

Pumps, Sensors & Meds, Oh My! New Treatments for Type 1 & Type 2 Diabetes



Community Medical School
November 13, 2018



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In Memory



Angel Elizabeth Dudley
June 21, 1961 - October 16, 2018

Outline for Tonight's Talk

- Review the prevalence of diabetes in the U.S. and around the world
- Discuss the cost of the current diabetes epidemic
- Investigate new treatments and technologies for patients with diabetes
- How can you take better care of your diabetes?

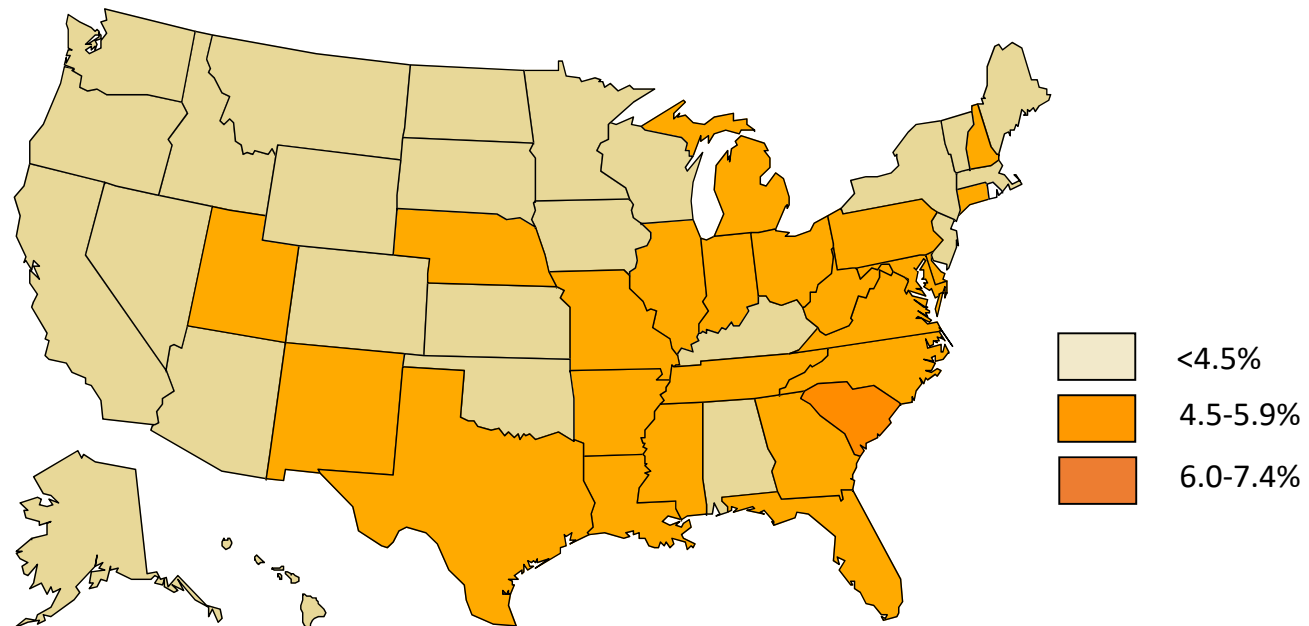
The Current State of Diabetes



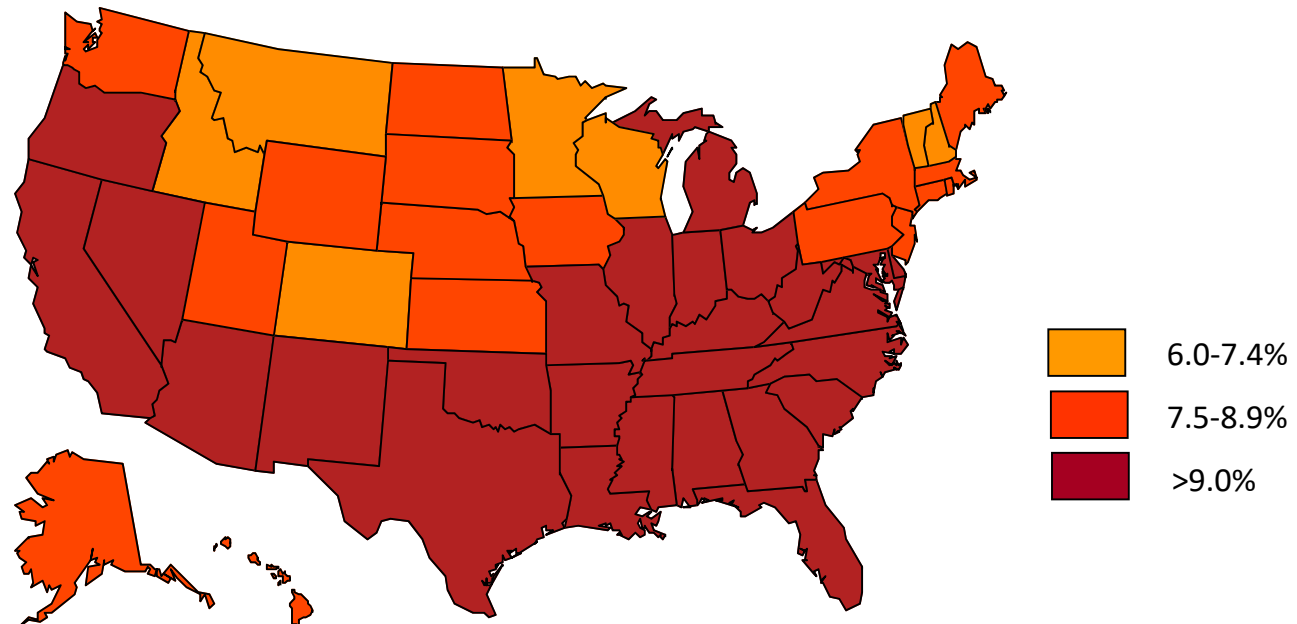
Prevalence of Diabetes in the U.S.-2017 Data

- 30.2 million (12.2% of the adult population) in the U.S. have diabetes
- Another 7.2 million are undiagnosed
- 34% of adults in the U.S. have prediabetes
- 25% of adults in the U.S. over the age of 65 have diabetes and 48% have prediabetes

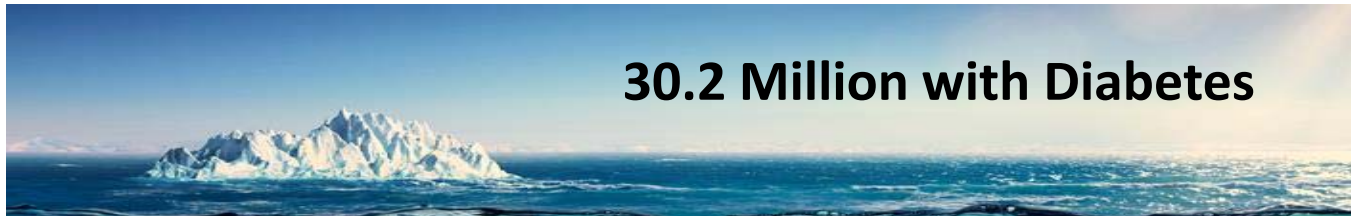
Prevalence of Diabetes in U.S. in 1994



Prevalence of Diabetes in U.S. in 2015

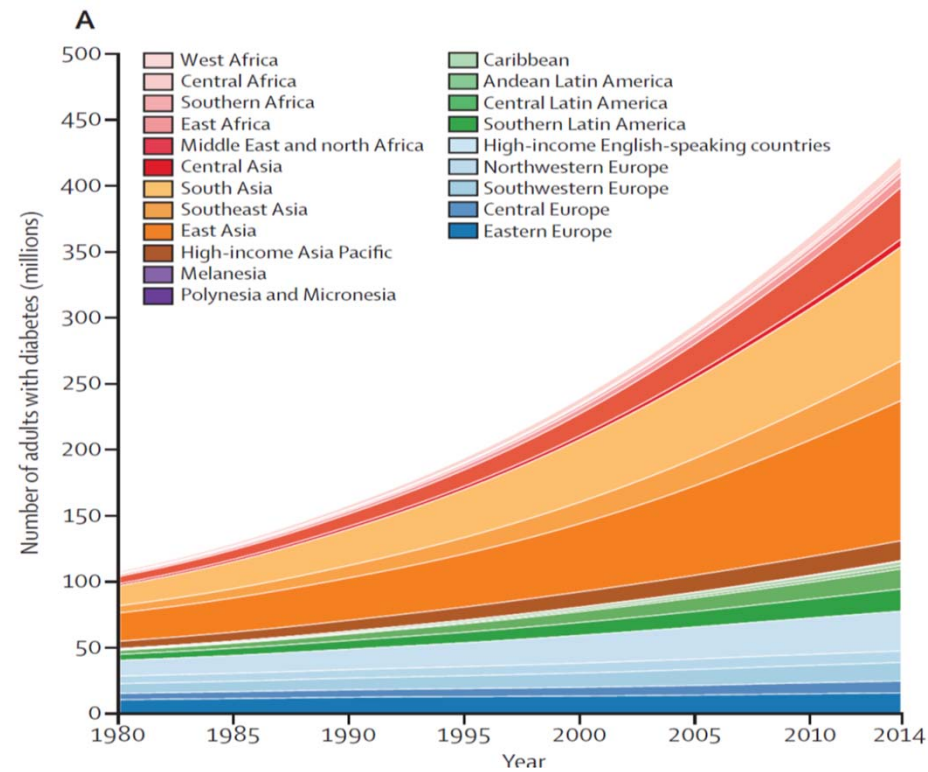


The Challenge



30.2 Million with Diabetes

Worldwide Prevalence of Diabetes



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NCD Risk Factor Collaboration. *Lancet* 2016;387:1513–1530. 9

Economic Cost of Diabetes in the U.S.

Diabetes Care Volume 41, May 2018

917



Economic Costs of Diabetes in the U.S. in 2017

American Diabetes Association

Diabetes Care 2018;41:917-928 | <https://doi.org/10.2337/dci18-0007>

THE COSTS OF DIABETES



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American Diabetes Association. *Diabetes Care*, 2018;41:917-928

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Economic Cost of Diabetes in the U.S.

