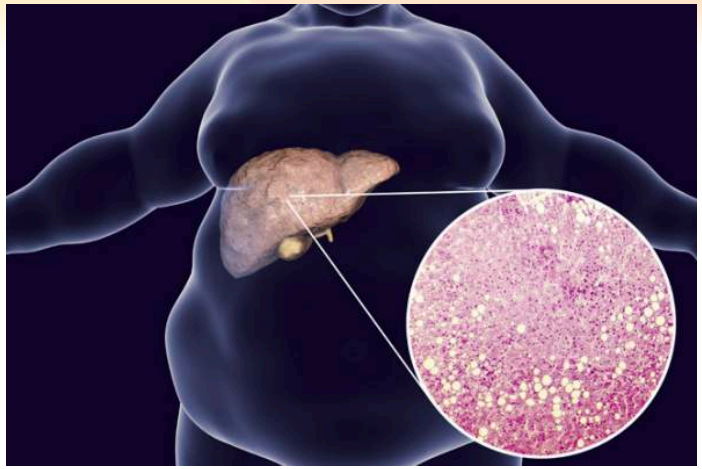
TRANSPLANT
WEBINAR SERIES



A Hefty Problem in Transplant: The Obesity Epidemic

April 23, 2020| 3-4pm ET

Speakers: Dr. Harmit Kalia| Dr. Violeta Popov

The Alliance

CEPTC Information

For more information:

Contact The Alliance at

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- You will receive a certificate via email upon completion of a certificate request or an evaluation.
- Group leaders, please share the follow-up email.

WEBINAR SPEAKERS

Moderator:

Maryanna Tosi, RD, CDN, CNSC
Registered Dietitian Nutritionist
Food and Nutrition Services
NYU Langone Health

Dr. Harmit Kalia
Clinical Associate Professor
Dept of Medicine
NYU Langone Health

Dr. Violeta Popov
Assistant Professor, Medicine in Division of Gastroenterology,
NYU Langone Health
Director of Bariatric Endoscopy,
VA New York Harbor Healthcare

The Alliance

NYU Langone Health

Transplant Institute

A HEFTY PROBLEM IN TRANSPLANT: THE OBESITY EPIDEMIC

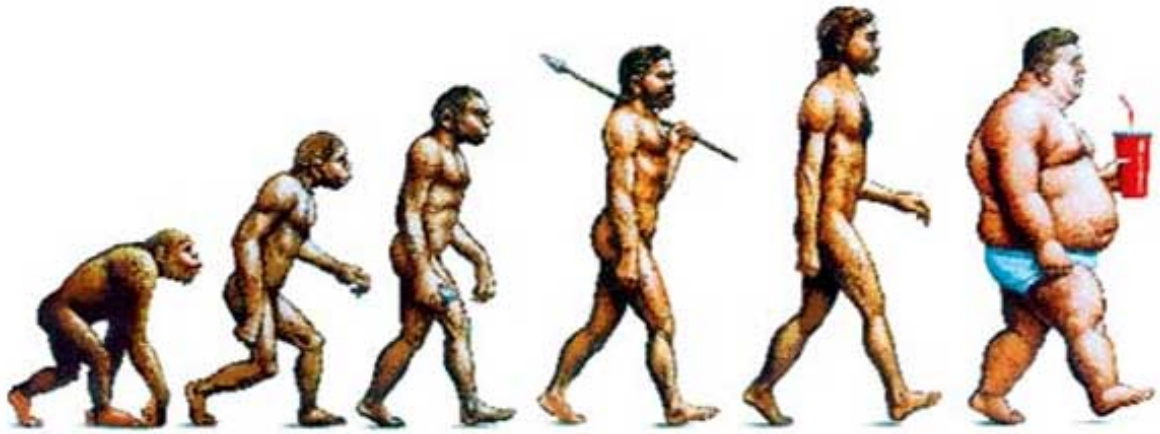
Harmit S Kalia DO

Transplant Hepatologist

Clinical Associate Professor of Medicine

Director, Liver Transplant Outreach

Human Evolution



http://www.paradigmshiftforhealth.com/wp-content/uploads/2014/07/the-evolution-of-obesity.jpg

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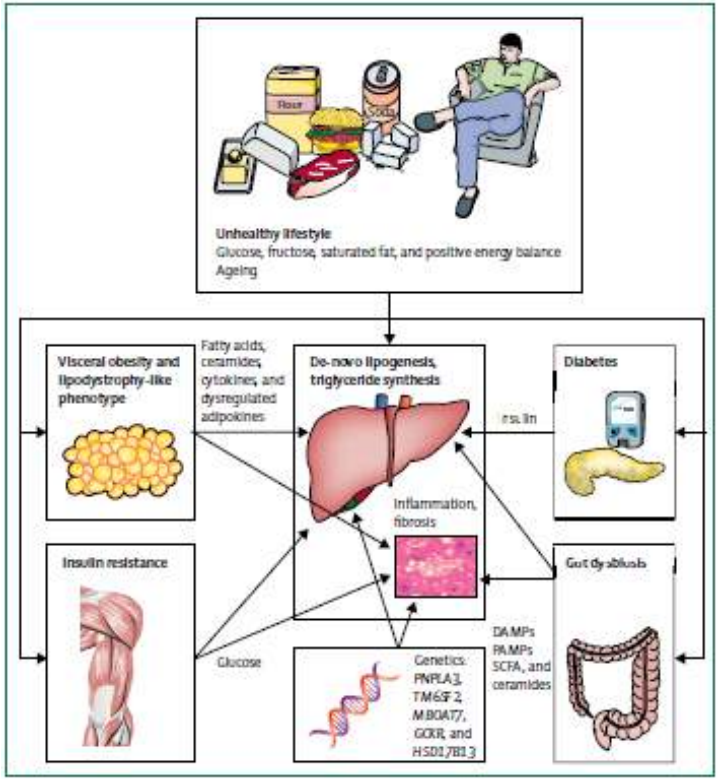
Objectives

- Recognize the relationship between the obesity epidemic and increasing prevalence of NAFLD.
- Appraise the impact of NAFLD on Liver Transplantation.

Causes of Obesity

- Genes Are Not Destiny
- Prenatal and Postnatal Influences
- Unhealthy Diets
- Too Much Television, Too Little Activity, and Too Little Sleep
- Toxic Environment-Food and Physical Activity

Causes of NAFLD



https://www.hsph.harvard.edu/obesity-prevention-source/obesity-causes/

Stefan N et al, Lancet Diabetes Endocrinol. 2018 August

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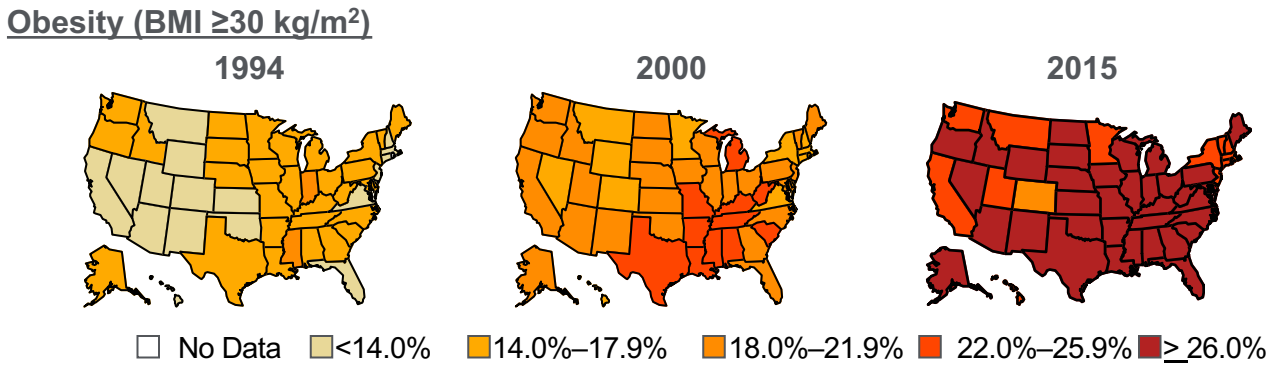
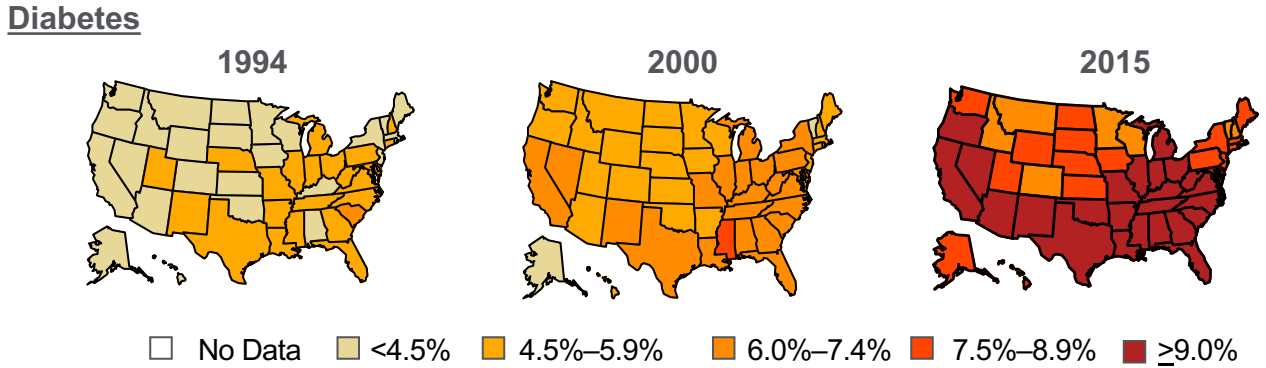
Age-adjusted Prevalence of Obesity and Diagnosed Diabetes Among US Adults



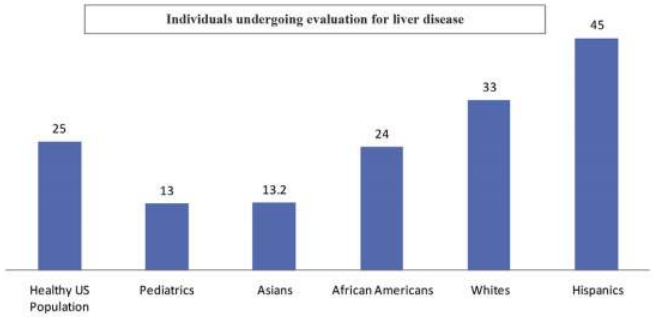


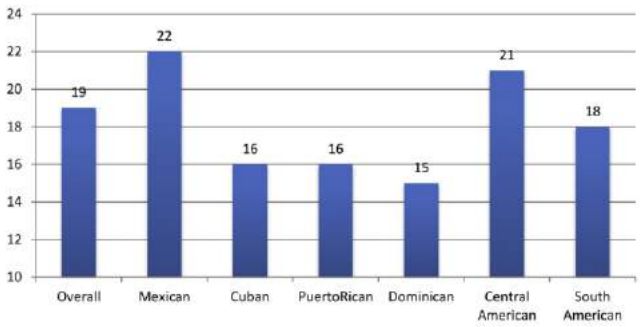
CDC's Division of Diabetes Translation. United States Surveillance System available at http://www.cdc.gov/diabetes/data

A Adults

If this trend continues, by 2030 86% of adult USA population will be overweight or obese

Prevalence of NAFLD in US population





Published data assessing NAFLD vary significantly based on how NAFLD is defined. Some studies use either laboratory, radiologic, or histologic criteria, or different combinations of these parameters, to demonstrate the prevalence of NAFLD

Note: not all Hispanic subgroups are equally affected.

Observations were not explained by differences in rates of the metabolic syndrome, physical activity, obesity, or diet when comparing individuals from different countries

Kalia, H. Clin Liver Dis.2016 May;20(2):215-24

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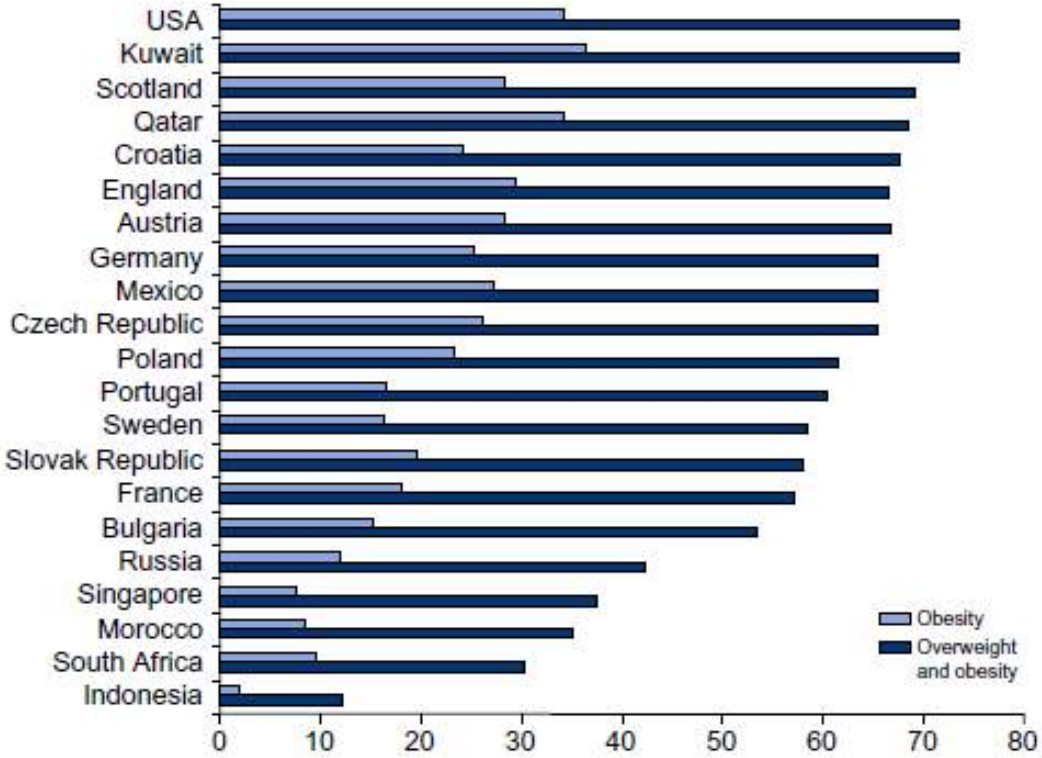
Countries with the highest adult prevalence rate of overweight and obesity



Younossi z, J Hepatol. 2018 Nov 9.

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Global Prevalence of NAFLD

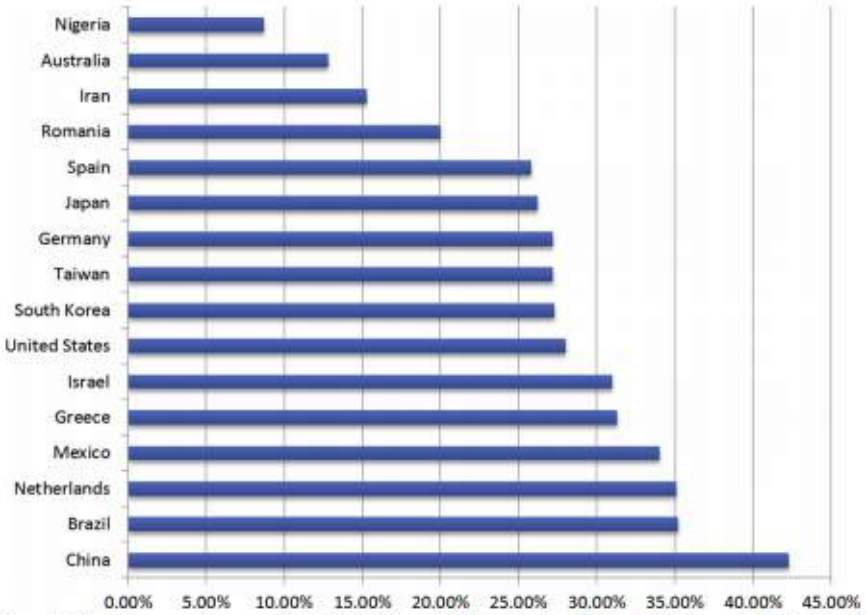

Fig. 1. Global prevalence of NAFLD (Nigeria,[28] Australia,[32] Iran,[56] Romania,[57] Spain,[22] Japan,[33] Germany,[58] Taiwan,[37] South Korea,[36] United States,[10] Israel,[7] Greece,[25] Mexico,[3] Netherlands,[26] Brazil,[18] and China[45]).

Most common cause of liver disease in the Western world

Sariney M. Clin Liver Dis. 2016 May;20(2):205-14

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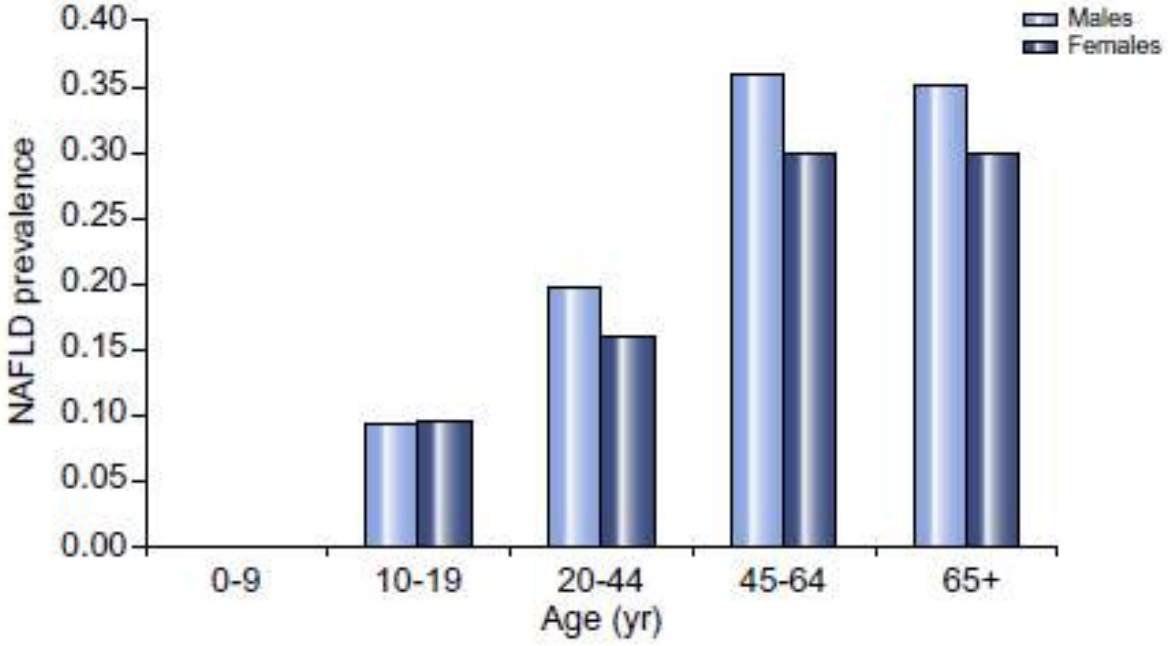
Trends in the prevalence of NAFLD by age



Younossi z, J Hepatol. 2018 Nov 9.

