Type 2 Diabetes Management

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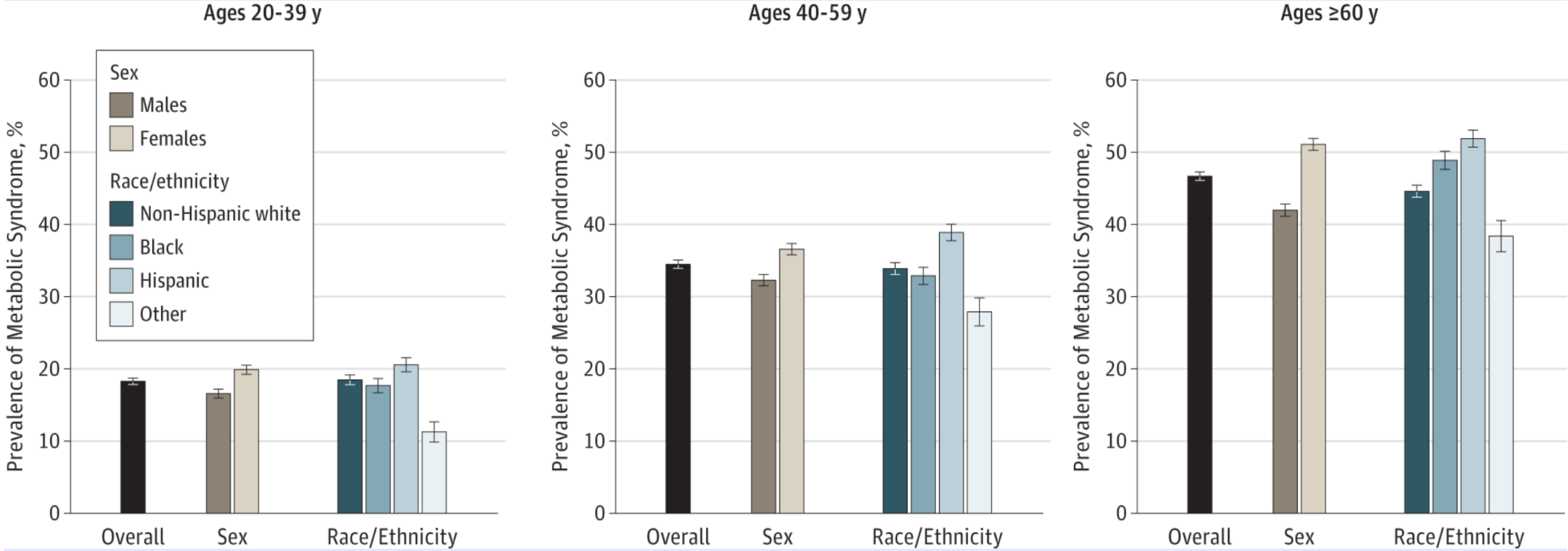
Age, Glucose Homeostasis and Diabetes

- Epidemiology
- Pathophysiology
- Recommendations

Age-Specific Prevalence of the Metabolic Syndrome by Sex and Race/Ethnicity



JAMA. 2015;313(19):1973-1974. doi:10.1001/jama.2015.4260

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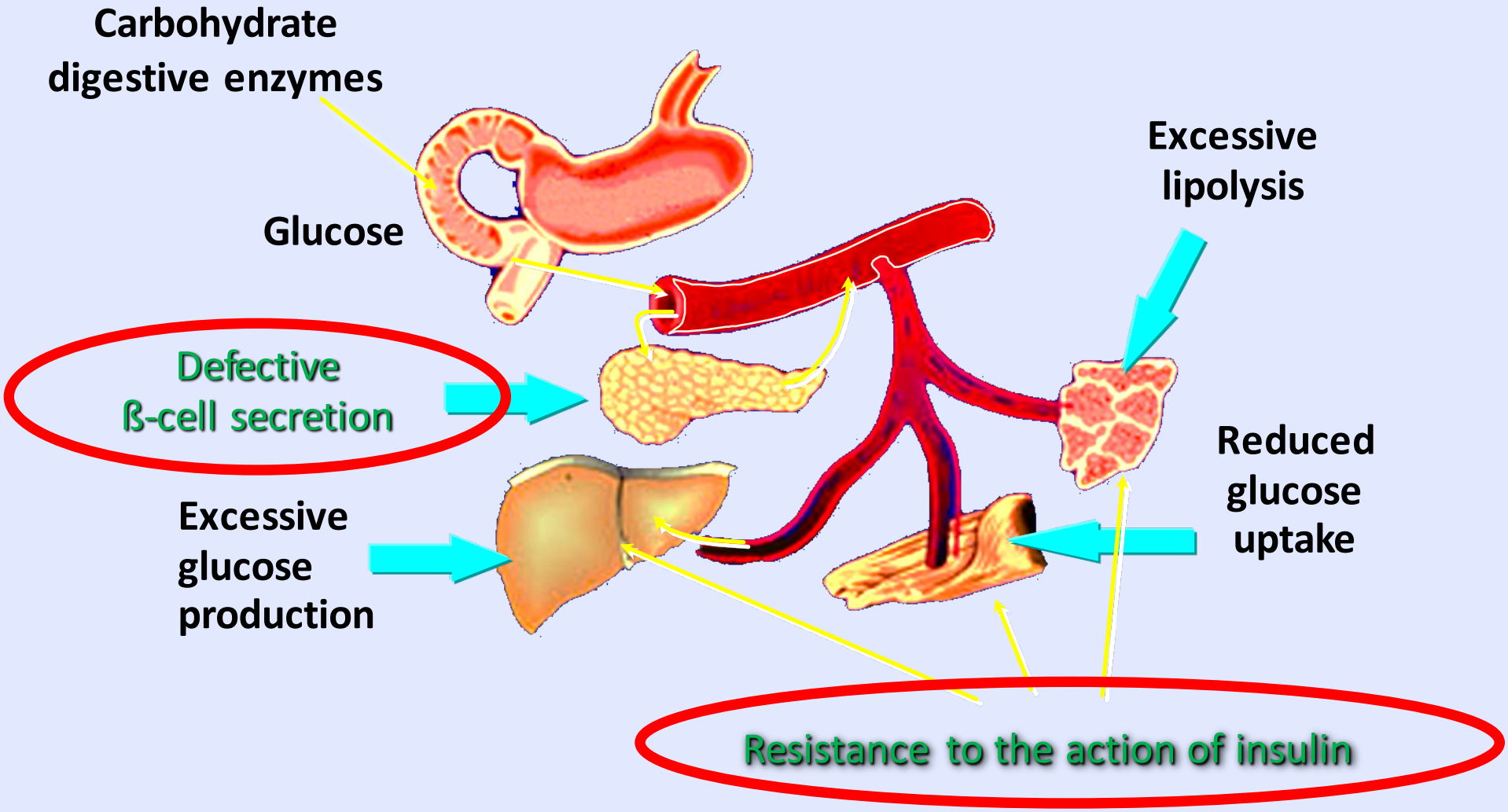
One in every two people age 65 and older have diabetes or pre-diabetes

Why Diabetes Risk Increases With Age?

Pathophysiology of Type 2 Diabetes

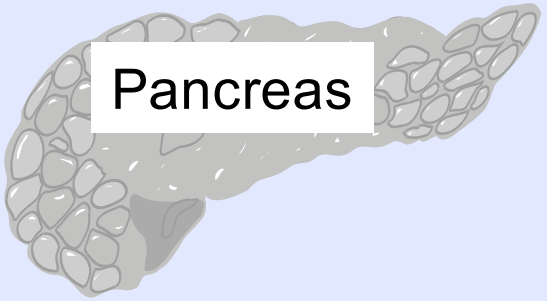


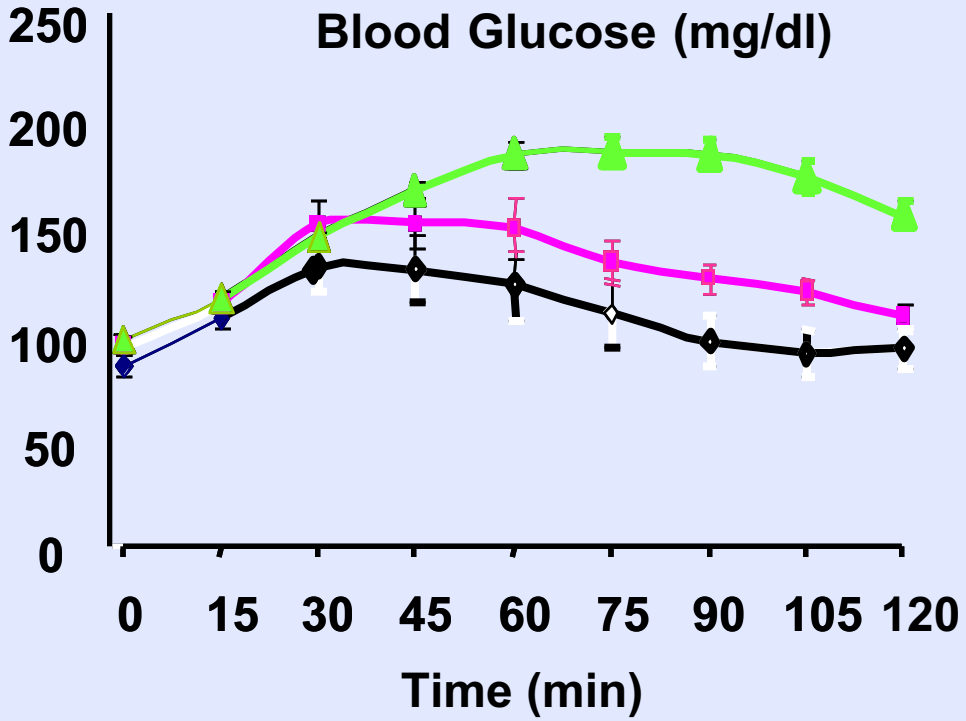
Effect of Age on Insulin Secretion

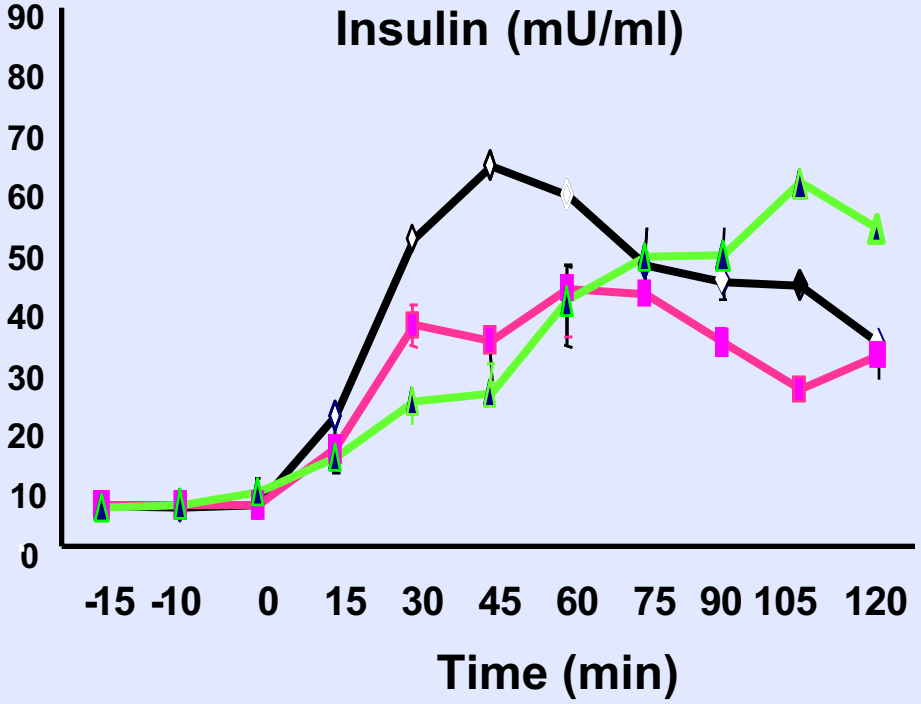
Young

Older Normal Glucose Tolerant

Old Impaired Glucose Tolerant







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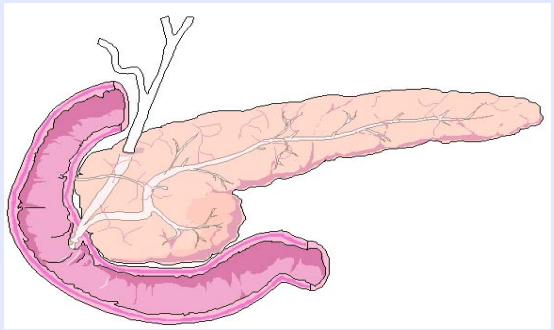
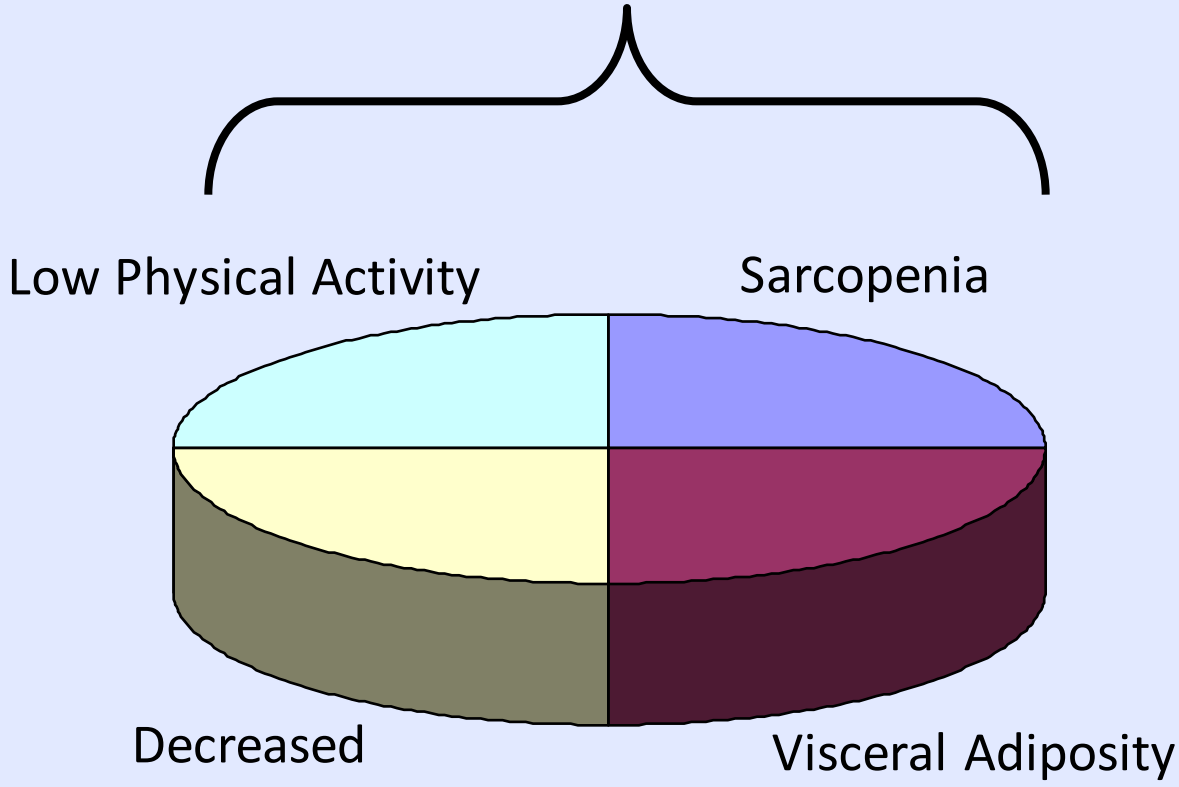
Type 2 Diabetes in Aging

β Cell Failure



Peripheral Insulin Resistance



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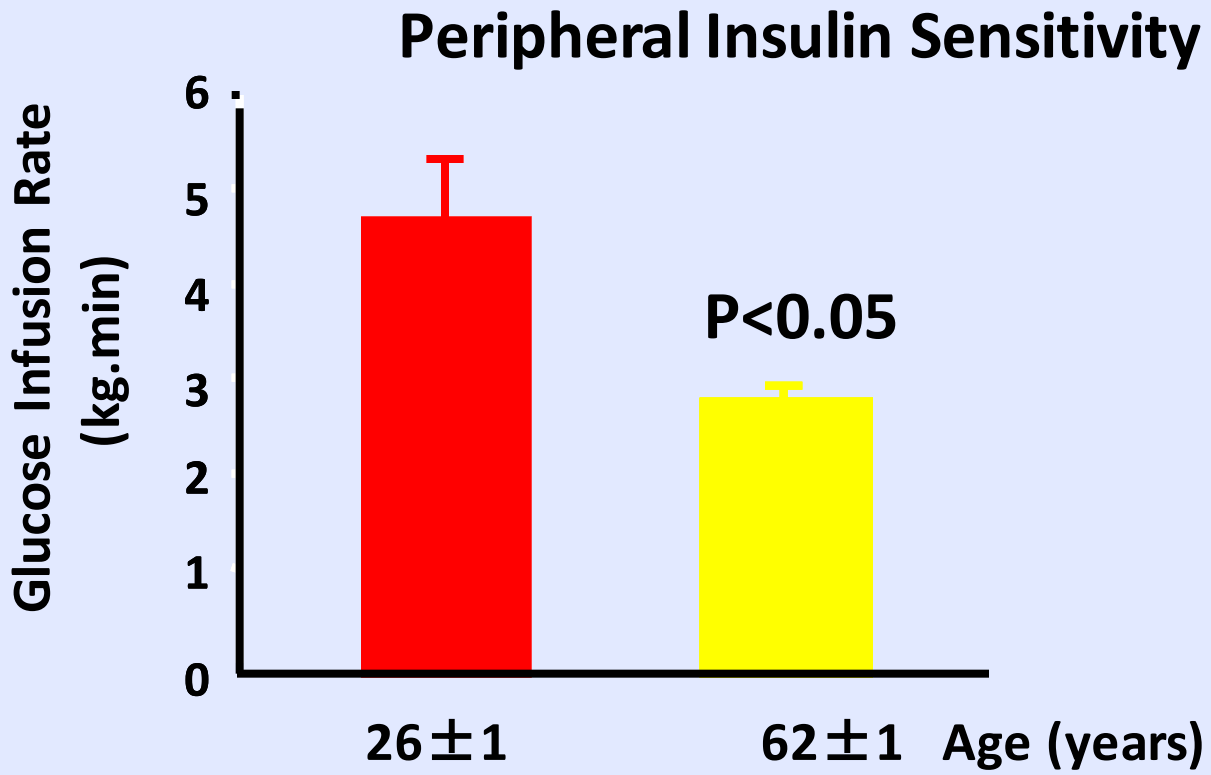
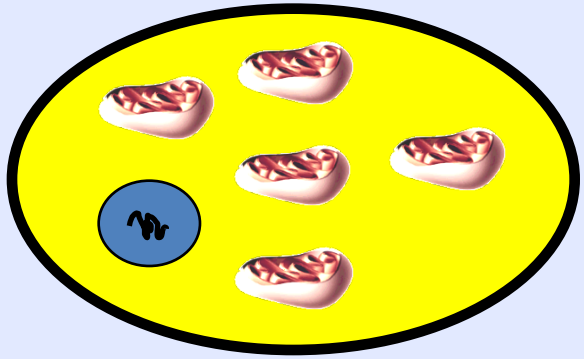
Are Older Patients More Insulin-Resistant?



