

# What's New in Gastroenterology and Hepatology

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# What's New in Gastroenterology and Hepatology

## *Overview*

- GERD management: PPIs (and beyond)
- Functional GI Disorders (FGID) and IBS
- Colon Cancer Screening
- Non-alcoholic Fatty Liver Disease (NAFLD)

# GERD Management PPIs (and Beyond)

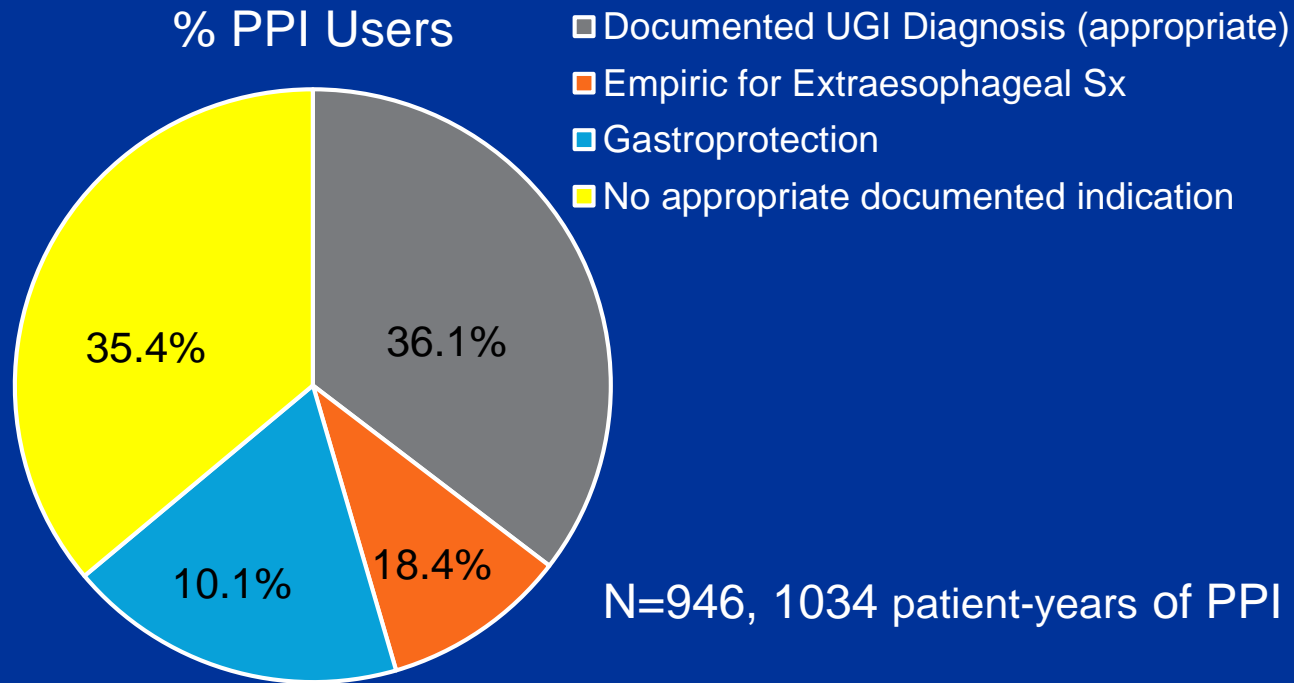
# PPI (Over) Use in the US

- Proton pump inhibitors (PPIs) among most widely used drug class in all of medicine
  - 8-10% of ambulatory adults prescribed PPI in past 30 days<sup>1</sup>
- PPI use particularly prevalent in elderly (3.5x higher use >60 yrs)<sup>2</sup>
- In 2009: \$7 billion spent on PPI prescriptions (not including OTCs!)<sup>3</sup>
- “Indications” for PPI use often unclear or inappropriate



# PPI Indications in the Ambulatory Setting

*Over 1/3 Rx have NO clearly documented indication!*



# Benefits of PPI Therapy

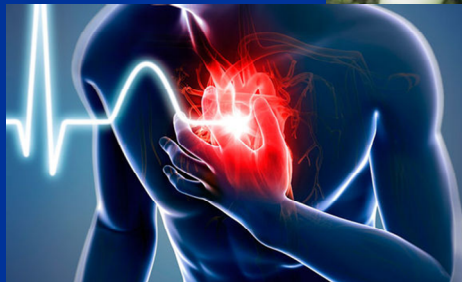
<u>Definitive indications</u>	<u>Consequences of stopping PPI</u>
Gastroesophageal reflux disease (GERD)	Erosive esophagitis
Erosive esophagitis, especially higher grades	Stricture recurrence
NERD with abnormal ambulatory reflux monitoring	Persistent symptoms
Long segment Barrett's esophagus	Reduced quality of life (Barrett's progression)
Peptic strictures	Increased health care costs
Eosinophilic esophagitis	Food impaction, dysphagia
Peptic ulcer disease including bleeding (short term therapy)	Bleeding, perforation, penetration, gastric outlet obstruction, death
<i>Helicobacter pylori</i> eradication	Persisting <i>H pylori</i> , atrophic gastritis, small risk of gastric cancer
Mucosa associated-lymphoid tissue (MALT) syndrome	Persisting MALT, symptoms
Gastro-protection with long term NSAID therapy	Peptic ulcer complications, dyspepsia
Hypersecretory states (Zollinger Ellison syndrome)	Peptic ulcer complications
Stress ulcer bleeding (short term therapy)	Bleeding, death
Chronic pancreatitis and refractory steatorrhea on pancreatic enzyme replacement therapy	Persisting steatorrhea

# Proton Pump Inhibitors (PPIs)

*Multiple Harmful Associations Identified*

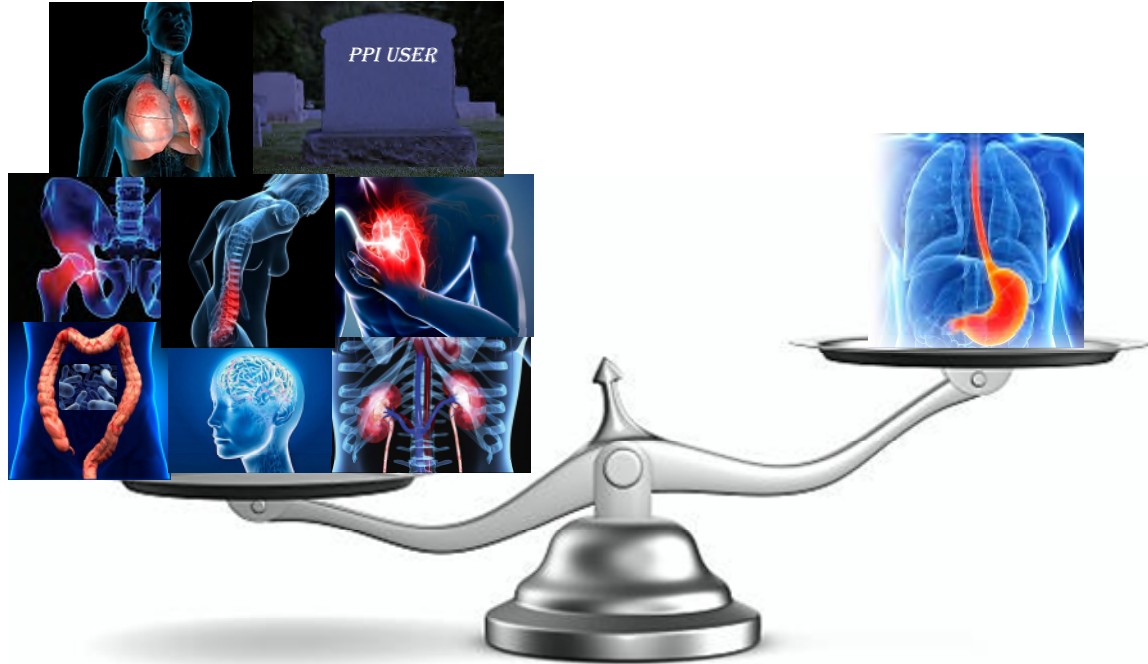


Acute cholecystitis  
Cholangitis  
Pancreatic cancer  
Atopic dermatitis  
Esophageal adenoCA  
Depression  
Gynecomastia



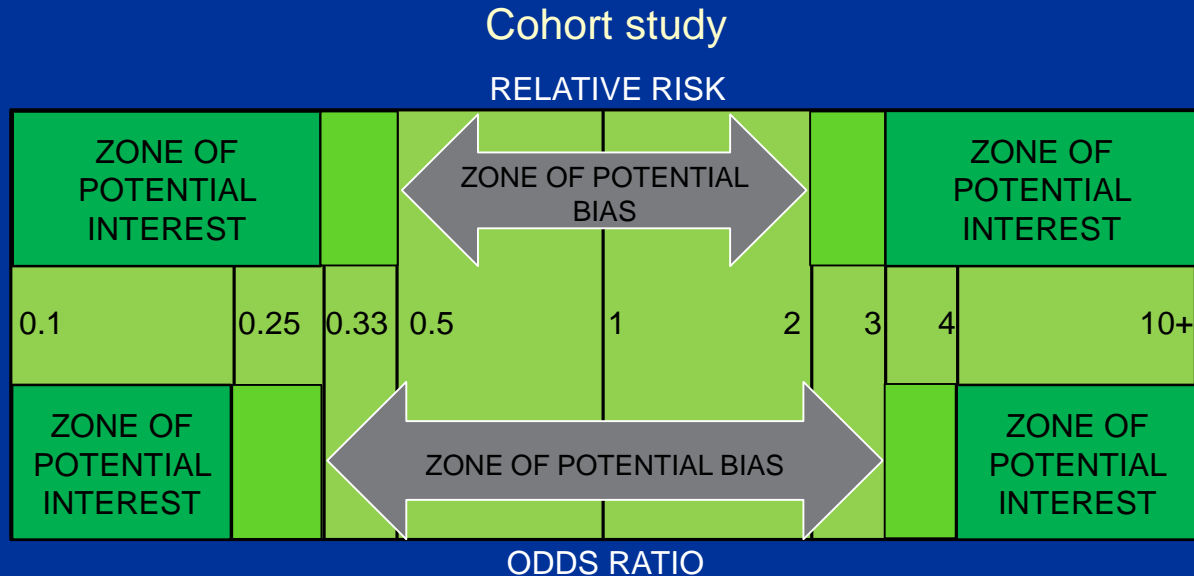
# PPI Use:

*An Unfavorable Risk: Benefit Balance?*



# False Alarms and Pseudo-epidemics\*

*Most reported associations in observational clinical research are FALSE!*



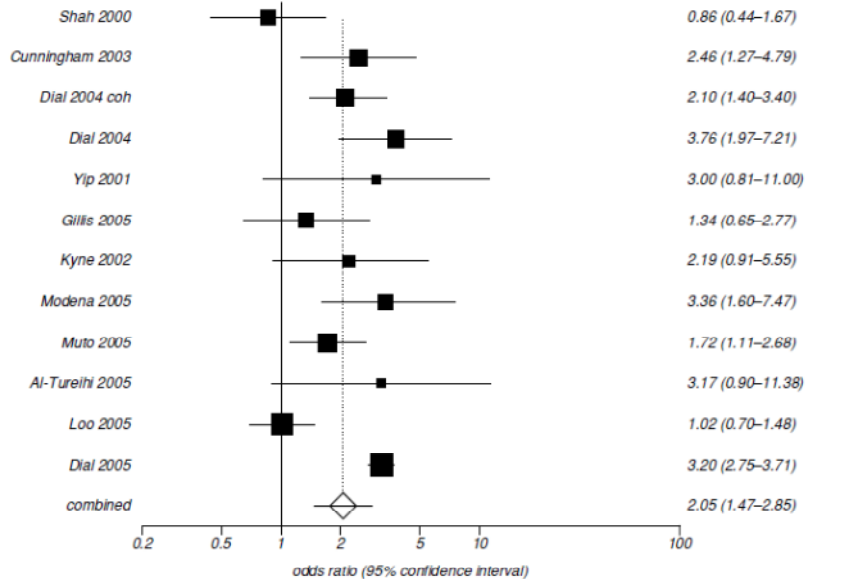
Weaker associations usually are related to study BIAS rather than CAUSALITY!

# PPI and Enteric Infections

## *Increased risk of C. difficile and other enteric infections*

### *Clostridium difficile colitis*

Summary meta-analysis plot [random effects]



RR PPI=2.05 (1.47, 2.85)

RR H2=1.47 (1.06, 2.05)

Control at higher risk

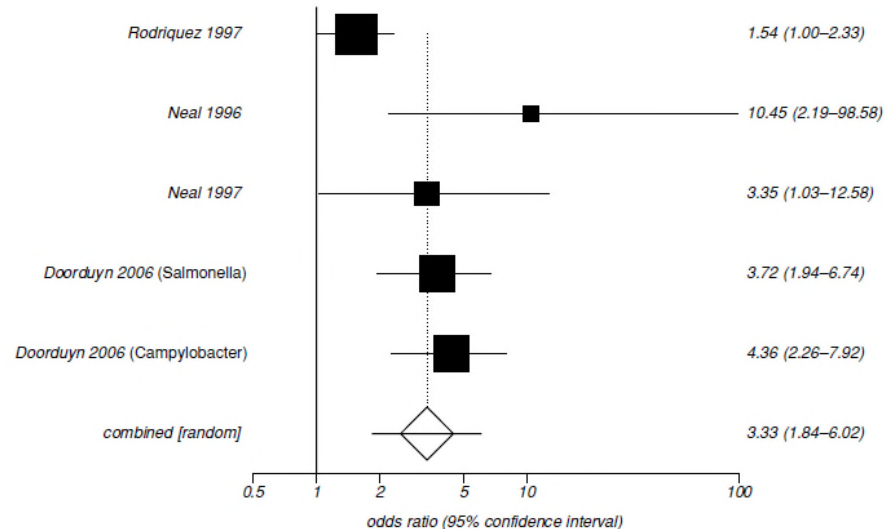
PPI at higher risk

12 papers, 2948 patients

Leonard J et al. Am J Gastroenterol 2007.

