billion
$176 billion (72%) direct health care expenditures
$69 billion (28%) lost productivity from
work-related absenteeism, reduced productivity at
work and home, unemployment from chronic
disability, and premature mortality.

Change from 2007-2012

Increase of $43 billion reflects:
1) 27% growth in diabetes prevalence,
2) changing demographics of people with diabetes,
3) growth in the utilization of certain types of health care services for treating diabetes and its comorbidities such as increased use of prescription medications and advanced treatment for cardiovascular disease,
4) rising prices for medical goods and services above general rate of inflation,
5) refinements to data and methods used to calculate cost of diabetes.
Impact of Diabetes in America

During the next hour:
A. 20 Americans will be diagnosed with diabetes.
B. 120 Americans will be diagnosed with diabetes.
C. 220 Americans will be diagnosed with diabetes.
D. 520 Americans will be diagnosed with diabetes.

During the next hour, 220 Americans will be diagnosed with diabetes.

Impact of Diabetes in America (cont.)

- Diabetes is the leading cause of kidney failure, accounting for 44% of all new cases of kidney failure in 2008.
- In 2008, 48,374 people with diabetes began treatment for end-stage kidney disease.
- In 2008, a total of 202,290 people with end-stage kidney disease from diabetes were living on chronic dialysis or with a kidney transplant.

What Was the Proportion of National Health Care Expenditures Devoted to Diabetes Care in 2007?

A. 10%
B. 15%
C. 20%
D. 25%
What Was the Proportion of Medicare Expenditures Devoted to Diabetes Care in 2007?

A. 15%
B. 20%
C. 27%
D. 32%

(Test strips cost $1 billion/year in 2006, 1.7 billion in 2010!)
Annual Health Care Costs for Patients With and Without Diabetes

<table>
<thead>
<tr>
<th>Food</th>
<th>20 Years Ago</th>
<th>Today</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bagel</strong></td>
<td>3-inch diameter</td>
<td>6-inch diameter</td>
</tr>
<tr>
<td></td>
<td>140 calories</td>
<td>350 calories</td>
</tr>
<tr>
<td><strong>Cheeseburger</strong></td>
<td>1 portion</td>
<td>1 portion</td>
</tr>
<tr>
<td></td>
<td>333 calories</td>
<td>590 calories</td>
</tr>
<tr>
<td><strong>Spaghetti and Meatballs</strong></td>
<td>1 cup spaghetti, sauce and 3 small meatballs</td>
<td>2 cups spaghetti, sauce and 3 large meatballs</td>
</tr>
<tr>
<td></td>
<td>500 calories</td>
<td>1,025 calories</td>
</tr>
<tr>
<td><strong>Soda</strong></td>
<td>6.5 ounces</td>
<td>about 20 ounces</td>
</tr>
<tr>
<td></td>
<td>85 calories</td>
<td>300 calories</td>
</tr>
<tr>
<td><strong>French Fries</strong></td>
<td>2.4 ounces</td>
<td>6.9 ounces</td>
</tr>
<tr>
<td></td>
<td>210 calories</td>
<td>610 calories</td>
</tr>
</tbody>
</table>
Chefs’ Estimates of Serving Sizes

Descriptions of typical portion sizes of all food, penne pasta, strip steak, and a vegetable side-dish, and size of dinner plates that chefs in this survey reported serving. In the current dietary guidelines, the U.S. Department of Agriculture recommends a 1-oz serving of pasta, 5.5 oz of meat per day, and a 2- to 3-oz portion of vegetables. Senior/Half, "early bird" or half-portion size; Full/Regular, standard portion size.
Coffee

20 Years Ago
Coffee
(with whole milk and sugar)

8 ounces, 45 calories

Today
Mocha Coffee
(with steamed whole milk and mocha syrup)

?? calories

A standard cup of coffee 20 years ago was 8 ounces and had 45 calories. How many calories do you think are in today's coffee?

☐ 100 ☐ 350 ☐ 450

Check Your Answer!
Correct!

Today’s 16 ounce cup of coffee has **350** calories. This is **305** calories more than a cup of coffee 20 years ago.

Keep in mind that many of today’s coffee drinks have a lot of added sugar, milk and syrup which increase the calories. It is best to stick with plain coffee and add your own milk and sweetener or ask for sugar free syrup.

