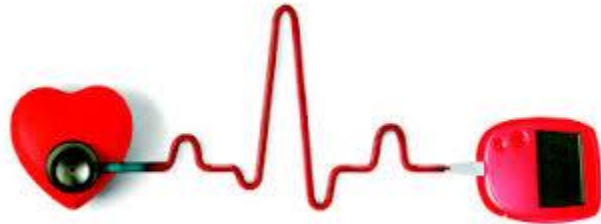# Diabetes and the Heart

Kathleen M. Dungan, MD

Division of Endocrinology, Diabetes & Metabolism
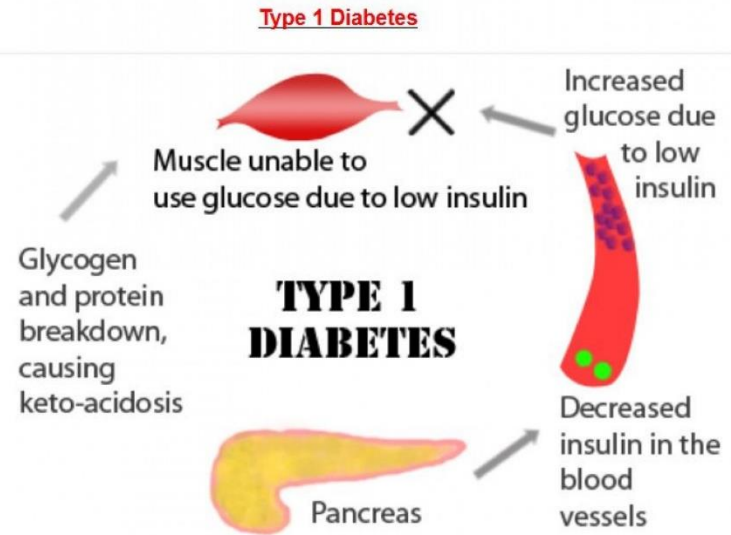
The Ohio State University

Disclosures

- I serve on advisory boards or perform consulting activities with Eli Lilly and Glaxo Smith Kline, Sanofi Aventis

- As director of our clinical trials unit, I also serve as an investigator for clinical trials sponsored by Astra Zeneca, Novo Nordisk, Sanofi Aventis, Glaxo
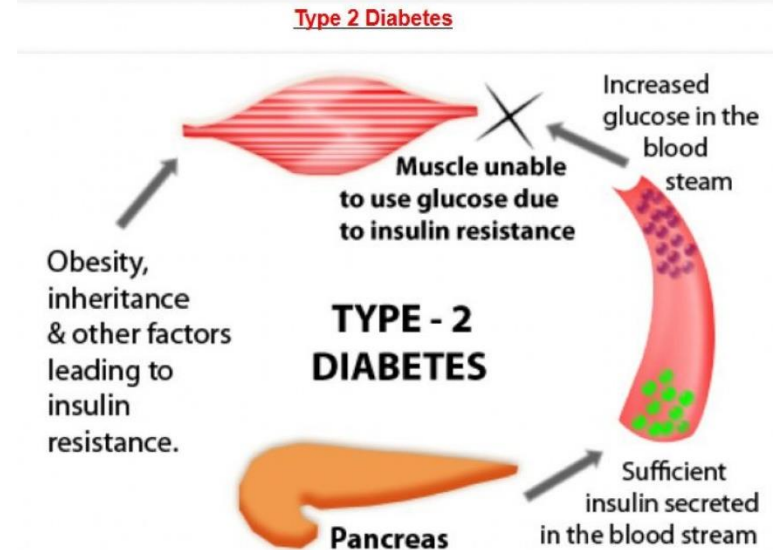
What is Diabetes?

- Diabetes is a group of diseases characterized by high blood glucose levels that result from defects in the body's ability to produce and/or use insulin.
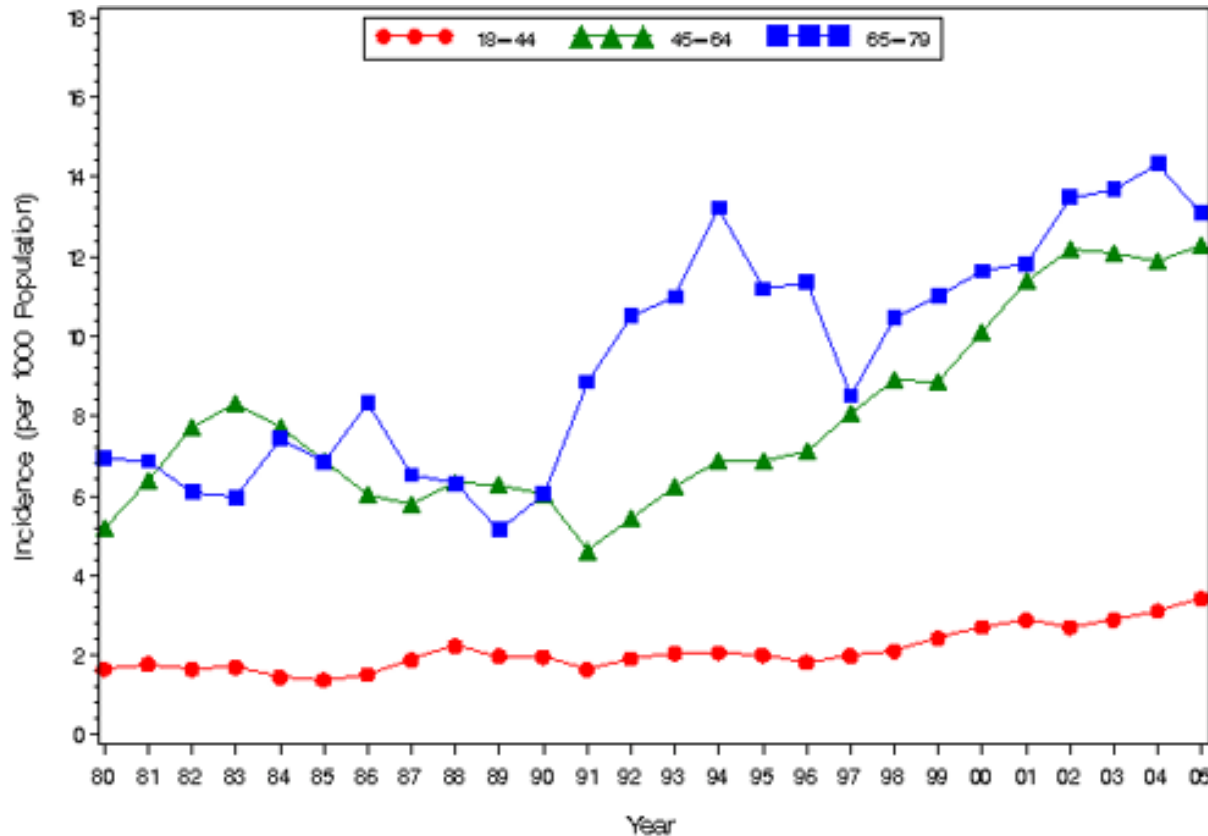
Types of Diabetes

- Type 1 diabetes

- Type 2 diabetes
  - **Pre-diabetes**
  - **Gestational diabetes**

Increased glucose due to low insulin

Muscle unable to use glucose due to low insulin

Glycogen and protein breakdown, causing keto-acidosis

TYPE 1 DIABETES

Decreased insulin in the blood vessels

Pancreas

Type 2 Diabetes

Increased glucose in the blood steam

Muscle unable to use glucose due to insulin resistance

Obesity, inheritance & other factors leading to insulin resistance.