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Risk Factors for NAFLD

Sariney M. Clin Liver Dis. 2016 May;20(2):205-14

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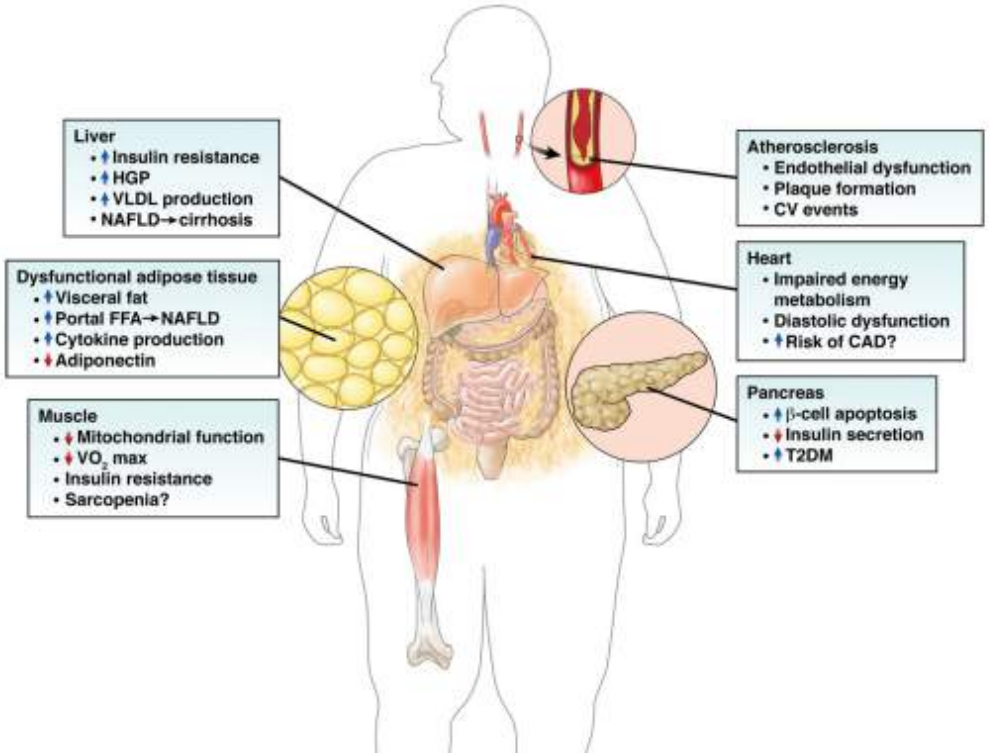
NAFLD: Pathophysiology



Cusi K GASTROENTEROLOGY 2012;142:711–725

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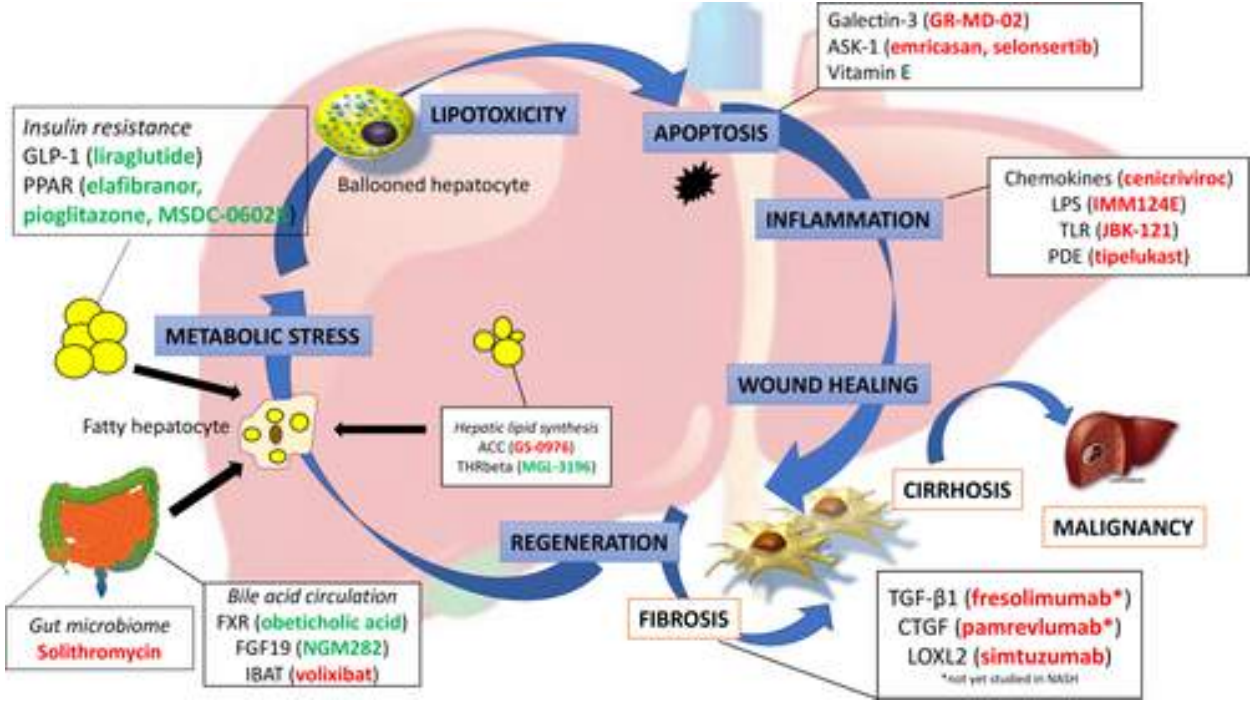
Disease pathways and molecular mechanisms of nonalcoholic steatohepatitis



Wegermann, K. , Diehl, A. M. and Moylan, C. A. (2018), Clinical Liver Disease, 11: 87-91.

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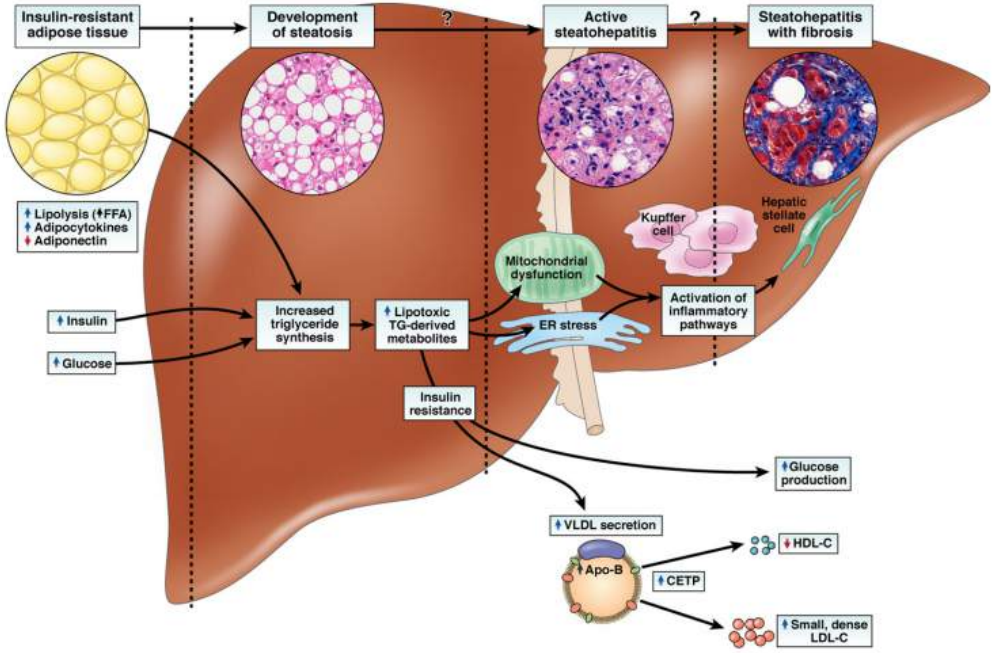
NAFLD: Pathophysiology



Cusi K GASTROENTEROLOGY 2012;142:711–725

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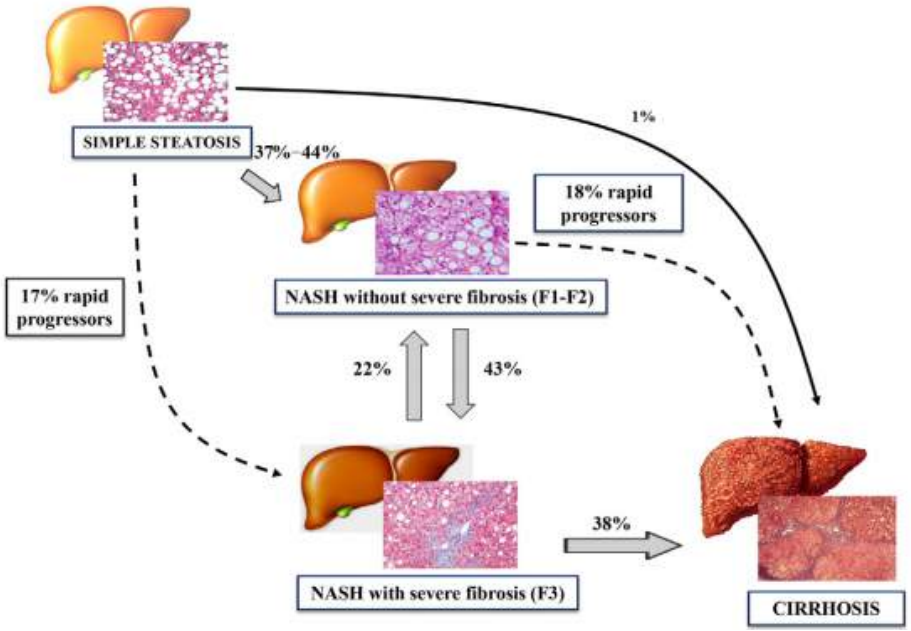
Natural History



NASH vs NAFL Liver Mortality: 7.3% vs 0.9%

-rate of fibrosis progression is at around 1 stage every 6 to 15 years in patients with NASH

-HCC incidence is growing in patients with NAFLD with or without cirrhosis, particularly among those with multiple metabolic risk factors

Marengo Clin Liver Dis. 2016 May;20(2):313-24

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NAFLD: Management

http://health.spectator.co.uk/content/uploads/2015/10/nhs-cover_se.jpg

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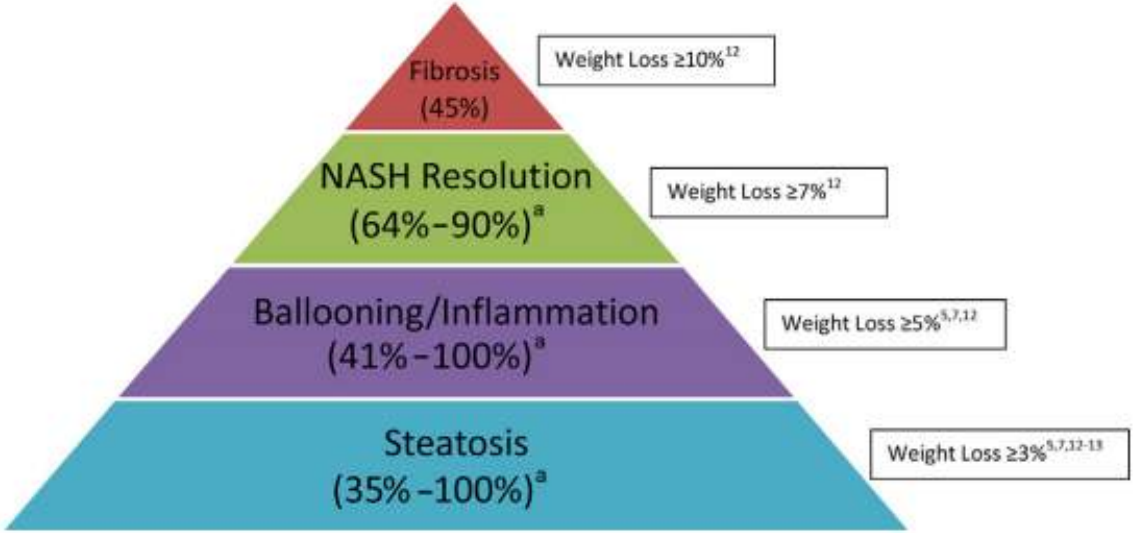
Management: Weight Loss



Lifestyle modifications to include diet, exercise, and weight loss remain the most effective therapy for nonalcoholic fatty liver disease (NAFLD)

Hannah. Clin Liver Dis. 2016 May;20(2):339-50

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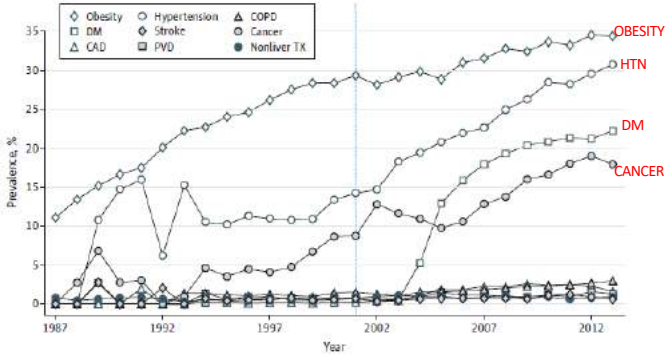
The Portrait of an Adult Liver Transplant Recipient in the United States from 1987 to 2013

Figure. The Prevalence of Comorbidities in Adult Liver Transplant Recipients by Year



Scientific Registry of Transplant Recipients (SRTR) analysis included all adult liver transplant recipients from 1987 to June 2013. A total of 108 707 adult liver transplants performed in 153 different transplant centers across the country were included

Liver transplant recipients in the United States have become older, predominantly male and with more comorbidities.

Increase in the rates of comorbidities related to metabolic syndrome, which may be explained by the increasing prevalence of obesity and its complications in the United States.

Stepanova M et al, JAMA Intern Med. 2014 Aug;174(8):1407-9.

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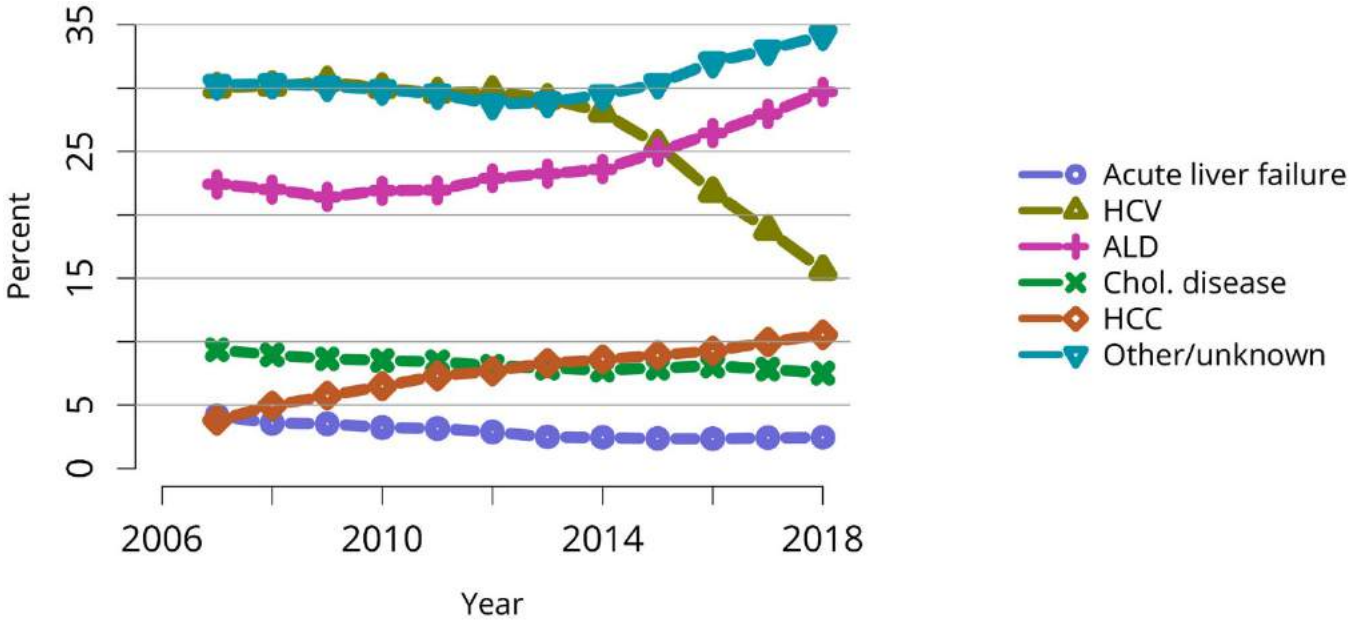
OPTN/SRTR 2018 Annual Data Report: Liver



American Journal of Transplantation, Volume: 20, Issue: s1, Pages: 193-299, First published: 02 January 2020, DOI: (10.1111/ajt.15674)

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Severe organ shortage and consequent high annual mortality on the liver waiting list

In 2017- 8082 Liver transplants were done, with 13869 patients remaining on the waiting list.

1169 died on the waiting list

1304 removed as they were too sick for transplant.

	To Date	2020	2019	2018	2017	2016	2015	2014	2013	2012	2011	2010
All Donor Types	175,269	2,199	8,896	8,250	8,082	7,841	7,127	6,730	6,455	6,256	6,342	6,291
Deceased Donor	167,831	2,071	8,372	7,849	7,715	7,496	6,768	6,450	6,203	6,010	6,095	6,009
Living Donor	7,438	128	524	401	367	345	359	280	252	246	247	282

Organ waiting list

All Organs	Kidney	Liver	Pancreas	Kidney / Pancreas	Heart	Lung	Heart / Lung	Intestine
112,690	94,858	12,754	877	1,777	3,625	1,250	51	241

Bodzin et al. Liver Transplantation 24 1470–1475 2018
Younossi ZM, et al. Transplantation 2019;103: 22–27

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Extrahepatic Manifestations of NAFLD/NASH : Impact on LT

- **High prevalence of metabolic comorbidities**:
- **Obesity** 53.4%-68%
- **T2DM** 49%-72.9%
- **HTN** 37.5-75%
- **CAD** 20%
- **CHF** 7%
- **CVA** 8%
- **Sarcopenia** 45%

- Barriers for being listed
- DM (pre/post LT) associated with higher complications/mortality
- Morbid obesity
  - Technical challenges
  - Increase pre-LT LOS in ICU
  - post LT infectious complications

Younossi ZM, et al. Transplantation 2019;103: 22–27

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Definition of Extended criteria donors

- Advanced age
- Macrovesicular steatosis
- DCD
- Organ dysfunction at procurement
  - ICU stay greater than 7 days
  - Hypernatremia greater than 165
  - Bilirubin greater than 3
  - Elevated AST/ALT
  - Vasopressor use
- Cause of death: anoxia, cerebrovascular accident
- Disease transmission
  - HBcAb
  - HBsAg
  - Hepatitis C virus
  - CDC high-risk donors
  - HIV positive
  - Extrahepatic malignancy
- CIT greater than 12 hours

Vodkin I Clin Liver Dis. 2017 May;21(2):289-301.

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Vodkin I Clin Liver Dis. 2017 May;21(2):289-301.

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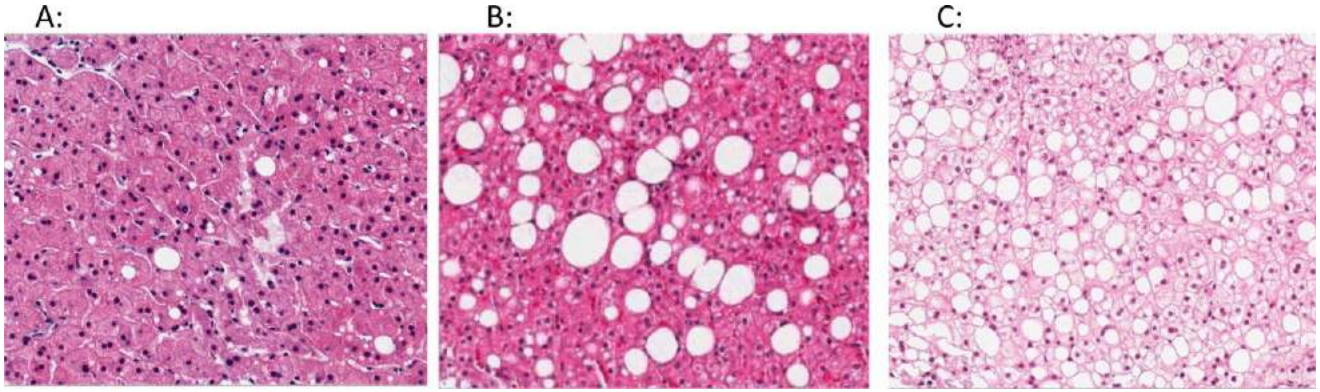
Donor and recipient effects on graft and patient survival



Clinical Liver Disease, Volume: 2, Issue: 4, Pages: 152-155

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Steatotic Liver Grafts for Transplantation: outcomes in current practice

- Mild Steatosis (<30%)
- -grafts with < 30% macrosteatosis, and microsteatosis regardless the percentage—is not associated with increased risk of:
  - primary graft nonfunction (PNF)
  - early allograft dysfunction (EAD)
  - safe for liver transplantation.