Now guess how long you will have to walk in order to burn those extra 305 calories?*

- 2 hours and 15 minutes
- 1 hour and 20 minutes
- 3 hours

*Based on a 130-pound person.
From Seattle Times, June 12, 2011: Changes from 1970 to 2008

- Sugar: 402 to 459 cal/day
- Fat: 410 to 641 cal/day
- Grains: 432 to 625 cal/day
Myths that get in our way

Reasons people say they don’t choose "healthy food"

- 40% It doesn’t taste good
- 75% It’s expensive
- 50% It’s hard to prepare

*Source: Food Marketing Institute*

Quick fixes make our day

**84%**

**Fast-Food Restaurants**
Parents who took their kids at least once in the past week

**Calories in Soda**
Number of calories in an average portion today vs. the 1950s

- 1950s: 88
- Today: 160 or more

**Cereals**
Sugar and sodium content of brands marketed to kids vs. adults

- Adult brands
  - Sugar: 85% more
  - Sodium: 60% more

*Source: Yale Rudd Center for Food Policy & Obesity; Journal of Public Health Nutrition*
TV’s influence

Foods advertised on Saturday morning television

- Restaurants 19%
- Snack foods 18%
- Cereal and cereal bars 27%
- Beverages 10%
- Other 13%

Note: Numbers do not add up to 100 due to rounding.

Source: Center for Science in the Public Interest
A. RAYMOND/THE SEATTLE TIMES
What Doctors Say...

“Eat healthy, drink in moderation, and be conscientious regarding blood sugar testing...”

What Patients Hear...

“Eat...drink...and be merry...”
Treatment Options

- Nutritional
- Physical activity
- Pharmacological
Classification

- Two major forms:
  - Type 2
  - Type 1
- Other:
  - Gestational
  - Chemical (steroid)
  - Endocrinological
  - LADA
  - Type 1.5

- Unusual diabetes:
  - Monogenic: MODY, MIDD
  - Pancreatic:
    - Tropical pancreatitis
    - Autoimmune pancreatitis
  - Cystic fibrosis
  - Post transplantation

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Cumulative Incidence of Diabetes from Three U.K. Birth Cohorts

Progressive Left Shift in Age of Onset


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The Faces of Type 1 Diabetes
Type 1 Diabetes: Not Just for Kids

- 20% of patients with type 1 diabetes develop the disease after the age of 30.
- There are variants with more latent onset.
- It follows a very waxing and waning course in terms of autoimmune antibody status.
Natural History of Type 1 Diabetes

- Genetic Risk
- Environmental Insult

Normal Islet Function

Onset Clinical Diabetes

“Pre-Clinical Period”

Time (Months or Years)
Type 2 Diabetes

- Can occur at any age  T/F
- 90% of all diabetes  T/F
- Major public health problem for America’s ethnic minorities
  - American Indians, Hispanics, Asian Americans, African Americans
- Two problems: resistance to insulin and insulin deficiency in the face of insulin resistance
- No immune markers, no good physical marker of insulin resistance
### Table 1: Genetic variants associated with T2DM at or near genome-wide levels of statistical significance