TYPE - 2 DIABETES

Sufficient insulin secreted in the blood stream

Pancreas

Incidence of Diabetes in the U.S. is climbing
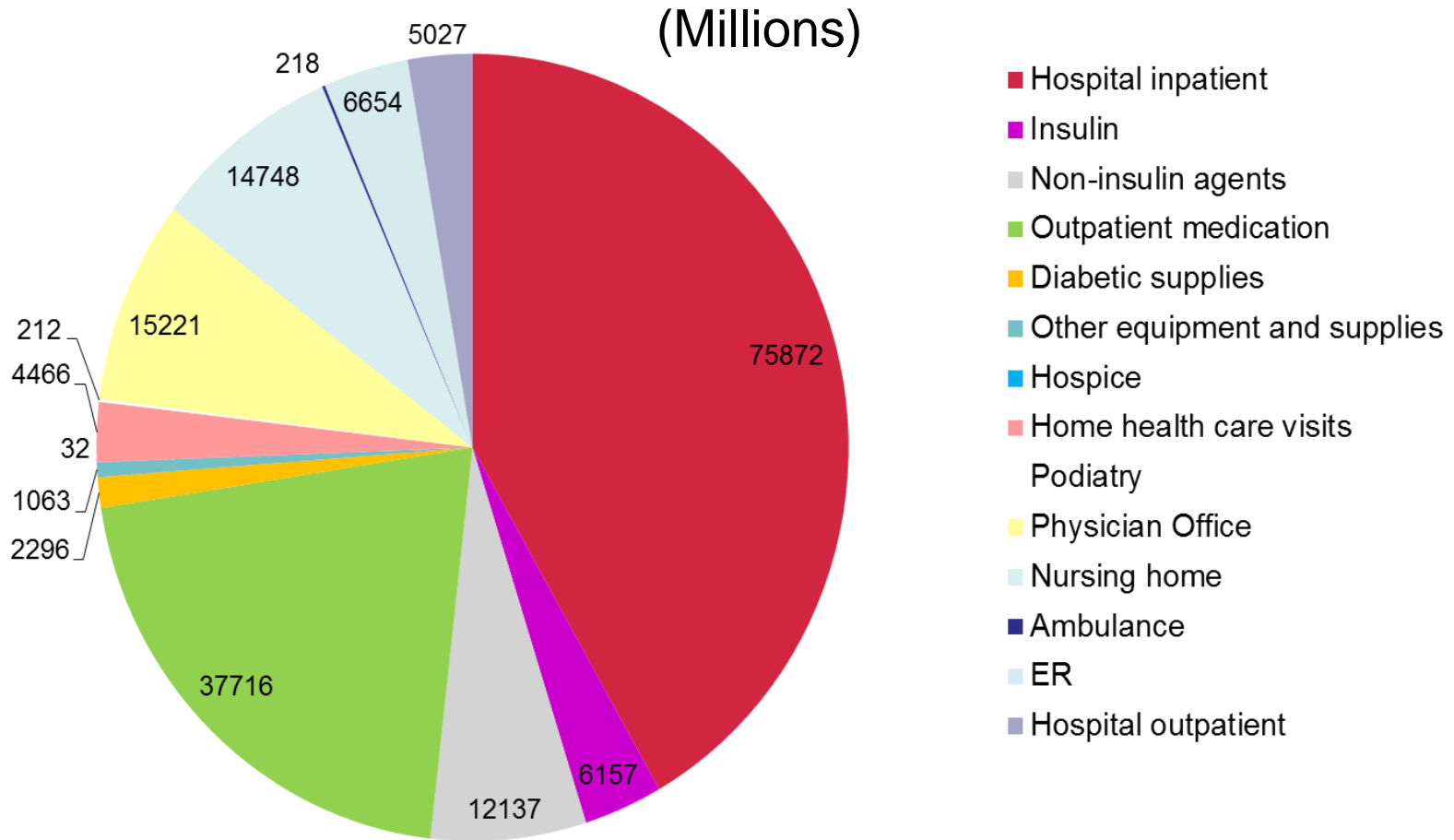## Age 18-79 Years

If current trends continue, 1 in 3 Americans and 1 in 2 minorities born in 2000 will develop diabetes during their lifetime!

*per 1000 Population

www.cdc.org

Map 3.1 Estimated age-adjusted prevalence of diabetes in adults (20-79), 2015

Legend:
- < 4%
- 4% – 5%
- 5% – 7%
- 7% – 9%
- 9% – 12%
- > 12%

International Diabetes Federation 2015

Costs Due to Diabetes in 2012

(Millions)

Pie chart values:
- 75872
- 6157
- 12137
- 37716
- 2296
- 1063
- 32
- 4466
- 212
- 15221
- 14748
- 218
- 6654
- 5027

Legend:
- Hospital inpatient
- Insulin
- Non-insulin agents
- Outpatient medication
- Diabetic supplies
- Other equipment and supplies
- Hospice
- Home health care visits
  Podiatry
- Physician Office
- Nursing home
- Ambulance
- ER
- Hospital outpatient

$176 billion (direct medical costs)
$ 69 billion (reduced productivity)

$245 BILLION (41% increase from 2007)

The toll of Diabetes

- 6th leading cause of death in the U.S.
    - Heart attack and stroke account for 65% of deaths
- Leading cause of new blindness in adults
- Leading cause of renal failure
- Leading cause of non-traumatic lower limb amputations

www.diabetes.org
Cheng et al Diabetes Care 2008;31:279-284

AT THE HEART OF DIABETES

Diabetes & Heart Disease By The #s

U.S. DIABETES PATIENTS HAVE:

2-3x
increased risk for heart disease

30%
of coronary stents implanted in 2011

280,000
heart attacks annually

2-4x
higher heart disease morbidity and mortality rates

60%
chance of dying from heart disease

Link between Diabetes, Heart Disease, and Stroke

- Conditions that increase the chance for heart disease or stroke
  - Overweight or obese
  - High blood pressure
  - High cholesterol
  - Family history of heart disease
  - smoking

Who should be tested for diabetes?

>45 years old

Or

RISK FACTORS
(1or more)

- Obesity/acanthosis
- CVD
- High risk ethnicity
- 1st degree relative with DM
- GestationalDM or baby > 9#
- HTN
- HDL (Good Cholesterol)<35
- TG >250 mg/dl
- Polycystic ovarian disease

Repeat screen every 3 years

ADA. *Diabetes Care* 2016; 39(Suppl 1):S1-S109.

TYPE 2 DIABETES?

American Diabetes Association

Diabetes Risk Test

1 How old are you?

Less than 40 years (0 points)
40—49 years (1 point)
50—59 years (2 points)
60 years or older (3 points)

Write your score in the box.