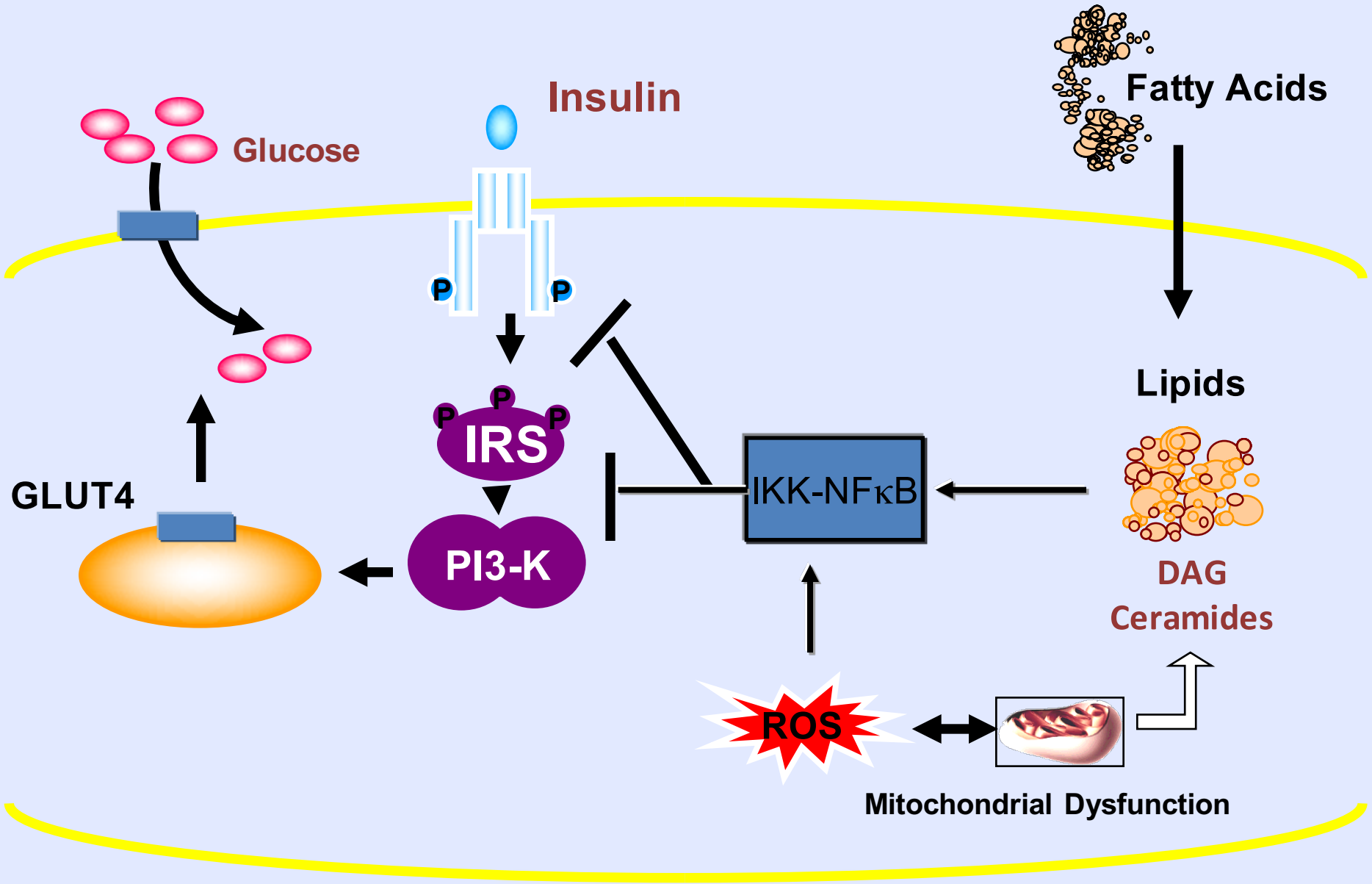
Age and Insulin Resistance



Mitochondrial Function

Insulin Resistance

Mechanism of Insulin Resistance in Aging



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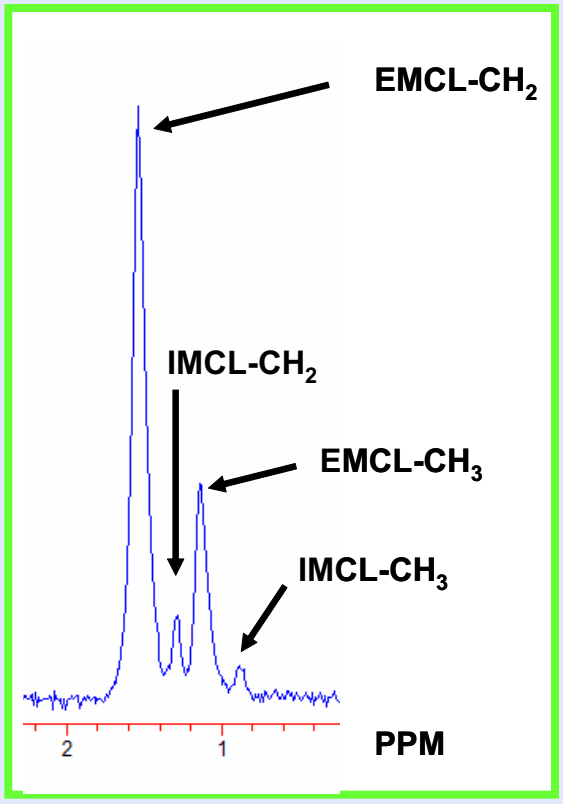
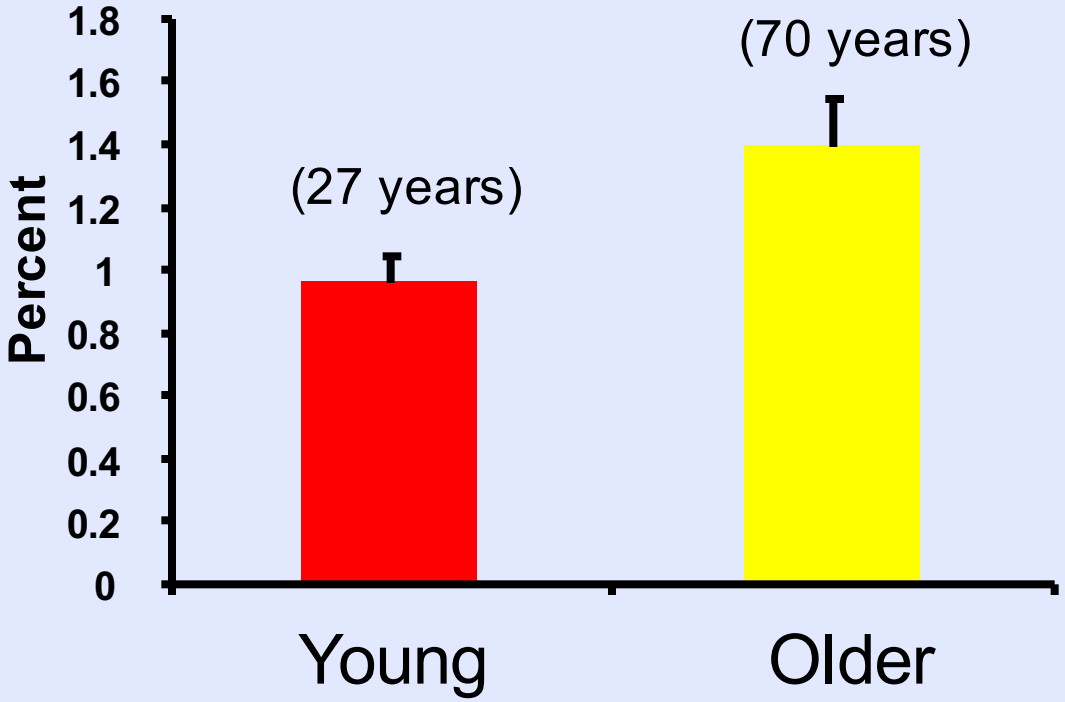
Effect of Age on Lipid Content

Magnetic Resonance Spectroscopy



Intramyocellular Lipid Content



(Petersen, Science, 2003)

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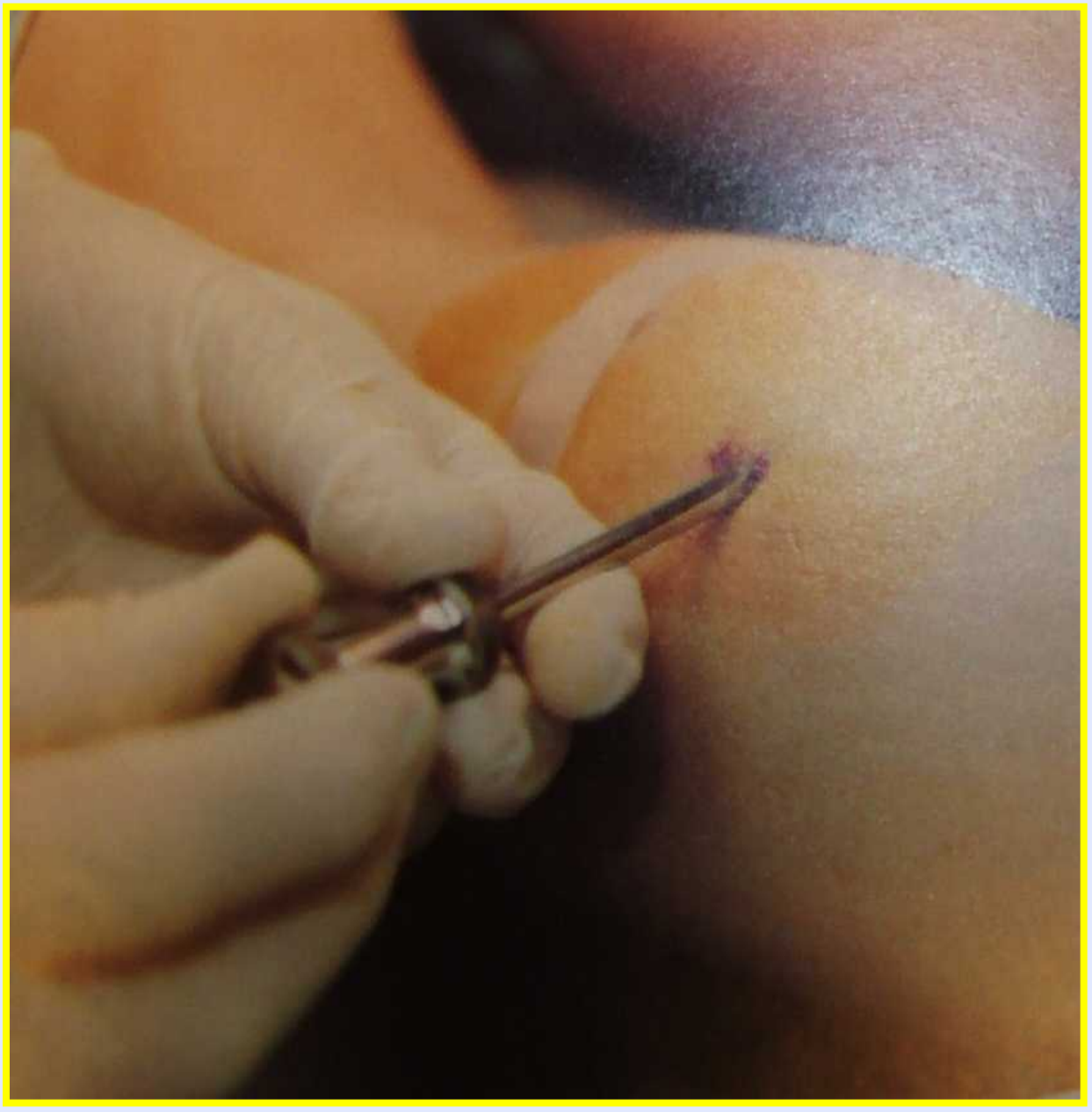
Needle Muscle Biopsy



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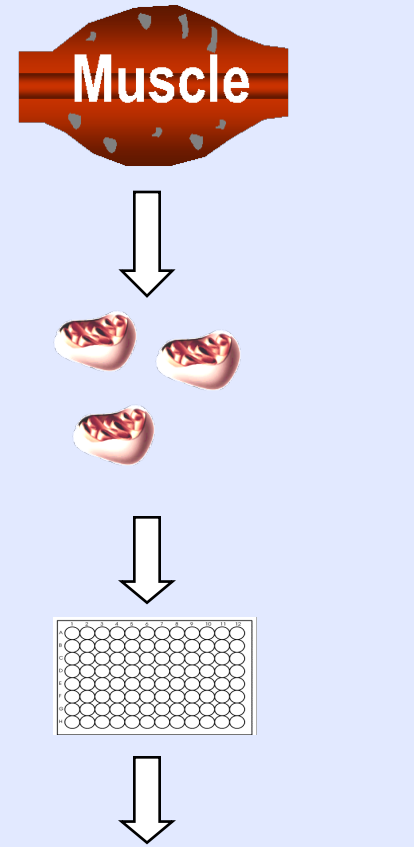
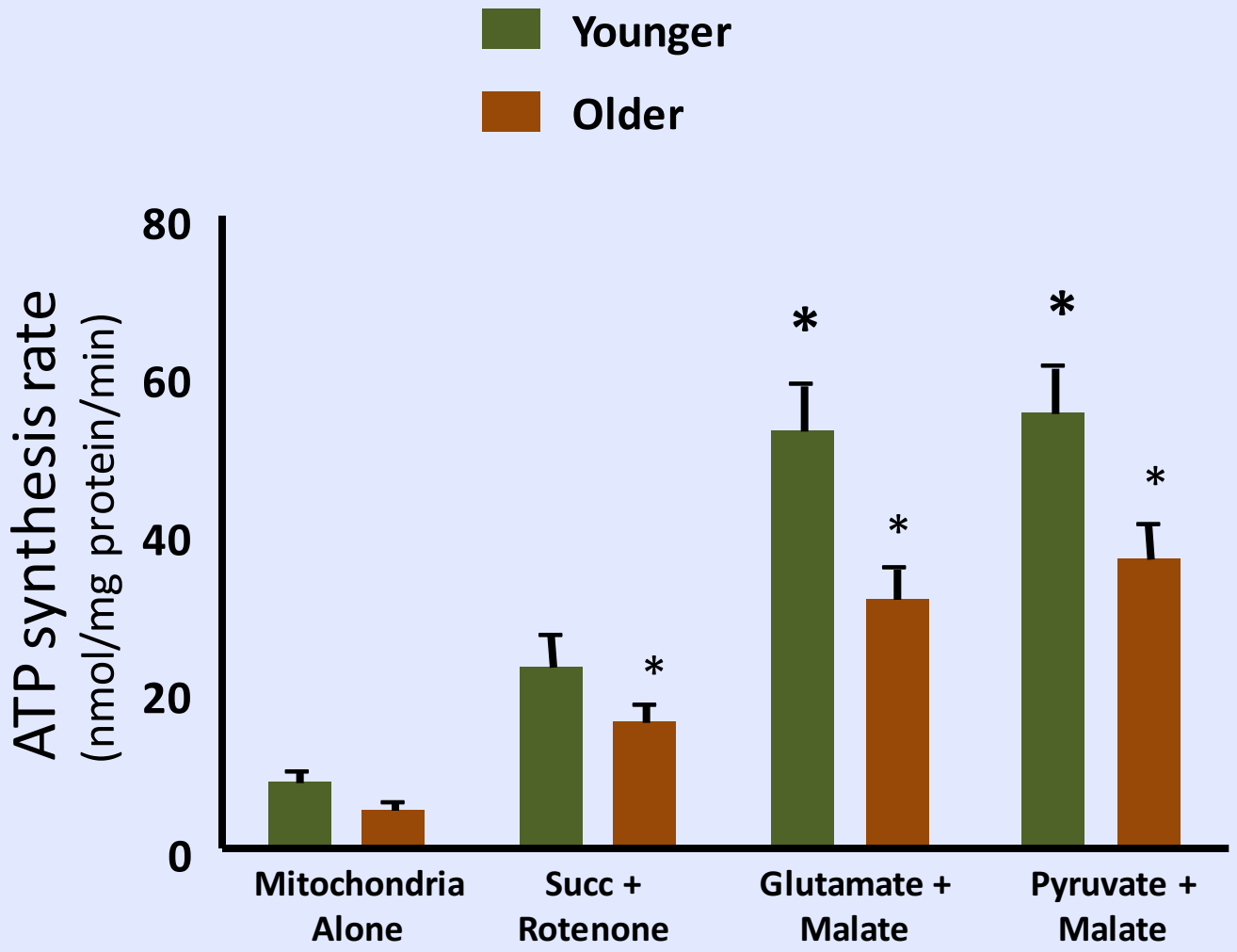
Effect of Age on Mitochondrial ATP Production





*P<0.05 vs. older group

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Aerobic Training Program

Warm up

Week 1

VO2 max

60% of effort

3 Day/week

20 mins/time

Wk 2 - Wk 4

65% of effort

3 Day/week

25 mins/time

Wk 5 - Wk 7

VO2 max

70% of effort

4 Day/week

35 mins/time

Wk 8 - Wk 11

80% of effort

4 Day/week

45 mins/time

Wk 12- Wk 15

VO2 max

VO2max and Insulin Sensitivity ~10%

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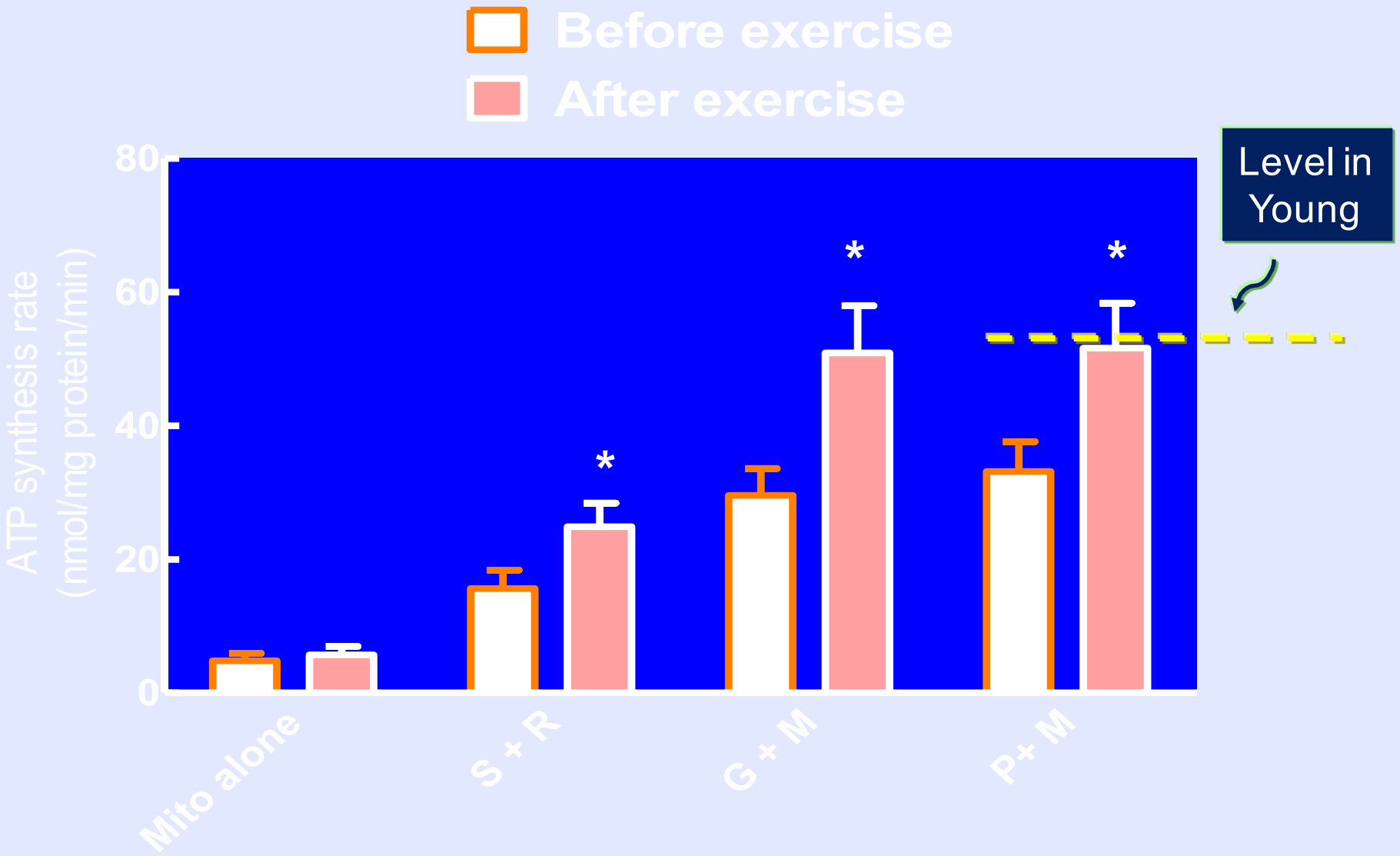
Effect of Aerobic Exercise on Mitochondrial ATP Production in Older Subjects



S+R: Succinate + Rotenone; G+M: Glutamate + Malate; P+M: Pyruvate + Malate

*, $P<0.05$ vs. older group before exercise.

