Diabetes Today: Implications for Disability

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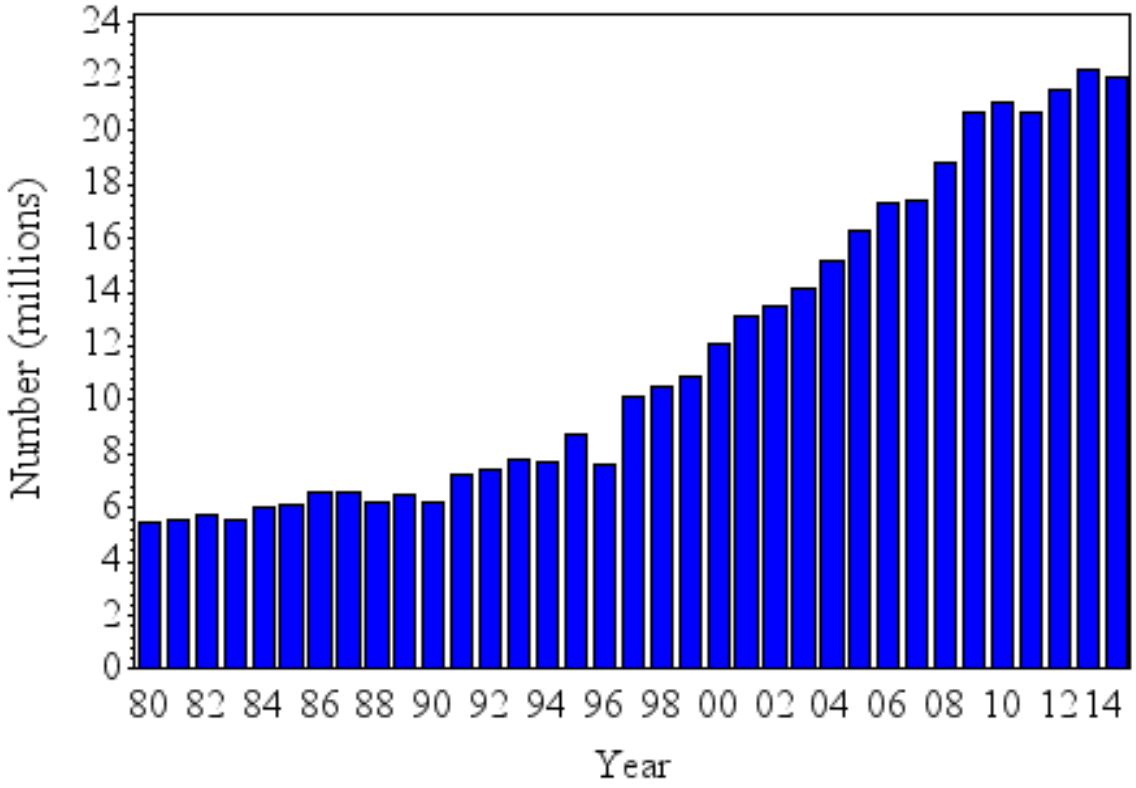
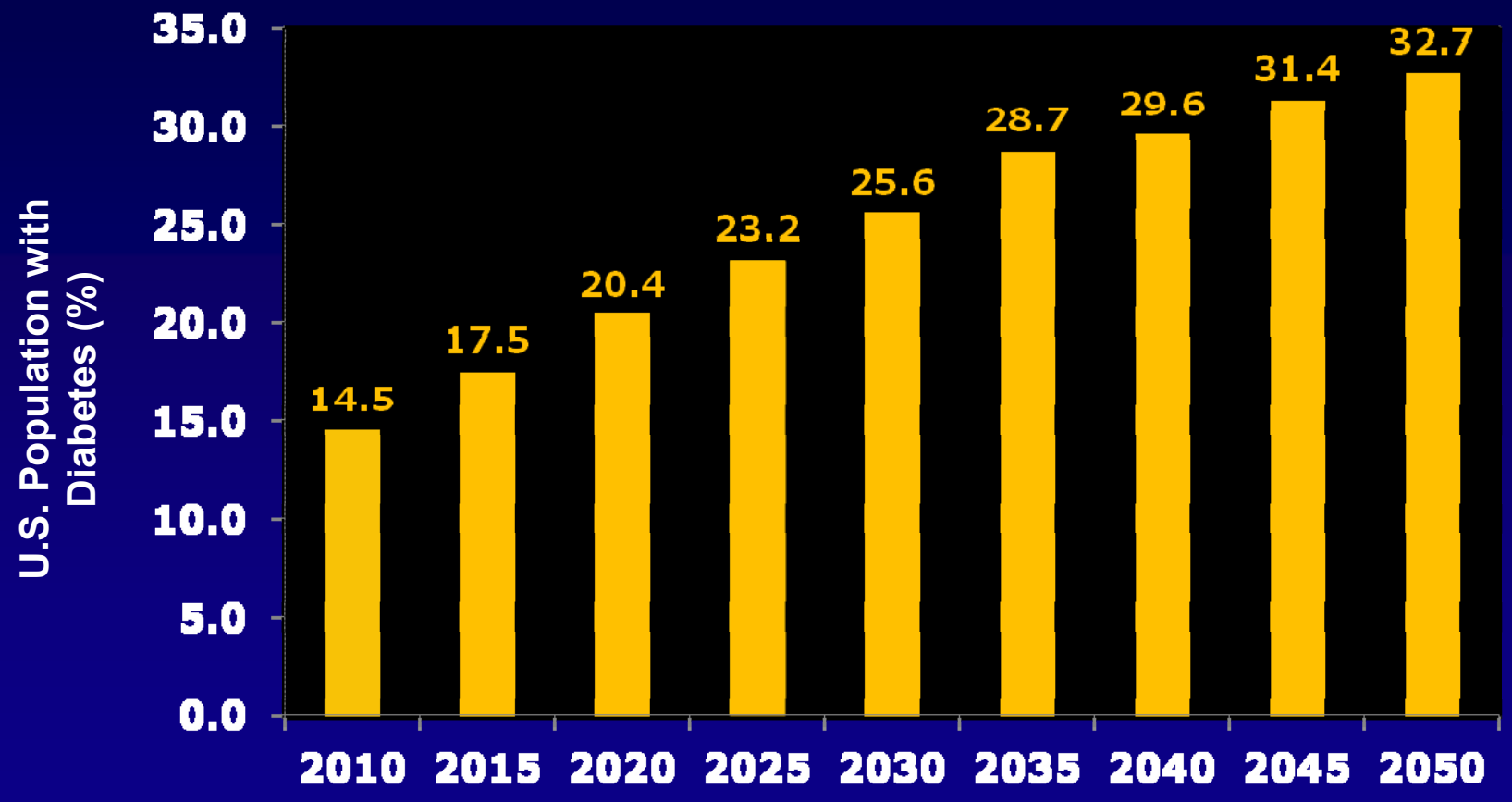
Number (in Millions) of Civilian, Non-Institutionalized Persons with Diagnosed Diabetes, United States, 1980-2014

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).



http://www.cdc.gov/diabetes/statistics/prev/national/figpersons.htm- **accesssed 4/5/2016**

Projecting the Future Diabetes Population: The Imperative for Change



American Diabetes Association.

Boyle JP, et al. *Popul Health Metr*. 2010;8(29):1-12.

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

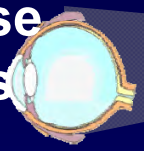
- •In 2014, 422 million adults (8.5% of the population) had diabetes, compared with 108 million (4.7%) in 1980.
- •Many diabetes related deaths (43%) occur prematurely, before age 70 years, and are largely preventable through adoption of policies to create supportive environments for healthy lifestyles and better detection and treatment of the disease

Accessed 04/06/2016 ,http://www.mdlinx.com/washington-report/index3.cfm

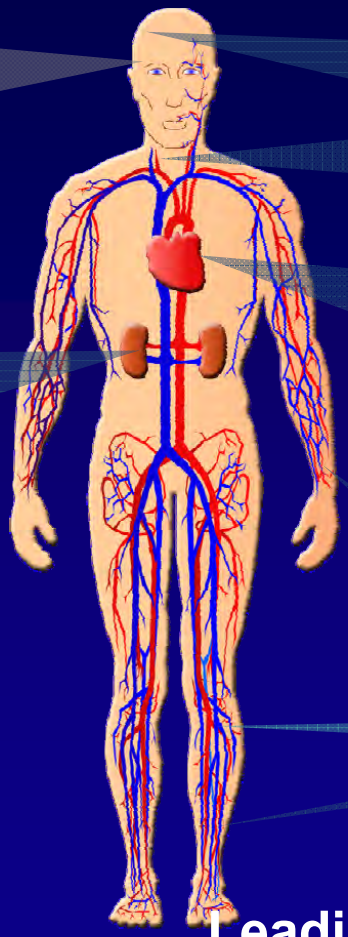
Long-term Complications of Diabetes

Consequences of Sustained Hyperglycemia

Leading cause of blindness in working age adults

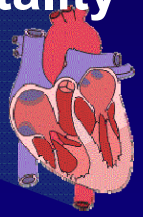


Diabetic Retinopathy



Stroke

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



Diabetic Nephropathy

Leading cause of end-stage renal disease

Cardiovascular Disease

Diabetic Neuropathy

Leading cause of nontraumatic lower extremity amputations

National Diabetes Information Clearinghouse. At: http://www.niddk.nih.gov/health/diabetes/pubs/dmstats/dmstats.htm.

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

Source: CDC. http://www.cdc.gov/diabetes/statistics/prev/national/figageadult.htm. Accessed June 23, 2011.

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.

American Diabetes Association. *Diabetes Care*. 2013;36:1033-46.

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.

Source: NIDDK, National Diabetes Statistics Fact Sheet. HHS, NIH, 2010.

Impact of Diabetes in America (cont.)

- Diabetes is 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.

Source: NIDDK. http://diabetes.niddk.nih.gov/dm/pubs/statistics/#Kidney. Accessed June 23, 2011.

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

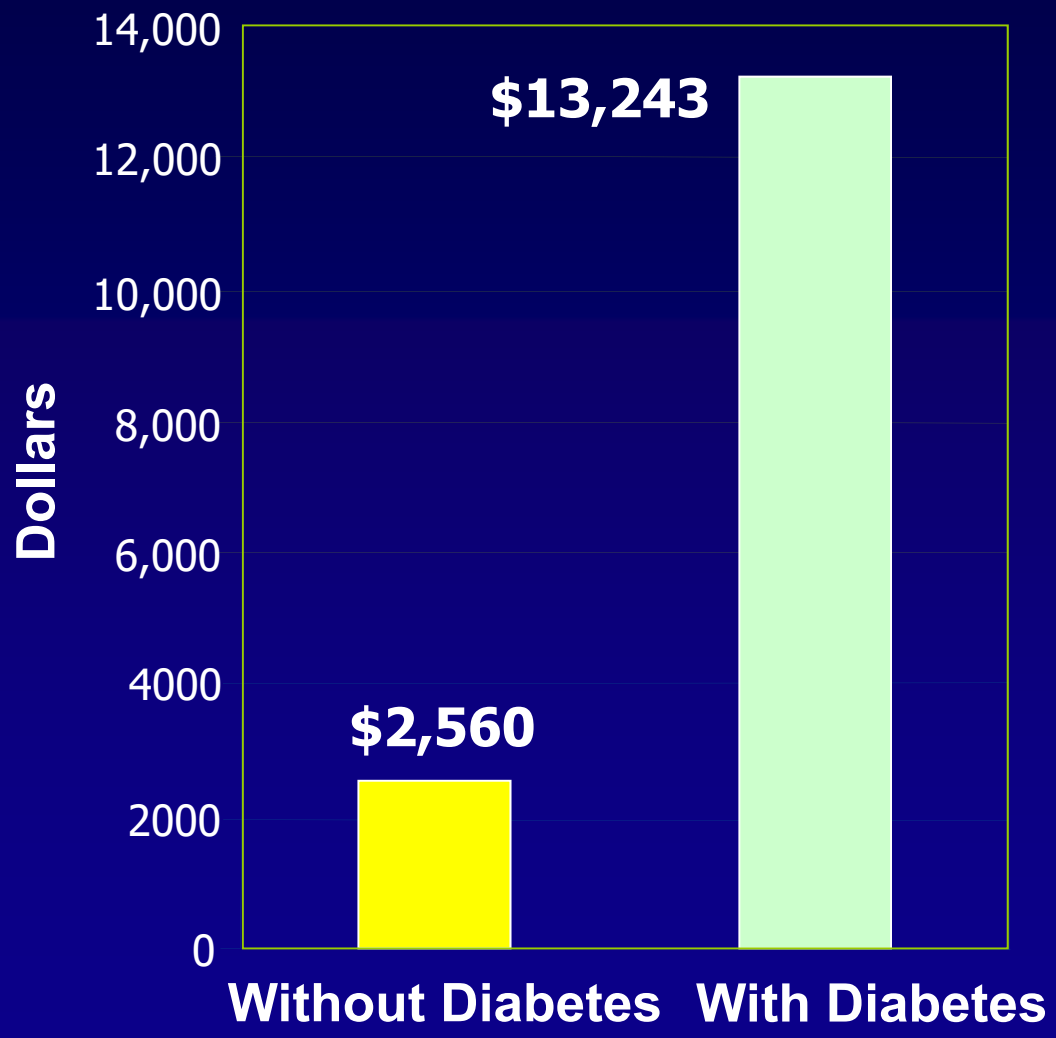
A. 10%
B. 15%
C. 20%
D. 25%

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!)

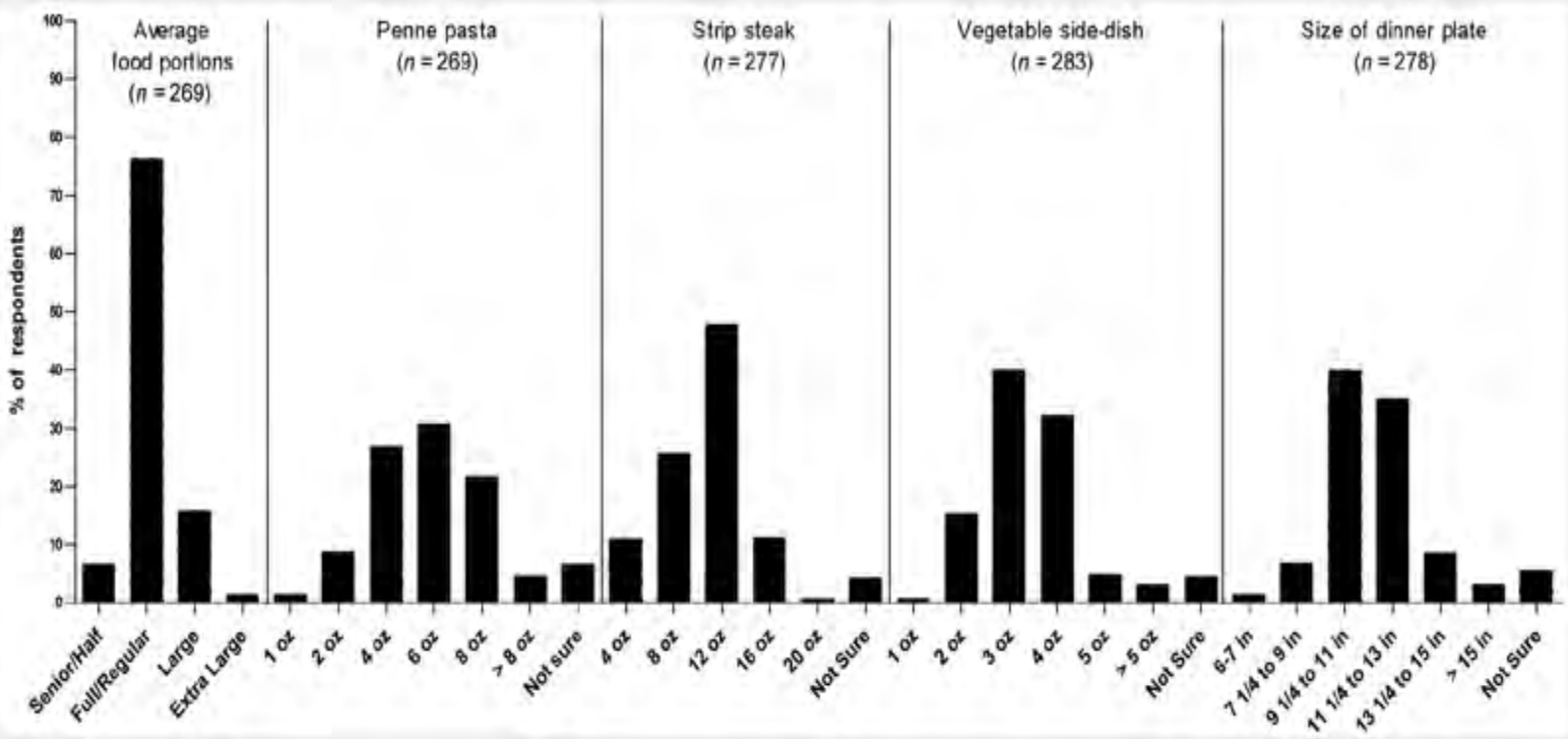
Annual Health Care Costs for Patients With and Without Diabetes



Source: Centers for Disease Control and Prevention Web site, 2006.

Food	20 Years Ago		Today	
Bagel				
	3-inch diameter	140 calories	6-inch diameter	350 calories
Cheeseburger				
	1 portion	333 calories	1 portion	590 calories
Spaghetti and Meatballs				
	1 cup spaghetti, sauce and 3 small meatballs	500 calories	2 cups spaghetti, sauce and 3 large meatballs	1,025 calories
Soda				
	6.5 ounces	85 calories	about 20 ounces	300 calories
French Fries				
	2.4 ounces	210 calories	6.9 ounces	610 calories

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.