2 Are you a man or a woman?

Man (1 point)   Woman (0 points)

3 If you are a woman, have you ever been diagnosed with gestational diabetes?

Yes (1 point)   No (0 points)

4 Do you have a mother, father, sister, or brother with diabetes?

Yes (1 point)   No (0 points)

5 Have you ever been diagnosed with high blood pressure?

Yes (1 point)   No (0 points)

6 Are you physically active?

Yes (0 points)   No (1 point)

7 What is your weight status? (see chart at right)

Height	Weight (lbs.)		
4' 10"	119-142	143-190	191+
4' 11"	124-147	148-197	198+
5' 0"	128-152	153-203	204+
5' 1"	132-157	158-210	211+
5' 2"	136-163	164-217	218+
5' 3"	141-168	169-224	225+
5' 4"	145-173	174-231	232+
5' 5"	150-179	180-239	240+
5' 6"	155-185	186-246	247+
5' 7"	159-190	191-254	255+
5' 8"	164-196	197-261	262+
5' 9"	169-202	203-269	270+
5' 10"	174-208	209-277	278+
5' 11"	179-214	215-285	286+
6' 0"	184-220	221-293	294+
6' 1"	189-226	227-301	302+
6' 2"	194-232	233-310	311+
6' 3"	200-239	240-318	319+
6' 4"	205-245	246-327	328+
	(1 Point)	(2 Points)	(3 Points)

You weigh less than the amount in the left column (0 points)

Add up your score.

If you scored 5 or higher:

You are at increased risk for having type 2 diabetes. However, only your doctor can tell for sure if you do have type 2 diabetes or prediabetes (a condition that precedes type 2 diabetes in which blood glucose levels are higher than normal). Talk to your doctor to see if additional testing is needed.

Adapted from Bang et al., Ann Intern Med 151:775-783, 2009. Original algorithm was validated without gestational diabetes as part of the model.

Type 2 diabetes is more common in African Americans, Hispanics/ Latinos, American Indians, and Asian Americans and Pacific Islanders.

For more information, visit us at www.diabetes.org or call 1-800-DIABETES

Visit us on Facebook
Facebook.com/AmericanDiabetesAssociation

Lower Your Risk

The good news is that you can manage your risk for type 2 diabetes. Small steps make a big difference and can help you live a longer, healthier life.

If you are at high risk, your first step is to see your doctor to see if additional testing is needed.

Visit diabetes.org or call 1-800-DIABETES for information, tips on getting started, and ideas for simple, small steps you can take to help lower your risk.

STOP DIABETES.

http://www.diabetes.org/diabetes-basics/prevention/diabetes-risk-test/

Diabetes Prevention Program

% of Patients developing Diabetes
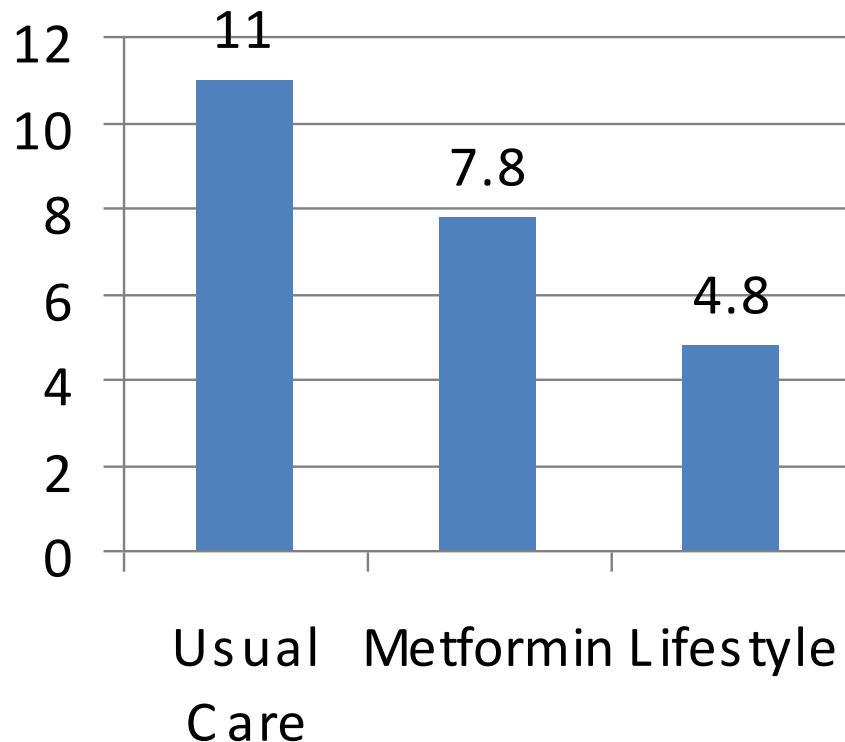
Intensive lifestyle changes prevent progression from prediabetes to diabetes:
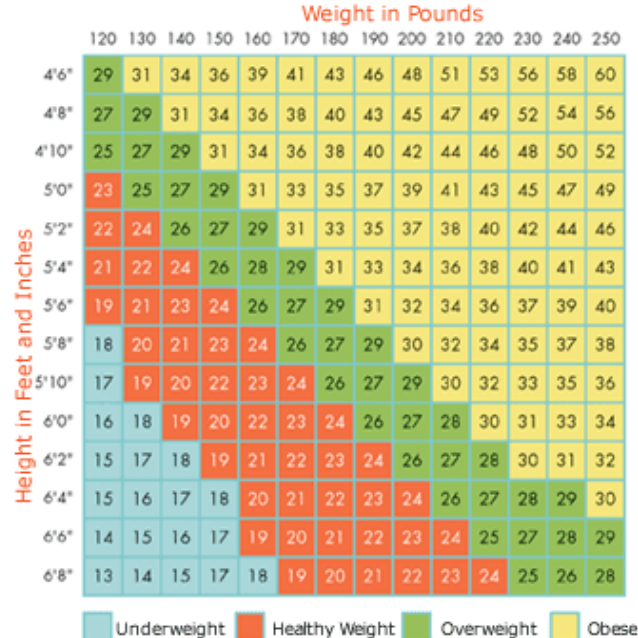
- 7% weight reduction
- Low-calorie, low fat diet
- Exercise 150 min/week
- Frequent contact with educators

3200 Adults with Prediabetes
Follow-up 2.8 years

N Engl J Med. 2002 Feb 7;346(6):393-403.

Weight loss

- The cornerstone of management for T2DM
- The goal is modest weight loss (5-7%): improves blood sugars and other risk factors for complications

Weight in Pounds

	120	130	140	150	160	170	180	190	200	210	220	230	240	250
4'6"	29	31	34	36	39	41	43	46	48	51	53	56	58	60
4'8"	27	29	31	34	36	38	40	43	45	47	49	52	54	56
4'10"	25	27	29	31	34	36	38	40	42	44	46	48	50	52
5'0"	23	25	27	29	31	33	35	37	39	41	43	45	47	49
5'2"	22	24	26	27	29	31	33	35	37	38	40	42	44	46
5'4"	21	22	24	26	28	29	31	33	34	36	38	40	41	43
5'6"	19	21	23	24	26	27	29	31	32	34	36	37	39	40
5'8"	18	20	21	23	24	26	27	29	30	32	34	35	37	38
5'10"	17	19	20	22	23	24	26	27	29	30	32	33	35	36
6'0"	16	18	19	20	22	23	24	26	27	28	30	31	33	34
6'2"	15	17	18	19	21	22	23	24	26	27	28	30	31	32
6'4"	15	16	17	18	20	21	22	23	24	26	27	28	29	30
6'6"	14	15	16	17	19	20	21	22	23	24	25	27	28	29
6'8"	13	14	15	17	18	19	20	21	22	23	24	25	26	28

Height in Feet and Inches

Underweight   Healthy Weight   Overweight   Obese

Do low carb diets work?

