Who and when should I refer to a hepatologist? To an endocrinologist?

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The First NAFLD Encounter

- Most likely with the primary care provider (PCP)
  - PCPs have a strong incentives to refer patients
    - Short visits, knowledge gap, liability, and patient demand
  - Little disincentive – usually no cost to the provider (some exceptions)
- Payers are concerned about excessive (costly) referrals to specialists
  - *1999-2009: physician referrals increased 4.8% → 9.3%
  - **More than 33% of patient are referred to a specialist each year
  - **More than 50% of office visits are with a specialist
- The specialist perspective
  - Depend on referrals, but many are inappropriate and reduce efficiency

*Barnett, ML, Song Z, Landon BE. Arch Intern Med. 2012; 172:163-170
**Mehrotra, A, Forrest, CB, Lin, CY. Millbank Q. 2011; 89: 39–68

Process improvement in NAFLD Care

- Most patients should be managed by primary care
  - Utilizes an existing professional relationship and lowers cost
- We need a payment structure that rewards extraordinary care
  - *Referrals are lower when PCPs have a financial stake
- On-line consultation/teaching
  - Asynchronous – written opinion and efficient referral without enhancing skills
  - Synchronous (e.g. Project ECHO®) – thematic clinics that improve skills
    - Time constraints frequently limit participation by PCPs and consultants
- Weight loss is the cornerstone, so the PCP needs the tools to succeed
  - Dietician, psychologist, exercise physiologist, social worker, weight loss drugs
- Assuming all the above, PCPs need some basic knowledge

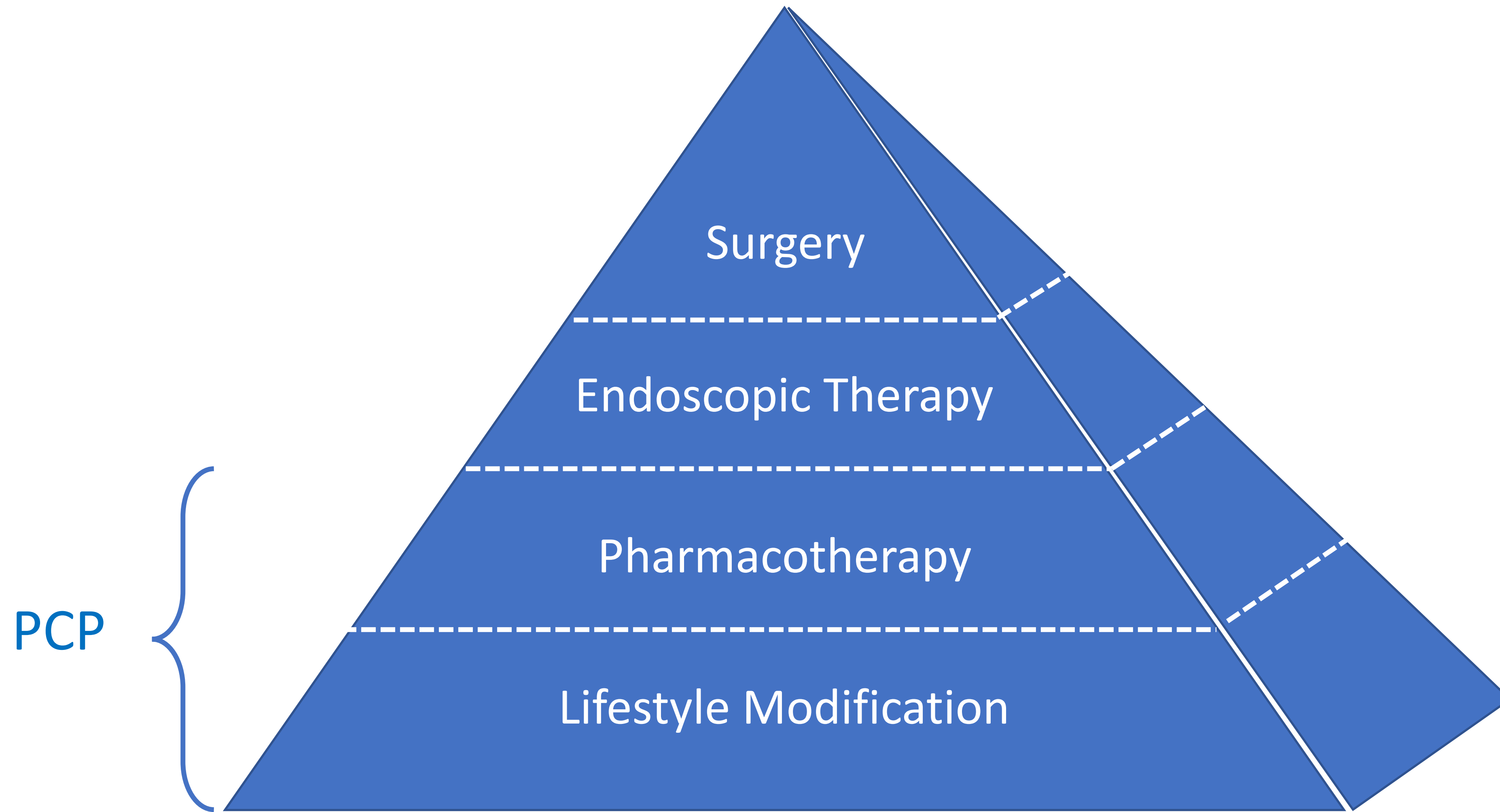
*Barnett, ML, Song Z, Landon BE. Arch Intern Med. 2012; 172:163-170