Condrasky M, et al *Obesity* 2007;15: 2086–2094

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Portion Distortion II Interactive Quiz

Healthy Weight Home | BMI Calculator | Menu Planner | WeCan! | OEI Home

Previous Question • Back to Beginning • Next Question

Coffee

20 Years Ago	Today
Coffee (with whole milk and sugar)	**Mocha Coffee** (with steamed whole milk and mocha syrup)
	
8 ounces, 45 calories	**??? 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!

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OEI Home Page • NHLBI Home • NIH Home
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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**

Check Your Answer!

*Based on a 130-pound person.

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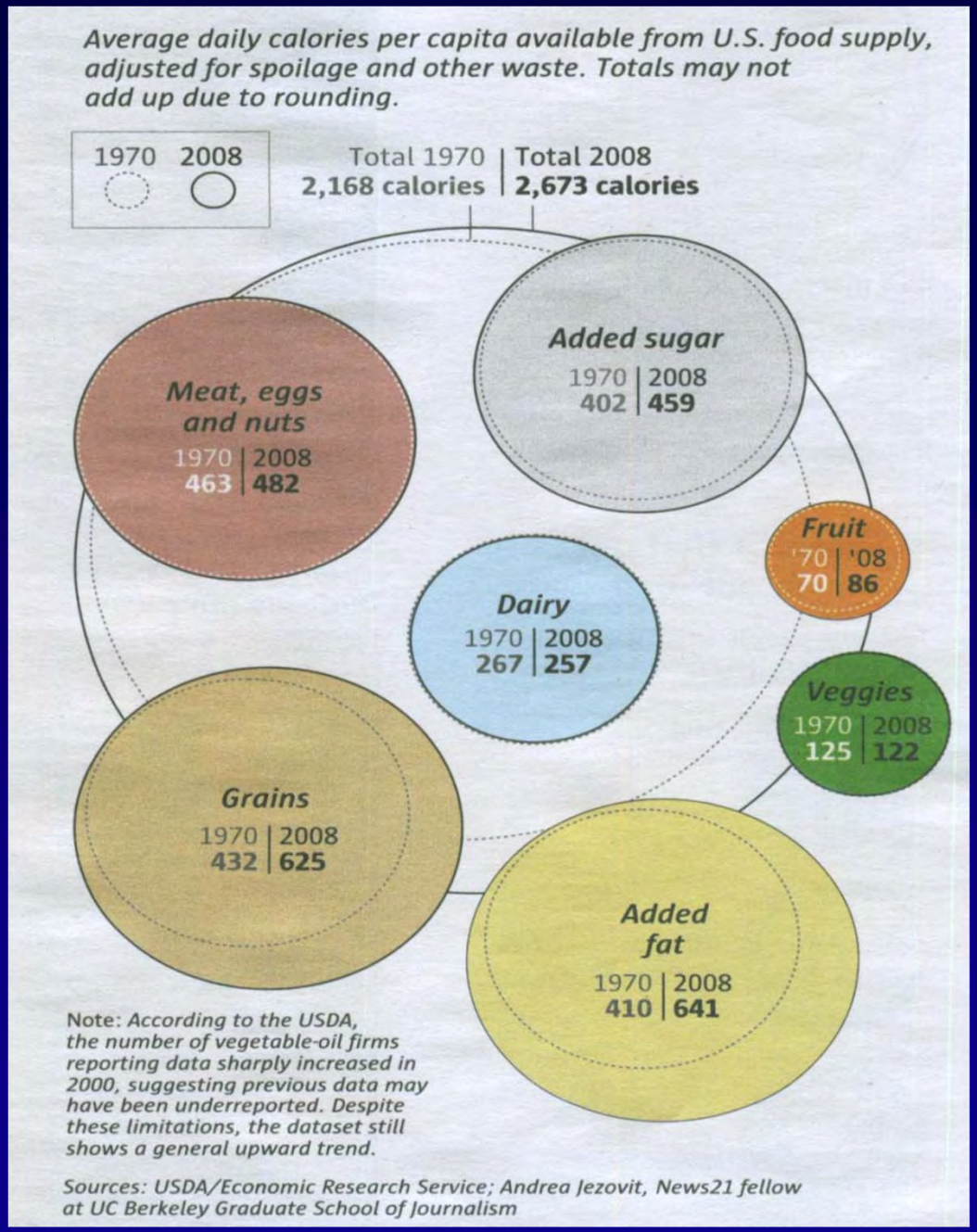
Department of Health and Human Services | National Institutes of Health | National Heart, Lung, and Blood Institute

hp2010.nhlbihin.net/portio

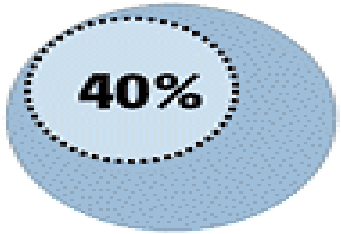


From *Seattle Times*, June 12, 2011: Changes from 1970 to 2008

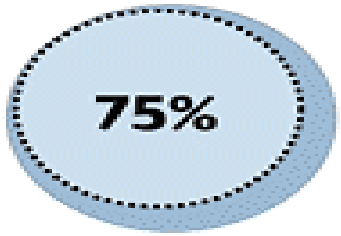
- Sugar: 402 to 459 cal/day
- Fat: 410 to 641 cal/day
- Grains: 432 to 625 cal/day

Myths that get in our way

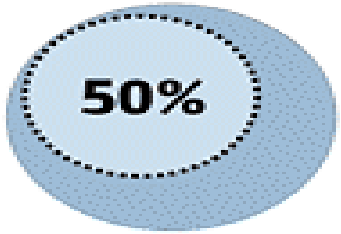
Reasons people say they don't choose "healthy food"



It doesn't taste good



It's expensive



It's hard to prepare

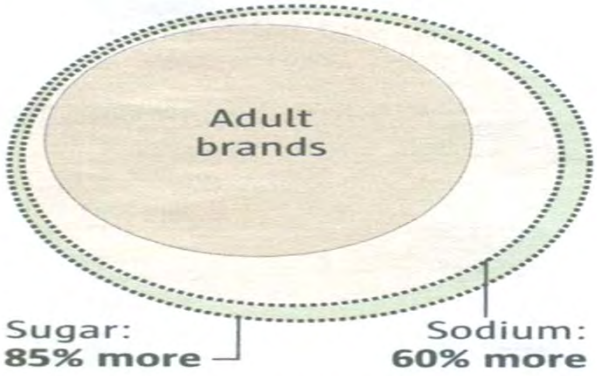
Source: Food Marketing Institute

Quick fixes make our day

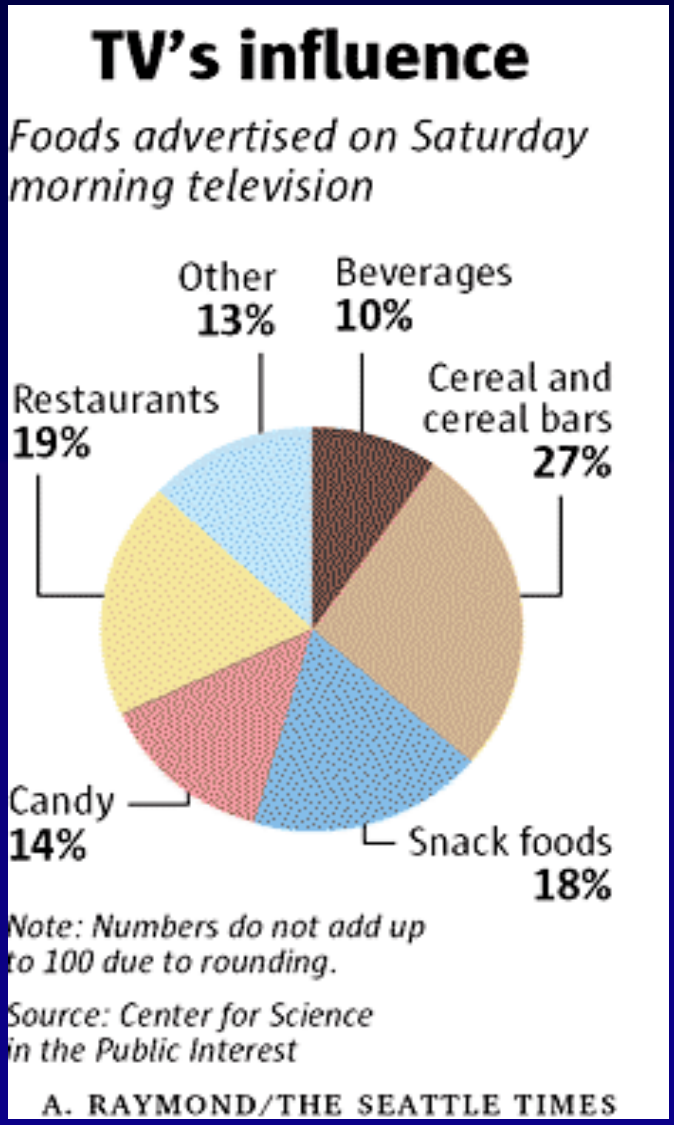
FAST-FOOD RESTAURANTS
Parents who took their kids at least once in the past week

CALORIES IN SODA
Number of calories in an average portion today vs. the 1950s

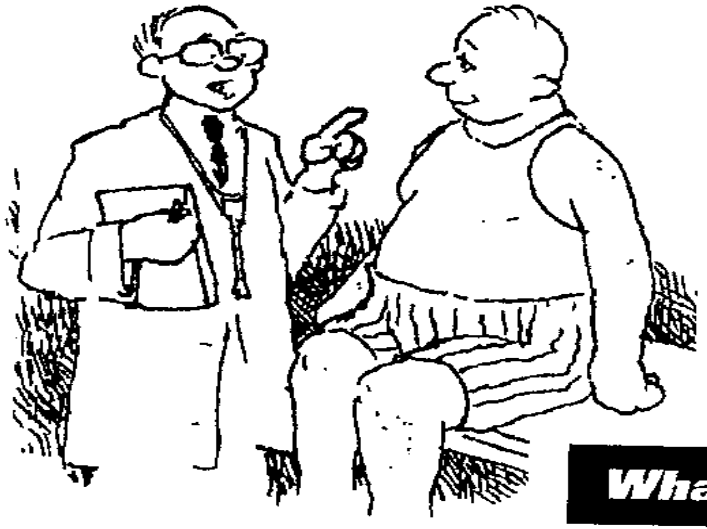
CEREALS
Sugar and sodium content of brands marketed to kids vs. adults



Source: Yale Rudd Center for Food Policy & Obesity; Journal of Public Health Nutrition



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

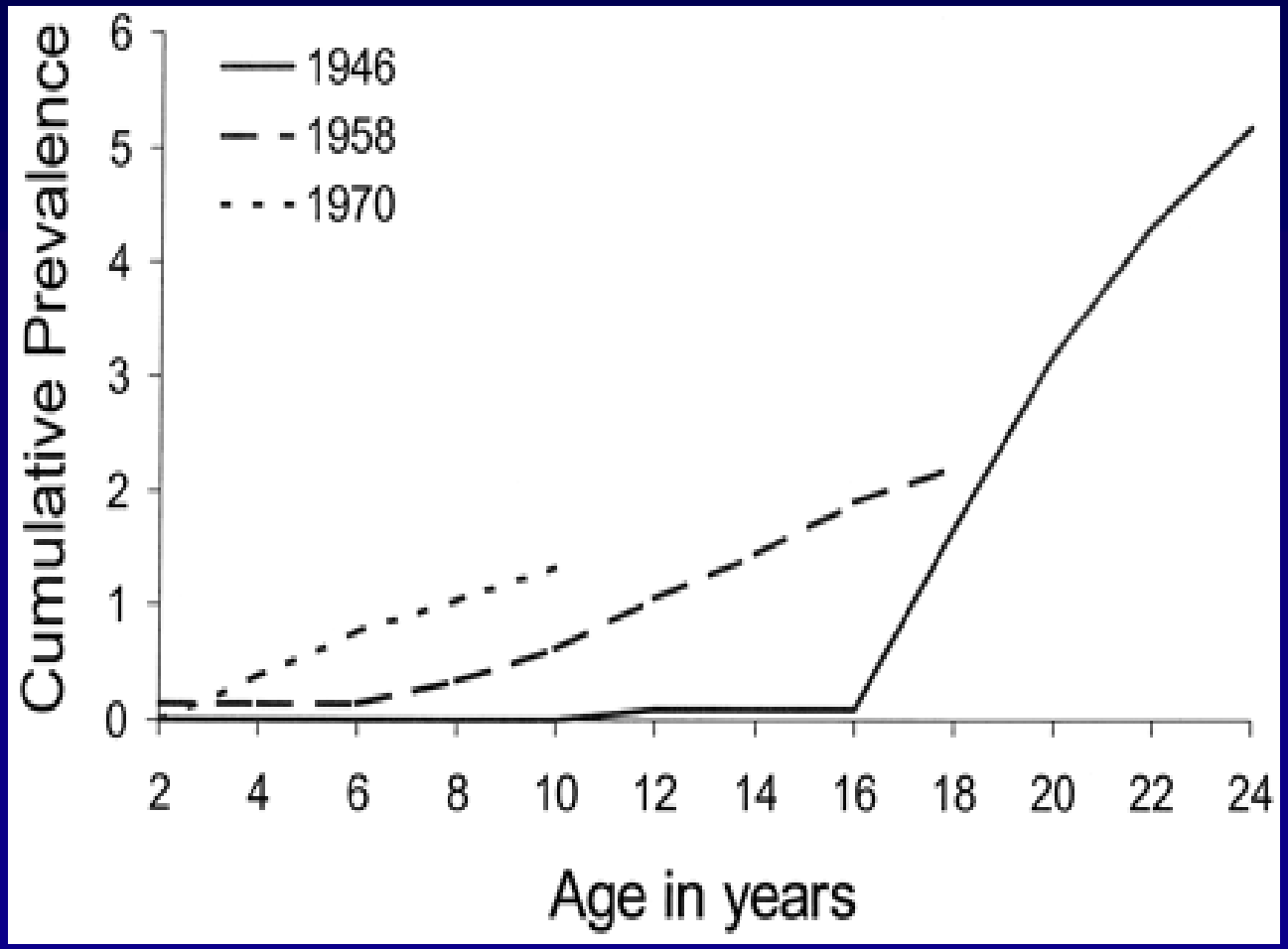
- Nutritional
- Physical activity
- Pharmacological

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

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

Progressive Left Shift in Age of Onset



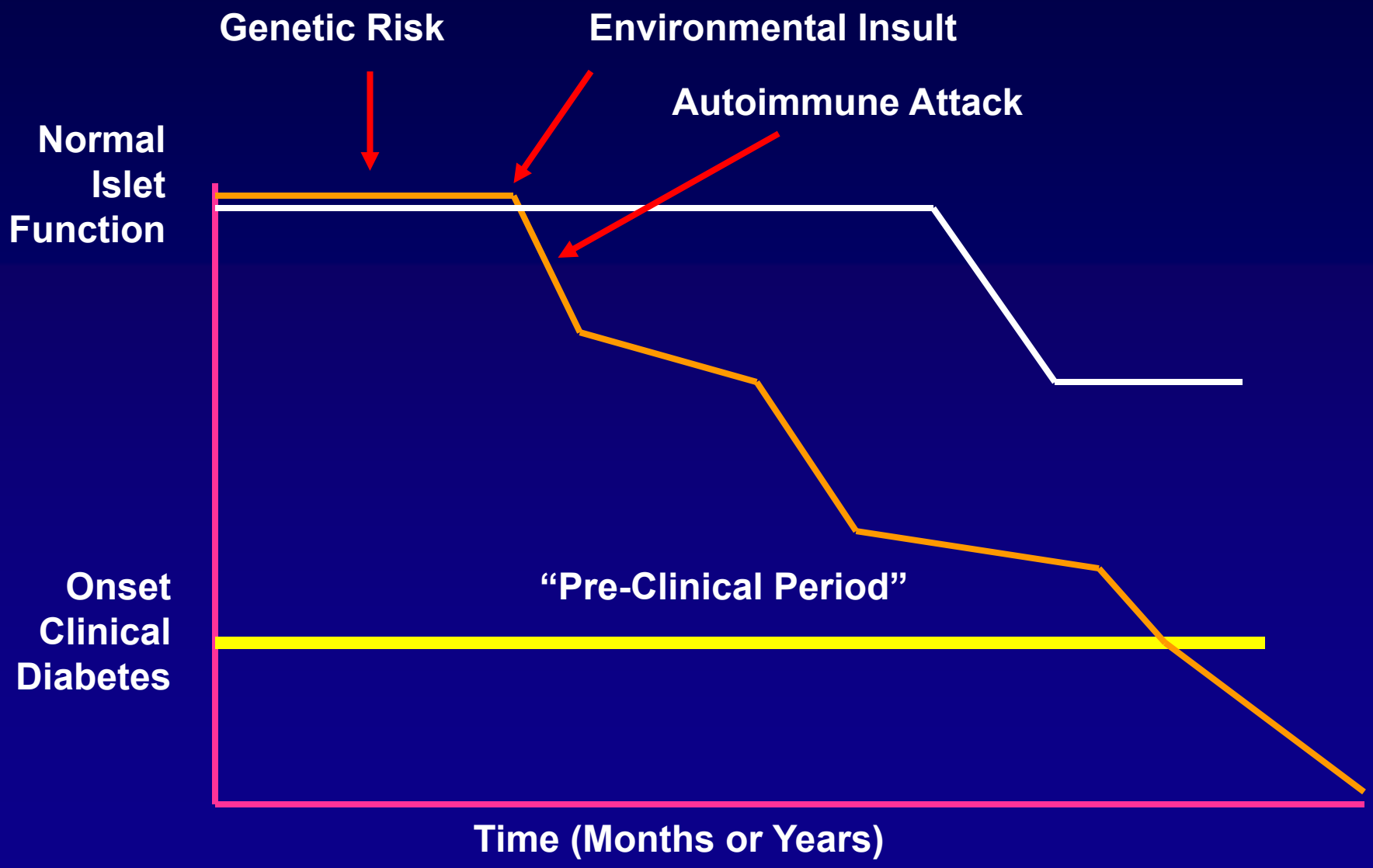
Gale EM. *Diabetes*. 2002;51:3353-3361.