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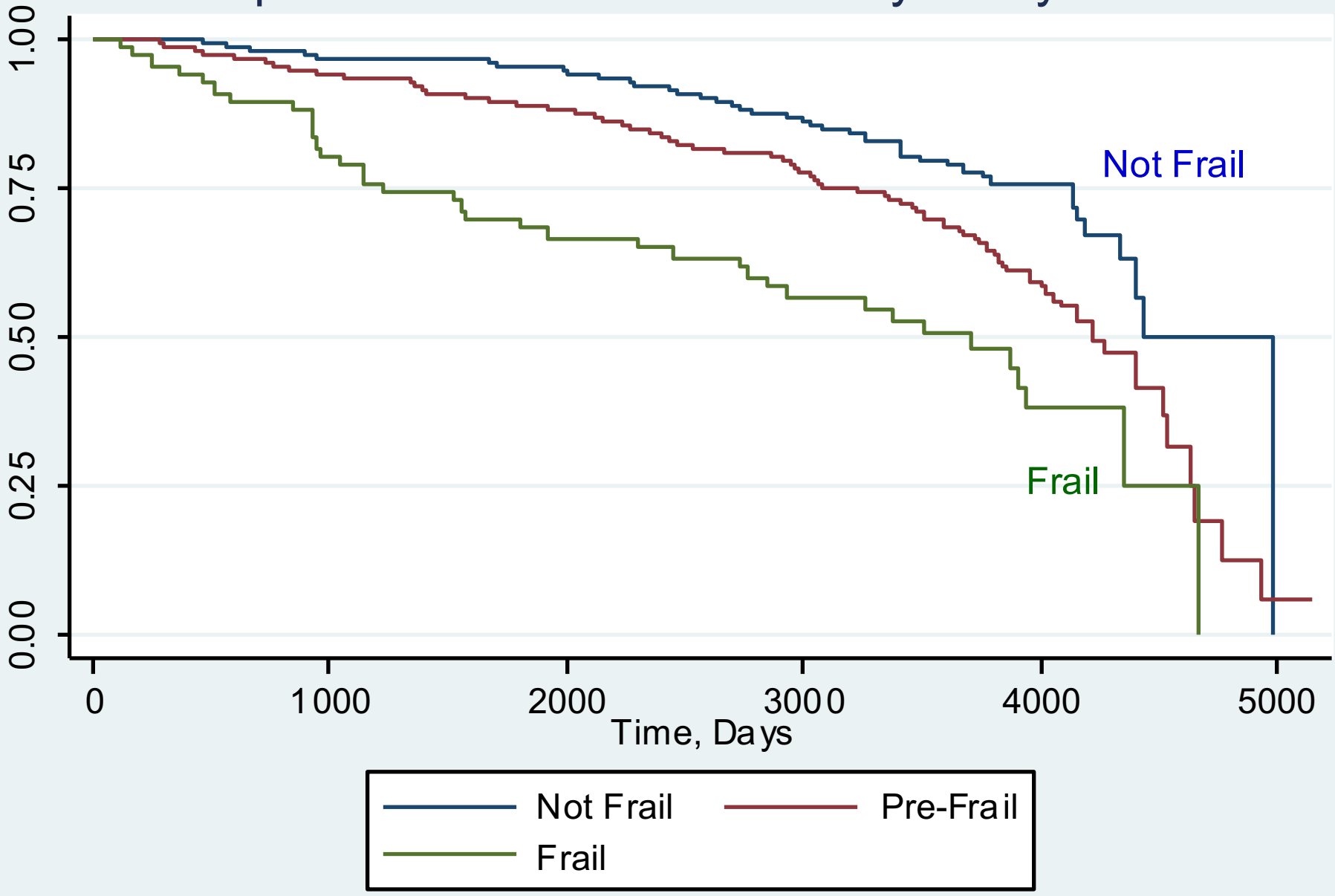
Recommendations

- Should we treat diabetes?
- Older subjects with diabetes
  - Higher rates of premature death, functional disability, HTN, CHD, and stroke
  - Higher rates of geriatric syndromes: polypharmacy, depression, cognitive impairment, urinary incontinence, falls, pain

Kaplan-Meier Survival Curves by Frailty Status



Espinoza, Hazuda (SALSA)

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ACCORD, ADVANCE and VADT Study Design

	ACCORD	ADVANCE	VADT
Major Endpoints	CV death, Non-fatal MI/Stroke	CV death, Non-fatal MI/Stroke, macrovacs event	CV death, Non-fatal MI/Stroke, CHF macrovacs event
Study	RCT	RCT	RCT
Design	Glucose Intensive vs Standard Arm 2x2 BP control +/-fenofibrate v placebo	Glucose Intensive vs Standard Arm 2x2 Perindopril +indamide v placebo	Glucose Intensive vs Standard Arm 2x1 All received BP and Lipid Rx

ACCORD Study Group, *NEJM* 2008, 358:2545-2559; ADVANCE Collaborative Group, *NEJM* 2008, 358:2560-2572; VADT Study Results ADA Scientific Session San Francisco, 2008; Diabetes Obesity and Metabolism, 2008

ACCORD, ADVANCE and VADT Demographics

	ACCORD	ADVANCE	VADT
# Participants	10,251	11,140	1,791
Population	North America	Europe /Asia	US
Male	62%	58%	97%
Age group mean age	40-79 62.2	>55 yrs 66	>40yrs 60.5
Non-Hispanic White Ethnic Representation	27% Hispanic, African Am	37% Asian	38% Hispanic, African Am, Native Am

ACCORD Study Group, *NEJM* 2008, 358:2545-2559; ADVANCE Collaborative Group, *NEJM* 2008, 358:2560-2572.
VADT Study Results ADA Scientific Session San Francisco, 2008; Diabetes Obesity and Metabolism, 2008

ACCORD, ADVANCE and VADT Baseline Clinical Characteristics

	ACCORD	ADVANCE	VADT
Weight	93.5	78 kg	97.2
BMI	32.2	28	31
Duration DM	10	8	11.5
Baseline A1c	8.3	7.5	9.4
Prior CVD	35%	32%	40%

ACCORD Study Group, *NEJM* 2008, 358:2545-2559; ADVANCE Collaborative Group, *NEJM* 2008, 358:2560-2572.
VADT Study Results ADA Scientific Session San Francisco, 2008; Diabetes Obesity and Metabolism, 2008

Therapeutic Approach: ACCORD, ADVANCE and VADT

	ACCORD	ADVANCE	VADT
Protocol	Provider Directed Formulary-based Poly-pharmacy	Stepped Approach: SU, Met, TZD, Insulin	Stepped Approach: Met BMI ≥27; SU BMI <27, TZD, Insulin
Meds (Inten v Std)			
Metformin	95 v 87 %	74 v 67 %	75 v 71%
TZD (Rosi)	91 v 58 %	17 v 11%	85 v 78%
Oral Hypoglycemic	87 v 74 %	94 v 84 %	55 v 45%
Insulin	73 v 58 %	41 v 24 %	90 v 74%
Exenatide	12 v 4 %	- - -	- - -
Follow-up intensive group	Q mo x 4, then q 2 mo	Q mo x 4, then Q 3 mo	-

ACCORD Study Group, *NEJM* 2008, 358:2545-2559; ADVANCE Collaborative Group, *NEJM* 2008, 358:2560-2572.
VADT Study Results ADA Scientific Session San Francisco, 2008; Diabetes Obesity and Metabolism, 2008

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Outcomes: Summary of ACCORD, ADVANCE and VADT

	ACCORD*	ADVANCE	VADT
A1C (%) (Intensive vs. Std)	6.4 vs.7.5 †	6.4 vs. 7.0 †	6.9 vs. 8.4 †
Nonfatal MI (%) (Intensive vs. Std)	3.6 vs 4.6% †	2.7 vs.2.8	6.3 vs. 6.1
CV Death (%) (Intensive vs. Std)	2.6 vs. 1.8 † (1.35 Hazard Ratio)	4.5 vs. 5.2	2.1 vs.1.7
Microvascular	-	nephropathy ↓ 21% retinopathy ↓ 5% NS	-
Take home	↓ risk MIs, but ↑ risk death in intensive arm	Glucose control has no impact on CV events, but ↓ Microvascular risk	Glucose control has no impact on CV events

*ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial halted intensive glucose group (2/6/08)

† significant difference between intensive and standard group

ACCORD Study Group, *NEJM* 2008, 358:2545-2559; ADVANCE Collaborative Group, *NEJM* 2008, 358:2560-2572.
VADT Study Results ADA Scientific Session San Francisco, 2008; Diabetes Obesity and Metabolism, 2008

Adverse Outcomes: ACCORD, ADVANCE and VADT

Intensive vs Std	ACCORD*	ADVANCE	VADT
Severe Hypoglycemia (% per yr)	3.0 vs 1.0	0.7 vs 0.4	-
Hypoglycemia requiring assistance (% per year)	4.6 vs 1.5	1.8 vs 0.6	2.3 vs 1.1
Weight Gain > 10Kg	27.8 % vs 14.1%	0.0 vs -1.0	-
Wt gain (Kg) Intensive group	3.5	0.7	6.8
Increased Mortality Rosigliatzone?	No	No	No

ACCORD Study Group, *NEJM* 2008, 358:2545-2559; ADVANCE Collaborative Group, *NEJM* 2008, 358:2560-2572.
VADT Study Results ADA Scientific Session San Francisco, 2008; Diabetes Obesity and Metabolism, 2008

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ACCORD, ADVANCE, and VADT Lessons Learned

- Intensive glucose control does not reduce CVD mortality in T2DM, and ***may*** increase risk, especially in patients with pre-existing CHD
- Aggressive A1c targets (<6.5%) were associated with a 3-fold increased risk of hypoglycemia
- No excess CVD mortality was seen with rosigliatazone

ACCORD, ADVANCE, and VADT Lessons Learned- Continued

- Intensive control associated with reduced risk for nephropathy in ADVANCE.
- To reach and maintain A1c targets of <6.5 required frequent adjustments of multiple anti-diabetic medications
- Aggressive targets (<6.5) are probably reasonable for healthy patients to reduce risk of micro-vascular complications

Recommendations (ADA, AGS)

Goals of Treatment (Tight Control?)

Consider:

1) Functional Status

2) Life expectancy

3) Cognitive Function

4) Clinical Heterogeneity (prone to complications?)

Recommendations (ADA, AGS)

Goals of Treatment (Tight Control?)

Functional, Cognitively Intact, Significant Life Expectancy:

- Similar Goals as Younger Person

- A1c ~ 7%

Recommendations (ADA, AGS)

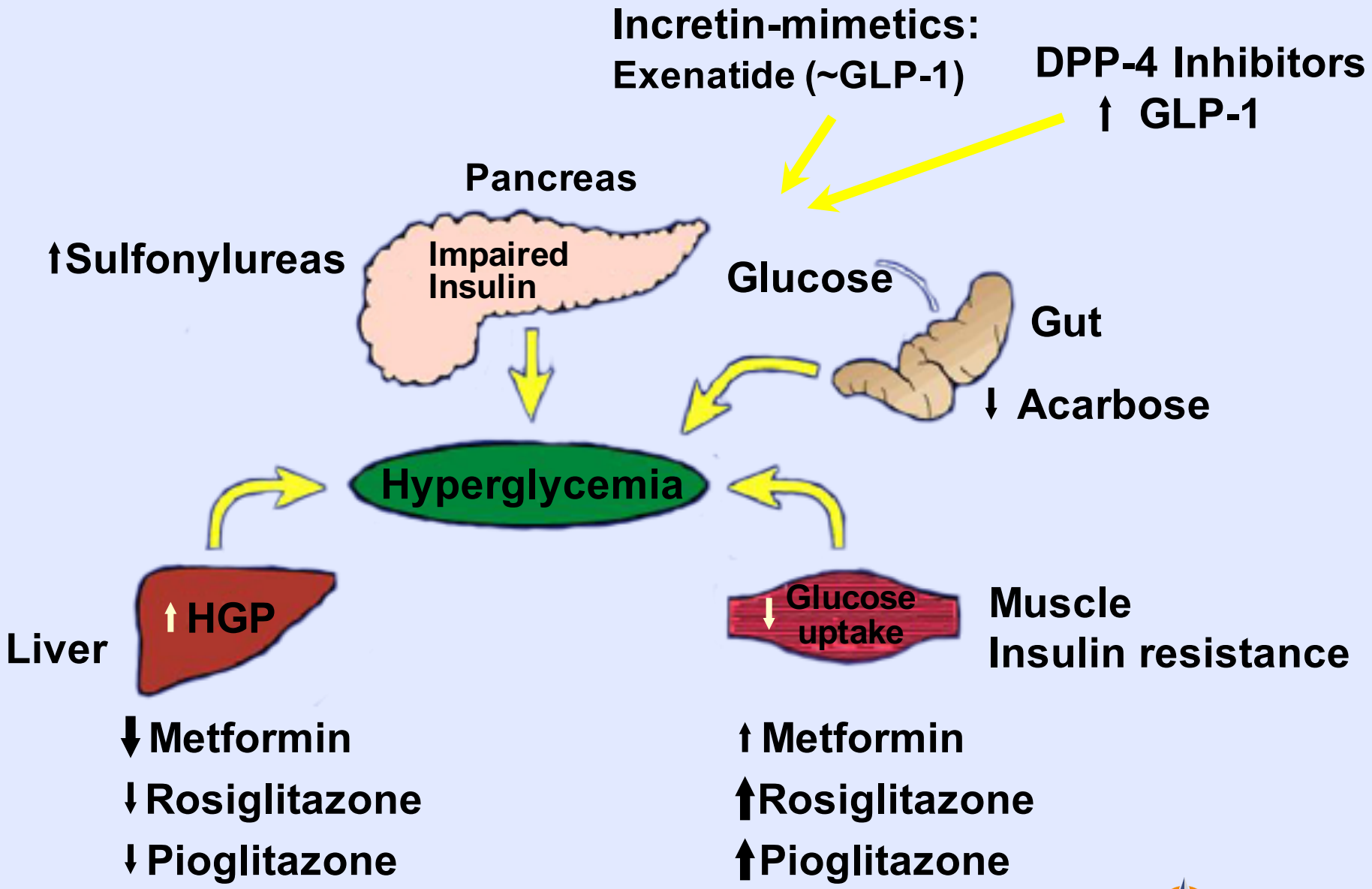
Goals of Treatment (Tight Control?)

Decreased Function/Cognition, Short Life Expectancy:

- Glycemic control can be relaxed

- Avoid hyperglycemic complications!

Oral Agents for the Treatment of T2DM



HGP = hepatic glucose production.

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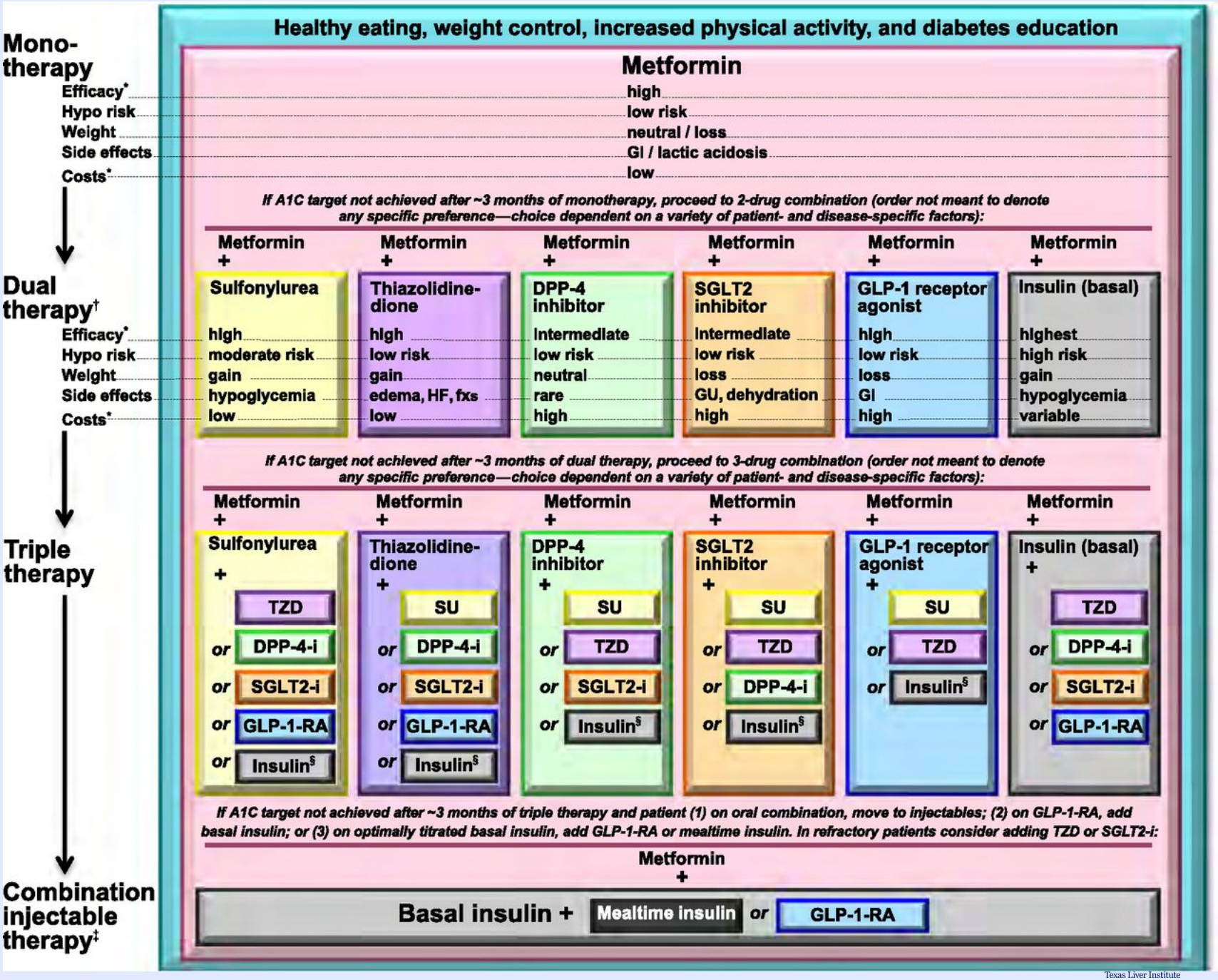
Antihyperglycemic therapy T2DM (ADA Standards, 2016)



Sulfonylureas

- Stimulate insulin release
- Lower A1c 1.5-2%
- Weight Gain
- Hypoglycemia 1-20%

Half life:	Chlorpopramide	36 h
	Glipizide	2-5 h
	Glyburide	10 h
	Glimepiride	5-9 h

* Aging: Half lives are prolonged

Metformin

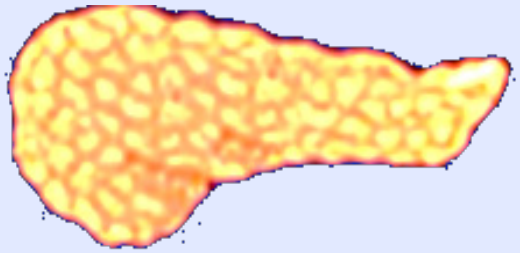
- Decrease Hepatic Glucose Output
- Lower A1c 1.4-2%
- No Weight Gain/Loss
- Noå Hypoglycemia
- Aging: Decreased Renal Clearance
- Precautions:
    - Lactic Acidosis Rare
    - Caution Age>80: Check Cr. Clearance
    - Contraindication: CHF, Renal/Liver Disease

TZDs (Pioglitazone/Rosiglitazone)

- Agonist of PPAR gamma nuclear receptor
- Improve insulin action in muscle and liver
- Lower A1c 0.3-1.9%
- Weight gain
- Hypoglycemia very rare (0.6%)
- Decreased bone density / increase bone fractures
- Aging: No difference in safety or effectiveness
- Precautions:
  - Check LFTs within 2 months then periodic.
  - Contraindication: CHF, Edema, Liver Disease, LFT >2.5 ULN

Incretin System

Delay Emptying



Insulin ↑
Glucagon ↓

GLP-1

Gut

Cleaved by DPP IV

Suppress Appetite

Incretin-Mimetics

Exenatide
Liraglutide

Agonist of GLP-1 (Incretin)

Increase Insulin Release/Inhibit Glucagon
Delay Gastric Emptying
Significant Weight Loss
No hypoglycemia unless used with Insulin or SU
Main Side Effect: Nausea (1/3)
Aging: No Difference in Safety or Effectiveness

Sitagliptin
Saxagliptin
Linagliptin

Inhibitors of DPP-IV (Breaks Down GLP-1)

Given Orally Once Daily
Increase Insulin Release/Inhibit Glucagon
No Weight Gain/Loss
No hypoglycemia unless used with Insulin or SU
Well Tolerated
Aging: No Difference in Safety or Effectiveness

Sodium-Glucose Transporter (SGLT)2 Inhibitors

- 180 g of glucose filtered daily
- All glucose is reabsorbed by proximal tubules (SGLT1 – 10% and SGLT2 – 90%)
- Dapagliflozin (5-10 mg), canagliflozin (100-300 mg), empagliflozin (10-25 mg) – all PO; once a Day
- A1c reduction – 0.7 – 1%
- Low risk of hypoglycemia
- Added benefits: weight loss (0.5-3 kg) and BP reduction (mean SBP reduced by 4 mmHg)

Sodium-Glucose Transporter (SGLT)2 Inhibitors

- Contraindicated: Severe liver and kidney failure (GFR less than 45-60 mL/min/1.73 m^2)
- Aging: Use low doses
- Issues:
  - Fungal infections (genitalia), UTI
  - Dehydration
  - Increase DKA
  - Decrease bone density / increase fracture risk

Summary

- Plan for Izzy?

