

2-6-2014

Gastric By-Pass and Remission of Type II Diabetes in Obese Adults

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Gastric By-Pass and Remission of Type II DM in Obese Adults

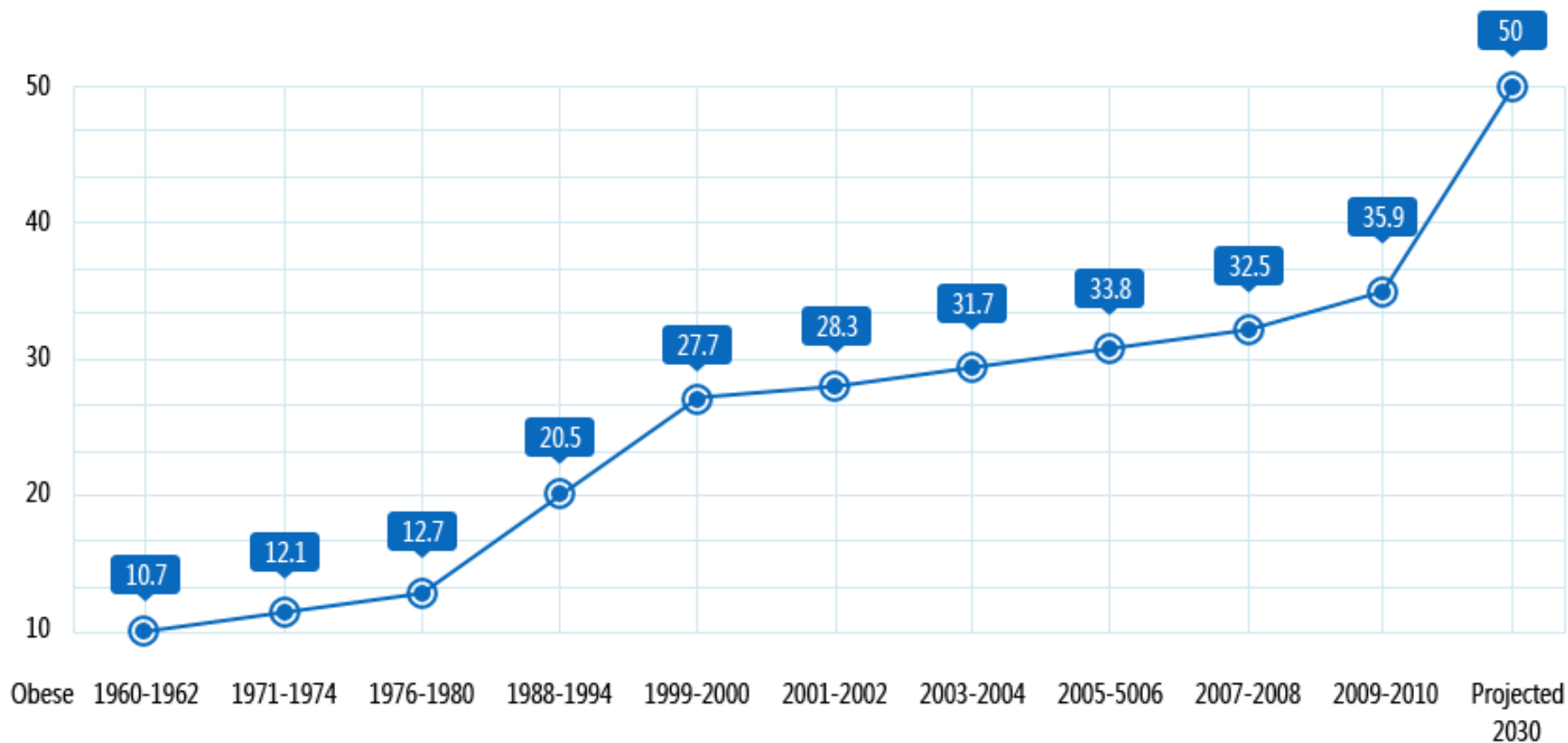
Kettering College
and Medical Center
February 2014



America....We Have A Problem...



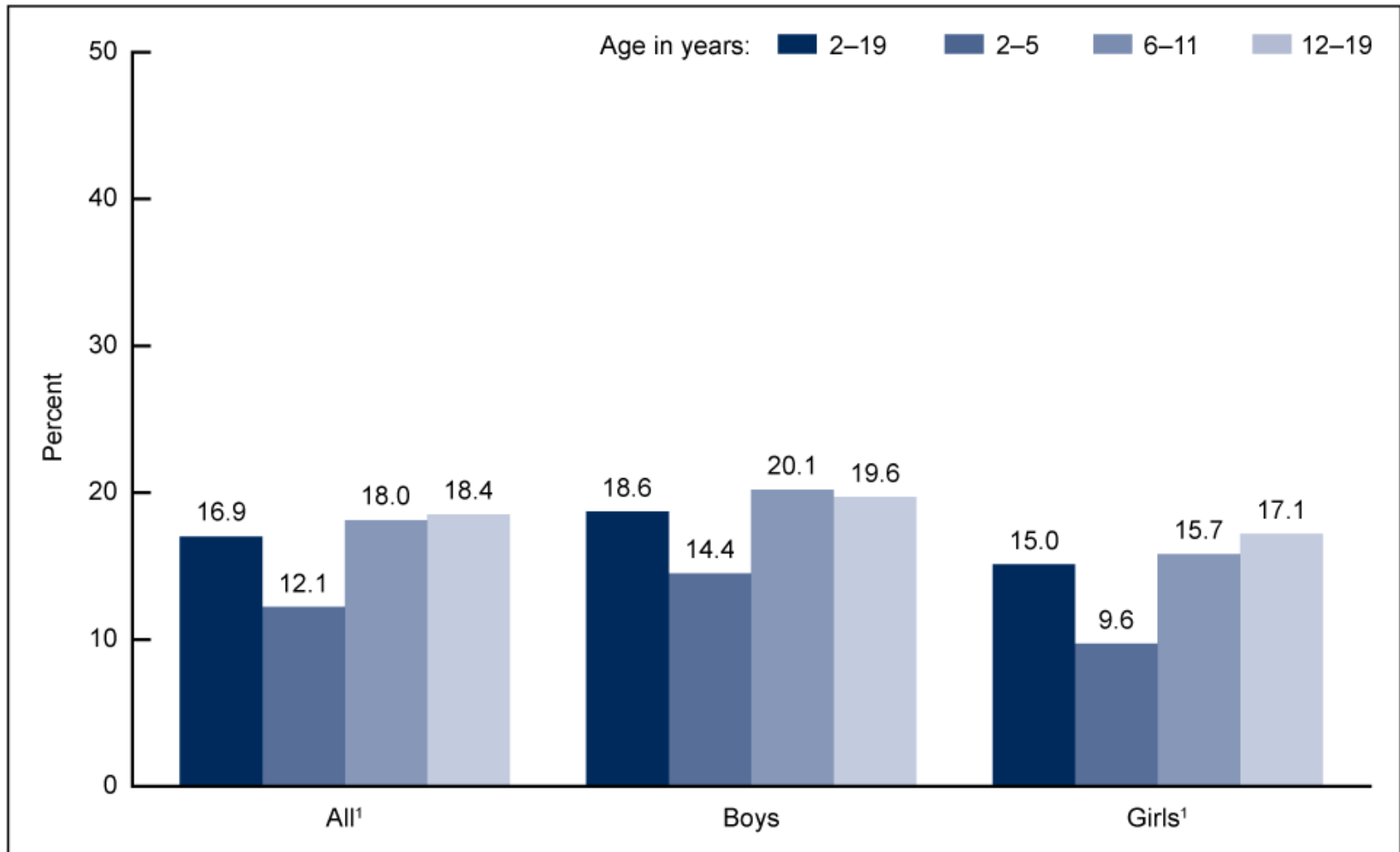
Prevalence of Obesity Among U.S. Adults Aged 20-74