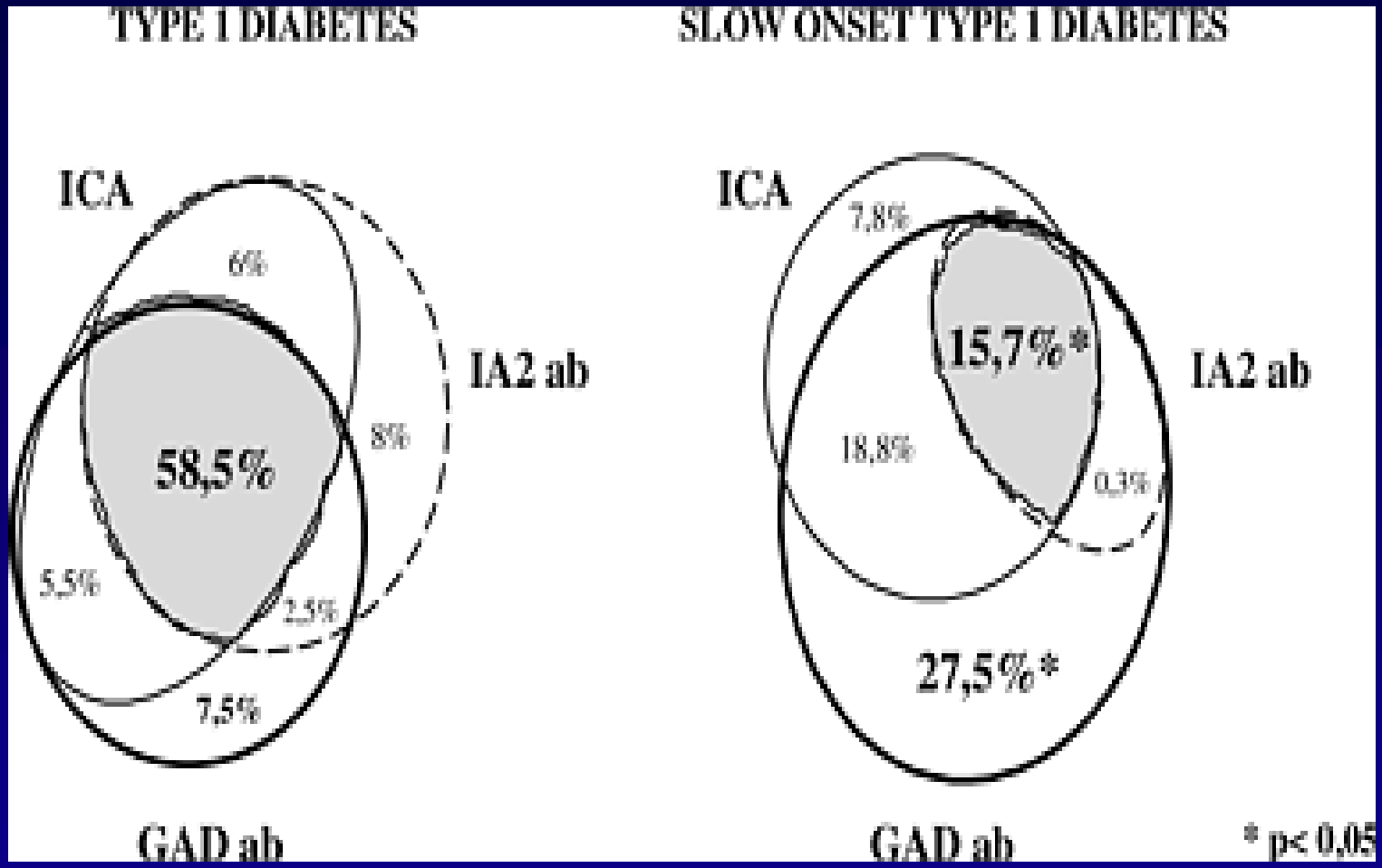
The Faces of Type 1 Diabetes

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





Desailloud R, Fajardy I, Vambergue A, Prevost G, Pigny P, Fontaine P. *Diabetes Metab.* 2000;26:353-360.

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[a]

Marker	Chromosome	Locus	Type of mutation	Function of gene	Risk allele	Odds ratio
rs10923931[36]	1	*NOTCH2*	Intronic	Transmembrane receptor involved in the formation of the pancreas	T	1.13
rs7578597[36]	2	*THADA*	Missense: Thr1187Ala	Expressed in thyroid adenomas; binds to PPARγ	T	1.15
rs4607103[36]	3	*ADAMTS9*	38 kb upstream	Secreted metalloproteinase expressed in muscles and pancreas	C	1.09
rs4402960[83]	3	*IGF2BP2*	Intronic	Growth factor binding protein involved in pancreatic development	T	1.14
rs1801282[84]	3	*PPARG*	Missense: Pro12Ala	Transcription factor involved in adipocyte development	C	1.19
rs10010131[83]	4	*WFS1*	Intron–exon junction	Transmembrane protein of the endoplasmic reticulum	G	1.15
rs7754840[83]	6	*CDKAL1*	Intronic	Islet glucose toxicity sensor; inhibits CDK5 activation	C	1.12
rs864745[36]	7	*JAZF1*	Intronic	Transcriptional repressor associated with prostate cancer	T	1.10
rs13266634[83]	8	*SLC30A8*	Missense: Arg325Trp	Zinc transporter involved in insulin storage and secretion	C	1.12
rs10811661[83]	9	*CDKN2A/B*	125 kb upstream	Cyclin-dependent kinase inhibitor and tumor suppressor involved in islet development	T	1.20
rs12779790[36]	10	*CDC123-CAMK1D*	Intergenic region	Cell-cycle regulator and protein kinase	G	1.11
rs7903146[13]	10	*TCF7L2*	Intronic	Transcription factor that regulates genes that encode proglucagon and insulin	T	1.37
rs1111875[83]	10	*HHEX*	7.7 kb downstream	Transcription factor involved in pancreatic development	C	1.13
rs5219[9]	11	*KCNJ11*	Missense: Glu23Lys	Potassium channel that regulates insulin secretion	T	1.14
rs2237892[38]	11	*KCNQ1*	Intronic	Pore-forming α subunit of potassium channel	C	1.42
rs1387153[44]	11	*MTNR1B*	28.3 kb upstream	High-affinity, G-protein-coupled receptor for melatonin	T	1.15
rs7961581[36]	12	*TSPAN8-LGR5*	Intronic	Cell-surface glycoprotein implicated in gastrointestinal tumors	C	1.09
rs8050136[83]	16	*FTO*	Intronic	Function unknown; affects BMI in general population	A	1.17
rs757210[83]	17	*HNF1B*	Intronic	Transcription factor involved in pancreatic development	A	1.12

[a]$P<5\times10^{-8}$. Abbreviation: T2DM, type 2 diabetes mellitus.

Stolerman ES,Florez JC. *Nat Rev Endocrinol*. 2009;5:429-436.

Associated with Prevention of Type 2 Diabetes

• Increased fiber and cereal grains	T	
• Dairy		F
• Vitamin D		F
• Alcohol	T	
• Caffeine	T	
• Mediterranean diet	T	

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)

Table 2— Estimated average glucose

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

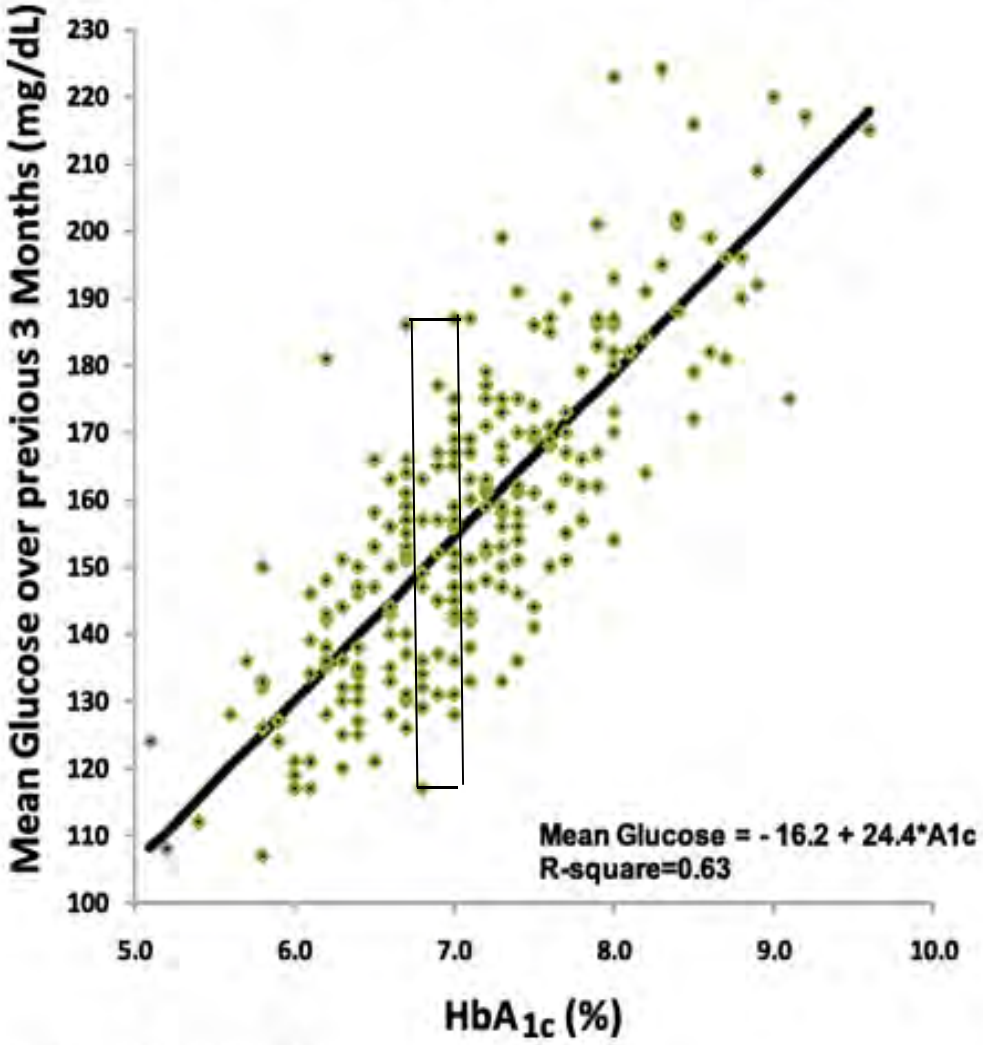
Data in parentheses are 95% CIs.

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

- 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)

Nathan D, et al. Diabetes Care 2008: 31;1473-1478.

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



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*

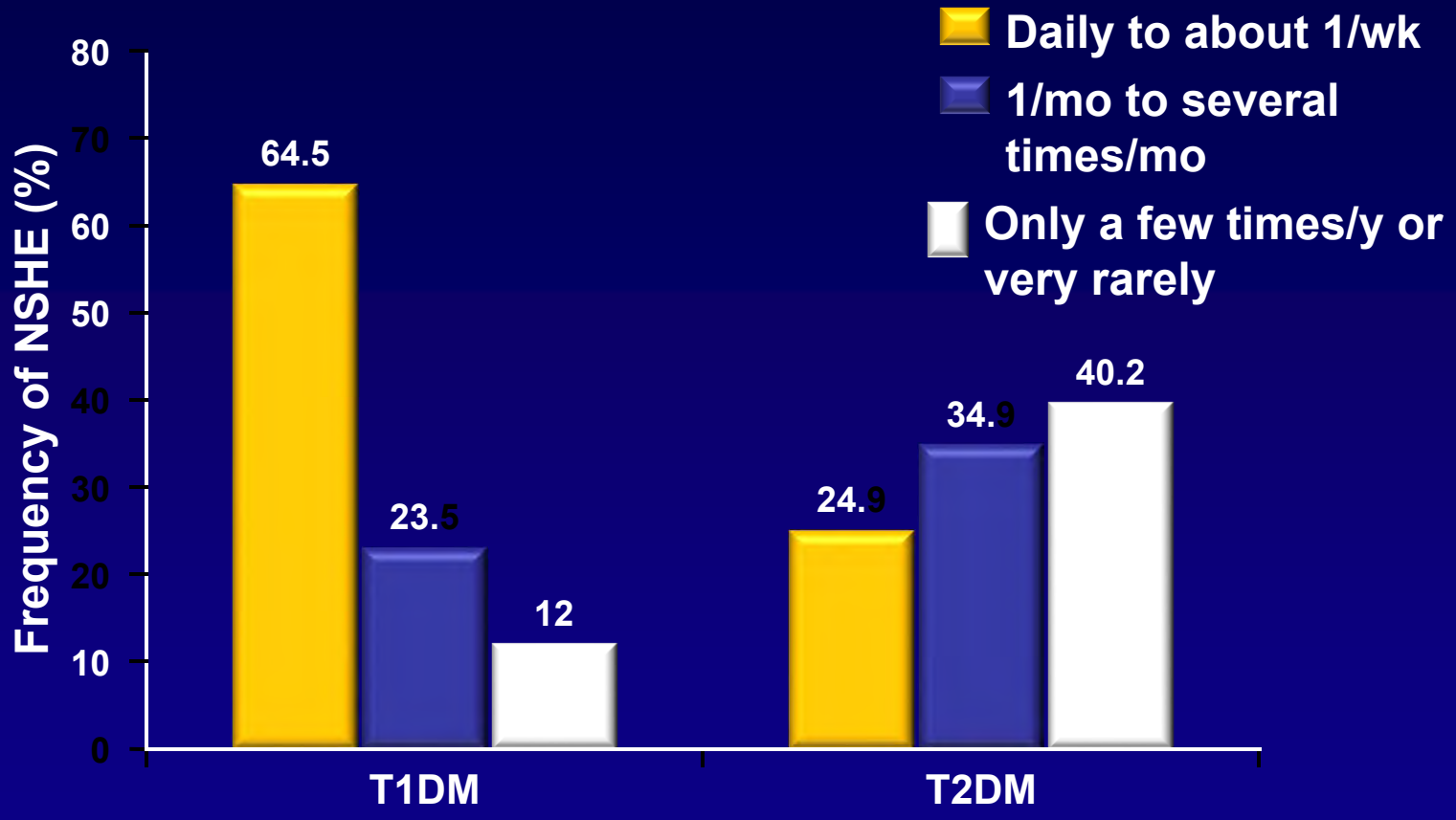
Medical Therapies
- Blood transfusion
- Hemodialysis

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?

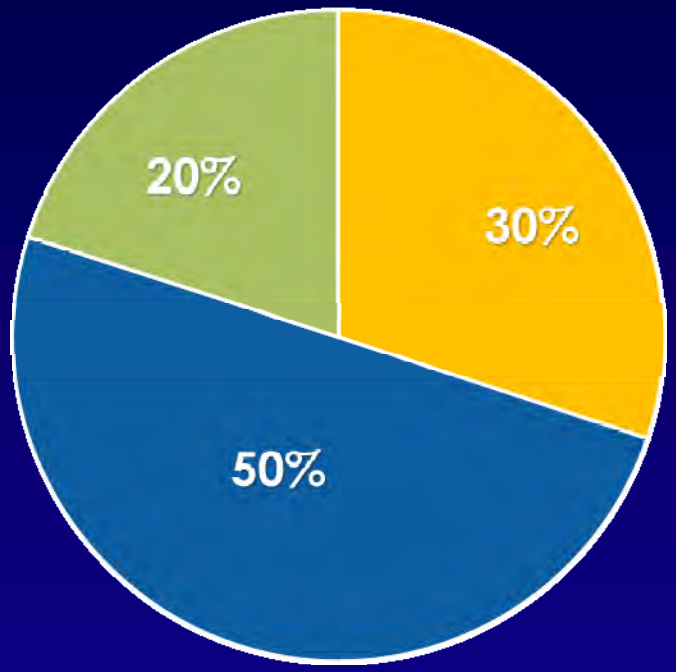


Wk, week; mo, month; T1DM, type 1 diabetes; T2DM, type 2 diabetes; NSHE, non-severe hypoglycemic events

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

Brod M, et al. *Value Health*. 2011;14:665-671.