Back to Dr. Liu

Izzy

- Visited PCP for checkup.
- Izzy recalled an ad campaign urging all baby boomers to get screened for chronic hepatitis C.
- While running bloodwork, her PCP ordered an HCV antibody test.
  - Her results came back AB+ and a subsequent HCV RNA test confirmed she had chronic HCV.
  - She was told she had genotype 1a and that she should go see Dr. Lawitz…

HCV: Is Metabolic Syndrome a Negative Predictive Factor?

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Chronic Hepatitis C

- Approximately 170 million people infected with HCV worldwide.
- Until 2011, only therapy available was peginterferon + ribavirin offering cures rates ~40%.
  - Primarily targeted towards the host.
- Standard of care now offers >90% cure rates with direct acting antiviral (DAA) agents.
  - Solely targeted towards the virus.

HCV Can Now Be Cured in Most Patients

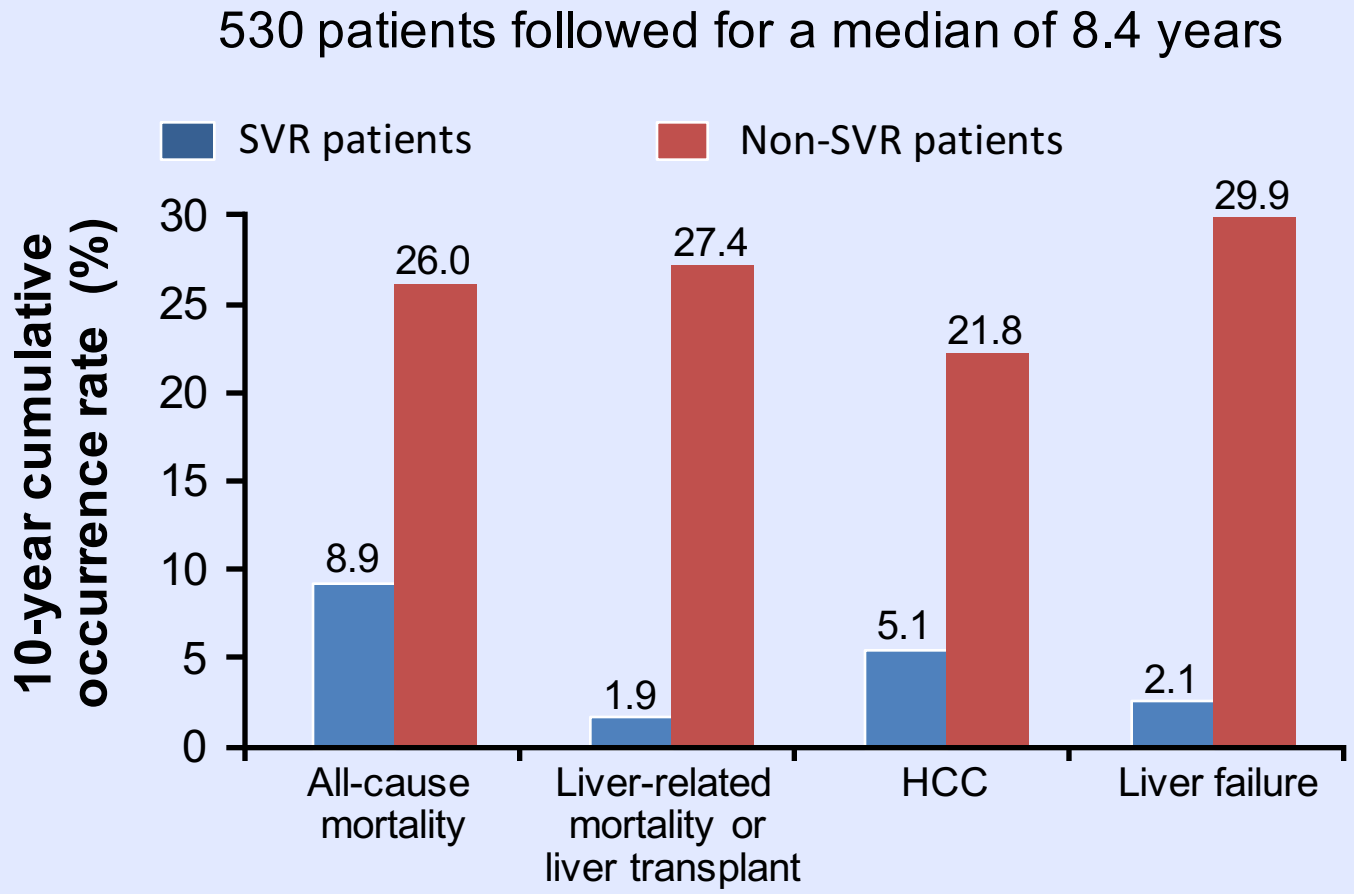
- Unlike HIV and HBV infection, HCV infection is a curable disease
  - HCV does not archive its genome
- What does cure mean?
  - Undetectable HCV RNA 12 weeks after completion of antiviral therapy
  - SVR12 is almost invariably durable

Ghany MG, et al. *Hepatology*. 2009;49(4):1335-1374.

SVR and All-cause Mortality in CHC Patients with Advanced Fibrosis

Baseline factors significantly associated with all-cause mortality:

- Older age
- GT 3 (2-fold increase in mortality and HCC)
- Higher Ishak fibrosis score
- **Diabetes**
- Severe alcohol use



Van der Meer A, et al. *JAMA* 2012; 308:2584–2593.

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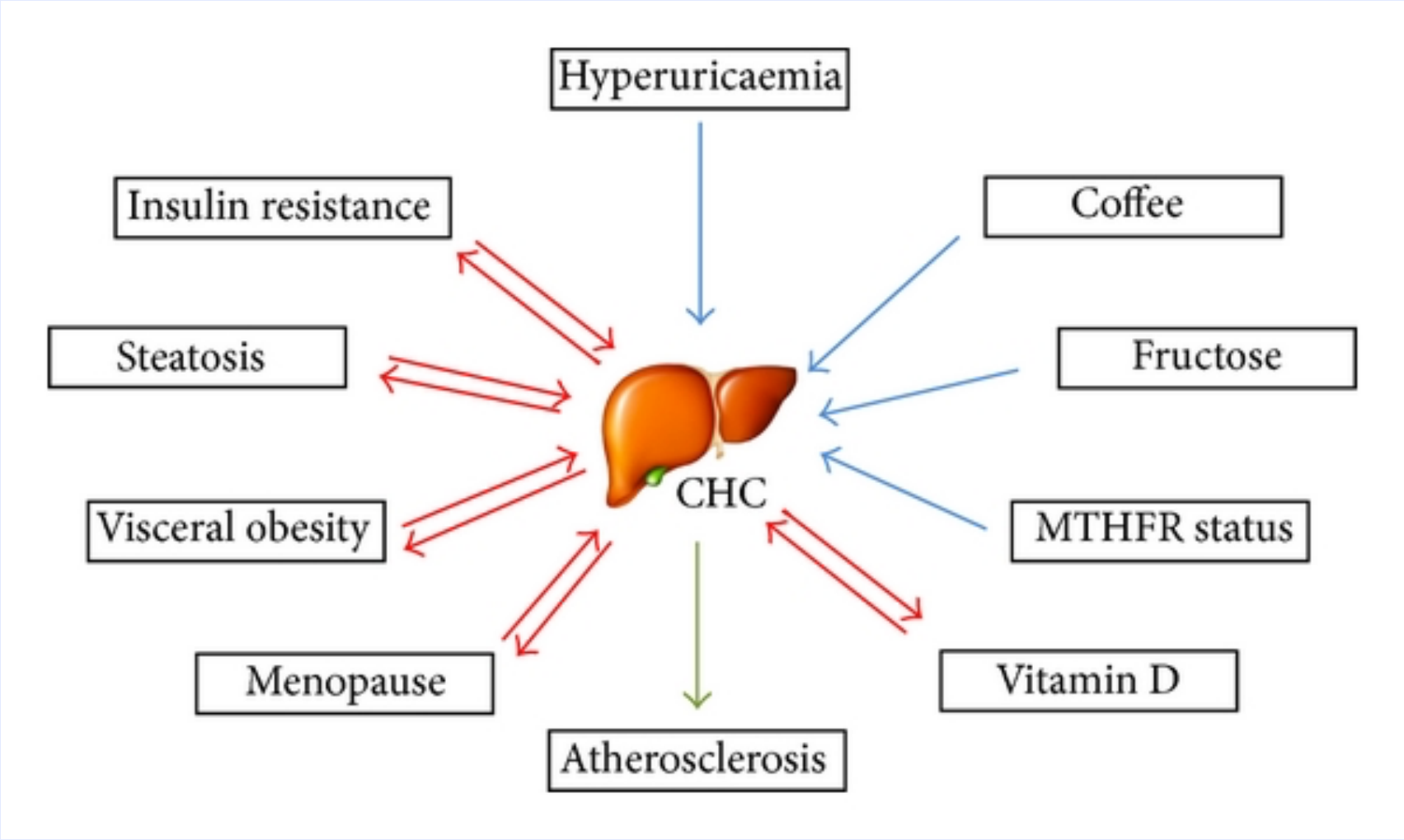
Factors Associated With Accelerated Fibrosis Progression

- **Modifiable**
  - **Alcohol consumption**
  - **Nonalcoholic fatty liver disease**
  - **Obesity**
  - **Insulin resistance**
- Non-modifiable
  - Fibrosis stage
  - Inflammation grade
  - Older age at time of infection
  - Male sex
  - Organ transplant

- **Viral**
  - Genotype 3
  - Coinfection with HBV or HIV

AASLD, IDSA, IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org.

Interplay Between Metabolic Factors and Chronic Hepatitis C (CHC)



Macaluso FS et al., BioMed Research International, Volume 2013 (2013), Article ID 564645, http://dx.doi.org/10.1155/2013/564645

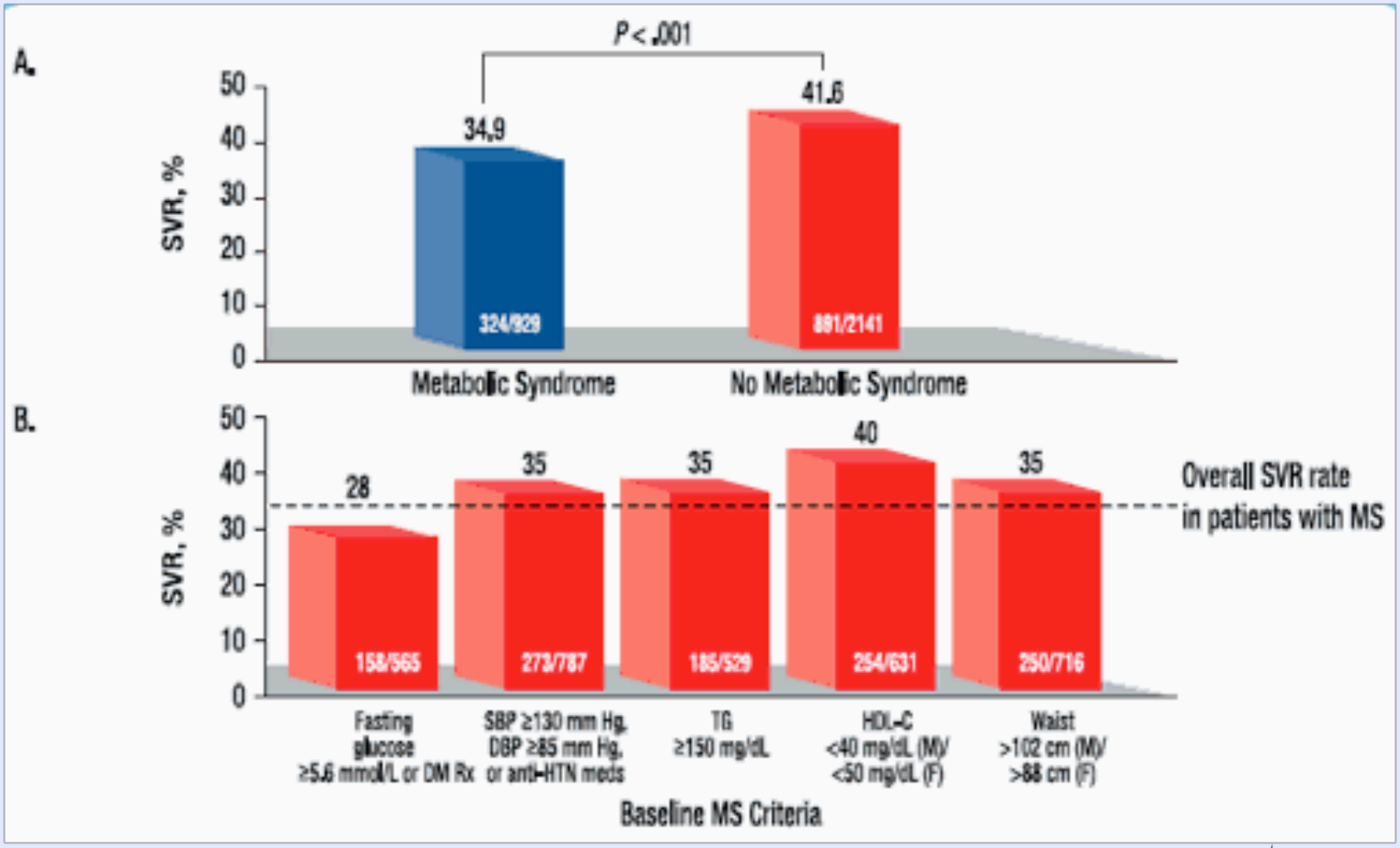
HCV and Metabolic Syndrome Factors

- Individuals with HCV infection are predisposed to develop T2DM at least one decade earlier than those without HCV infection.[1]
- Eradication of HCV infection is associated with reduced incidence of glucose metabolism disturbances after treatment, independent of other predisposing factors.[2]
- Pioglitazone does not produce significant reductions in viral load.[3]

[1]Sulkowski M et al., *Ann Intern Med* 2000; 133: 592-599. [2]Arase Y et al., *Hepatology* 2009; 49: 739-744; [3]Harrison SF et al., *J Hepatol* 2010; 52(Suppl 1): S129.

Peginterferon + Ribavirin: The Distant Past

Peginterferon/Ribavirin in GT1: Presence of Metabolic Syndrome Led to Lower Response Rates



Sulkowski M et al., EASL 2010

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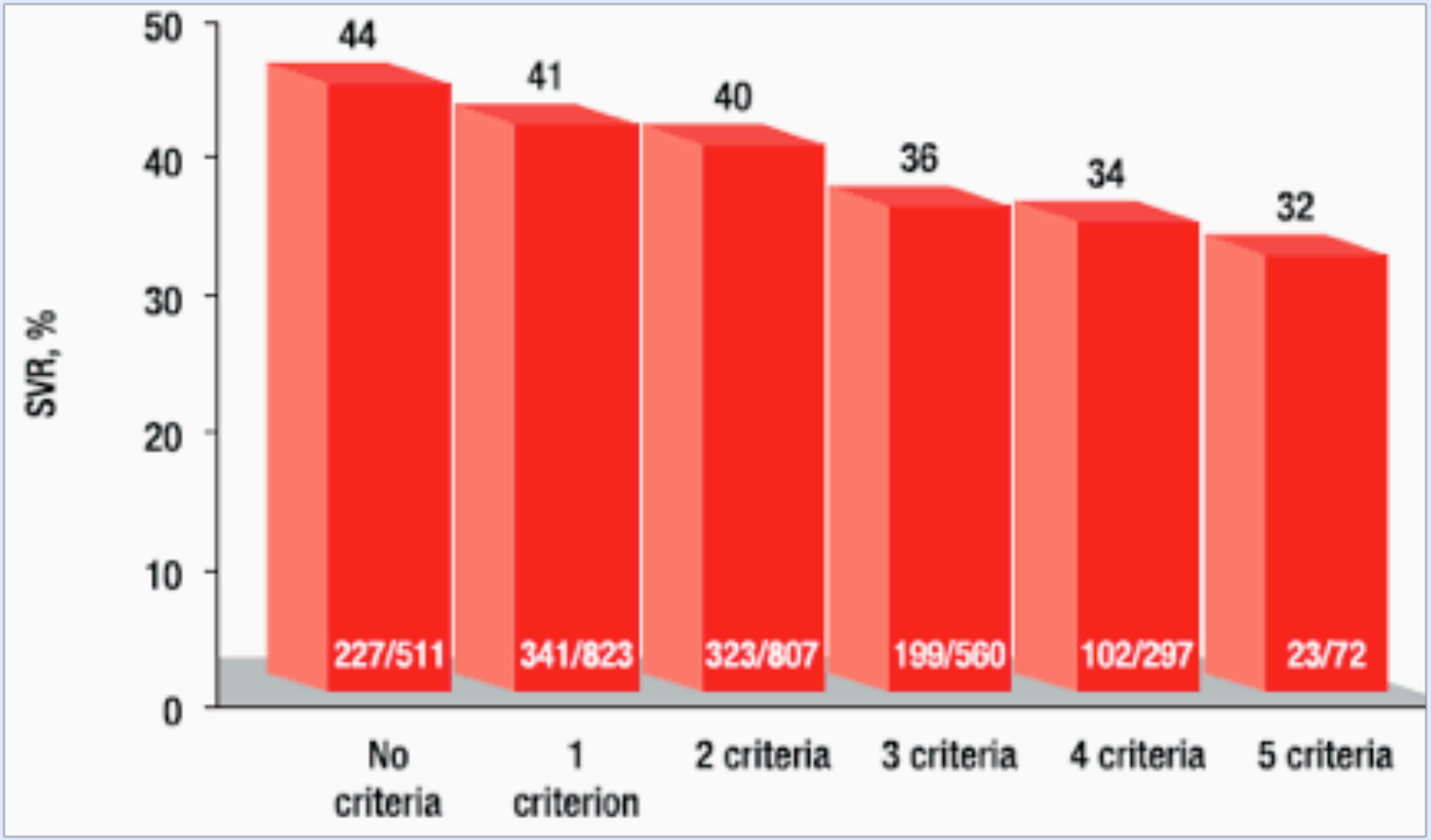
The Higher Number of Metabolic Syndrome Criteria Met, The Lower The Chance of Cure (SVR) with PEG-IFN/RBV Treatment



Sulkowski M et al., EASL 2010

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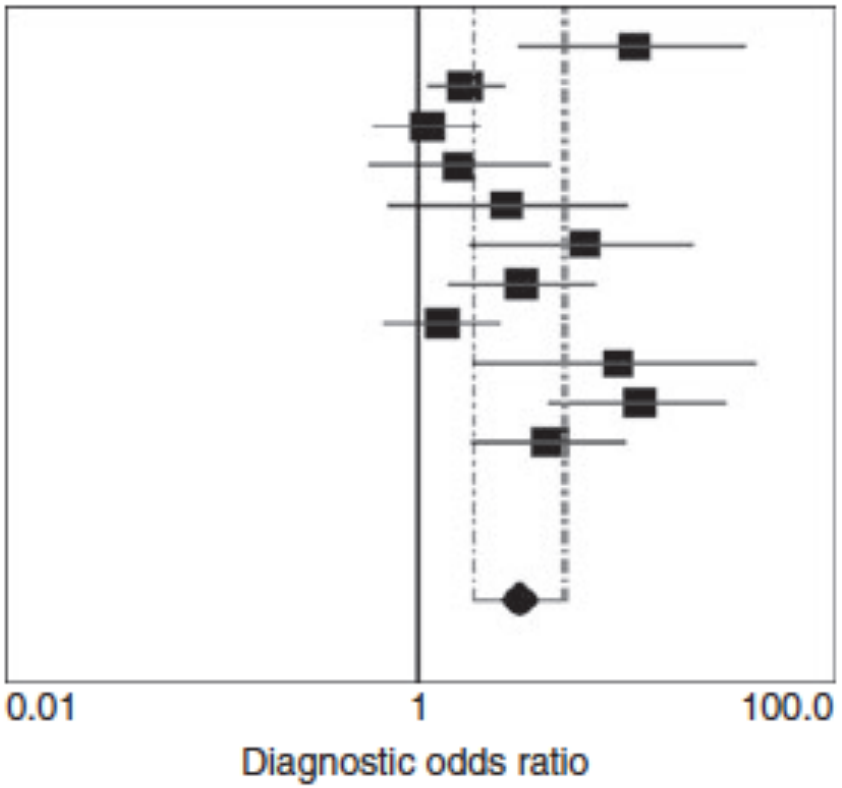
Insulin Resistance Defined by HOMA-IR> 2 and Achievement of SVR with PEG-IFN/RBV