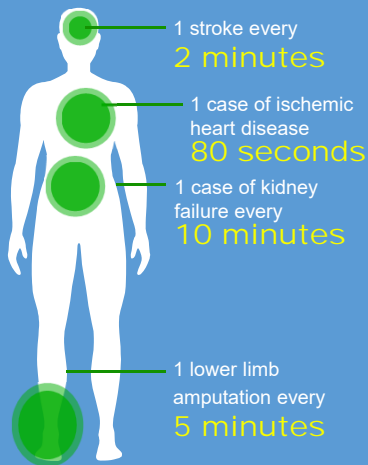
- \$327 billion were spent in 2017 on patients with diabetes
 - \$237 billion in direct medical costs and \$ 90 billion in reduced productivity
- Direct medical costs represent a 26% increase since 2012
- More than 300 million work days are lost to the economy due to diabetes
- Diabetes resulted in 277,000 premature deaths in 2017

Economic Cost of Diabetes in the U.S.

- Medications directly used to treat diabetes = \$31 billion
- \$15 billion of which is for insulin
 - Increase of 45% over the last 5 year
- 1 in every 4 health care dollars spent was for the care of people with the diagnosis of diabetes
- 1 of every 7 health care dollars can be attributed directly to the care of diabetes

DEATHS DUE TO DIABETES COMPLICATIONS CONTINUE AT ALARMING RATE

IN THE US, DIABETES^a
CONTRIBUTES TO, ON AVERAGE¹:



DIABETES CONTRIBUTES TO THE DEATH OF
1 PERSON EVERY 2 MINUTES IN THE
UNITED STATES



That's more than
768 people a day

OPIOID OVERDOSE CRISIS
IN THE UNITED STATES, IN 2016, 1 PERSON DIES
EVERY 52 MINS. FROM OPIOID OVERDOSE³

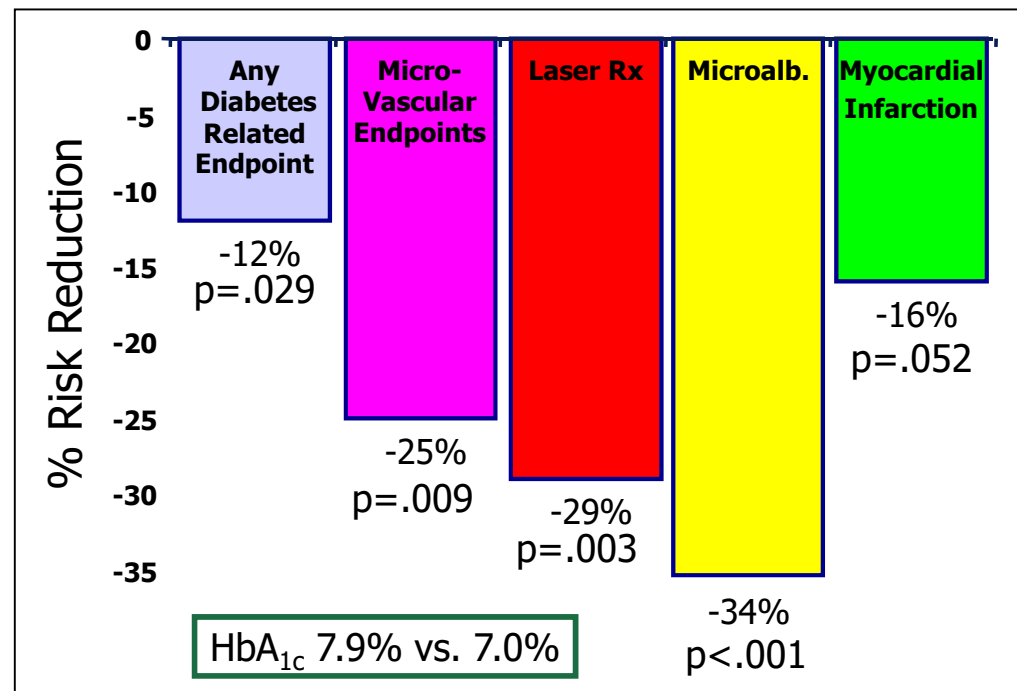


That's more than
46 people a day

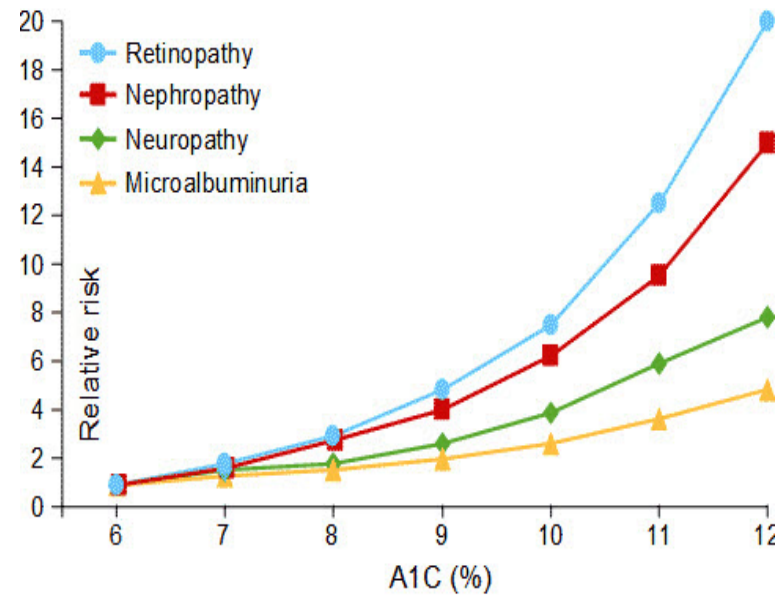
^aType 1 or Type 2 diabetes.

1. CDC. *National Diabetes Statistics Report 2017*. www.cdc.gov/statistics. 2. . IDF Diabetes Atlas, 8th edition. 2017. International Diabetes Foundation ; <https://www.cdc.gov/drugoverdose/data/overdose.html>

How do we prevent complications of diabetes?



Preventing Complications

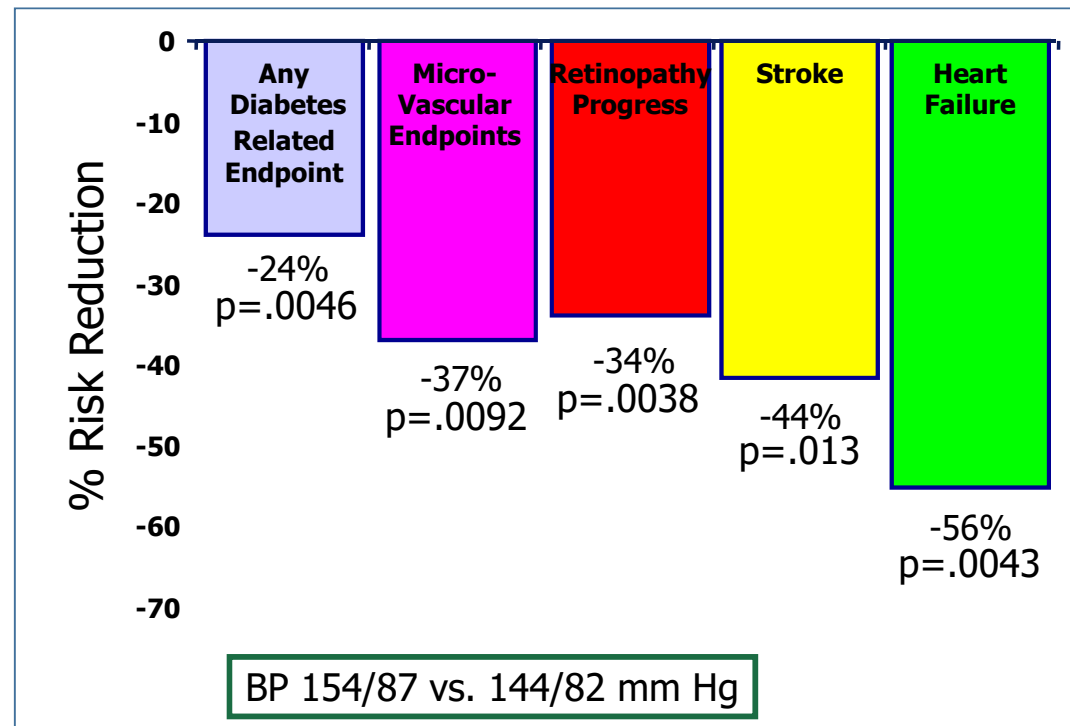


Patients with type 1 diabetes (n=1,441)
Adapted from DCCT, Diabetes 1995;44:968-43.



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How do we prevent complications of diabetes?