- The most effective diet is the one that *you* can continue long-term
- High-protein, low-carb diets
  - o Improved sugars
  - o But may also increase LDL cholesterol (the bad stuff)
- Carbs: the total amount is more important than the type in determining effect on glucose levels

- <u>Fat Matters, Carbs Count, but Calories are King!</u>
(Allan Borushek)

ADA. Diabetes Care 31 (Suppl 1):S61-S78

Is all fat the same?

Short answer: *no*

Legend:
- 🟩 ☺ Good fats
- 🟨 😐 limit
- 🟧 ☹ eliminate

Fats	Source	HDL ☺	LDL ☹
Omega-3	Fatty fish (salmon, mackerel & herring), flaxseeds/oil, walnuts	↑→	↓→
Monounsaturated	Olive, peanut, & canola oils, avocado, nuts	↑→	↓
Polyunsaturated	Vegetable oils (safflower, corn, sunflower, soy, cottonseed), nuts	↑→	↓
Saturated	Animal fats, coconut & palm oil	↑→	↑
Trans-fats	"Partially hydrogenated", commercial baked goods, fried foods, shortening, margarine	↓	↑

But remember, all fats have calories! The goal is to substitute the bad fats for the good ones.

But I already know what I need to do...
Effectiveness of Education

Pastors et al. *Diabetes Care* 2002;25:608-613
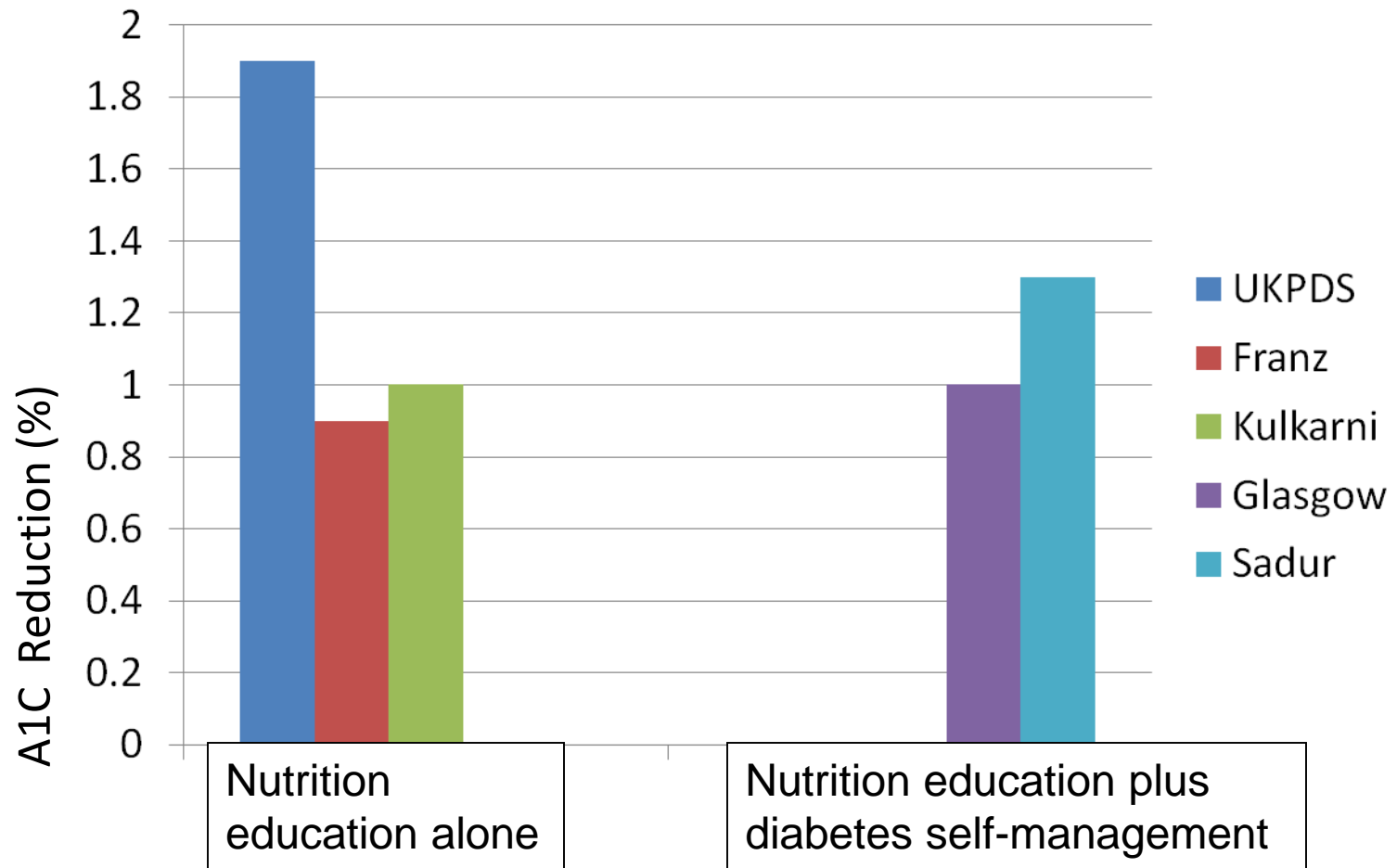
Exercise

- Minimum 30 min/day

- Important for keeping weight off.

- Most weight loss results from ↓ calories

- Benefit in reducing sugars and risk of heart disease beyond that produced by weight reduction alone.

ADA. Diabetes Care 31 (Suppl 1):S61-S78

So you want to start an exercise program…

- Talk to your doctor to make sure it is safe

- You may need an exercise stress test

- See your doctor if you experience chest pain or discomfort, shortness of breath or racing heart

Where should my sugars be?
Measuring Success
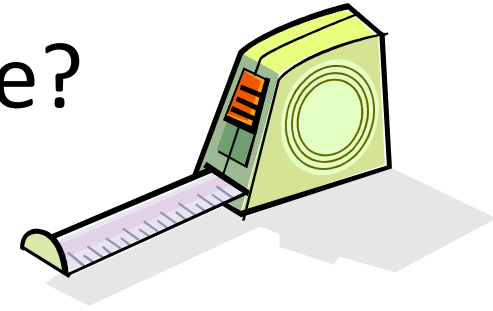
	ADA[1]
A1C	<7%
Fasting/premeal glucose	90-130
Postmeal glucose	<180 (peak)