	Diagnostic OR (95% CI)
Chu *et al.*	10.64 (3.06–36.95)
Conjeevaram *et al.*	1.69 (1.11–2.58)
Fattovich *et al.*	1.11 (0.62–2.01)
Grasso *et al.*	1.58 (0.58–4.29)
Mayaaki *et al.*	2.65 (0.72–9.80)
Mizuta *et al.*	5.98 (1.76–20.32)
Romero-Gómez *et al.*	3.13 (1.42–6.88)
Fattovich *et al.*	1.30 (0.69–2.46)
Poustchi *et al.*	8.77 (1.87–41.18)
Khattab *et al.*	11.26 (4.30–29.47)
Moucari *et al.*	4.18 (1.82–9.61)

Random effects model
Pooled diagnostic odds ratio = 3.05 (1.88–4.93)
Cochran-Q = 35.90; df = 10 (P = 0.0001)
Inconsistency (I^2) = 72.1 %
τ^2 = 0.4363

- Differences greatest in individuals with higher insulin resistance and individuals with advanced fibrosis

Eslam M et al., *Alimentary Pharmacology and Therapeutics*, 2011; 34: 297-305

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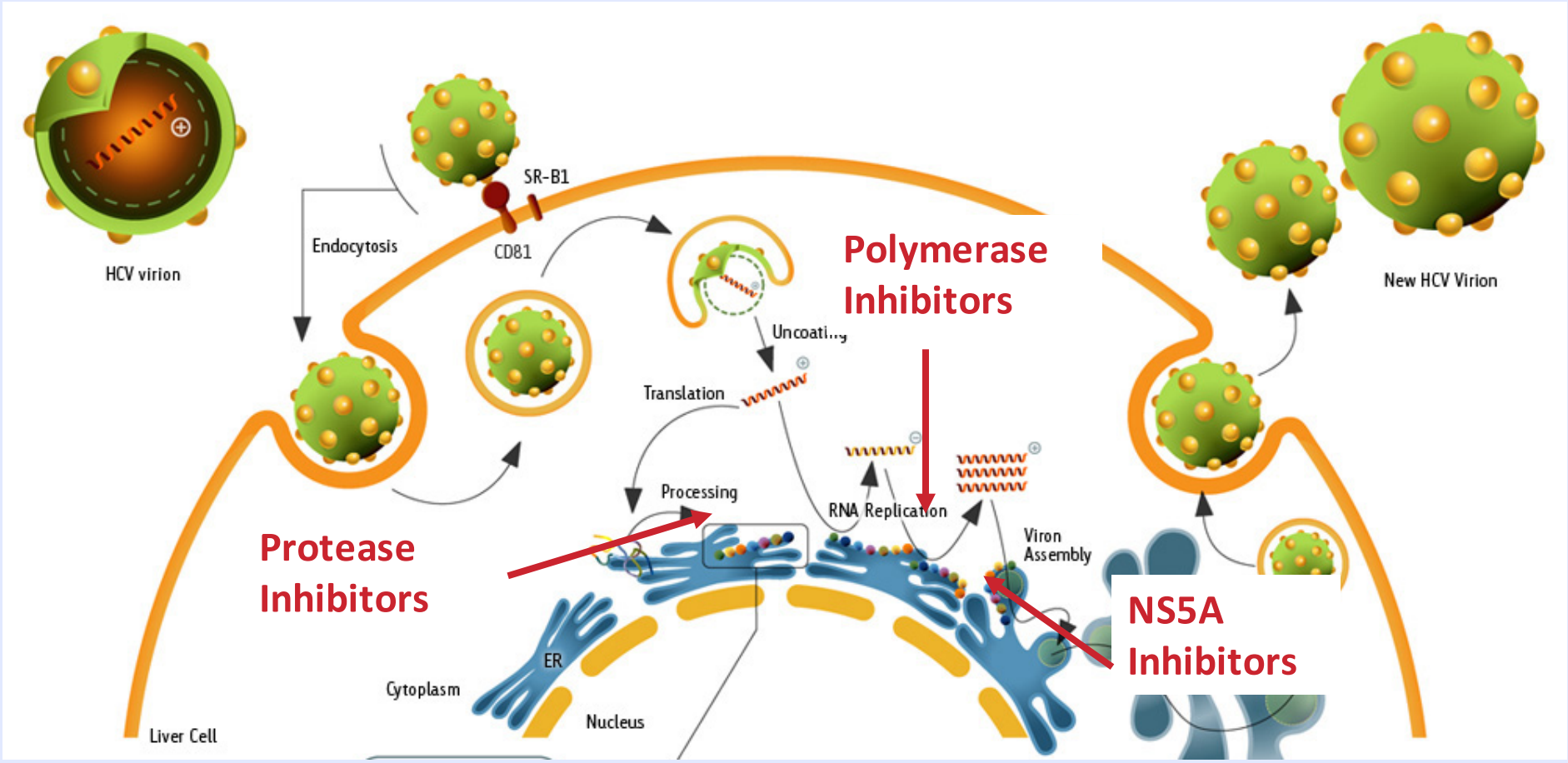
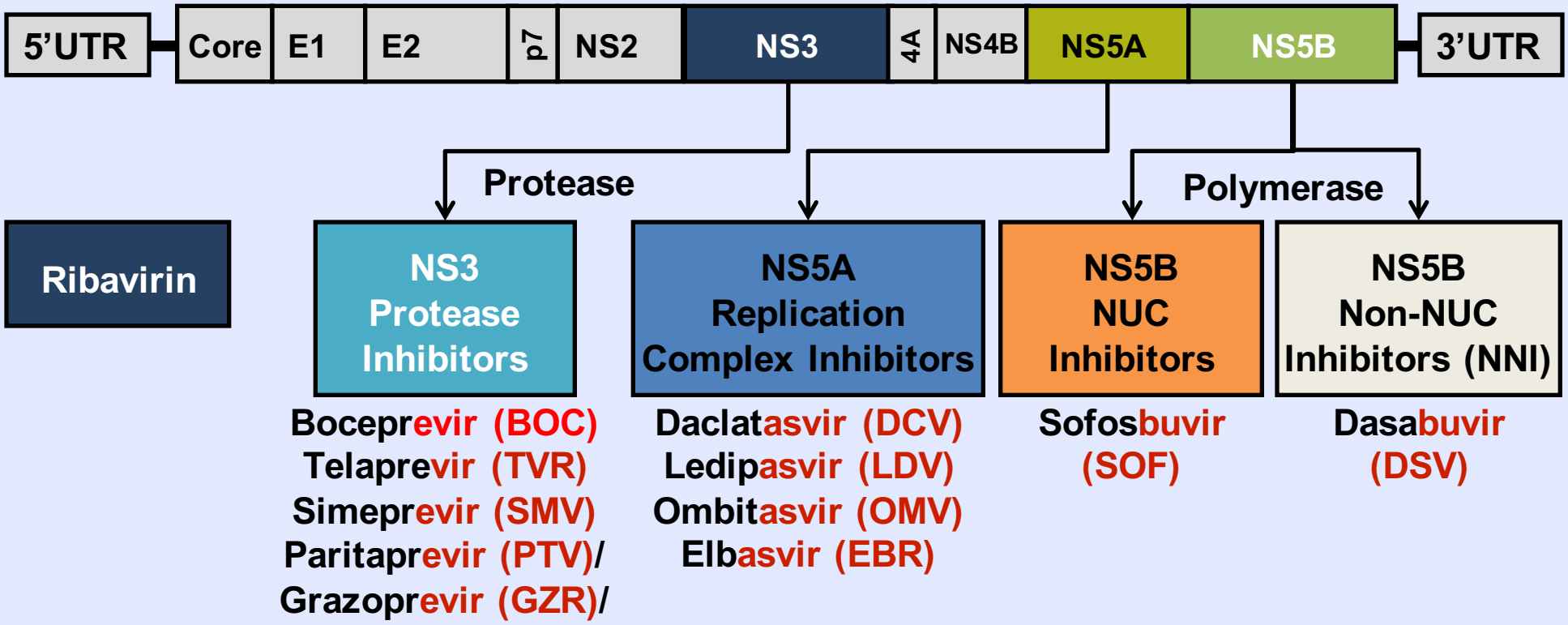
Is Direct-Acting Antiviral Therapy Also Negatively Impacted by Metabolic Syndrome?

The HCV Lifecycle: Multiple Targets



Manns. *Nat Rev*. 2007.

FDA Approved Direct-Acting Antiviral Agents (DAAs) from Multiple Classes



Note the common root name for each drug class

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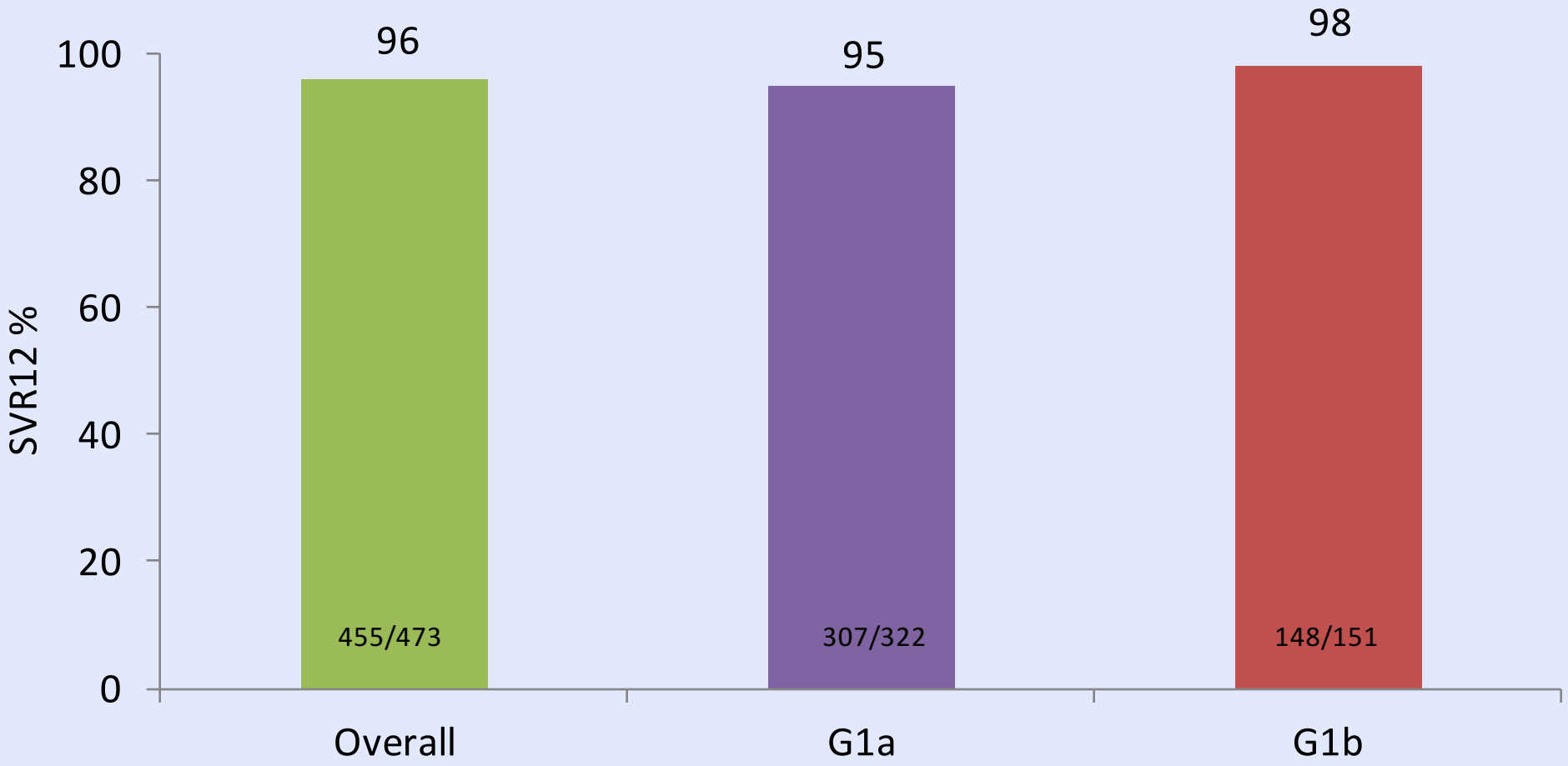
Principles of All Oral Regimens for HCV

- Combine drugs from different classes
  - Target multiple targets to increase efficacy
  - Decrease risk of viral resistance
- If done properly
  - Near universal efficacy
  - Shortened duration of therapy
  - Adverse events have minimal impact on patient's quality of life

Ombitasvir/Paritaprevir/r + Dasabuvir + RBV: SAPPHIRE-I

Genotype 1, treatment-naïve, noncirrhotic,12 weeks, n=473



Feld JJ, et al. *N Engl J Med*. 2014;370:1594-1603.

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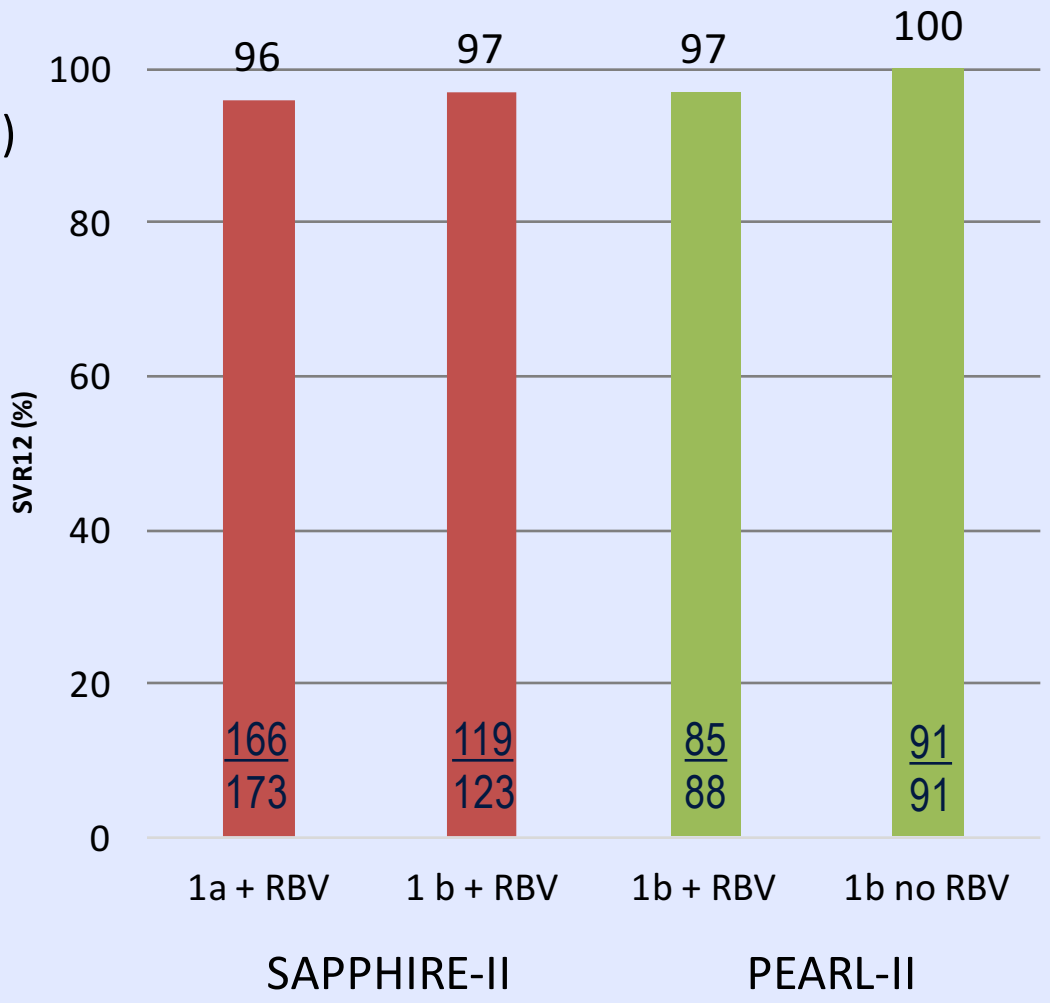
SAPPHIRE-II & PEARL-II

Ombitasvir/Paritaprevir/r + Dasabuvir, No Cirrhosis

- Ombitasvir/paritaprevir/r + dasabuvir
- Treatment-experienced patients (PEG/RBV)
- Duration: 12 weeks
- SAPPHIRE-II
  - 1a and 1b
  - Ribavirin for all
  - Sample size 394
- PEARL-II
  - 1b only
  - +/- ribavirin
  - Sample size 179



Zeuzem S, et al. *N Engl J Med.* 2014;370:1604-1614.
Andreone P, et al. *Gastroenterology.* 2014;147:359-365.

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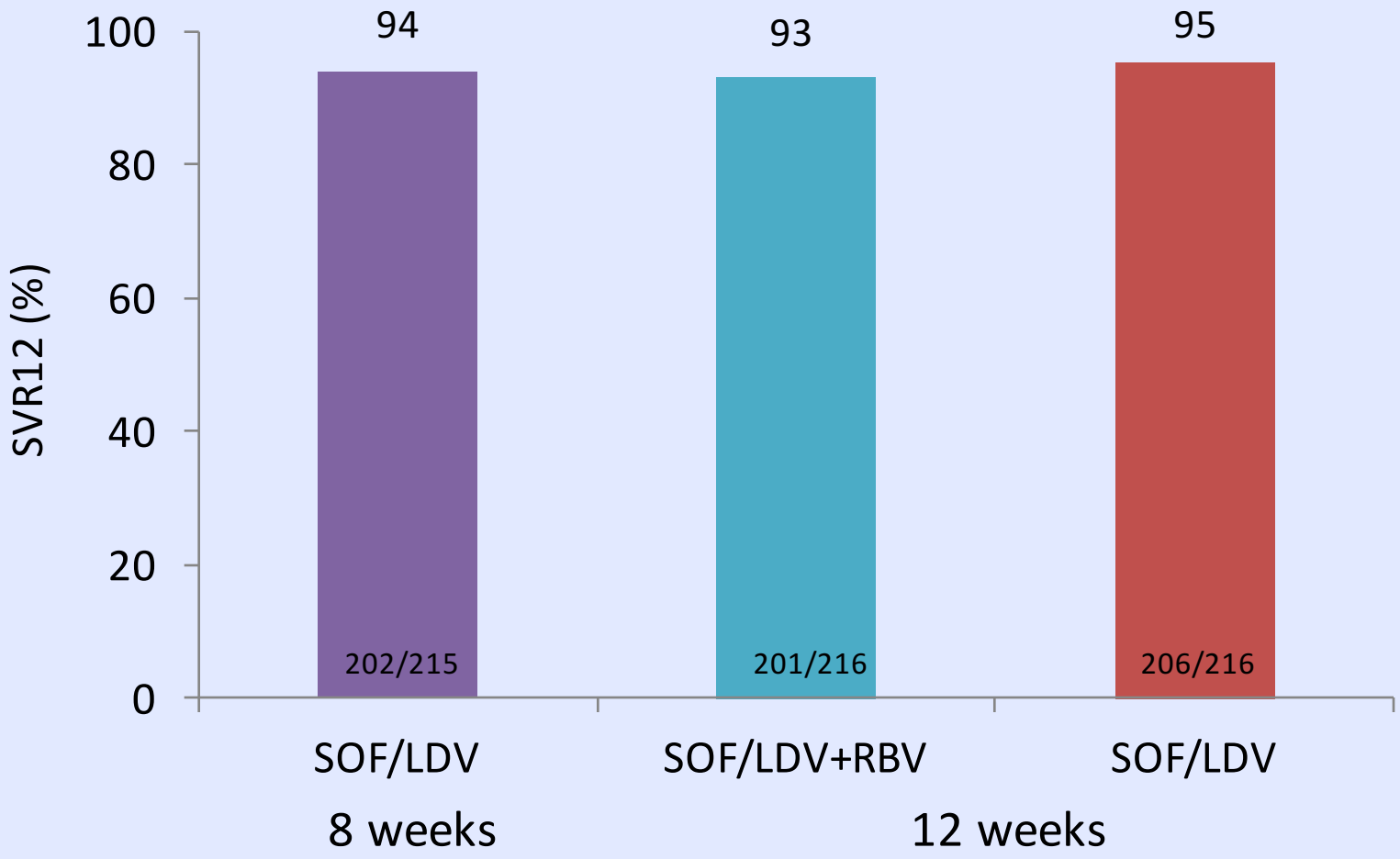
ION-3: Ledipasvir/Sofosbuvir ± RBV GT1 Treatment Naïve Noncirrhotic: 8 Weeks vs 12 Weeks



Kowdley K, et al. *N Engl J Med.* 2014:370:1879-1888.