Derived from NHANES data

Not Just Adults...Children and Teens Too

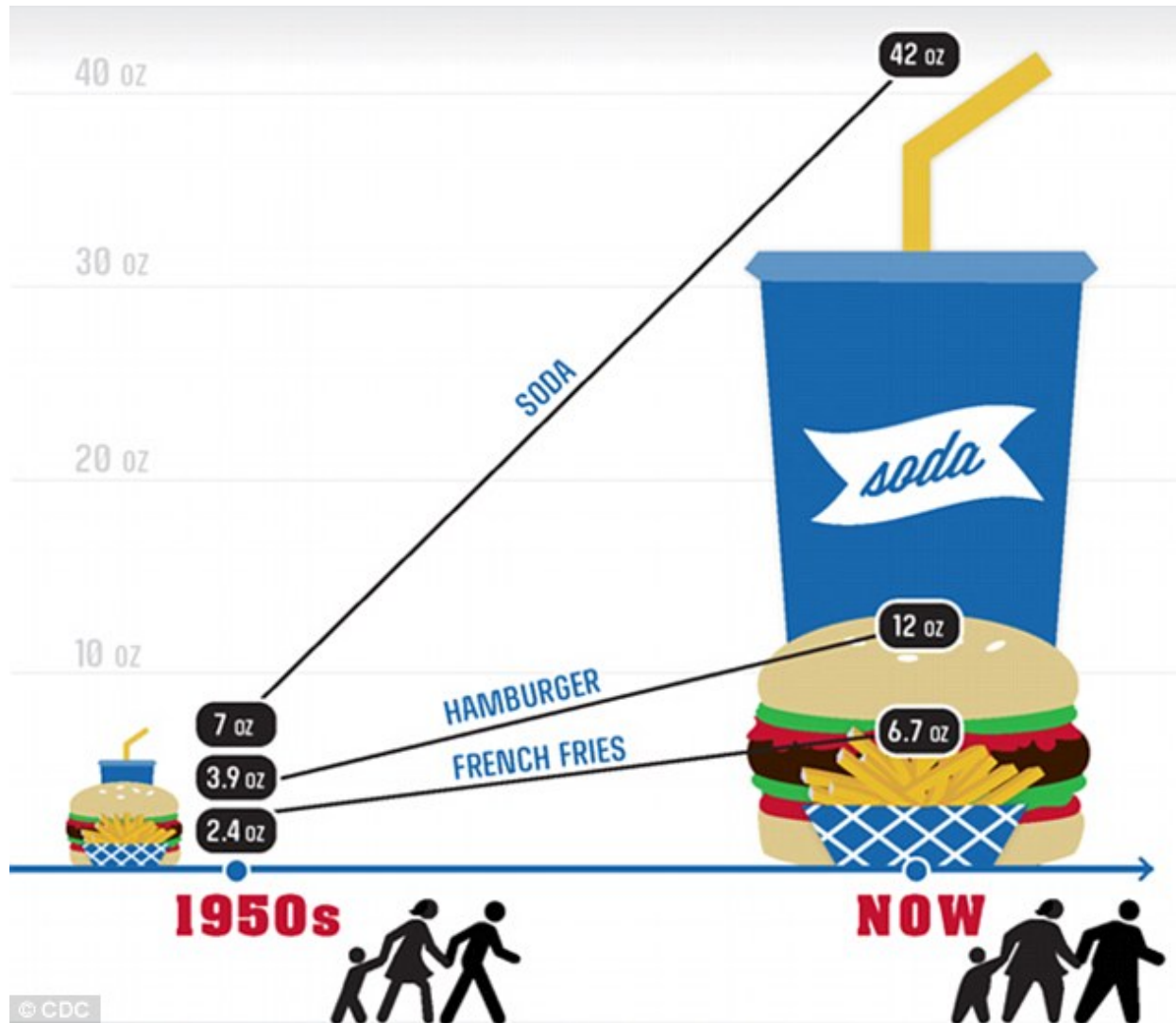
Figure 2. Prevalence of obesity among children and adolescents aged 2–19, by sex and age: United States, 2009–2010



¹Significant increasing linear trend by age ($p < 0.005$).

SOURCE: CDC/NCHS, National Health and Nutrition Examination Survey, 2009–2010.

We've Been "Super-Sized"



On Average, Servings and Meals Are Bigger



A tasty 750
calories

And so are
we.....



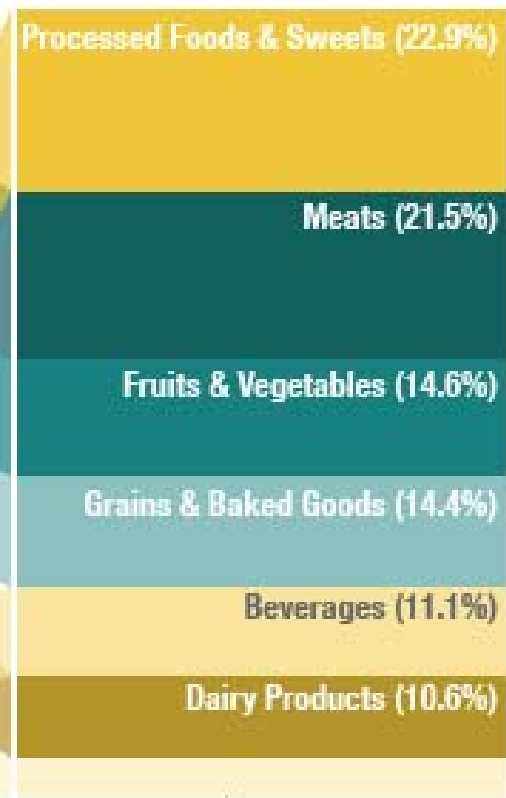
Our Grocery-buying Habits Have Changed

Breakdown Of Money Spent On Groceries

1982



2012



Adults and Children Spend Most of Their Time Sitting



Siri Stafford, Getty Images



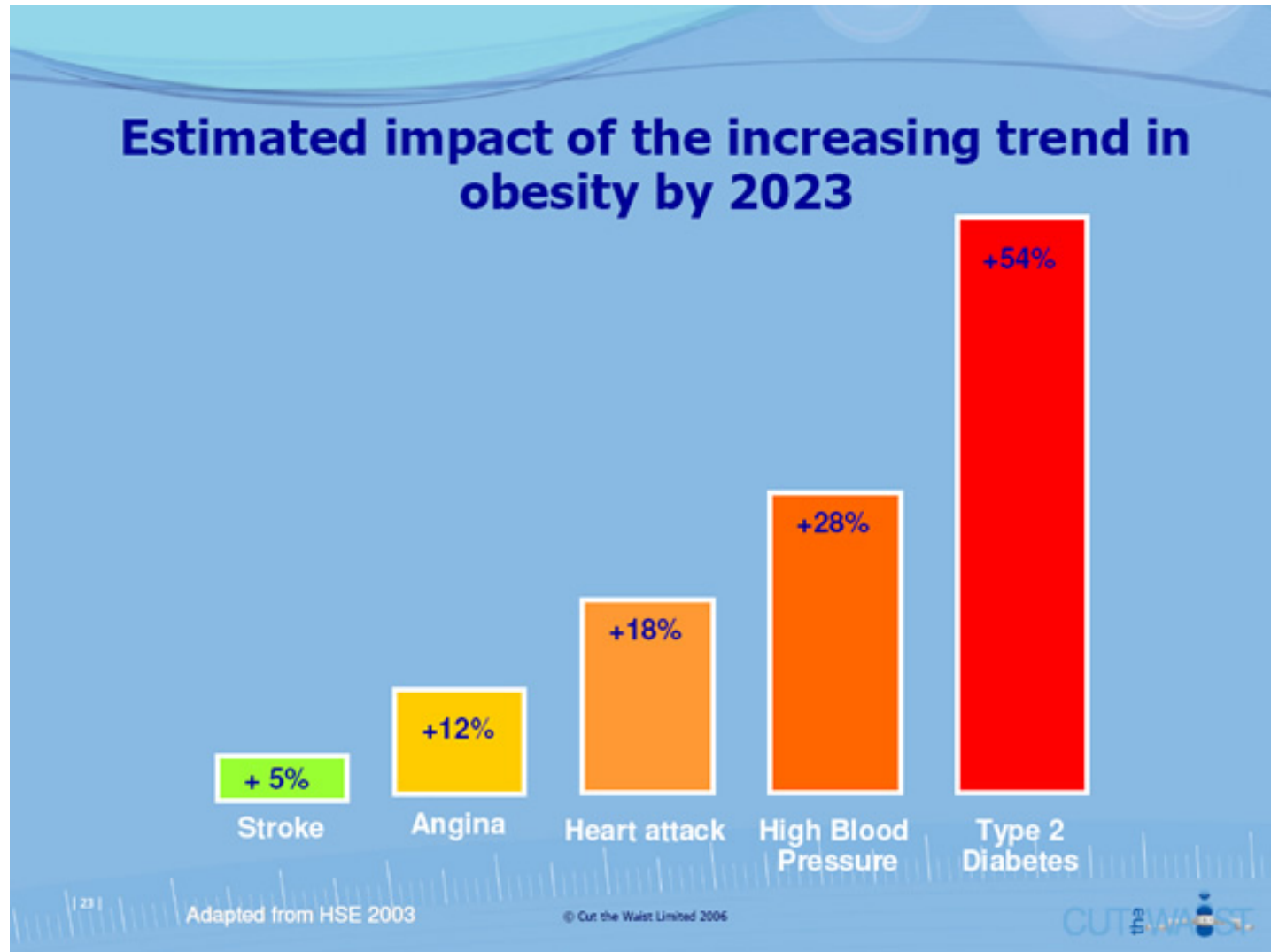
wiseGEEK



And Too Little of Our Time in Physical Activity



So...What Does Our “Weight Problem” Have to Do With Health??