Linares et al.Transplantation 2019;103: 78–90

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Steatotic Liver Grafts for Transplantation: outcomes in current practice

- Moderate Steatosis (30-60%) – Use of these organs is controversial (high risk or allograft dysfunction, graft failure; longer ICU and LOS

Clinical studies and outcomes of patients transplanted with moderate steatotic livers (30-60%) in last decade

Author	Year	Sample size	PNF	EAD	1-y Graft survival	3-y Patient survival
Chavin et al[72]	2013	N:27	0% (0/27)	35% (10/27)	81% (22/27)	70% (19/27)
Gabrielli et al[73]	2012	N:6	0% (0/6)	—	100%	100% (6/6)
de Graaf et al[74]	2012	N:7	0% (0/7)	29% (2/7)	100% (7/7)	—
Deroose et al[23]	2011	N:19	0% (0/19)	53% (10/19)	73% (14/19)	79% (15/19)
Doyle et al[24]	2010	N:22	0% (0/22)	—	82% (18/22)	70% (15/22)
Noujaim et al[75]	2009	N:6	0% (1/6)	0% (0/6)	50% (3/6)	50% (3/6)
Li et al[71]	2009	M:23	4% (1/23)	22% (5/23)	91% (21/23)	—
Gao et al[76]	2009	N:24	0% (0/24)	20.8% (5/24)	83% (20/24)	—
Burra et al[77]	2009	N:11	0% (0/11)	—	82% (9/11)	82% (9/11)
Angele et al[25]	2008	N:50	4% (2/50)	—	72%	58%[a]

[a] 5-y Patient survival.

Linares et al.Transplantation 2019;103: 78–90

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Steatotic Liver Grafts for Transplantation: outcomes in current practice

- Severe Steatosis (>60%)
- In the past, severe macrosteatosis had been considered to be an absolute contraindication for liver transplantation

Clinical studies and outcomes of patients transplanted with severely steatotic (>60%) livers in the last decade

Authors	Years	Patient number	PNF	EAD	1-y Graft survival	3-y Patient survival
Wong et al[78]	2016	N:19	0% (0/19)	0% (0/19)	95% (18/19)	95% (18/19)
Chavin et al[72]	2013	N:11	0% (0/11)	—	82% (9/11)	82% (9/11)
Gabrielli et al[73]	2012	N:9	22% (2/9)	60% (4/7)	67% (6/9)	67% (6/9)
De Graaf et al[74]	2012	N:4	50% (2/4)	25% (1/4)	25% (1/4)	—
Sharkey et al[79]	2011	N:12	0% (0/12)	17% (2/12)	—	—
Deroose et al[23]	2011	N:15	13% (2/15)	73% (11/15)	73% (11/15)	67% (10/15)
Noujaim et al[75]	2009	N:5	20% (1/5)	80% (4/5)	40% (2/5)	40% (2/5)
Li et al[71]	2009	N:18	6% (1/18)	28% (5/18)	90% (16/18)	—

PNF, Primary nonfunction.

Some believe that severely macrosteatotic grafts might be accepted for liver transplantation but only with a very careful patient selection (low MELD score, donor and recipient age, short CIT, no retransplant)

Linares et al.Transplantation 2019;103: 78–90

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Analysis of Discarded Livers for Transplantation

All donor harvesting procedures performed from 1988 to 2004 were retrospectively studied

Comparison was made between transplanted and discarded livers

Total # of Donors	754
Accepted/Transplanted Livers	628
Discarded livers	126 (17.5%)
Hepatic causes	110
Chronic dz/cirrhosis	33 (26.4%
Ischemic/infection (liver)	22 (16.8%)
Steatosis	55 (44%)

Obesity and the finding of steatosis in US exam were the only two factors that maintained statistical significance upon multivariate analysis

Transplantation Proceedings, 37, 3859–3860 (2005)

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Liver Biopsy Results in Potential Donor Evaluation in Living donor Transplant

- 612 living-related liver donor candidates who received liver biopsies between January 2001 and June 2017 (Turkey)
- 416 liver biopsies (68%) were reported as normal and 196 liver biopsies (32%) had pathologic findings.
- Of 196 donors with pathologic findings, 86 (44%) had fatty changes and 24 (12%) had portal inflammation.

Exp Clin Transplant. 2018 Mar;16 Suppl 1(Suppl 1):35-37.

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Outcome of Living-Donor Liver Transplantation Using Grafts from Donors Treated for Fatty Liver

- Adult-to-adult LDLTs
- Donors diagnosed with FL (FL group) received diet–exercise and pharmacological treatment and compared to non FL group

Case No.	Sex/ age	Coexisting diseases	Alcohol intake	Pharmaco-logical treatment	Treatment duration (days)	Body weight (kg)		BMI (kg/m²)		CT_L (HU)		$CT_{L/S}$		MaS in confir-mation Bx
						Before	After	Before	After	Before	After	Before	After	
1	M/47	None	Social	Lipitor, EPL	40	78.6	72.4	24.8	22.9	32.7	61.3	0.85	1.18	5%
2	M/50	None	None	none	36	71.0	68.0	25.2	24.1	52.3	65.3	1.03	1.38	<10%
3	M/47	None	Social	none	106	85.0	81.0	27.4	26.1	50.5	60	0.99	1.18	5–10%
4	M/21	None	None	EPL	46	68.4	62.3	24.1	22	44.7	67.7	0.91	1.46	5%
5	M/28	None	Social	EPL	75	72.9	62.9	28.5	24.6	38.3	60.3	0.75	1.2	10%
6	M/37	Hyper-lipidemia	Social	Lipitor, EPL	109	69.0	65.6	26.1	24.8	63	60.7	1.06	1.21	<5%
7	M/34	Migraine headache	Social	EPL	35	64.8	61.6	21.9	20.8	48.5	61.3	1.05	1.21	<5%
8	M/34	None	None	none	70	64.4	56.5	23.5	20.6	34.7	61.9	0.62	1.12	10%

EPL – essential phospholipid; $CT_{L/S}$ – liver-to-spleen attenuation ratio on CT scan; CT_L – hepatic attenuation value on CT scan; MaS – macrosteatosis; N.S. – not stated.

Early graft function and donor postoperative course were comparable in the 2 groups

Ann Transplant, 2020; 25: e920677

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THANK YOU

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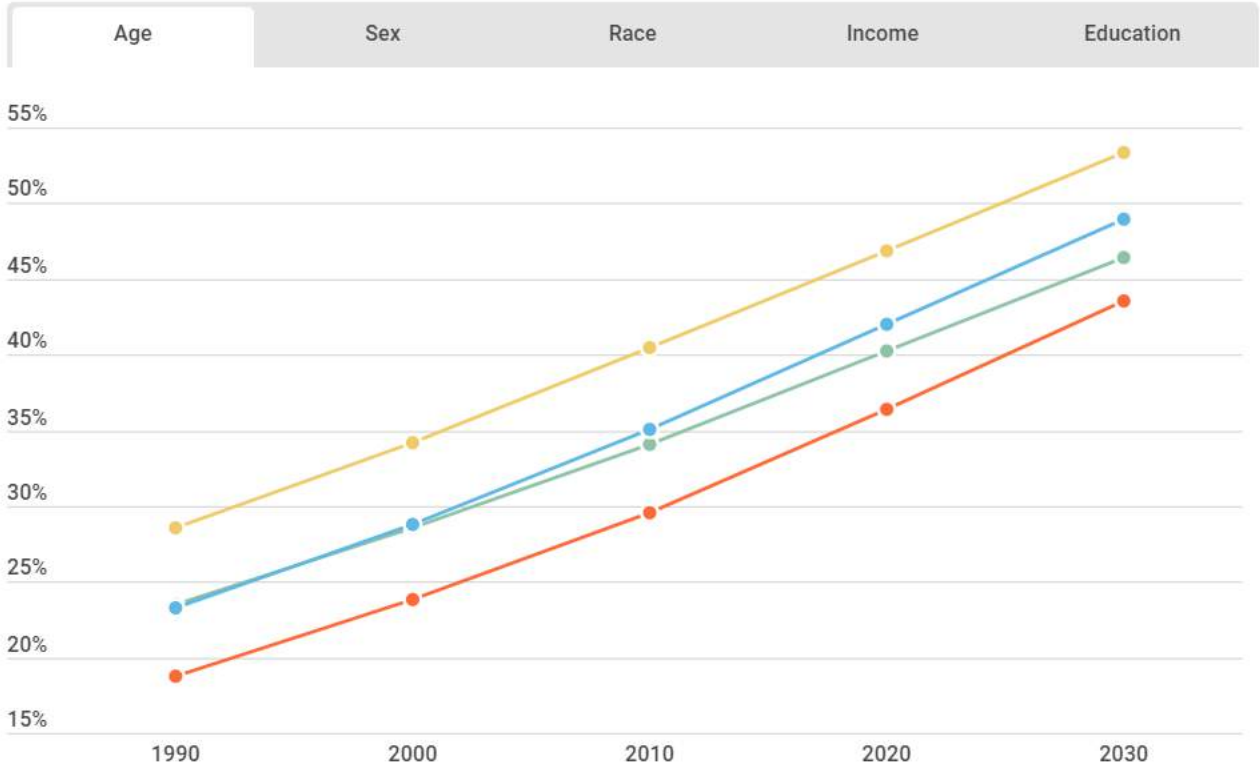
NYU Langone MEDICAL CENTER

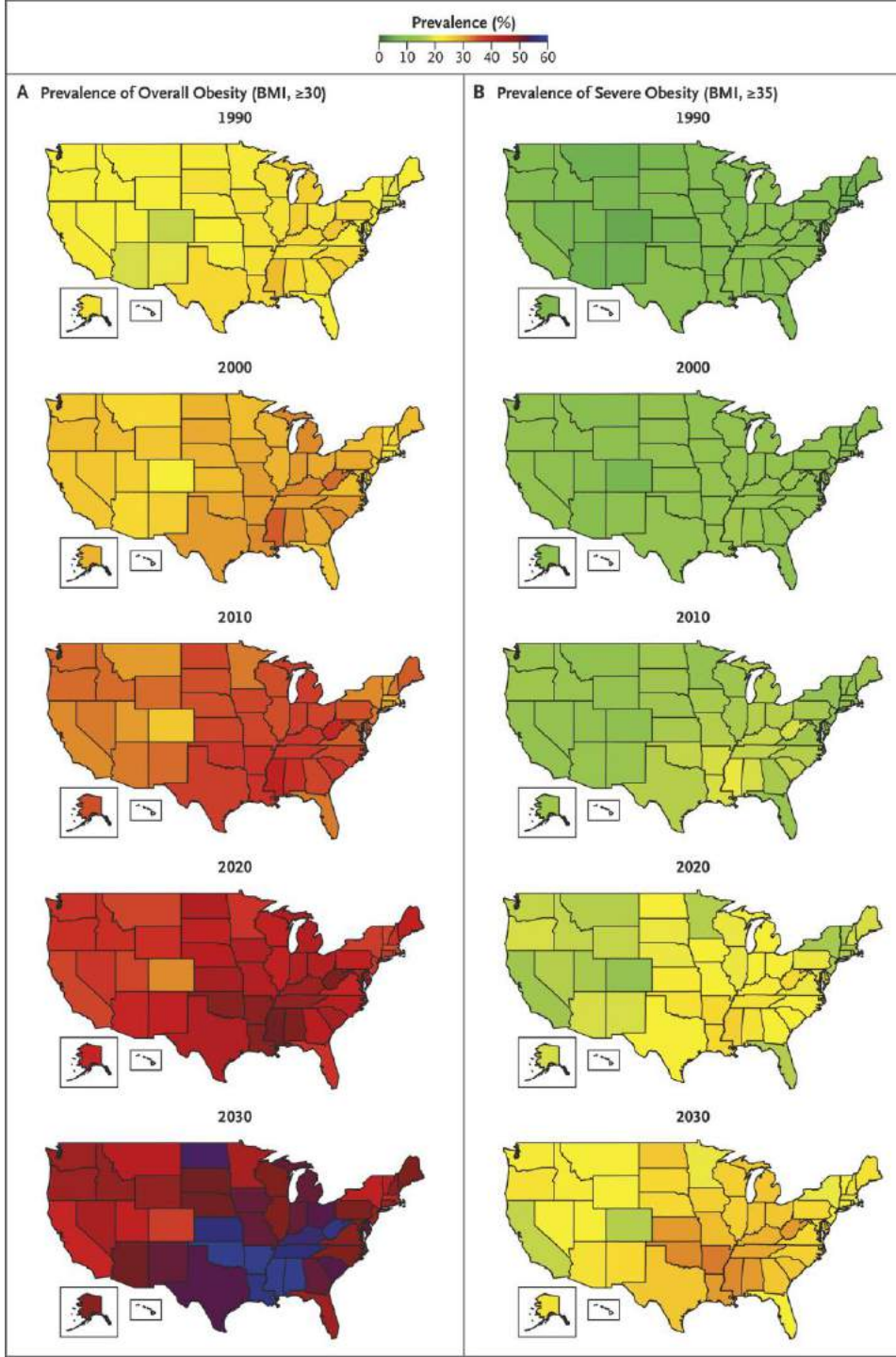
Intragastric Balloons and Other Endoscopic Bariatric Therapies for NAFLD

Violeta Popov, MD PhD FACG
Assistant Professor of Medicine
Director of Bariatric Endoscopy, NY VA Harbor Healthcare
New York University School of Medicine

@PopovVioleta

Obesity Is On The Rise





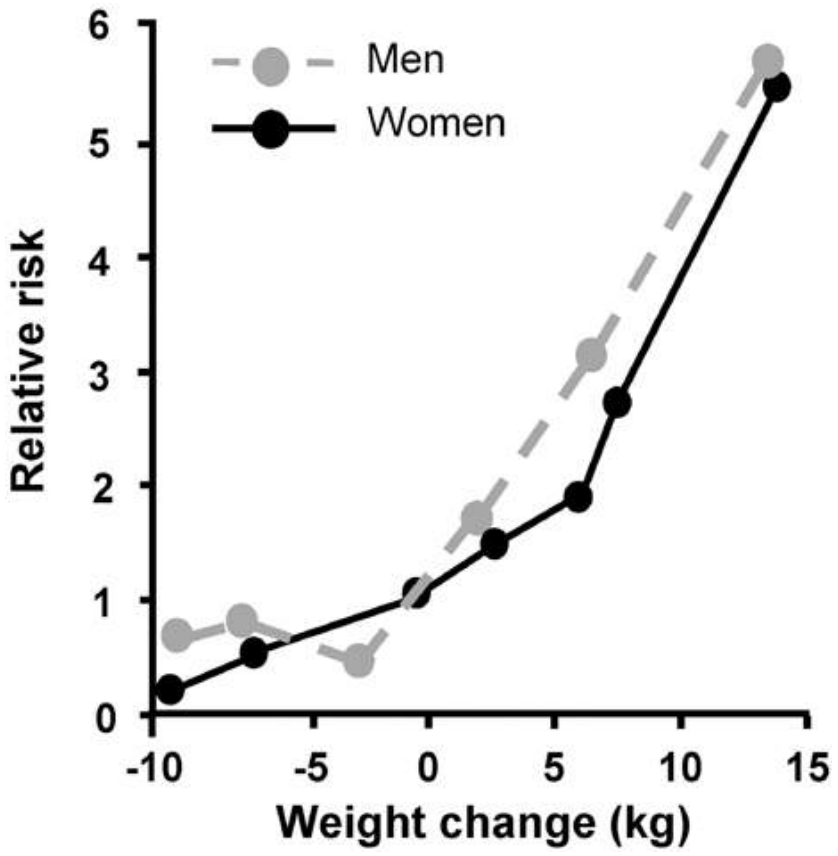
Advisory.com
Ward Z, et al. N Engl J Med 2019

Risk of Metabolic Comorbidities Increases with BMI

Association of BMI and the Relative Risk of Metabolic Comorbidities

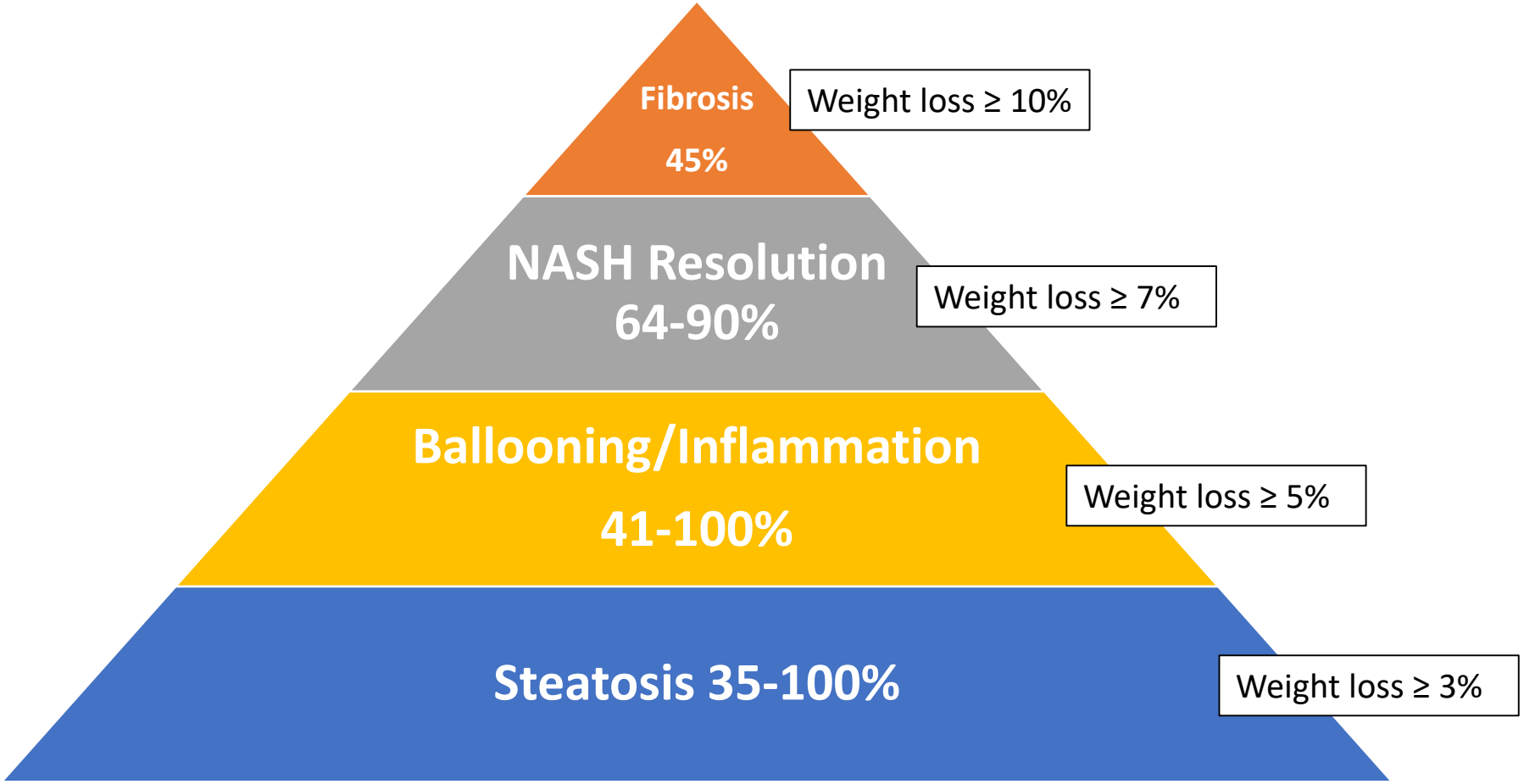
	PREVALENCE	
	BMI < 25 (%)	BMI > 40 (%)
Hypertension	18.1	53.2
Diabetes	2.4	14.2
Dyslipidemia	8.9	19
Metabolic Syndrome	13.6	39.2
Sleep apnea	2-4	50-98

Association of Weight Gain and the Relative Risk of Diabetes



Blaffner SM, Obesity 2016, Issue S6
Nguyen NT, et al. J Am Coll Surg. 2008

Weight Loss Can Reverse NASH



Villar-Gomez et al, Gastroenterol 2015

Obesity Treatment Guide

Intervention	BMI Category (kg/m)					Effectiveness	Complications
	25-26.9	27-29.9	30-34.9	35-39.9	≥40		
Diet, Exercise, Behavior Tx	✓	✓	✓	✓	✓	↓	↓
Pharmaco-therapy		With co-morbidities	✓	✓	✓		
Surgery			? diabetes	With co-morbidities	✓		

Treatment Gap

TOS Obesity Treatment Guidelines 2013

Weight Loss Interventions: Lifestyle

- Weight loss is hard to achieve/sustain through lifestyle changes alone:
  - 76,704 men and 99,791 women with obesity followed 2004-2014 in the UK Clinical Practice Research Datalink
  - 1 in 701 men and 1 in 408 women with obesity class 2 achieved normal weight
  - 1 in 8 had probability of 5% weight loss in 1 year
  - 78% regained the weight within 5 years

Fildes A, et al. Am J Public Health 2015;105(9);e54-9
Anderson JW, et al. Am J Clin Nutr 2001