Percentage Weight Loss vs Histologic Improvement in NAFLD

Weight Loss	Outcome Among Patients Achieving Weight Loss	Sustained Weight Loss at 1 Yr[1]
≥ 10%[1]	Fibrosis regression (45% of patients)	< 10%
≥ 7%[1]	NASH resolution (64% to 90% of patients)	18%
≥ 5%[1-3]	Ballooning/inflammation (41% to 100% of patients)	30%
≥ 3%[1-4]	Steatosis (35% to 100% of patients)	Not reported

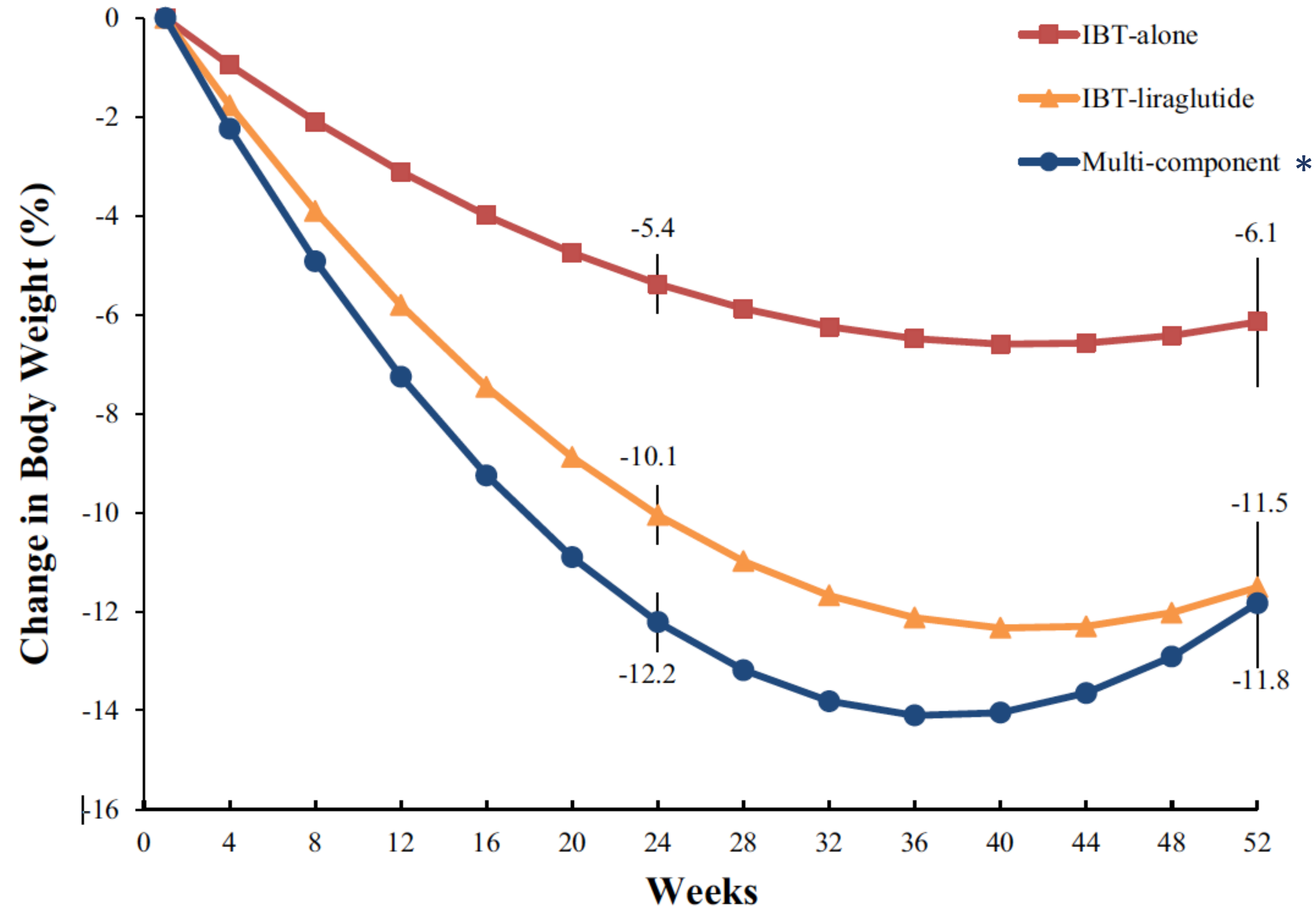
[1] Vilar-Gomez, E et al. Gastroenterology. 2015;149:367-378	[3] Harrison, SA et al. Hepatology. 2009;49:80-86
[2] Promrat, K et al.. Hepatology. 2010;51:121-129	[4] Wong, VW-S at al. J Hepatol. 2013;59:536-542