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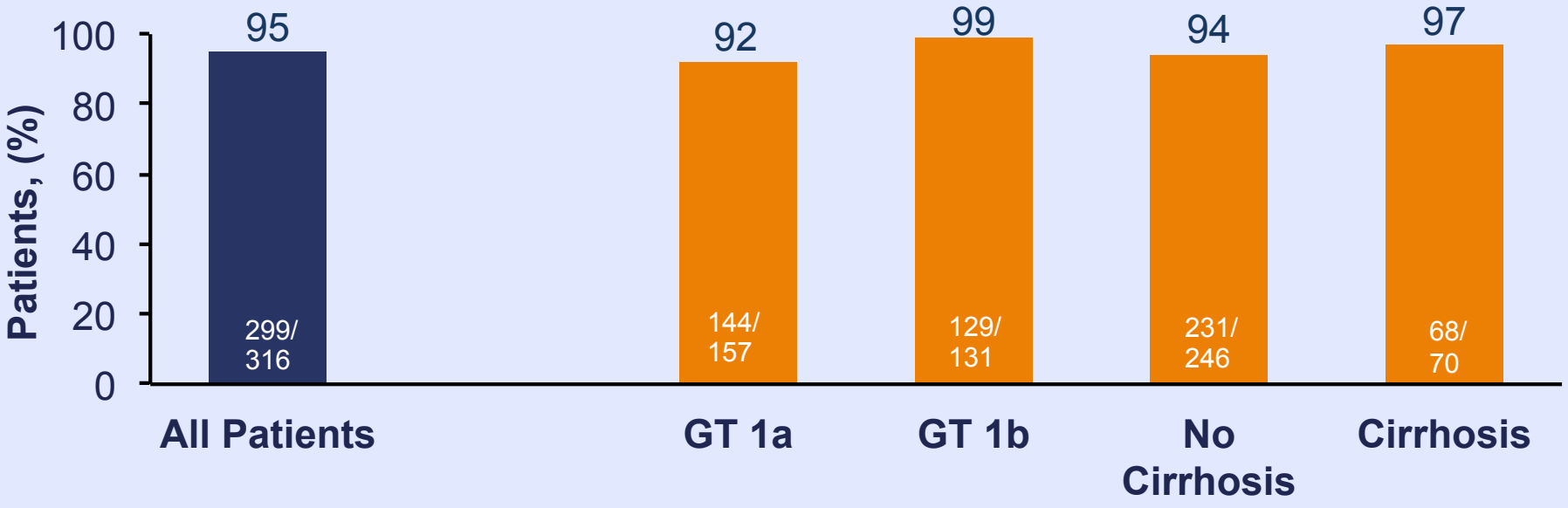
C-EDGE: Grazoprevir/Elbasvir (GZR/EBR) for 12 Weeks in GT 1 Treatment-Naïve Patients

- 67% of failures due to relapse
- Most common adverse events were headache, fatigue, nausea and arthralgia (no difference from placebo arm)



Zeuzem et al., Abstract G07, EASL 2015; published online at *Ann Intern Med* (www.annals.org) on 24APR15.

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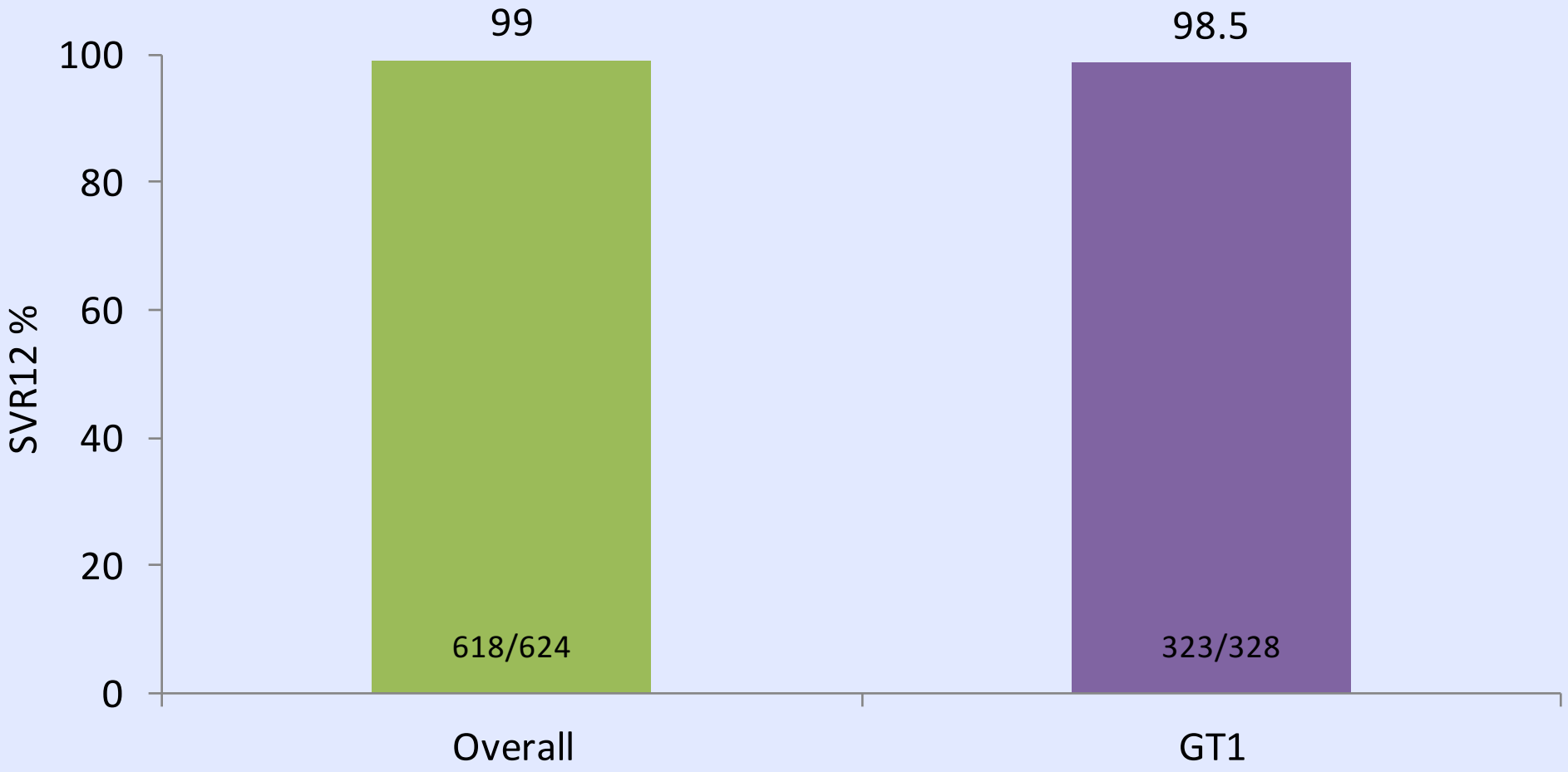
ASTRAL-1: Sofosbuvir/Velpatasvir ± RBV x 12 Weeks in Tx-naïve Patients



Velpatasvir (VEL, GS-5816): pangenotypic HCV NS5A inhibitor; 22.3% Cirrhosis

Feld JJ, et al. NEJM 2015

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Reviewing Potential Drug: Drug Interactions is Important

Is the patient taking any drugs that could have a potential drug:drug interaction with a DAA?

- Antiarrhythmics e.g. digoxin, amiodarone
- PPIs/acid reducing agents
- Herbal supplements
- HIV antivirals e.g. tenofovir, lopinavir/ritonavir
- Drugs that are renally cleared

Is a co-medication contraindicated or is a dose adjustment required?

Can plasma levels of co-medications be easily monitored to ensure they remain within the established therapeutic range?

Great reference tool: www.hep-druginteractions.org

Summary

- Treating patients with diabetes and other components of metabolic syndrome is safe and highly efficacious.
- Multiple all-oral options with cure rates >95%.
- Typical treatment duration is 12 weeks (as short as 8 weeks in some; up to 24 weeks in others).
- Important to review concomitant medications and make appropriate modifications, if necessary.

Back to Dr. Liu

Izzy

- Treated with a DAA regimen, achieved SVR12 and was cured of HCV.
- 3 months later was involved in motor vehicle accident requiring 6 months of PT.
- In that time period, she stopped exercising and gained 30 lbs.
- BMI now 37.
- Hypertension, T2DM and dyslipidemia under control.
- Her friend recently underwent bariatric surgery and looked great and Izzy wants to know if she can do the same…

Obesity Management

Nicole Basa, M.D., F.A.C.S.
Assistant Professor of Surgery,
Texas A&M Medical School
Cedar Park Surgeons, P.L.L.C.
Cedar Park, Texas

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Obesity Pandemic

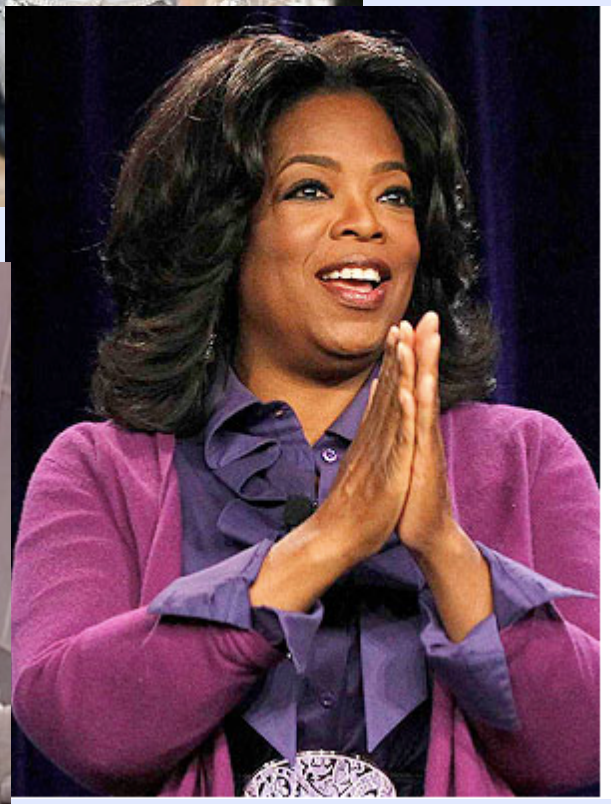
- In the United States it is more common to be overweight than not.
  - Over 2/3 of the population meet the criteria
    - BMI over 25
  - Over 1/3 are obese
    - BMI over 30

Strategies for Weight Loss

- Diet and Exercise
- Medications
- Surgery

Diets

- An estimated 60 million Americans go on some form of diet each year.
- Over $50 billion a year is spent on diets, pills and other dietary products.
- Programs tend to be good at initial weight loss but does not include counseling to sustain weight loss.
- Research has shown that 95% of those who lose weight gain it back within 3 years.



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Diet and Exercise

- Persistent Metabolic Adaptation 6 years after "The Biggest Loser" Competition, *Obesity Biology and Integrated Physiology 2016*
  - 14 out of 16 "Biggest Loser" competitors from season 8 were followed for 6 years
    - Resting Metabolic Rate Measured
      - RMR at baseline was 2607 kcal/day and fell to 1996 kcal/day after the 30 week competition
      - "Metabolic Adaptation" or "adaptive thermogenesis," occurs

Metabolic Adaptation

- Weight loss is accompanied by a slowing of resting metabolic rate (RMR)
- The RMR after weight loss is lower than would be expected based on the measured changes in body composition
- In a study several years ago 16 people who competed in “Biggest Loser” body composition was measured
  - Weight was lost primary from fat mass (FM) with relative preservation of fat-free mass (FFM)

Diet and Exercise vs. Surgery

- Metabolic Adaptation increased 6 years after the “Biggest Loser” competition
- Bariatric Surgery- Roux en Y Gastric Bypass patients had significant metabolic adaptation 6 months after surgery and no detectable metabolic adaptation after 1 year
  - It is possible that the lack of long-term metabolic adaptation may reflect a permanent resetting of the body weight set-point

Weight Loss Long-term

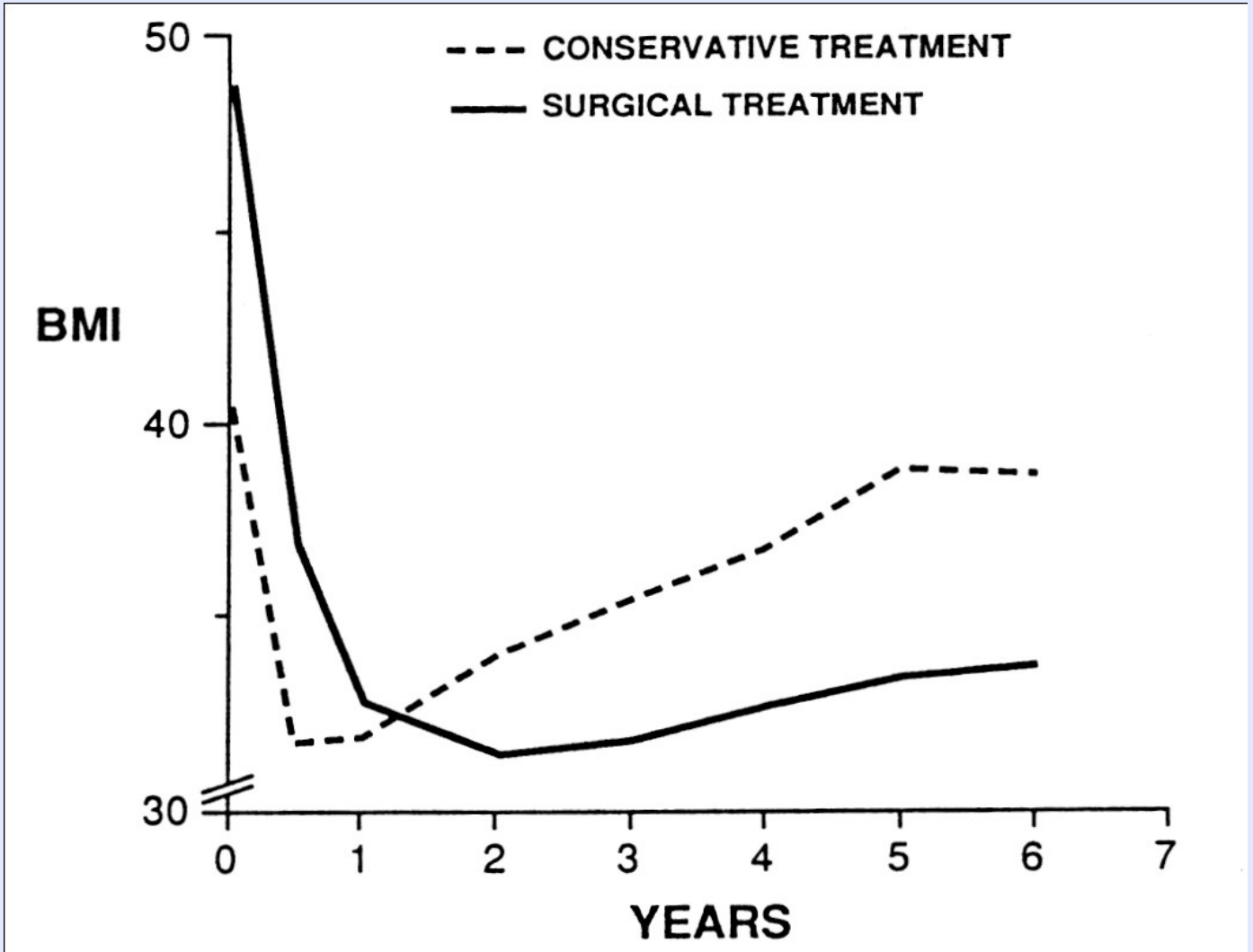

Figure 3. The weight loss curves for patients treated conservatively and surgically (Adapted from Martin FL et al. Comparison of the costs associated with medical and surgical treatment of obesity. Surgery 1995; 118: 599-607. Used with permission).

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Medications

- Qsymia (Phentermine/Topiramate)
  - 5-10% weight loss
- Lorcaserin(Belviq)
  - Serotonin 2C receptor agonist in hypothalamus
- Liraglutide 3.0 mg (Saxenda)
  - GLP 1 agonist

Bariatric Surgery

- Basic Criteria:

  BMI ≥ 40 or

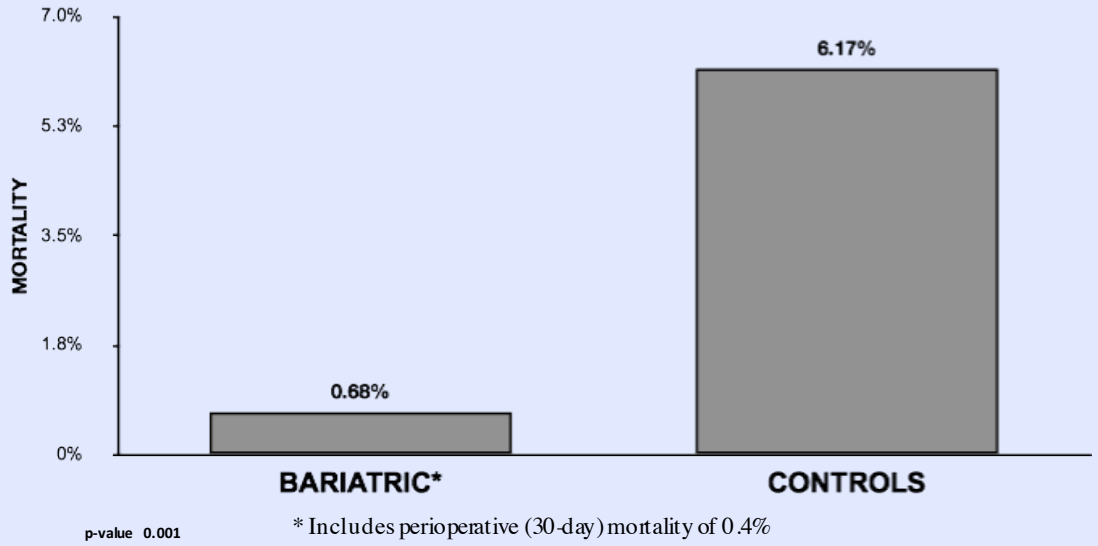
  BMI ≥ 35 with one or more obesity related comorbidity

Most likely **insurance approved** comorbidities:

1. Sleep Apnea
2. Diabetes Mellitus
3. Hypertension on multiple medications

Mortality Reduction

Surgical Patients Had Nine Times Lower Risk of Dying Within the Study Period



* Includes perioperative (30-day) mortality of 0.4%

Christou NV, Sampalis JS, Liberman M, et al. Surgery Decreases Long-Term Mortality, Morbidity, and Health Care Use in Morbidly Obese Patients. Annals of Surgery 2004;240(3):416-424.