Bariatric Surgery

Lap-Band

10.6% total
body weight loss

Roux-en-Y Bypass

27.5% total
body weight loss

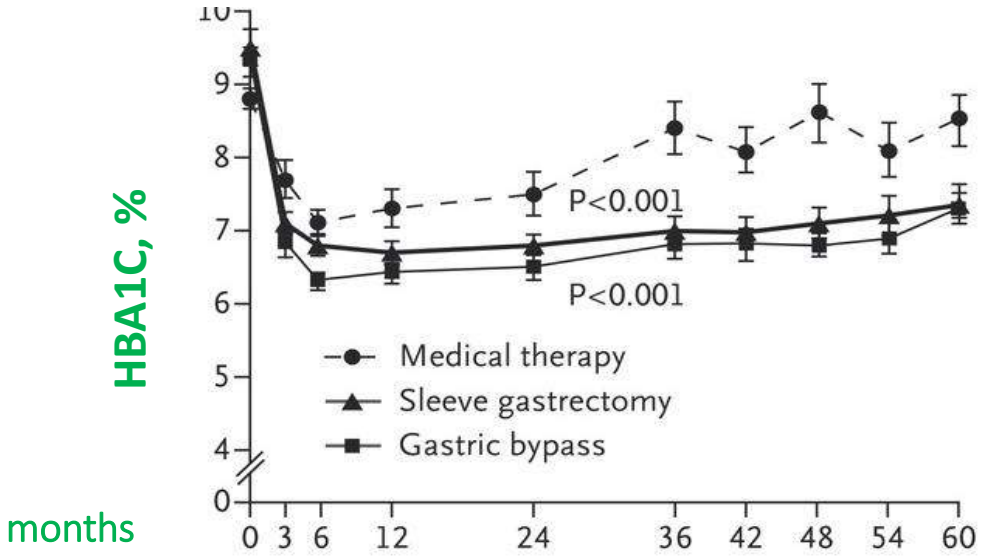
Sleeve gastrectomy

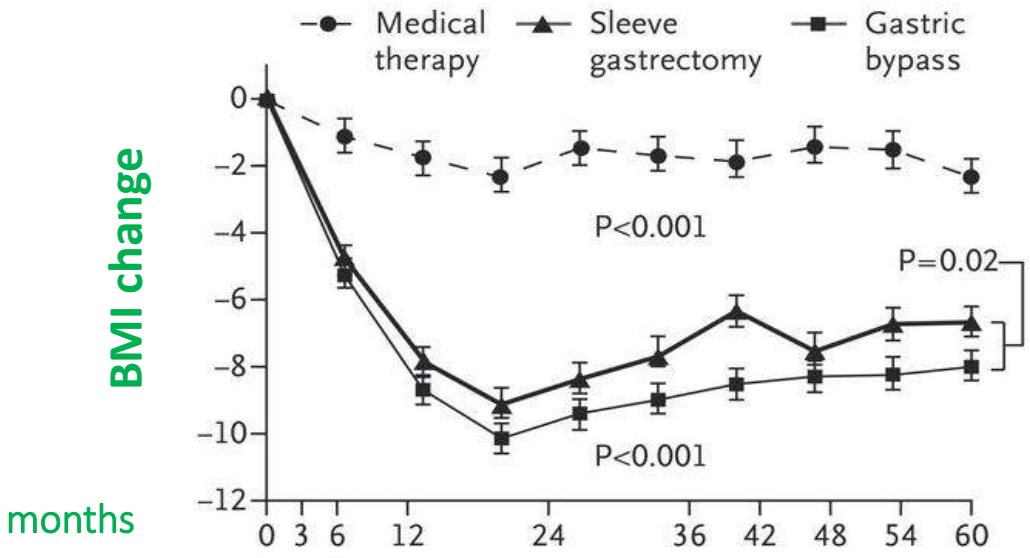
17.8% total
body weight loss

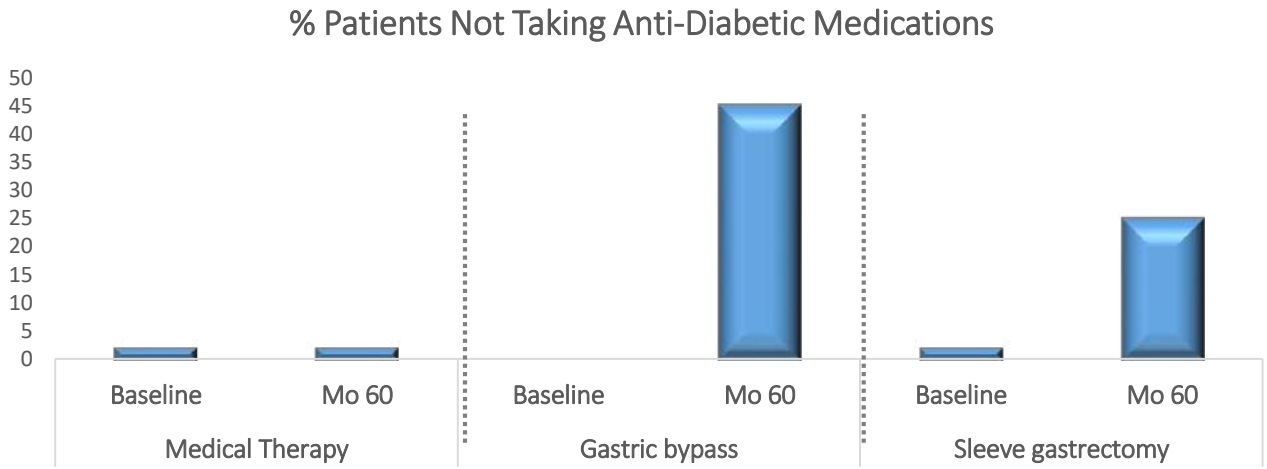
- mortality is 0.2-1%
- serious adverse events are greater than 26%
- significant weight regain in greater than 25%
- reoperation rate is 4.3-8.3%

Maciejewski M, et al.JAMA Surgery 2016; Larder, Nat Med 2012
Bolen SD, 2012; Ilias EJ 2013; Brolin RE. JAMA 2002; Castaneda, Popov, 2017
Genco, SOARD 2016

Bariatric Surgery Is More Effective Than Medical Therapy For Treatment Of Diabetes: The STAMPEDE Trial





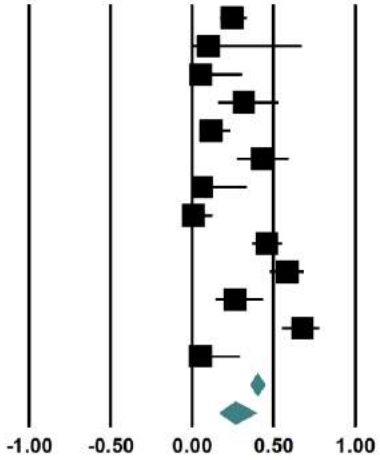


Schauer P, et al. N Engl J Med 2017

Bariatric Surgery, Liver Fibrosis, NAFLD - a Systematic Review and Meta-Analysis

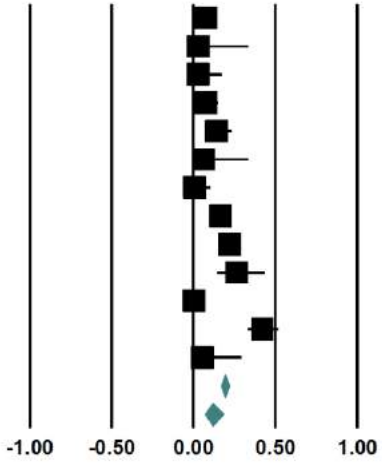
27 % of subjects with initial fibrosis had worsening of fibrosis

Model	Study name	Statistics for each study: Event rate	Lower limit	Upper limit	p-Value
	Taitano 2015	0.25	0.17	0.34	0.00
	De Almeida 2006	0.10	0.01	0.67	0.14
	Liu 2007	0.06	0.01	0.31	0.01
	Silverman 1992	0.32	0.16	0.53	0.10
	Stratopoulos 2005	0.12	0.05	0.24	0.00
	Moretto 2012	0.43	0.28	0.59	0.40
	Csendes 2006	0.06	0.01	0.34	0.01
	Mattar 2005	0.01	0.00	0.13	0.00
	Mathurin-1 2009	0.46	0.37	0.55	0.39
	Mathurin -5 2009	0.59	0.48	0.69	0.12
	Dixon(Skoien) 2004	0.26	0.14	0.44	0.01
	Kral 2004	0.68	0.55	0.78	0.01
	Barker	0.05	0.01	0.29	0.00
Fixed		0.40	0.36	0.45	0.00
Random		0.27	0.17	0.39	0.00



12 % of subjects who had no fibrosis initially developed fibrosis over time

Model	Study name	Statistics for each study: Event rate	Lower limit	Upper limit	p-Value
	Taitano	0.08	0.04	0.13	0.00
	De Almeida 2006	0.03	0.00	0.34	0.01
	Liu 2007	0.03	0.00	0.17	0.00
	Silverman 1992	0.08	0.04	0.15	0.00
	Moretto 2012	0.14	0.08	0.24	0.00
	Csendes 2006	0.06	0.01	0.34	0.01
	Mattar 2005	0.01	0.00	0.10	0.00
	Mathurin-1 2009	0.17	0.13	0.22	0.00
	Mathurin -5 2009	0.22	0.17	0.28	0.00
	Skoien(Dixon) 2013	0.26	0.14	0.44	0.01
	Weiner 2010	0.00	0.00	0.06	0.00
	Kral 2004	0.42	0.33	0.52	0.10
	Barker	0.05	0.01	0.29	0.00
Fixed		0.19	0.17	0.22	0.00
Random		0.12	0.07	0.18	0.00



Popov, Schoenfeld, Park, Thompson DDW 2016

Liver Fibrosis Progression Depends On Time Of Follow-up:

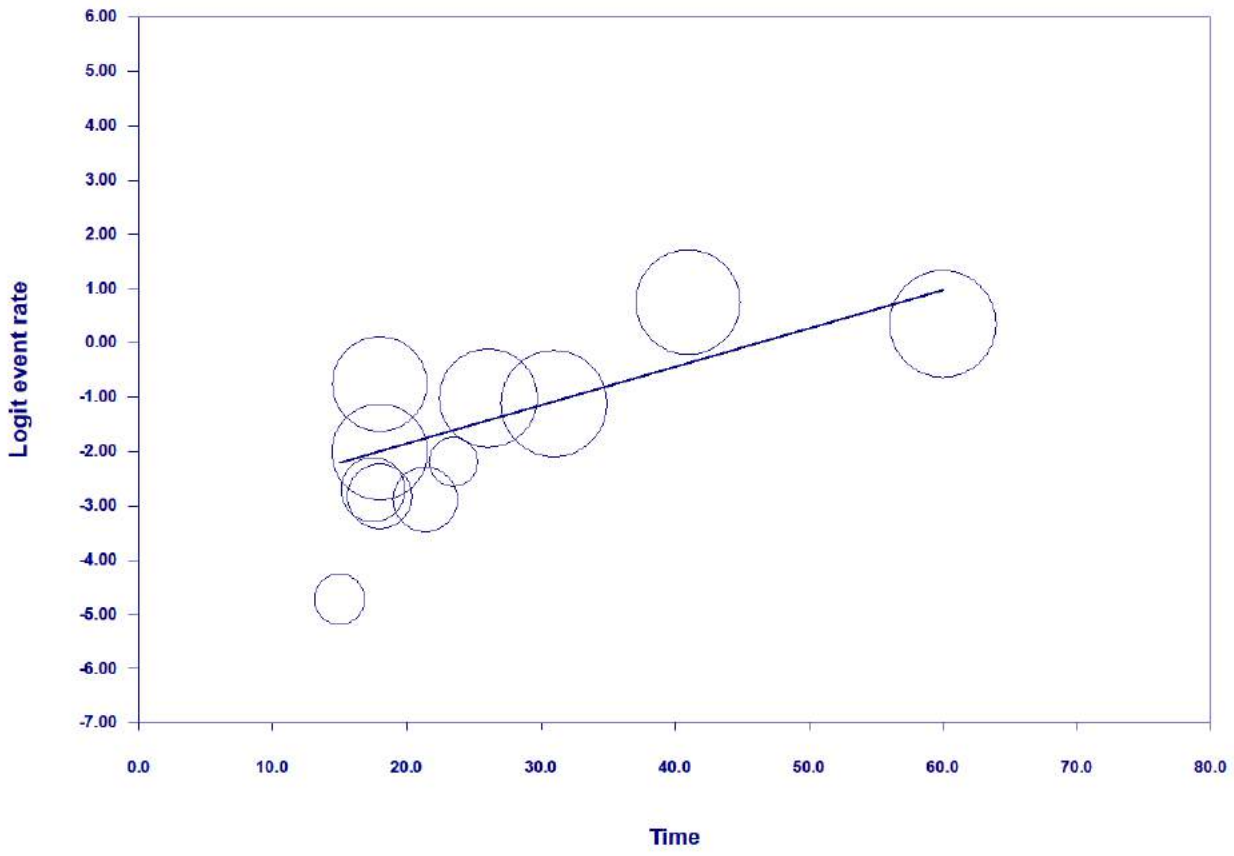
Subgroup analysis:

- Follow-up < 18 mo:

10 % had worsening in fibrosis (95% CI 4, 25)

- Follow-up > 18 mo:

36 % had worsening in fibrosis (95% CI 21, 55), P=0.004 for difference



Popov, Schoenfeld, Park, Thompson ACG 2016

The bottom line…

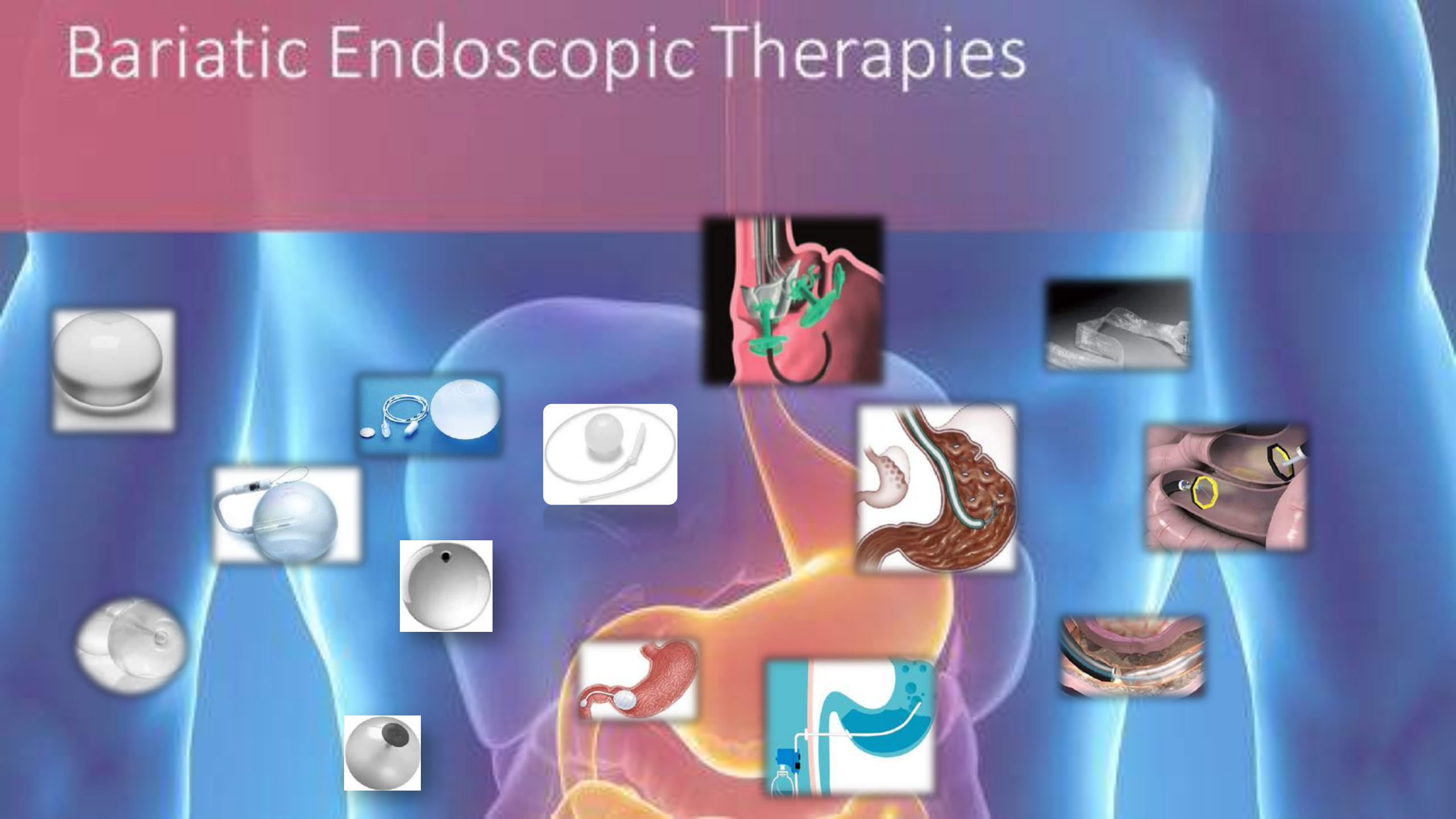
- Lifestyle/medications *alone* are hard to maintain, low efficacy

- Surgery *alone* cannot contain the obesity epidemic:
  - Only 1% of eligible patients undergo surgery

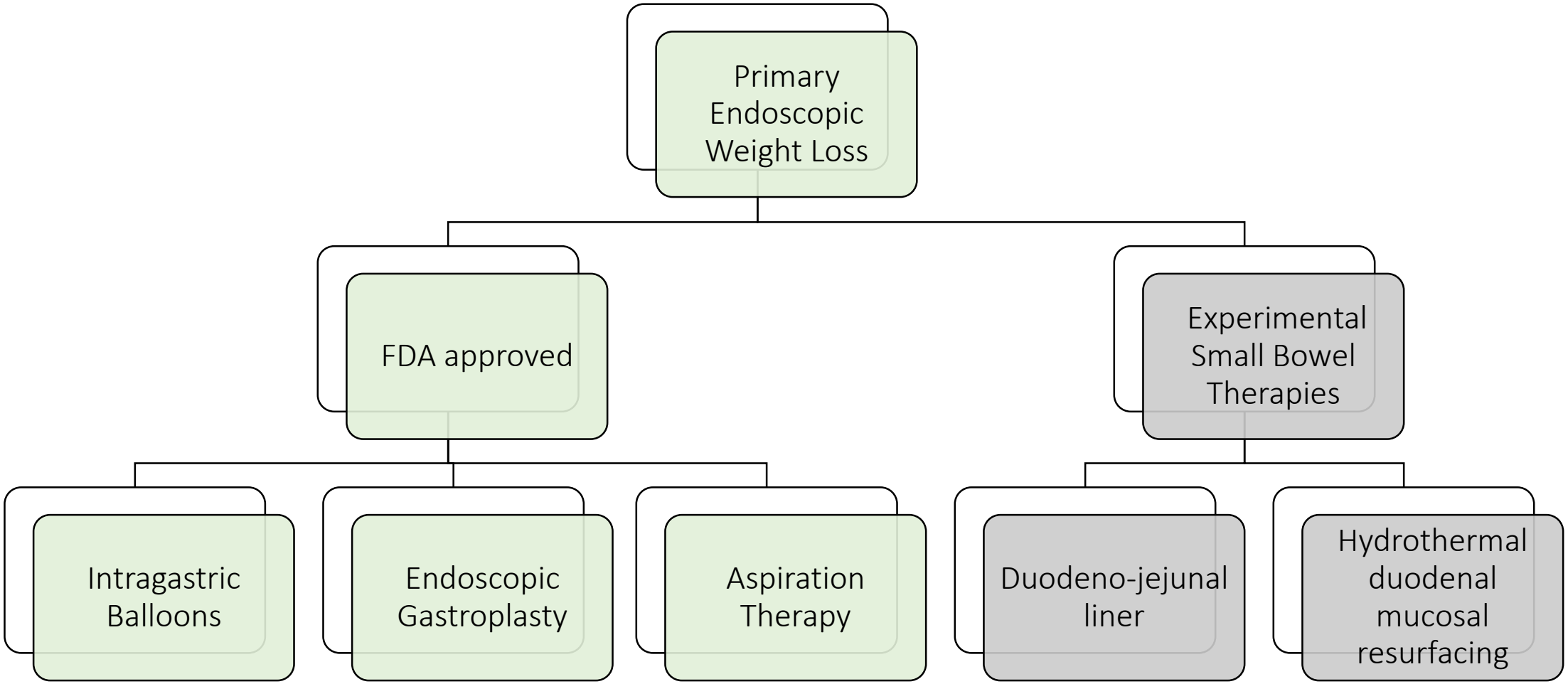
- New Therapeutic options that are more effective that medications and less invasive than surgery are needed

Martin M et al. Surg Obes Rel Dis 2010; 6(1); 8-15.