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)
Brod M, et al. *Value Health.* 2011;14:665-671

NSHE, non-severe hypoglycemic events

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

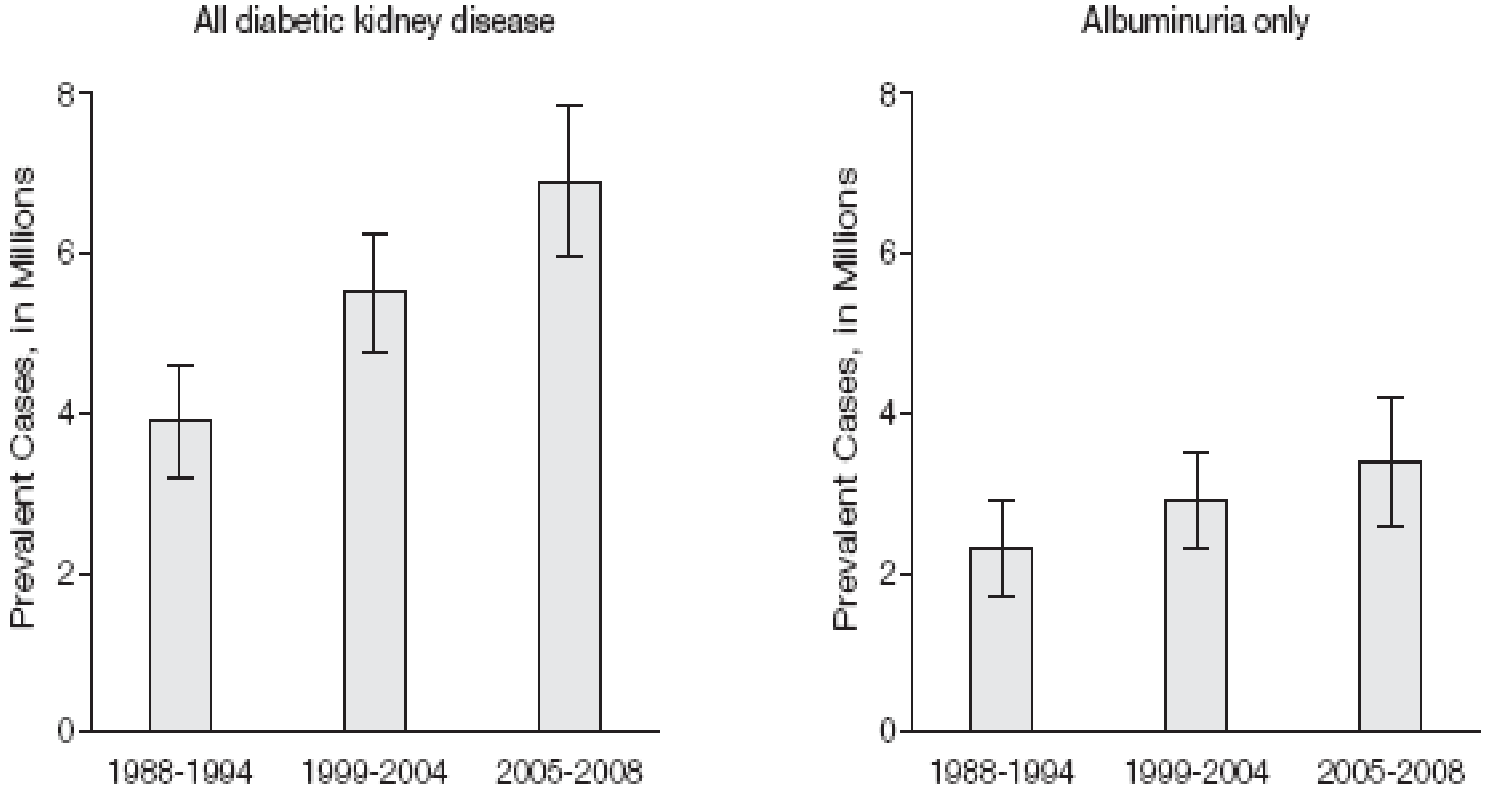
- **Falls**
- **Accidents with injury**

Cryer PE, et al. *Diabetes Care. 2003;*26:1902-1912.
Desouza CV, et al. *Diabetes Care.* 2010;33:1389-1394.

TIA, transient ischemic attack

Temporal Trends in Diabetic Kidney Disease

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



de Boer IH, Rue TC, Hall YN, Heagerty PJ, Weiss NS, Himmelfarb J. *JAMA*. 2011;305:2532-2539.

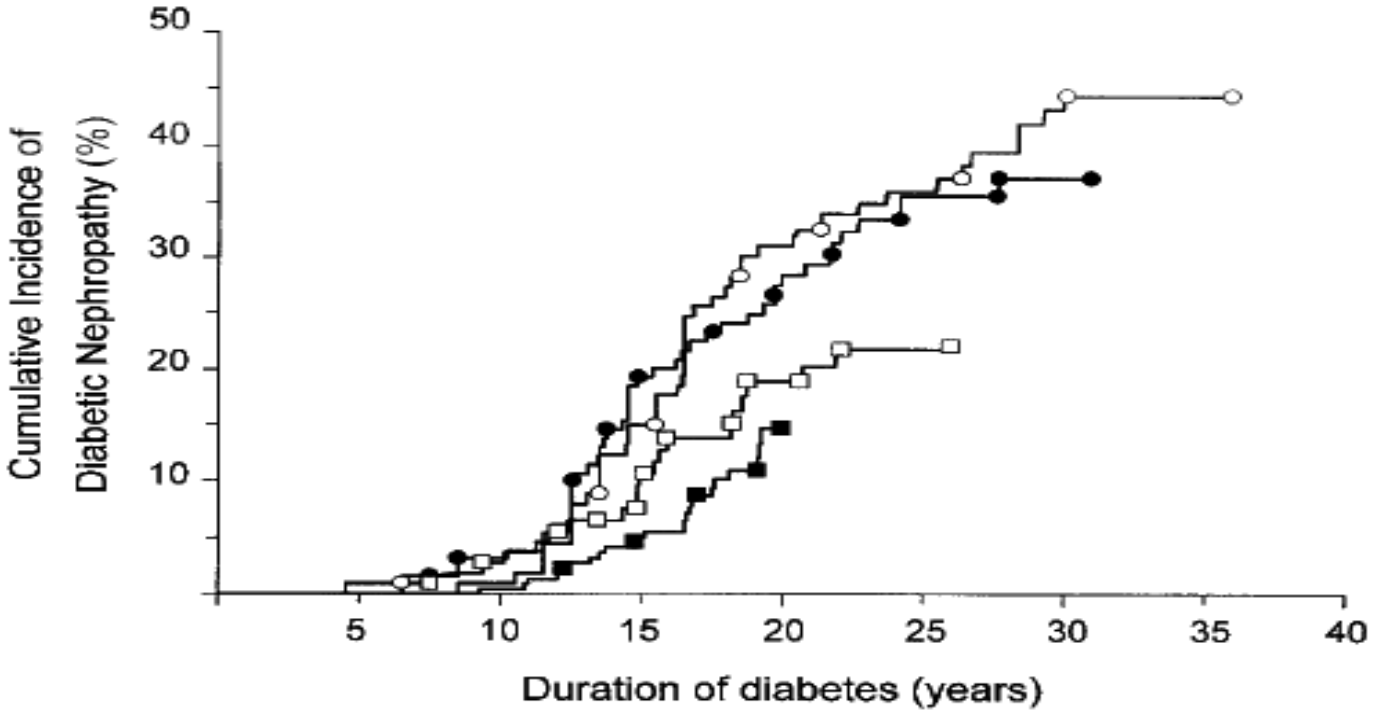


Figure 1—*Cumulative incidence of diabetic nephropathy in 600 type 1 diabetic patients with onset of diabetes from 1965 to 1969* (n = *113, group A* [○]), *1970 to 1974* (n = *130, group B* [●]), *1975 to 1979* (n = *113, group C* [□]), *and 1979 to 1984* (n = *244, group D* [■]). P < *0.001, log-rank 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.

Hovind P, et al Diabetes Care 2003; 26:1258–1264

Declining Rates of Hospitalization for Nontraumatic Lower-Extremity Amputation in the Diabetic Population Aged 40 Years or Older: U.S., 1988–2008

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NILKA RIOS BURROWS, MPH[2]
EDWARD W. GREGG, PHD[2]
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LINDA S. GEISS, MA[2]

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.

Diabetes Care 35:273–277, 2012

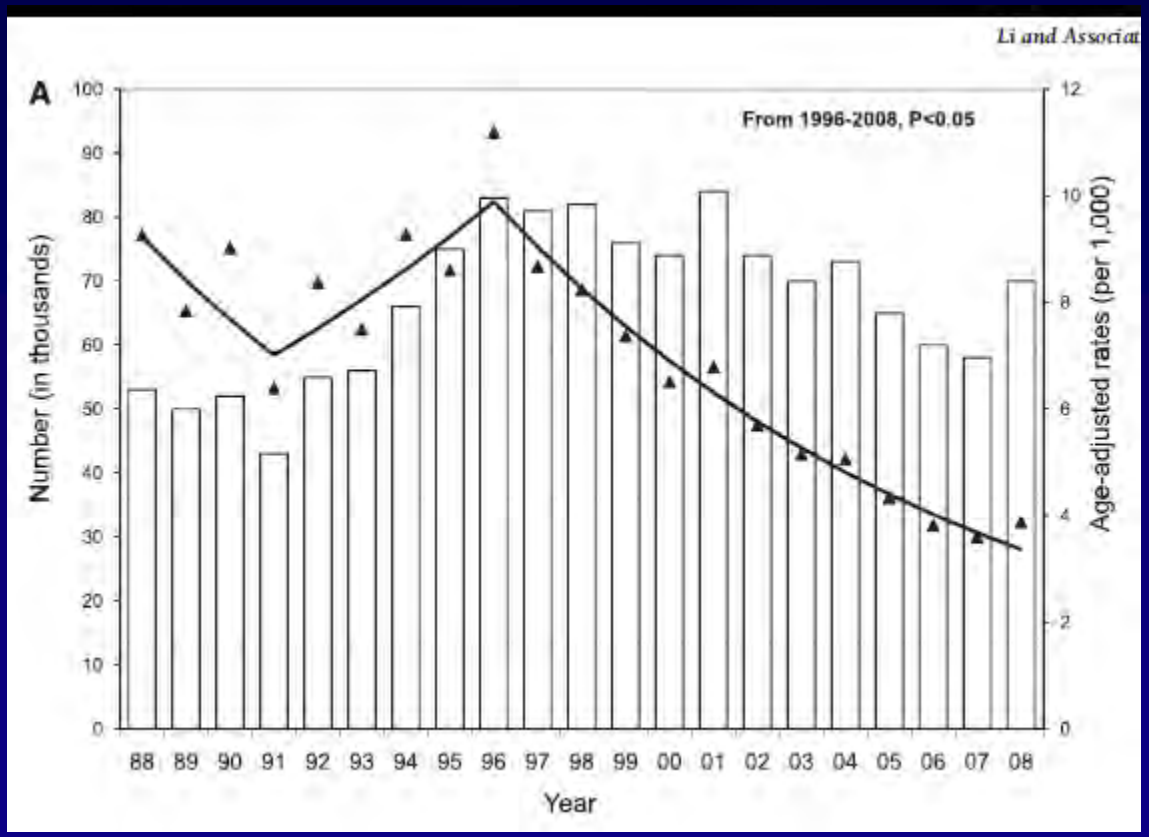
reductions in rates of diabetes-related complications (5,6) and cardiovascular disease (6).

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.