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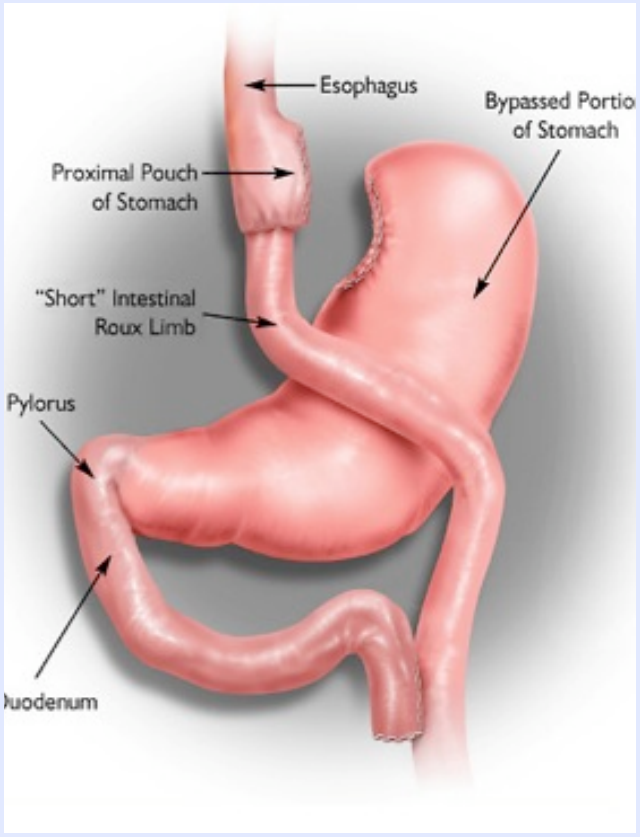
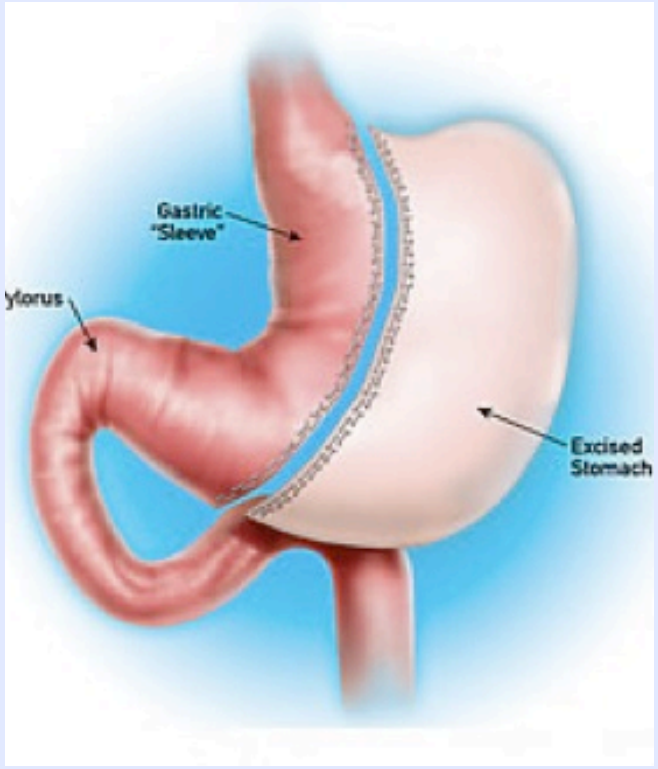
Gastric Bypass



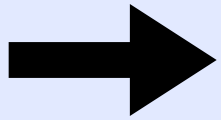
75% Excess Wt. Loss

Malabsorptive
& Restrictive

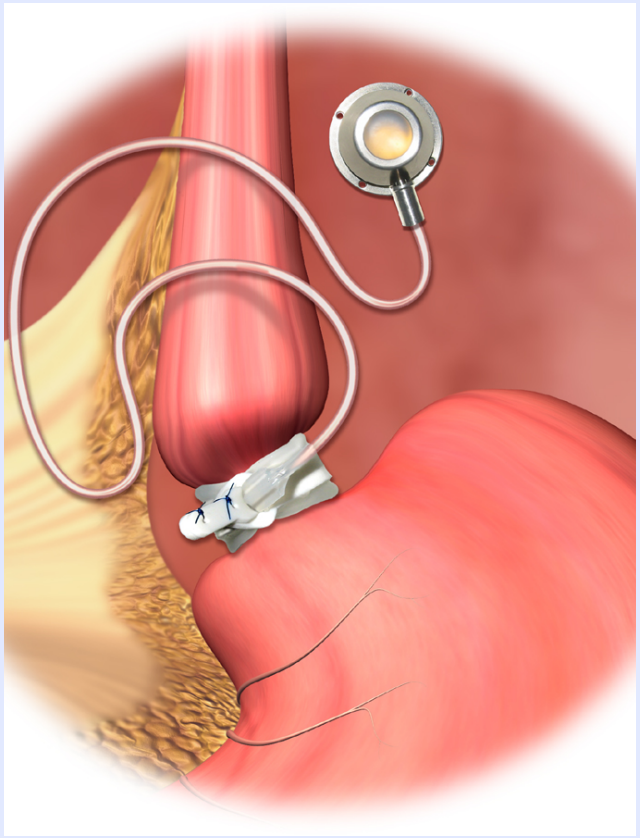
Sleeve



65% Excess Wt. Loss



Lap Band



40% Excess Wt. Loss

Restrictive

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Hunger Hormones

- Ghrelin
  - Increases right before a meal
  - Appetite stimulant

“Fullness” Hormones

- **GLP-1 and Insulin**
  - Decreases food intake
  - Appetite suppressant
- **Peptide YY**
  - Causes fullness after a meal
  - Appetite suppressant

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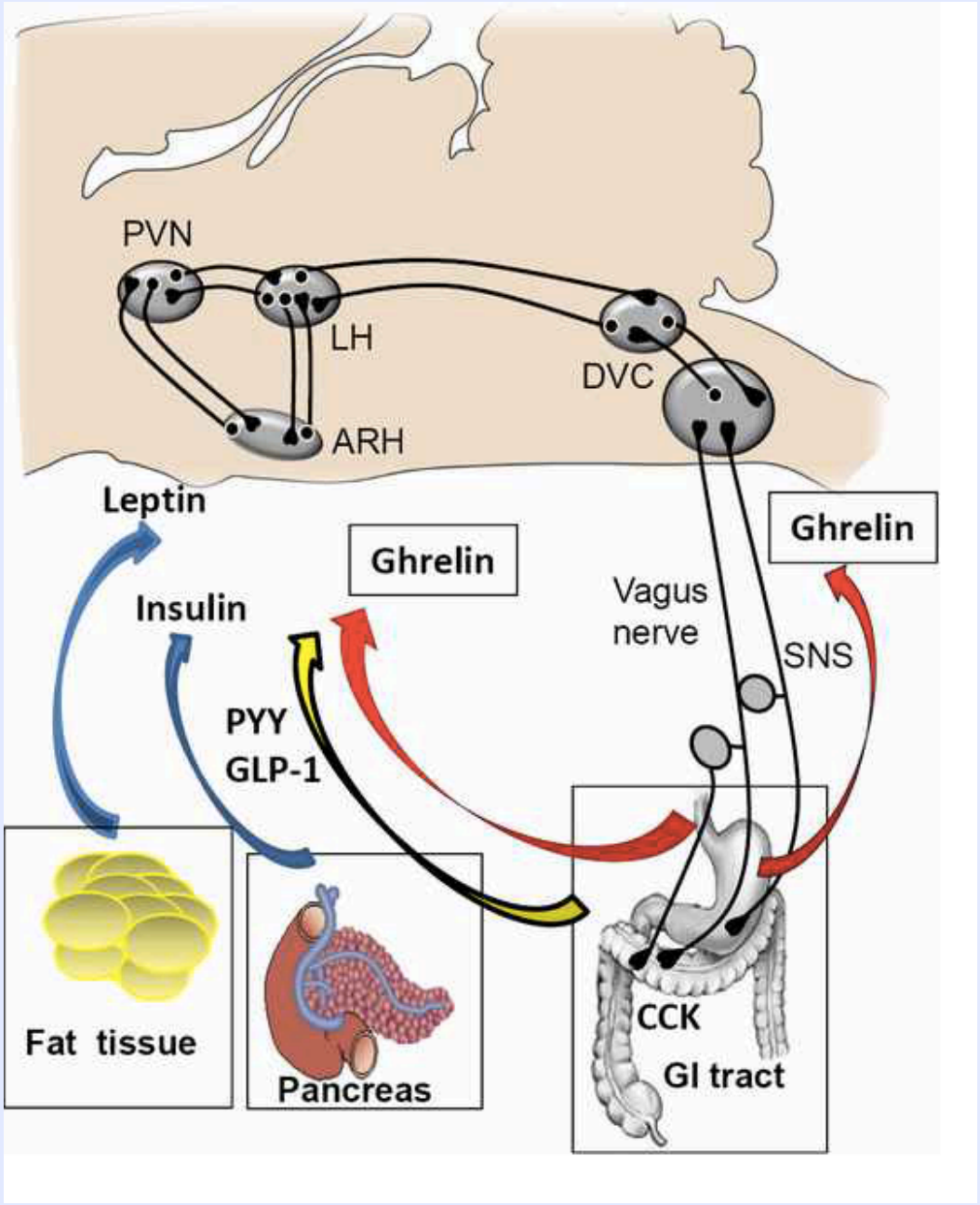
Neurohormonal control of appetite



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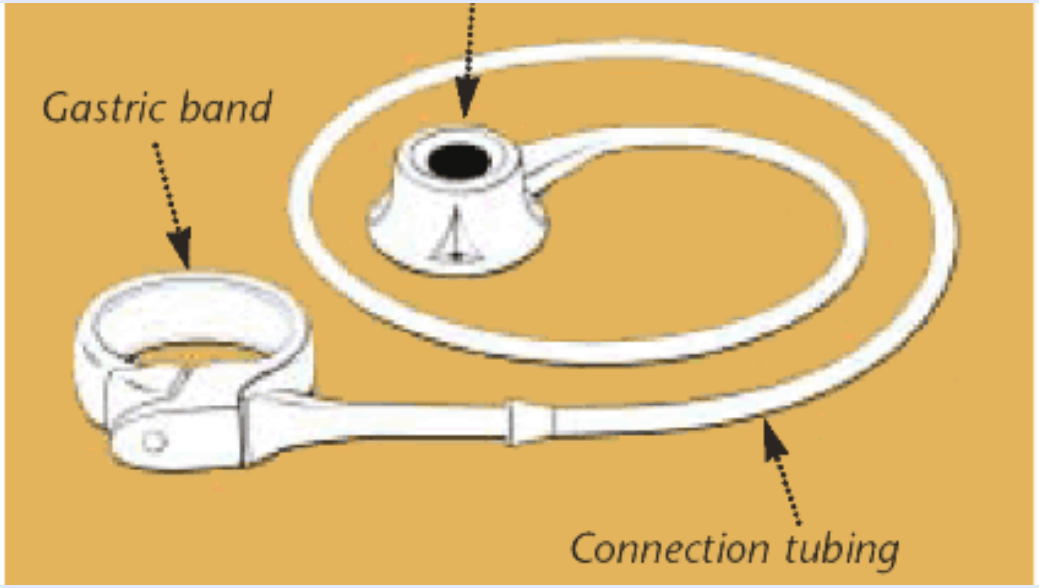
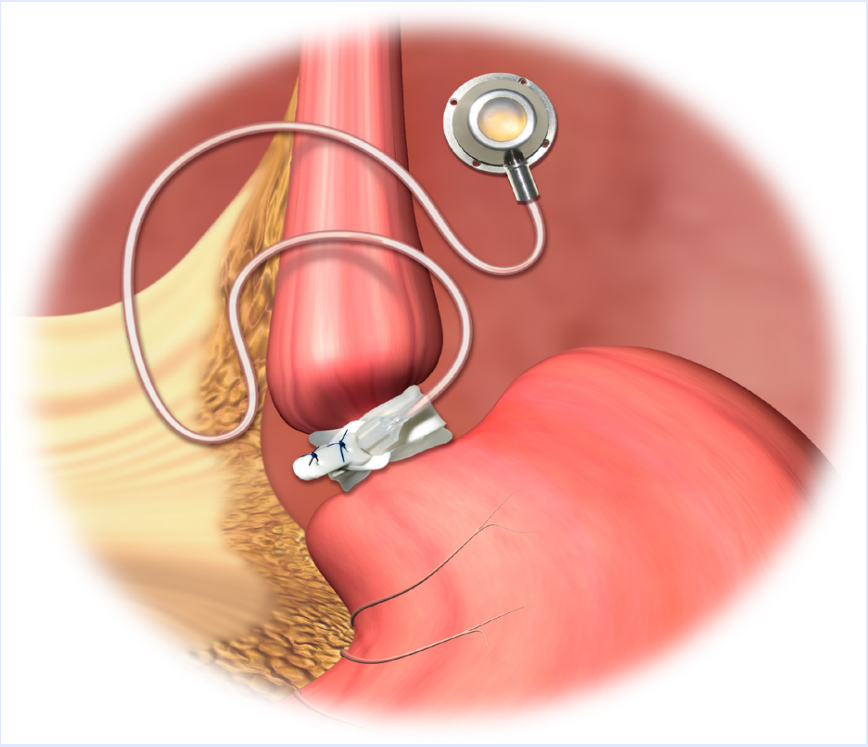
Lap Band

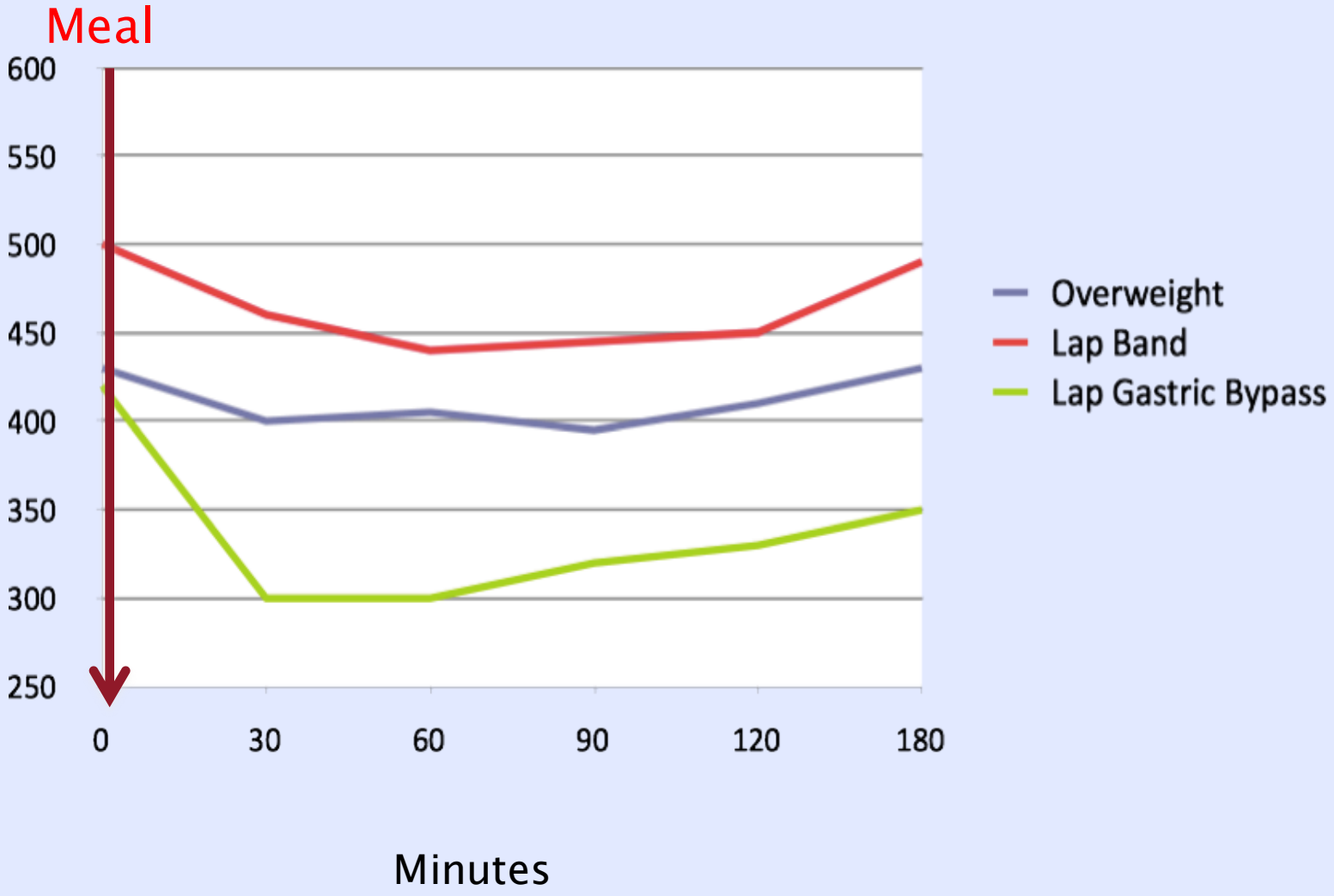




Lap Band

- Peak placement in 2008
- Currently only 10% of bariatric procedures worldwide
- Banding exerts a temporary weight loss
  - Weight loss due to decreased food intake
  - No direct neuro-hormonal effects
  - Ghrelin levels are elevated

Ghrelin - Hunger



Korner et al. Differential effects of Gastric Bypass and Banding on Circulating Gut hormone and Leptin Level, Obesity, Sept 2006

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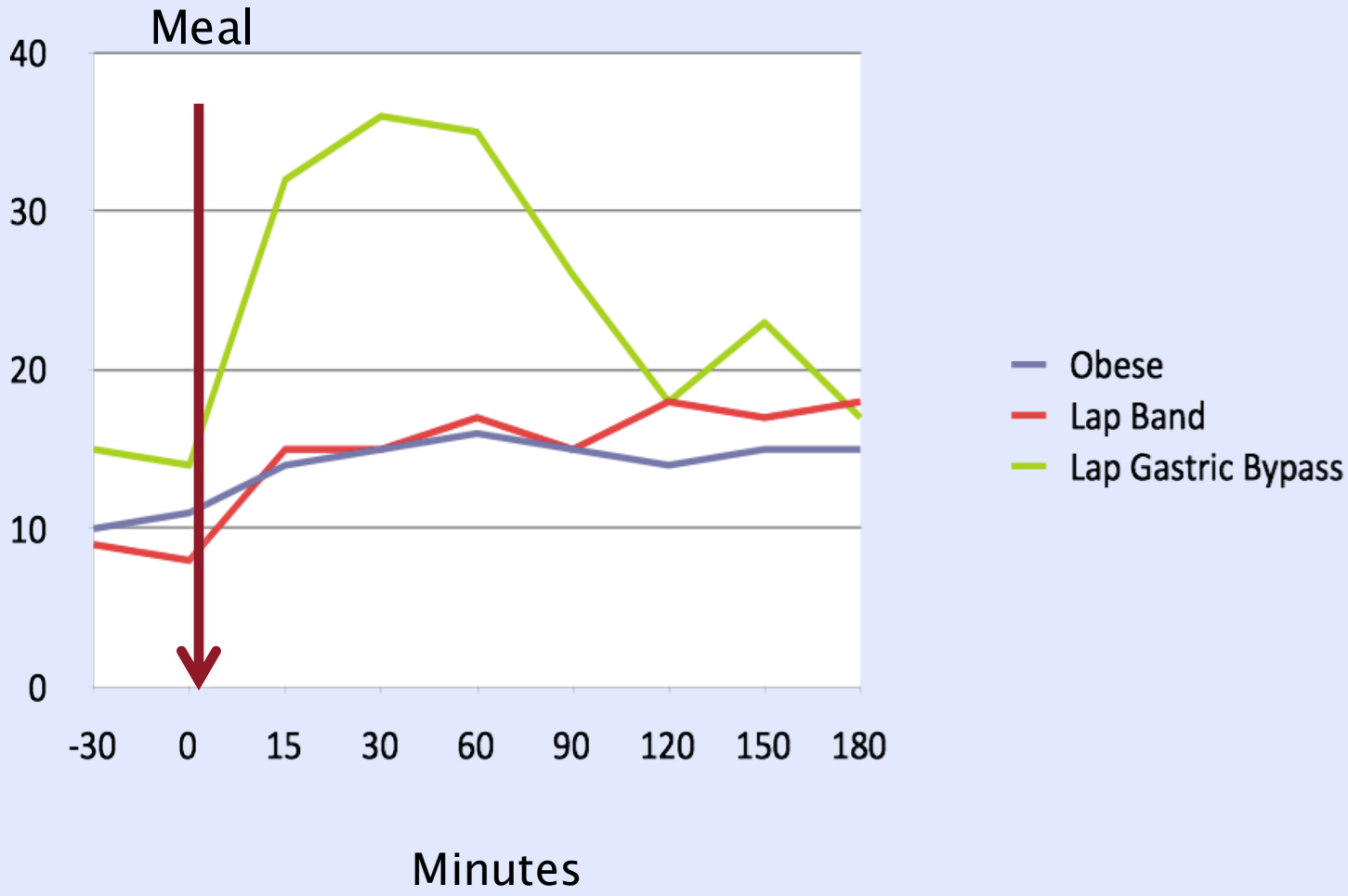
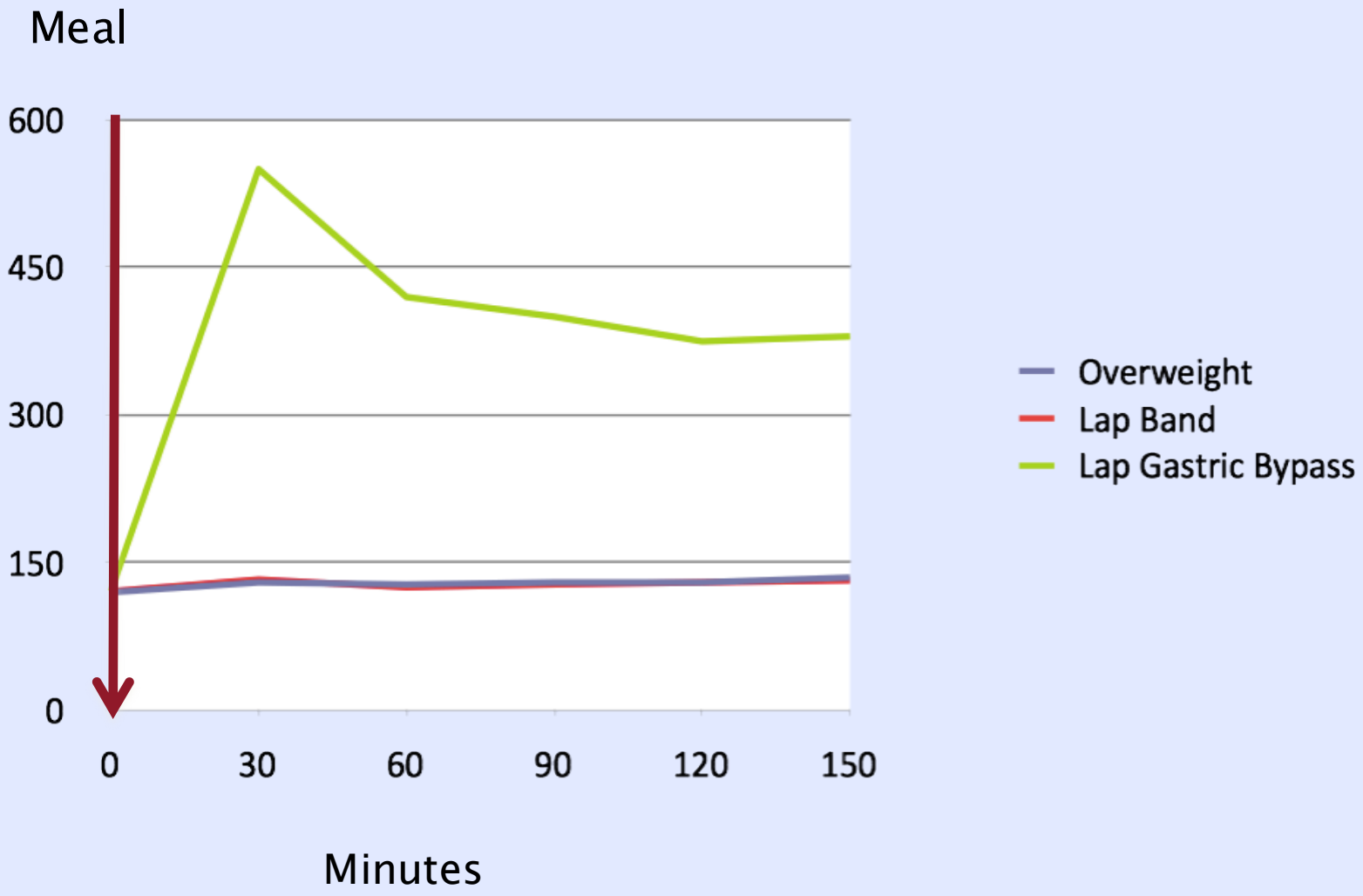
GLP-1 Causes Fullness