<table>
<thead>
<tr>
<th>Marker</th>
<th>Chromosome</th>
<th>Locus</th>
<th>Type of mutation</th>
<th>Function of gene</th>
<th>Risk allele</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs10923931&lt;sup&gt;36&lt;/sup&gt;</td>
<td>1</td>
<td>NOTCH2</td>
<td>Intronic</td>
<td>Transmembrane receptor involved in the formation of the pancreas</td>
<td>T</td>
<td>1.13</td>
</tr>
<tr>
<td>rs7578597&lt;sup&gt;36&lt;/sup&gt;</td>
<td>2</td>
<td>THADA</td>
<td>Missense: Thr1187Ala</td>
<td>Expressed in thyroid adenomas; binds to PPARγ</td>
<td>T</td>
<td>1.15</td>
</tr>
<tr>
<td>rs4607103&lt;sup&gt;36&lt;/sup&gt;</td>
<td>3</td>
<td>ADAMTS9</td>
<td>38 kb upstream</td>
<td>Secreted metalloproteinase expressed in muscles and pancreas</td>
<td>C</td>
<td>1.09</td>
</tr>
<tr>
<td>rs4402960&lt;sup&gt;83&lt;/sup&gt;</td>
<td>3</td>
<td>IGF2BP2</td>
<td>Intronic</td>
<td>Growth factor binding protein involved in pancreatic development</td>
<td>T</td>
<td>1.14</td>
</tr>
<tr>
<td>rs1801282&lt;sup&gt;84&lt;/sup&gt;</td>
<td>3</td>
<td>PPARG</td>
<td>Missense: Pro12Ala</td>
<td>Transcription factor involved in adipocyte development</td>
<td>C</td>
<td>1.19</td>
</tr>
<tr>
<td>rs10010131&lt;sup&gt;83&lt;/sup&gt;</td>
<td>4</td>
<td>WFS1</td>
<td>Intron-exon junction</td>
<td>Transmembrane protein of the endoplasmic reticulum</td>
<td>G</td>
<td>1.15</td>
</tr>
<tr>
<td>rs7754840&lt;sup&gt;83&lt;/sup&gt;</td>
<td>6</td>
<td>CDKAL1</td>
<td>Intronic</td>
<td>Islet glucose toxicity sensor; inhibits CDK5 activation</td>
<td>C</td>
<td>1.12</td>
</tr>
<tr>
<td>rs864745&lt;sup&gt;36&lt;/sup&gt;</td>
<td>7</td>
<td>JAZF1</td>
<td>Intronic</td>
<td>Transcriptional repressor associated with prostate cancer</td>
<td>T</td>
<td>1.10</td>
</tr>
<tr>
<td>rs13266634&lt;sup&gt;83&lt;/sup&gt;</td>
<td>8</td>
<td>SLC30A8</td>
<td>Missense: Arg325Trp</td>
<td>Zinc transporter involved in insulin storage and secretion</td>
<td>C</td>
<td>1.12</td>
</tr>
<tr>
<td>rs10811661&lt;sup&gt;83&lt;/sup&gt;</td>
<td>9</td>
<td>CDKN2A/B</td>
<td>125 kb upstream</td>
<td>Cyclin-dependent kinase inhibitor and tumor suppressor involved in islet development</td>
<td>T</td>
<td>1.20</td>
</tr>
<tr>
<td>rs12779790&lt;sup&gt;36&lt;/sup&gt;</td>
<td>10</td>
<td>CDC123-CAMK1D</td>
<td>Intergenic region</td>
<td>Cell-cycle regulator and protein kinase</td>
<td>G</td>
<td>1.11</td>
</tr>
<tr>
<td>rs7903146&lt;sup&gt;13&lt;/sup&gt;</td>
<td>10</td>
<td>TCF7L2</td>
<td>Intronic</td>
<td>Transcription factor that regulates genes that encode proglucagon and insulin</td>
<td>T</td>
<td>1.37</td>
</tr>
<tr>
<td>rs1111875&lt;sup&gt;83&lt;/sup&gt;</td>
<td>10</td>
<td>HHEX</td>
<td>7.7 kb downstream</td>
<td>Transcription factor involved in pancreatic development</td>
<td>C</td>
<td>1.13</td>
</tr>
<tr>
<td>rs5219&lt;sup&gt;9&lt;/sup&gt;</td>
<td>11</td>
<td>KCNJ11</td>
<td>Missense: Glu23Lys</td>
<td>Potassium channel that regulates insulin secretion</td>
<td>T</td>
<td>1.14</td>
</tr>
<tr>
<td>rs2237892&lt;sup&gt;38&lt;/sup&gt;</td>
<td>11</td>
<td>KCNQ1</td>
<td>Intronic</td>
<td>Pore-forming a subunit of potassium channel</td>
<td>C</td>
<td>1.42</td>
</tr>
<tr>
<td>rs1387153&lt;sup&gt;44&lt;/sup&gt;</td>
<td>11</td>
<td>MTN1B</td>
<td>28.3 kb upstream</td>
<td>High-affinity, G-protein-coupled receptor for melatonin</td>
<td>T</td>
<td>1.15</td>
</tr>
<tr>
<td>rs7961581&lt;sup&gt;36&lt;/sup&gt;</td>
<td>12</td>
<td>TSPAN8-LGR5</td>
<td>Intronic</td>
<td>Cell-surface glycoprotein implicated in gastrointestinal tumors</td>
<td>C</td>
<td>1.09</td>
</tr>
<tr>
<td>rs8050136&lt;sup&gt;83&lt;/sup&gt;</td>
<td>16</td>
<td>FTO</td>
<td>Intronic</td>
<td>Function unknown; affects BMI in general population</td>
<td>A</td>
<td>1.17</td>
</tr>
<tr>
<td>rs757210&lt;sup&gt;83&lt;/sup&gt;</td>
<td>17</td>
<td>HNF1B</td>
<td>Intronic</td>
<td>Transcription factor involved in pancreatic development</td>
<td>A</td>
<td>1.12</td>
</tr>
</tbody>
</table>

*P<5×10⁻⁸. Abbreviation: T2DM, type 2 diabetes mellitus.*


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## Associated with Prevention of Type 2 Diabetes

<table>
<thead>
<tr>
<th>Item</th>
<th>T/F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased fiber and cereal grains</td>
<td>T</td>
</tr>
<tr>
<td>Dairy</td>
<td>F</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>F</td>
</tr>
<tr>
<td>Alcohol</td>
<td>T</td>
</tr>
<tr>
<td>Caffeine</td>
<td>T</td>
</tr>
<tr>
<td>Mediterranean diet</td>
<td>T</td>
</tr>
</tbody>
</table>
Associated with Increased Risk for Type 2 Diabetes

- Lack of sleep
- Smoking
- Lack of exercise
Type 1.5 Diabetes (cont.)