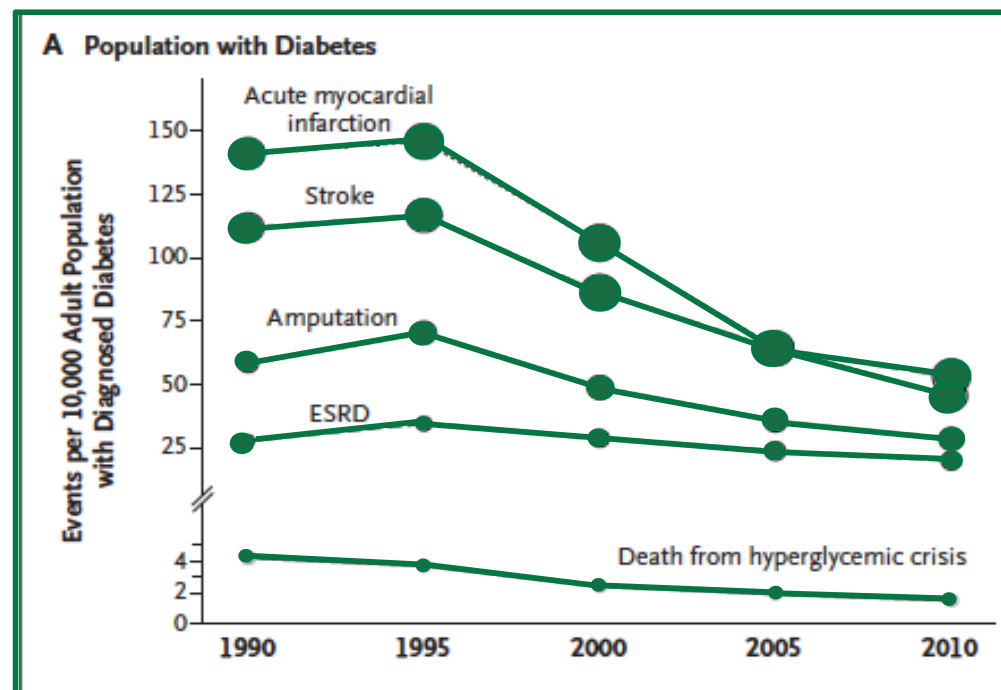


Preventing Complications



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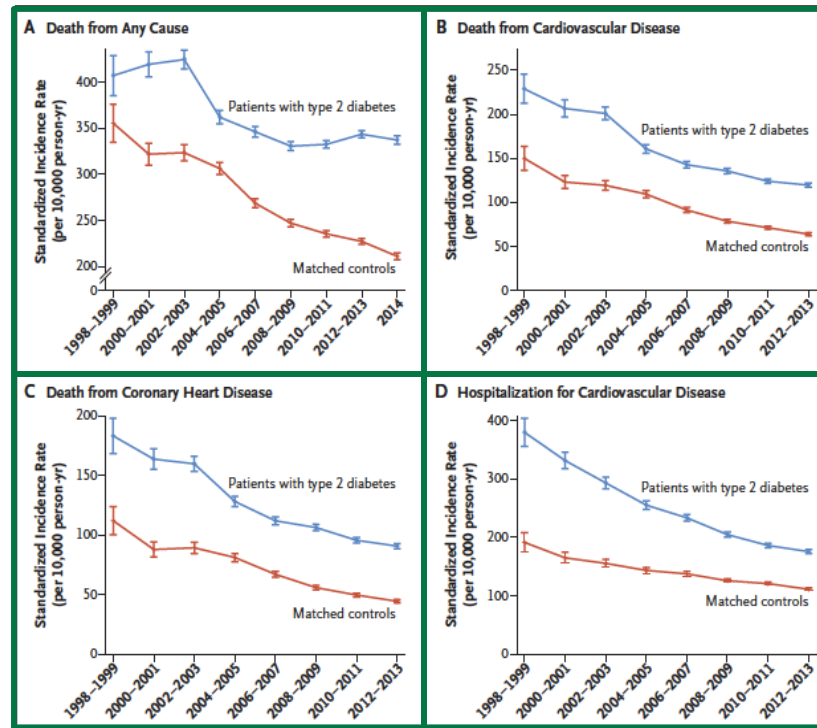
How are we doing?



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Gregg EW et al. *N Engl J Med* 2014;370:1514-1523 18

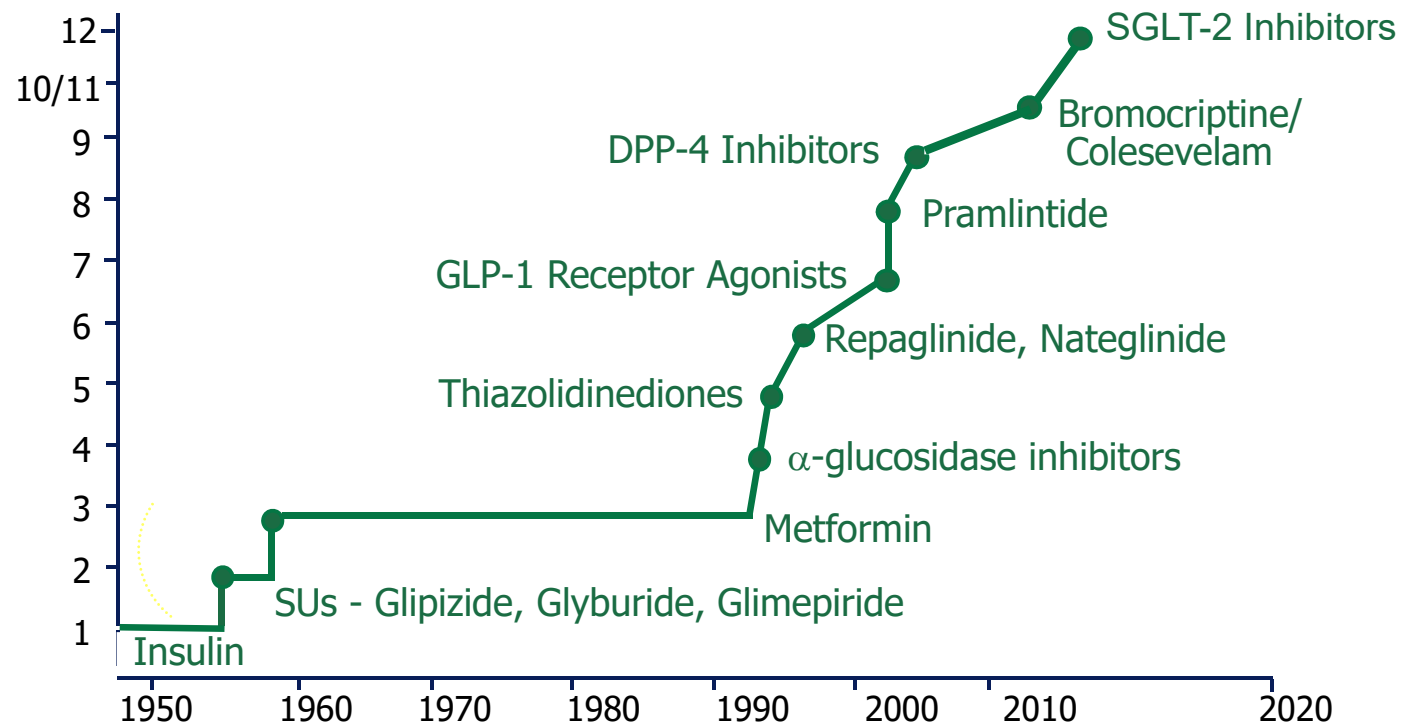
How are we doing?



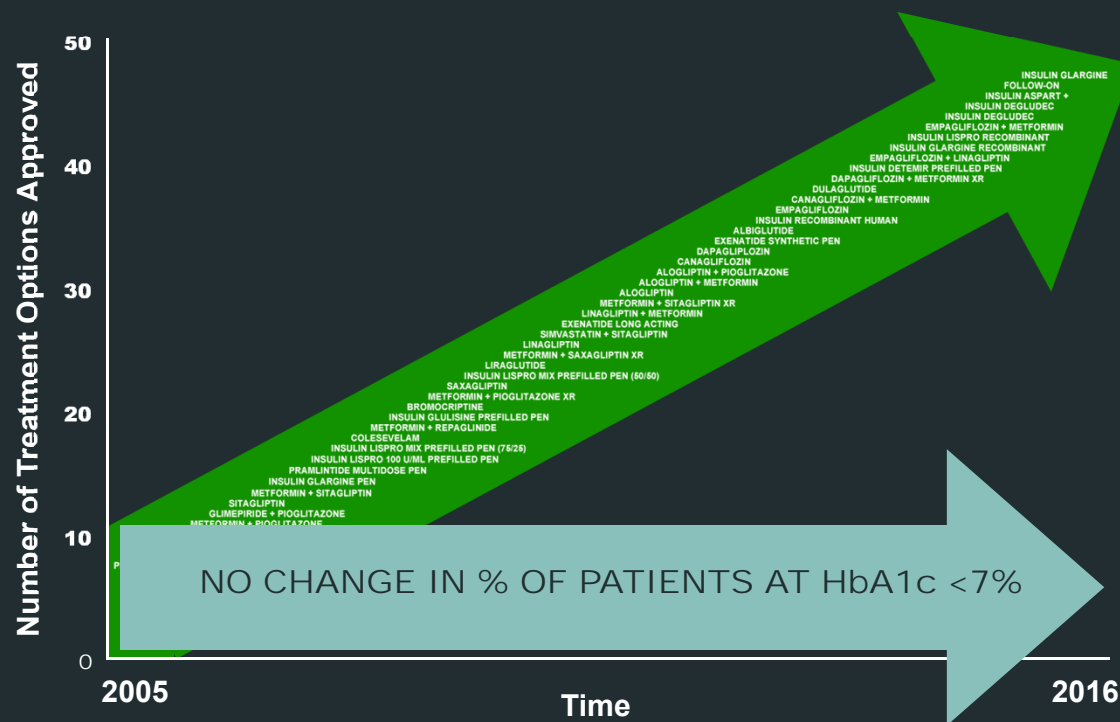
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Rawshani A et al. *N Engl J Med* 2017;376:1407-1418 19

Drug Development for Diabetes 1950-Present



MORE THAN 40 T2DM TREATMENT OPTIONS HAVE BEEN APPROVED SINCE 2005



Type 2 diabetes U.S. drug approvals: 2005-2015, Food and Drug Administration website.
<https://www.accessdata.fda.gov/scripts/cder/drugsatfda/>.