Le Roux et al. Annals of Surgery Jan, 2006

PYY Causes Fullness

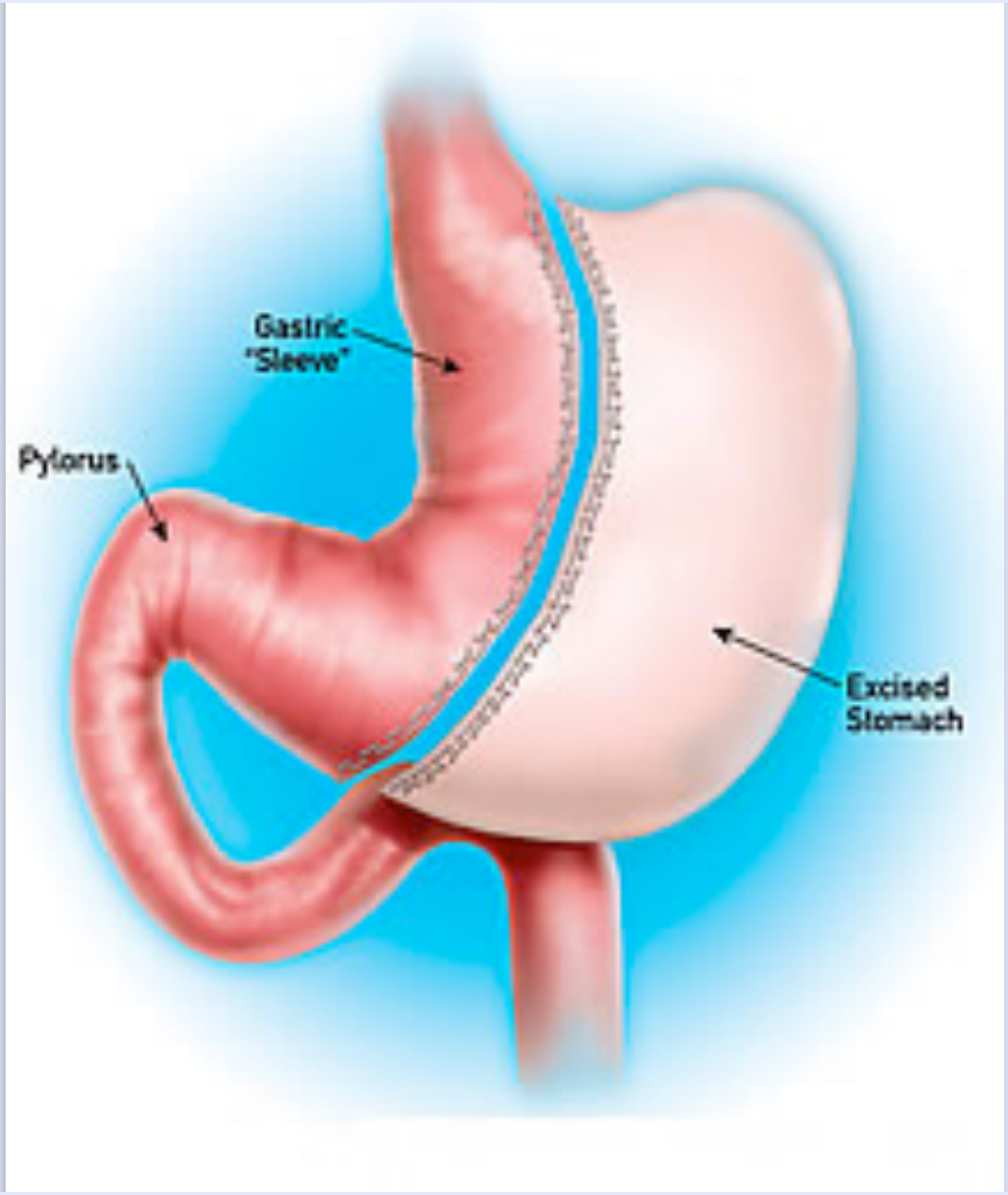


Le Roux et al. Annals of Surgery Jan, 2006

Lap Band Outcomes

Studies	Length of Follow up (mean)	Patient number	Reoperations (% of patients)	Conclusions
Tolonen et al.	7 years	123	25%	Failure rate 15% 1-3yr 40% 8-9 yrs
Suter et al.	8 years	317	21.7% 33% developed late complications	Failure rate 40% at 5 years
Camerini et al.	13 years	45	60% of bands removed	Longest Follow up. Discouraged band placement

Sleeve Gastrectomy



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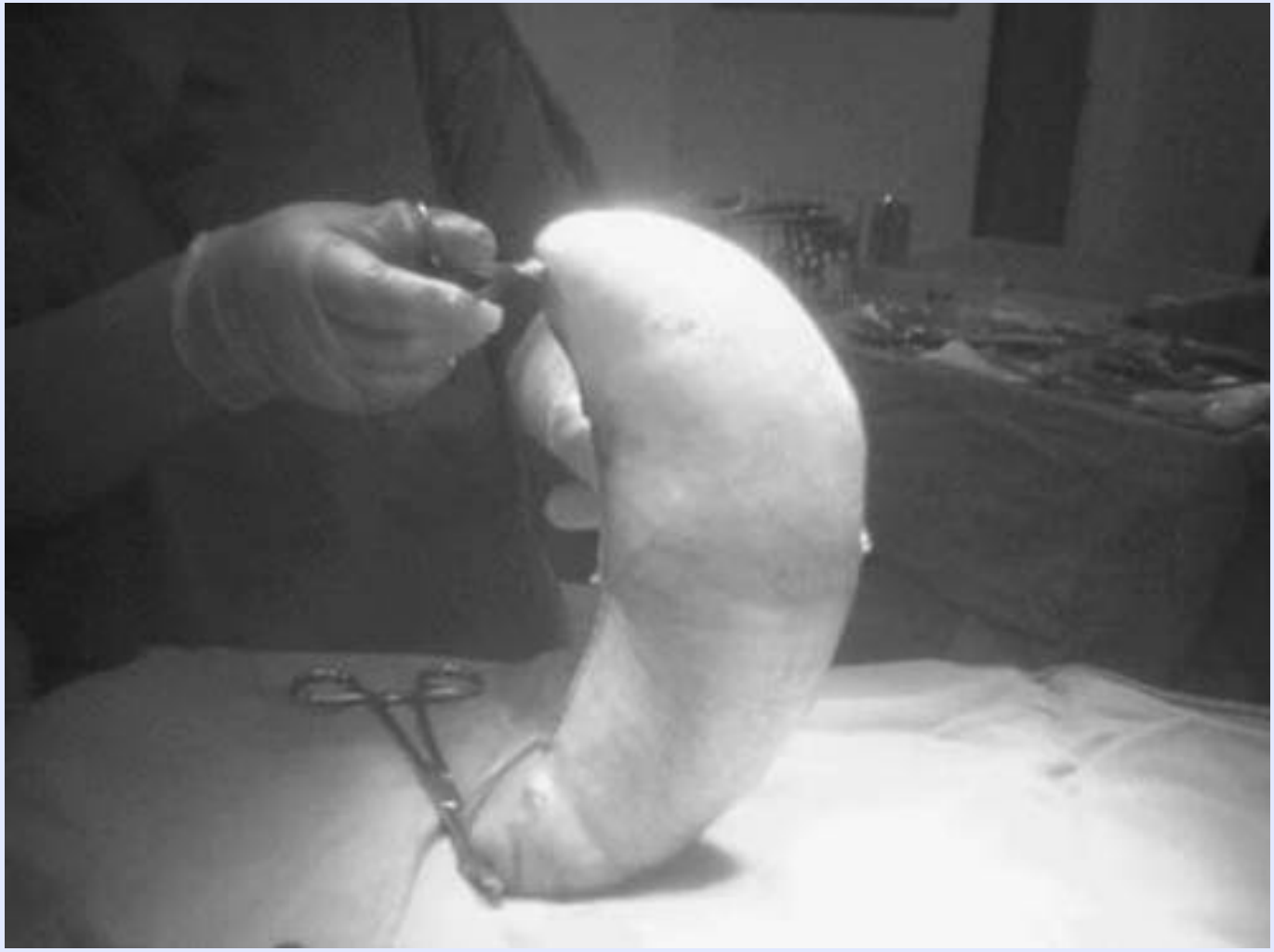
Remnant Stomach



Comorbidity Resolution with the Sleeve Gastrectomy

Table 2
Comorbidity resolution after sleeve gastrectomy

Author	Patients (n)	Follow-up	T2DM	HTN	Hyperlipidemia	Sleep apnea	DJD/joint pain	GERD	Peripheral edema	Depression
Cottam et al (2006)[3]	126	1 yr	81% R 11% I	78% R 7% I	73% R 5% I	80% R 7% I	85% R 6% I	70% R 8% I	91% R 3% I	67% R 9% I
Hamoui et al (2005)[4]	118	2 yr	47% R 22% I	15% R 16% I	—	—	—	—	—	—
Moon Han et al (2005)[5]	60	1 yr	100% R	93% R 7% I	45% R 30% I	100% R	76% R 24% I	80% R 20% I	—	—
Silecchia et al (2006)[6]	41	18 mo	79.6% R 15.4% I	62.5% R 25% I	—	56.2% R 31.2% I	—	—	—	—

T2DM = Type 2 diabetes mellitus; HTN = hypertension; DJD = degenerative joint disease; GERD = gastroesophageal reflux; R = resolved; I = improved.

- Vidal from Spain reports that at 4 months the resolution of Type II DM was similar in Lap Sleeve (51.4%) patients compared to the Lap Roux en Y Gastric Bypass (62%) patients

Position Statement Sleeve Gastrectomy as a Bariatric Procedure Clinical Issues Committee of the ASMBS, SOARD 2007; 3: 573-576.

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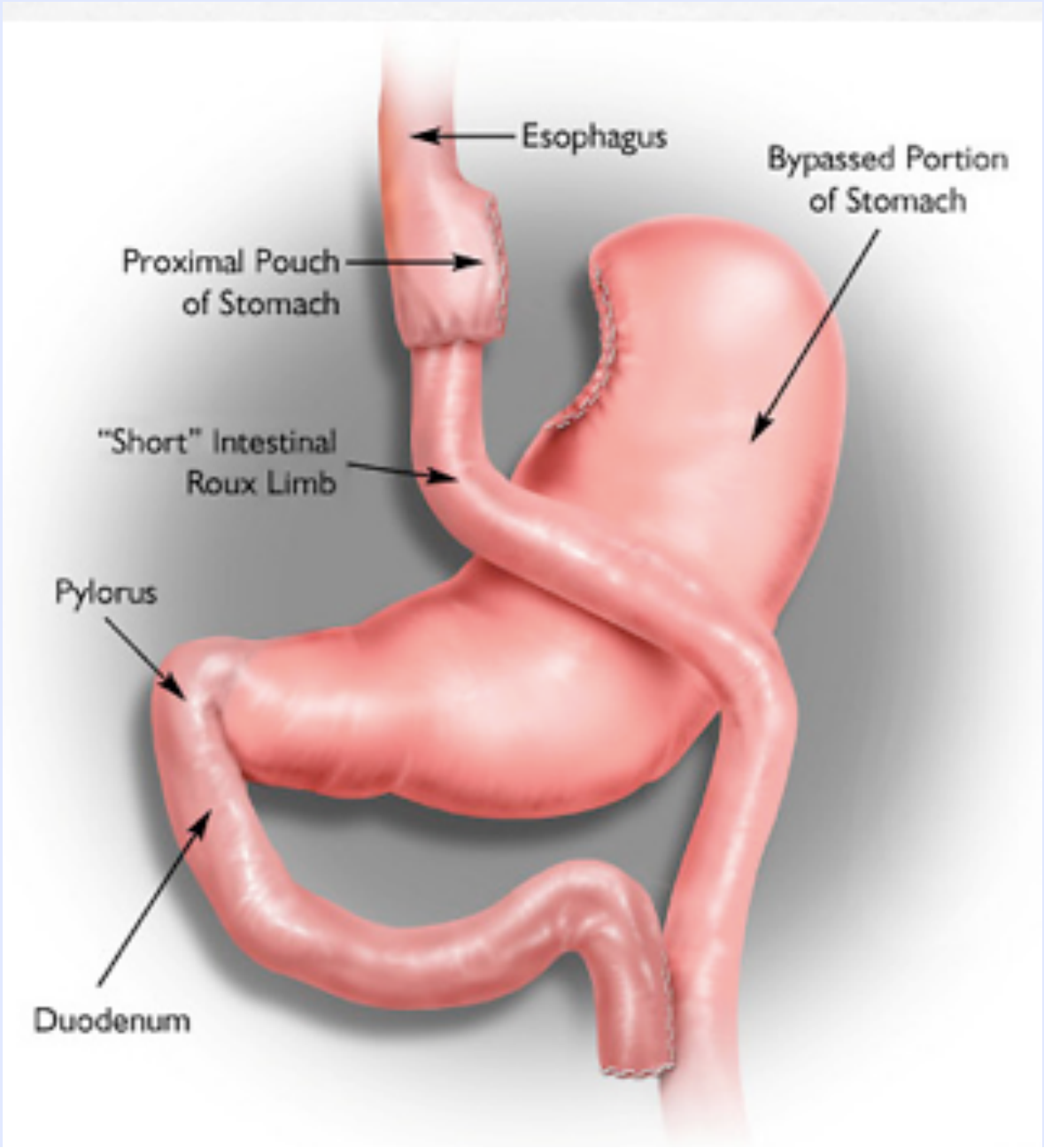
Roux-en-Gastric Bypass



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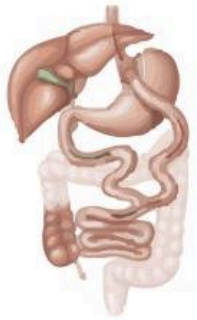
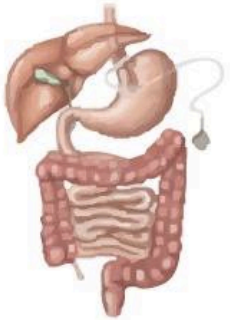
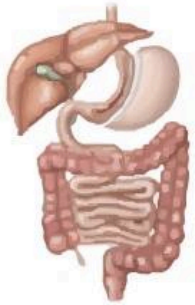
Roux en Y Gastric Bypass

- Gold standard procedure
- Works through restriction and malabsorption
- Resolution of diabetes prior to weight loss
- Decrease in hunger hormones
- Increase in satiety

	RYGB	AGB	VSG
			
Lipid homeostasis	Elevated HDL Reduced triglycerides Reduced total cholesterol, LDL	Elevated HDL Reduction in triglycerides not as dramatic as RYGB or VSG	Elevated HDL Reduced triglycerides
Glucose homeostasis	Improved fasting blood glucose and insulin sensitivity, prior to weight loss	Improvements are slower and not as dramatic as after VSG or RYGB	Improved fasting blood glucose and insulin sensitivity, prior to weight loss
Role of gastric restriction	Has not yet been directly tested	Failure of band leads to less gastric restriction and less weight loss	Gastric restriction is not the critical factor preventing hyperphagia
Gastric emptying	Few published studies	No overall change in gastric emptying rate; Emptying rate of proximal pouch created by band is enhanced	Most papers show increase
Energy expenditure	Controversial	Not reported	Unchanged, but only reported in one study
Leptin	Circulating leptin levels lower than expected for body weight Changes to leptin sensitivity not tested	Plasma leptin reduced, as expected for body weight; Changes to leptin sensitivity not tested	Circulating leptin levels lower than expected for body weight; Body weight changes not driven by changes to leptin sensitivity
Ghrelin	Reduced total ghrelin; Controversial, but no change in acyl-ghrelin levels	Increased circulating ghrelin	Reduced total ghrelin; Controversial, but no change in acyl-ghrelin levels
CCK	No change	No change	Not measured
GLP-1 (postprandial)	Weight loss-independent postprandial increase	Increased circulating GLP-1 but much less than RYGB or VSG	Weight loss-independent increase comparable to RYGB
PYY (postprandial)	Increased postprandial PYY levels; Reduced body weight loss in PYY knockout mice	No change	Increased postprandial PYY levels, comparable to levels after RYGB
Bile acids	Increased plasma bile acids	Not reported	Increased plasma bile acids
Diet Change	Decreased fat intake, more fruits and vegetables	Decrease bread intake and increase in caloric liquids; Greater fat intake and fewer fruits/ vegetables than RYGB	Decreased fat intake, similar to RYGB
Food Intolerance	Some dumping syndrome, usually well-tolerated	More persistent and problematic than RYGB; Mainly vomiting	Little or none

Sleeve and Gastric Bypass Hormonal Changes

- Ghrelin decreased
- Peptide YY increased
- GLP-1 increased
- Leptin decreased
- Resistin decreased

2016 ADA Guidelines

Table 6.1—Treatment for overweight and obesity in type 2 diabetes

	BMI category (kg/m^2)				
Treatment	23.0* or 25.0–26.9	27.0–29.9	30.0–34.9	35.0–39.9	≥40
Diet, physical activity, and behavioral therapy	†	†	†	†	†
Pharmacotherapy		†	†	†	†
Bariatric surgery				†	†

†Treatment may be indicated for selected motivated patients.
*Cutoff points for Asian American individuals.

Diabetes Care 2016; 39(Suppl. 1): S47-S51/DOI: 10.2337/dc16-S009

Back to Dr. Liu

Izzy (2007)

- Izzy undergoes lap band procedure.
- Over 6-9 months, successfully achieves substantial weight loss; hypertension, diabetes and dyslipidemia well controlled.
- She swears that she will eat well and exercise regularly in order to maintain the weight loss.

Panel Discussion/Q&A