- Distinct from LADA
- Phenotypically appears more like type 2 diabetes
  - Obese, insulin resistant
- However, one of Abs is *positive*, suggesting autoimmune β-cell destruction
- Best therapy unclear, although UKPDS data show >90% of these patients require insulin after 6 years
Diagnostic Criteria in Non-Pregnant People

- Fasting glucose: >125 mg/dL on two separate days
- Blood glucose 2 hours after 75 g load: >200 mg/dL
- Random blood glucose: ≥200 mg/dL and symptoms of hyperglycemia
- Hyperglycemia and acute decompensation
- A1C
A1c Measurement

• Considered the gold standard for measurement of glycemic control
• Not patient dependent
• Serves as surrogate for risk of both microvascular as well as macrovascular complications
### Estimated Average Glucose (eAG)

- 507 subjects, 2700 glucose points
- DM1, DM2, non-DM
- A1c matched to 3 days/wk 7 point fingerstick, min 2 days/mo continuous glucose sensor (blinded)

#### Table 2 — Estimated average glucose

<table>
<thead>
<tr>
<th>A1C (%)</th>
<th>mg/dl*</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>97 (76–120)</td>
</tr>
<tr>
<td>6</td>
<td>126 (100–152)</td>
</tr>
<tr>
<td>7</td>
<td>154 (123–185)</td>
</tr>
<tr>
<td>8</td>
<td>183 (147–217)</td>
</tr>
<tr>
<td>9</td>
<td>212 (170–249)</td>
</tr>
<tr>
<td>10</td>
<td>240 (193–282)</td>
</tr>
<tr>
<td>11</td>
<td>269 (217–314)</td>
</tr>
<tr>
<td>12</td>
<td>298 (240–347)</td>
</tr>
</tbody>
</table>

Data in parentheses are 95% CIs.

* Linear regression eAG(mg/dl) = 28.7 × A1C – 46.7.

Mean glucose versus HbA1c: mean glucose measured by the CGM device over 3 months (91 days) before the HbA1c measurement (n = 252).

Mean Glucose = -16.2 + 24.4 * A1c
R-square = 0.63

Dia Care 2011;34:540-544
What Alters A1C

Hematologic conditions
- Anemia
- Accelerated erythrocyte turnover
  - Thalassemia
  - Sickle cell disease
  - Reticulocytosis
  - Hemolysis

Physiologic States
- Aging
- Pregnancy

Drugs/Medications
- Alcohol
- Opioids
- Vitamin C
- Vitamin E
- Aspirin
- Erythropoetin
- Dapsone
- Ribavirin

Disease States
- HIV infection
- Uremia
- Hyperbilirubinemia
- Dyslipidemia
- Cirrhosis
- Hypothyroidism*

Medical Therapies
- Blood transfusion
- Hemodialysis

Miscellaneous
- Glycation rate
- Protein turnover
- Race and ethnicity*
- Mechanical heart valves*
- Laboratory assay

In a typical primary care practice, there are LOTS of reasons why A1C may be falsely low (or high); in the DCC 15-25% of patients A1C “doesn’t work”
Complications of Diabetes
How Often Does Hypoglycemia Occur in Diabetes?

Frequency of NSHE (%)

- Daily to about 1/wk
- 1/mo to several times/mo
- Only a few times/y or very rarely

Wk, week; mo, month; T1DM, type 1 diabetes; T2DM, type 2 diabetes; NSHE, non-severe hypoglycemic events

Survey 409 US patients with T1DM (n = 200) and with T2DM (n = 209)


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When Does Hypoglycemia Occur with Diabetes?

1/5 of all nonsevere hypoglycemia occurs nocturnally.

Survey 409 US patients with T1DM (N=200) and with T2DM (N=209)

NSHE, non-severe hypoglycemic events

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## Potential Complications of Hypoglycemia

### Central Nervous System
- Cognitive Dysfunction
- Intellectual Decline
- Coma
- Brain Damage
- Seizure
- Focal Neurological Lesions (Rare)
- TIA, Stroke

### Heart
- Cardiac arrhythmias
- Myocardial ischemia

### Eye
- Vitreous Hemorrhage
- Worsening of retinopathy?

### Other
- Falls
- Accidents with injury

---


TIA, transient ischemic attack

---

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Temporal Trends in Diabetic Kidney Disease

Figure. Prevalent Cases of Diabetic Kidney Disease in the United States


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Figure 1—Cumulative incidence of diabetic nephropathy in 600 type 1 diabetic patients with onset of diabetes from 1965 to 1969 (n = 113, group A [O]), 1970 to 1974 (n = 130, group B [●]), 1975 to 1979 (n = 113, group C [□]), and 1979 to 1984 (n = 244, group D [■]). P < 0.001, log-rank test, pooled over strata. Not all patients in group D have yet been followed for 20 years. For pairwise log-rank test over strata after 20 years of diabetes, see RESULTS.