Obesity Management Pyramid



Modified, courtesy of Sam Klein, MD

Intensive Behavioral Therapy (IBT) + Liraglutide (ITT)



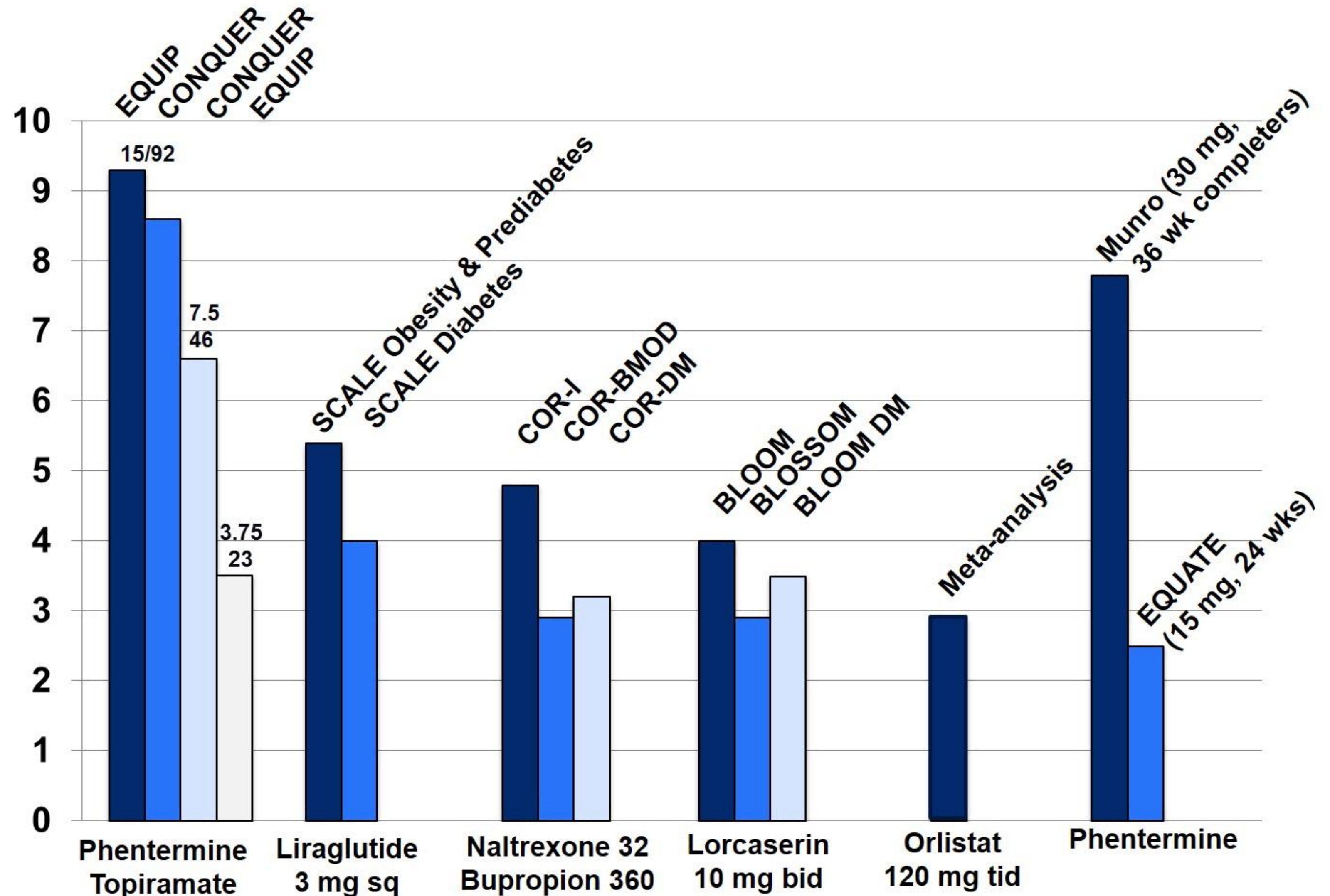
* Multi-component included shakes and frozen meals from week 4-12