Bariatic Endoscopic Therapies



Bariatric Endoscopic Therapies: Primary Weight Loss

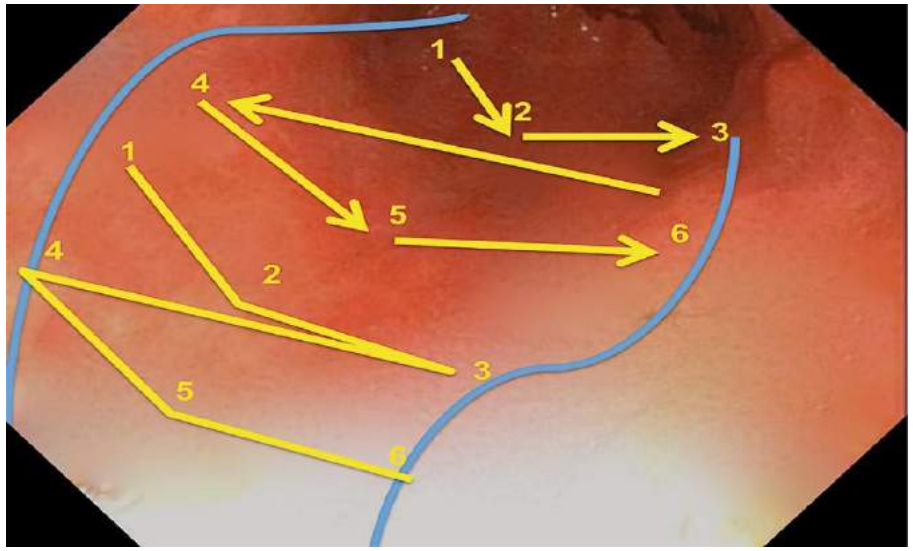


Gastric Remodeling (or Endoscopic Gastroplasty)

- Mimics surgical gastroplasty with the OverStitch (Apollo) or USGI IOP device
- Belt- and-suspenders with

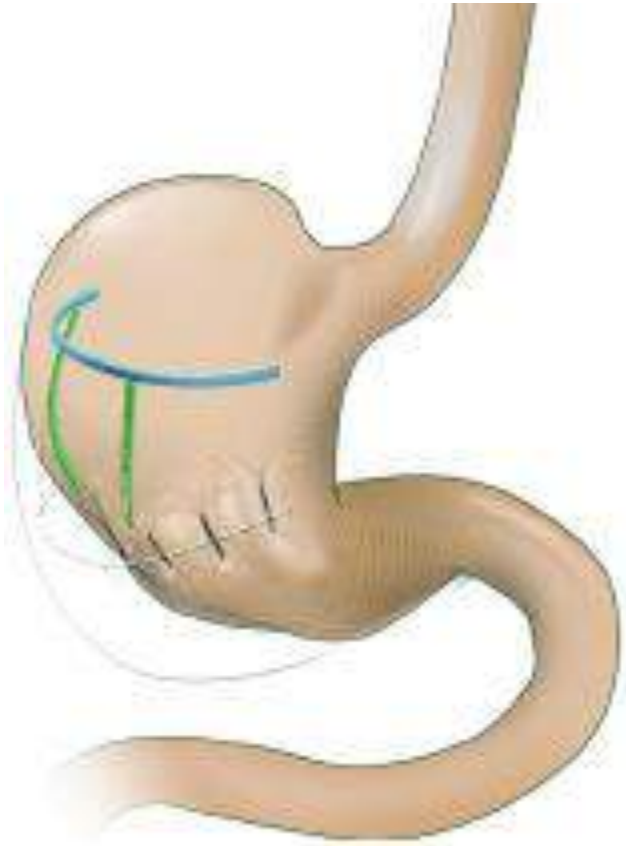
USGI IOP device

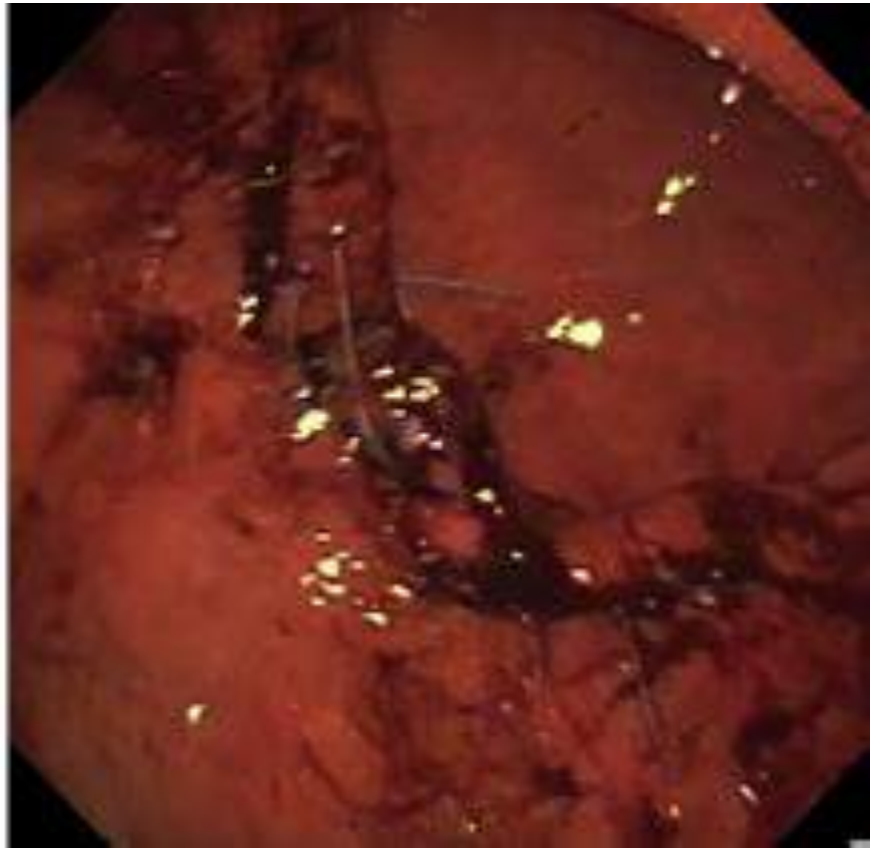
- Serious AE in 2-10%:
  - Perigastric fluid collections
  - PE
  - Pneumoperitoneum



Lopez-Nava, et al DDW 2016
Sharaiha R, et al. Endoscopy 2015
Jirapynio, Thomspon CC. Video GIE 2018

Incisionless Operating System for Gastric Remodeling





Jirapinyo, Thompson CC, Video GIE 2018

Video of Endoscopic Gastroplasty

- Video 1

Gastric Remodeling (or Endoscopic Gastroplasty)

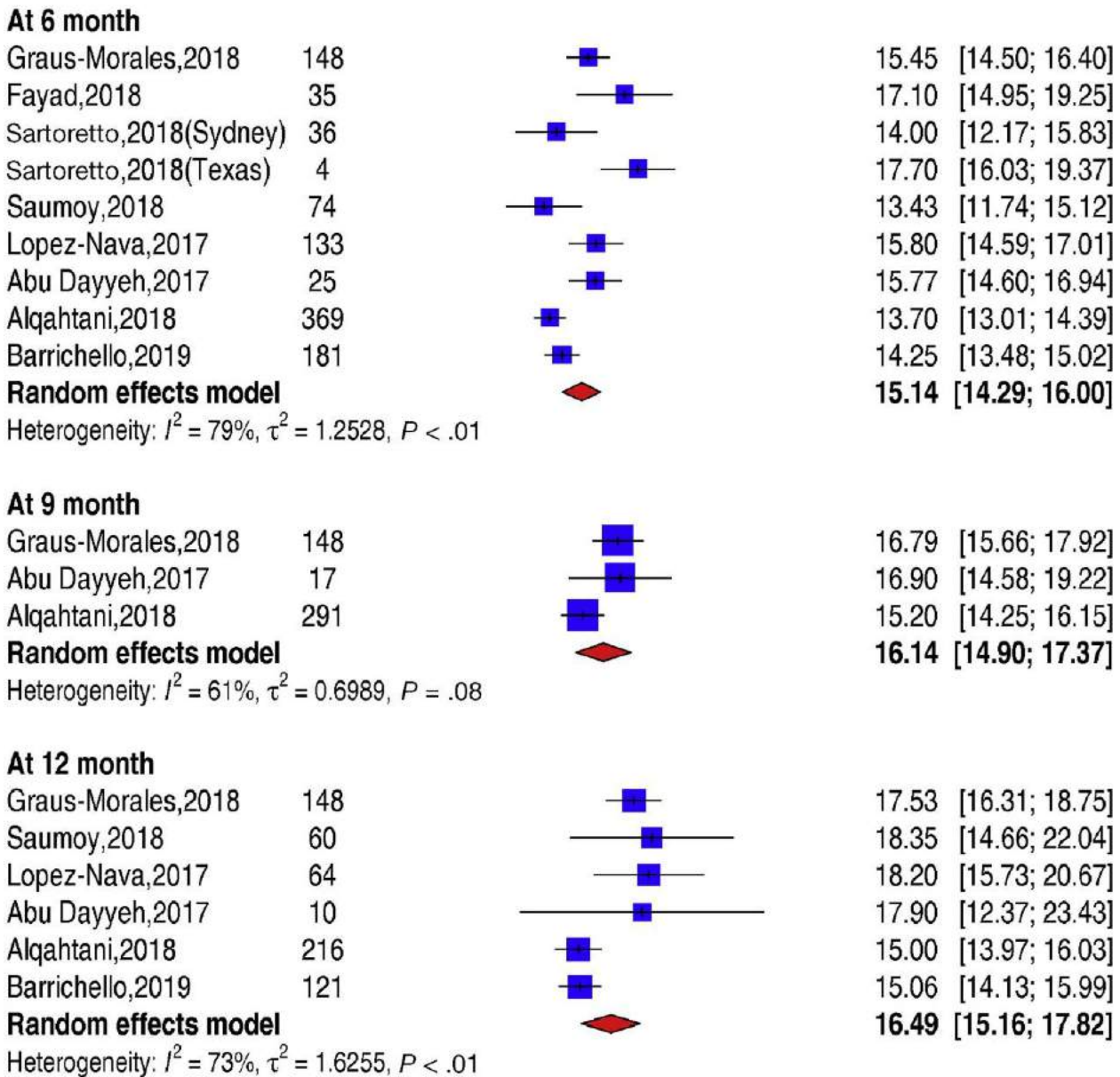
- A meta-analysis of 8 studies,
- 1172 subjects:

  - Pooled **16.49%** weight loss at 12 months

- First data in adolescents:

  - 109 subjects, age 17±2.2 yrs, BMI of 33± 4.7

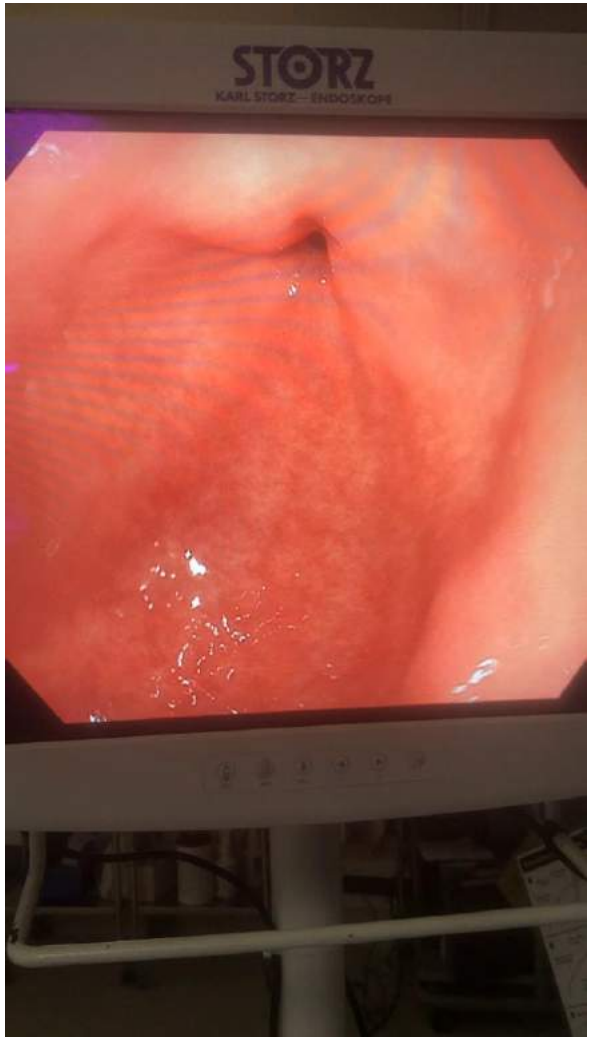
  - **16.2% ± 8.3%** weight loss at 12 months



Alqahtani A, et al. A J Gastro 2019
Hedjoudje A, et al. Clin Gastroenterol Hepatol. 2019

Endoscopic Gastroplasty and NAFLD

- In a study of 10 subjects with transient elastography
- Baseline BMI 36.8 (± 2.9)
- CAP score decreased from 319 (± 20.5) dB/m to 182.3 (± 54.5) dB/m
- Fibrosis score decreased from 6.6 (± 1.6) kPa to 4.5 (± 1.6) kPa from baseline



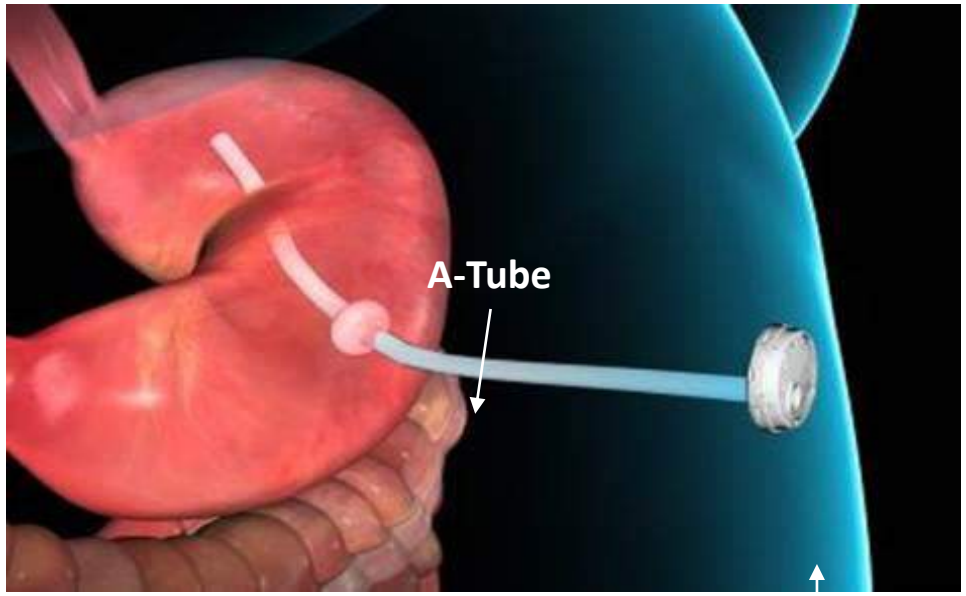
Sidhu S, Lin E, Popov V.

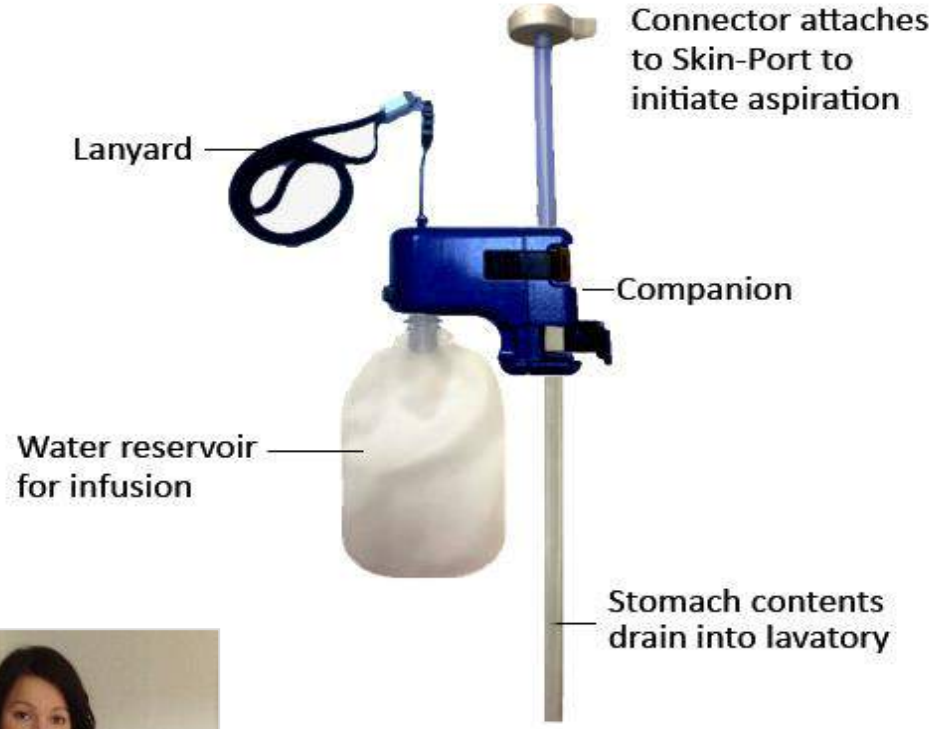
FDA-Approved Therapies: Aspiration Therapy

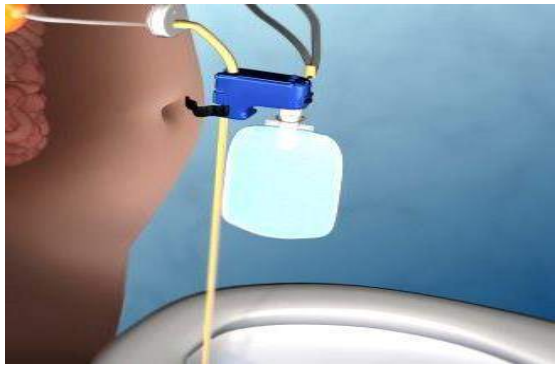
- FDA approved in 2016
- Approved for age 22-65
- Indicated for BMI of 35 to 55 kg/m^2
- Approved for long-term use
- Requires a nutritionist follow-up
- Adverse events in 3.6 %: pain/granulation tissue at PEG site

Sullivan S, et al. Gastroenterology 2013
Thompson et al, Am J Gastro., Dec 2017
Thompson CC, et al. SOARD 2019