Yanfeng Li, MD, MPH1,2
Nilka Rios Burrows, MPH2
Edward W. Gregg, PhD2
Ann Albright, PhD, RD2
Linda S. Geiss, MA2

OBJECTIVE—To assess trends in rates of hospitalization for nontraumatic lower-extremity amputation (NLEA) in U.S. diabetic and nondiabetic populations and disparities in NLEA rates within the diabetic population.

RESEARCH DESIGN AND METHODS—We calculated NLEA hospitalization rates, by diabetes status, among persons aged ≥40 years on the basis of National Hospital Discharge Survey data on NLEA procedures and National Health Interview Survey data on diabetes prevalence. We used joinpoint regression to calculate the annual percentage change (APC) and to assess trends in rates from 1988 to 2008.

RESULTS—The age-adjusted NLEA discharge rate per 1,000 persons among those diagnosed with diabetes and aged ≥40 years decreased from 11.2 in 1996 to 3.9 in 2008 (APC = −8.6%; P < 0.01), while rates among persons without diagnosed diabetes changed little. NLEA rates in the diabetic population decreased significantly from 1996 to 2008 in all demographic groups examined (all P < 0.05). Throughout the entire study period, rates of diabetes-related NLEA were higher among persons aged ≥75 years than among those who were younger, higher among men than women, and higher among blacks than whites.

CONCLUSIONS—From 1996 to 2008, NLEA discharge rates declined significantly in the U.S. diabetic population. Nevertheless, NLEA continues to be substantially higher in the diabetic population than in the nondiabetic population and disproportionately affects people aged ≥75 years, blacks, and men. Continued efforts are needed to decrease the prevalence of NLEA risk factors and to improve foot care among certain subgroups within the U.S. diabetic population that are at higher risk.


reductions in rates of diabetes-related complications (5,6) and cardiovascular disease (6).

Although results of several recent studies (6–9) have shown encouraging trends in rates of NLEA in various populations and evidence of subgroup disparities among people with diabetes, no comprehensive studies have examined trends in NLEA rates or characteristics associated with diabetes-related NLEAs in the overall U.S. population. In this study, we used data from two nationally representative surveys to assess trends in NLEA hospital discharge rates by patients' diabetes status and to determine whether disparities in NLEA rates within the diabetic population persist.

RESEARCH DESIGN AND METHODS

Data sources
Our study was based on 1988–2008 data from the National Hospital Discharge Survey (NHDS) and the National Health Interview Survey (NHIS). The NHDS is a national probability survey of short-stay, nonfederal hospitals in all 50 states and...
Between 1996 and 2008, NLEA rates decreased by 67%.
Diabetic retinopathy
Neovascularization
Diabetic Peripheral Neuropathy

• Diabetic peripheral neuropathy (DPN) is a frequent complication of diabetes associated with significant morbidity and mortality¹
  – Risk factor for ulcers and amputations²
  – Impairs quality of life¹

• Significant resources are spent to treat patients with DPN
  – Estimated total annual cost in US $4.6 - $13.7 billion³

• Only effective intervention is prevention by tight control of patient’s diabetes

DPN affects the limbs symmetrically and progresses from distal to proximal over time.

- DPN is characterized by a stocking and glove distribution:
  - Bilateral symmetrical distribution of signs and symptoms
  - Affects lower limbs first
  - Progresses from distal (toes) to proximal (knee) over time.

Diabetic Neuropathy (Boulton), 2001
# Epidemiology

Reliable epidemiological information is complicated by differences in: Definition; Methodology and Diagnostic Criteria

<table>
<thead>
<tr>
<th>Study Population</th>
<th>Data Collection</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rochester Diabetic Neuropathy Study*</td>
<td>1986</td>
<td>54% - Type I</td>
</tr>
<tr>
<td></td>
<td></td>
<td>45% - Type II</td>
</tr>
<tr>
<td>San Luis Valley Diabetes Study†</td>
<td>1984 – 1986</td>
<td>25.8%</td>
</tr>
<tr>
<td>Pittsburgh Epidemiology of Diabetes Complications Study‡</td>
<td>1984 – 1988</td>
<td>34.0%</td>
</tr>
</tbody>
</table>

DPN diagnosed on basis of: *Positive symptoms and electrophysiological testing¹; †Neurological exam²; ‡Presence of two out of three: abnormal sensory or motor signs, symptoms, decreased tendon reflexes³

---

Figure 34.1 Failure of palmar surfaces of interphalangeal joints to approximate in patient with stiff joints and waxy skin.
Relative risks for cardiovascular autonomic neuropathy and mortality in 15 studies.