Goals should be individualized

1. ADA Clinical Practice Recommendations. Diabetes Care 2015

Prevalence of HbA1c <7% among people with diabetes
NHANES Data
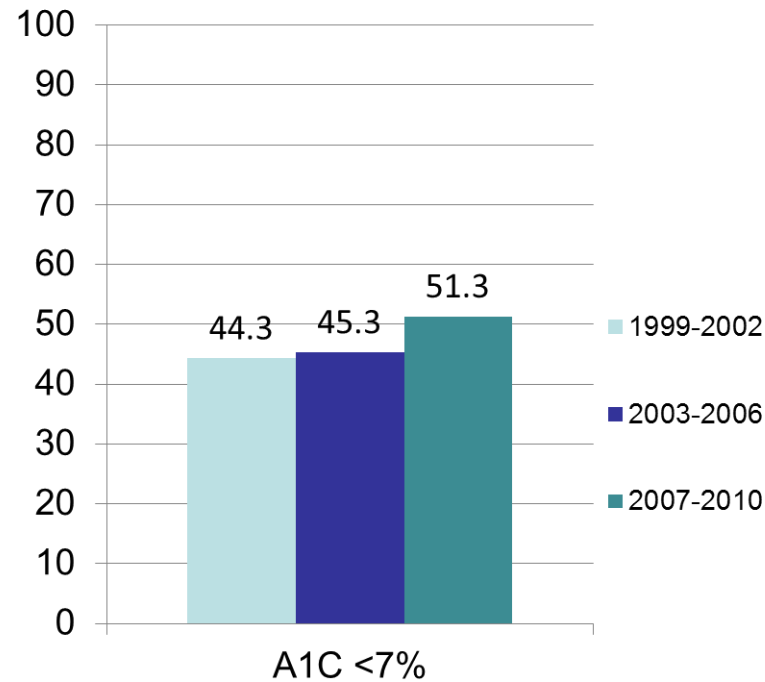
Ali et al. N Engl J Med. 2013;368(17):1613-24

Frequency of Glucose Monitoring Predicts Glycemic Control
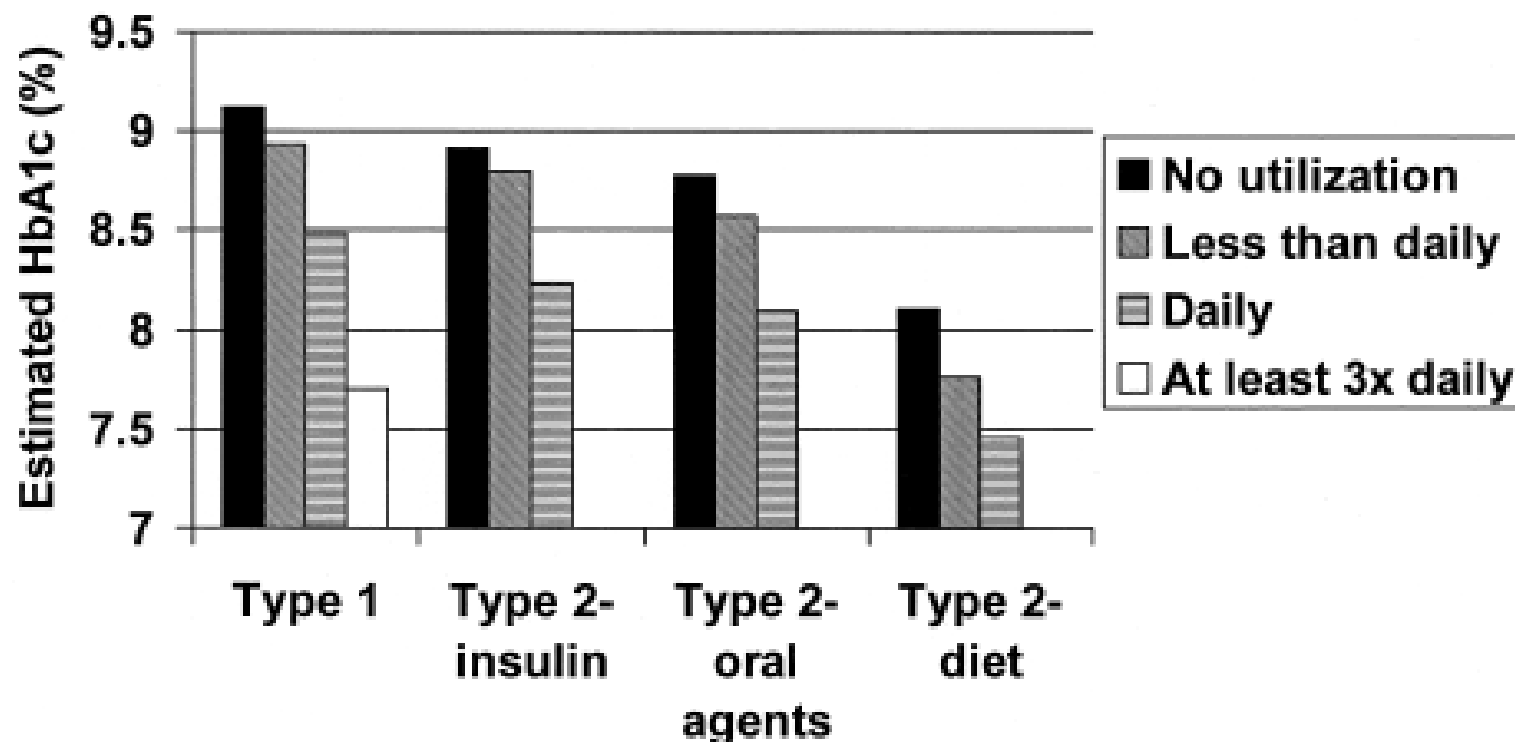
Am J Med. 2001;111:1–9.

Frequency of Testing

- Depends upon medications used
  - Insulin: 3+ times/day
  - Oral Hypoglycemics: 1+ time/day

But it only improves glucose control if you use the information!

Can you find the pattern?