Aspiration System



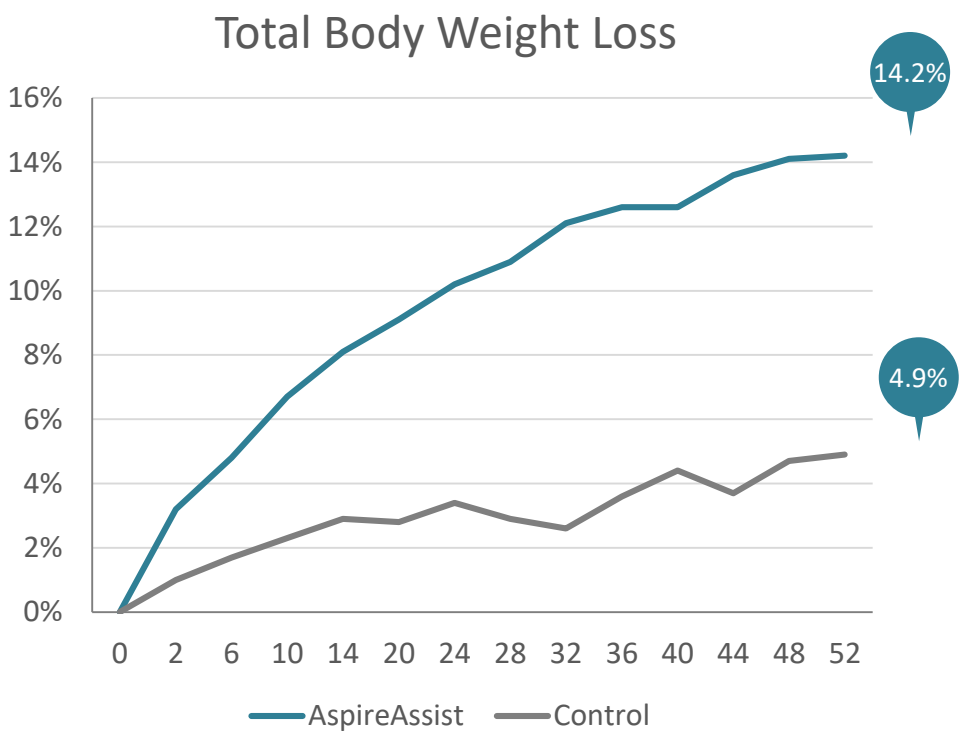


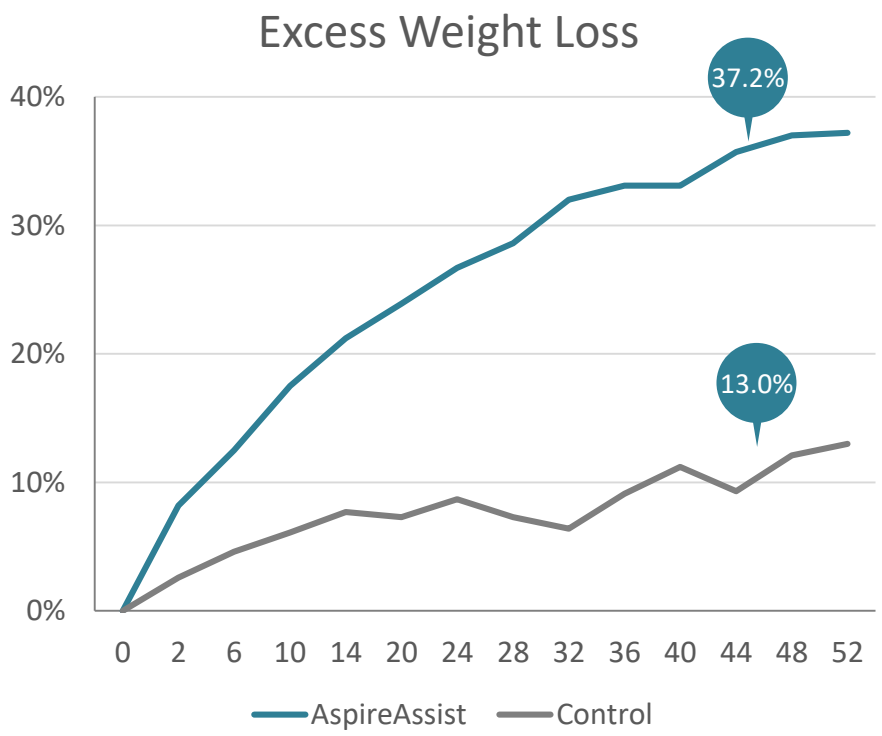


Device in Use

Device Not in Use

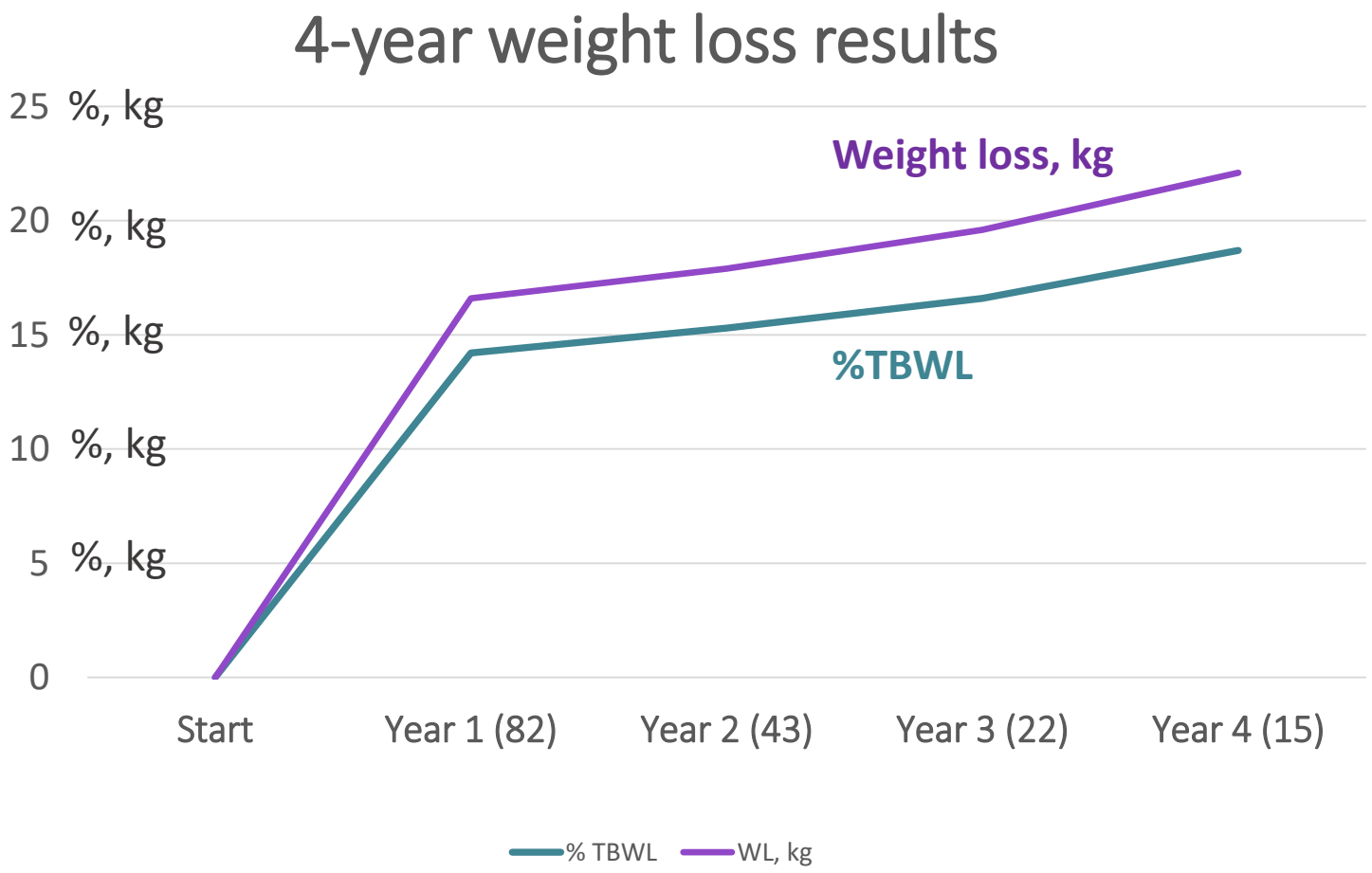
PATHWAY* Study: Weight Loss Results





*US Data: Per Protocol. Thompson C et al. The AspireAssist Is an Effective Tool in the Treatment of Class II and Class III Obesity: Results of a One-Year Clinical Trial. Gastroenterology. April 2016 Volume 150, Issue 4, Supplement 1, Page S86. [Presented at DDW 2016]. N=171 Subjects.

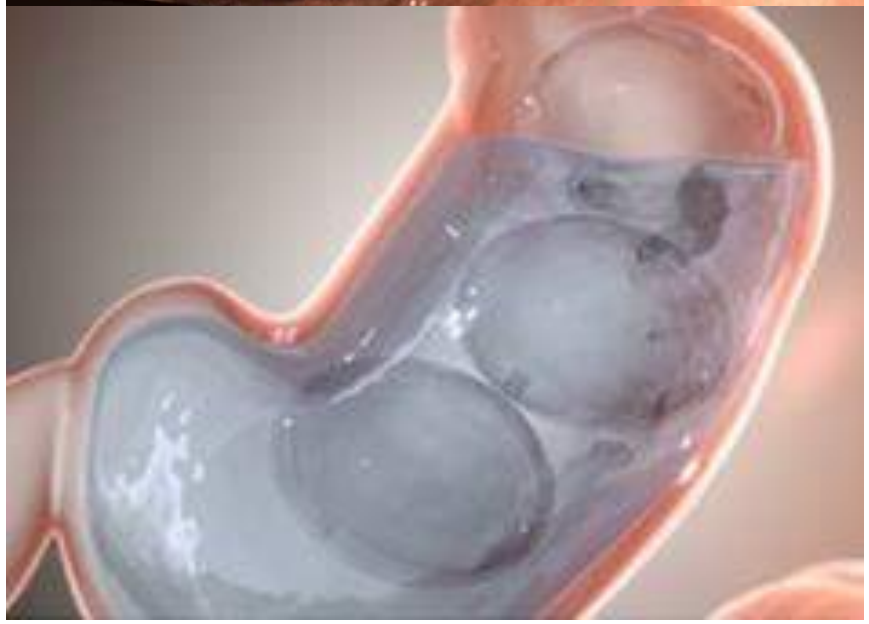
PATHWAY Study: Long-Term Results



Thompson CC, et al. SOARD 2019

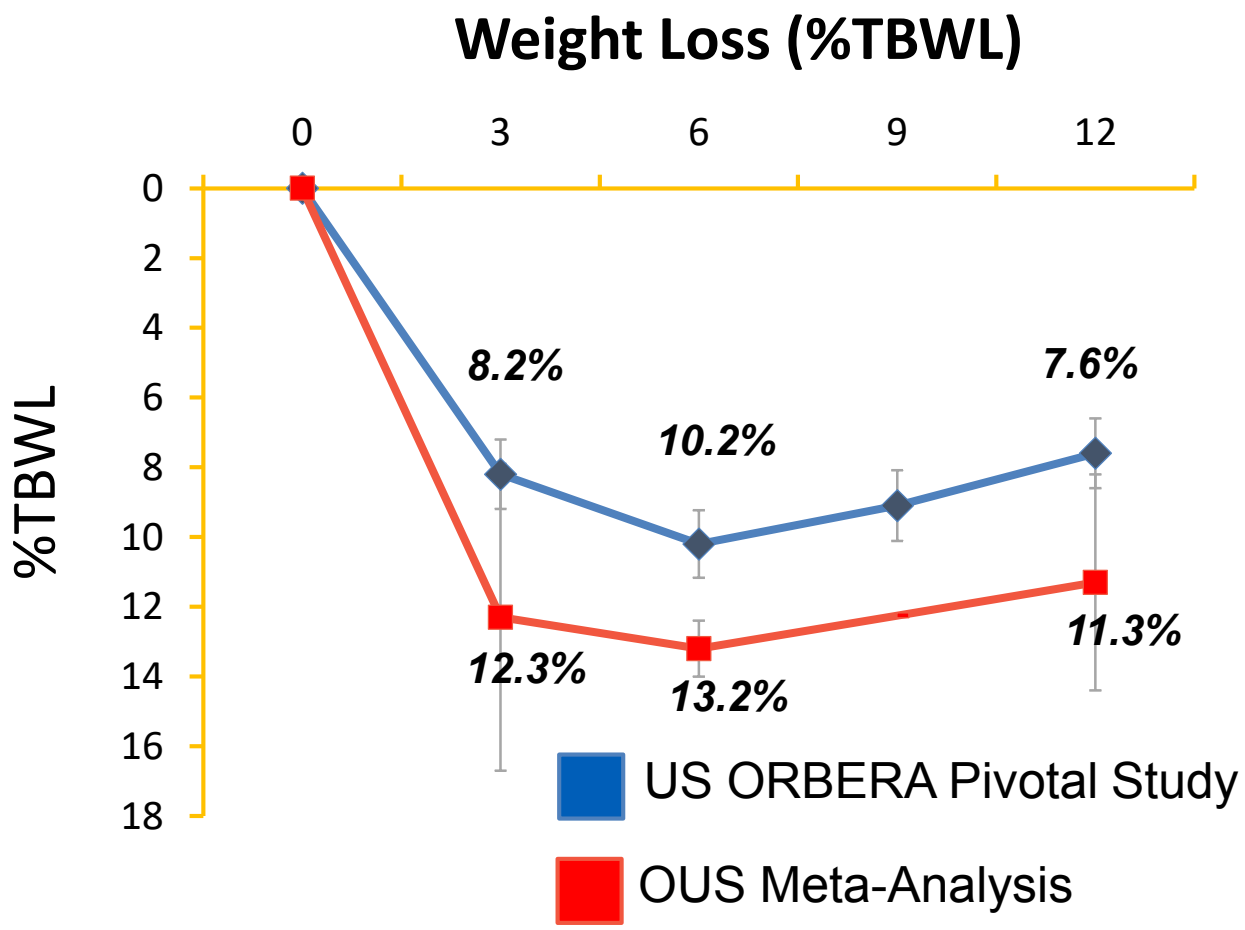
FDA-Approved Therapies: Intragastric Balloons (IGB)

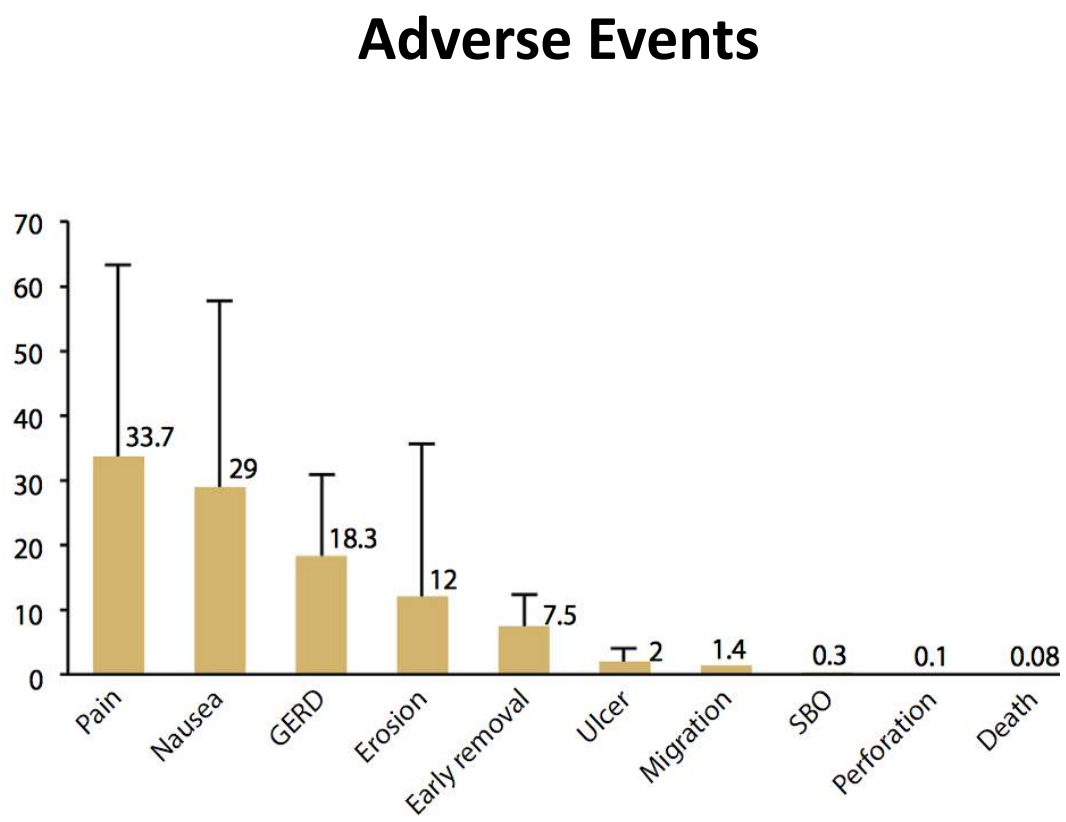
- Silicone gas- or fluid-filled balloon placed in the stomach for 6 months
- Weight loss of 10-12% of body weight
- Adverse events:
  - Nausea/vomiting x 7 days;
  - Obstruction(0.3%);
  - Perforation(0.01%)
- Two FDA-approved devices: Obalon and Orbera™



Imaz et al, 2008
Abu Dayyeh et al, GIE 2015

Extensive Global Experience with Low Adverse Events: Meta-analysis of 55 Published Studies (over 3,000 patients)





Abu Dayyeh B, et al GIE 2015

Impact of IGB on Metabolic Outcomes

Metabolic Syndrome

Insulin Resistance

- ⇓ FBG by **12.4 mg/dL** than controls
- ⇓ HGA1C by **1.1%** than controls
- Odds ratio for DM2 resolution **1.4 (1.3, 1.6)**

Visceral Obesity

- ⇓ waist circ. by **4.1 cm** than controls

High Blood Pressure

- ⇓ SBP by **3.4 mmHg** than controls (*p* is ns)
  - -by **9.1 mmHg** from baseline
- ⇓ DBP by **2.9 mmHg** than controls
- Odds ratio for HTN resolution **2.0 (1.8, 2.2)**

Dyslipidemia

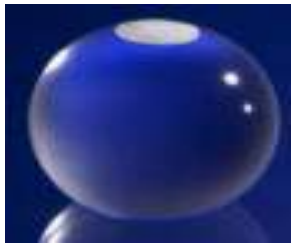
- ⇓ TG **by 22.3% (-33.4 mg/dL)** from baseline
- Odds ratio for Dyslipidemia resolution **1.7 (1.2, 2.6)**

Non-alcoholic fatty liver disease

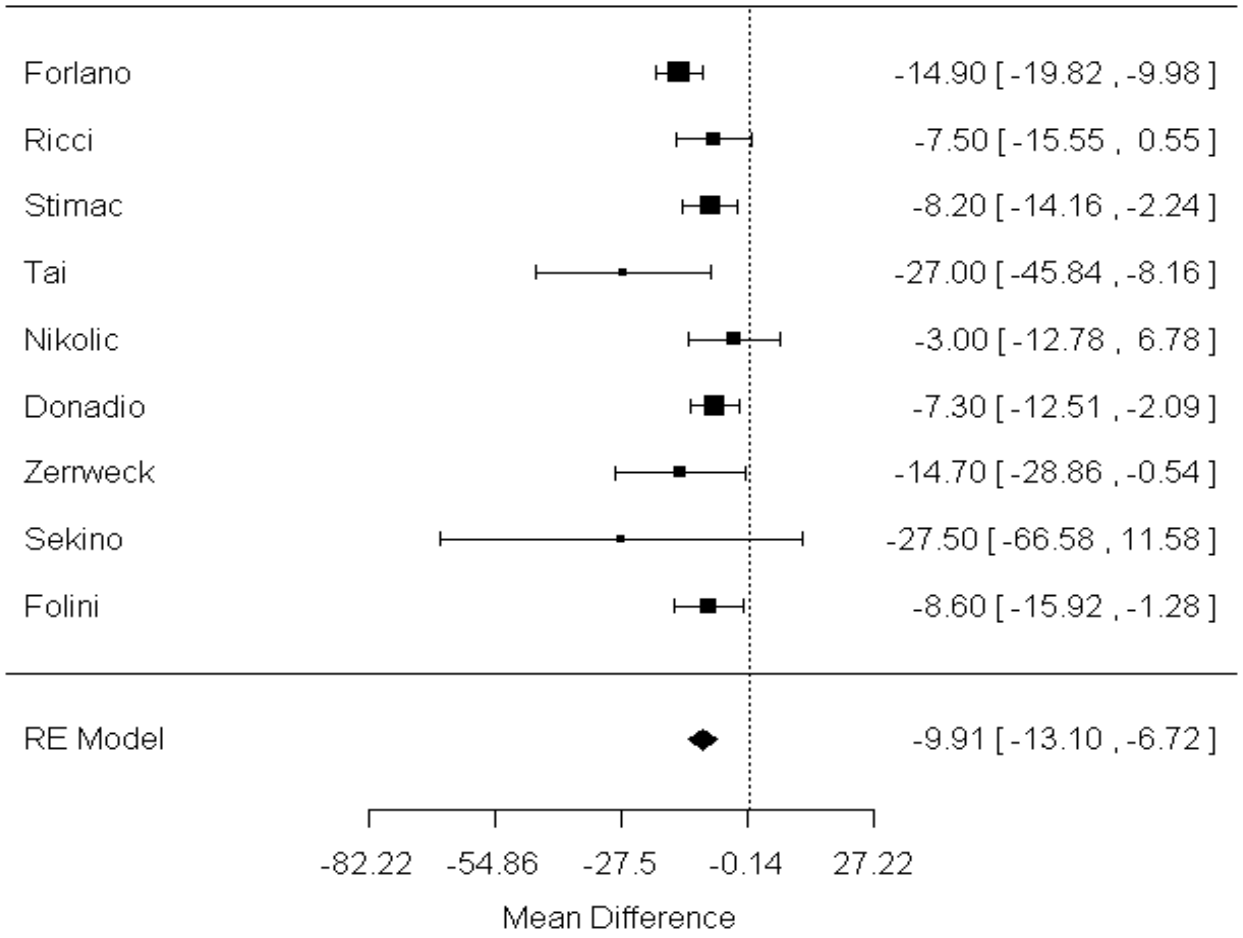
- ⇓ ALT by **29% (- 9 U/L)** from baseline