A New(ish) Approach to Treatment of Type 2 diabetes



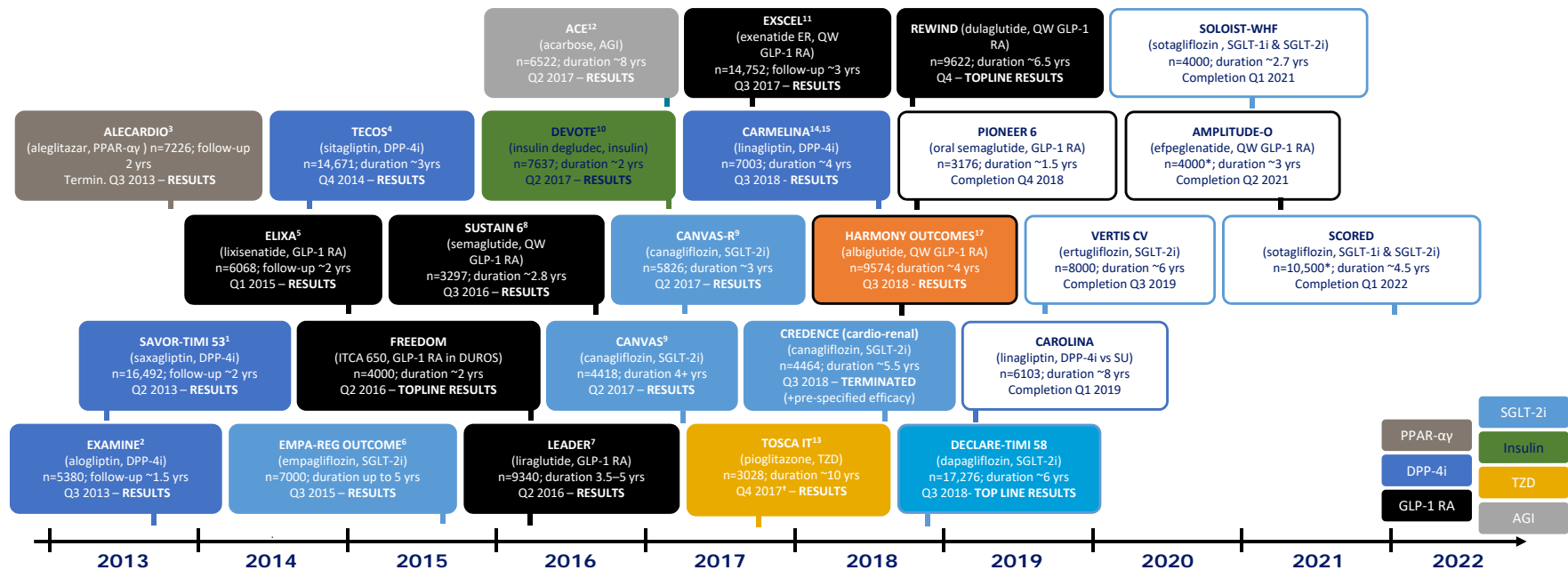
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Cardiovascular Safety of Diabetes Medications



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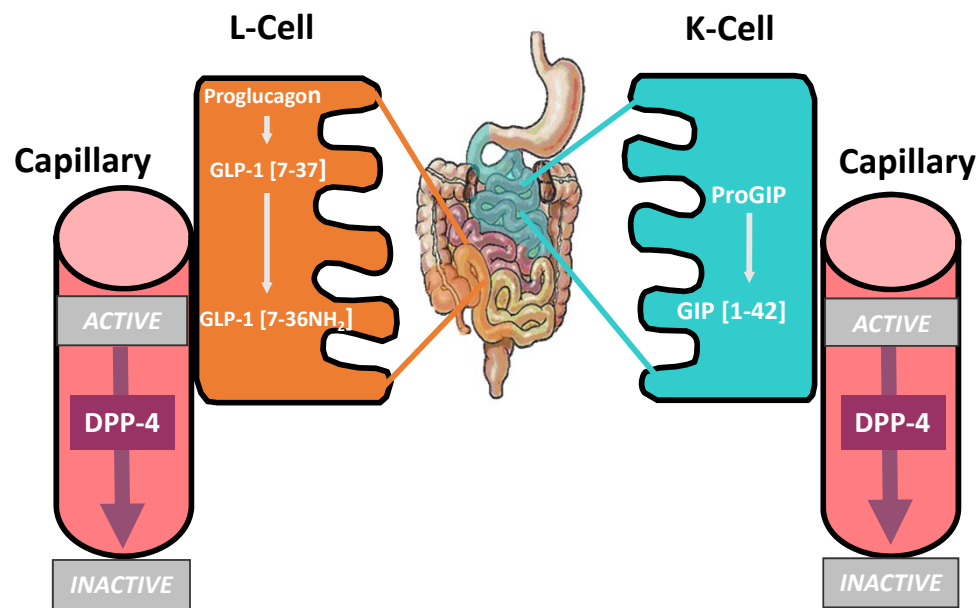
Contemporary Cardiovascular Outcome Trials (CVOT) in Diabetes



Biology of Incretin Hormones

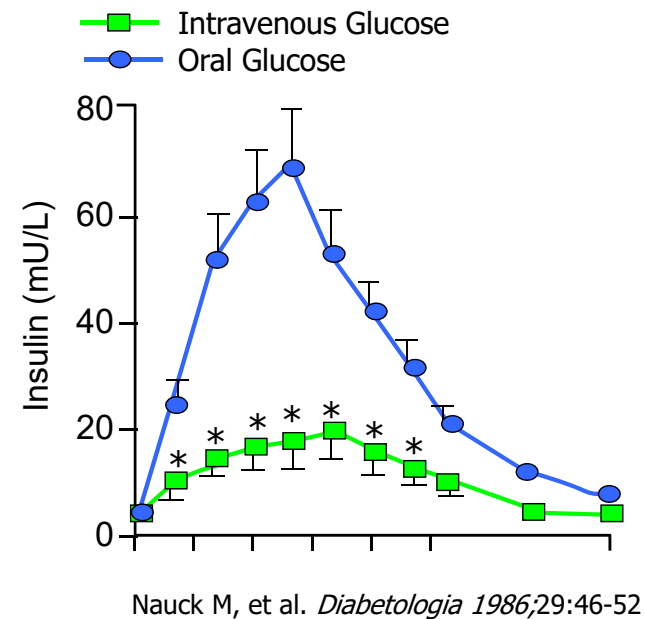
- Concept that “factors” from the intestine stimulate the endocrine pancreas is not new ¹
- The term “incretin” arrived in the 1930’s ²
- Development of the radioimmunoassay confirmed the “communication” between the intestine and endocrine pancreas

Biology of Incretin Hormones

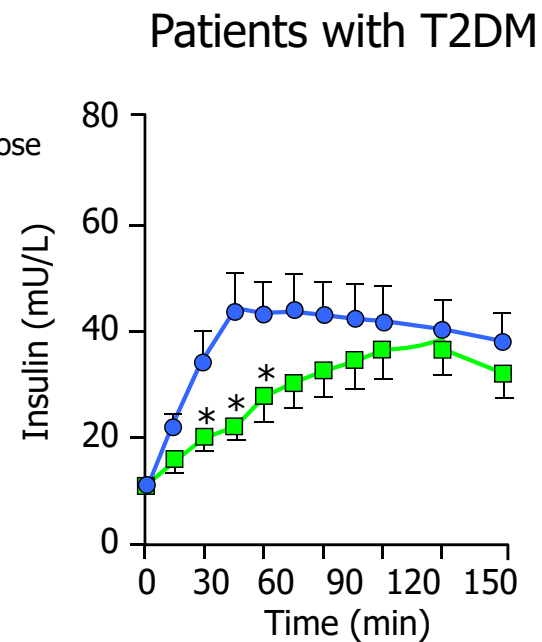
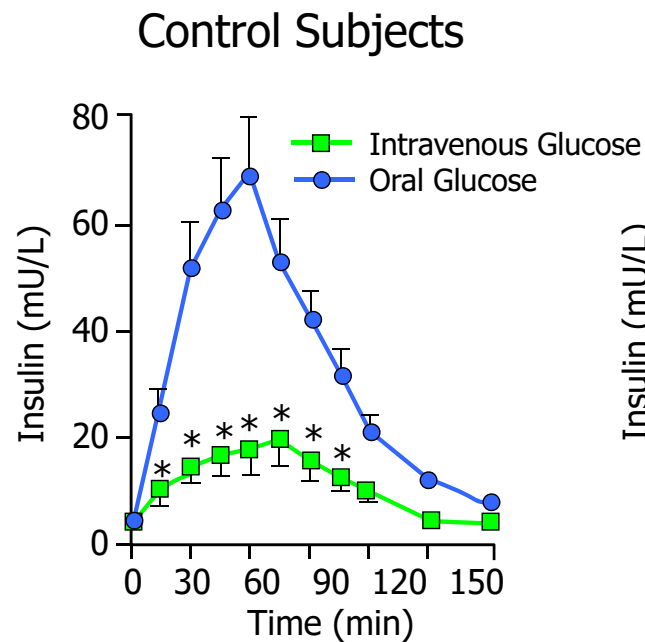


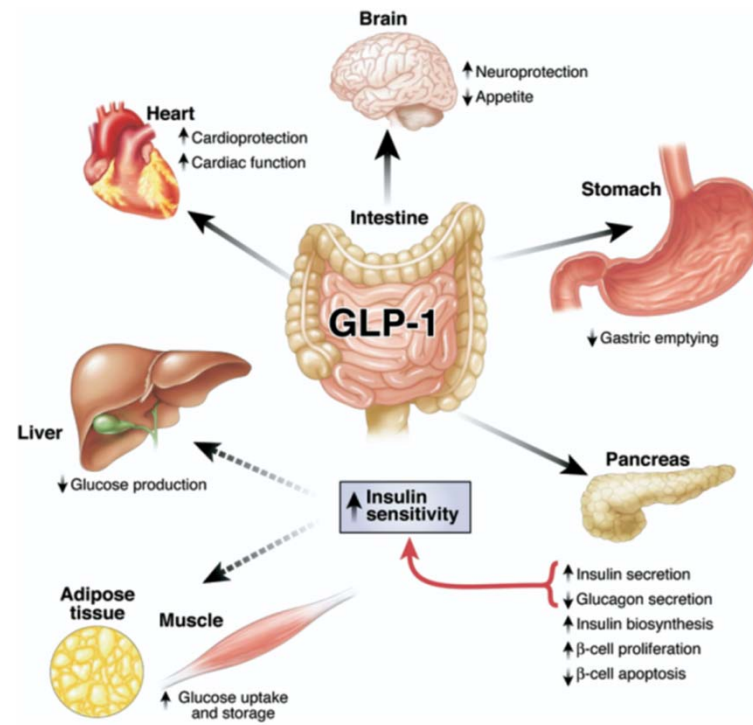
Biology of Incretin Hormones

- “Incretin effect”
- May account for 50-70% of total insulin secreted after a meal
- Incretins are hormones that enhance glucose-stimulated insulin secretion



Reduced Incretin Effect





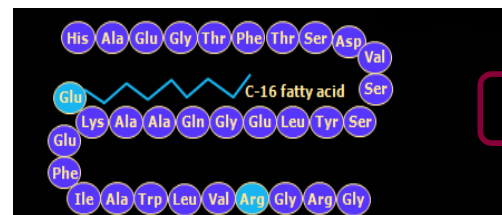
Incretin Therapies

- Glucagon-like peptide-1 receptor agonists (GLP-1 RA) and dipeptidyl peptidase-4 inhibitors (DPP-4i)
- DPP-4i block the breakdown of GLP-1 and GIP in the body
- GLP-1 RA mimic the action of human GLP-1, but are not easily broken down by natural DPP-4 found in the gut.