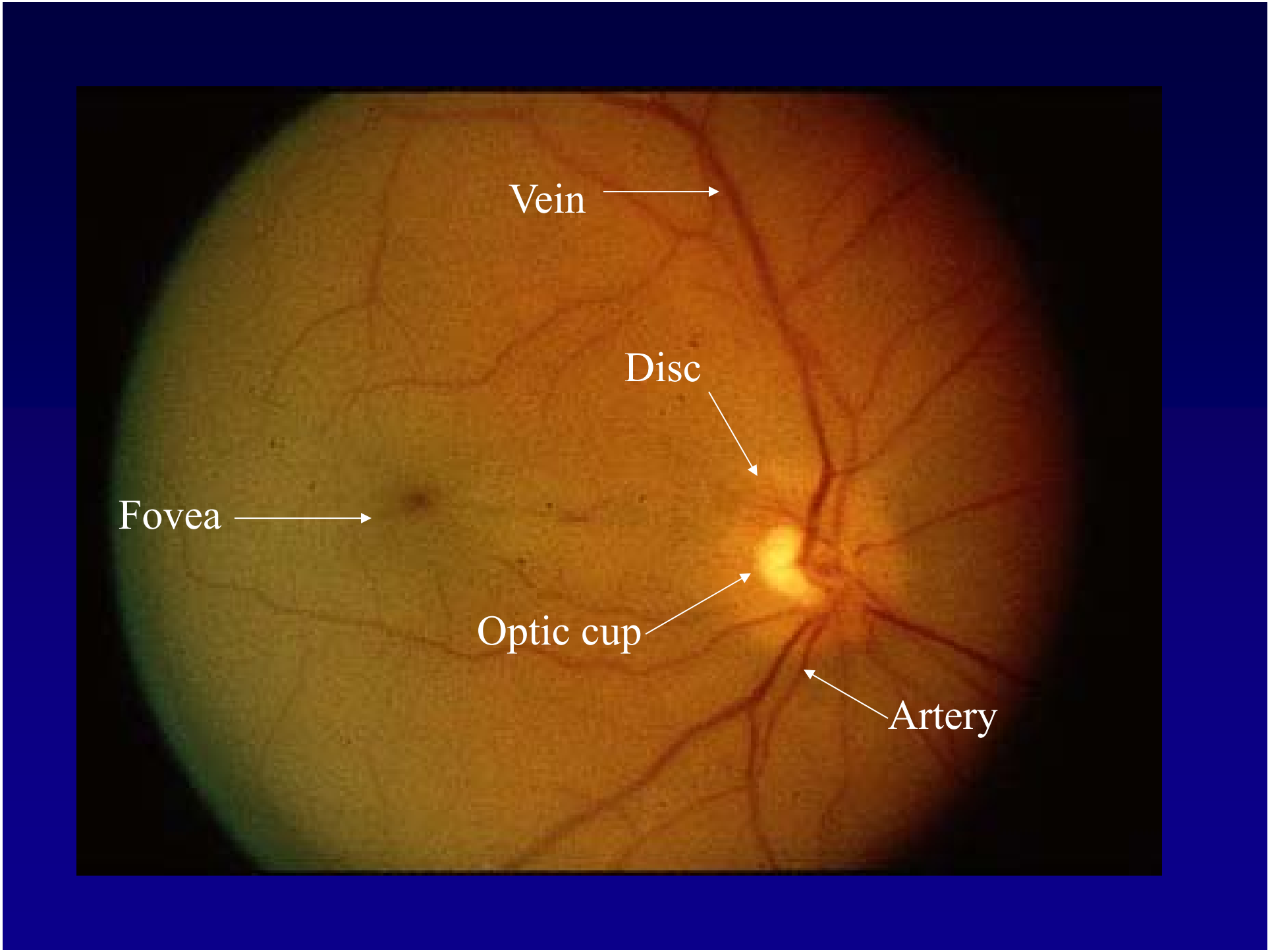
RESEARCH DESIGN AND METHODS

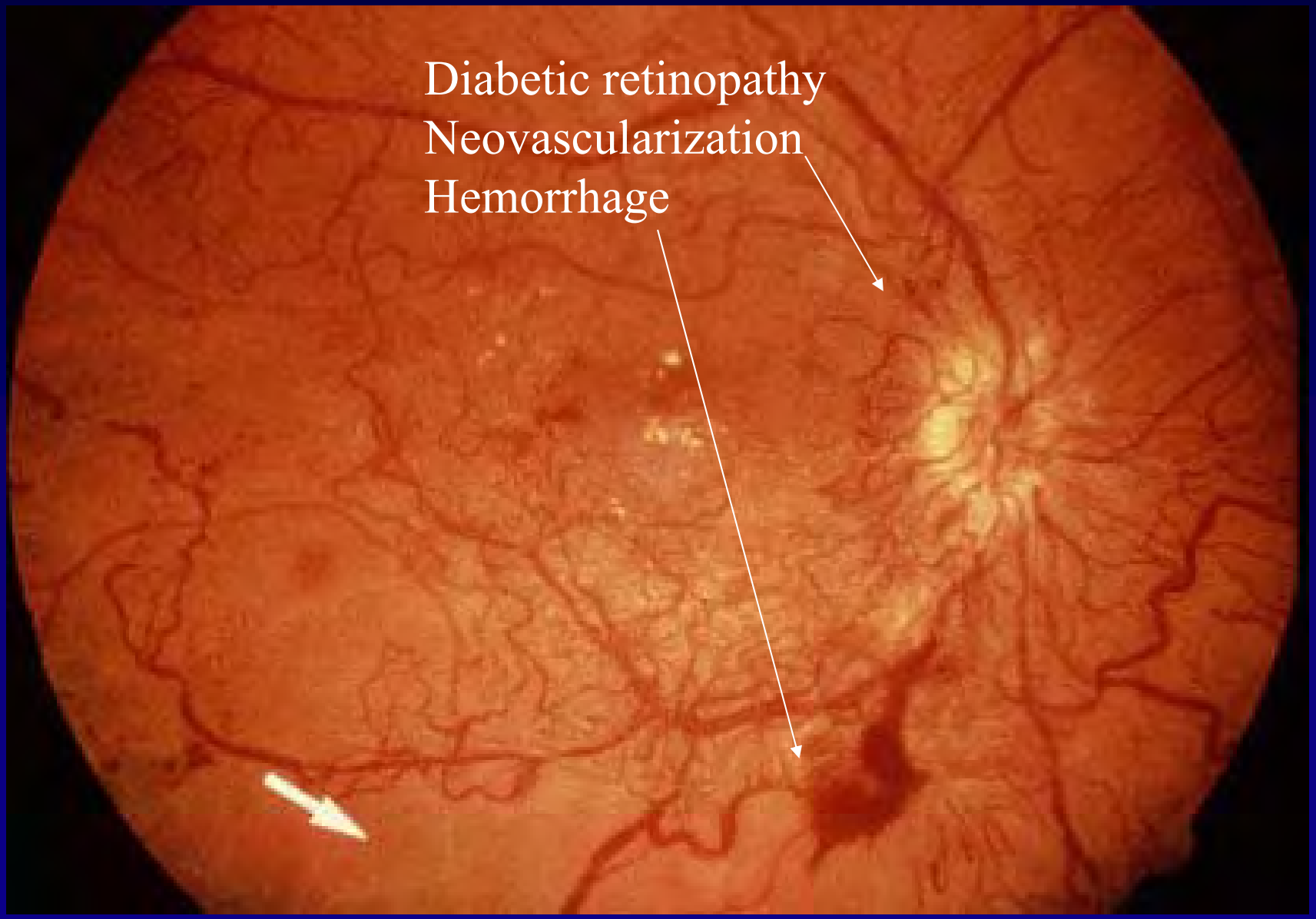
Data sources

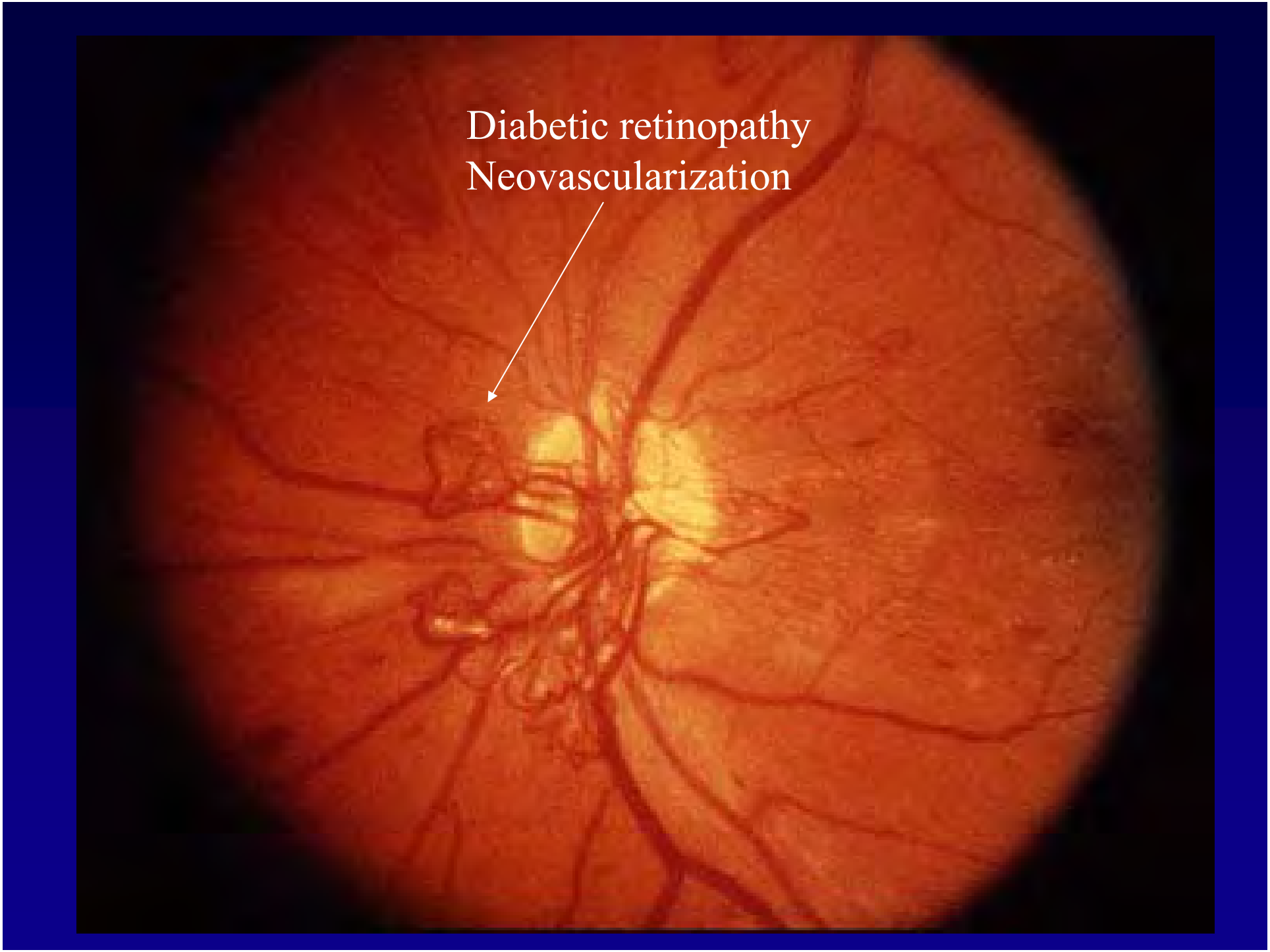
Our study was based on 1988–2008 data from the National Hospital Discharge Survey (NHDS) and the National Health Interview Survey (NHIS). The NHDS is a national probability survey of short-stay, nonfederal hospitals in all 50 states and

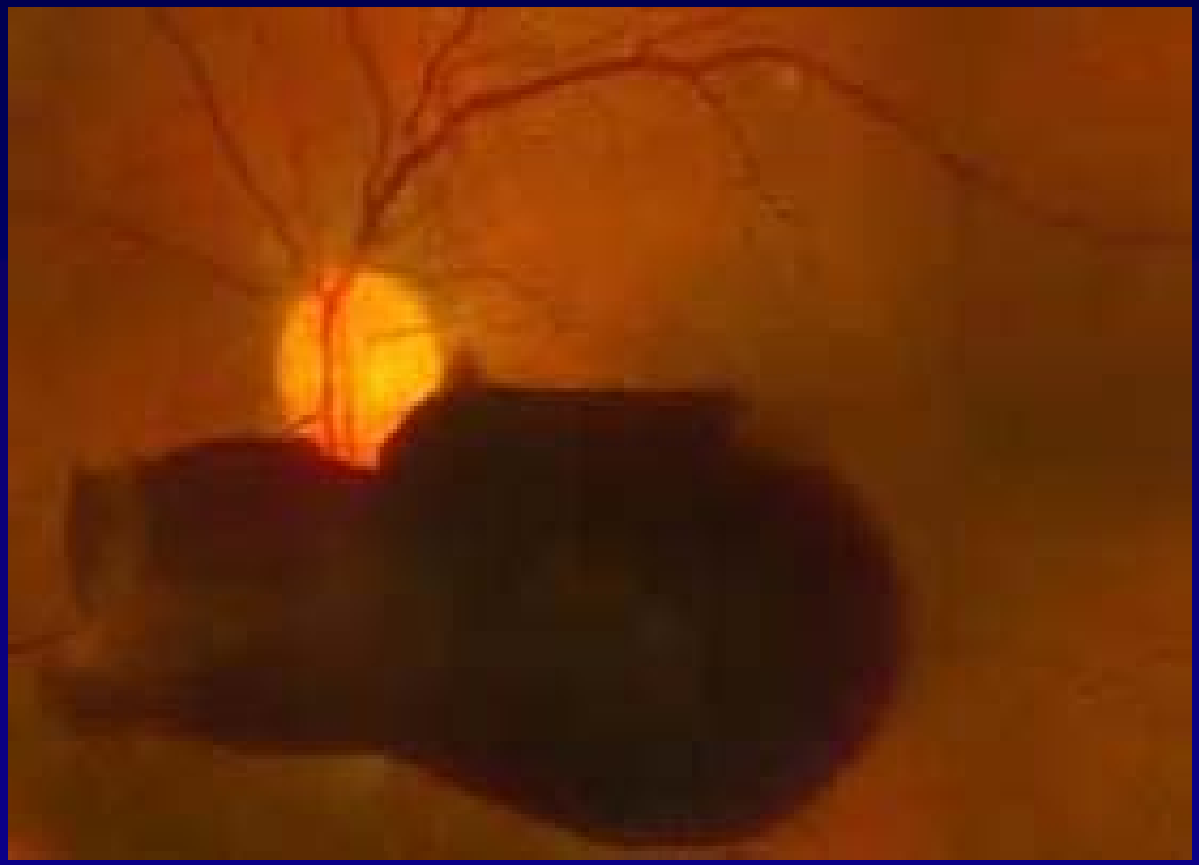


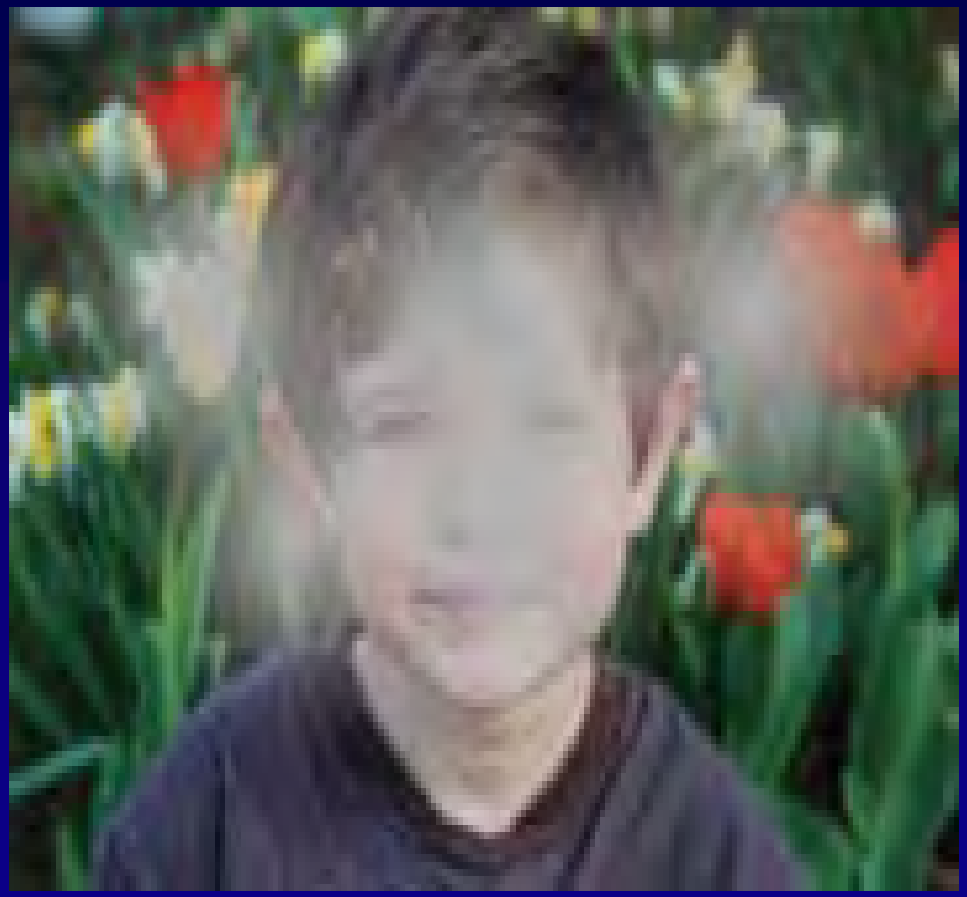
Between 1996 and 2008,NLEA rates decreased by 67%.

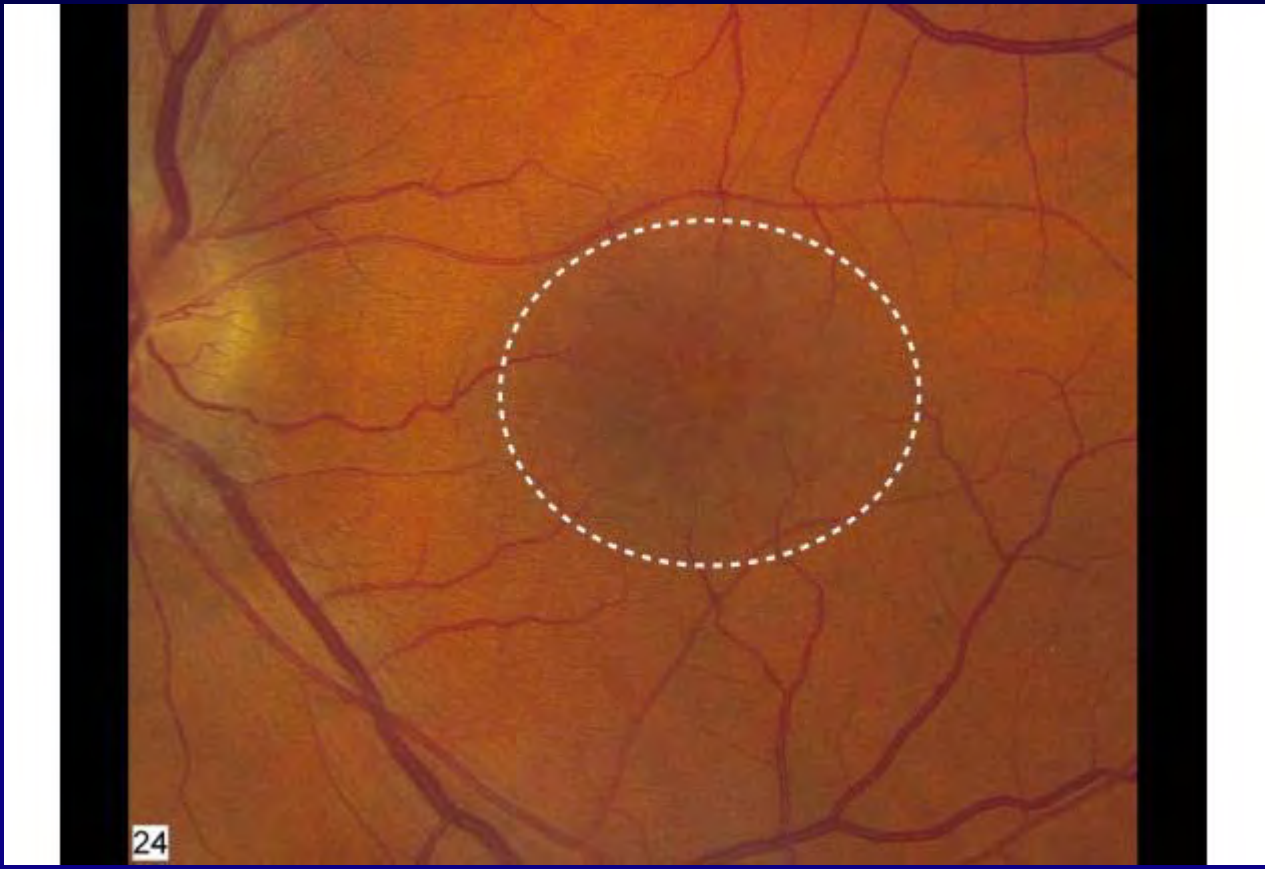












Diabetic Peripheral Neuropathy

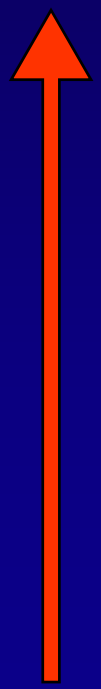
- Diabetic peripheral neuropathy (DPN) is a frequent complication of diabetes associated with significant morbidity and mortality[1]
  - Risk factor for ulcers and amputations[2]
  - Impairs quality of life[1]
- Significant resources are spent to treat patients with DPN
  - Estimated total annual cost in US $4.6 - $13.7 billion[3]
- Only effective intervention is prevention by tight control of patient's diabetes

1. Vinik AI, et.al. *Diabetologia* 2000;43: 957-973.
2. Standards of Medical Care in Diabetes. *Diabetes Care*. 2004;S1:15-35.
3. Gordois A, et.al. *Diabetes Care.* 2003;26: 1790-1795

Clinical Manifestations

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.



Signs and symptoms progress from distal to proximal over time

Diabetic Neuropathy (Boulton), 2001

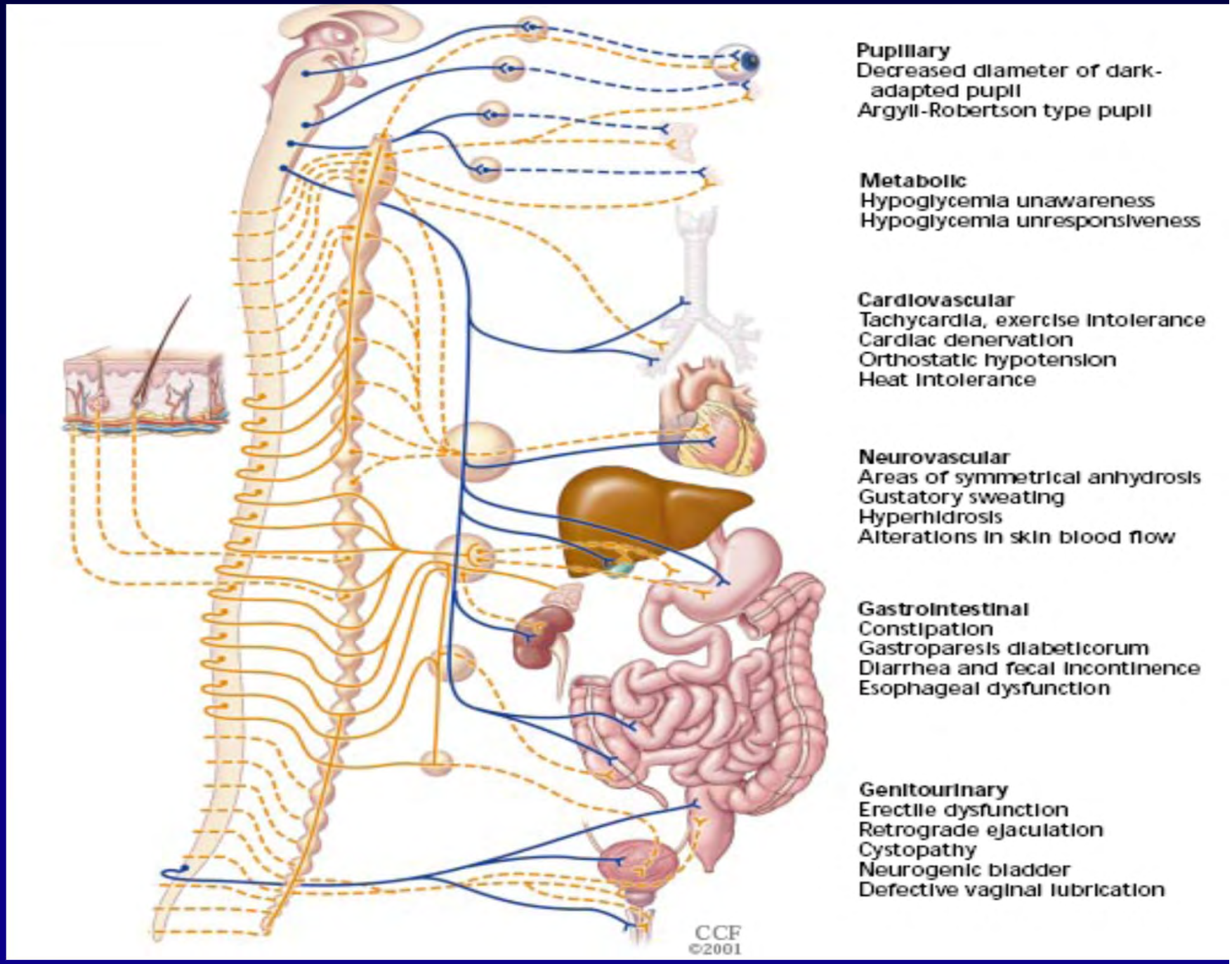
Epidemiology

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

Study Population	Data Collection	Prevalence (%)
Rochester Diabetic Neuropathy Study*	1986	54% - Type I 45% - Type II
San Luis Valley Diabetes Study†	1984 – 1986	25.8%
Pittsburgh Epidemiology of Diabetes Complications Study‡	1984 – 1988	34.0%

DPN diagnosed on basis of: *Positive symptoms and electrophysiological testing[1];
† Neurological exam[2]
‡ Presence of two out of three: abnormal sensory or motor signs, symptoms, decreased tendon reflexes[3]

1. Dyck PJ, et.al. *Neurology*. 1993;43: 817-24.
2. Franklin GM, et.al. *Am J Epidemiol* 1990;131:633-43.
3. Maser RE, et.al. *Diabetes* 1989;38(11):1456-61.