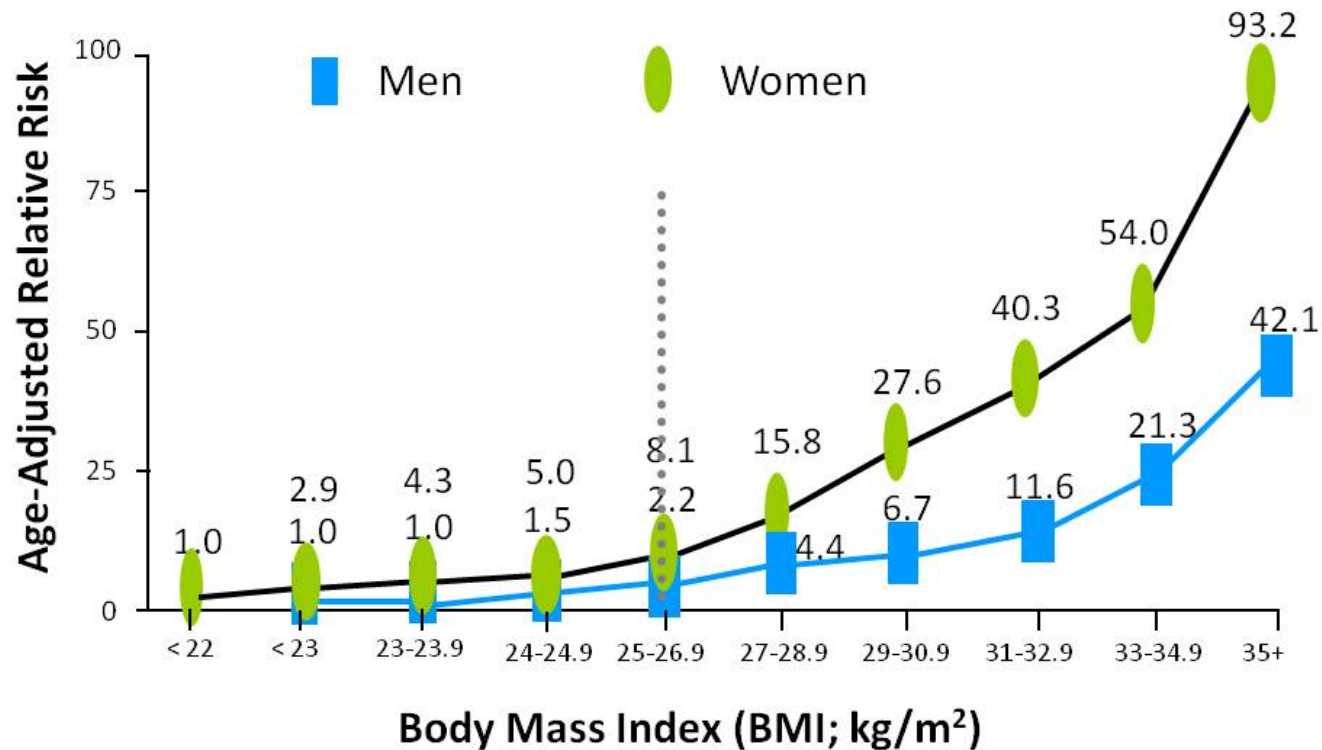


Overweight and Obesity are “Warning Signs



Our “Weight Problem” and Type 2 DM

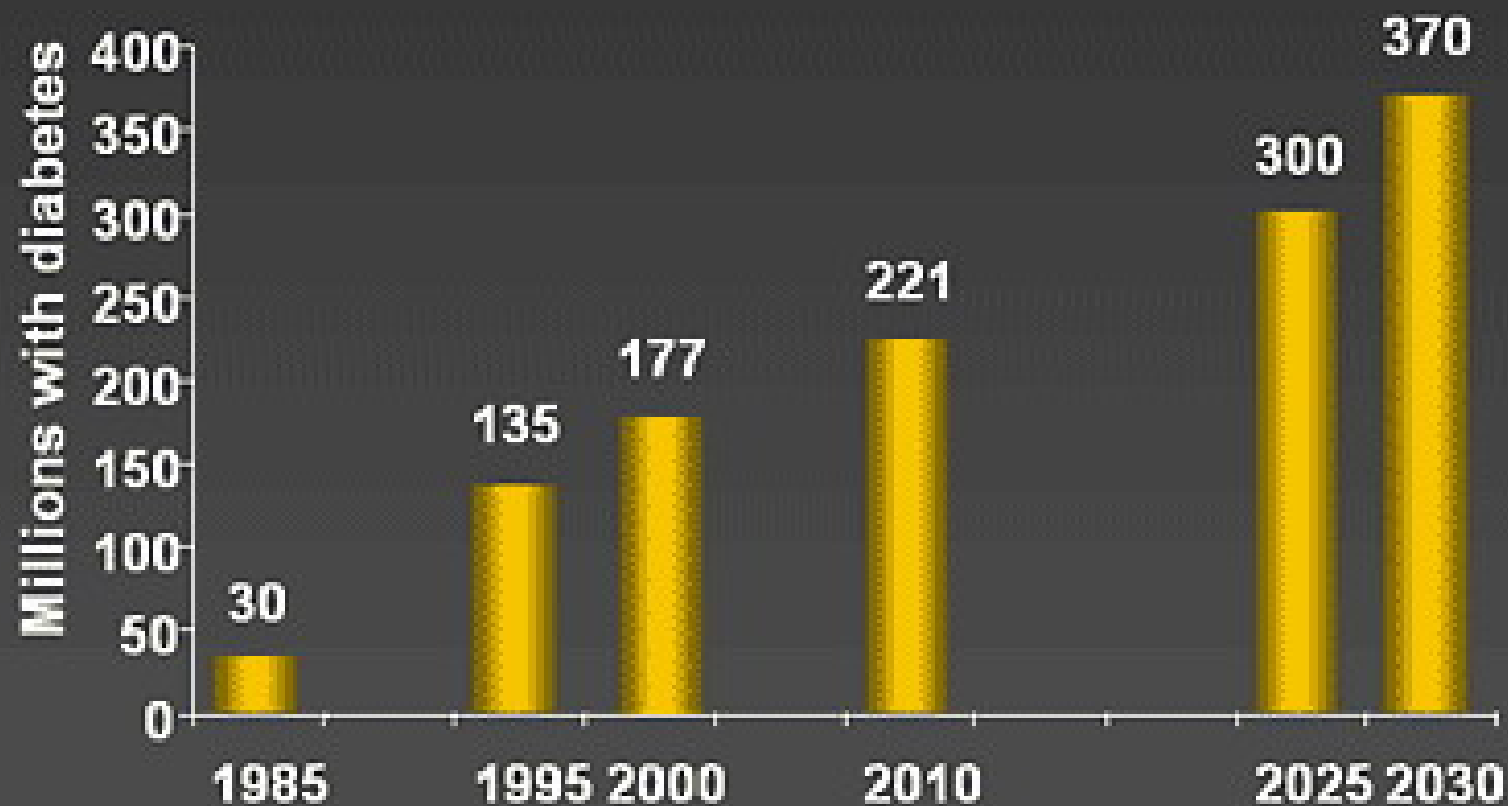
Relationship Between BMI and Risk for Type 2 Diabetes Mellitus



Chan J, et al. *Diabetes Care*. 1994;17:961-969.