Connecting and Downloading

Apps
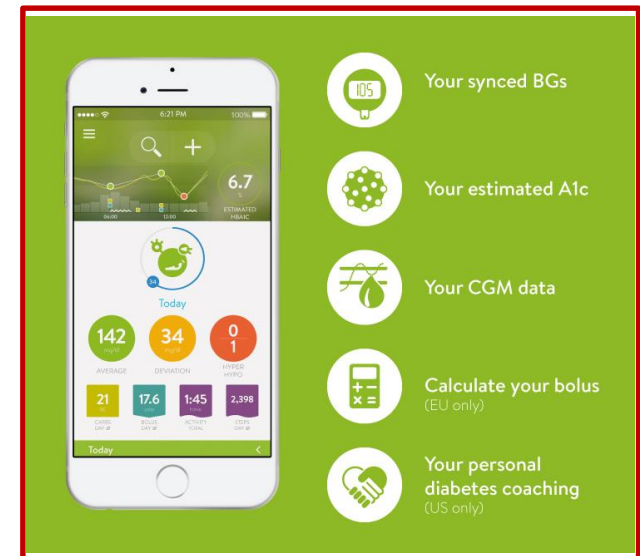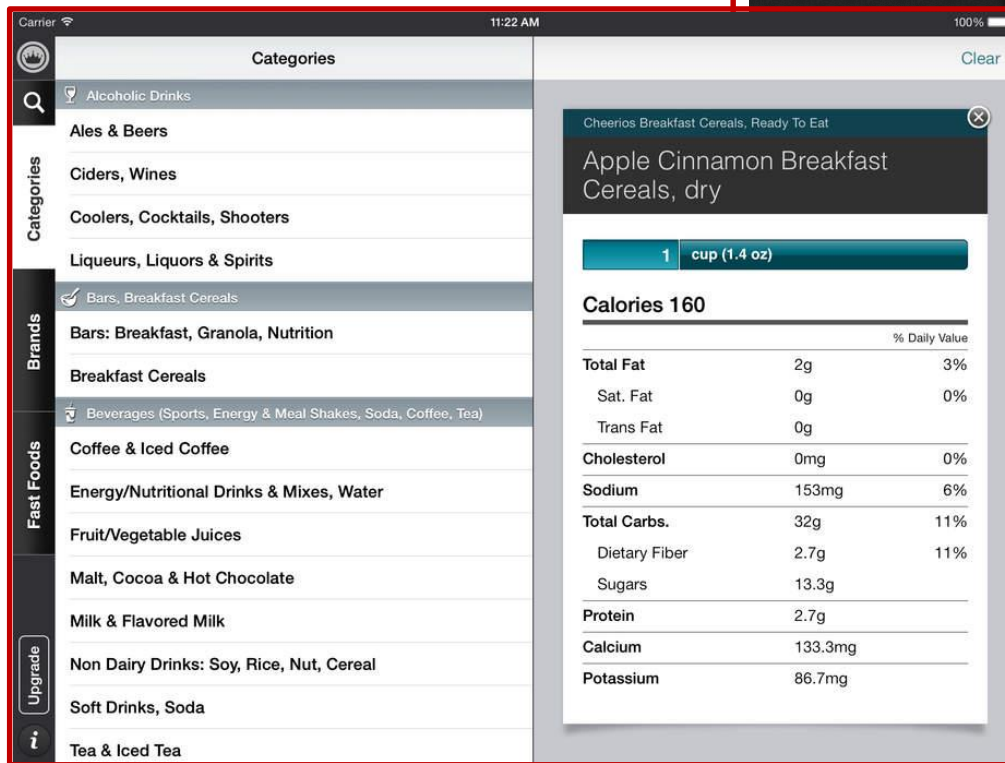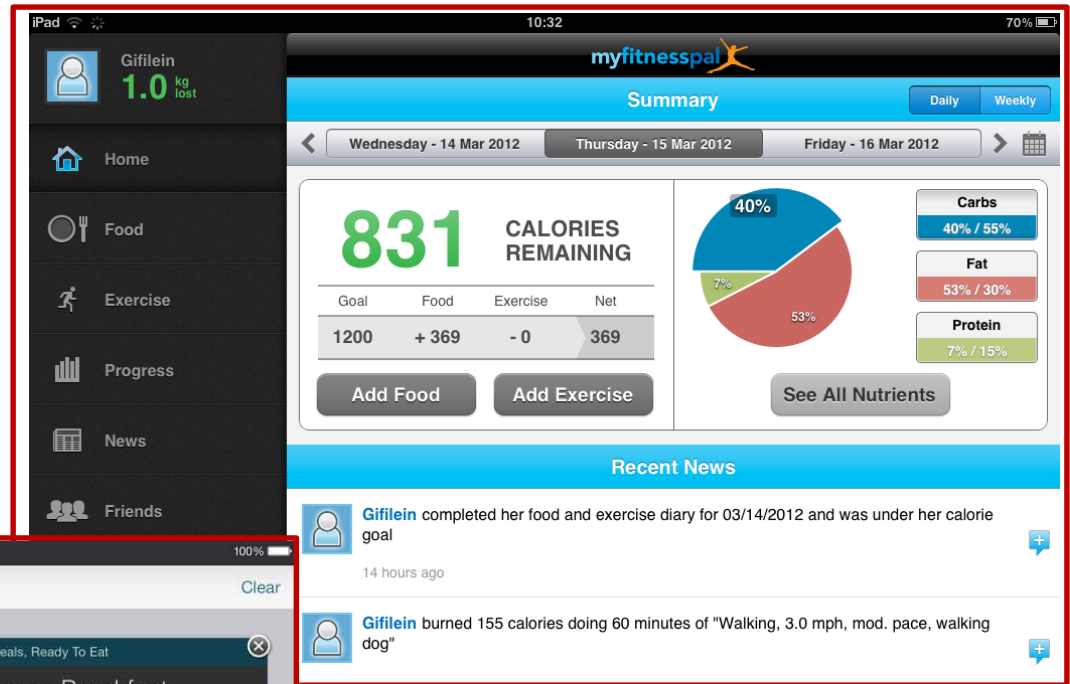
Apps

	Diabetes
	Diet
	Lifestyle
	Exercise

App Name	Device Compatibility	Ratings	Cost (iOs, Android)	Features
Dlife	iOs	No Rating	Free	Gives a range of advice on Type I Diabetes. And give reminders to check blood sugar.
Glucose Buddy	iOs, Android	4.4	Free, Free	Glucose Buddy is a data storage utility for people with diabetes.
MySugr	iOs, Android	4.8	Free, Free	mySugr Logbook is a charming, sometimes outspoken diabetes manager that focuses on making your diabetes data useful in everyday life.
Meal Memory	iOs	No Rating	$1.99	Logging a meal is as simple as taking a picture. Now with Apple Health integration, Meal Memory can import your blood sugar readings and link them to your meals automatically.
MyDiabetes	iOs, Android	No Rating	$0.99	App manages your Blood Glucose, Blood Pressure, Food, Exercise, Water intake and Medication all in one simple-to-use application.
Calorie King	iOs, Android	3.6	Free, Free	Contains over 70,000 foods 260 fast food chains and restaurants.
Figwee	iOs	3.5	$1.99	visual, using over 28,000 photos of meticulously weighed portions. Use a slider to adjust how much is in the bowl, on the plate, or in the glass,
Fooducate	iOs, Android	4.5	Free, Free	Products are awarded a nutrition grade of A, B, C, or D by an automatic algorithm
Go Meals	iOs, Android	3	Free, Free	GoMeals includes tools for eating healthy, staying active, and tracking your blood glucose levels. food tracker, activity tracker, glucose tracker, and restaurant locator.
HealthyOut	iOs, Android	4.4	Free, Free	Find healthy meals from local restaurunts in your area. Filters by Cuisine, ingredients, type of dish, low carb, and by dietary restriction like vegan, vegetarian, and etc.
My FitnessPal	iOs, Android	4.7	Free, Free	The largest food database (over 5,000,000 foods) and amazingly fast and easy food and exercise entry. Can connect with 50+ other apps and tracks goals and reports them.
SPARKPEOPLE	iOs, Android	4	Free, Free	This app brings the fitness tracking and calorie counting tools, exercise demos, reporting, and the detailed food database
Daily Workouts	iOs, Android	4.8	Free, Free	Daily Workouts FREE is a 10 to 30 minute daily workout routine for men and women that steps you through some of the best exercises you can do in the comfort of your own home No internet required to do the workouts.
Run Keeper	iOs, Android	4.4	Free, Free	With Runkeeper, turn your phone into a GPS tracker or track your runs without your phone with our Apple Watch app.