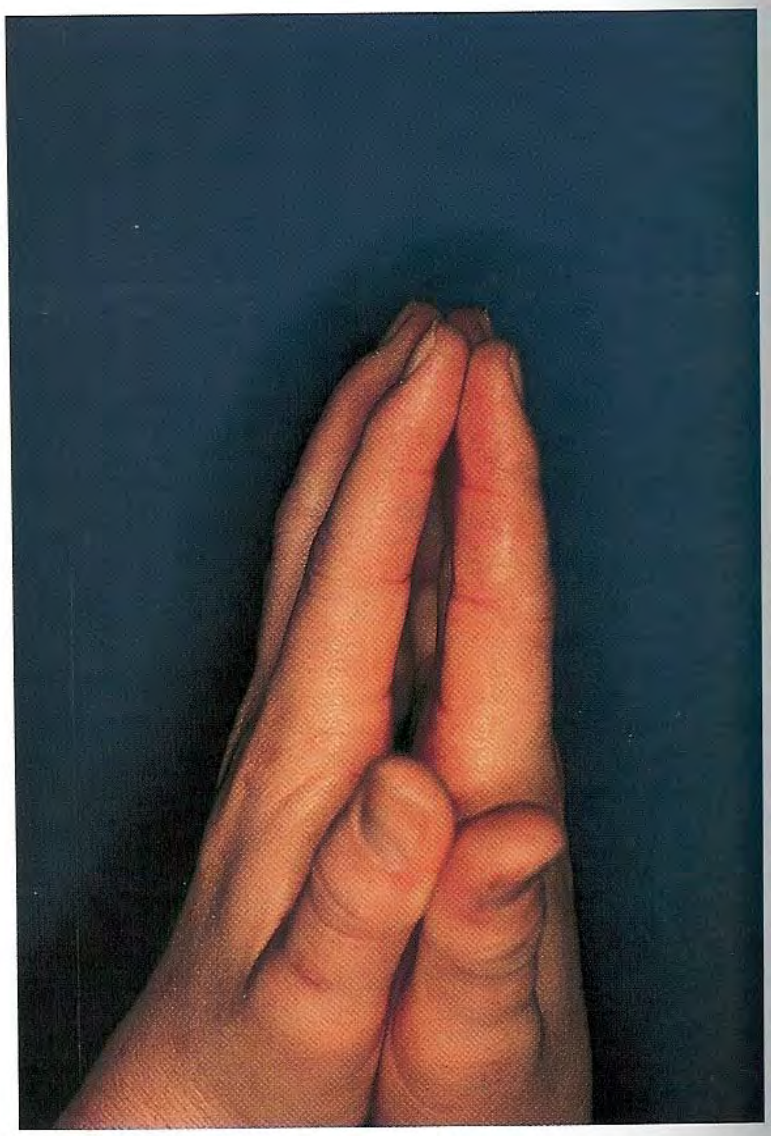
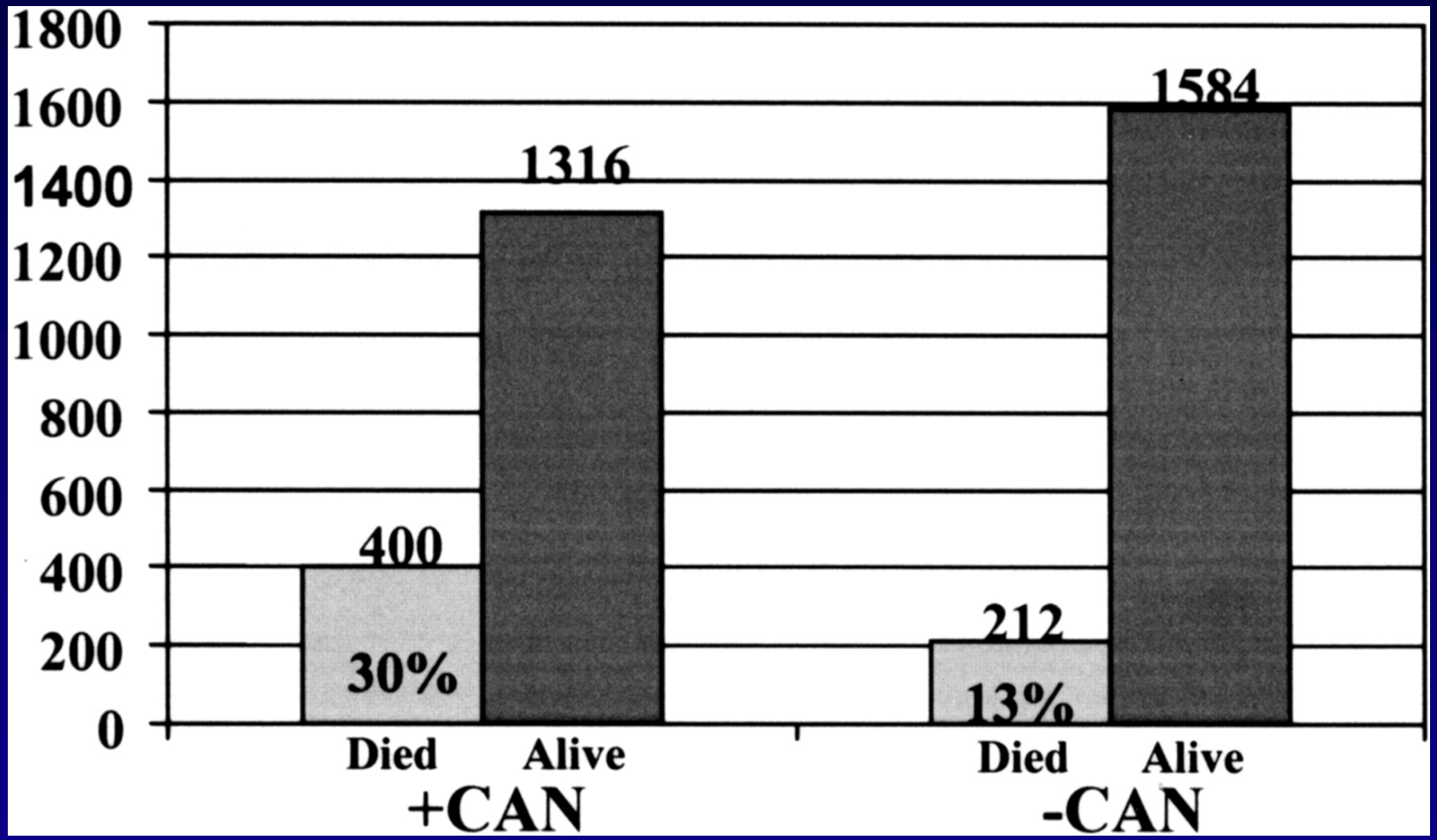


Figure 34.1 Failure of palmar surfaces of interphalangeal joints to approximate in patient with stiff joints and waxy skin.

Relative risks for cardiovascular autonomic neuropathy and mortality in 15 studies.