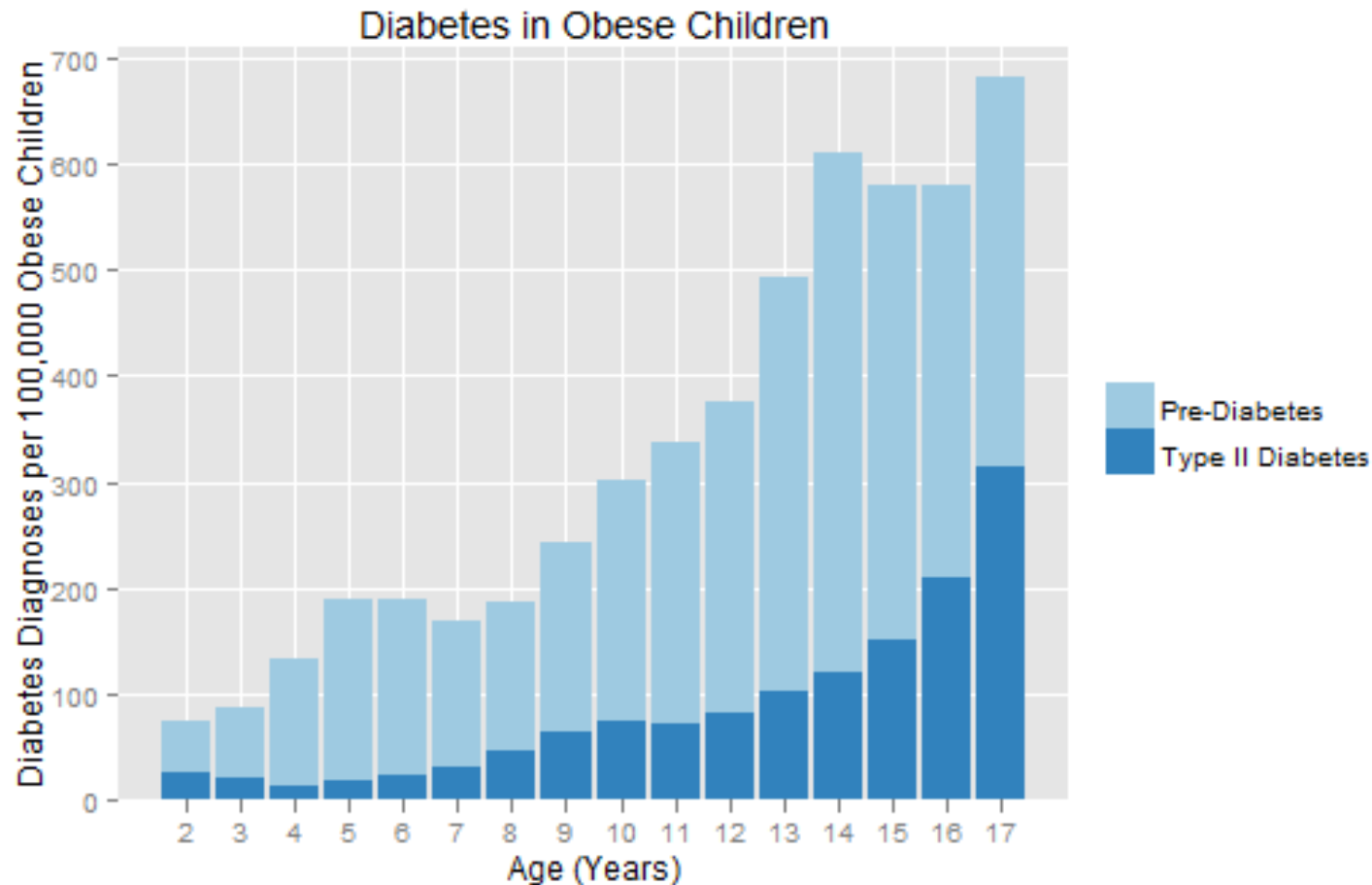
Colditz G, et al. *Ann Intern Med*. 1995;122:481-486.

The Worldwide Epidemic: Diabetes Trends



Sources: www.who.int; www.idf.org; Zimmet P, et al. *Nature*. 2001;414:782-787.

Remember When T2DM Was “Adult Onset” Diabetes???



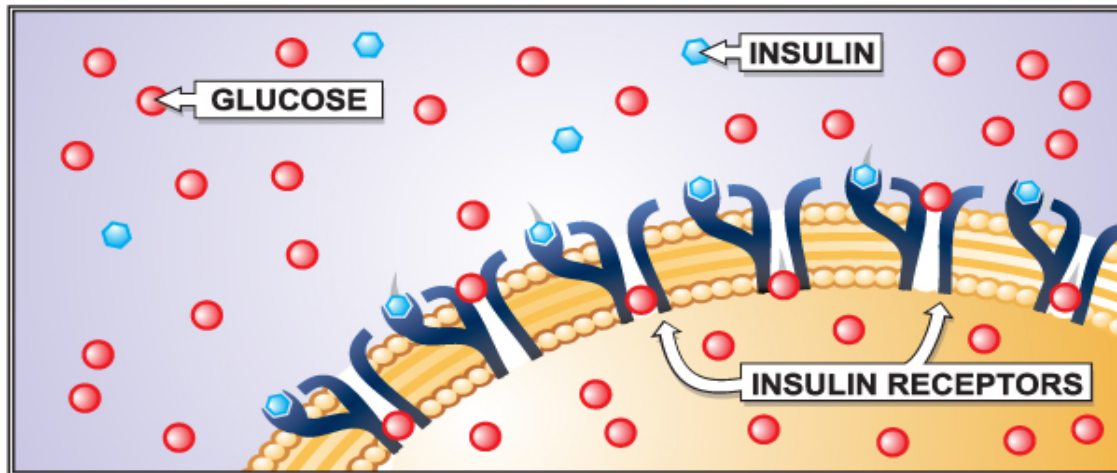
A Word About “BMI” As A Designator of Overweight and Obesity

- It is based simply on height and weight
- $\text{BMI} = \text{wt. (lbs)} \times 703 \div \text{ht. (in. squared)}$
- Does not take into account lean body mass
- Waist : hip ratio might be a better classifier
- However...it is quick, based on simple to obtain measures
- There is no doubt that a $\text{BMI} \geq 35$ indicates obesity, and a $\text{BMI} \geq 40$ indicates “morbid” obesity
- 25.6% of those with BMI's ≥ 40 have type 2 diabetes

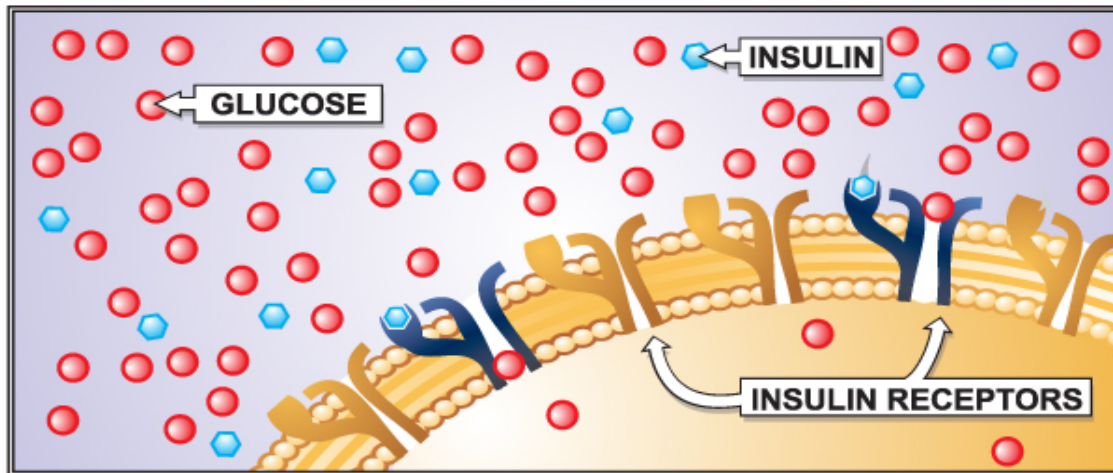
Development of Type 2 Diabetes

- Many of us consume foods high in sugars and starches
- Bombarded by high amounts of glucose, beta cells of pancreas secrete more insulin
- So much that, in time, cells' insulin receptors become resistant, so that cells are unable to take up glucose effectively
- Blood glucose level remains chronically high