Available Therapies
Anti-hyperglycemic Agents In US 2015


Insulin, Sulfonylurea, TZDs, Glinides, Metformin, α Glucosidase inhibitors, Sitagliptin, Saxagliptin, Bromocriptine, Linagliptin

U-300, Inhaled Insulin, U-200, Exenatide once weekly, Colesevelam, Liraglutide, SGLT 2
How to Choose Diabetes Therapies – 2016

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More complex insulin strategies

If combination therapy that includes basal insulin has failed to achieve HbA1c target after 3-6 months, proceed to a more complex insulin strategy, usually in combination with 1-2 non-insulin agents.

<table>
<thead>
<tr>
<th>Drug Combinations</th>
<th>Efficacy (↓HbA1c)</th>
<th>Hypoglycemia</th>
<th>Weight</th>
<th>Major side effect(s)</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin + Sulfonylurea</td>
<td>high moderate risk gain hypoglycemia</td>
<td>high</td>
<td>low risk</td>
<td>gain edema, HF, fx's</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + Thiazolidinedione</td>
<td>high low risk</td>
<td>neutral</td>
<td>rare</td>
<td>GI</td>
<td>high</td>
</tr>
<tr>
<td>Metformin + DPP-4 Inhibitor</td>
<td>intermediate low risk</td>
<td>neutral</td>
<td>rare</td>
<td>GI</td>
<td>high</td>
</tr>
<tr>
<td>Metformin + GLP-1 receptor agonist</td>
<td>high low risk</td>
<td>loss</td>
<td>GI</td>
<td>high</td>
<td>variable</td>
</tr>
<tr>
<td>Metformin + Insulin (usually basal)</td>
<td>highest high risk</td>
<td>gain hypoglycemia</td>
<td>variable</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Initial drug monotherapy

Healthy eating, weight control, increased physical activity

Metformin

- high
- low risk
- neutral/loss
- GI / lactic acidosis
- low

If needed to reach individualized HbA1c target after ~3 months, proceed to 2-drug combination (order not meant to denote specific preference)

<table>
<thead>
<tr>
<th>Drug Combinations</th>
<th>Efficacy (↓HbA1c)</th>
<th>Hypoglycemia</th>
<th>Weight</th>
<th>Side effects</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin + Sulfonylurea</td>
<td>high</td>
<td>moderate risk gain</td>
<td>hypoglycemia</td>
<td>low risk</td>
<td>moderate risk gain hypoglycemia</td>
</tr>
<tr>
<td>Metformin + Thiazolidinedione</td>
<td>high</td>
<td>low risk</td>
<td>gain edema, HF, fx's</td>
<td>low</td>
<td>low</td>
</tr>
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<td>Metformin + DPP-4 Inhibitor</td>
<td>intermediate</td>
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<td>highest</td>
<td>high risk</td>
<td>gain hypoglycemia</td>
<td>variable</td>
<td></td>
</tr>
</tbody>
</table>

Inzucchi SE, et al., Diabetes Care 2012;35:1364–1379
# Individualization Of HbA1c Targets

<table>
<thead>
<tr>
<th>Target HbA1c Goal</th>
<th>Patient Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c &lt; 7.0%</td>
<td>Nonpregnant adults for prevention of complications</td>
</tr>
<tr>
<td></td>
<td>- Microvascular disease</td>
</tr>
<tr>
<td></td>
<td>- Macrovascular disease</td>
</tr>
<tr>
<td>Lower than the general goal of &lt; 7.0% (without hypoglycemia)</td>
<td>Patients with:</td>
</tr>
<tr>
<td></td>
<td>- Short duration of diabetes</td>
</tr>
<tr>
<td></td>
<td>- Long life expectancy</td>
</tr>
<tr>
<td></td>
<td>- No significant cardiovascular disease</td>
</tr>
<tr>
<td>Less stringent than the general goal of &lt; 7.0%</td>
<td>Patients with:</td>
</tr>
<tr>
<td></td>
<td>- History of severe hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>- Limited Life expectancy</td>
</tr>
<tr>
<td></td>
<td>- Advanced chronic complications</td>
</tr>
<tr>
<td></td>
<td>- Extensive comorbidities</td>
</tr>
<tr>
<td></td>
<td>- Long-standing diabetes in whom the general goal has been difficult to achieve despite comprehensive approach to glucose lowering including education, monitoring and progressive pharmacologic therapy</td>
</tr>
</tbody>
</table>

Adapted from Diabetes Care 2011; 34 (suppl 1) S11
Individualizing A1C Targets for Patients with T2DM