### *Other enteric infections*

Odds ratio meta-analysis plot [random effects]



RR PPI=3.33 (1.84, 6.02)

RR H2=2.03 (1.05, 3.92)

Control at higher risk

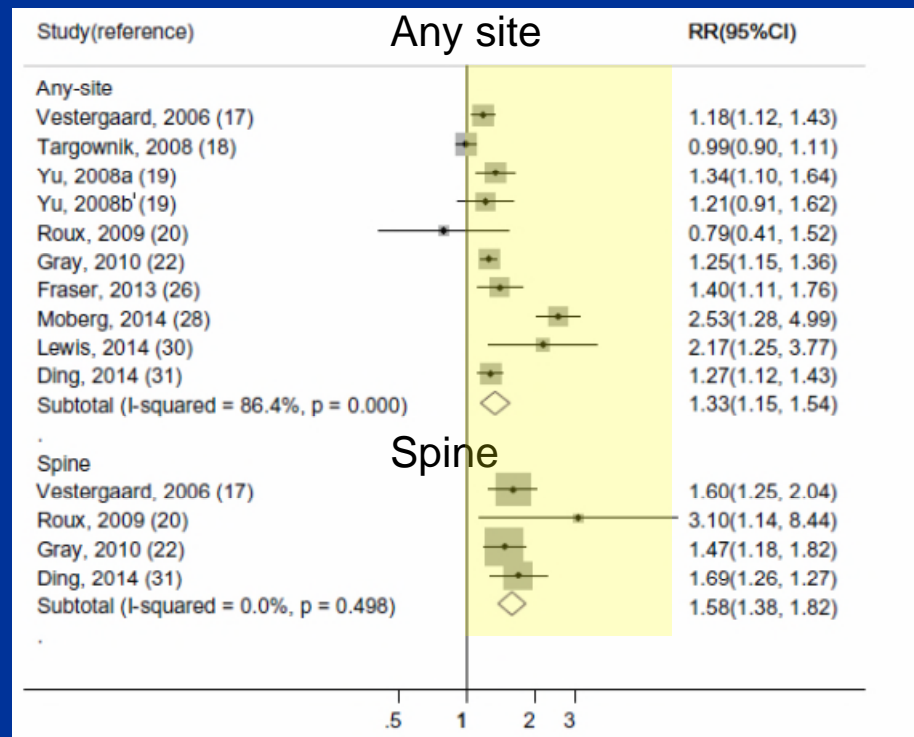
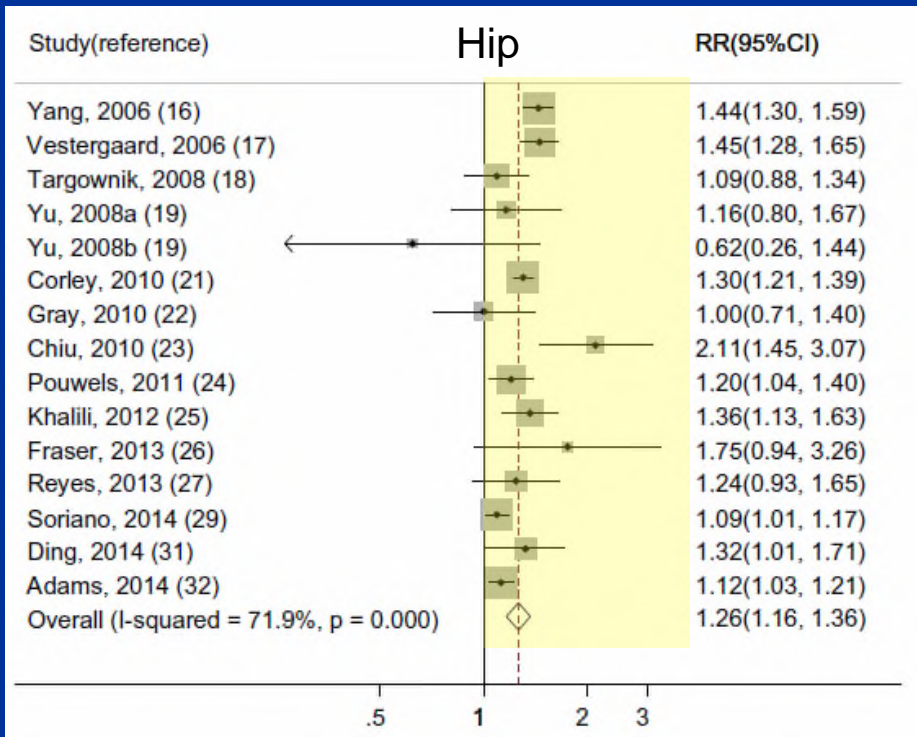
PPI at higher risk

6 papers, 11,280 patients



# PPI and Bone Fractures

*Increased risk of hip, spine, and all-site fractures*



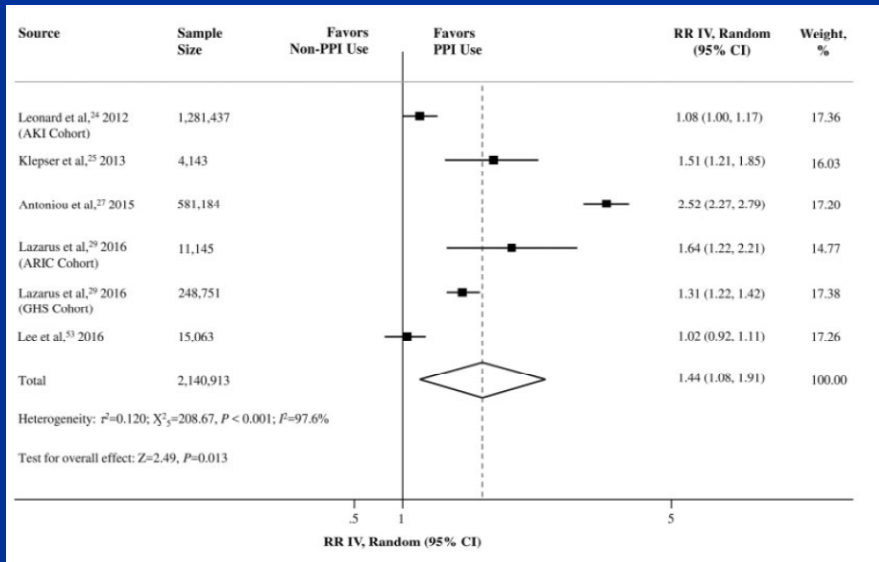
18 studies, 244,109 fracture cases included in analysis

Zhou B *et al. Osteoporosis Int* 2016.

# PPI and Kidney Disease

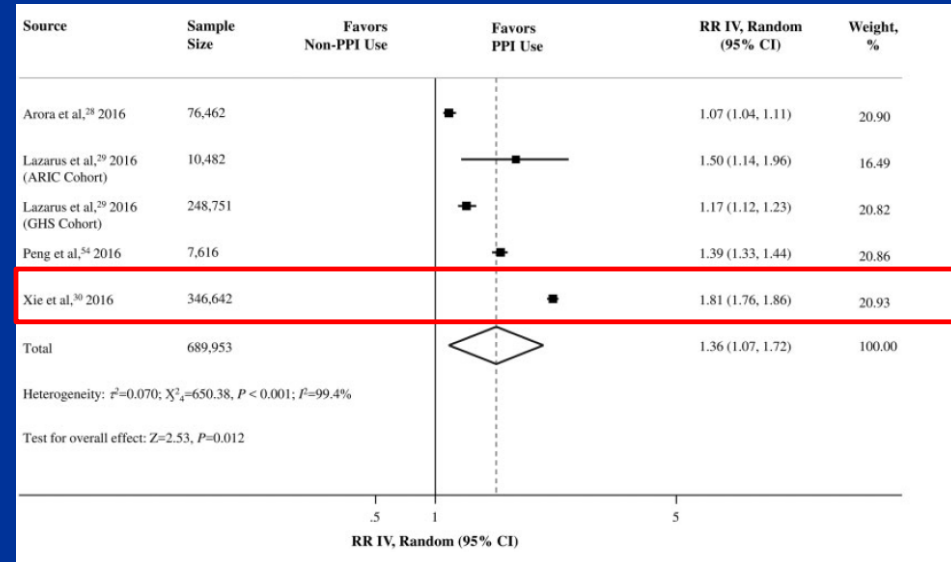
## *Increased risk of acute and chronic kidney disease*

### Acute kidney injury (AKI)



RR=1.44 (1.08-1.91), n=2,140,913

### Chronic kidney disease (CKD)



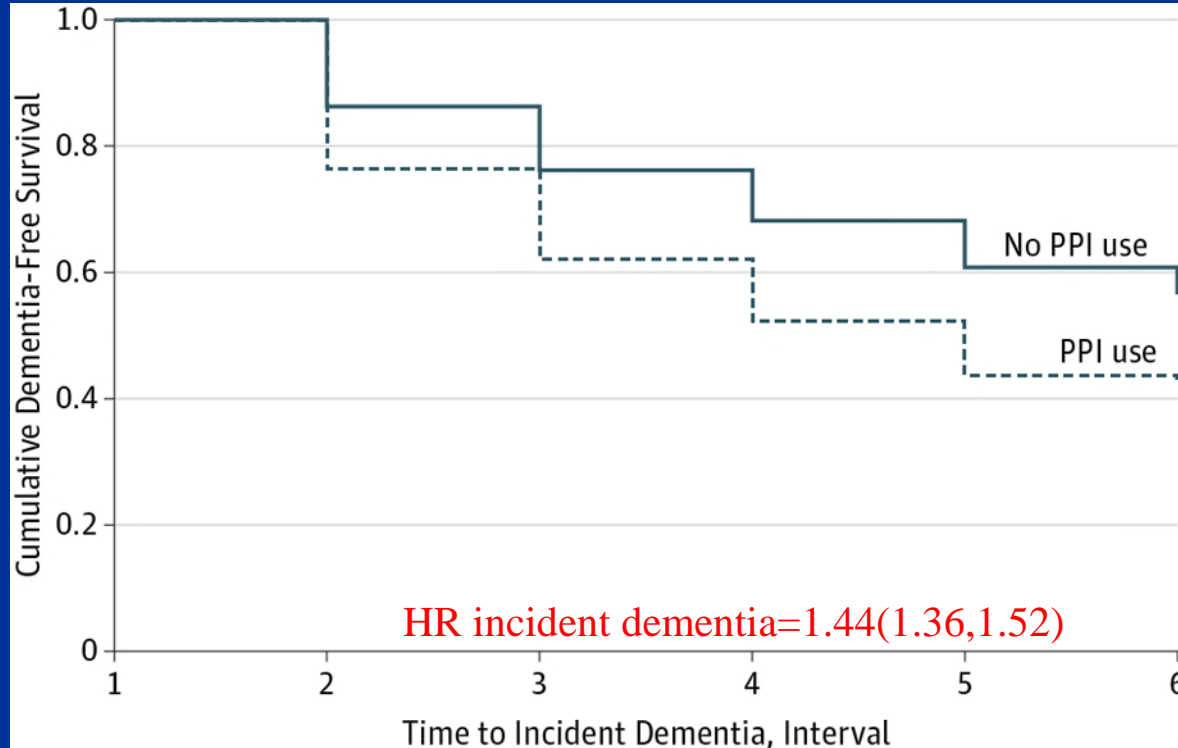
RR=1.36 (1.07-1.72), n=689,953

Nochaiwong S et al. Nephrol Dial Transplant 2017.



# PPI and Dementia

*Decreased dementia-free survival with PPI use*

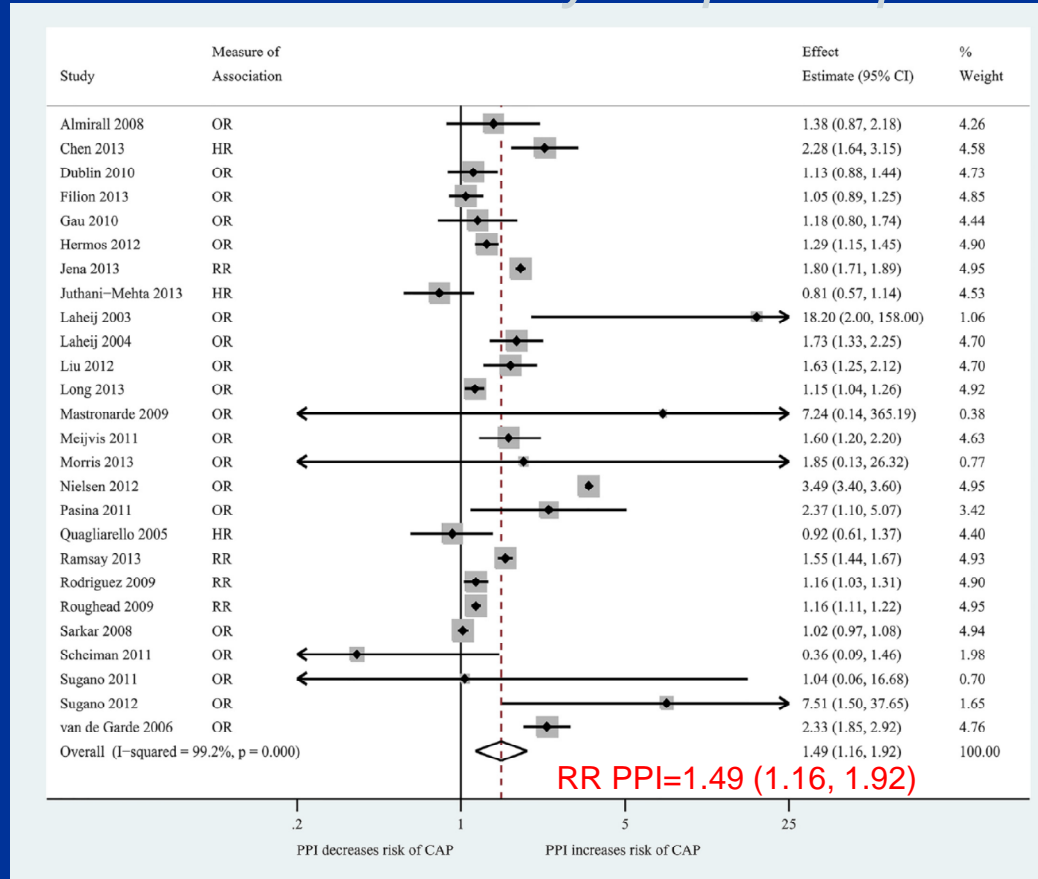


German statutory health insurer (Allgemeine Ortskrankenkassen), n=73,679 PPI users, n=70,729 controls  
>75 years old

Gomm W *et al. JAMA Neurol* 2016.