NORMAL CELL



INSULIN RESISTANT CELL



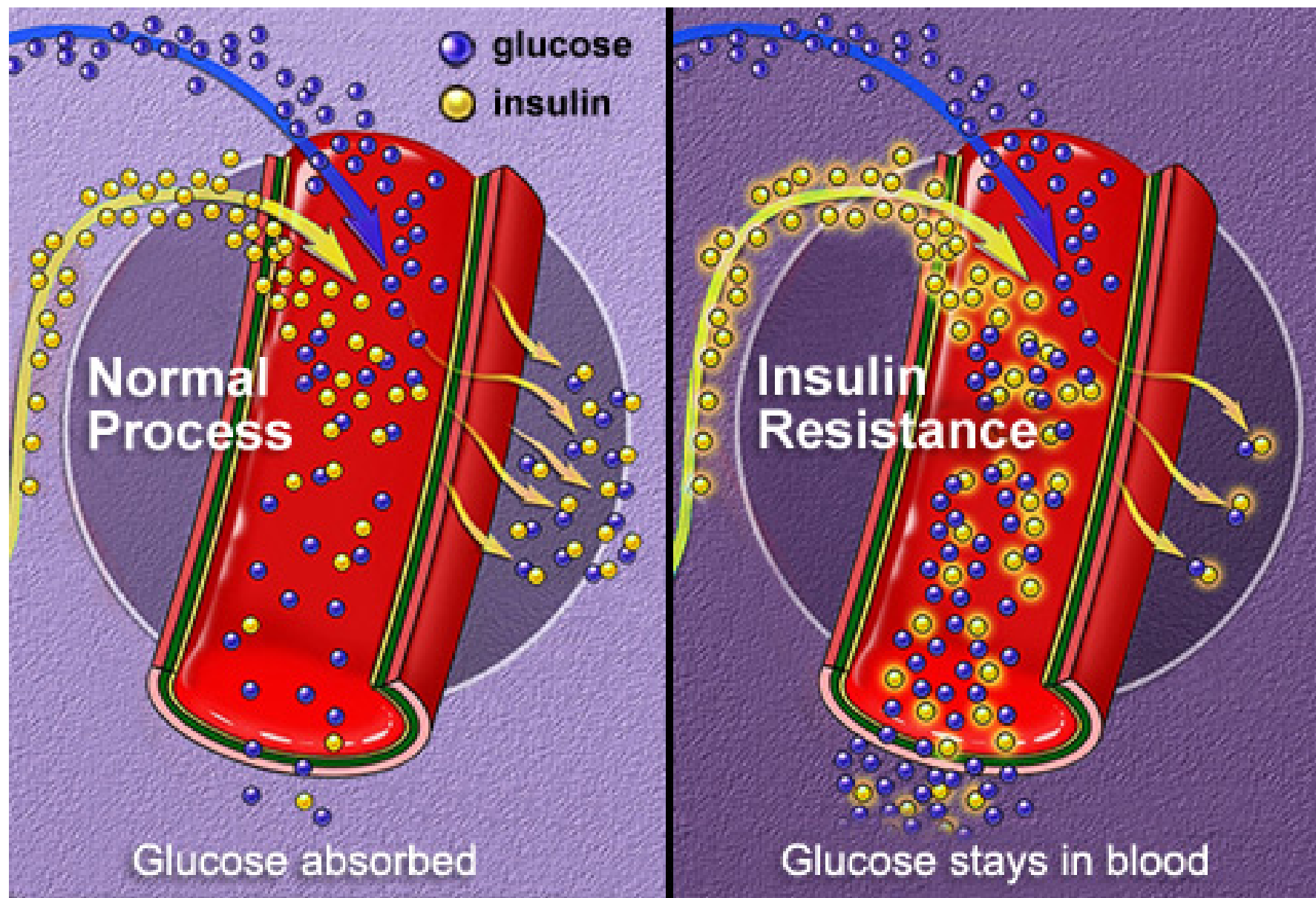
● glucose
● insulin

Normal
Process

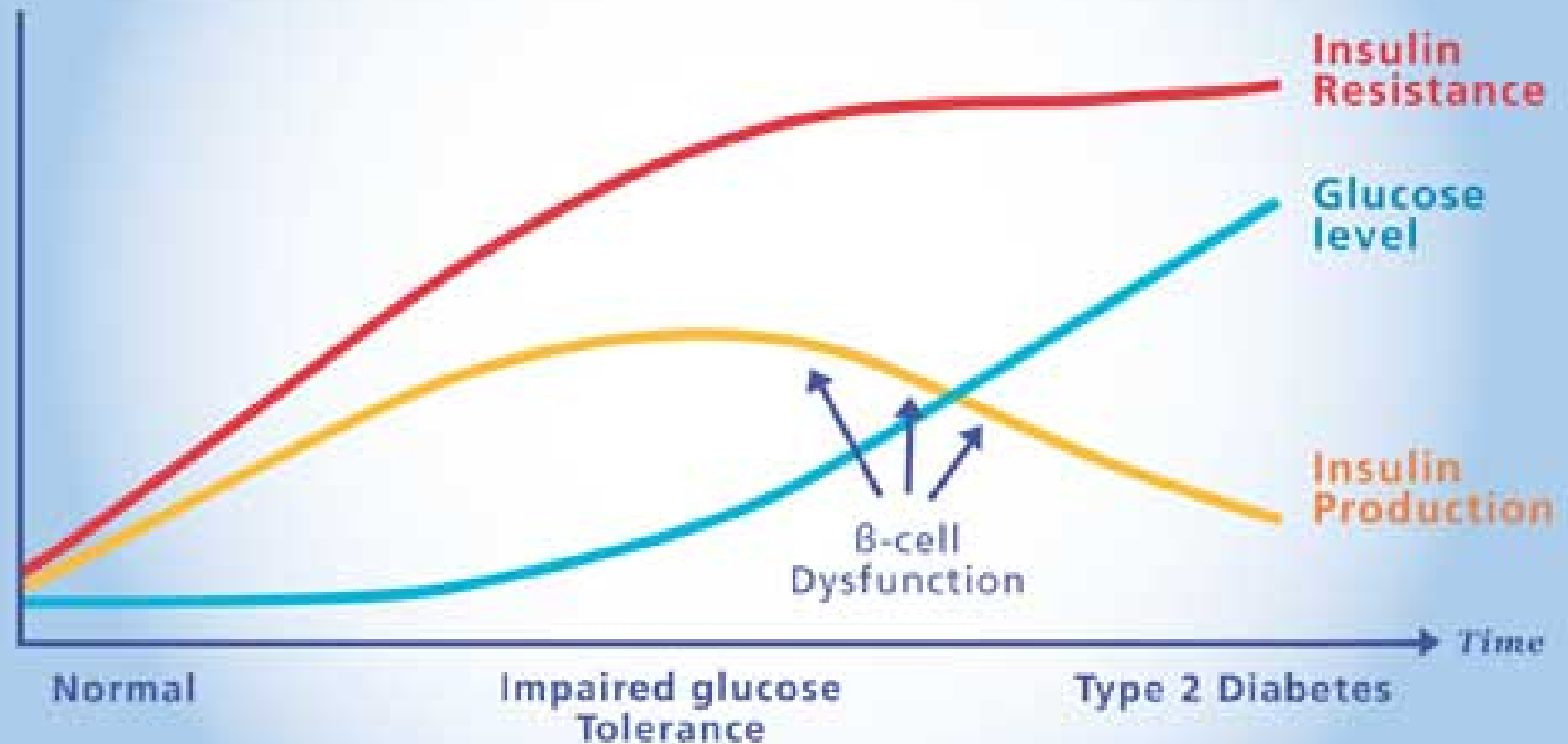
Glucose absorbed

Insulin
Resistance

Glucose stays in blood



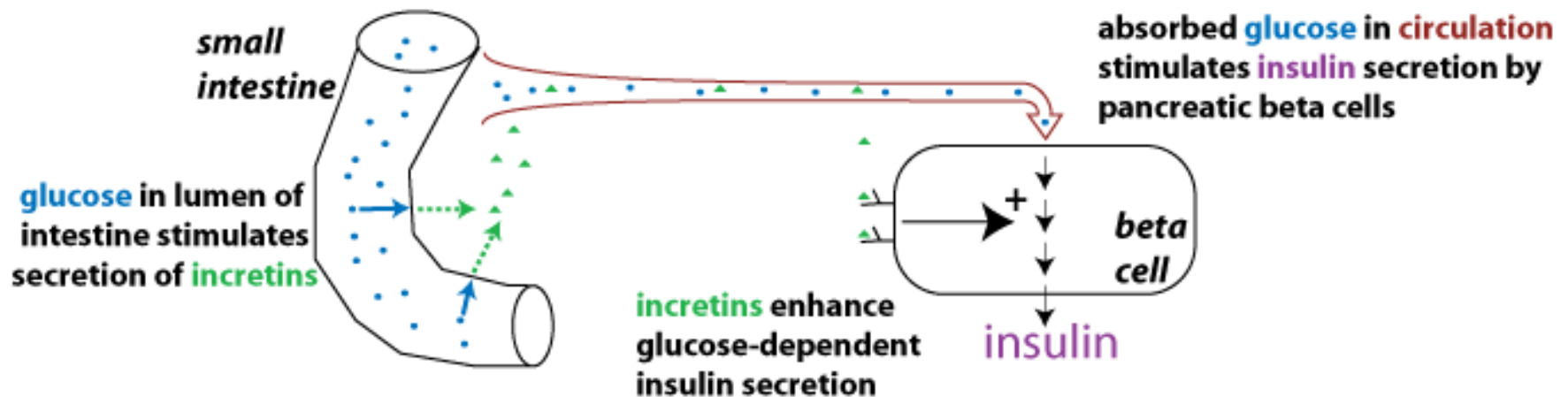
Natural History of Type 2 Diabetes



Henry, *Am J Med* 1998 ;105(1A):20S-6S

Insulin Production Also Mediated by Hormones Known as Incretins

Intestine – mediated Secretion of Insulin

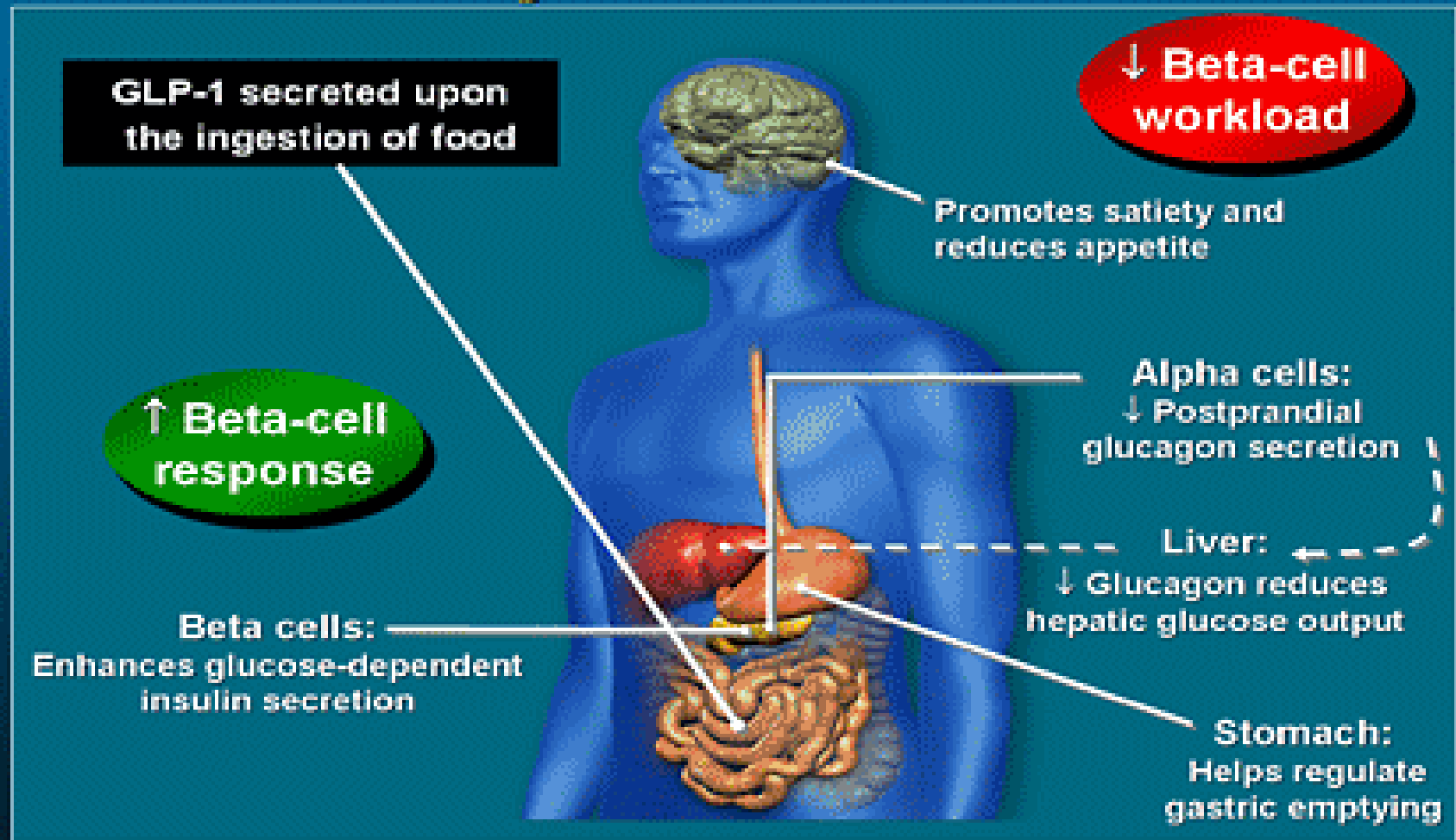


Glucagon-Like Peptide 1 & Glucose-dependent Insulinotropic Polypeptide

- Both are secreted by cells in the intestine, in response to food entering the intestine
- Enhance insulin release in response to food intake – particularly carbohydrates
- In non-diabetics, account for up to 50% of insulin released
- Have a protective effect on beta cells, reduction in rate of apoptosis and enhancing neogenesis
- Incretin effects are blunted in type 2 diabetes

GLP-1 Effects in Humans

Understanding the Natural Role of Incretins



Adapted from Flint A et al. *J Clin Invest*. 1998;101:515-520.

Adapted from Larsson H et al. *Acta Physiol Scand*. 1997;160:413-422.

Adapted from Nauck MA et al. *Diabetologia*. 1996;39:1546-1553.

Adapted from Drucker DJ. *Diabetes*. 1998;47:159-169.

Progressive Deterioration of β -Cell Function

- By the time of diagnosis, the process of beta cell “fatigue” and acceleration of apoptosis may have been ongoing for as much as 10-12 years
- Beta cell mass may be decreased as much as 50%
- Effects of hyperglycemia may have brought about damage to kidneys, nerves, and blood vessels

At Time of Diagnosis, Typical T2 Diabetic Has:

- BMI ≥ 35 , usually with truncal obesity
- HgbA1c ≥ 10
- Elevated blood pressure
- Elevated blood lipids
- Possibly some symptoms of peripheral neuropathy (tingling, numbness-hands/feet)
- Possibly some blurring of vision

Progression of Therapies

- Lifestyle modification: diet, exercise, stop smoking + oral medications + education and everything we can think of to encourage compliance
- Among compliant patients, some achieve good control ($\text{HgbA1c} \leq 6.5$)
- Alas, compliance is not a common trait, and many progress to a regimen of long-and-short acting insulins
- Treatment is costly; an oral med + two insulins, over 10 years = \$86,800.

Some Encouraging New Agents

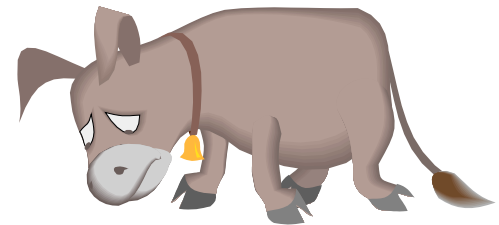
- Agents that inhibit DPP-4 enzyme – that’s the one that inactivates incretins
 - Sitagliptin (Januvia). Saxagliptin (Onglyza) and Linagliptin (Tradjenta)
 - They can work well, but tend to be “top tier” on the insurance coverage ladder; can cost \$200 or more/month
- GLP1 agonists : extenatide (Byetta) and Liraglutide (Victoza) –short and long-acting synthetic extendin
- These are also quite expensive, and often either not covered, or are “top tier”, with high co-pay

Extendin – Extracted From Saliva of the Gila Monster



For the Majority of Type 2 Diabetics:

- Once insulin is added, obesity is increased
- Added weight increases back and joint stress
- Control of glucose level waxes and wanes; even among compliant patients, the “24-7” average blood glucose is 150-160
- Slow, inexorable damage is done to kidneys, nerves, blood vessels, and heart
- It’s a “No Win” situation



So...What About Bariatric Surgery?