Wadden, TA et al. Obesity. 2018; 0:1-12. doi:10.1002/oby.22359

Placebo-subtracted Weight Loss of Obesity Medications (% weight loss at 1 year, ITT-LOCF*)

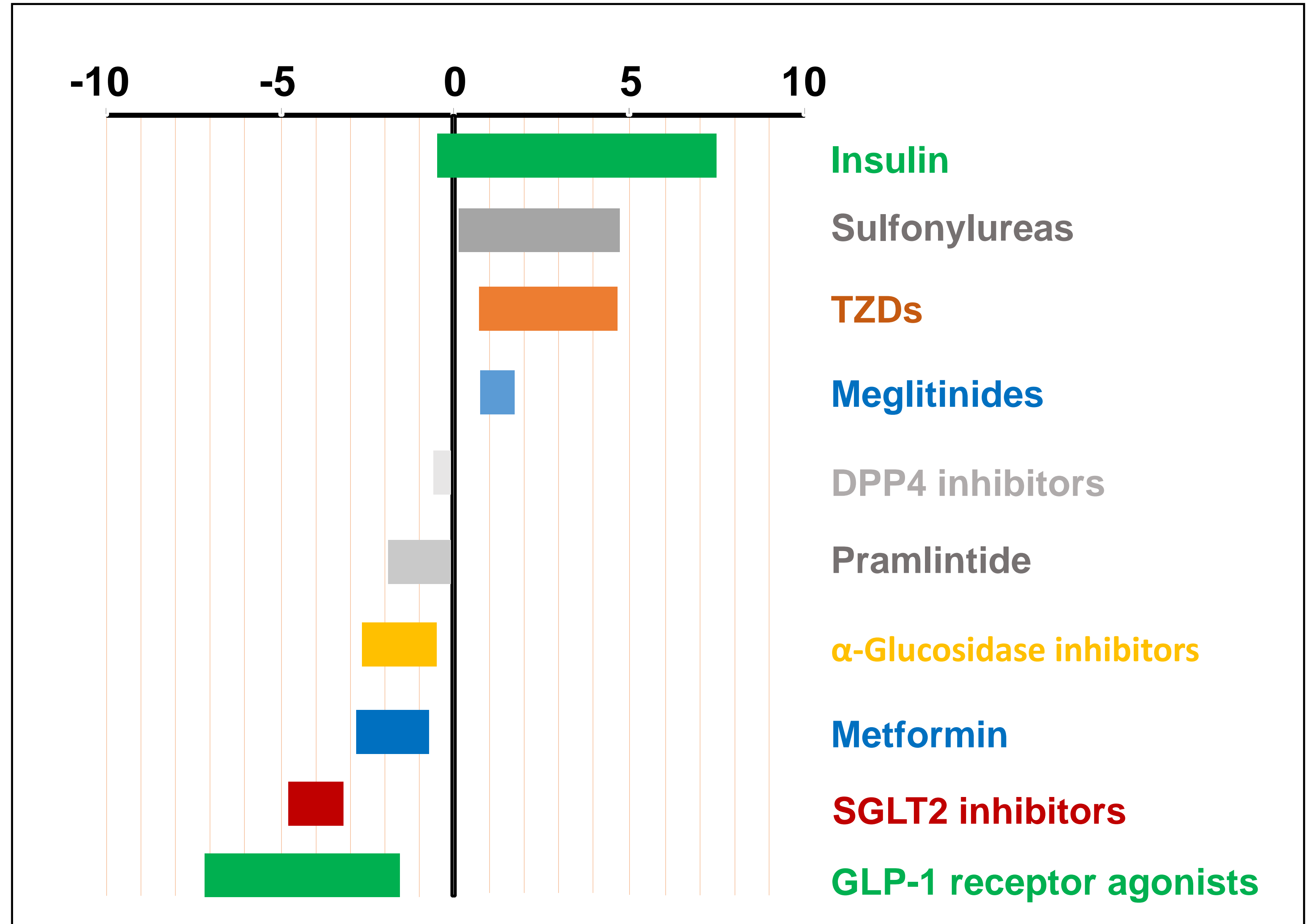
Cost per Month (GoodRx)