# PPI and Pneumonia

*Increased risk of community acquired pneumonia (CAP)*

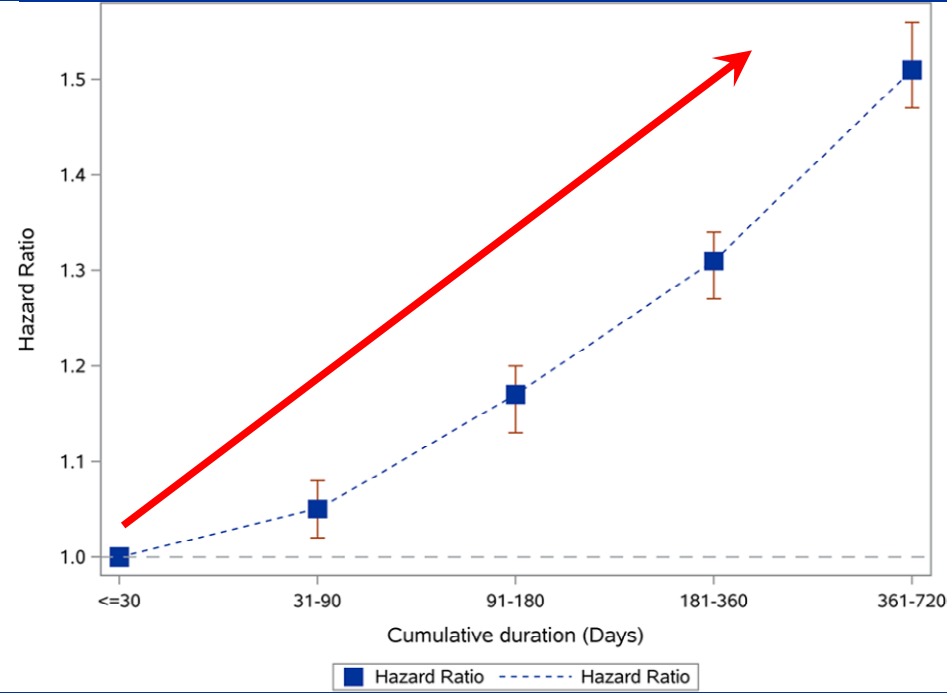
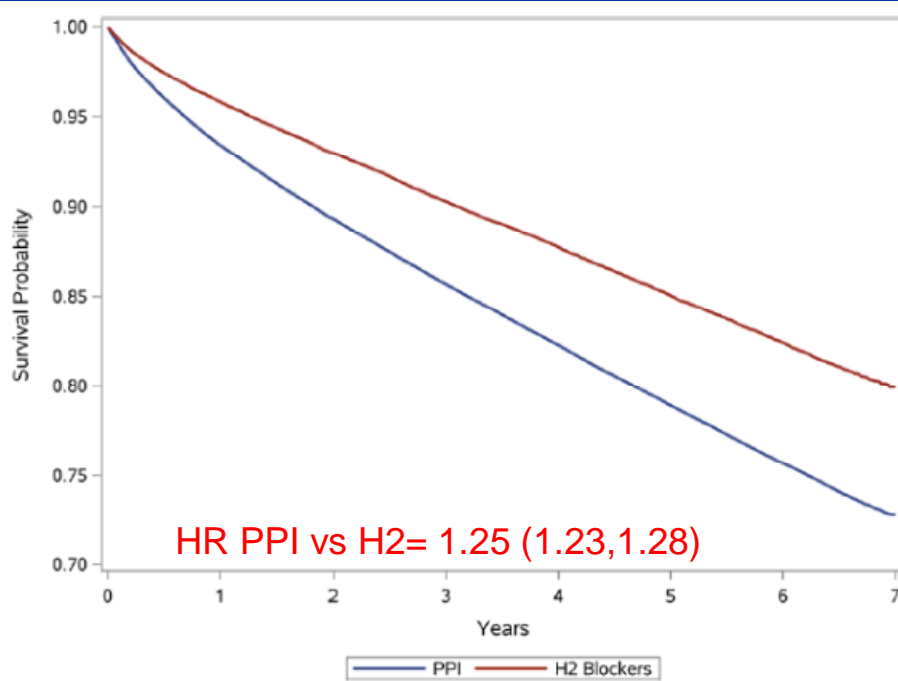


26 studies,  
n=226,769 cases of CAP

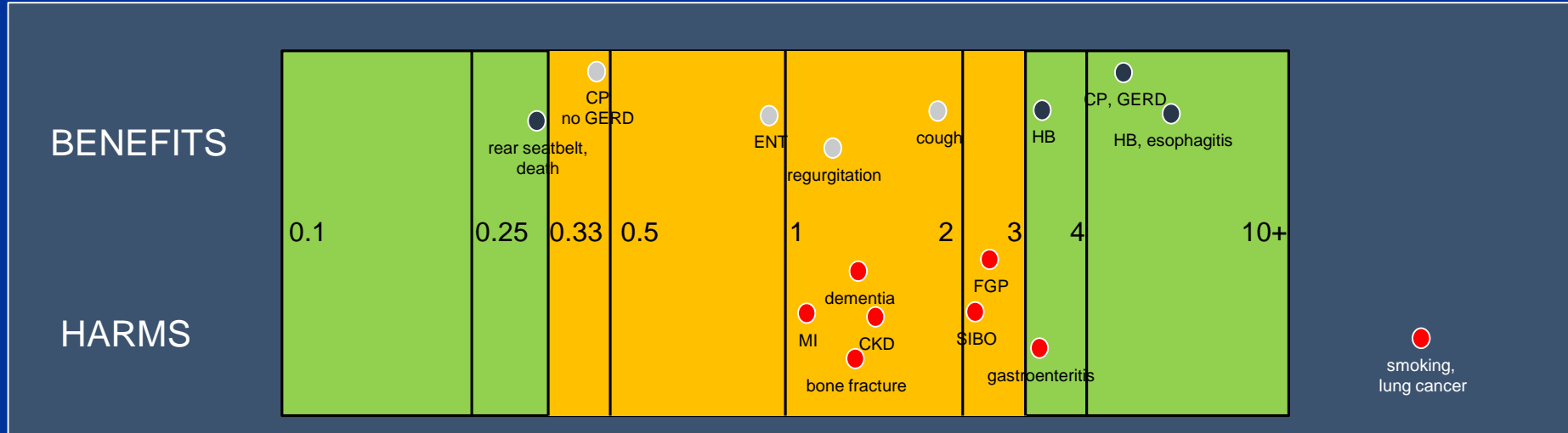
Lambert AA *et al.*  
*PLoS ONE* 2015.

# PPI and Mortality

*Excess risk of death among PPI users*



# “False Alarms and Pseudo-Epidemics”?



CP=chest pain, ENT=laryngopharyngeal symptoms, HB=heartburn, CKD=chronic kidney disease, SIBO=small intestinal bacterial overgrowth, FGP=fundic gland polyps

# Studies Reporting Risk of PPIs have Major Limitations

- Retrospective design
  - Bias and misinterpretation
  - Suboptimal design to assess safety
- Channeling bias
- Failure to satisfy Hill criteria
- Often not confirmed (or even refuted) by better quality studies

# Channeling bias













- Tendency of clinicians to prescribe a treatment based on the patient's prognosis
  - i.e., OLDER and SICKER patients are more likely to be prescribed a PPI than are younger, healthier individuals

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- Failure to satisfy Hill criteria

# Hill Criteria and PPIs

## *Soft evidence of causation*

	Enteric infection	Fracture	Renal dysfunction	Dementia	Pneumonia
Strength	Moderate	Weak	Weak	Very weak	Weak
Consistency		X	X	X	X
Specificity	X	X	X	X	X
Temporality					
Gradient		X	X	X	X
Plausibility			?	X	
Coherence		?	?	X	?
Experiment	X	X	X	X	X
Analogy		X	X	X	X



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# Prospective PPI Safety Data

- Randomized, double-blinded study on patients  $\geq 65$  with stable CV disease
  - ASA 100 mg a day
  - ASA 100 mg a day + rivaroxaban 2.5 mg bid
  - Rivaroxaban 5 mg bid
- Pts NOT on PPI randomized to pantoprazole 40 mg a day or placebo
- 3 year followup, 53,000 pt-years

# Prospective PPI Safety Data

*(Mostly) lack of significant effect*

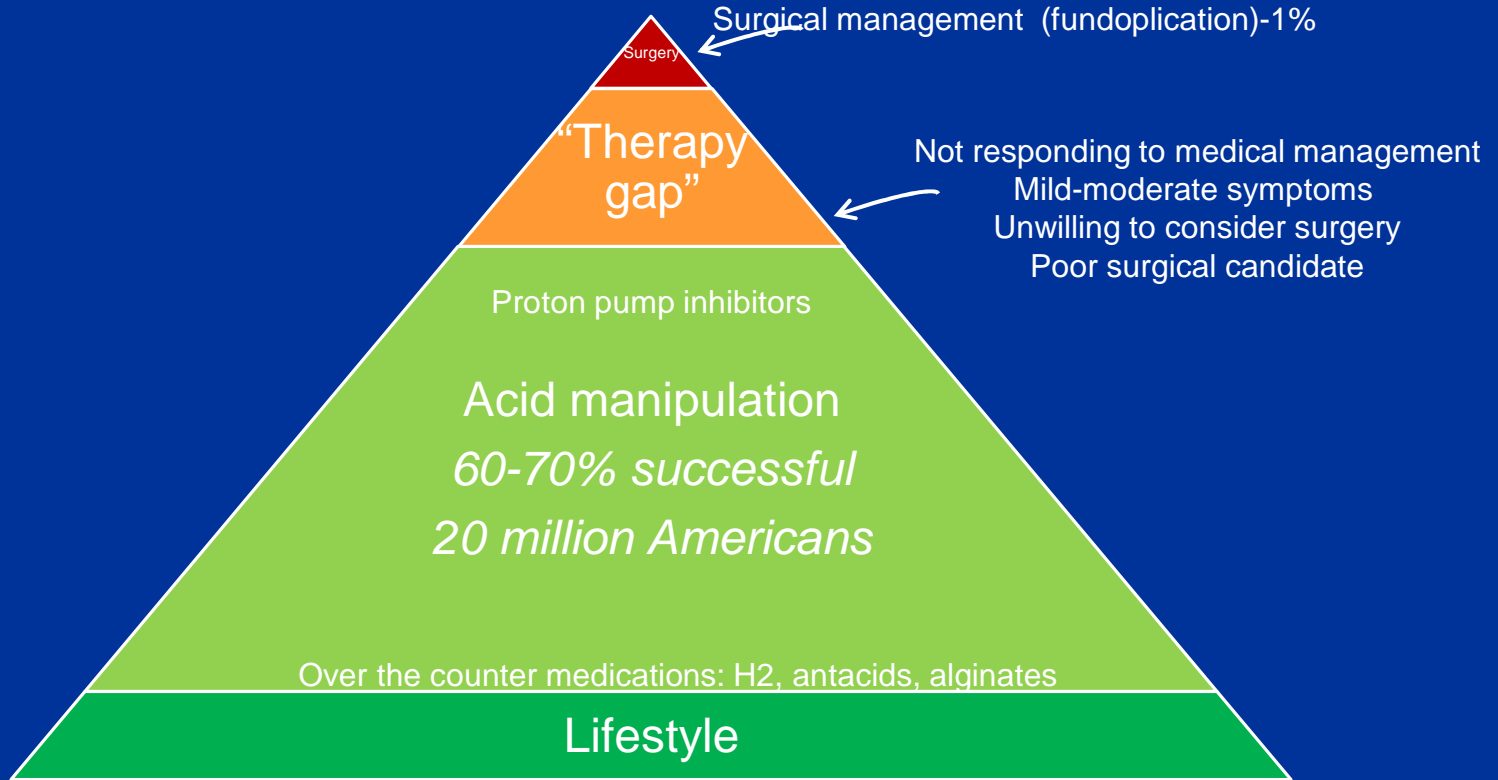
	Pantoprazole 40 mg <i>qd</i> (N=8791)	Placebo <i>qd</i> (N=8807)	Pantoprazole v. placebo	
	No. (%) of first events		OR (95% CI)	P
<i>C. difficile</i>	9 (0.1)	4 (<0.1)	2.26 (0.70 to 7.34)	0.18
Other enteric infections	119 (1.4)	90 (1.0)	1.33 (1.01 to 1.75)	0.04
Fracture	203 (2.3)	211 (2.4)	0.96 (0.79 to 1.17)	0.71
Renal dysfunction	184 (2.1)	158 (1.8)	1.17 (0.94 to 1.45)	0.15
Dementia	55 (0.6)	46 (0.5)	1.20 (0.81 to 1.78)	0.36
Pneumonia	318 (3.6)	313 (3.6)	1.02 (0.87 to 1.19)	0.82

Moayyedi P *et al.*  
*Gastroenterol* 2019.

# Approach to Responsible PPI Use

- Review indication for PPI therapy
- Review dose of PPI therapy
  - Lowest effective dose
- Discuss risk-benefit with patient

# GERD Management



# Anti-reflux surgery

## *A good alternative to PPI?*

- Objective: restore antireflux barrier, ↓ GERD
- Success rates variable (67-95%)
  - Dependent on: surgical expertise, pre-op eval, patient selection
- Serious peri-operative (30-day) complications low
  - Mortality (0.1-0.2%), infection (1.1%), bleeding (0.9%), perforation (0.9%)
  - BUT: acute dysphagia: 50%
- Prolonged complications are common
  - Structural: 30% (disruption, herniation, slippage, stenosis)
  - Functional: dysphagia, gas-bloat, inability to belch/vomit, chest pain, diarrhea (18-31%)
- 62% surgical patients back on PPI *within a decade!*

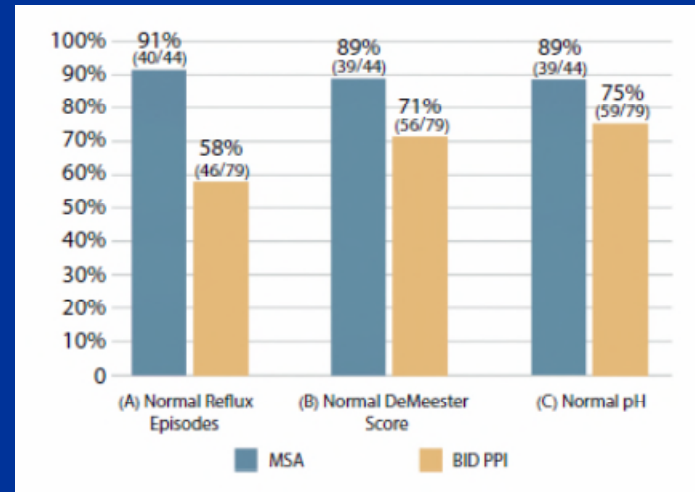
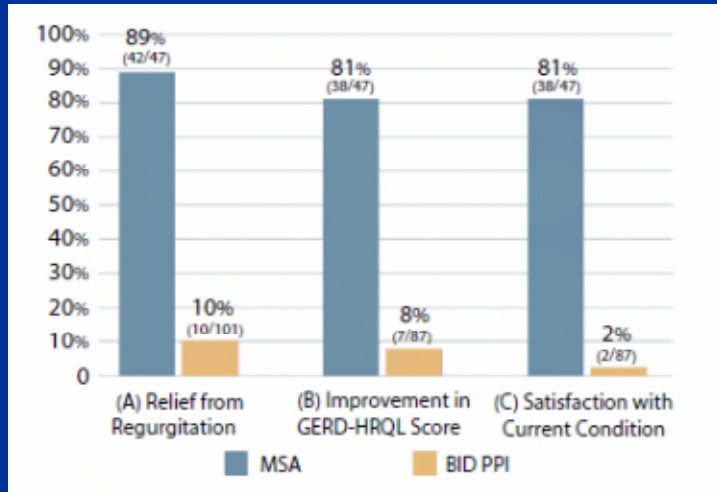
# Magnetic LES Sphincter Augmentation (MSA, LINX)



# Magnetic Sphincter Augmentation (MSA) Advantages



# Magnetic Sphincter Augmentation vs BID PPI



# MSA vs. Nissen

## *Meta-analysis of 3 studies*

- 688 patients (n=273, Lap Nissen, n=415 MSA)
  - **Better with MSA:**
    - Belching (95.2 vs. 65.9%,  $p < 0.00001$ )
    - Emesis (93.5 vs 49.5%,  $p < 0.0001$ )
  - **No difference:**
    - Dysphagia
    - Bloating
    - PPI dependence