Popov VB, Ou A, et al, Am J Gastroenterol. 2017

Effect of Intragastric Balloon on Liver Enzymes: ALT, AST and GGT Decrease After IGB

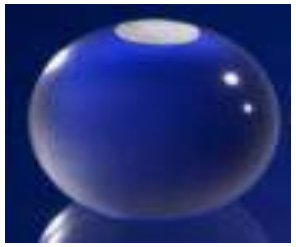


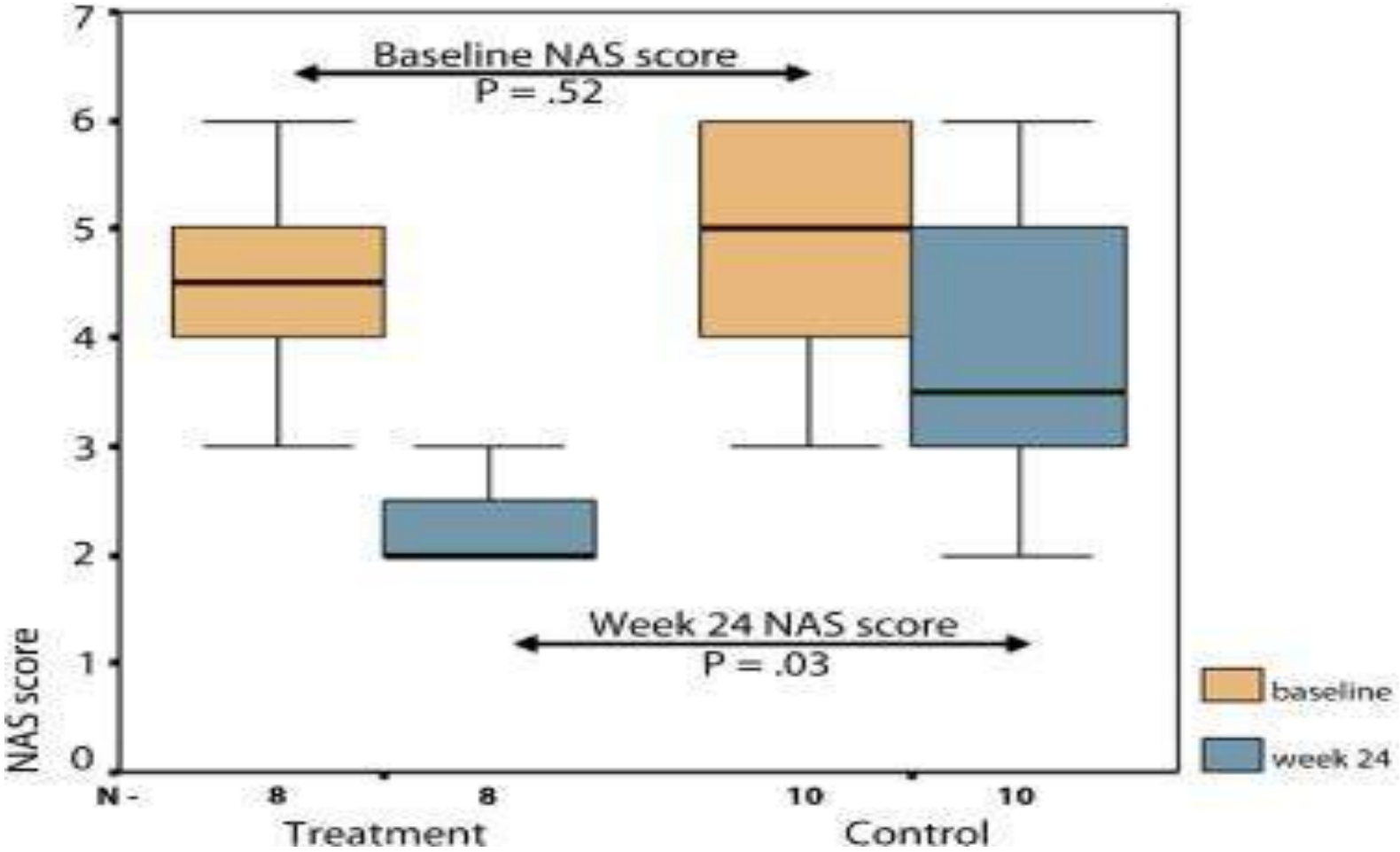
Change in ALT, U/l, with IGB treatment for 6 months



Popov V, Thompson C et al, Dig Dis Sci 2016

Intragastric Balloon Improves NAFLD Activity Score: an RCT of 20 patients

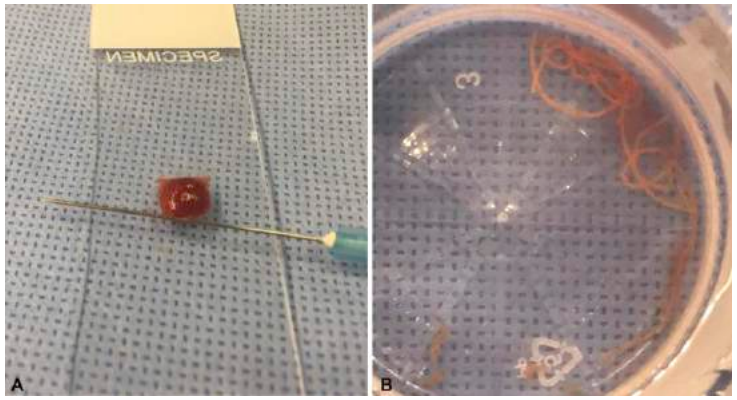




Lee YM, et al. Gastrointest Endosc 2012

Orbera, NASH and EUS-core Liver Biopsy: prospective study at Mayo Clinic

- 20 patients with biopsy-proven NASH
- EUS- guided core liver biopsy; MRE
- **All patients with early fibrosis (stages 1A, 1B, and 1C) regressed fibrosis stage**
- **65% o**f patients achieved resolution of NASH on biopsy
- **80%** of patients had a ≥2 point improvement in NAFLD activity score



Bazerbachi F, et al. DDW 2018
Bazerbachi F, Storm A, Abu Dayyeh B et al. GIE 2019

IGB and Liver Trasnplantation

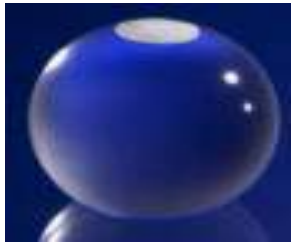


Table 1 Details of patients

From: Intragastric balloon as a novel modality for weight loss in patients with cirrhosis and morbid obesity awaiting liver transplantation

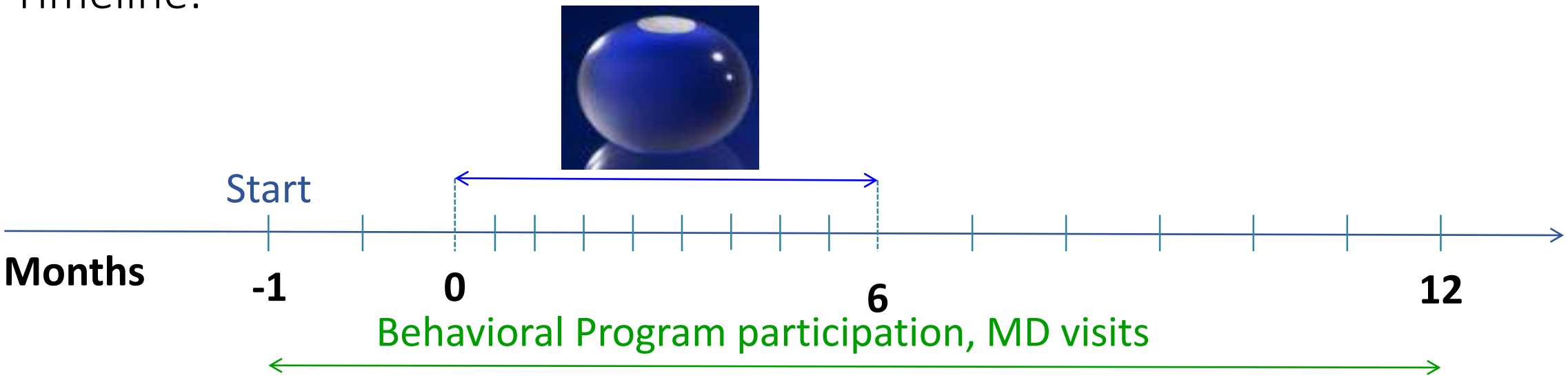
S. no	Age, sex	BMI before balloon placement	Weight loss (% of weight)	BMI before liver transplant	Balloon placement to transplant interval	Type of balloon	Etiology of cirrhosis	CTP, MELD
1	61, M	48.3	24 kg (18.8)	39.2	6 months	BIB	Cryptogenic	9, 14
2	43, M	38.7	5.4 kg (5)	33.6	25 days	BIB	ALD	9, 17
3	45, F	39.2	13 kg (13.9)	33.7	5 months	BIB	HCV	9, 16
4	45, M	51	15 kg (12)	44.8	1 months	Spatz	HBV CLD, HCC	9, 17
5	46, F	54.5	none	Wait list	6 months	Spatz	Cryptogenic	8, 10
6	43 M	42.5	36 kg (26.4)	Wait list	9 months	Spatz	Cryptogenic	8, 17
7	46 M	38.2	22 kg (21.1)	30.1	2 months	Spatz	HBV, HCC	5, 12
8	44 M	35.6	10 kg (10.4)	Balloon removed after 6 weeks, patient opted out from list due to personal reasons	1 months	Spatz	Cryptogenic	11, 22

BMI body mass index, *CTP* Child-Turcotte-Pugh, *MELD* model for end-stage liver disease, *BIB* bioenteric intragastric balloon, *ALD* alcoholic liver disease,

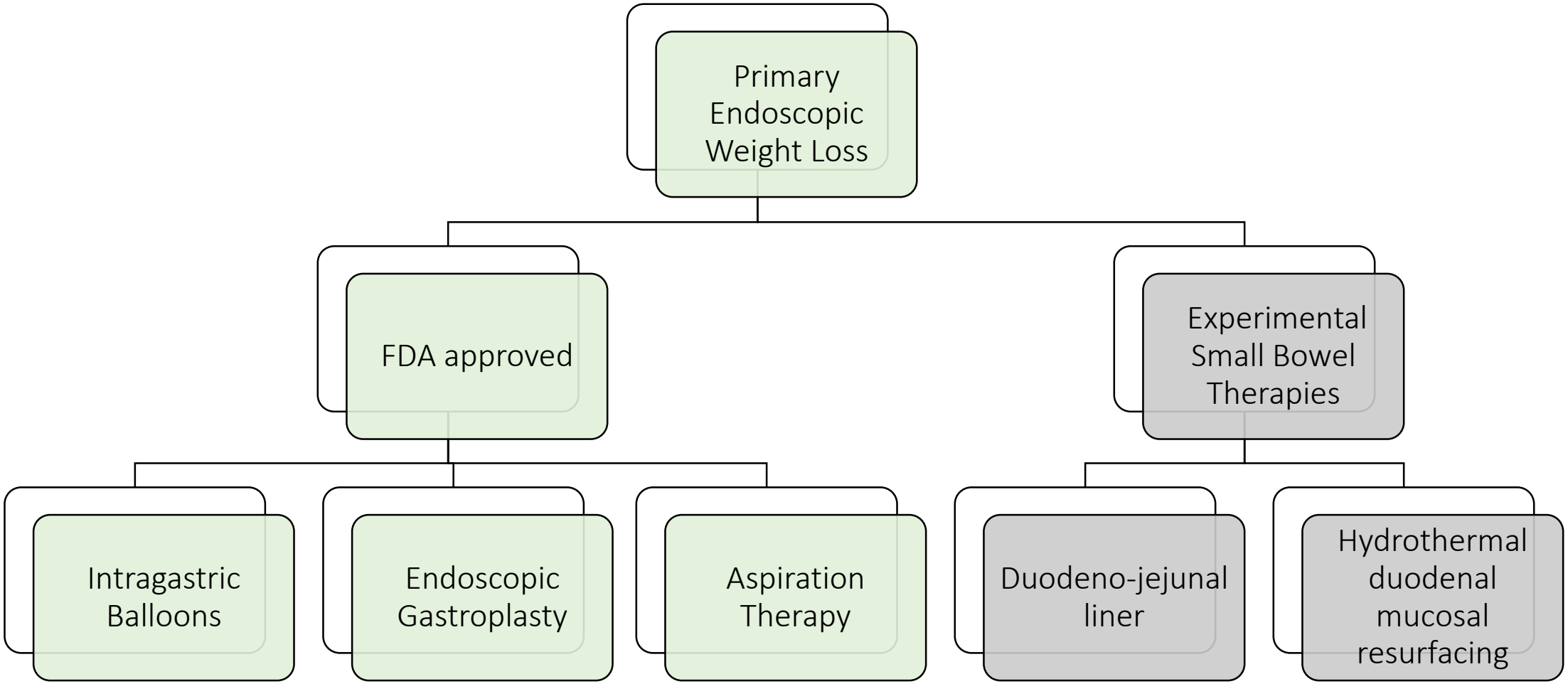
Choudhary NS, et al. Indian J Gastroenetrol 201

Intragastric Balloon in Practice: Partnership with a Behavioral Modification Program

- Indications: patients with BMI 30 – 40 kg/m2 who are not candidates for bariatric surgery or do not want to undergo surgery
- Exclude patients with prior stomach surgery
- 12-13 months minimum commitment with the program
- Timeline:

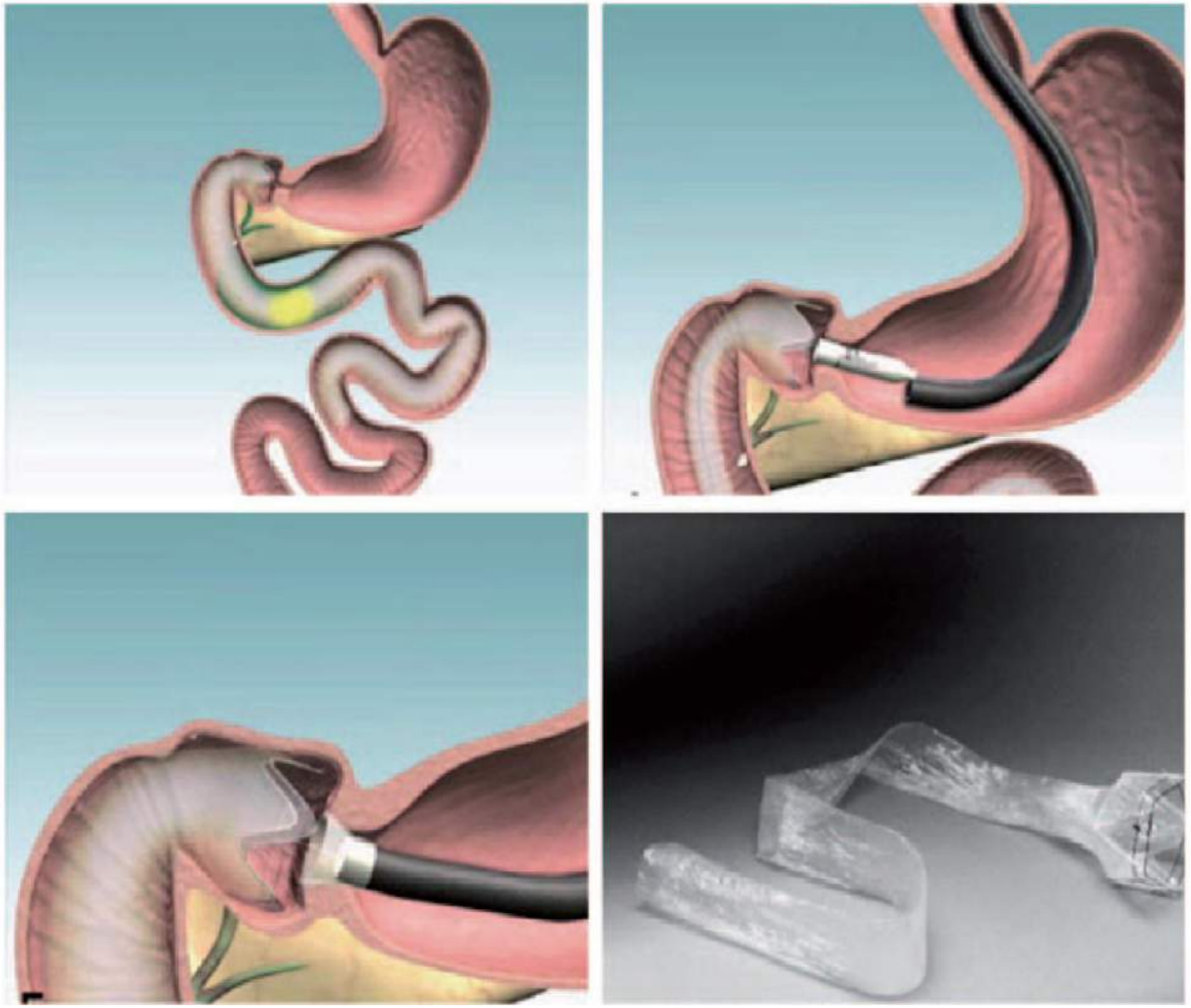


Bariatric Endoscopic Therapies: Primary Weight Loss



Small Bowel Therapies: Duodenal-Jejunal Sleeve

- Duodeno-jejunal bypass sleeve open at both ends
- Pooled %EWL was 35%(25, 46) after 12 months of DJ liner
- Pooled HbA1c decrease was -1.1% greater in the DJ liner group than in controls



Escalona A et al. Ann Surg 2012
Abu Dayyeh et al, Gastrointest Endosc 2015

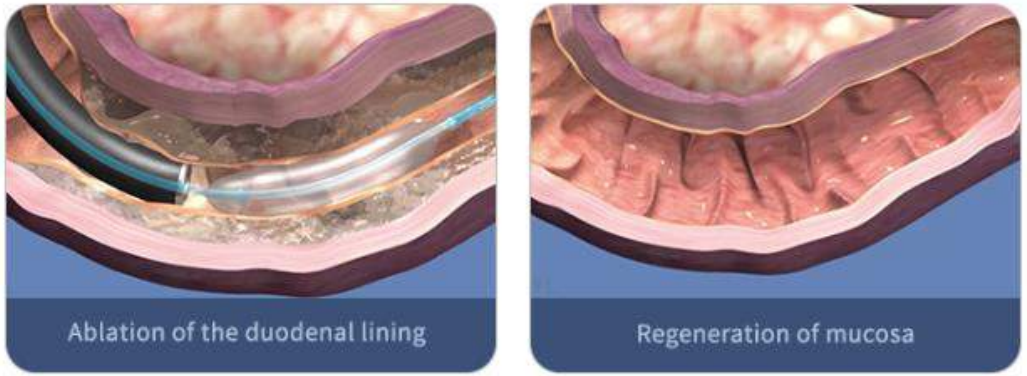
Duodenal-Jejunal Sleeve Improved Liver Enzymes

- 17 obese subjects treated with DJB for 24 weeks
- Liver tests decreased :
  - ALT: from 54 to 28 U/L, $P<0.05$
  - AST: from 35 to 28 U/L
  - GGT: from 66 to 35 U/L, $P<0.05$
- Results were maintained 6 months after removal of the device
- Presently, multi-center trial is undergoing in the US