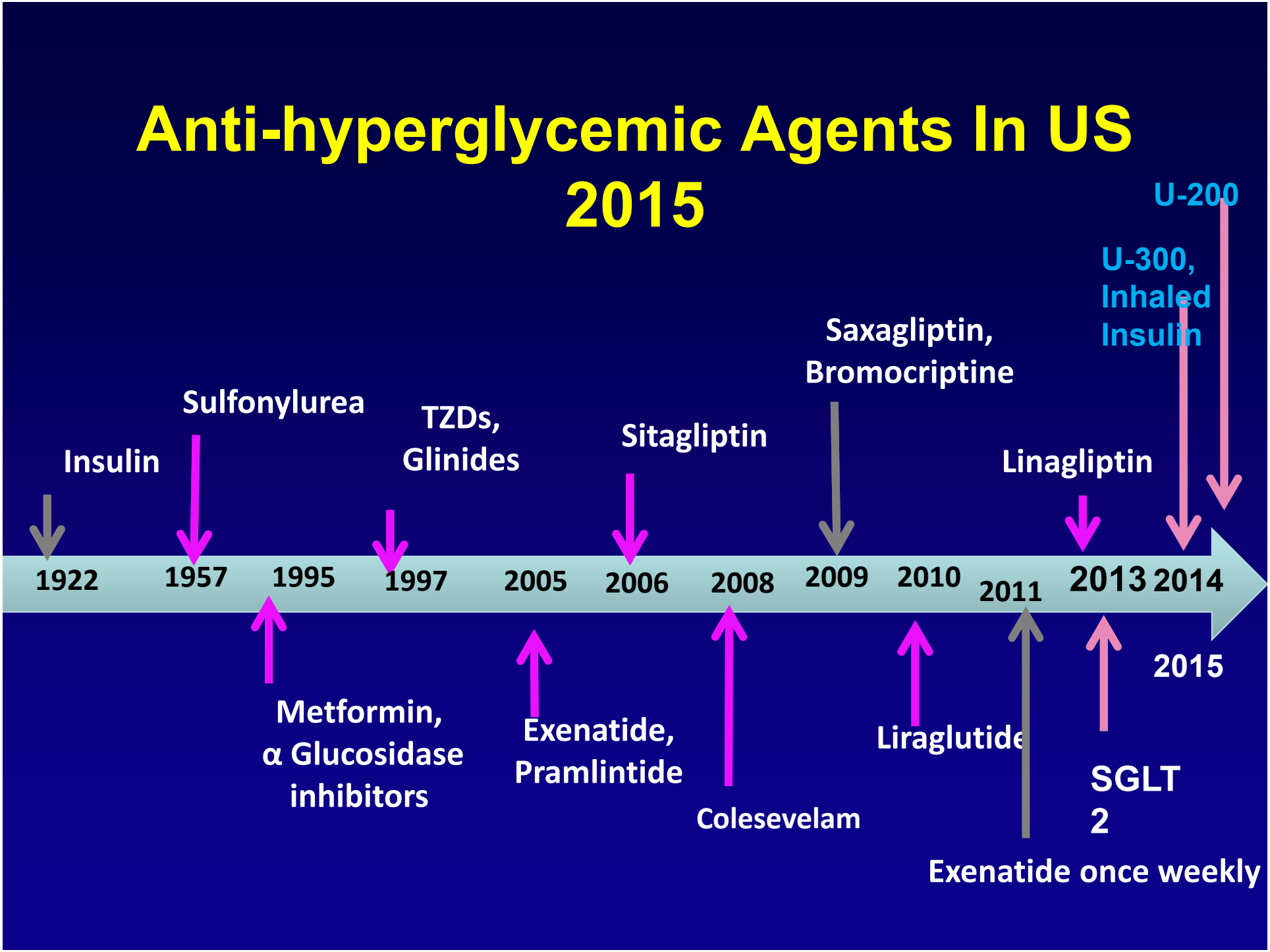


Aaron I. Vinik, and Dan Ziegler Circulation. 2007;115:387-397

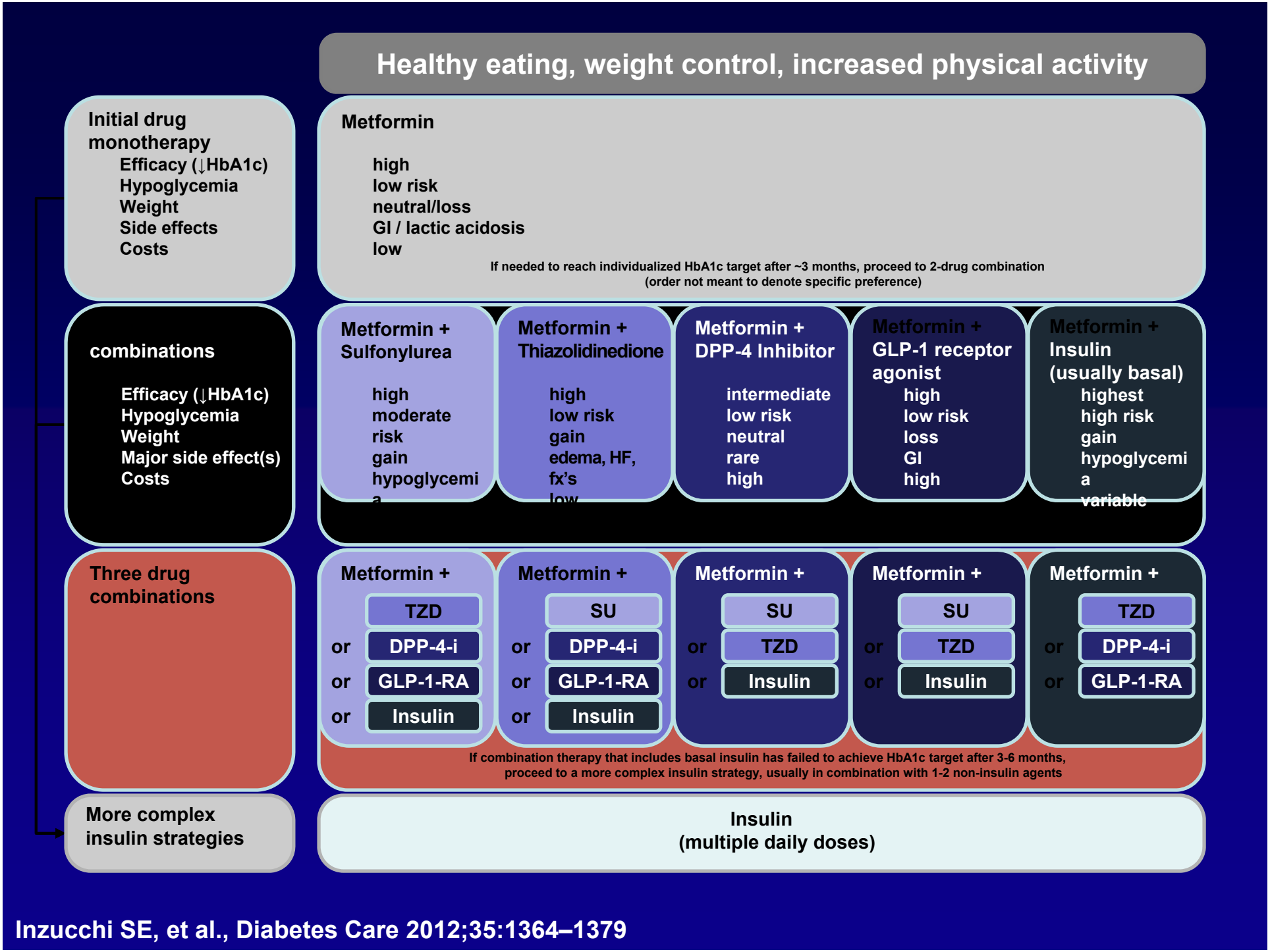
American Heart Association

Available Therapies

Anti-hyperglycemic Agents In US 2015

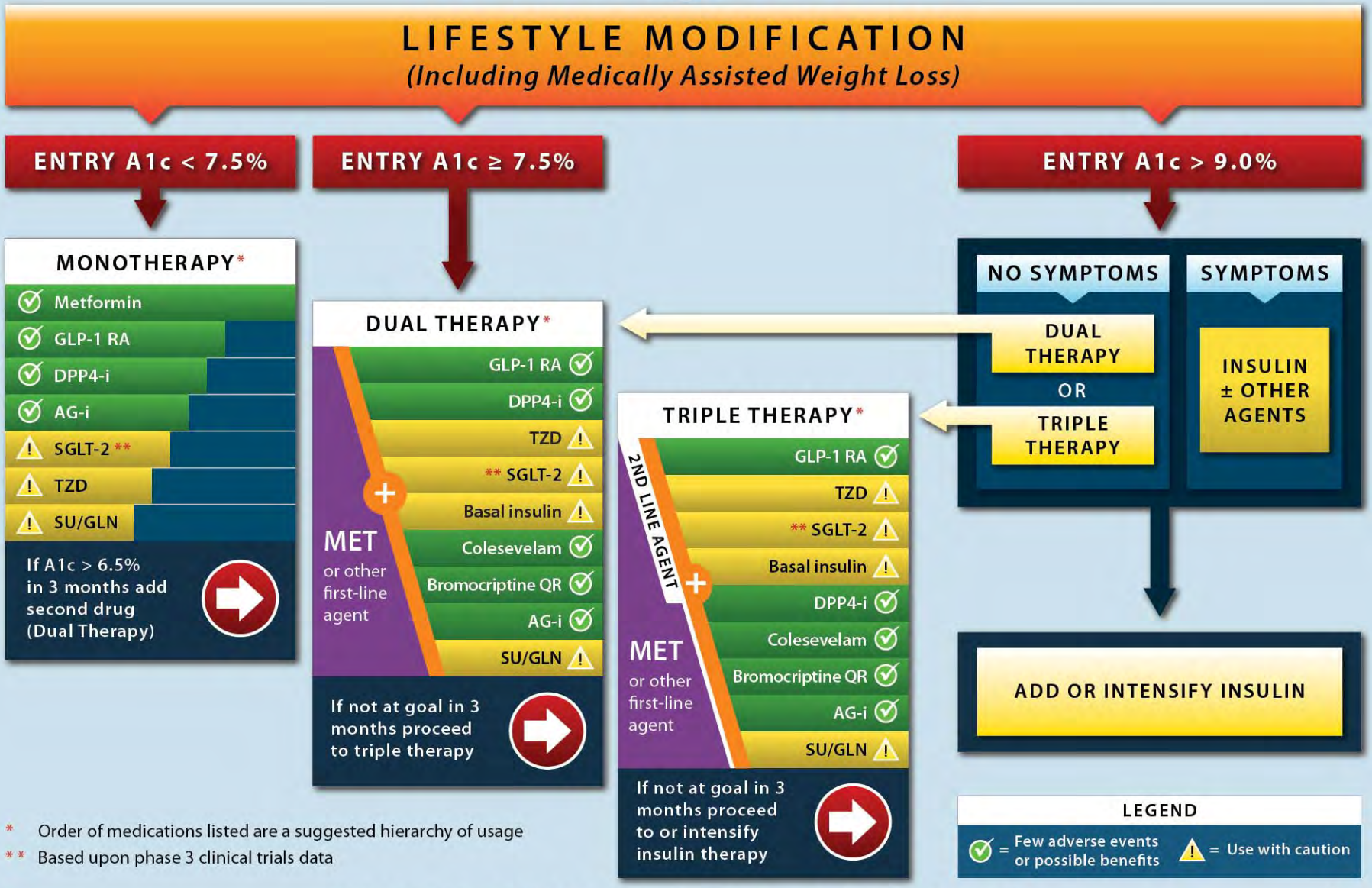


How to Choose Diabetes Therapies – 2016



Inzucchi SE, et al., Diabetes Care 2012;35:1364–1379

Glycemic Control Algorithm

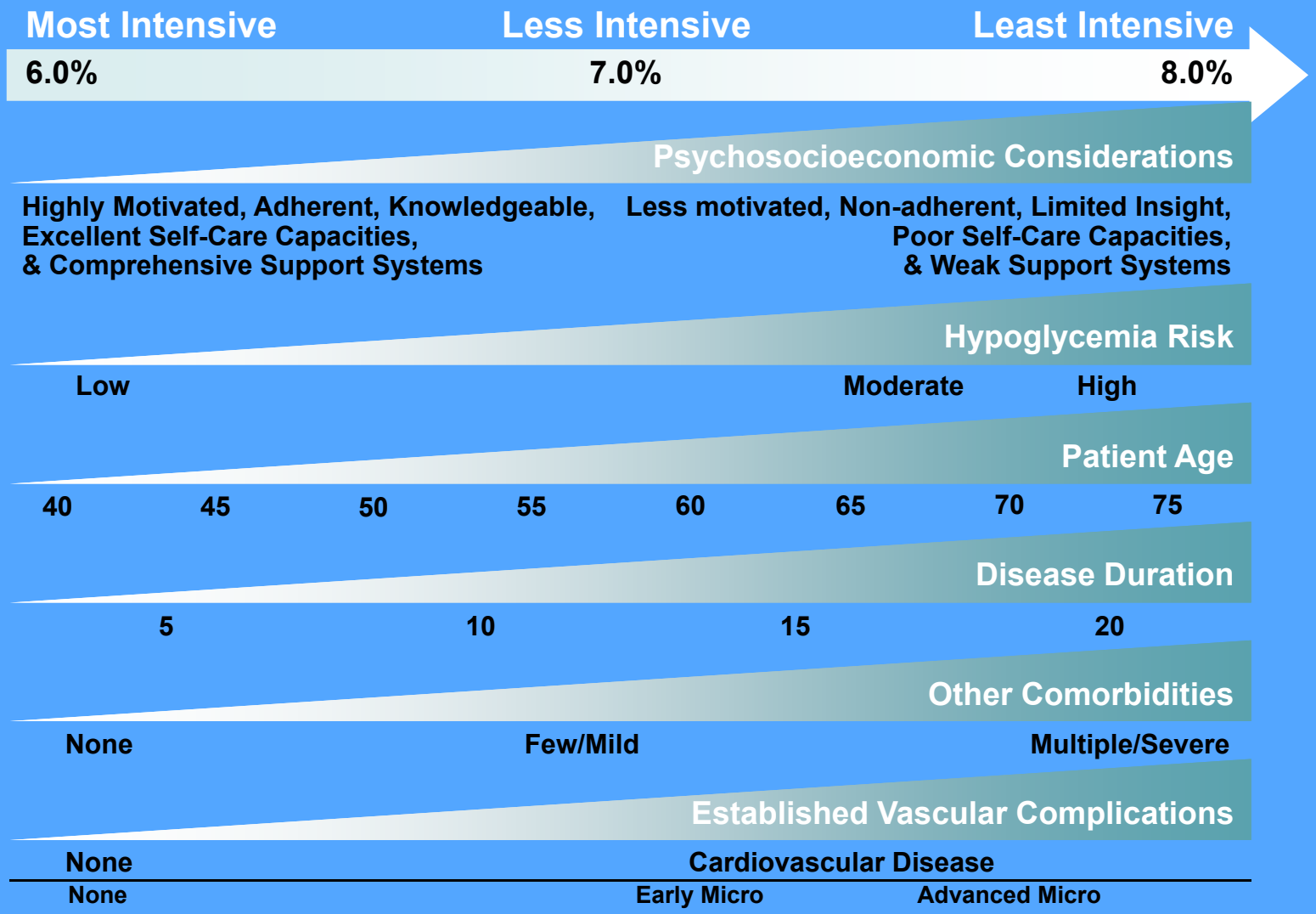


Individualization Of HbA1c Targets

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

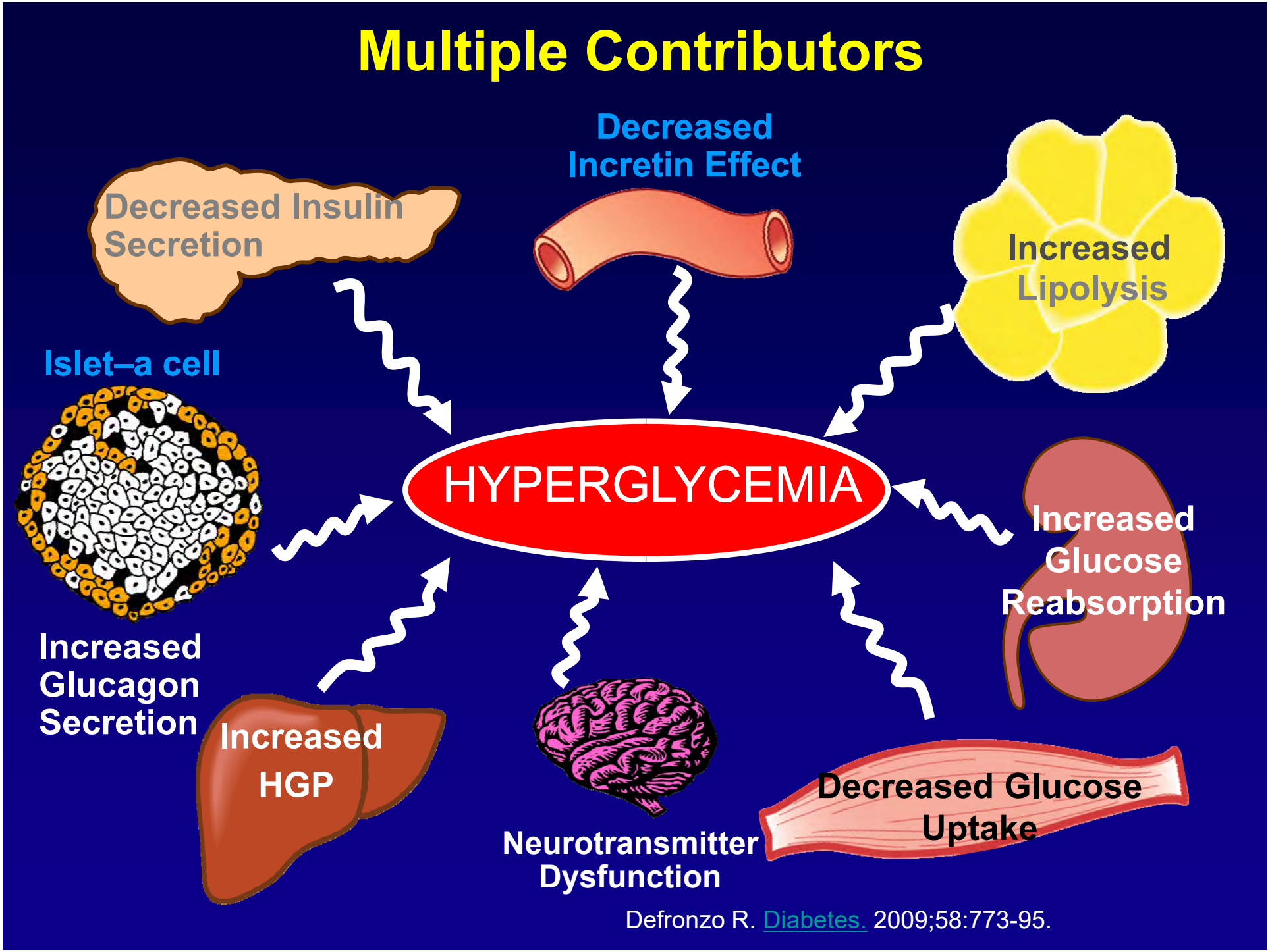
Adapted from Diabetes Care 2011; 34 (suppl 1) S11

Individualizing A1C Targets for Patients with T2DM



Data from Ismail-Beigi F, et al. *Ann Intern Med*. 2011;154(8):554-9.

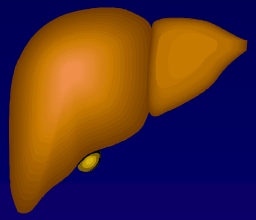
Multiple Contributors



Defronzo R. Diabetes. 2009;58:773-95.

Sites of Action by Therapeutic Options Presently Available for T2DM

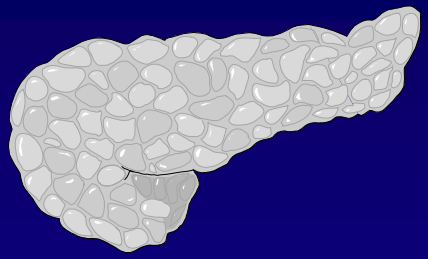
LIVER



GLUCOSE PRODUCTION
Biguanides
(Thiazolidinedione)

BRAIN
GLP-1 agonists
Dopamine agonists

PANCREAS

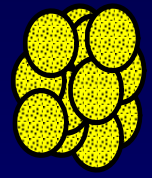


INSULIN SECRETION/REPLACEMENT
Sulfonylureas
Meglitinides
GLP-1 agonists?
DPP4 Inhibitors?
Insulin

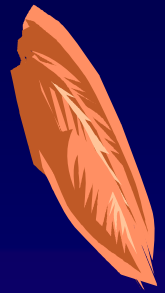
KIDNEY

GLUCOSE EXCRETION
SGLT2 Inhibitors

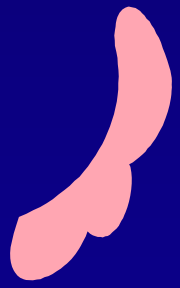
ADIPOSE TISSUE



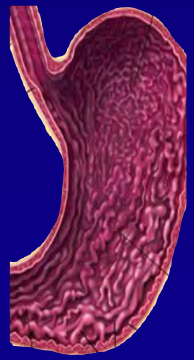
MUSCLE



PERIPHERAL GLUCOSE UPTAKE
Biguanides
(Thiazolidinedione)



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



STOMACH
DELAYED EMPTYING GLP-1 agonists (Exenatide, Liraglutide)
Pramlintide

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

Sonnenberg GE, et al. *Curr Opin Nephrol Hypertens*. 1998;7(5):551-555.

JS1

Slide 75

JS1 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

Box 356176
Seattle , WA 98195-6176
Phone: 206-598-4882
Fax: 206-598-4976

3:23
Pam Thoms

DM Statistics

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

[redacted]

	NIGHT 00:00-05:00	Breakfast 05:00-09:00	MID-AM 09:00-11:00	Lunch 11:00-14:00	MID-AFTERN 14:00-17:00	Dinner 17:00-20:00	MID-EVENIN 20:00-22:00	BED! 22:00-00:00	Aggregate
# of Readings	48 % 24	44 % 22	4 % 2	4 % 2					100% 50
Maximum	375	341	329	264					375
75th Percentile	318.50	311.75	318.75	249.50					316.00
Median	287.50	302.00	308.50	235.00					289.50
25th Percentile	259.00	284.00	298.25	220.50					276.50
Minimum	169	150	288	206					150
Mean	290	296	308	235					291
Std Dev	45.21	38.19	20.51	29.00					42.73
Events									
Hypo (<60)	0	0	0	0					0
Hyper (>180)	23	21	2	2					48
Above Target(>140)	100% 24	100% 22	100% 2	100% 2					100% 50
On Target(100-140)	0 % 0	0 % 0	0 % 0	0 % 0					0 % 0
Below Target(<100)	0 % 0	0 % 0	0 % 0	0 % 0					0 % 0

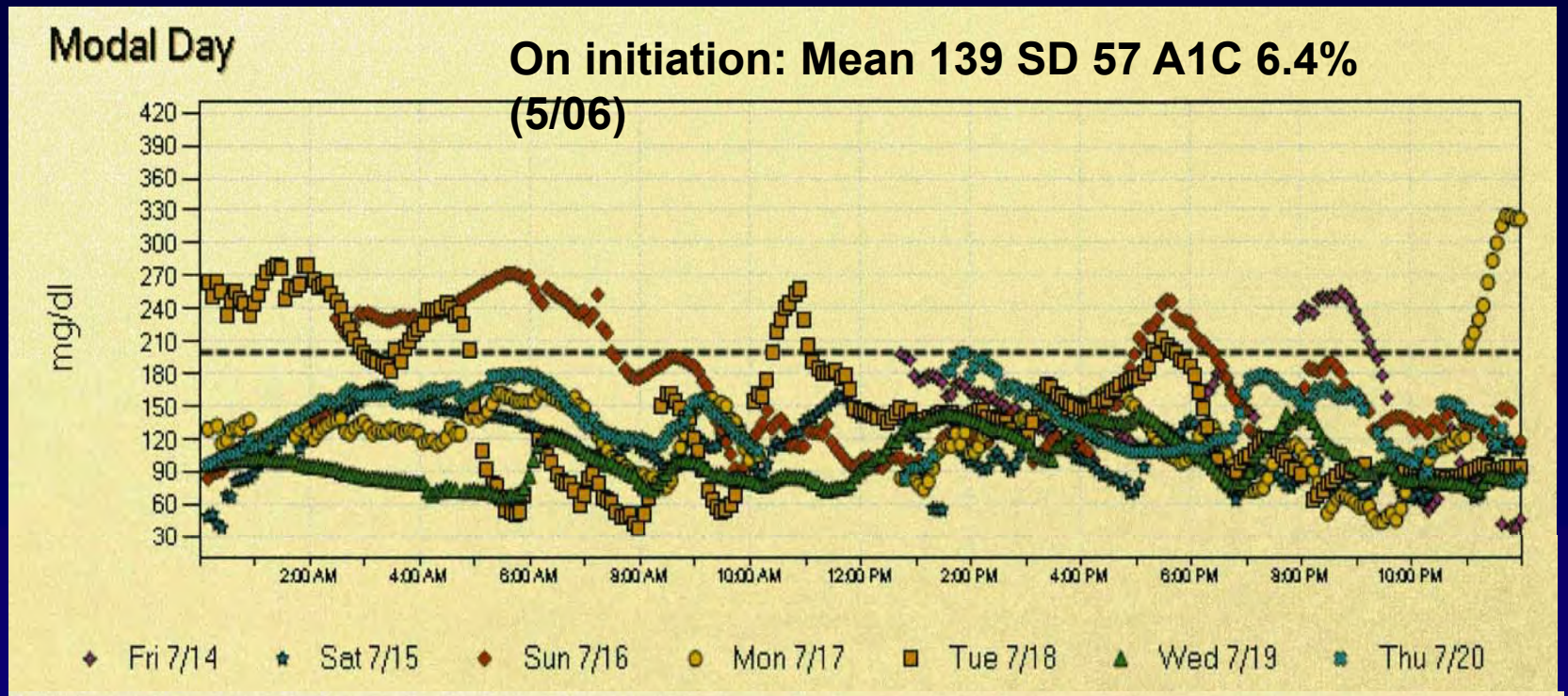
[redacted]