# The Ideal MSA Patient

- Typical GERD Sx (heartburn, regurgitation)
- Normal esophageal peristalsis on manometry
- Good symptom correlation on pH testing
- Want a quick recovery
- Smaller hiatal hernia
- No anticipated need for MRI

# Functional GI Disorders (FGID) & Irritable Bowel Syndrome (IBS)

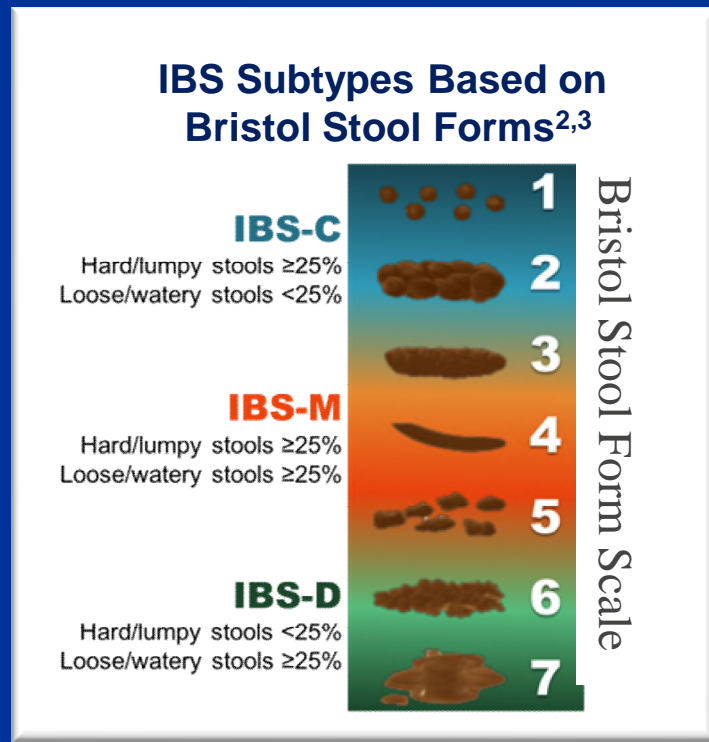
# Defining and Characterizing IBS

## Rome IV Criteria for IBS<sup>1</sup>

Recurrent **abdominal pain**, on average,  $\geq 1$  day per week in the last 3 months, associated with  $\geq 2$  of the following:

- Related to *defecation*
- Change in *frequency* of stool
- Change in *form* (appearance) of stool

Criteria should be fulfilled for the *last 3 months* with symptom *onset*  $\geq 6$  months before diagnosis



IBS-C, irritable bowel syndrome with constipation; IBS-D, irritable bowel syndrome with diarrheal IBS-M, irritable bowel syndrome with mixed symptoms.

1. Lacy BE et al. *Gastroenterology*. 2016;150:1393-1407; 2. Longstreth GF et al. *Gastroenterology*. 2006;130:1480-1491;

3. O' Donnell LJD et al. *BMJ*. 1990;300:439-440.

# The Dichotomy of IBS Diagnostic Approaches

**Rome criteria + for IBS**



**Diagnose IBS**



**IBS is a “diagnosis of exclusion”**



**Rule out ALL other diagnoses**

*Basic laboratories*

*Specialized lab testing*

*Stool studies*

*Multiple endoscopic procedures*

*Multiple imaging studies*



**Diagnose IBS**

# The Dichotomy of IBS Diagnostic Approaches

## Rome criteria + for IBS

*No red flag symptoms*  
*High somatization/anxiety*  
*Normal CBC, Hb, CRP*



**Diagnose IBS**

***LR +17.3, Specificity 99%***



## IBS is a diagnosis of exclusion



**Rule out ALL other diagnoses**

*Basic laboratory tests*  
*Specialized testing*



*Multiple endoscopic procedures*  
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**Diagnose IBS**

# *“Diagnosis IBS and Treat...”*

*Reconsider if No Response or New Symptoms Develop*

## **Rome criteria + for IBS**

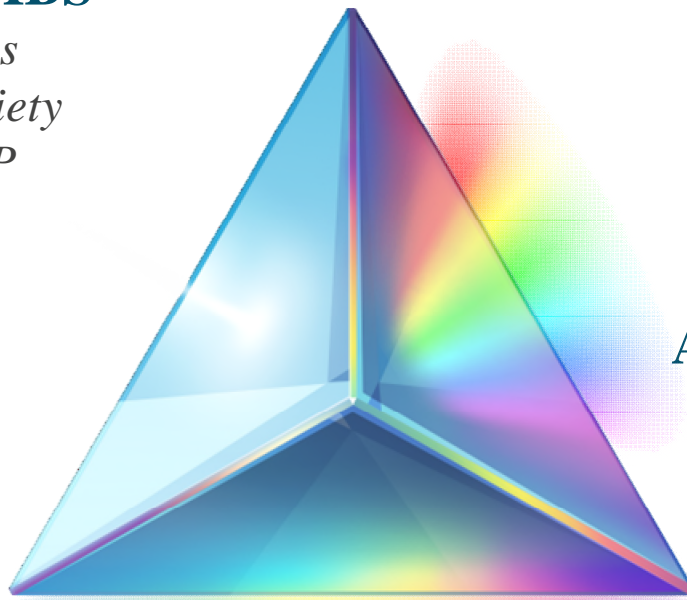
*No red flag symptoms*

*High somatization/anxiety*

*Normal CBC, Hb, CRP*



**Diagnose IBS  
and Treat**



**Expand Differential  
To Consider  
Additional Diagnoses,  
& Pursue Further  
Evaluation**

***No Response to Rx, New Red Flags***



# IBS Pharmacotherapy

*Remember when?*



# IBS Pharmacotherapy

## *Tegaserod for IBS with constipation*



# Tegaserod for IBS with constipation

*“Not all smiles”*



- March 30, 2007: FDA “discontinued marketing” of tegaserod “for safety reasons.”
- Retrospective review of 29 premarketing trials (11,614 tegaserod-treated subjects):
  - 10-fold increase in the RR of significant pooled cardiovascular events:
  - 0.1% in tegaserod vs. 0.01% in placebo
  - Number needed to harm (NNH) was 1,111
- FDA: because tegaserod was used for a “nonlife-threatening condition”, risk of serious cardiovascular events was felt to be disproportionate to any potential benefit.

# Tegaserod for IBS with constipation

## *Evidence against a CV risk*

- Large matched, case-control study of tegaserod-treated patients (n = 2603), matched 1:6 with untreated (n = 15,618) patients, followed for an average of 2.5 years.
- Cardiovascular event rates were low and similar in both cohorts
  - Primary composite CV endpoint, 54 (0.35%) untreated and 12 (0.46%) treated pts (untreated OR = 1.27, 95% CI: 0.68-2.38, P = .46).
  - A total of 12 (0.1%) untreated and 1 (<0.1%) treated pts were hospitalized for a myocardial infarction (MI).
  - A total of 6 (<0.1%) untreated and NO treated pts died from cardiac causes.
- Failed to confirm a reported large event differential for tegaserod incidentally noted in earlier clinical trials database
  - *\*\*Suggesting that the prior observation may have been due to chance.*

# IBS Pharmacotherapy

## *“What’s old is new again”*

Healio > Gastroenterology > Motility

FDA NEWS PERSPECTIVE

## FDA approves reintroduction of Zelnorm for IBS-C in certain women

April 3, 2019

+ ADD TOPIC TO EMAIL ALERTS



COMMENT



SAVE

The FDA has approved the reintroduction of Zelnorm, a twice-daily oral treatment for irritable bowel syndrome with constipation in women aged under 65 years, according to a company press release.

The FDA originally approved [tegaserod](#) (Zelnorm, Sloan Pharmaceuticals) in 2002 for the treatment of IBS-C in women. However, Novartis, the drug’s previous manufacturer, voluntarily pulled tegaserod from the U.S. market in 2007 due to possible cardiac-related side effects.

### SEE ALSO

[First opioid lawsuit settlement raises questions with...](#)

[Top 5 stories you may have missed in March](#)

[Advanced liver cancer therapy meets overall survival...](#)

Tegaserod has been available in the U.S., but only through an FDA-authorized expanded access program.

“We are excited about what the reintroduction of Zelnorm means for patients suffering from irritable bowel syndrome with constipation,” **P. Breckinridge Jones**, CEO of U.S. WorldMeds, said in the press release. “We have continually heard from patients and clinicians alike that the IBS-C community is eager to have Zelnorm return to the U.S. as an available treatment option.”

# IBS Pharmacotherapy

## *"What's old is new again"*

Healio > Gastroenterology > Motility

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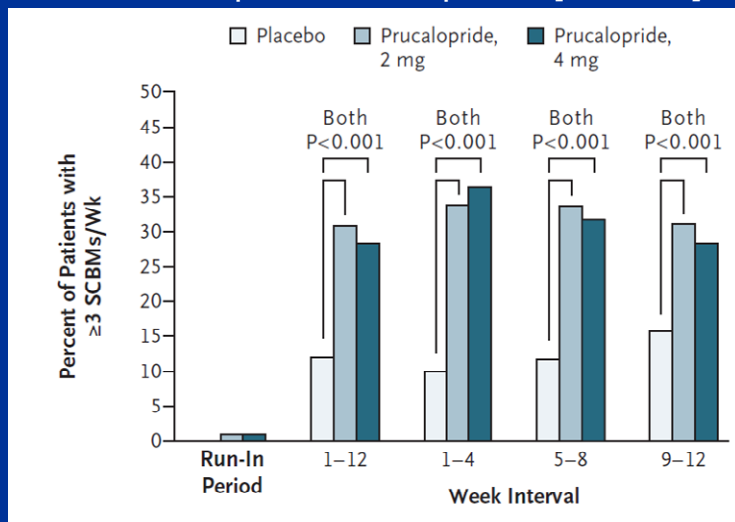
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# Prucalopride as a “Newer” prescription option

## • 5-HT<sub>4</sub> receptor agonist

- Improves colonic motility, (decreases colonic transit time)
- Increase spontaneous complete bowel movements (SCBMs)
- In chronic idiopathic constipation [NNT ~5]



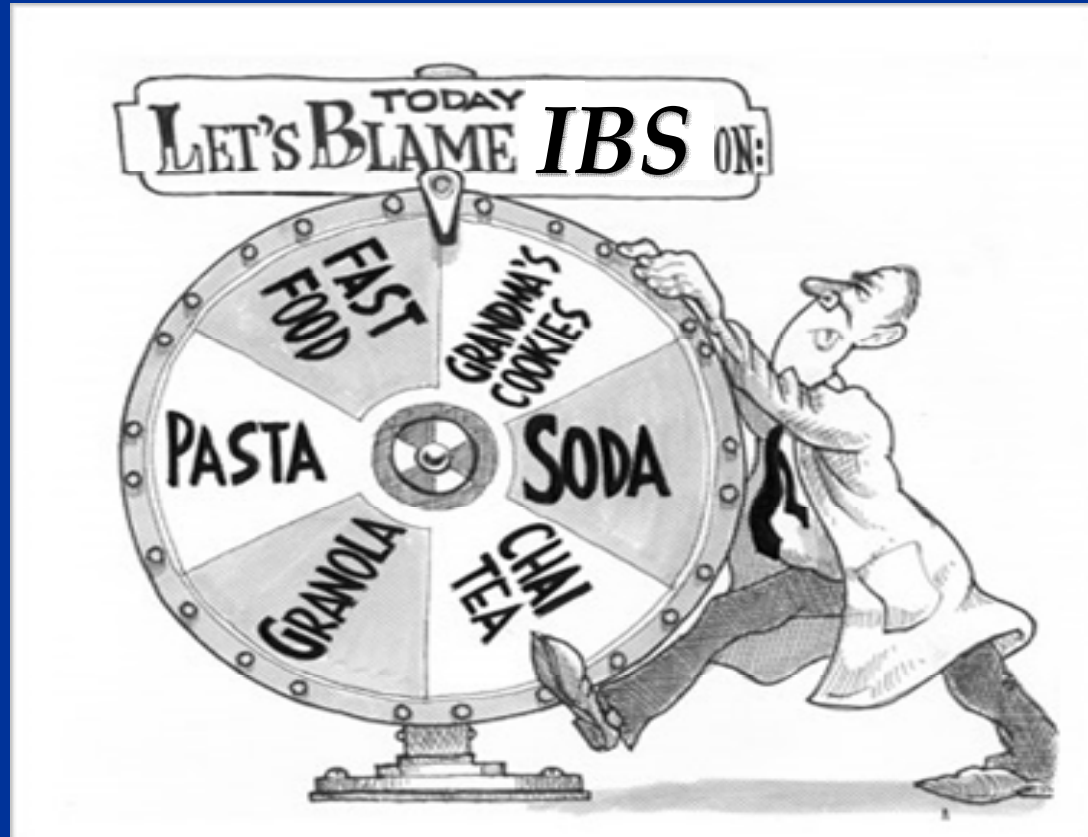
- More specific 5-HT<sub>4</sub> receptor activity than predecessors
- No observed increase in cardiac events or QTc
- Systemic effects: Nausea, headache
- “Suicidal ideation and behavior” warning

Drug	Receptor binding profile at therapeutic concentrations					
	5-HT <sub>4</sub>	5-HT <sub>3</sub>	5-HT <sub>2</sub>	5-HT <sub>1</sub>	D <sub>2</sub>	hERG
Cisapride	+	+	+			+
Tegaserod	+	+	+	+		
Renzapride	+	+				
Cleopride	+	+			+	
Mosapride	+	+				
Prucalopride	+					
Velusetrag	+					
Naropride	+					

Tack J, Camilleri M, et al. AP&T 2012.

Mohammad S, Zhou Z, et al. Am J Physiol 1997.