<table>
<thead>
<tr>
<th>Most Intensive</th>
<th>Less Intensive</th>
<th>Least Intensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.0%</td>
<td>7.0%</td>
<td>8.0%</td>
</tr>
</tbody>
</table>

**Psychososocioeconomic Considerations**
- Highly Motivated, Adherent, Knowledgeable, Excellent Self-Care Capacities, & Comprehensive Support Systems
- Less motivated, Non-adherent, Limited Insight, Poor Self-Care Capacities, & Weak Support Systems

**Hypoglycemia Risk**
- Low
- Moderate
- High

**Patient Age**
- 40
- 45
- 50
- 55
- 60
- 65
- 70
- 75

**Disease Duration**
- 5
- 10
- 15
- 20

**Other Comorbidities**
- None
- Few/Mild
- Multiple/Severe

**Established Vascular Complications**
- None
- Early Micro
- Advanced Micro

Multiple Contributors

- Decreased Incretin Effect
- Decreased Insulin Secretion
- Increased Glucagon Secretion
- Increased Lipolysis
- Increased Glucose Reabsorption
- Decreased Glucose Uptake
- Neurotransmitter Dysfunction


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Sites of Action by Therapeutic Options Presently Available for T2DM

T2DM = type 2 diabetes mellitus; GLP-1 = glucagon-like peptide-1; DPP-4 = dipeptidyl peptidase-4.

GLUCOSE PRODUCTION
- Biguanides (Thiazolidinedione)

GLUCOSE ABSORPTION
- α-Glucosidase Inhibitors, bile-acid resin binder

GLUCOSE PRODUCTION
- Biguanides (Thiazolidinedione)

INSULIN SECRETION/REPLACEMENT
- Sulfonylureas
- Meglitinides
- GLP-1 agonists?
- DPP4 Inhibitors?
- Insulin

GLUCOSE EXCRETION
- SGLT2 Inhibitors

PERIPHERAL GLUCOSE UPTAKE
- Biguanides (Thiazolidinedione)

PANCREAS
- BRAIN
  - GLP-1 agonists
  - Dopamine agonists

MUSCLE
- Peripheral glucose uptake

KIDNEY
- Glucose excretion

LIVER
- Glucose production

STOMACH
- Delayed emptying
- GLP-1 agonists (Exenatide, Liraglutide)
- Pramlintide

ADIPOSE TISSUE
- Glucose excretion

INTESTINE
- Glucose absorption

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Testing Made Small and Simple
For CME reasons, we cannot include product images in the presentation. We’d also prefer to avoid using brand names, if at all possible.

Jessica Steuerman, 8/27/2013
### DM Statistics

**Date Range: 7/19/2005 - 8/18/2005**

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Aggregate</th>
<th>NIGHT 00:00-05:00</th>
<th>Breakfast 05:00-09:00</th>
<th>MID-AM 09:00-11:00</th>
<th>Lunch 11:00-14:00</th>
<th>MID-AFTER 14:00-17:00</th>
<th>Dinner 17:00-20:00</th>
<th>MID-EVENING 20:00-22:00</th>
<th>BED 22:00-00:00</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong># of Readings</strong></td>
<td>100%</td>
<td>50</td>
<td>50</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

#### Maximum
- Night: 375
- Breakfast: 341
- Mid-AM: 329
- Lunch: 264
- Mid-Afternoon: 375
- Dinner: 316.00
- Mid-Evening: 289.50
- Bed: 289.50
- Aggregate: 289.50

#### 75th Percentile
- Night: 318.50
- Breakfast: 311.75
- Mid-AM: 318.75
- Lunch: 249.50
- Mid-Afternoon: 316.00
- Dinner: 289.50
- Mid-Evening: 276.50
- Bed: 276.50
- Aggregate: 276.50

#### Median
- Night: 287.50
- Breakfast: 302.00
- Mid-AM: 308.50
- Lunch: 235.00
- Mid-Afternoon: 289.50
- Dinner: 276.50
- Mid-Evening: 265.00
- Bed: 265.00
- Aggregate: 265.00

#### 25th Percentile
- Night: 259.00
- Breakfast: 284.00
- Mid-AM: 298.25
- Lunch: 220.50
- Mid-Afternoon: 276.50
- Dinner: 265.00
- Mid-Evening: 243.25
- Bed: 243.25
- Aggregate: 243.25

#### Minimum
- Night: 169
- Breakfast: 150
- Mid-AM: 288
- Lunch: 206
- Mid-Afternoon: 150
- Dinner: 150
- Mid-Evening: 150
- Bed: 150
- Aggregate: 150