Structure of GLP-1 Medications

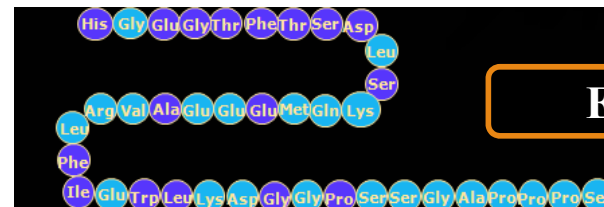


Native human GLP-1



Liraglutide

97% amino acid
homology to
human GLP-1



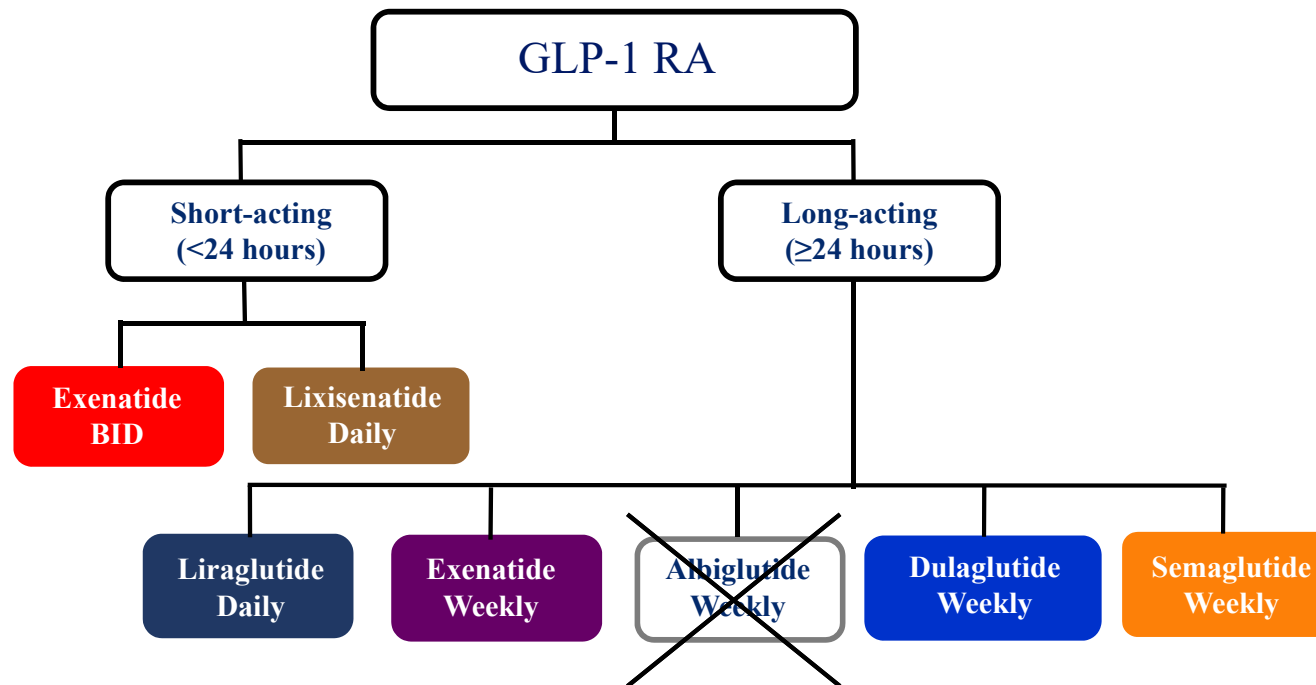
Exenatide

53% amino acid
homology to
human GLP-1



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GLP-1 Receptor Agonists



GLP-1 RA Clinical Characteristics

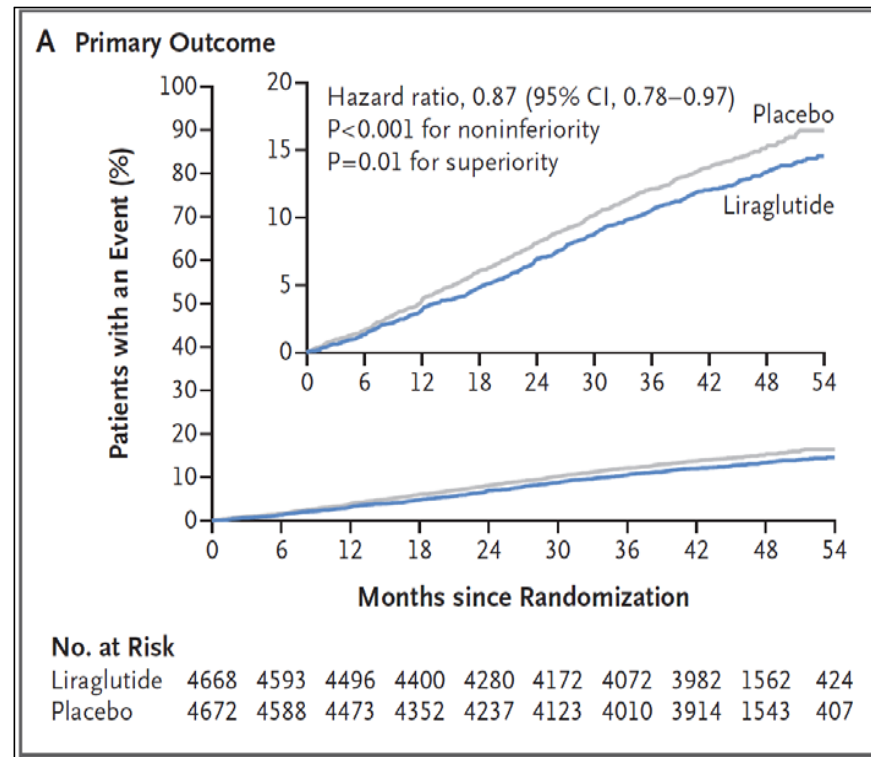
- Injectable medications (twice daily, daily, weekly)
- Lower A1c by 1-1.5%
- Promote weight loss (3-5 kg)
- Nausea is a common side effect of this class of medication
- Low rates of hypoglycemia

LEADER Trial

- Cardiovascular effect of liraglutide in patients with T2DM
- Double-blind, randomized control trial of liraglutide vs. placebo
- Patients with high CV risk (CAD, CVA, PVD, CHF or CKD)
- Total of 9340 patients were randomized
- Mean follow-up was 3.8 years
- Primary **composite outcome** was comprised of CV death, nonfatal MI and nonfatal stroke



LEADER Trial

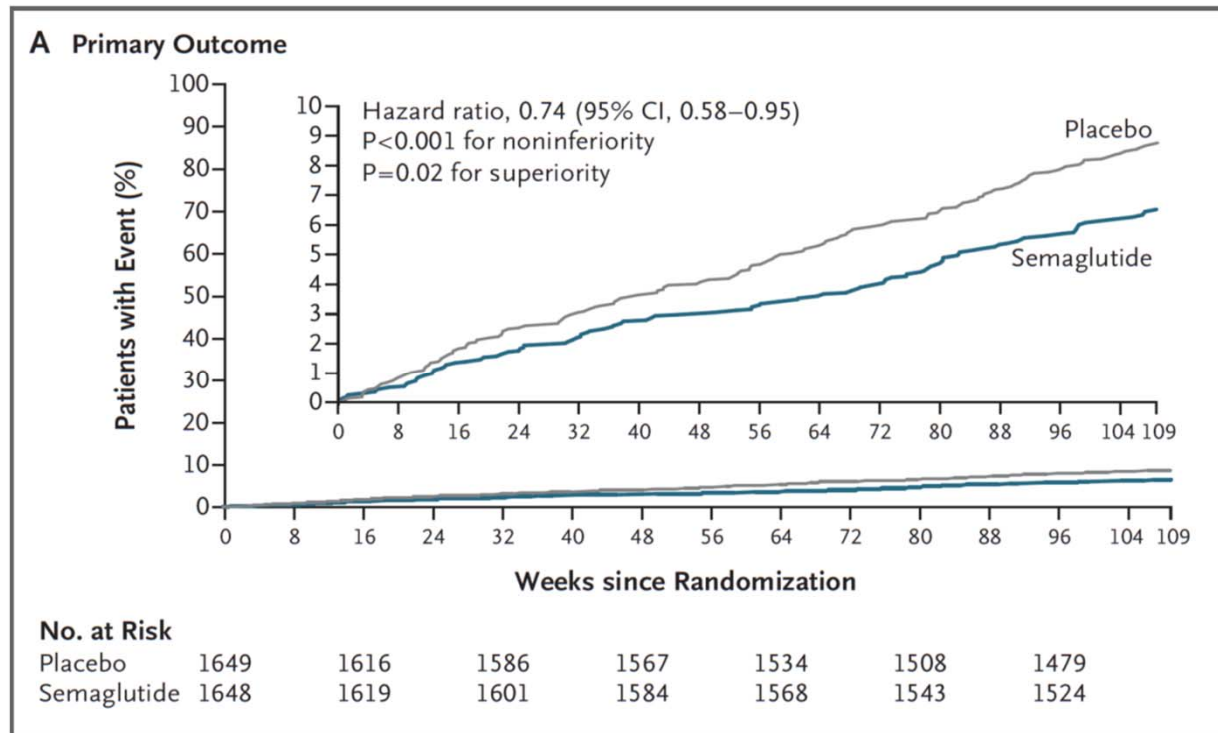


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Marso SP, et al. *NEJM*. 2016;375:311-322