# Diet and IBS...*circa 2000*





# Diet and IBS...2019



# What are FODMAPs?

## Fermentable **O**ligo-, **D**i-, **M**onosaccharides **A**nd **P**olyols



### **Excess Fructose**

Honey, apples, pears,  
peaches, mangos, fruit  
juice, dried fruit

### **Fructans**

Wheat (large amounts), rye  
(large amounts), onions,  
leeks, zucchini

### **Sorbitol**

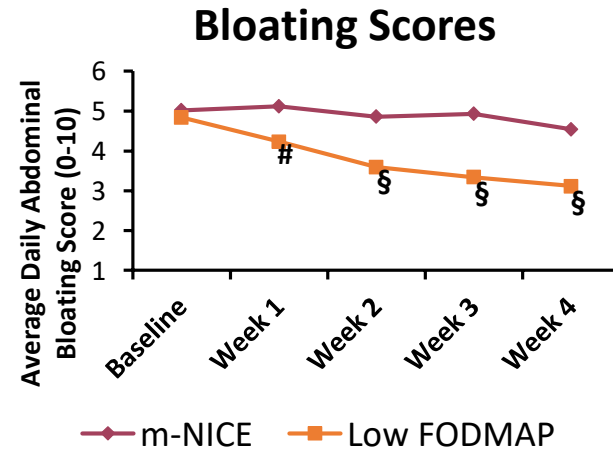
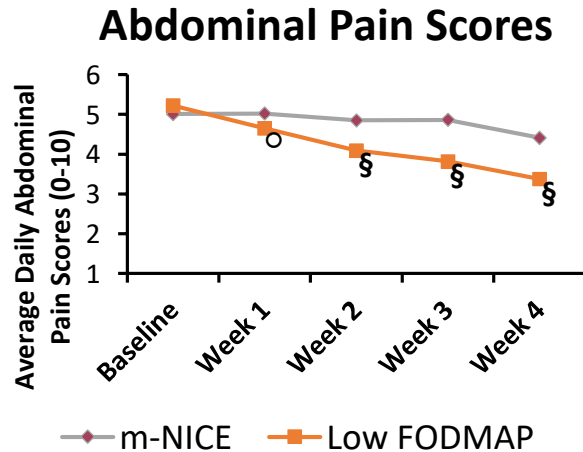
Apricots, peaches, artificial  
sweeteners, artificially  
sweetened gums

### **Raffinose**

Lentils, cabbage, brussels  
sprouts, asparagus,  
green beans, legumes

# Dietary Management of IBS

*FODMAP > mNICE for abdominal pain and bloating*

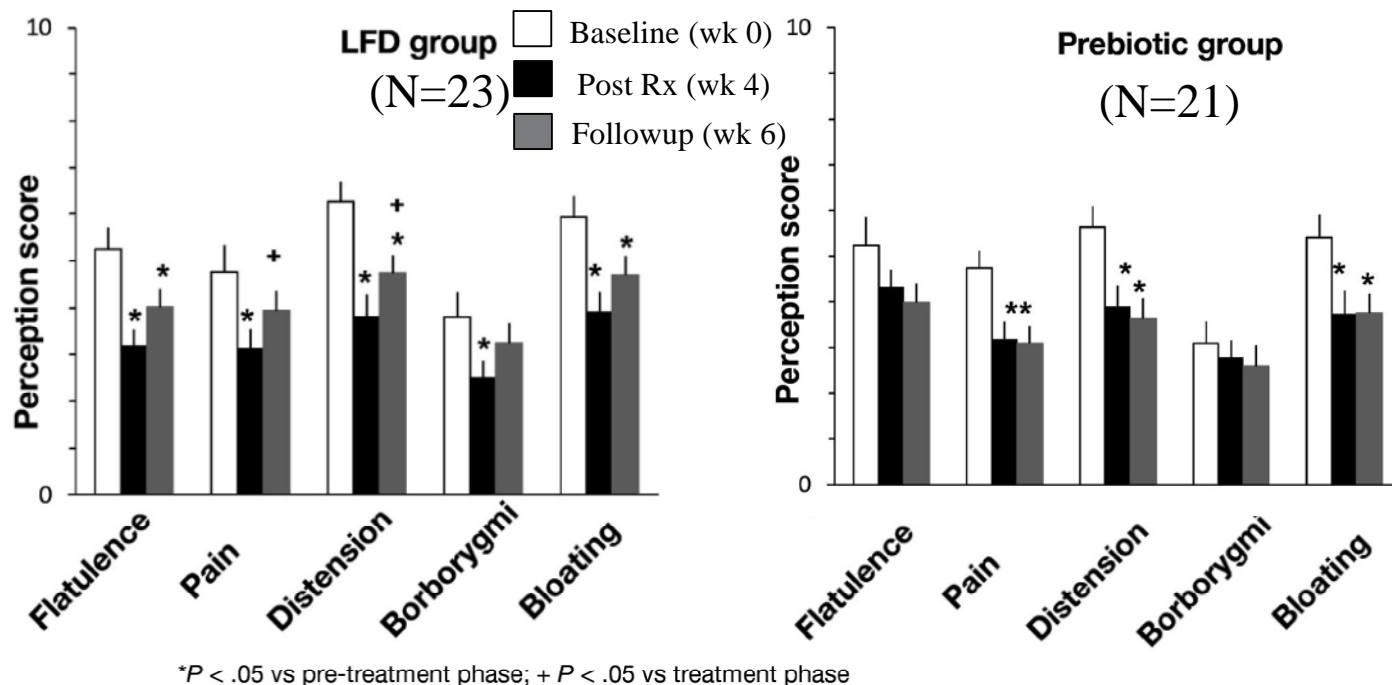


*P values refer to the change WITHIN group comparing to baseline score.*

*\*P≤0.05; °P≤0.001; §P≤0.0001.*

# Prebiotics for IBS

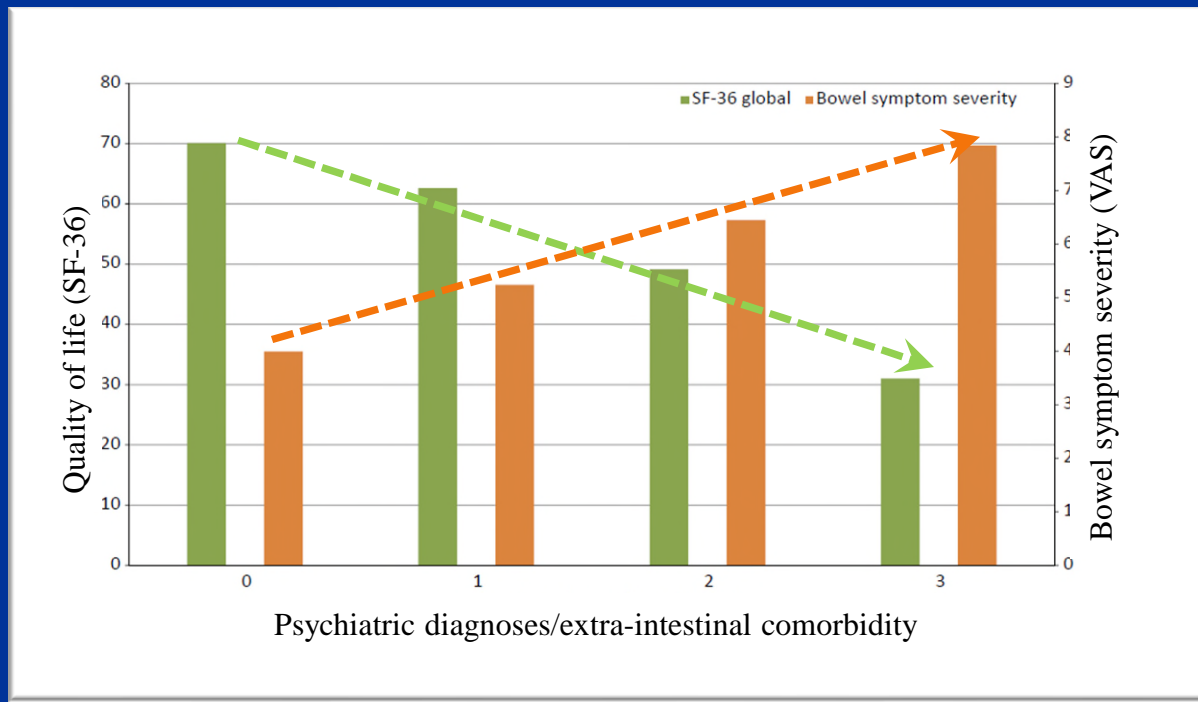
*As effective as low FODMAP diet (with continued benefit!)*



*LFD = low FODMAP diet*

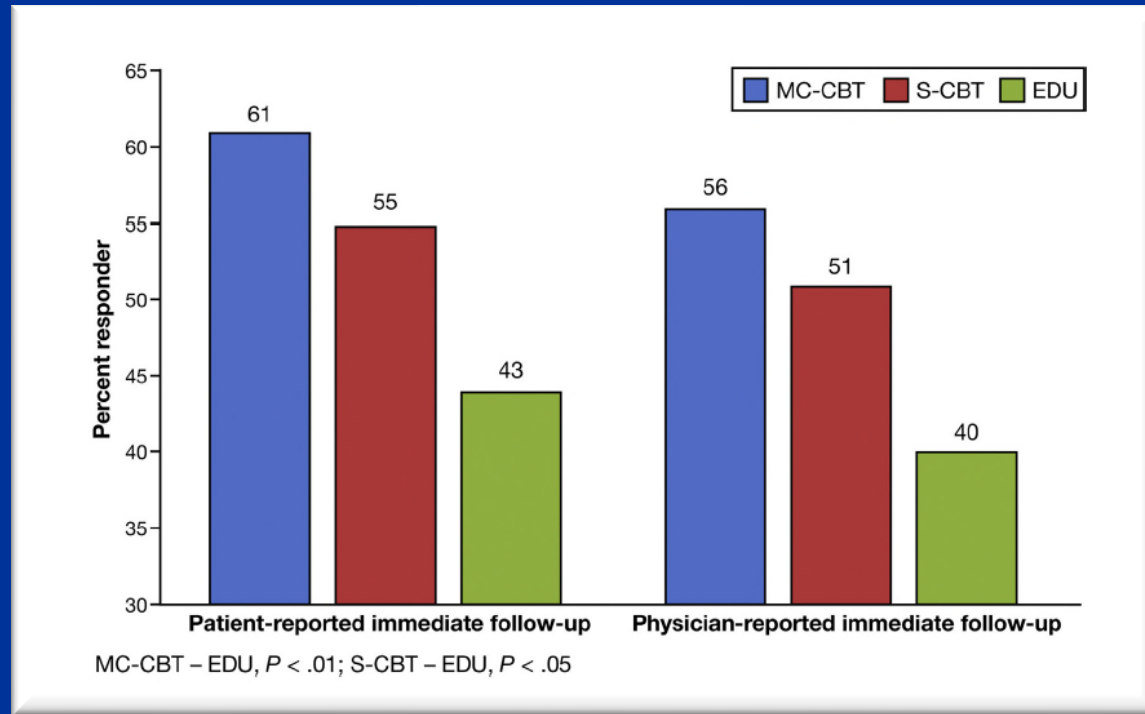
# Psychiatric and Extra-intestinal Comorbidities in IBS

*Additive worsening of **HRQOL** and **Bowel Symptoms***



# Cognitive Behavioral Therapy (CBT) for IBS

*Minimal contact (and standard) CBT improves refractory IBS symptoms*



MC-CBT = minimal contact cognitive behavioral therapy

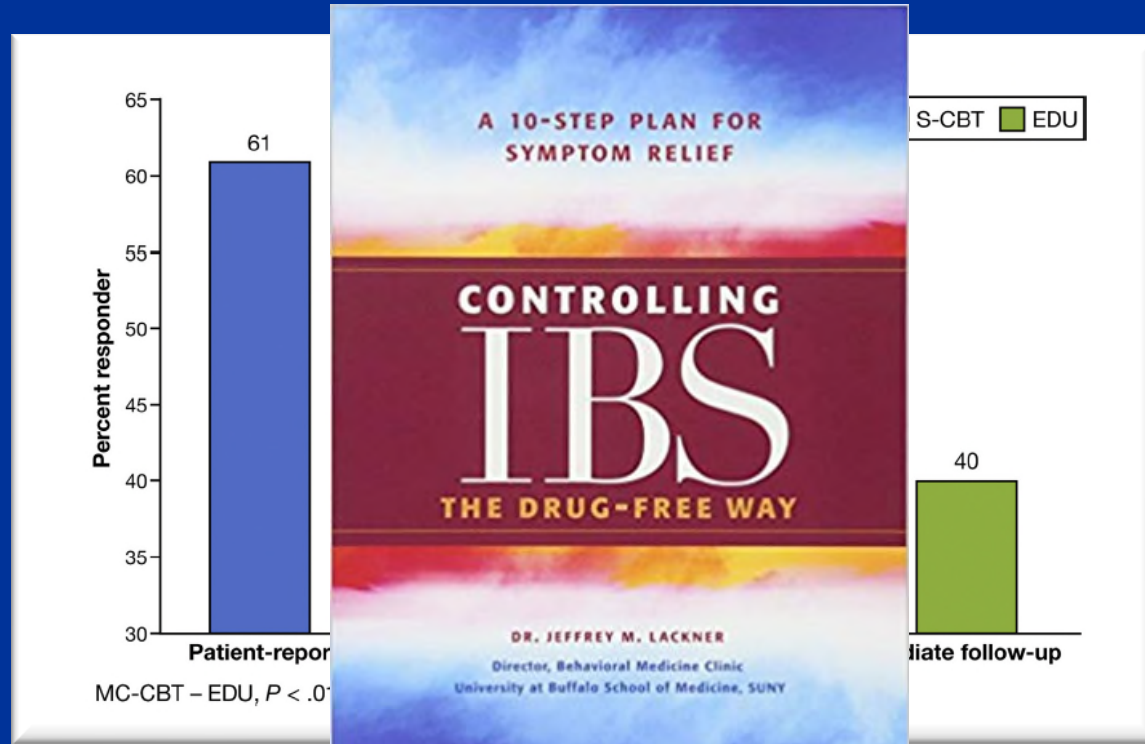
S-CBT = standard cognitive behavioral therapy

EDU = education control

Lackner J *et al. Gastroenterol* 2018.

# Cognitive Behavioral Therapy (CBT) for IBS

*Minimal contact (and standard) CBT improves refractory IBS symptoms*



MC-CBT = minimal contact  
S-CBT = standard cognitive  
EDU = education control

Lackner J *et al. Gastroenterol* 2018.