De Jonge et al, Clin Gastroenterol Hepatol. 2013

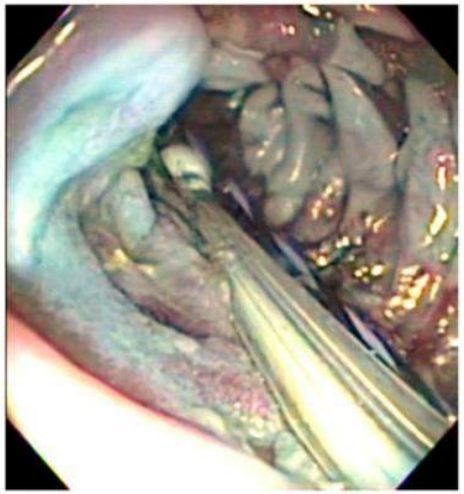
Small Bowel Therapies: Duodenal Mucosal Resurfacing

- Thermal ablation of the duodenal mucosa with a catheter
- Most studies in diabetic patients with obesity
- Modest weight loss

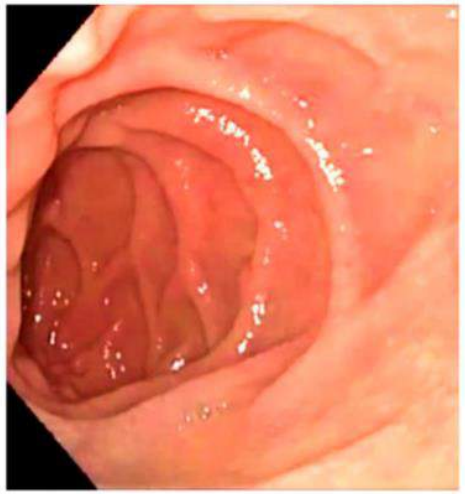


Duodenum before DMR

Immediately after DMR

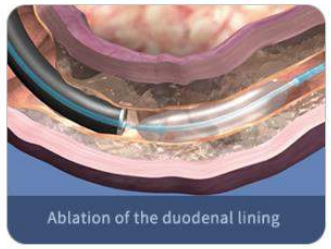


One month after DMR

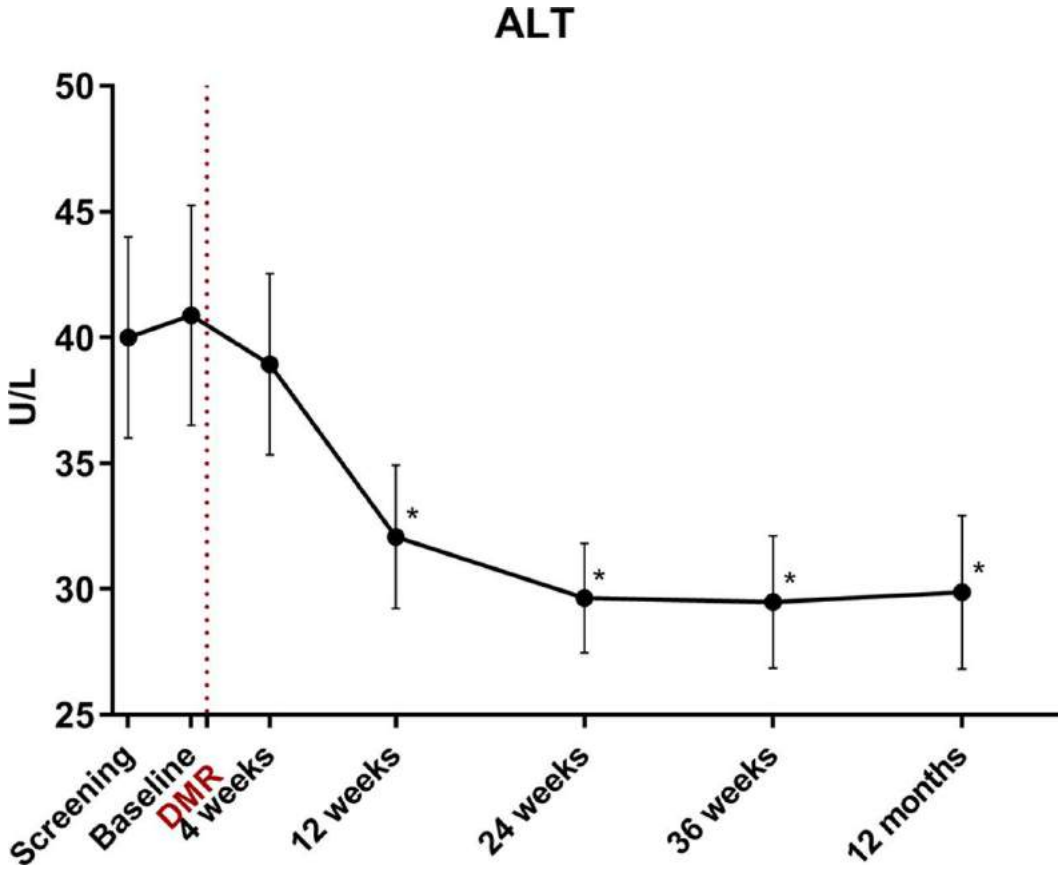


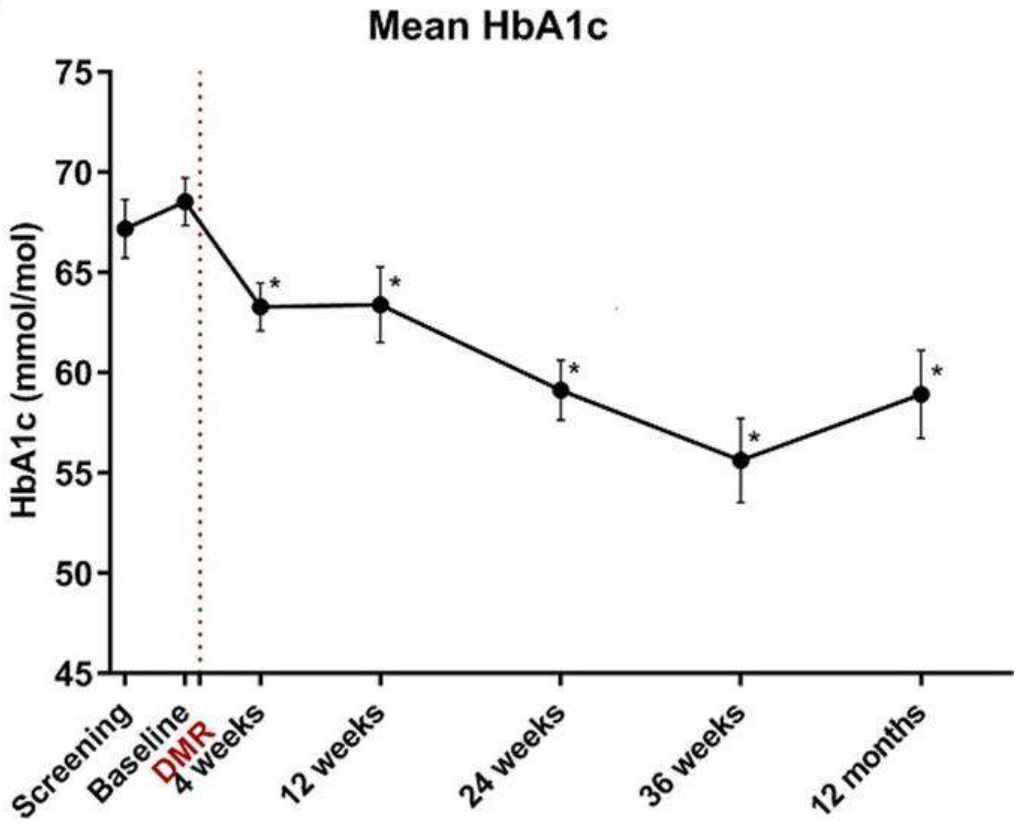
Rajagopalan H et al. Diabetes Care 2016
Galval Neto M et al. Video GIE 2019

Duodenal Mucosal Resurfacing Open Label Trial, 12 months



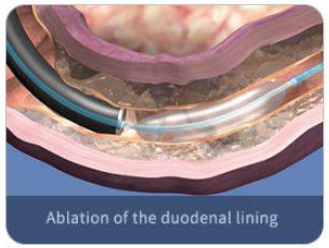
- 9 countries, 37 pts





Van Baar, et al. Gut 2019

Duodenal Mucosal Resurfacing RCT



- First sham-controlled, double-blind, prospective study
- 11 sites (9 in EU, 2 in Brazil)
- Eligible patients (HbA1c of 7.5-10%, BMI ≥24 to ≤40kg/m2, on ≥1 oral anti-diabetic medication)
- Randomized 1:1 to receive DMR or sham procedure
- 108 patients were enrolled (DMR, n=56; sham, n=52)

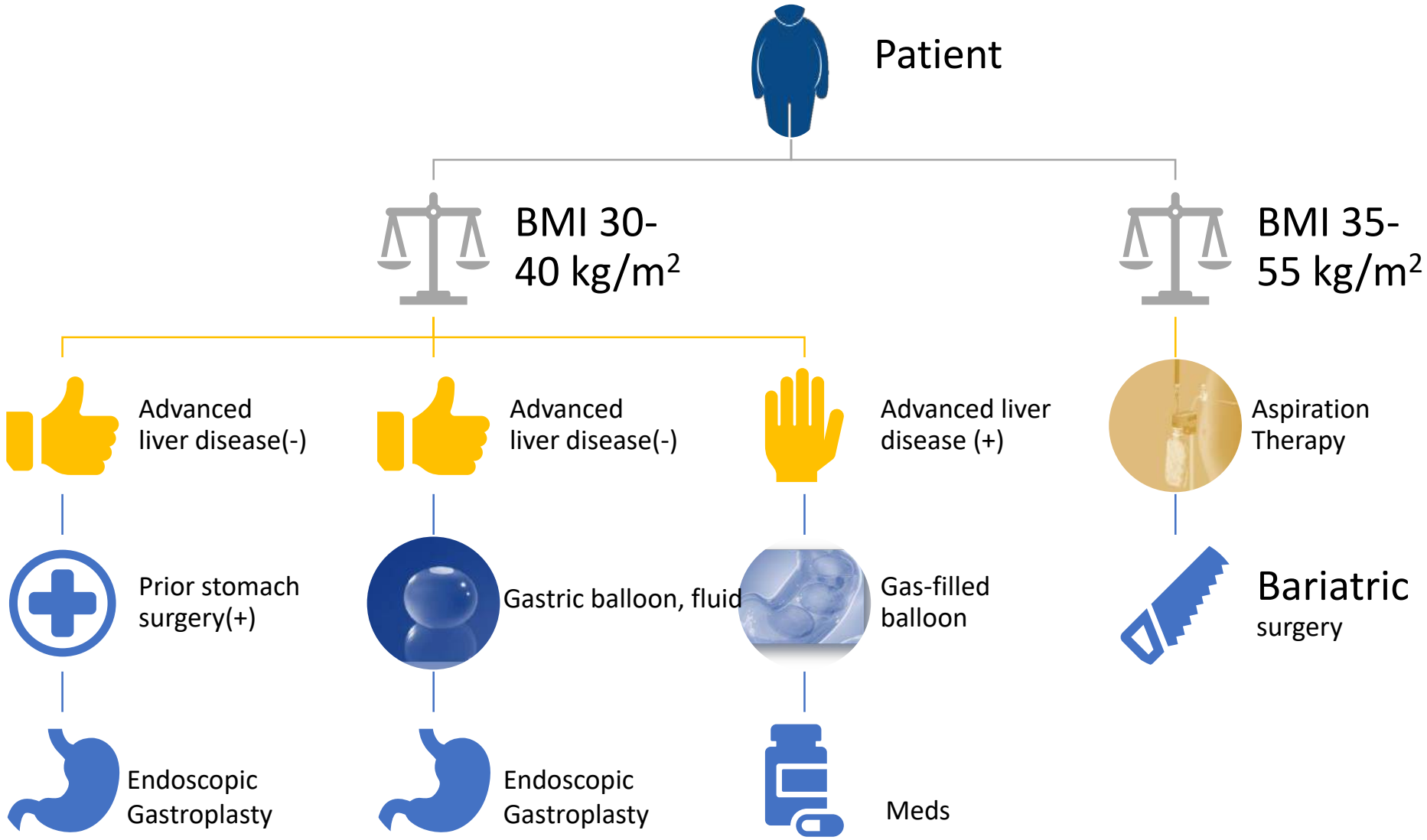
	DMR(n=39)	Sham(n=36)	P value
Change in liver MRI-PDDF baseline – 12 wks	- 5.4	-2.4	<0.05
Weight change baseline-24 wks, kg	-2.4	-1.4	<0.05
HbA1c change from baseline, 12 wks. %	-0.8	-0.3	<0.05

Bergman J, Deviere J, et al. AASLD 2019

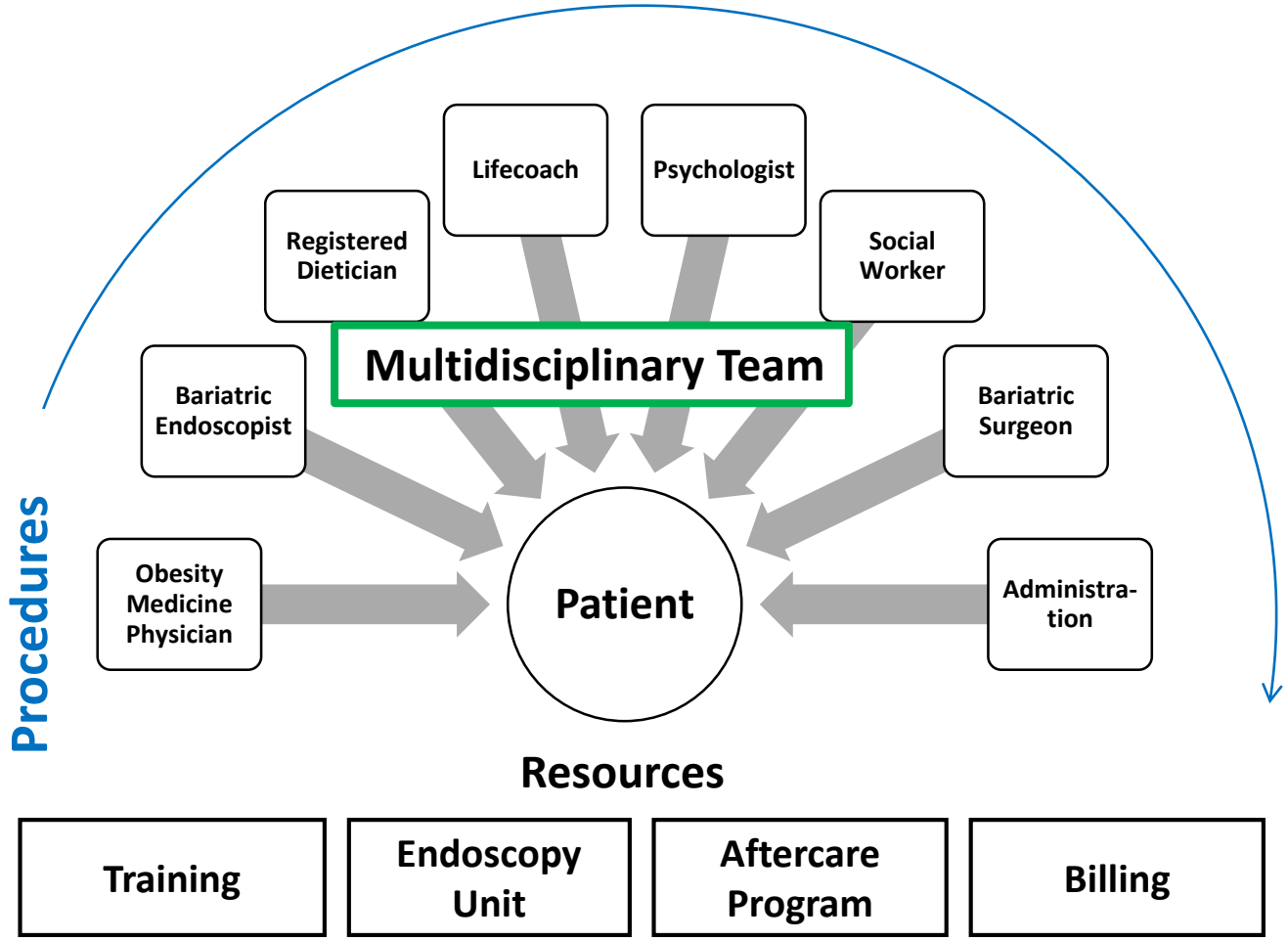
Patient Selection

- Patients have to show commitment to lifestyle changes and insight about factors leading to obesity
- For aspiration, the patients need to be prepared to aspirate 3 x a day- should describe plan
- Stable social situation
- Use of anti-thrombotic agents almost always a contraindication
- Generally, patients with end-stage liver disease are poor candidates
- Esophageal or gastric varices; GAVE; Portal gastropathy exclusion criteria
- Meet other inclusion-exclusion criteria

Patient Selection

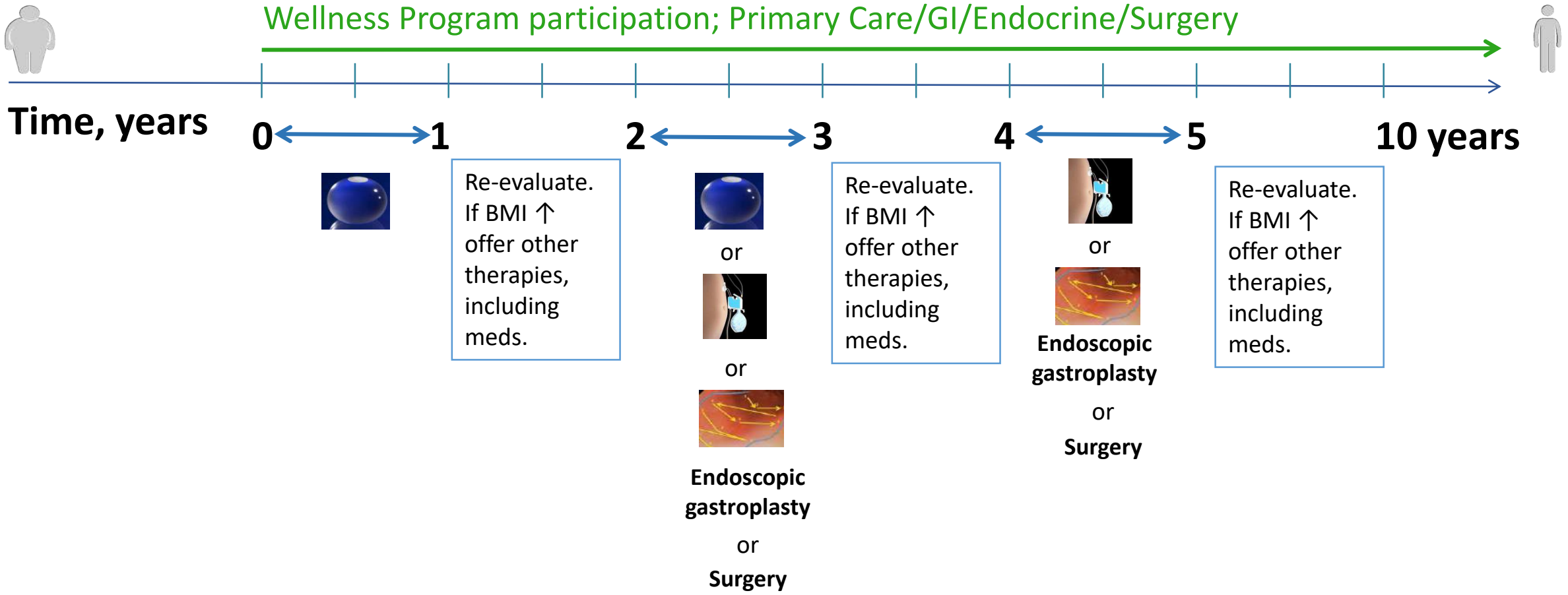


The Multidisciplinary Team



Comprehensive approach

- Obesity is a **chronic** disease that requires **<u>long-term multidisciplinary</u>** management plan and standards of care.



EBTs Are **Safe And Effective Weight Loss Adjunct** to Lifestyle Interventions & May Be Beneficial in NAFLD

Intervention	BMI Category (kg/m)					Effectiveness	Complications
	25-26.9	27-29.9	30-34.9	35-39.9	≥40		
Diet, Exercise, Behavior Tx	✓	✓	✓	✓	✓		
Pharmaco-therapy		With co-morbidities	✓	✓	✓		
Endoscopic therapies			✓	✓	✓		
Surgery				With co-morbidities	✓		

NYU Langone MEDICAL CENTER

Thank you!

@PopovVioleta