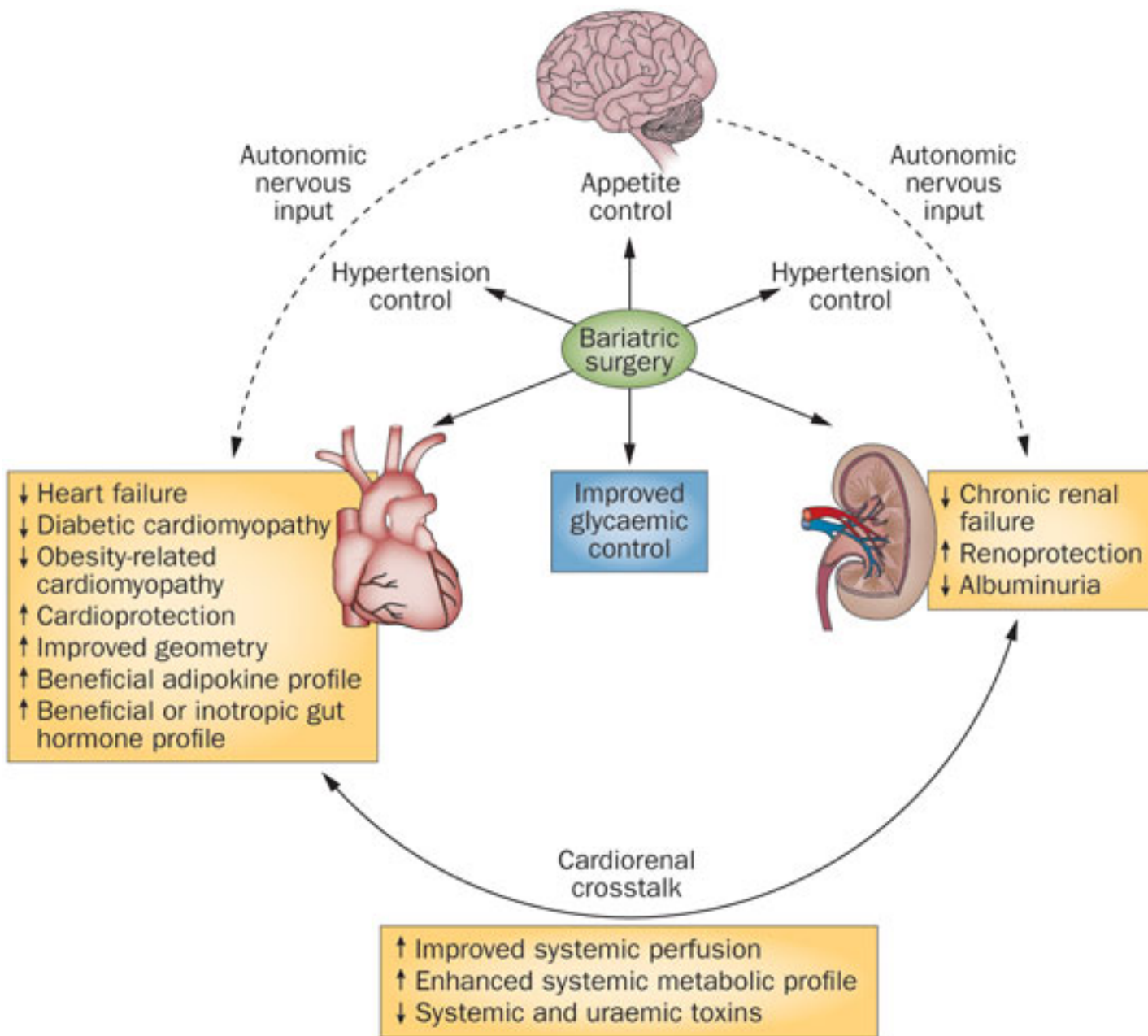
- Your patients usually have BMI's ≥ 40 ; i.e. they are “morbidly obese”
- It's “come a long way” since the early days of open surgical gastric bypass
- Laparoscopic procedures now the “state of the art”; patients usually discharged on 2nd or 3rd post-op day
- ...And blood glucose levels fall long before curtailed calorie intake and weight loss could bring about decreases

It's Time to Consider It

- STAMPEDE study (2012): 6-yr. follow-up – 50% achieved complete or partial remission, 24% with no medication, and 26% needing only an oral agent, typically metformin, to hold $\text{HgbA1c} \leq 6.0$. Signs of diabetic nephropathy improved or stabilized as well
- A Utah study followed 418 obese diabetics post gastric bypass surgery. At 6 yrs. Post-op, 62% had total or partial remission of diabetes, and significant improvement in blood lipid profiles, and hypertension.
- Swedish study followed 600 diabetics for 20 yrs. Post- GBP; 72% remission at 2 yrs., dropping to 36% at 10 yrs., and 18% at 20 yrs. All had fewer co-morbidities at 20 yrs than diabetics who had not had bariatric surgery

But....Findings Beyond Diabetes Remission.....

- At 20 years, the GBP group had a much lower incidence of complications involving kidneys, eyes, circulation, and peripheral nerves compared to the control group of diabetics who did not have gastric by-pass (20% / 45%)
- It's those complications that account for the vast majority of diabetics requiring dialysis, amputations, and coronary stents or grafts

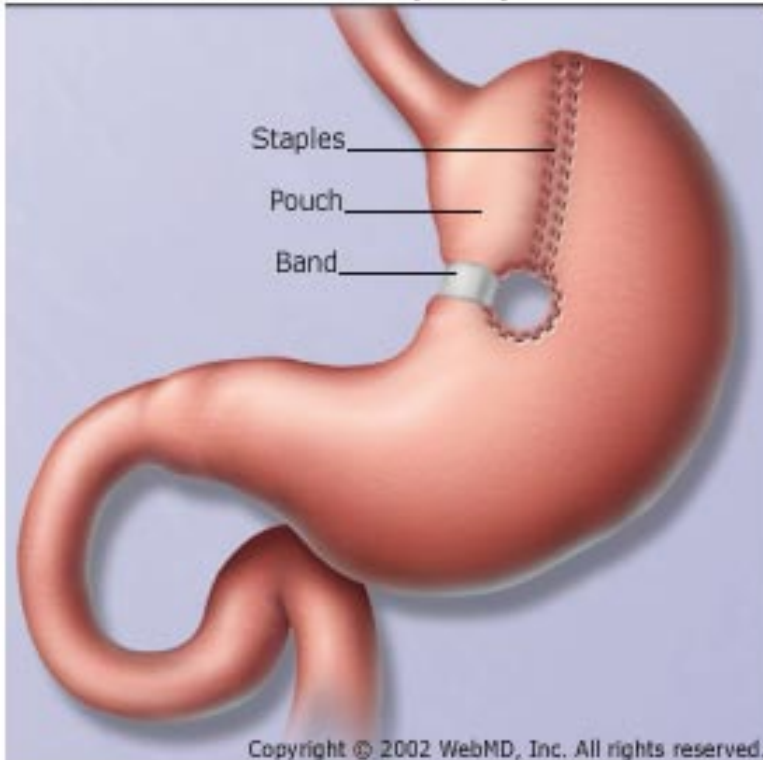


Bariatric Procedures

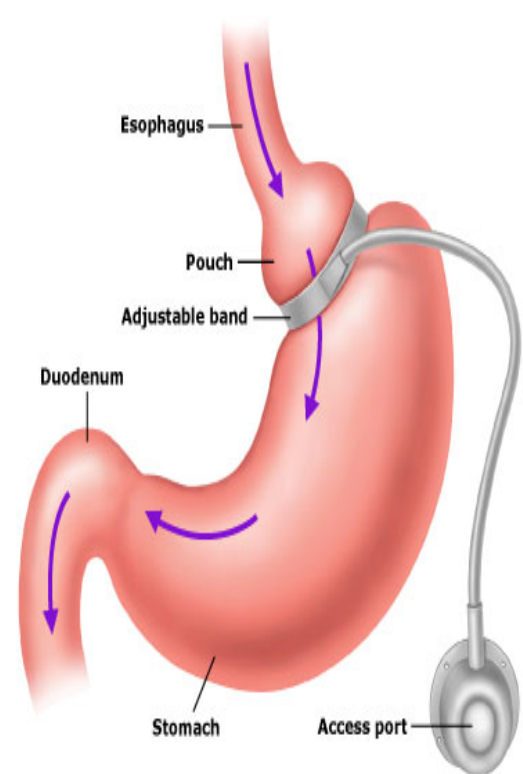
- Restrictive:
 - Limited intake capacity; normal flow of food preserved
- Restrictive + Reduced Absorption of Nutrients
 - Limited intake capacity; absorption length of small intestine moderately shortened; gut hormone effect on pancreas and liver enhanced; digestive hormones from stomach and duodenum preserved

Restrictive Bariatric Procedures

Vertical Banded Gastroplasty

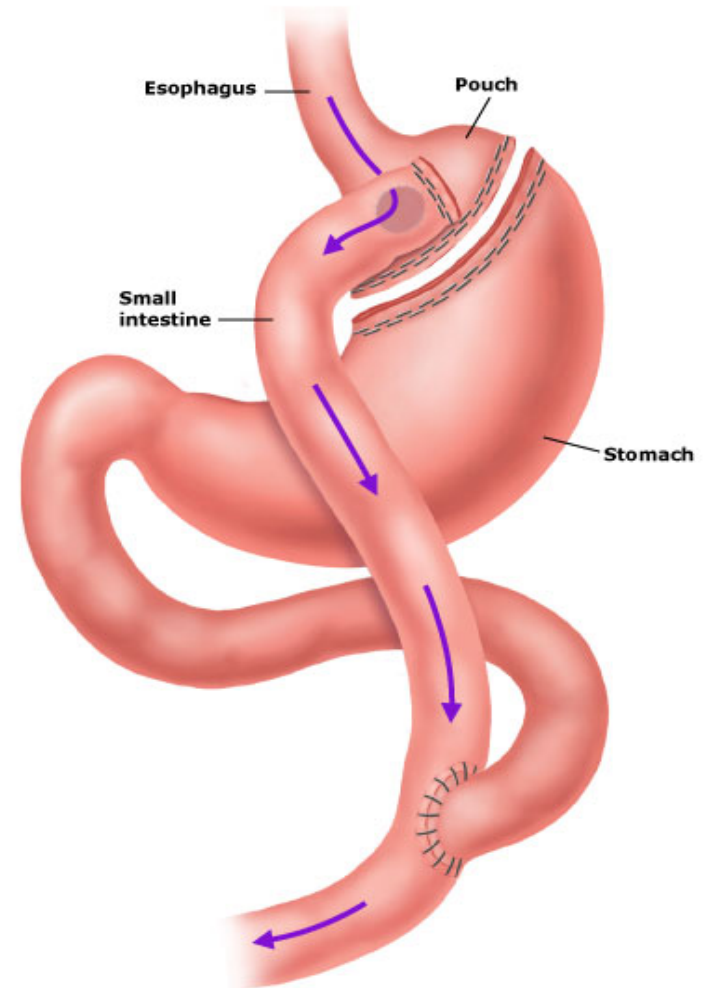


Adjustable Band Gastroplasty



Roux-en-Y: Combination of Restrictive and Altered Pathway

- Choice for 80% of patients in most centers; pouch about 30 ml. capacity; most of absorptive length preserved; stomach, duodenum and short segment of jejunum bypassed; upper limb re-connected, restoring continuity