# Colon Cancer Screening



# Bowel Prep for Colonoscopy

*Poor prep = poor study*

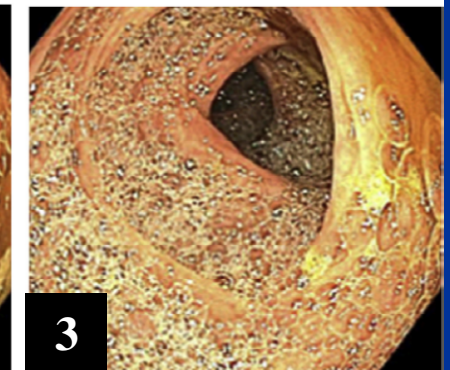
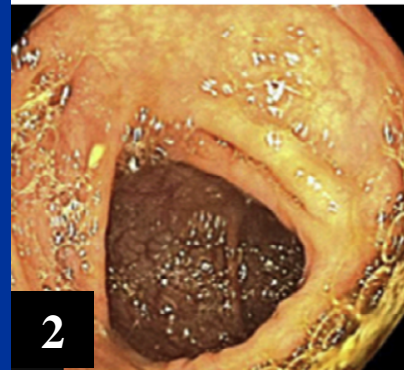
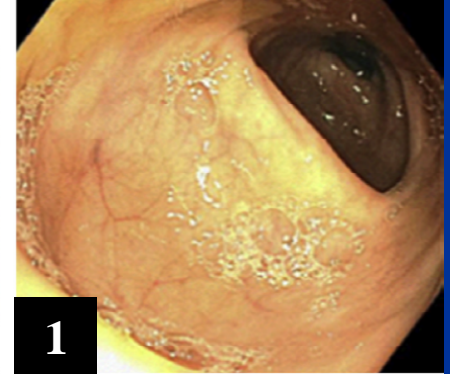
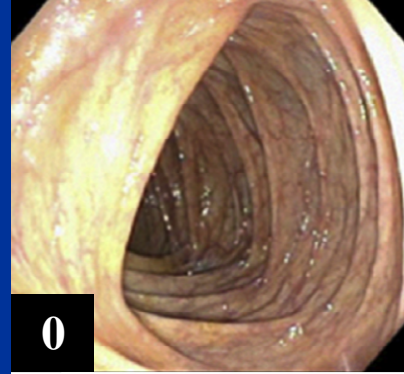
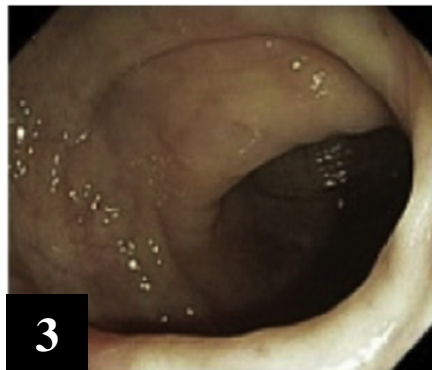
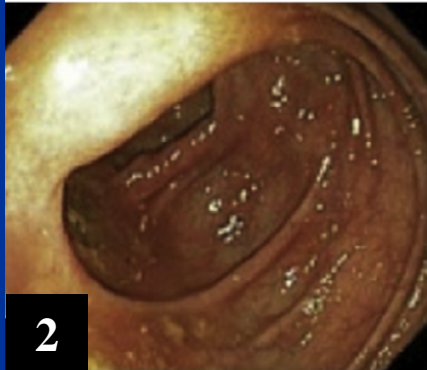
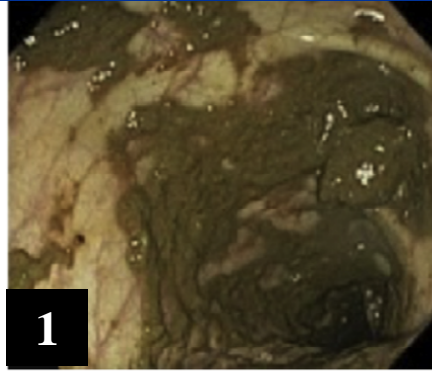
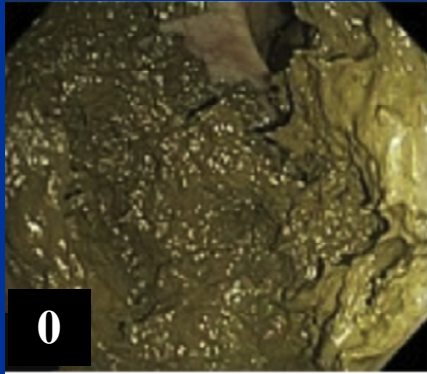
- Even with excellent prep, colonoscopy is imperfect
  - 5% miss rate clinically significant lesions (polyp  $\geq 1$ cm)
- Prep is inadequate in up to 25% of examinations
- Split-dose better than single dose (85 vs. 63% adequate)
- Inadequate bowel preparation increases:
  - Risk of adverse events during procedure
  - Missed polyps
  - Insertion time, overall procedure time
  - Incomplete procedures
  - Number of procedures needed

# Patient risk factors for poor bowel prep

- Prior inadequate preparation
- Hx constipation
- Constipating medications (e.g., TCAs and opioids)
- Dementia or Parkinson disease
- Male sex
- Low health literacy/cognitive skills
- Low patient engagement
- Overweight/obese
- Diabetes mellitus
- Previous colorectal surgery
- Cirrhosis

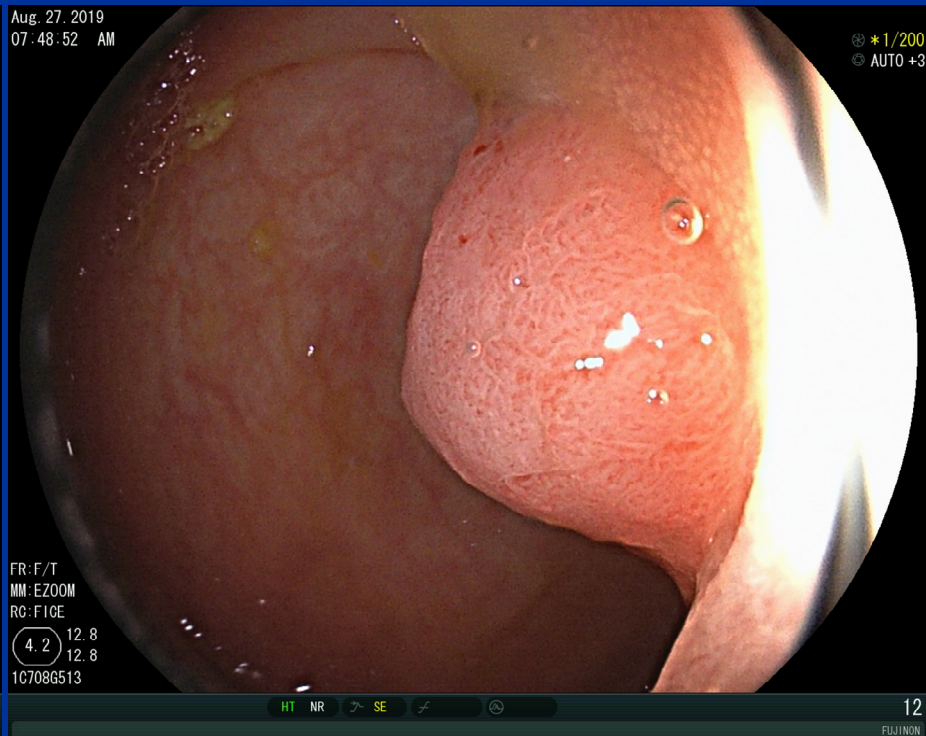
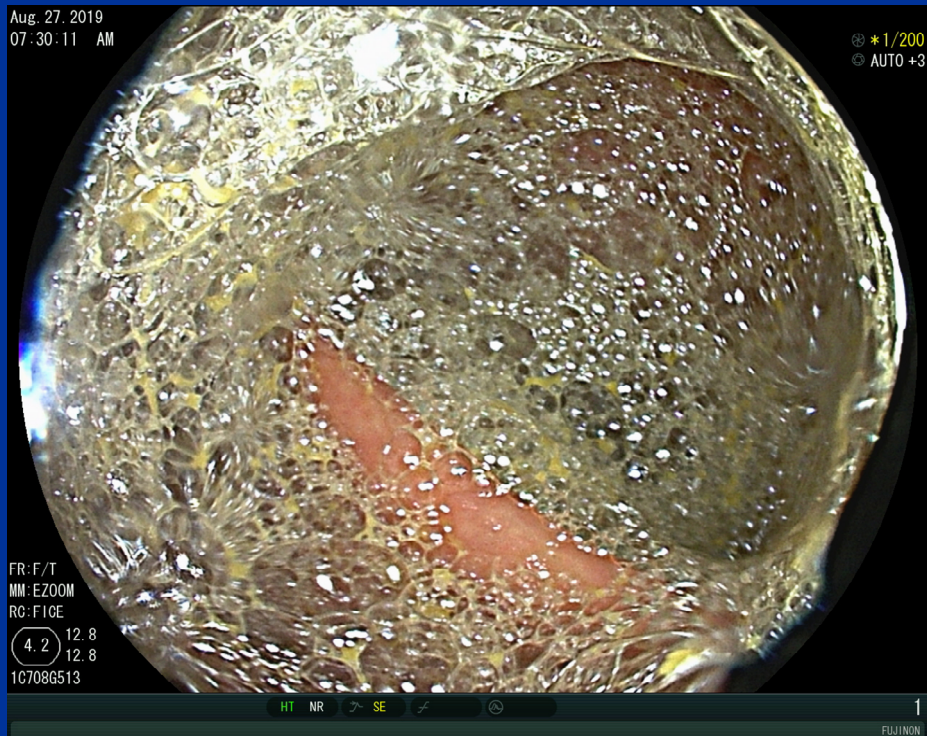
# Bowel prep quality

*Boston Bowel prep score (BBPS) and Bubble score*

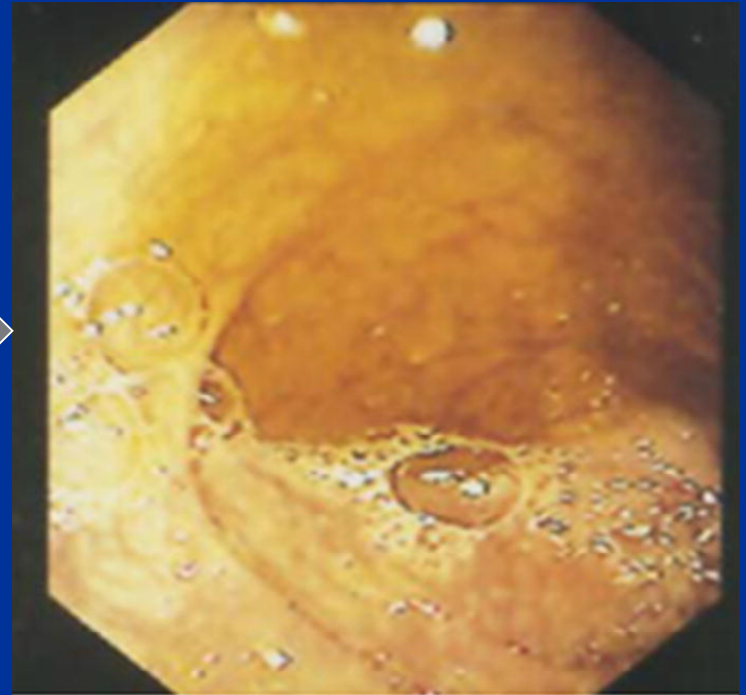
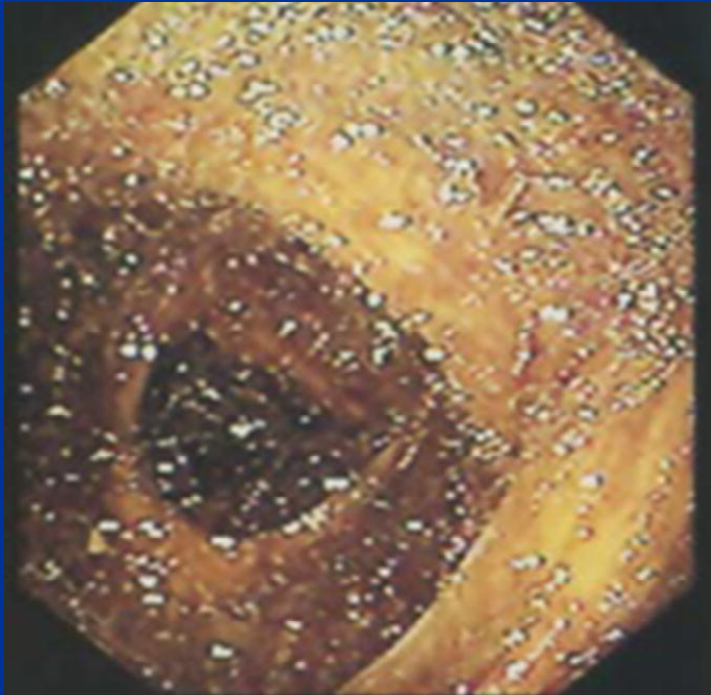




# A Recent Case...



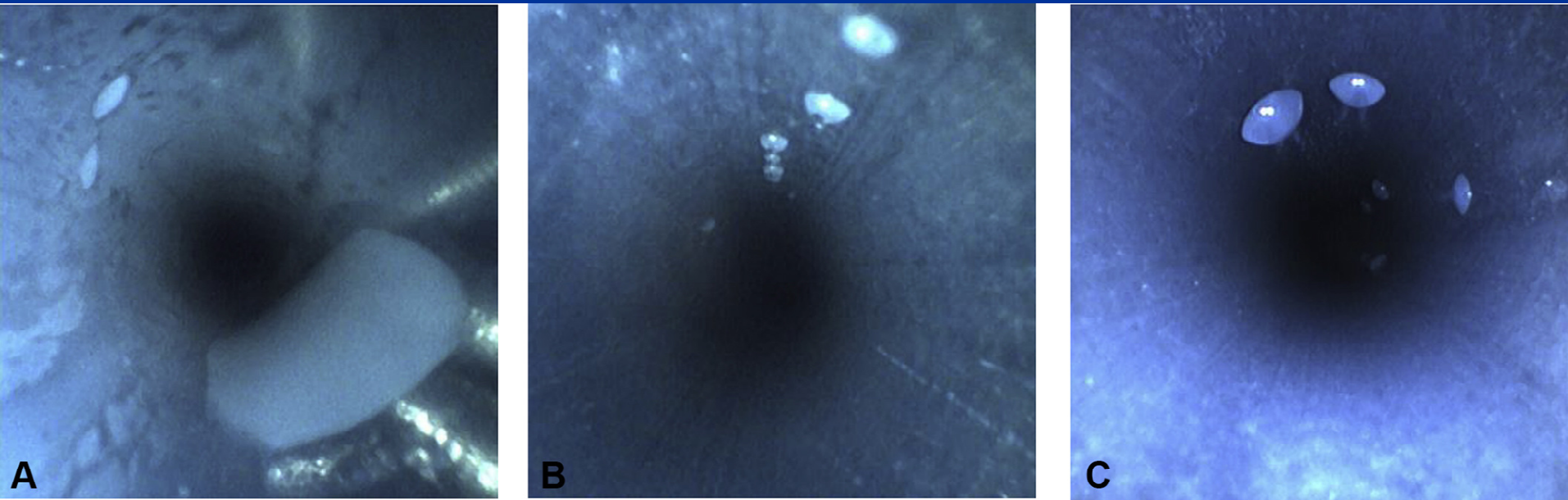
# Simethicone helps reduce colon bubbles



Kim H, et al. *Digestive Dis Sci* 2019.



# But...Is Simethicone safe?



Olfstead CM *et al.* *Am J Infection Control* 2016. Bakarar MT *et al.* *Gastrointest Endoscopy* 2019.  
Olympus Corporation of the Americas [US]. *Use of simethicone and other non-water soluble additives with Olympus flexible endoscopes* June 29, 2018. Cited 20 August 2018. Available from URL:  
<https://medical.olympusamerica.com/sites/us/files/pdf/Customer-Letter-Use-of-simethicone-and-lubricants.pdf>

# But...Is Simethicone safe?

“Olympus does not recommend the use of non-water-soluble additives with our flexible endoscopes or ancillary equipment. These products may be difficult to remove during manual cleaning and may reduce the efficacy of the reprocessing procedure.”