#### Mean
- Night: 290.8
- Breakfast: 296.0
- Mid-AM: 306.6
- Lunch: 235.0
- Mid-Afternoon: 291.0
- Dinner: 291.0
- Mid-Evening: 291.0
- Bed: 291.0
- Aggregate: 291.0

#### Std Dev
- Night: 45.21
- Breakfast: 38.19
- Mid-AM: 20.51
- Lunch: 29.00
- Mid-Afternoon: 42.73
- Dinner: 42.73
- Mid-Evening: 42.73
- Bed: 42.73
- Aggregate: 42.73

#### Events
- Hypo (<60):
  - Night: 0
  - Breakfast: 0
  - Mid-AM: 0
  - Lunch: 0
  - Mid-Afternoon: 0
  - Dinner: 0
  - Mid-Evening: 0
  - Bed: 0
  - Aggregate: 0
- Hyper (>180):
  - Night: 2
  - Breakfast: 2
  - Mid-AM: 2
  - Lunch: 2
  - Mid-Afternoon: 2
  - Dinner: 2
  - Mid-Evening: 2
  - Bed: 2
  - Aggregate: 2

#### Above Target (>140)
- Night: 100%
- Breakfast: 100%
- Mid-AM: 100%
- Lunch: 100%
- Mid-Afternoon: 100%
- Dinner: 100%
- Mid-Evening: 100%
- Bed: 100%
- Aggregate: 100%

#### On Target (100-140)
- Night: 0%
- Breakfast: 0%
- Mid-AM: 0%
- Lunch: 0%
- Mid-Afternoon: 0%
- Dinner: 0%
- Mid-Evening: 0%
- Bed: 0%
- Aggregate: 0%

#### Below Target (<100)
- Night: 0%
- Breakfast: 0%
- Mid-AM: 0%
- Lunch: 0%
- Mid-Afternoon: 0%
- Dinner: 0%
- Mid-Evening: 0%
- Bed: 0%
- Aggregate: 0%
Current Continuous Sensors Available in the US
DexCom SC Glucose Sensor
Continuous Glucose Sensors Available Outside US
On initiation: Mean 139 SD 57 A1C 6.4% (5/06)

After 8 weeks on CGM: Mean 130 SD 49 A1C 6.2% (8/06)
Drawbacks to CGM

- Can be overwhelming for some patients
- Alarms can be annoying, discontinued
- Cost; not covered by Medicaid or Medicare
- Comfort
- Accuracy
- Frustration- analog (fast) insulin is slow!
Benefits of CGM?

- A1C lowering with less hypoglycemia
  - 0.5% for adults with type 1 DM
- Hypoglycemia warning for individuals with hypoglycemia unawareness
Insulin Pens

More convenient than traditional vial and syringe

More accurate, repeated doses

Easier to use for those with visual or fine motor skill impairments

Less injection pain (Needles are not dulled by insertion into vial diaphragm before a second insertion into the skin)

Most insurance companies are covering insulin pens

But more expensive! (2 X)

Combined glucose sensing and insulin delivery
Week 1 on sensor-augmented pump

Mean = 162

Week 2 on sensor-augmented pump

Mean = 115
Glucose monitoring apps

Several apps for both Android and iOS are available to facilitate data tracking, trending and communication with providers.

- BG Monitor
- BlueLoop
- OnTrack Diabetes

- Some studies suggest positive results using mobile phone based interventions for DM control
- Apps specific for the needs of minorities with diabetes are needed

Diabetes Technol Ther. 2011 May;13(5):563-9
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

ABSTRACT

BACKGROUND
Adults with type 2 diabetes mellitus often have limitations in mobility that increase with age. An intensive lifestyle intervention that produces weight loss and improves fitness could slow the loss of mobility in such patients.

METHODS
We randomly assigned 5145 overweight or obese adults between the ages of 45 and 74 years with type 2 diabetes to either an intensive lifestyle intervention or a diabetes support-and-education program; 5016 participants contributed data. We used hidden Markov models to characterize disability states and mixed-effects ordinal logistic regression to estimate the probability of functional decline. The primary outcome was self-reported limitation in mobility, with annual assessments for 4 years.

RESULTS
At year 4, among 2514 adults in the lifestyle-intervention group, 517 (20.6%) had severe disability and 969 (38.5%) had good mobility; the numbers among 2502 participants in the support group were 656 (26.2%) and 798 (31.9%), respectively. The lifestyle-intervention group had a relative reduction of 48% in the risk of loss of...
Figure 2. Prevalence of the Four States of Clinical Disability during the 4-Year Study.

The numbers in each color block are the percentages of participants at each state of mobility-related disability among those receiving diabetes support and education and those receiving an intensive lifestyle intervention. Values at follow-up visits for years 1 to 4 have been adjusted for baseline values.