Complication Rates for Laparoscopic Bariatric Surgeries

- Mortality:
 - AGB : 0.05%; RYGBP: 0.5%
- Bleeding
 - AGB: 0.1%; RYGBP: 0.4-4.0%
- Deep vein thrombosis
 - AGB: 0.-1%; RYGBP: 0% - 1.3%
- Pulmonary embolus
 - AGB: 0.1%; RYGBP: 0% - 1.1%

T2 Diabetes Remission: RYGBP and AGB Procedures

Medscape

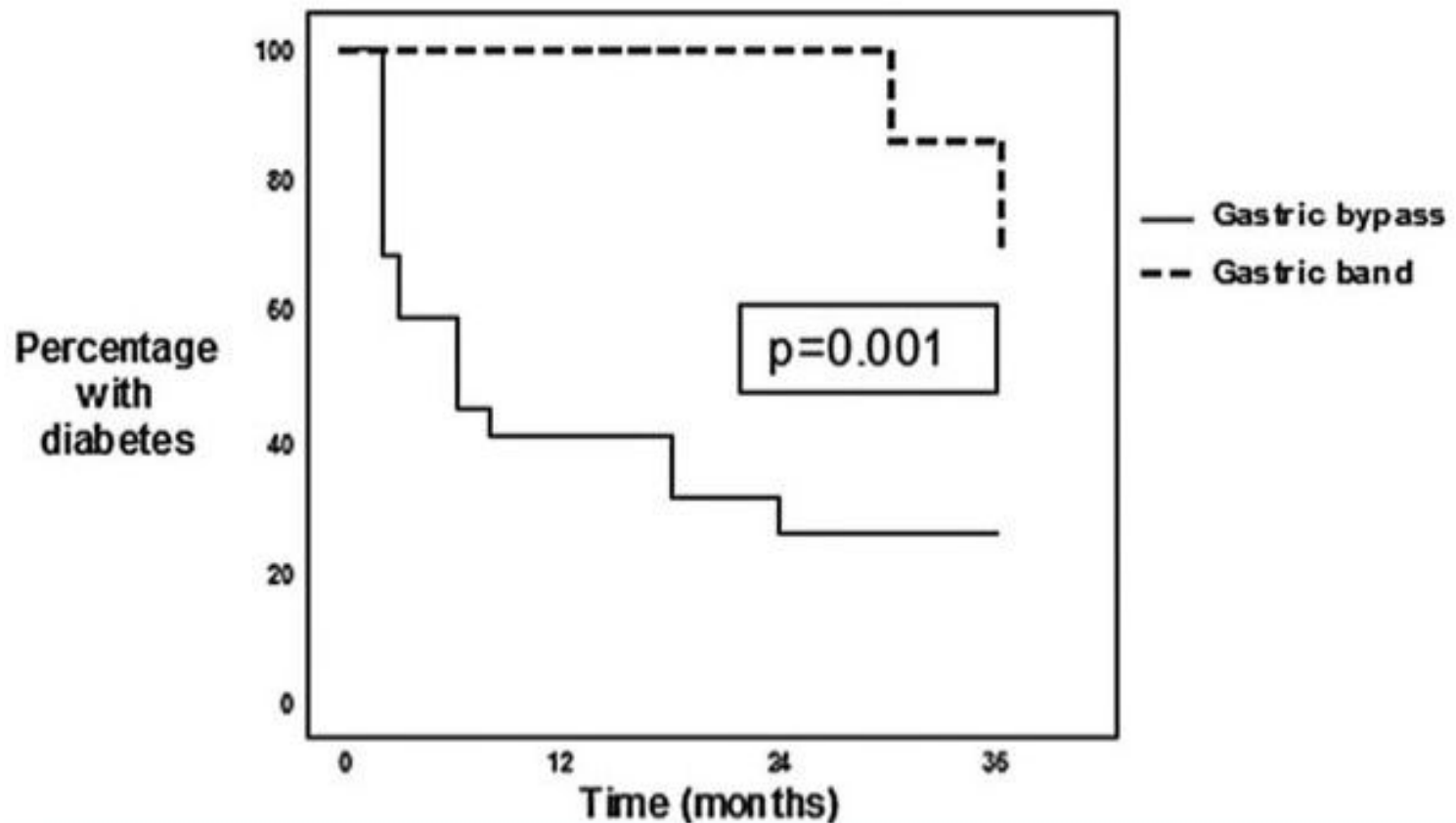


Table. Rates of Remission of Type 2 Diabetes Reported after Bariatric Surgery

Procedure	Remission Rate (%)
Vertical banded gastroplasty	75-83
Laparoscopic adjustable silicone gastric banding	40-47
Roux-en-Y gastric bypass	83-92

Table 2. Glycemic Control Following Bariatric Surgery

	Roux-En-Y Gastric Bypass	Sleeve Gastrectomy	Adjustable Gastric Banding
HbA1C (%) preoperative	8.1±1.9	7.5±1.5	7.7±1.5
HbA1C (%) postoperative	6.2±1.2*	6.8±1.7*	6.3±0.7*

*p<0.001 compared with preoperative.

Results: Wt. Loss and Blood Glucose Control

- Patients receiving any type of bariatric surgery lose weight; RYGBP \geq AGB
- Remission of type 2 diabetes
 - RYGBP: 80.3%; AGB: 56.7%
 - Total remission persists for varying lengths of time; 2 – 10 years reported in most studies. In patients who need medication to maintain glycemic control, typically one oral drug, or a GLP-1 agonist like victoza is sufficient

Why Does This Happen, and Why Does Roux-en-Y Seem More Effective?

- Decreased caloric intake
- Somewhat lessened intestinal absorption of nutrients
- Food enters incretin-producing portion of intestine sooner, stimulating release of the incretins and peptide YY
- Those stimulate release of insulin, and produce feeling of satiety.

Who Is A Candidate?

- BMI ≥ 40 ; type 2 diabetes, or BMI ≥ 35 plus a comorbidity (hyperlipidemia; sleep apnea; arthritis)
- Patient who have demonstrated compliance with glucose monitoring, medication regimens
- Patients who demonstrate understanding of post-surgery eating patterns, and need for life-long vitamin supplements (A, D, E, K, C, Iron, Zinc, and B₁₂) and will commit to long-term follow-up

What's the Cost?

- It depends on where you are located; large cities typically have practices specializing in bariatric surgeries
- In New York, cost average is \$21,000, which includes surgery and follow-up, anesthesia, and hospital stay. In Houston, \$21-22,000.
- A clinic in Michigan offers an all-inclusive “package” for \$19,500
- Medicare and most insurances do provide coverage
- There likely will be visits to nutritionist periodically; patients will require life-long supplements: A,D,E,K,C,B₁₂, iron, zinc
- Not to mention...new clothes, or lots of alterations!

Sounds Expensive...But Consider...

- An obese type 2 diabetic, age 40, who does not have the surgery will spend \$373,600 on the typical regimen of diabetes medications over the next 20 years
- Add to that the cost of anti-hypertensive and anti-hyperlipidemic drugs they will likely need, and the cost of surgery doesn't look like a big obstacle

Intangible “Quality of Life” Benefits

Self-esteem; ability to work, and perhaps be considered more “employable”

Able to enjoy physical activity and its benefits

Enjoy a better “energy level”

Having to take fewer medicines

Overall, just “feel better”



After All This...My Answer Is YES!

- I was a “nay-sayer” as regards bariatric surgery for diabetics...or anyone!
- But after seeing some dramatic changes in our patients who’ve chosen to have it...and reviewing research...I’ve changed my mind!
- We should present it as an option
- Yes, they will have to be willing to be compliant, and may still require some medicine...and still need to monitor BG, but all-in-all, it seems to offer significant advantages!