Olfstead CM *et al.* *Am J Infection Control* 2016. Bakarar MT *et al.* *Gastrointest Endoscopy* 2019.  
Olympus Corporation of the Americas [US]. *Use of simethicone and other non-water soluble additives with Olympus flexible endoscopes* June 29, 2018. Cited 20 August 2018. Available from URL:  
<https://medical.olympusamerica.com/sites/us/files/pdf/Customer-Letter-Use-of-simethicone-and-lubricants.pdf>

## Deadly CRE Germs Linked to Hard-to-Clean Medical Scopes



Officials at the U.C.L.A. Medical Center reported this week that a superbug had infected seven people, killing two of them. Damian Dovarganes/Associated Press

By Sabrina Tavernise

Feb. 19, 2015



WASHINGTON — Federal officials warned health care providers across the country on Thursday that difficult-to-clean medical scopes inserted down the throat might be infecting patients with deadly drug-resistant bacteria.

Yet....there are no published reports of adverse events related *specifically* to the use of simethicone.



# Is Simethicone OK to use for colonoscopy?

*It depends on who you ask!*

- **The Gastroenterology Society of Australia (2019):** “The *continued use* of simethicone is considered reasonable as it improves mucosal inspection during colonoscopy.”
- **The American Society for Gastrointestinal Endoscopy (2016):** “*Insufficient evidence to recommend a change* to current clinical practice.”
- **The Canadian Association of Gastroenterology:** “*Unable to make clear recommendations* on the use of simethicone at this time.”
- **The British Society of Gastroenterology (2017):** “*Concentration of simethicone should be kept to a minimum* and that it be administered orally or via the biopsy channel”
- **The European Society of Gastrointestinal Endoscopy:** “*Recommend adding simethicone to standard bowel preparation* for colonoscopy.”

# The role of oral simethicone on the adenoma detection rate and other quality indicators of screening colonoscopy: a randomized, controlled, observer-blinded clinical trial

Sharareh Moraveji, MD,<sup>1</sup> Nancy Casner, CRC,<sup>1</sup> Mohammad Bashashati, MD,<sup>2</sup> Cesar Garcia, MD,<sup>3</sup> Alok Dwivedi, PhD,<sup>4</sup> Marc J. Zuckerman, MD,<sup>1</sup> Andres Carrion, MD,<sup>1</sup> Antonio Mendoza Ladd, MD<sup>1</sup>

El Paso, Texas, USA

	PEG + SIM (n = 129)	PEG (n = 139)	P value
Cecal intubation time, mean ( $\pm$ SD), sec	363.6 ( $\pm$ 222.7)	371.6 ( $\pm$ 277.3)	.71
Withdrawal time, mean ( $\pm$ SD), sec	395.7 ( $\pm$ 69.2)	399.0 ( $\pm$ 76.7)	.79
Effective procedure time, mean ( $\pm$ SD), sec	759.3 ( $\pm$ 253.1)	800.2 ( $\pm$ 459.6)	.37
Polyp detection rate, %	46.5%	49.6%	.61
Adenoma detection rate, %	33.3%	38.8%	.88
Intraprocedural use of SIM, no. (%)			< .05
Yes	2 (1.6%)	68 (48.9%)	
No	127 (98.4%)	71 (51.1%)	

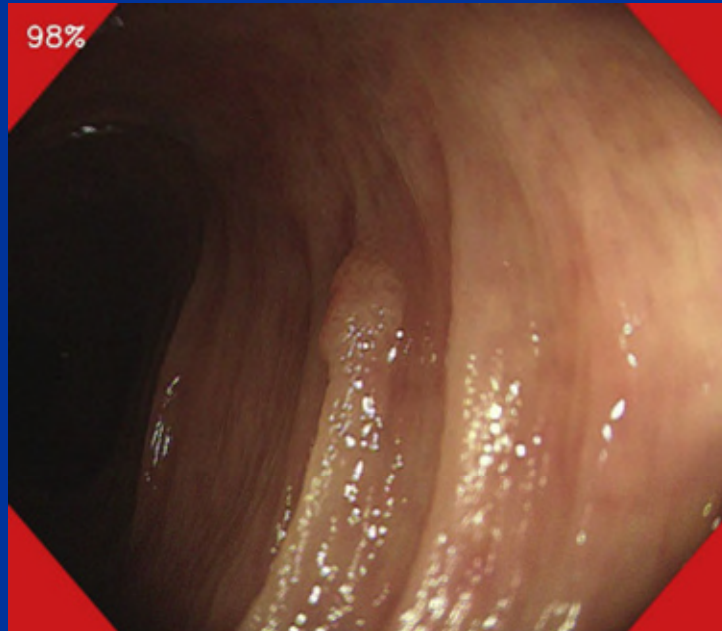
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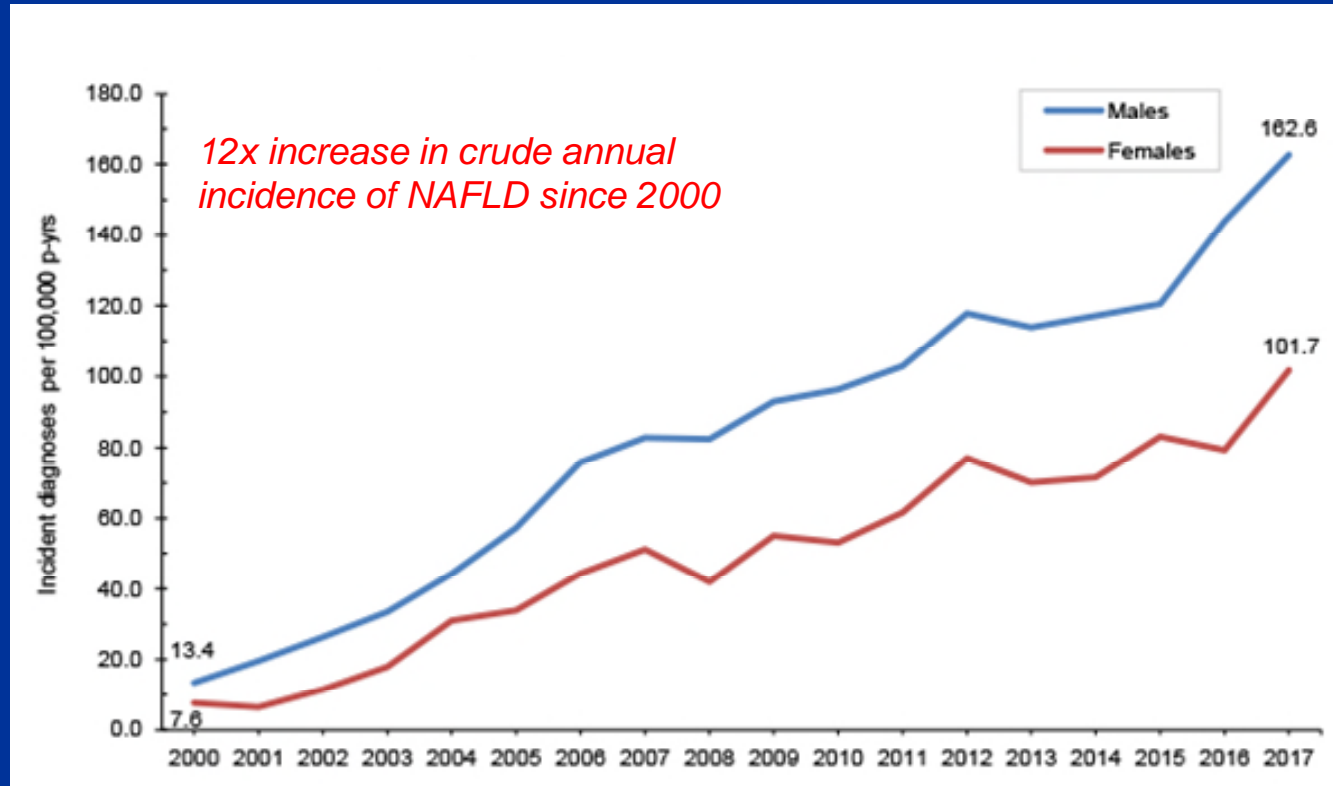
	PEG + SIM (n = 129)		PEG (n = 139)		P value	
	Bubble scale	BBPS	Bubble scale	BBPS	Bubble scale	BBPS
Endoscopist 1: total mean ( $\pm$ SD)*	0.1 ( $\pm$ 0.2)	8.9 ( $\pm$ 0.4)	2.1 ( $\pm$ 2.1)	8.9 ( $\pm$ 0.4)	$\dagger < .001$	$\dagger .87$
Rectosigmoid colon	0.01 ( $\pm$ 0.09)	2.98 ( $\pm$ 0.13)	0.34 ( $\pm$ 0.74)	2.98 ( $\pm$ 0.15)	$< .001$	.73
Transverse colon	0.02 ( $\pm$ 0.13)	2.99 ( $\pm$ 0.09)	1 ( $\pm$ 1.05)	2.99 ( $\pm$ 0.12)	$< .001$	.62
Ascending colon	0.01 ( $\pm$ 0.09)	2.97 ( $\pm$ 0.18)	0.75 ( $\pm$ 0.89)	2.93 ( $\pm$ 0.29)	$< .001$	.21

# The Future?...Computer Aided Detection of Colon Polyps

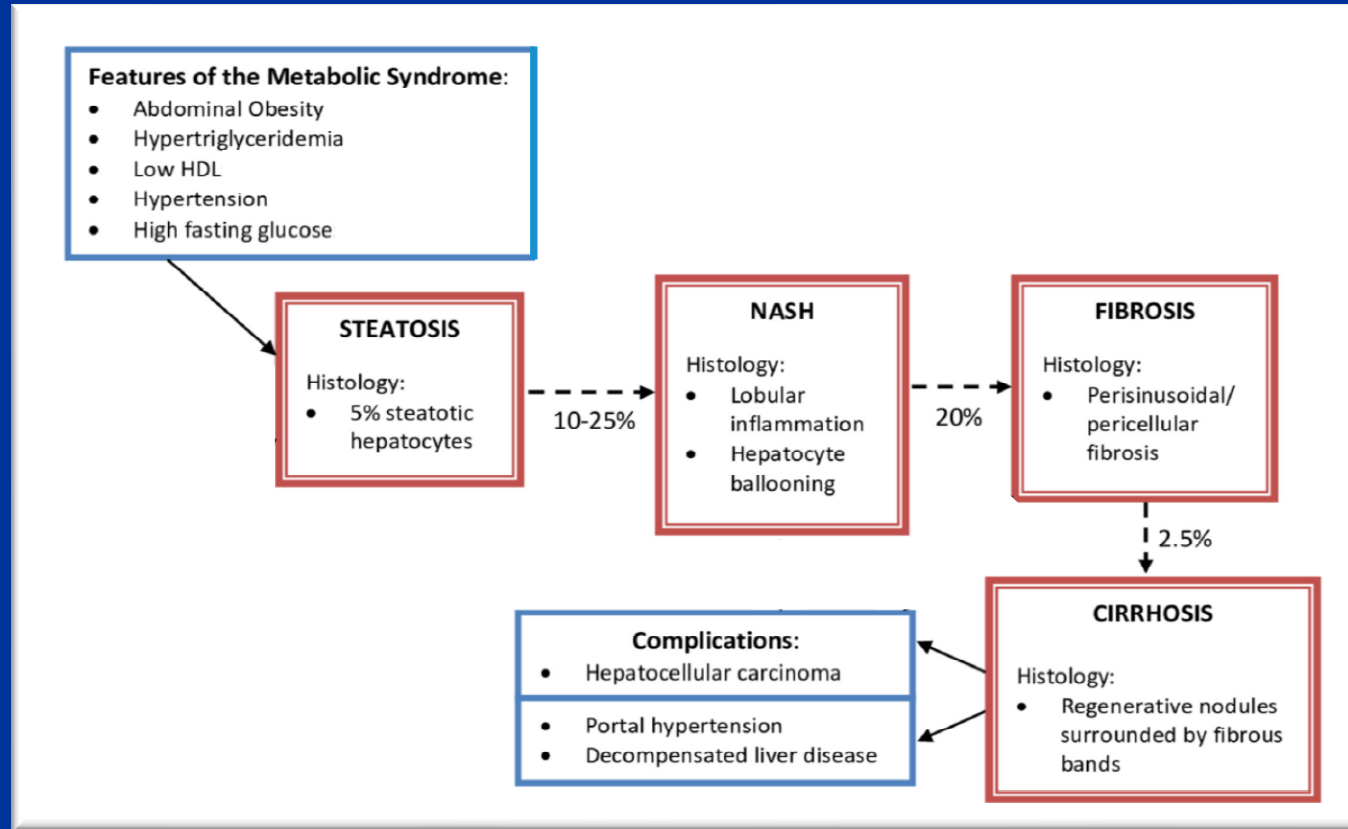


# Non-alcoholic Fatty Liver Disease (NAFLD)

# Annual Rates Incident NAFLD, US Armed Forces



# The Natural History of Non-Alcoholic Fatty Liver (NAFLD)



# Management of NAFLD...circa 2000



“You need to lose weight”

6 mo



“You still need to lose weight”

6 mo



“Keep working to lose weight”

6 mo



Pray patient doesn't  
develop cirrhosis/cancer



“You REALLY need to lose weight!”