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SUSTAIN-6 Trial



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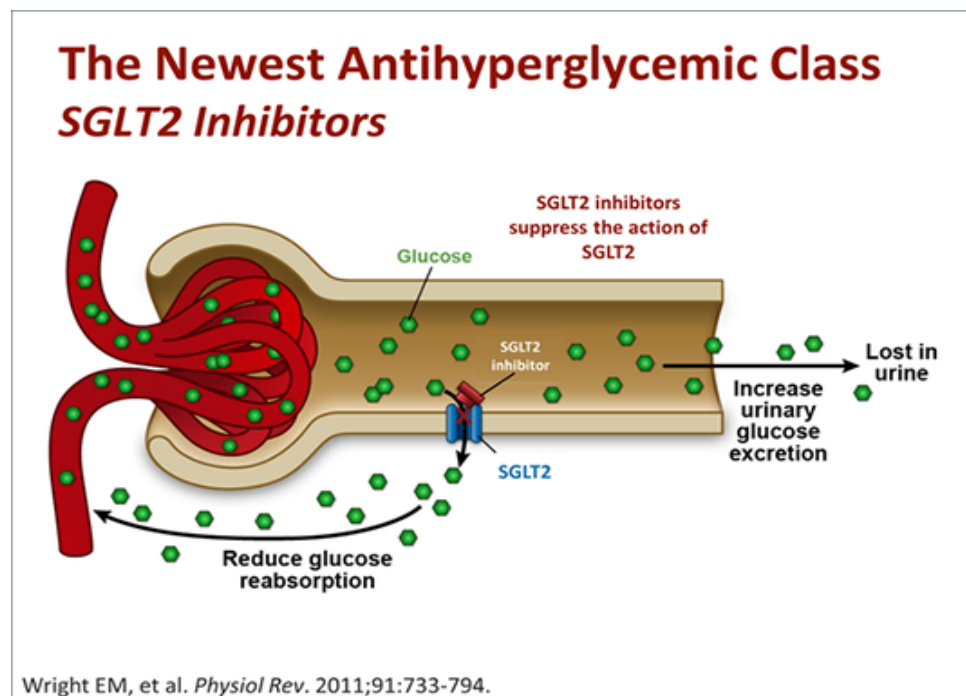
Marso SP, et al. *NEJM*. Epub September 15, 2016

37

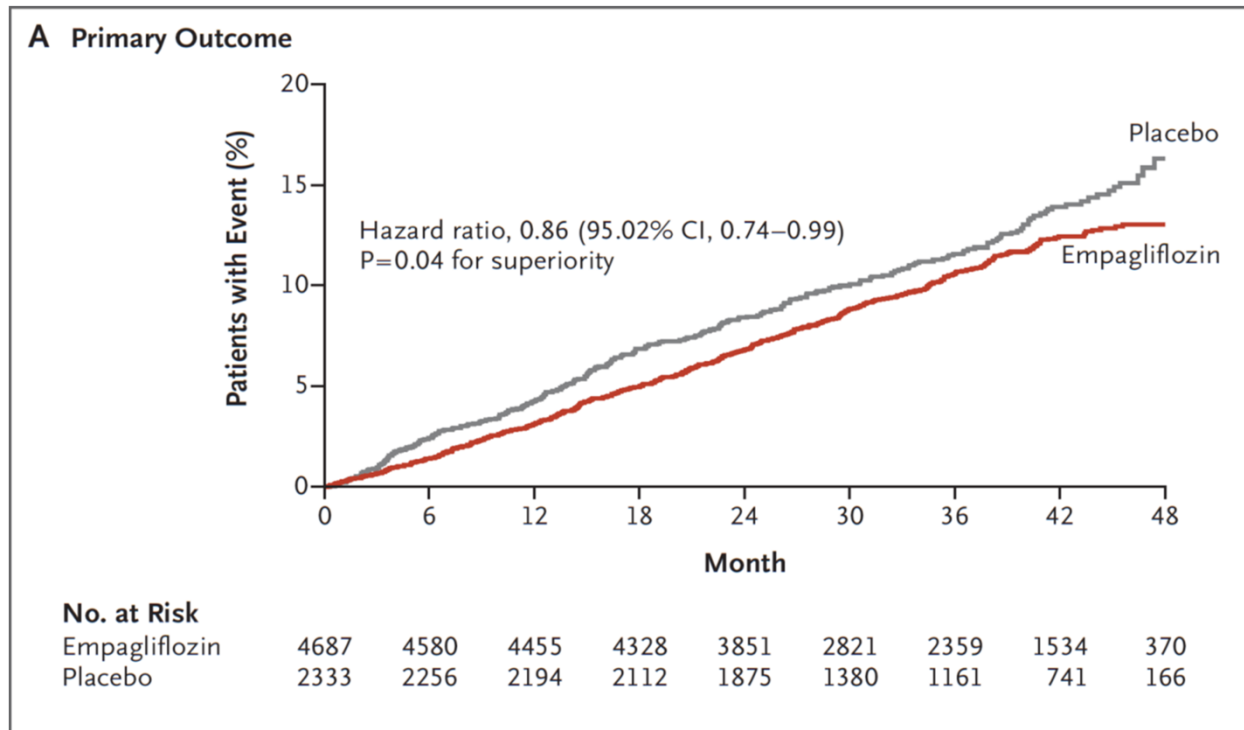
SGLT-2 Inhibitors

- Newer class of medications
- Block the reabsorption of glucose by the kidney
- Low risk of hypoglycemia
- Weight loss
- Increase risk of infections and dehydration from increased urine output

How do SGLT-2 Inhibitors Work?



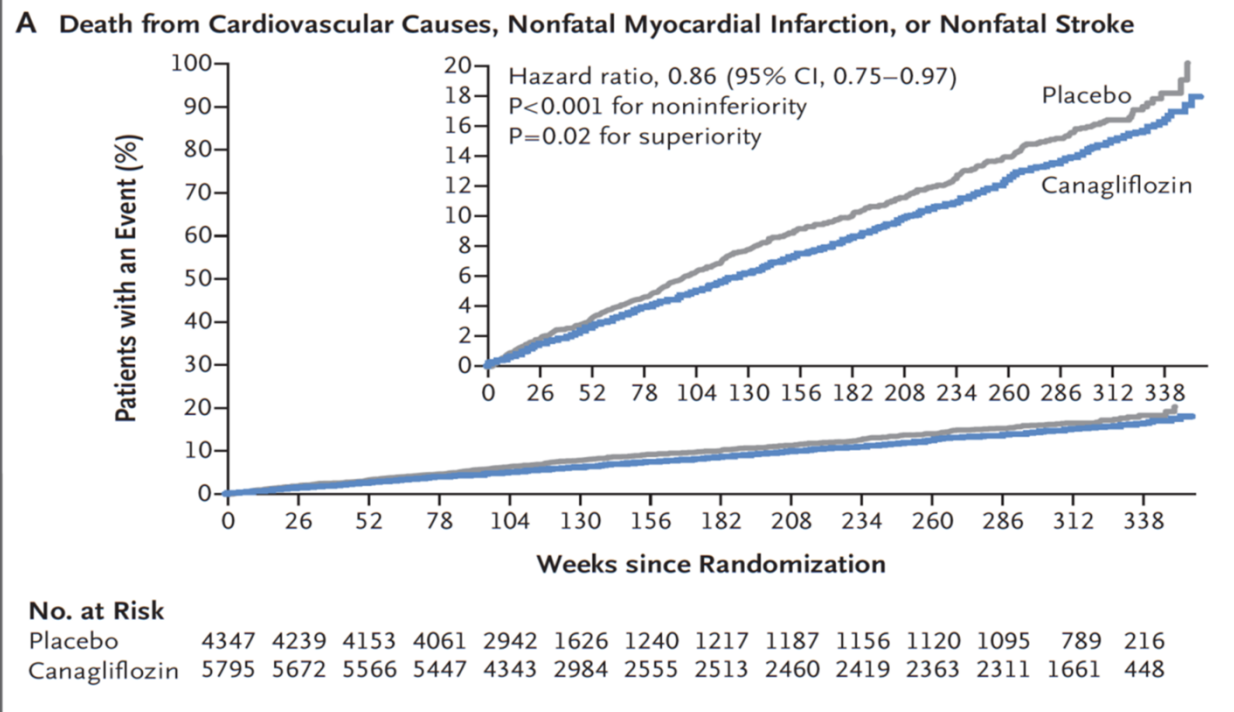
EMPA-REG OUTCOM Trial



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Zinman B, et al. NEJM. 2015 40