Two Week Glucose Summary with Logbook

Glucose Target Ranges | Glucose Readings
Low | Within | High | Manual (BG) △ Glucose (BG) • Glucose (CM)
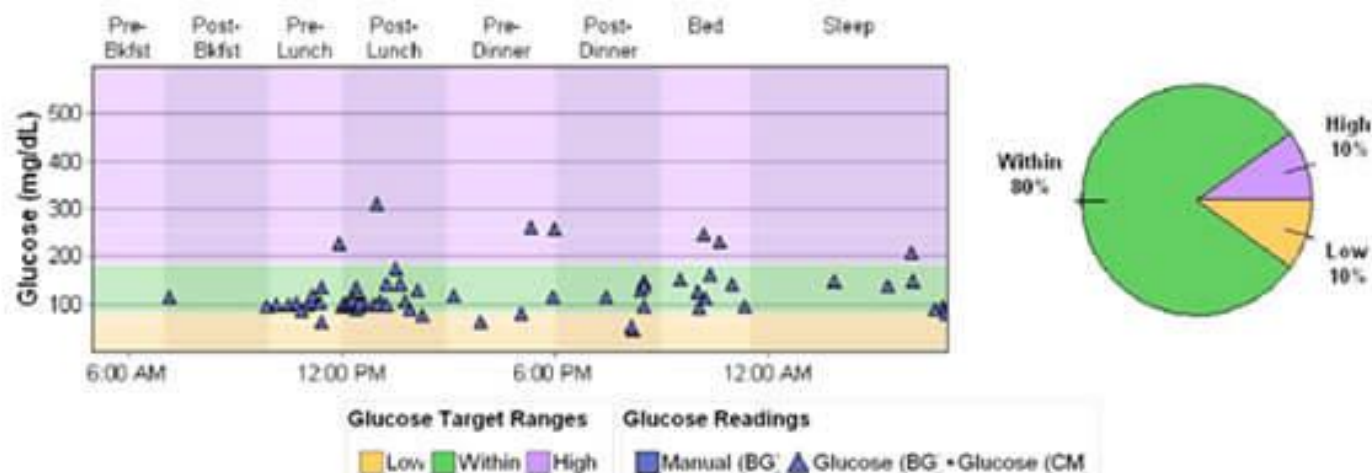
Glucose Statistics	Breakfast		Lunch		Dinner		Bed & Sleep	
(mg/dL)	5:01 AM-7:00 AM-10:00 AM		10:01 AM-12:00 PM-3:00 PM		3:01 PM-6:00 PM-9:00 PM		9:01 PM-11:30 PM-5:00 AM	
	Pre	Post	Pre	Post	Pre	Post	Bed	Sleep
# Readings		2	11	28	6	7	9	8
Highest	N/A	116	226	311	262	147	246	209
Lowest	N/A	97	62	77	62	47	92	78
Average		107	112	115	149	103	151	124
Standard Deviation	N/A	N/A	39.8	42.4	80.5	37.4	52.3	42.1
Within %	N/A	100%	82%	92%	33%	71%	78%	76%

CGM: continuous glucose monitoring

- Eras of glucose measurement

| Urine Glucose | → | Fingerstick | → | CGM? |

Pre-1978   **1978-2006**   **2006 -**

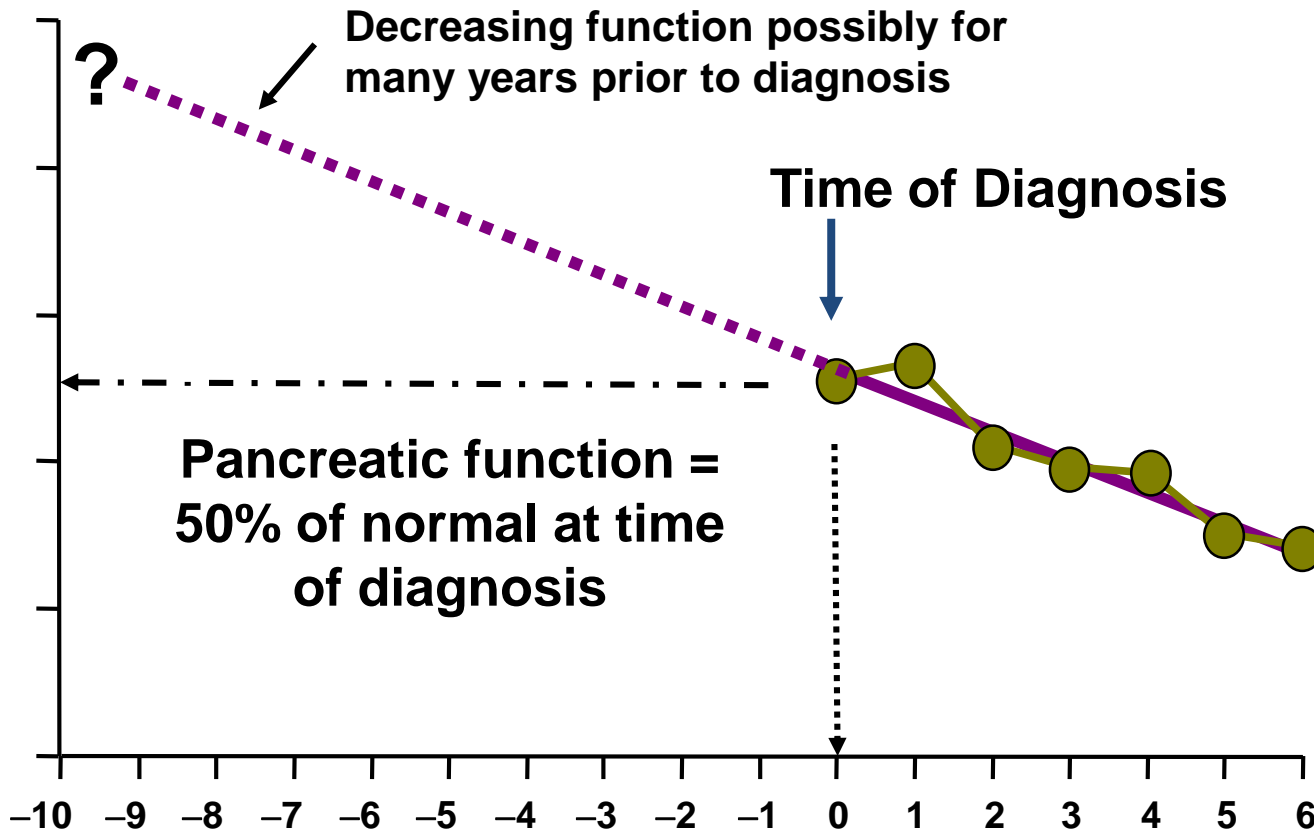- Tiny filament inserted just under the skin samples glucose levels every 5 minutes

So many drugs…
Can't I just take whatever is cheapest?

- In general, treatment has to be tailored to fit you
- Safety
- Hypoglycemia
- Weight gain
- Effectiveness: ~1% reduction in A1c for each agent
- Blood sugar patterns
- Durability
- Cost

But it worked for me before!
Declining Pancreas Function in T2DM

?