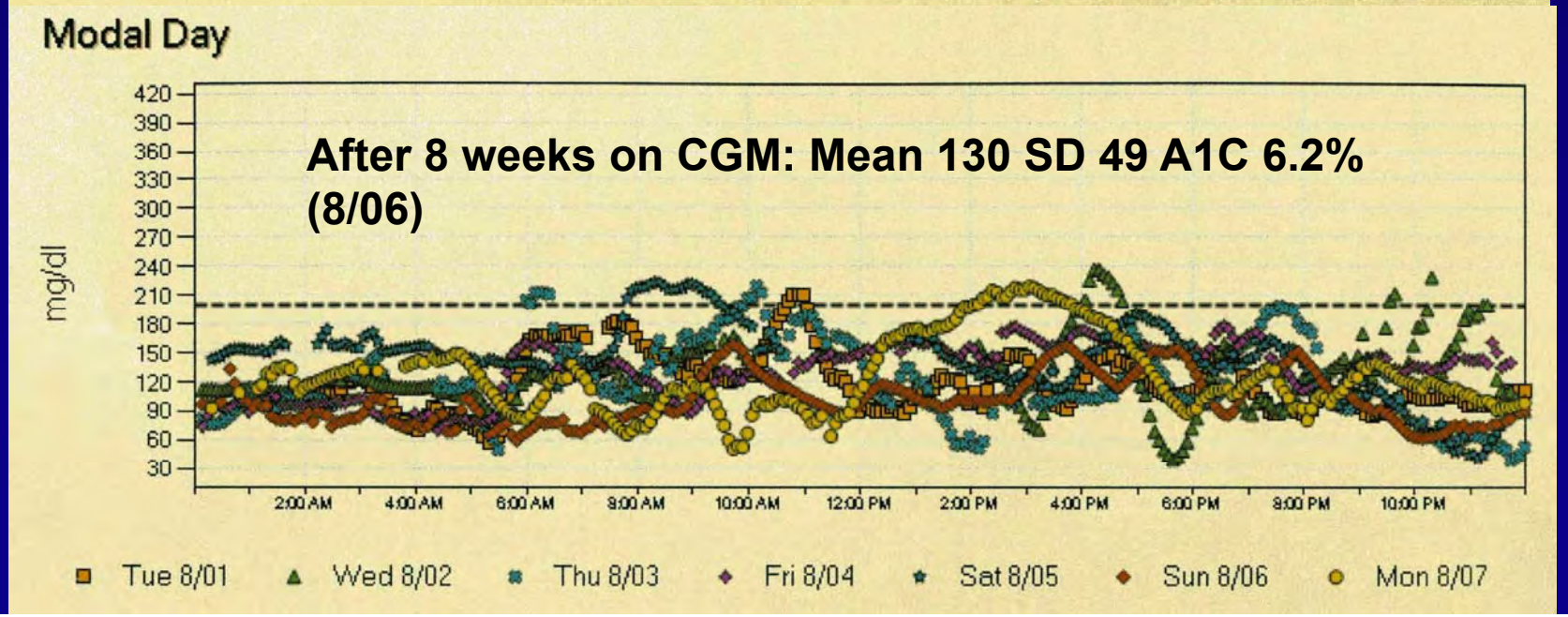
	NIGHT 00:00-05:00	Breakfast 05:00-09:00	MID-AM 09:00-11:00	Lunch 11:00-14:00	MID-AFTERN 14:00-17:00	Dinner 17:00-20:00	MID-EVENIN 20:00-22:00	BED! 22:00-00:00	Aggregate
# of Readings	13 % 16	17 % 21	10 % 12	11 % 13	9 % 11	15 % 18	20 % 25	5 % 6	100% 122
Maximum	185	188	187	187	219	311	228	217	311
75th Percentile	144.50	150.00	163.25	123.00	141.00	165.25	178.00	183.50	151.75
Median	124.00	133.00	145.50	107.00	123.00	130.00	130.00	89.00	125.00
25th Percentile	102.75	106.00	120.00	87.00	118.50	110.00	106.00	56.00	106.25
Minimum	86	58	106	75	108	82	47	41	41
Mean	129	131	143	109	134	142	139	116	132
Std Dev	33.07	31.55	24.52	29.01	29.36	52.33	50.19	71.51	42.67
Events									
Hypo (<60)	0	1	0	0	0	0	1	2	4
Hyper (>180)	2	1	1	1	1	2	6	2	16
Above Target(>140)	25 % 4	43 % 9	50 % 6	8 % 1	27 % 3	44 % 8	40 % 10	33 % 2	35 % 43
On Target(100-140)	50 % 8	43 % 9	50 % 6	54 % 7	73 % 8	39 % 7	36 % 9	17 % 1	45 % 55
Below Target(<100)	25 % 4	14 % 3	0 % 0	38 % 5	0 % 0	17 % 3	24 % 6	50 % 3	20 % 24

Current Continuous Sensors Available in the US

DexCom SC Glucose Sensor

Continuous Glucose Sensors Availale Outside US



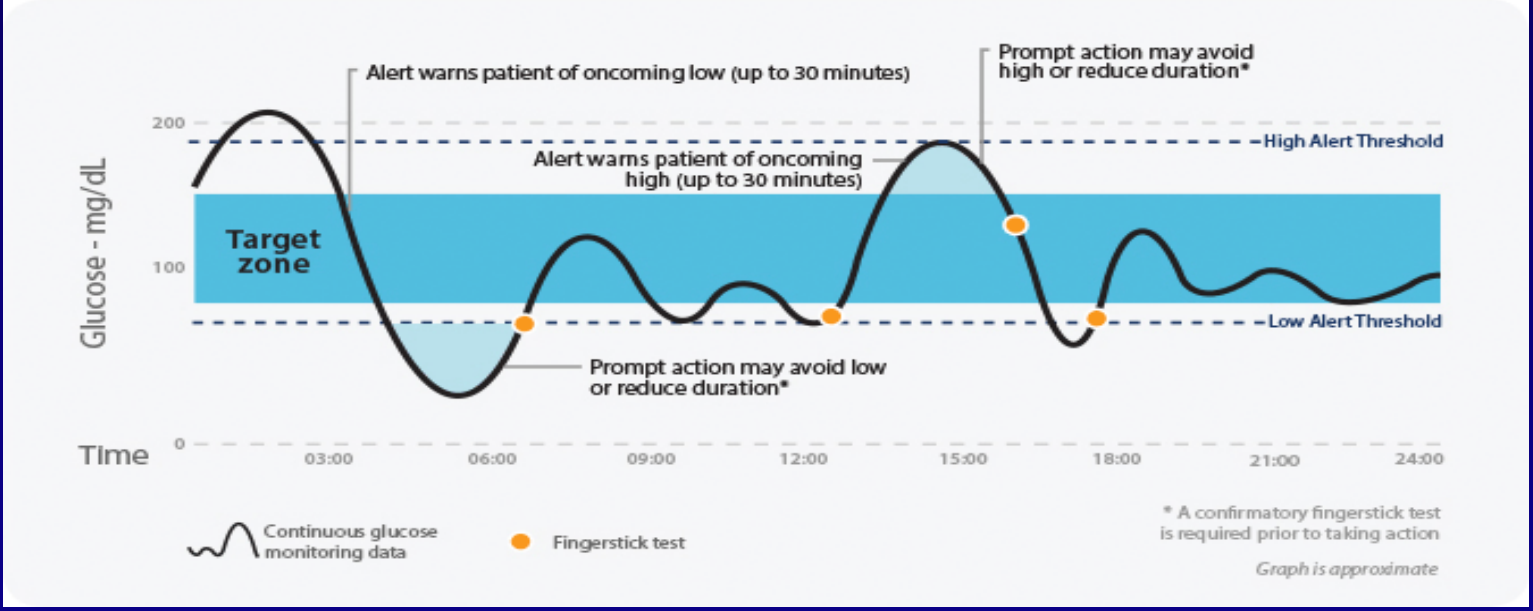


Drawbacks to CGM

- 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)

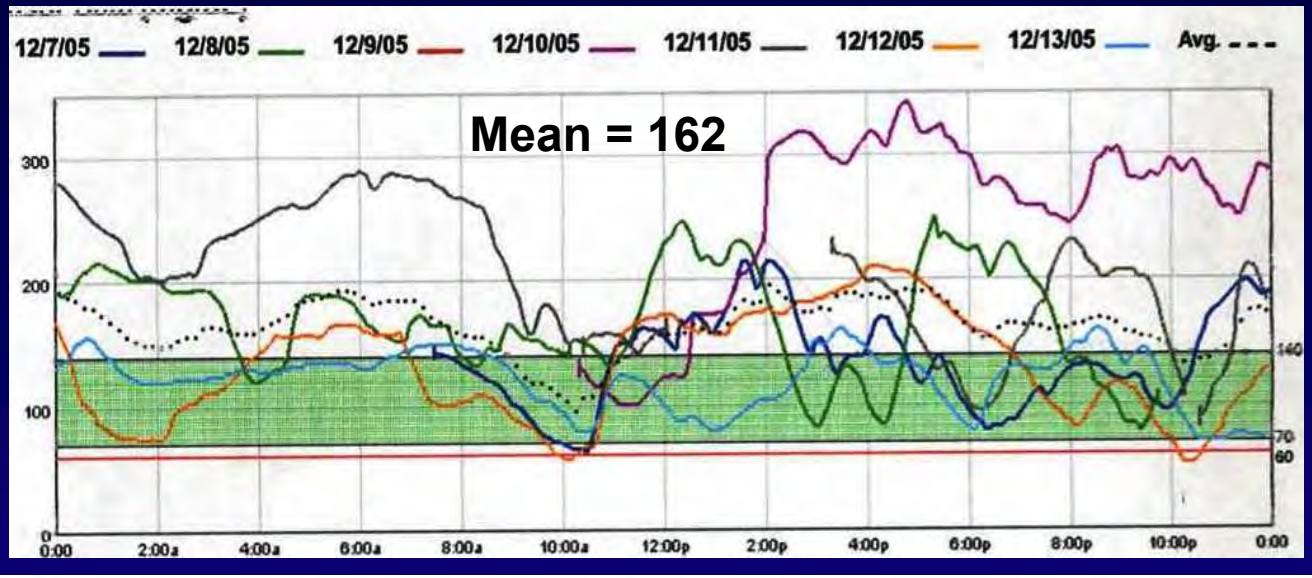
Most insurance companies are covering insulin pens

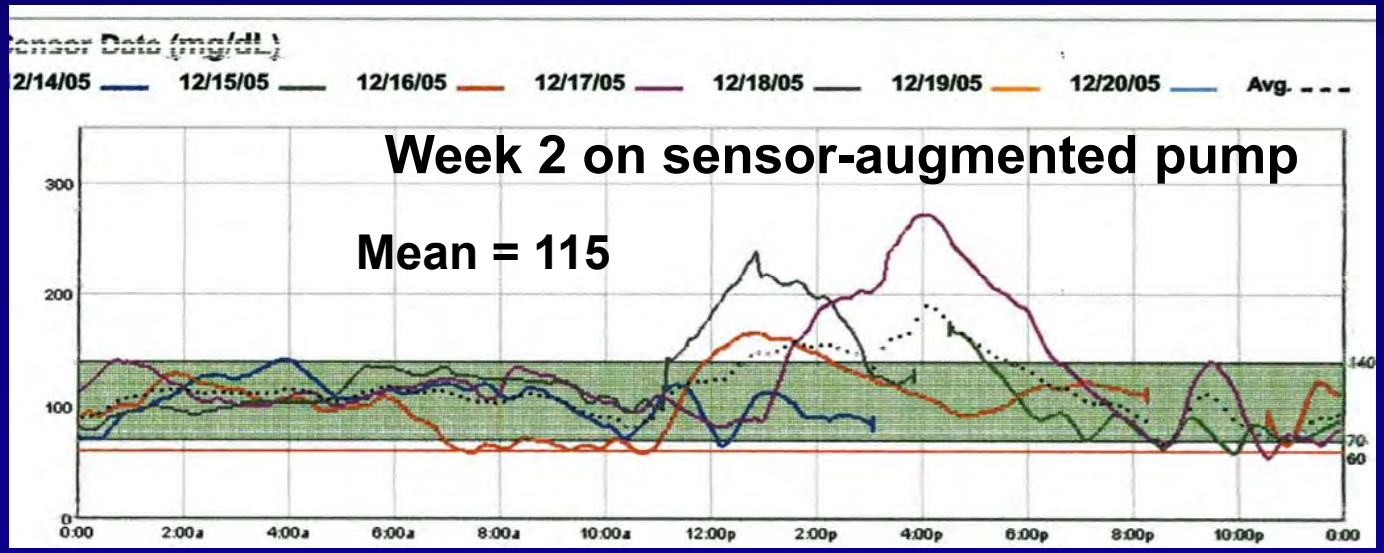
But more expensive! (2 X)

Asamoah E. *J Diabetes Sci Technol*. 2008;2(2):292-296.

Combined glucose sensing and insulin delivery

Week 1 on sensor-augmented pump





Glucose monitoring apps

Several apps for both Android and iOS are available to facilitate data tracking, trending [illegible] providers

BG Monitor **BlueLoop** **OnTrack Diabetes**

-Some studies suggest positive results using mobile phone based interventions for DM contro

- Apps specific for the needs of minorities with diabetes are needed

Diabetes Technol Ther. 2011 May;13(5):563-9
World J Diabetes 2015 March 15l 6(2): 225-233

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

From the Reynolda Campus (W.J.R
the School of Medicine (E.H.I., A
Q.Z.), Wake Forest University, Wi
Salem, NC; the Pennington Biom
Research Center, Louisiana State U
ty, Baton Rouge (G.A.B.); Baylor C
of Medicine, Houston (G.E.); and t
vision of Diabetes Translation, Cent
Disease Control and Prevention, A
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ment of Health and Exercise Sci
Box 7868, Winston-Salem, NC 27
at rejeski@wfu.edu.

*Investigators in the Look AHEAD (
for Health in Diabetes) Research
are listed in the Supplementary A
dix, available at NEJM.org.

N Engl J Med 2012;366:1209-17.

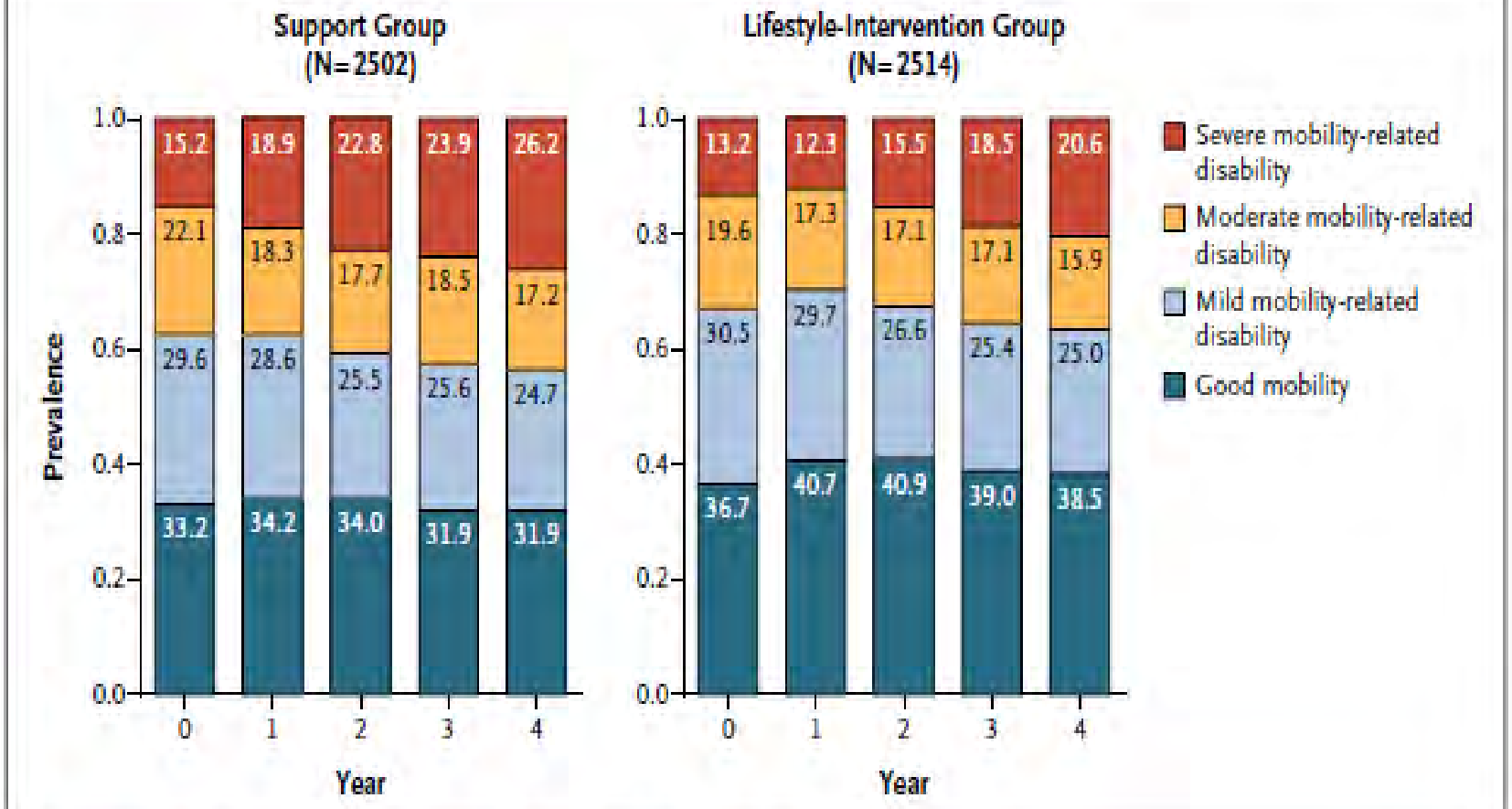

Figure 2. Prevalence of the Four States of Clinical Disability during the 4-Year Study.

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.