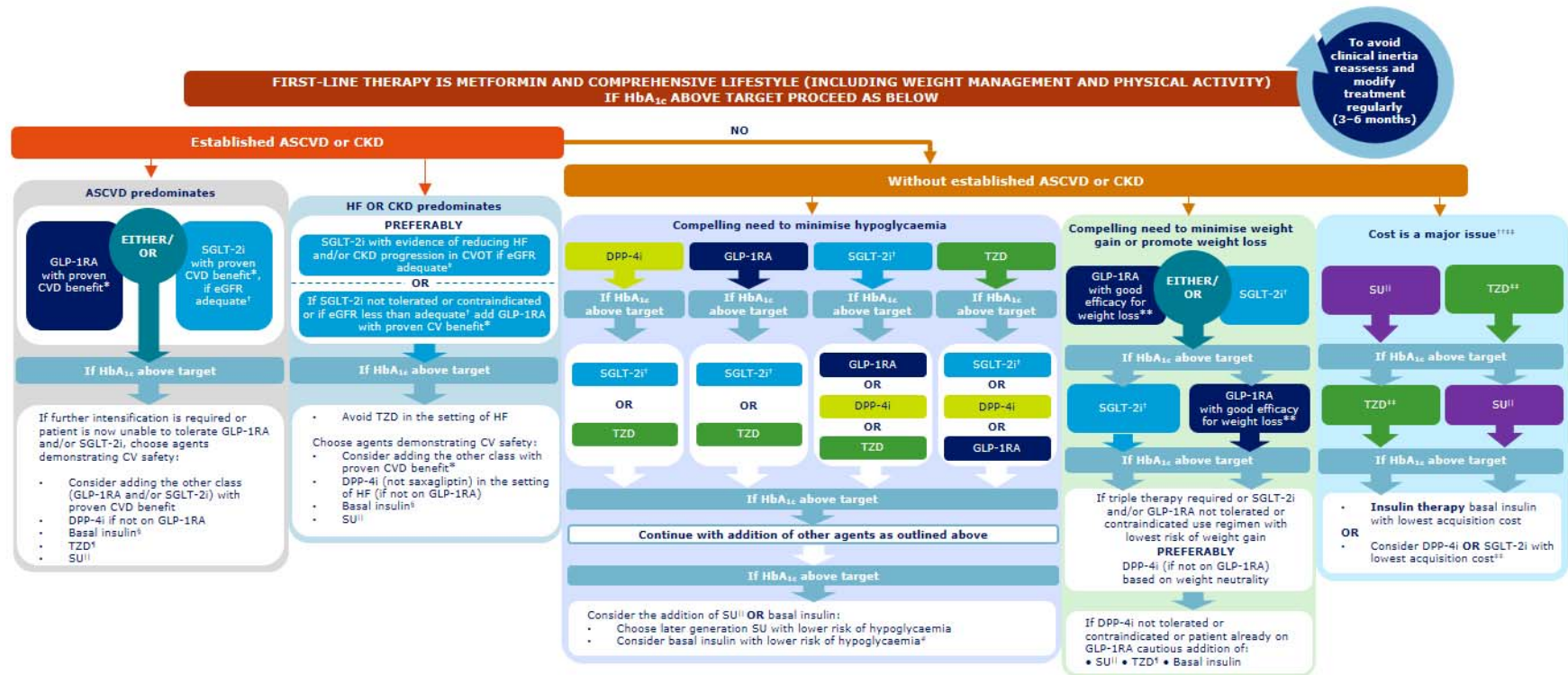
CANVAS PROGRAM



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Neal B, et al. NEJM. 2017;377:644 41

2018 ADA/EASD Consensus Guidelines



New Technologies for the Treatment of Diabetes



New Technologies for the Treatment of Diabetes



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DEXCOM G6 Continuous Glucose Monitor® (CGM)



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DEXCOM G6 Continuous Glucose Monitor® (CGM)



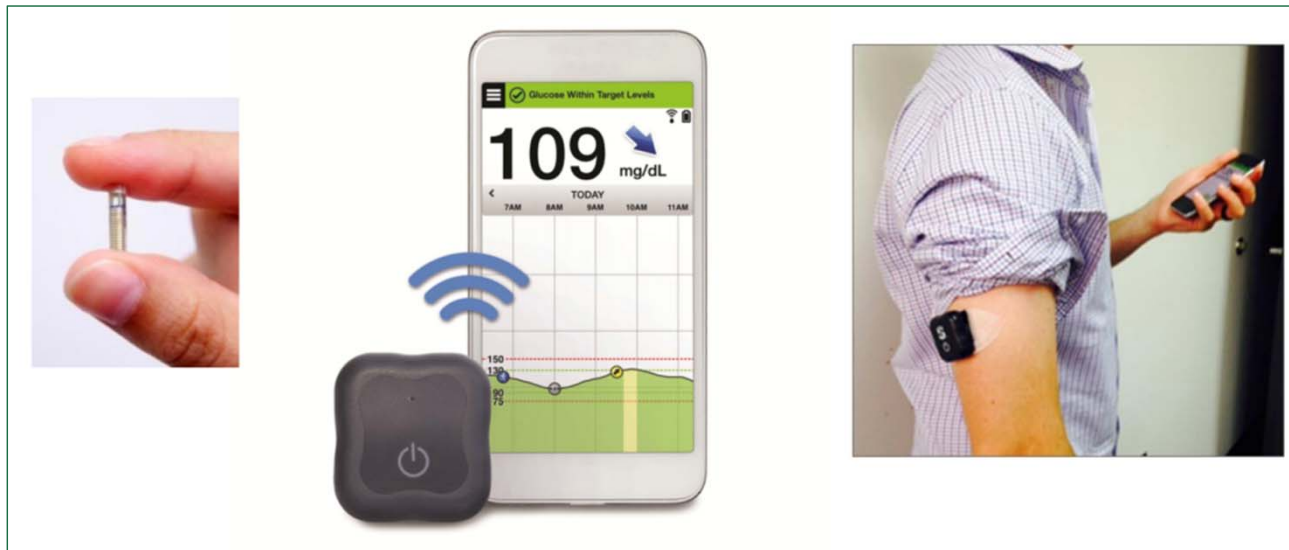
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FreeStyle Libre Flash CGM®



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Eversense®



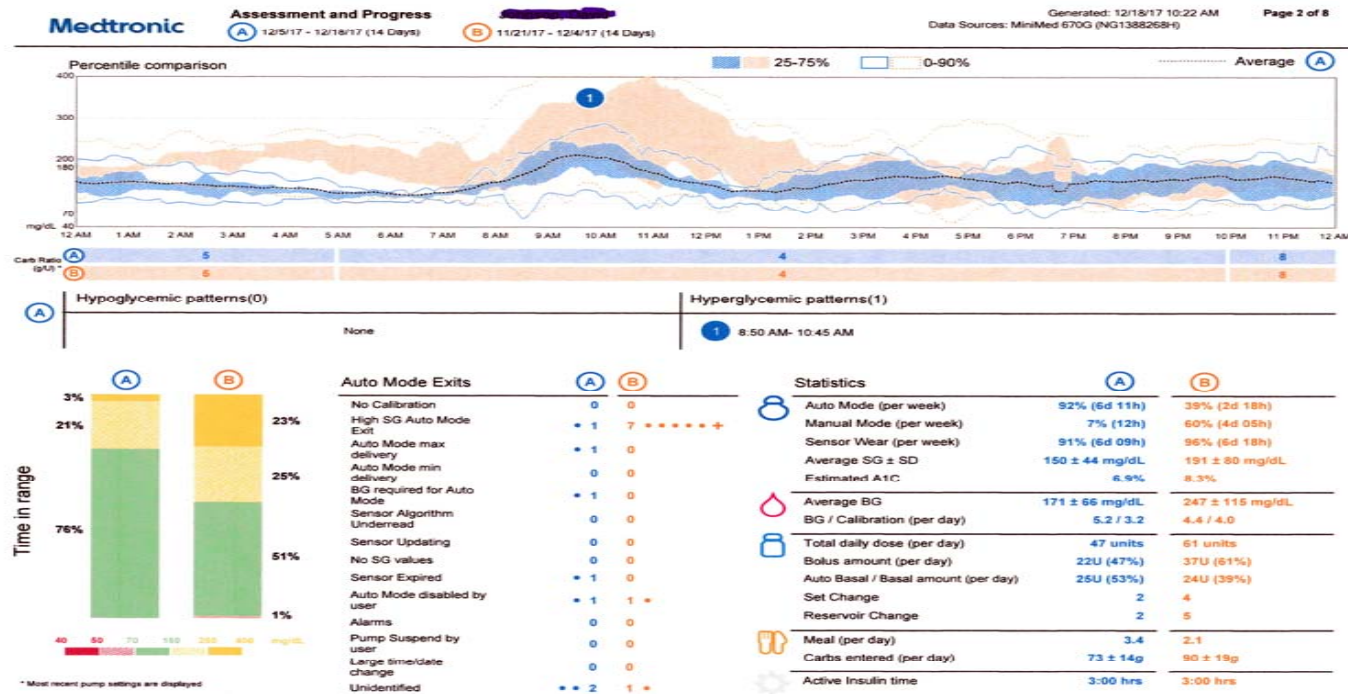
New Technologies for the Treatment of Diabetes



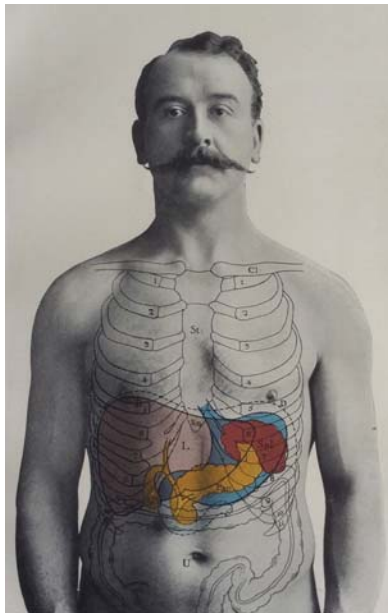
Medtronic 670G® Closed Loop Insulin Pump



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Artificial Pancreas



What Can You Do to Help Reduce Your Risk



What can you do help?

- See your doctor regularly (Every 3-6 months)
- See your dentist regularly (Every 3-6 months)
- See your eye provider for **dilated** eye exam (Annually)
- Exercise on a regular basis and lose weight if you need to (5-7%)
- Work on your diet (CDE or CDE/RD or RD)

What can you do help?

- Obtain urine test to look for early sings of kidney damage (microalbuminuria)
- Check your blood pressure on a regular basis using a home blood pressure monitor
- Get your cholesterol level checked
- **Take your medication**
- Stay informed regarding new treatments
- Ask your provider if there are any new treatments or technologies that might benefit you

What can you do help?