6 mo

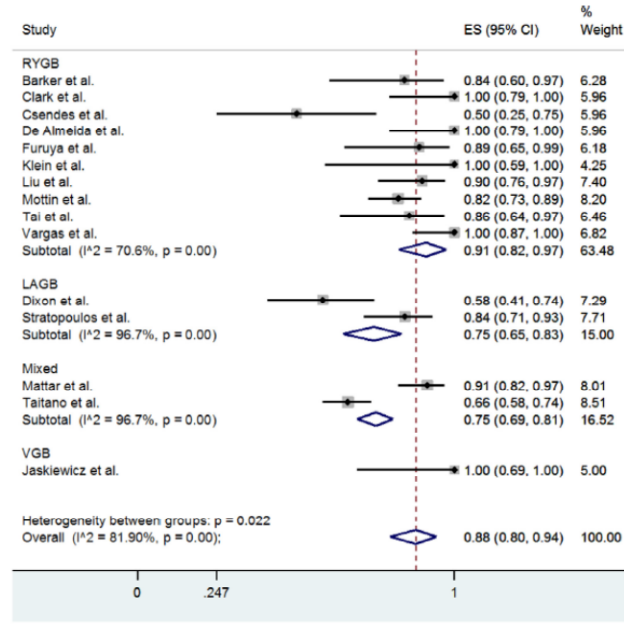


Liver biopsy to confirm  
NAFLD/NASH

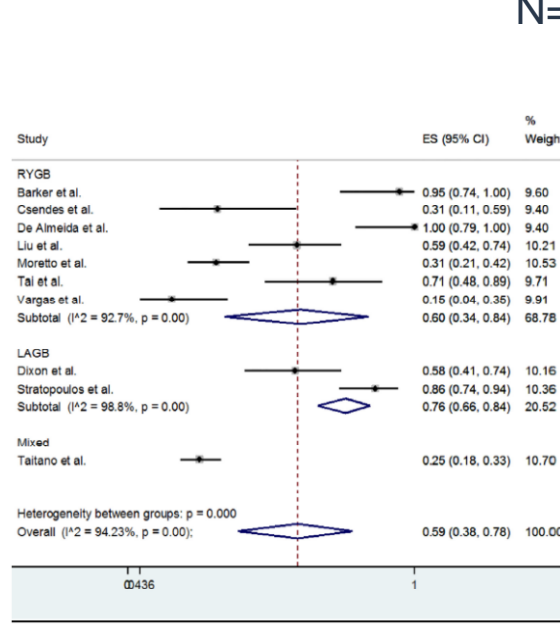


# Bariatric surgery outcomes in NAFLD

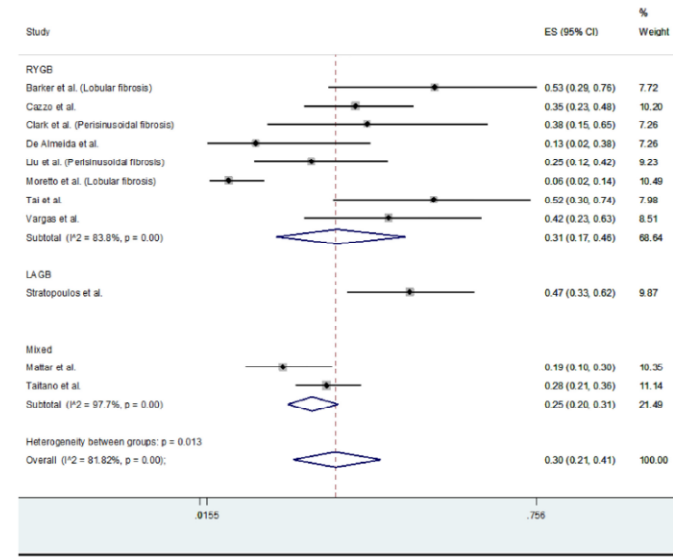
N=2374 patients



Improvement/resolution steatosis  
88% (88-94%)



Improvement/resolution steatohepatitis  
59% (38-78%)



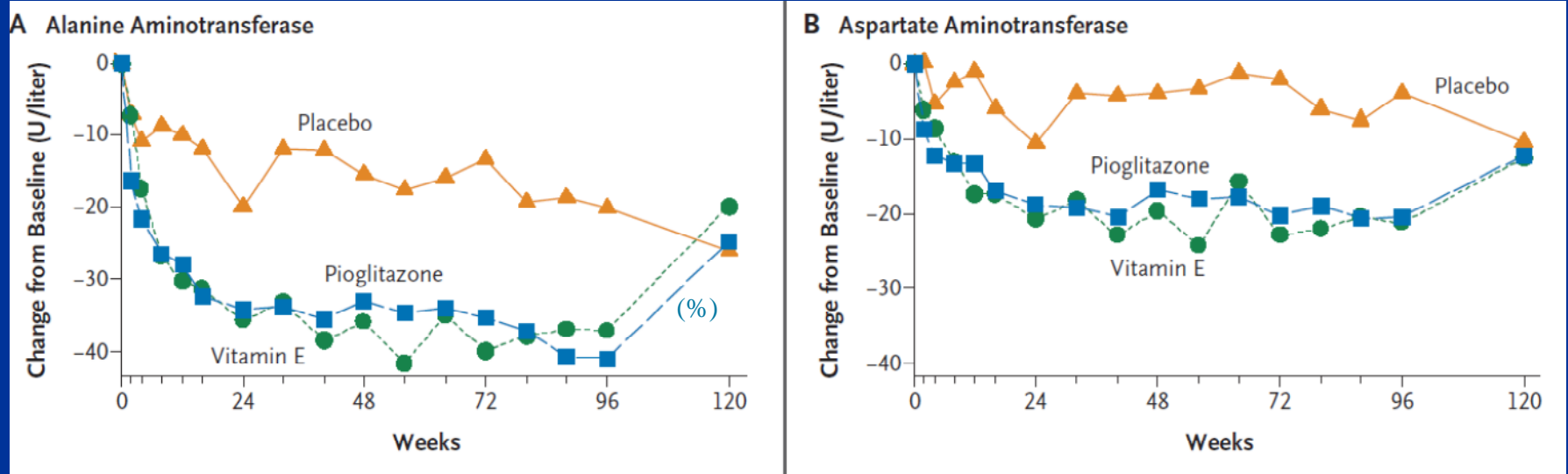
Improvement/resolution fibrosis  
30% (21-48%)

*RYGB more effective than other surgeries at improving NAFLD histology*

# Vitamin E and Pioglitazone

## *The good: Improvement in transaminases*

*247 non-diabetic patients with steatohepatitis*



# Vitamin E and Pioglitazone

*The good: Improvement in histology*

	Placebo	Vitamin E	Pioglitazone
<b>Steatosis</b>	31	54	60
<b>Lobular inflammation</b>	35	54	60
<b>Fibrosis</b>	31	41	44
<b>Resolution of NAFLD</b>	21	36	47

# Vitamin E and Pioglitazone

*The not so good*

## Pioglitazone

- Diabetics only
- Weight gain!
- Heart failure
- Fracture risk
- ? Bladder cancer risk

## Vitamin E

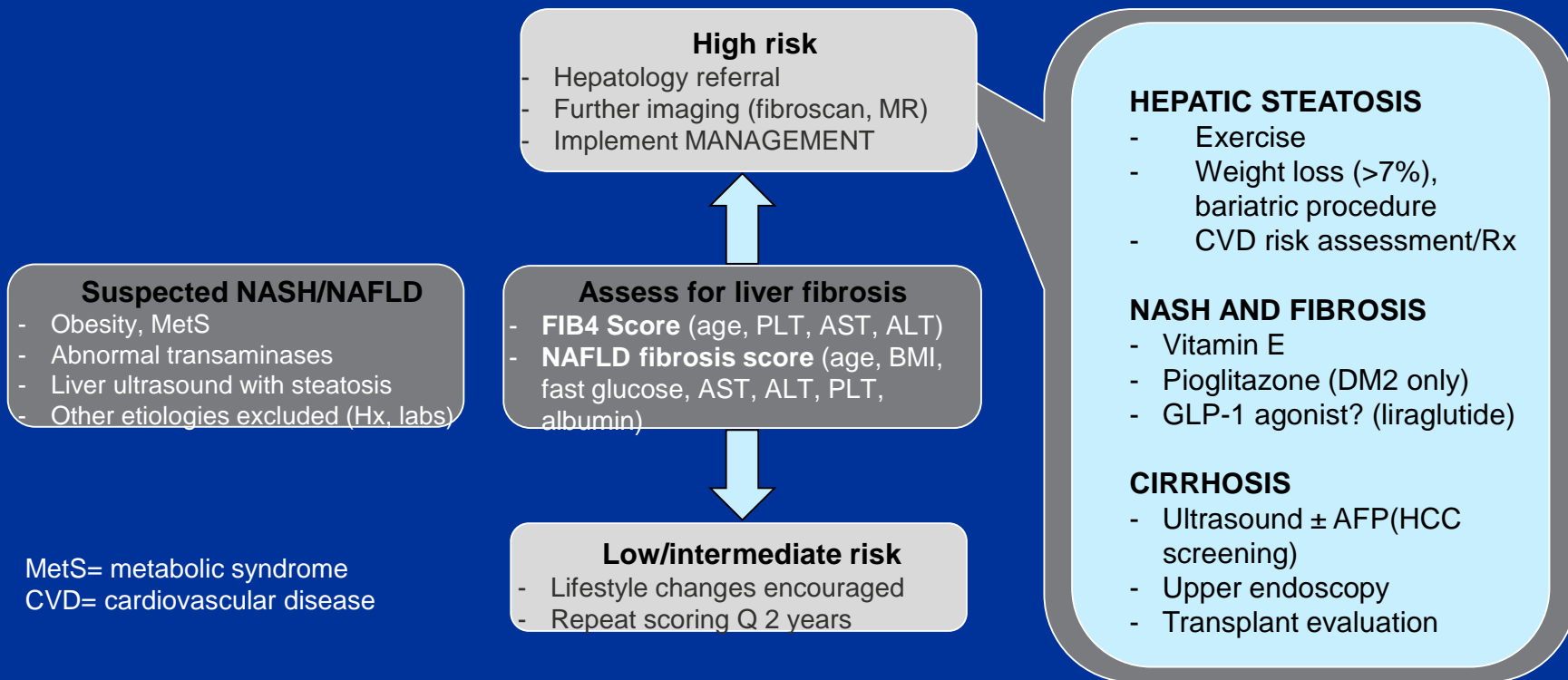
- Not studied in diabetics or decompensated cirrhosis
- Increase in all cause mortality?
- Increase risk prostate cancer (SELECT)

2018 AASLD Practice Guidelines, Non-alcoholic fatty liver disease,  
<http://aasldv2019stg.aasld.org/sites/default/files/2019-06/NAFLD%20Guidance%202018.pdf>.

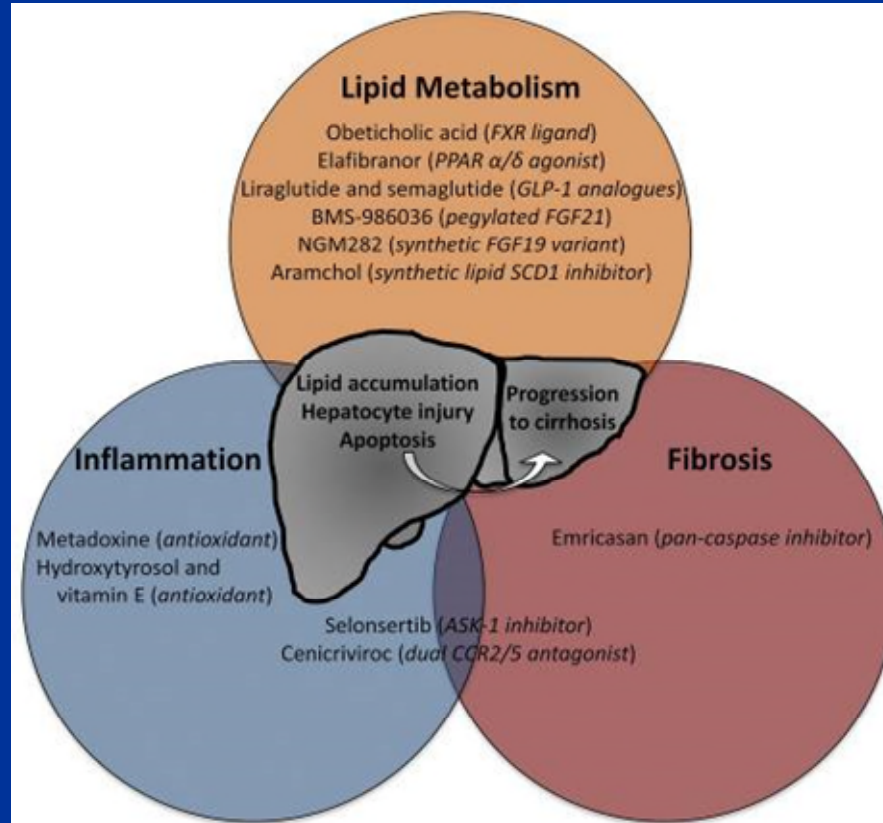
Lippmann SM, *et al.* JAMA 2009.

# Management of NAFLD in 2019

*Fibrosis is the key of liver-related and all-cause mortality*



# The Future of NAFLD Treatment?

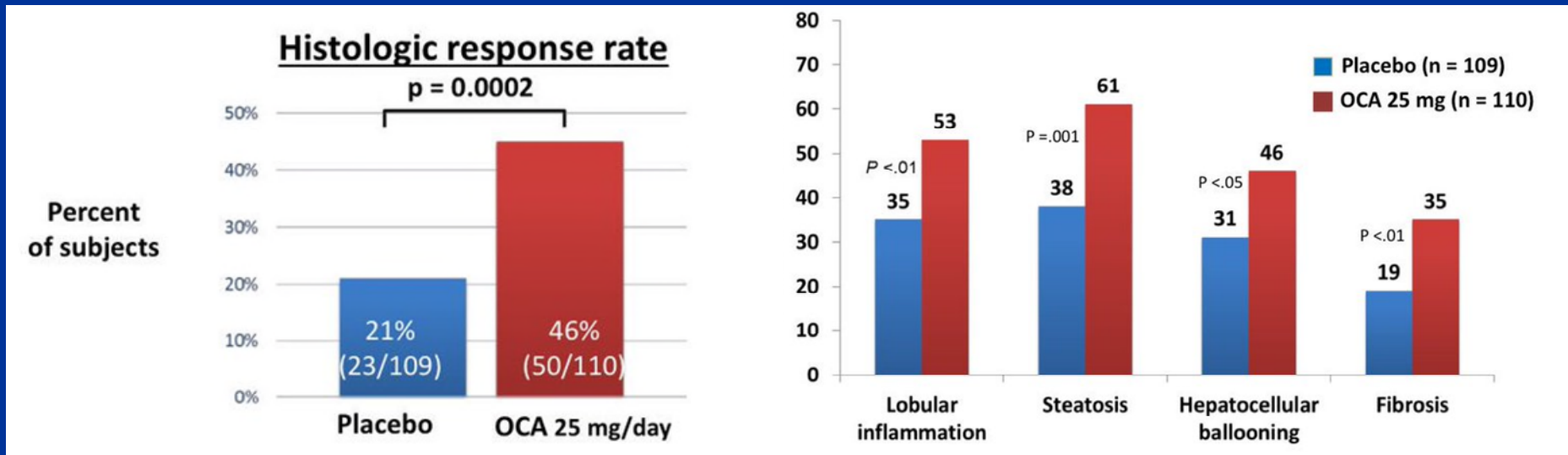


# The Future of NAFLD Treatment?

## *Obetacholic acid*

Primary endpoint

Key Secondary Endpoints—72 wks



\* Improvement in NAFLD Activity Score (NAS)  $\geq 2$   
[Steatosis (0-3) + Inflammation (0-3) + Ballooning (0-2)]

\* No worsening of hepatic fibrosis

\*\**BUT: worsening lipid profile ( $\uparrow$  LDL,  $\downarrow$  HDL, pruritis)*

Neuschwander-Tetri B *et al*, *Lancet* 2015.

# What's New in Gastroenterology and Hepatology

## *A Summary*

- PPI's overall are safe; use, where indicated, at lowest effective doses.
- Consider magnetic sphincter augmentation as a good GERD surgical option.
- Symptom are sufficient to diagnose IBS (99% accurate).
- IBS therapy: what's new is old (tegaserod); use diet, prebiotic, and psychological strategies to control symptoms.
- Colonoscopy remains a mainstay of colon cancer screening; improving prep (recognize risk, split dose) and bubbles (simethicone) optimizes visualization.
- Computer aided detection of polyps is around the corner.
- NAFLD is increasing in incidence; aggressive weight loss (bariatrics) mainstay; Vit E and pioglitazone for some patients.
- Novel NAFLD therapies are on the horizon. Ultimate goal is to prevent fibrosis and cirrhosis.