Liraglutide	$1,332
Nalrex/buprop	$292
Phent/topir	$198
Phentermine	$11



*LOCF: Last observation carried forward
Modified, courtesy of Sam Klein, MD

Effect of Diabetes Medications on Body Weight



Courtesy of Sam Klein, MD

When to refer to Endocrinology

- Treatment paradigm: dual goals of weight loss and euglycemia
  - These are not mutually exclusive
  - Referral depends on PCP skill and interest
- Who to refer
  - Consecutive Hb A1C >8% over 3-6 months despite non-insulin medication
  - Any type II diabetic on insulin
  - PCP unfamiliar or unable to prescribe new diabetes agents
    - GLP-1 agonists reduce cardiovascular risk
    - SGLT2 inhibitors improve heart failure
  - High cardiovascular risk score increases the urgency
    - Install a cardiovascular risk calculator in EHR

Cardiovascular Risk Stratification (ACC/AHA Score)

Field	Value
Age (years)	65
Gender	(•) Male ( ) Female
Race	(•) African American ( ) Other
Total cholesterol (mg/dL)	240
HDL cholesterol (mg/dL)	35
Systolic blood pressure (mmHg)	140
Diastolic blood pressure (mmHg)	90
Treated for high blood pressure	( ) No (•) Yes
Diabetes	(•) No ( ) Yes
Smoker	( ) No (•) Yes

Calculate

34.6%

10-year risk of heart disease or stroke

On the basis of your age and calculated risk for heart disease or stroke over 7.5%, the ACC/AHA guidelines suggest you should be on a **moderate to high intensity statin.**

http://www.cvriskcalculator.com/

When to refer to Hepatology

- Most referrals are for abnormal liver tests or an echogenic liver
- Biopsy findings make the <u>diagnosis</u> of NASH, but
- *Fibrosis stage is the only histologic predictor of <u>outcome</u>
- **Non-invasive predictors of advanced fibrosis – two stage testing
  - Stage 1: FIB4 (calculator and alert should be installed in EHR)
  - Stage 2: ELF or liver stiffness measurement (e.g. VCTE)

*Angulo, P et al. Gastroenterology 2015;149:389-397
**Anstee, QM et al. Hepatology 2019;70:1521-1530

When to refer to Hepatology (Cont.)

- Advanced fibrosis by any test
- Liver tests don’t improve after weight loss
- More than one potential cause of elevated liver tests
- Need for a potentially hepatotoxic drug
- Liver biopsy shows disease, inflammation, or advanced fibrosis
- Liver tumor

*Angulo, P et al. Gastroenterology 2015;149:389-397
**Anstee, QM et al. Hepatology 2019;70:1521-1530

Take Home Points – When to Refer to Endocrine

- Primary care needs the tools to manage simple cases of NAFLD
  - Install calculators and alerts in EHR (Cardiovascular risk and FIB4)
  - Advocacy for ancillary services
  - Stop drugs that increase body weight
  - Use appetite suppressants when appropriate
- Endocrine referral
  - Poorly controlled diabetes (Hb A1c >8%)
  - Type II diabetic on insulin

Take Home Points – When to Refer to Hepatology

- Advanced fibrosis by any test (noninvasive or invasive)
- Liver tests fail to normalize after weight loss
- The patient has more than one cause for elevated liver tests
- The patient requires a potentially hepatotoxic drug
- Liver biopsy shows serious pathology
  - Any defined disease, inflammation or advanced fibrosis
- Liver tumor seen on abdominal imaging

The End