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Conclusions

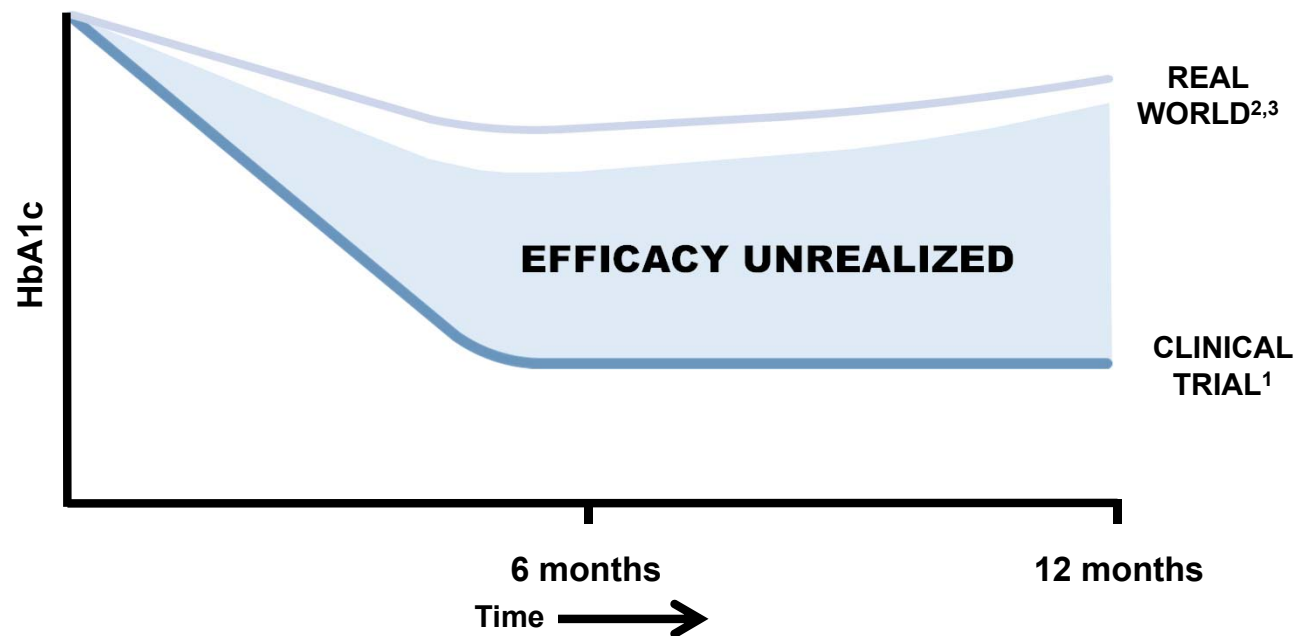
- Diabetes is a world-wide epidemic
- Significant financial and human costs
- Newer treatments are changing the everyday life of people with diabetes
- Newer treatments are providing additional benefits than lowering blood sugars
- Stay up to date and ask your provider regarding new treatments or technologies
- Take care of yourself!



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Improvements in clinical trials is not translating to the real world



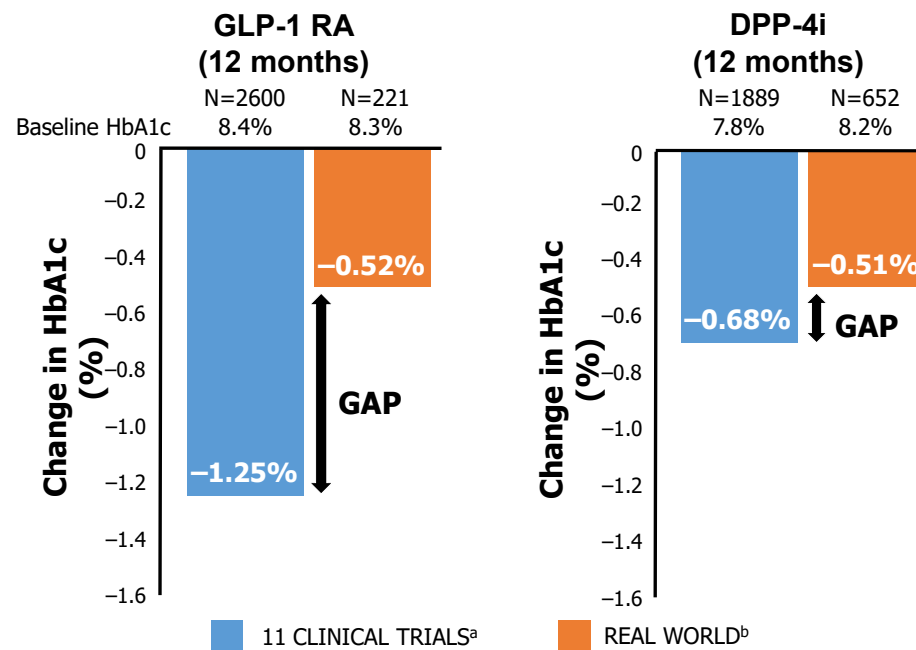
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1. Garber A et al. *Lancet*. 2009;373:473-481.

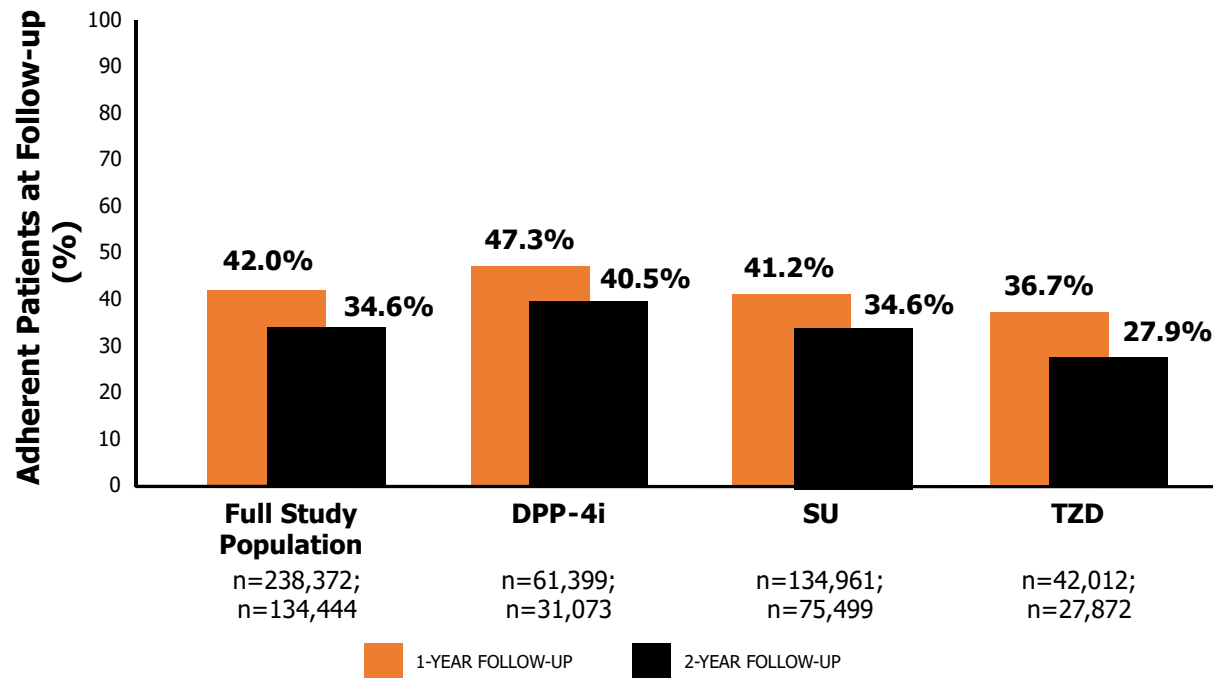
2. Singhal M et al. ISPOR Annual International Meeting. May 16-20, 2015. Poster PDB10.

3. Why are reductions in HbA1c greater in clinical trials compared to the real-world? Identifying the contribution of poor adherence. 76th ADA Scientific Sessions. June 10-14, 2016.

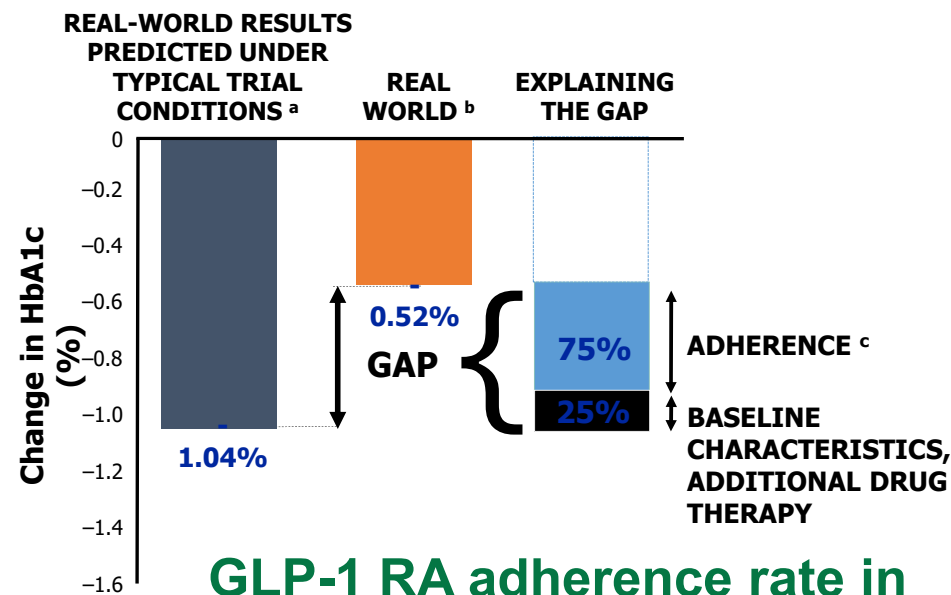
The efficacy gap between clinical trial and real-world results



Adherence rates for oral agents are less than 50%



Poor adherence is the key contributor to the efficacy gap



RCT, randomized clinical trial.

^a Linear regression model fitted to estimate the change in HbA1c 1 year after initiating GLP-1 RA or DPP-4i based on baseline and treatment characteristics. ^b Optum/Humedica SmartFile database (2007-2014) was used (GLP-1 RA 221 patients; DPP-4i 652 patients). Change in HbA1c measured from drug initiation to 365±90 days later. ^c Medical adherence classified as poorly adherent if percentage of days covered (PDC) <80%. Carls GS et al. 76th ADA Scientific Sessions. June 10–14, 2016. New Orleans, LA. Poster 117-LB.