Decreasing function possibly for many years prior to diagnosis

Time of Diagnosis

Pancreatic function = 50% of normal at time of diagnosis

−10 −9 −8 −7 −6 −5 −4 −3 −2 −1 0 1 2 3 4 5 6

HOMA = homeostasis model assessment

Adapted from Holman RR. *Diabetes Res Clin Pract*. 1998;40(suppl):S21-S25.
UKPDS Group. *Diabetes*. 1995;44:1249-1258. Reproduced with permission from Elsevier.

Long-term safety

- The FDA requires all new diabetes drugs to demonstrate long-term safety to the heart
  - Requires very large trials ~10,000 patients
  - Patients usually have known vascular disease
  - Typically 3-5 years

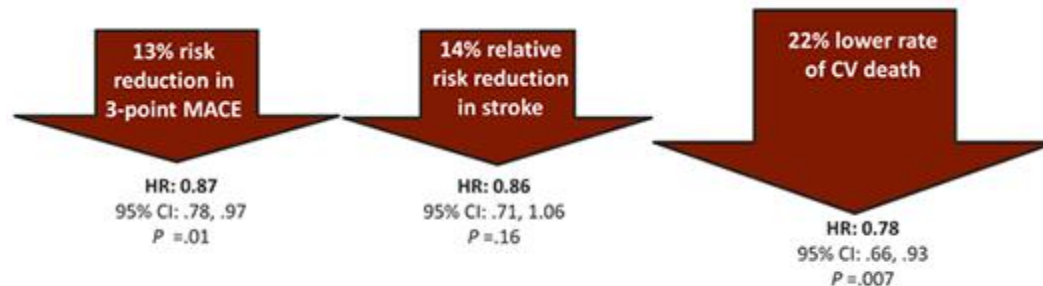# The first diabetes drug to demonstrate reduced cardiac events

ORIGINAL ARTICLE

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

"…significantly lower rates of death from cardiovascular causes (3.7%, vs. 5.9% in the placebo group; 38% relative risk reduction), hospitalization for heart failure (2.7% and 4.1%, respectively; 35% relative risk reduction), and death from any cause (5.7% and 8.3%, respectively; 32% relative risk reduction)."

ORIGINAL ARTICLE

Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes

Steven P. Marso, M.D., Gilbert H. Daniels, M.D., Kirstine Brown-Frandsen, M.D., Peter Kristensen, M.D., E.M.B.A., Johannes F.E. Mann, M.D., Michael A. Nauck, M.D., Steven E. Nissen, M.D., Stuart Pocock, Ph.D., Neil R. Poulter, F.Med.Sci., Lasse S. Ravn, M.D., Ph.D., William M. Steinberg, M.D., Mette Stockner, M.D., Bernard Zinman, M.D., Richard M. Bergenstal, M.D., and John B. Buse, M.D., Ph.D., for the LEADER Steering Committee on behalf of the LEADER Trial Investigators*

13% risk reduction in 3-point MACE	14% relative risk reduction in stroke	22% lower rate of CV death
HR: 0.87 95% CI: .78, .97 P =.01	HR: 0.86 95% CI: .71, 1.06 P =.16	HR: 0.78 95% CI: .66, .93 P =.007

- 9340 adults with type 2 diabetes and high risk for heart and vascular disease
- Duration: 3.8 years

Does this mean I can't eat the pumpkin pie?

- If you *must* splurge
  - Portion control
  - Substitute one carb for another
  - Take an extra walk after the meal
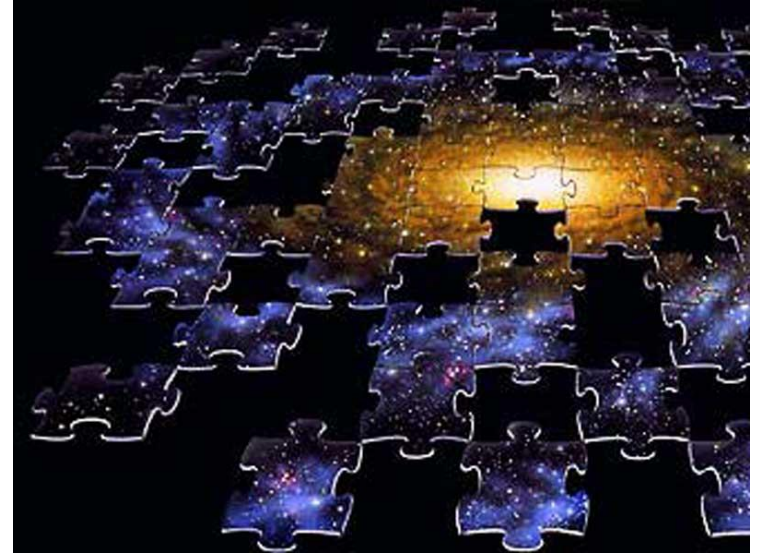 - Learn to count carbs and adjust your medication

Should I take this supplement?

- Supplements are not regulated by the FDA
  - Not required to vigorously study safety or effectiveness
  - Contents may not be consistent with the label
- "Natural" does not necessarily mean "safe"
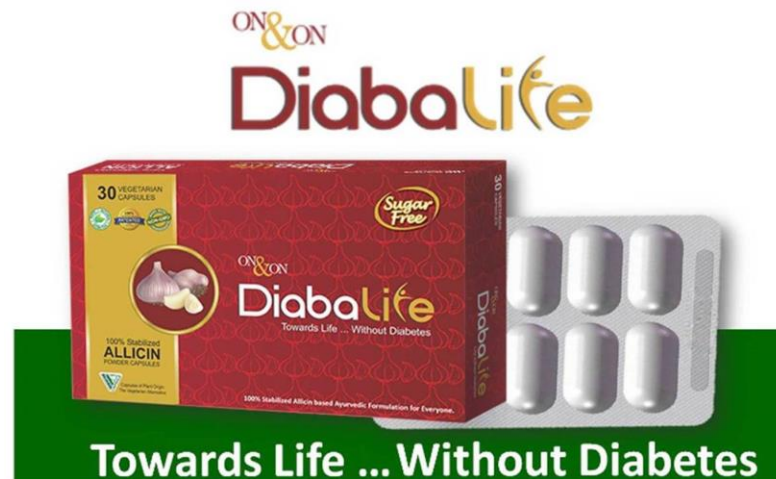
Global Treatment of T2DM

- **Glucose control is only one of the pieces of the treatment puzzle for diabetes mellitus**
- **Aggressive therapy is necessary for**
  - **Blood pressure**
  - **Cholesterol**
- **Aggressive multiple risk factor interventions prevent complications**

Gaede et al. N Engl J Med. 2008;358:580-91.

KEY TESTS/EXAMS

Hemoglobin A1c	Quarterly if treatment change
	At least twice/yr if stable
Dilated eye exam	Yearly
Foot exam	Yearly (at risk often)
Lipid profile	1-2 years
Urine Microalbumin	Yearly
Blood pressure	Each visit
Weight	Each visit
GYN/family planning	Each visit

When to see a specialist

- Uncontrolled despite working closely with your doctor

- Special devices (insulin pumps and continuous glucose monitors)

- Severe hypoglycemia

Don't treat your heart to diabetes

Conclusions

- Diabetes places a substantial clinical and economic burden on the U.S.

- Lifestyle changes, as part of a multi-pronged approach, can prevent or delay DM and prevent complications

- Glucose lowering therapy should be individualized and goal-directed