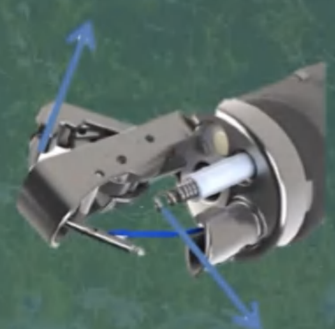
Endoscopic Bariatric Techniques: Are They Viable Alternative to Surgery?

Reem Sharaiha MD MSc

Associate Professor of Medicine

Director of Therapeutic Endoscopy

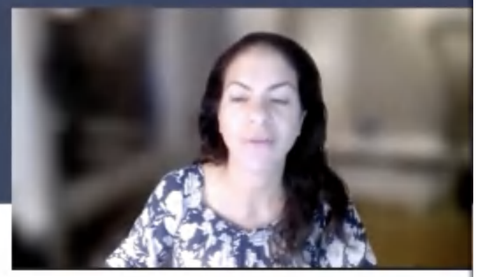
Weill Cornell Medical College



Disclosure

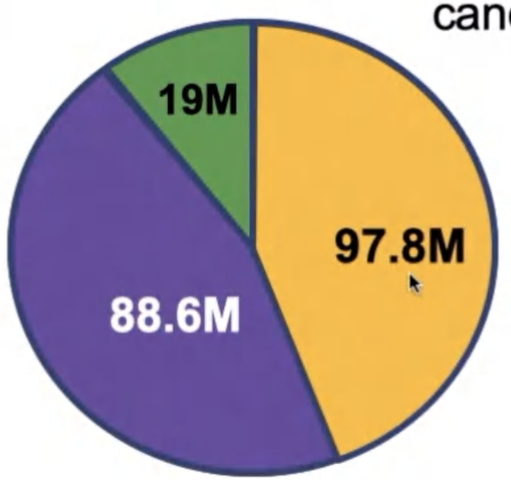
- **Consultant and research support**
  - **Boston Scientific**
  - **Olympus**
  - **Lumendi**
  - **Wilson Cook**

Management of obesity: the problem



Surgical candidates: only 2% choose this
BMI >40kg/m2
BMI >35 with >1 comorbid condition

Super obese-poor surgical candidates



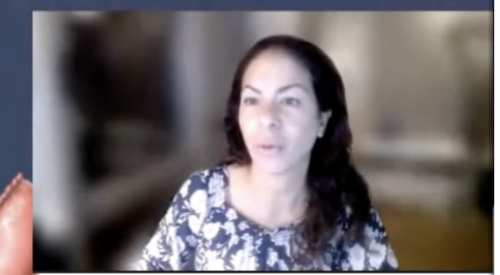
Overweight: risk for metabolic Diseases (NASH, DM)

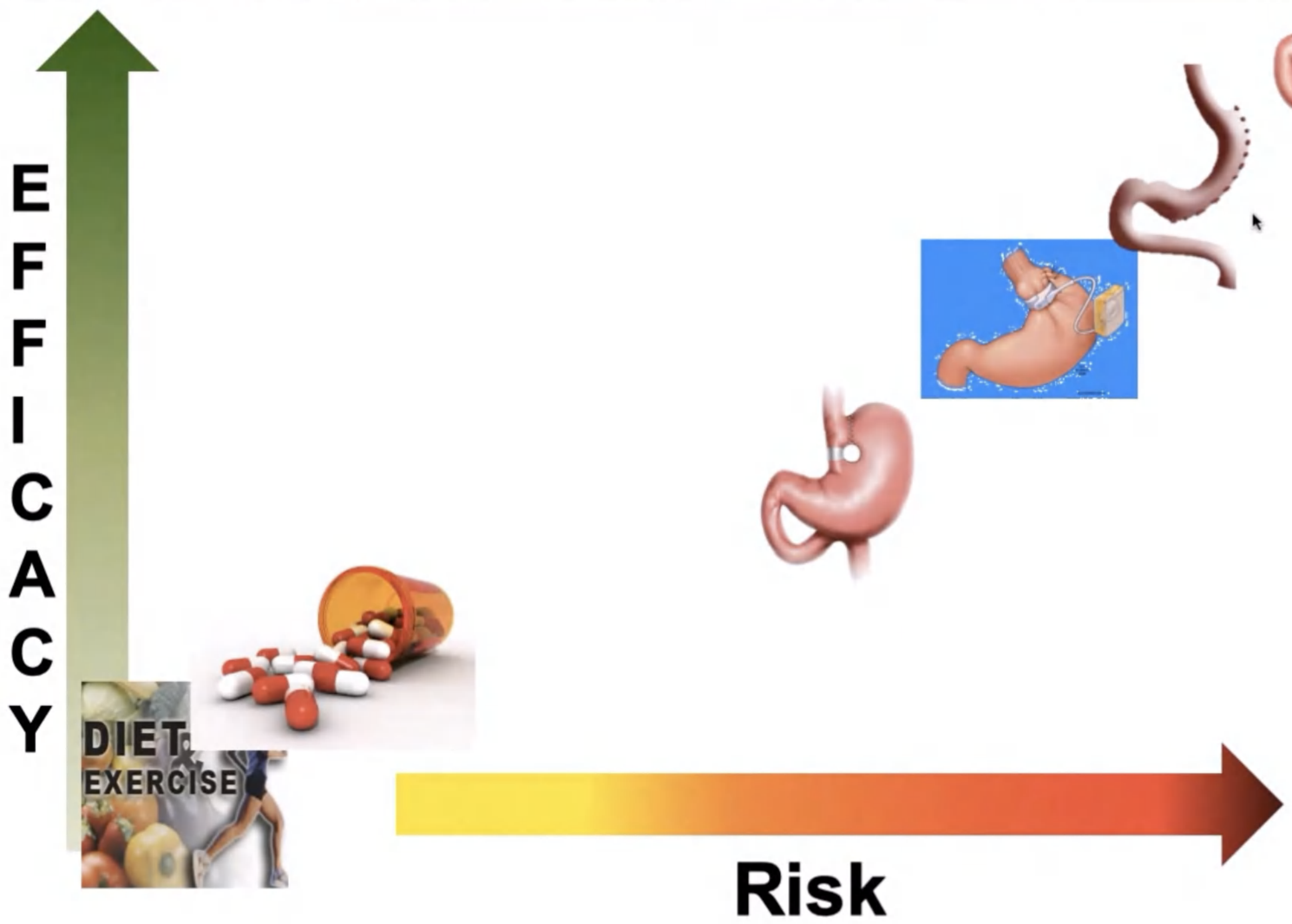
Obese: don't qualify for surgery, Diet and exercise failed

Prevalence >200 million obese/overweight

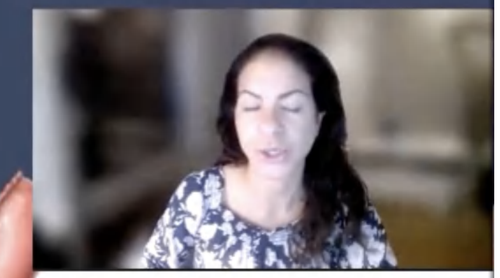
Ponce J et al. Surg Obses Rel Dis 2015

Treatments for obesity



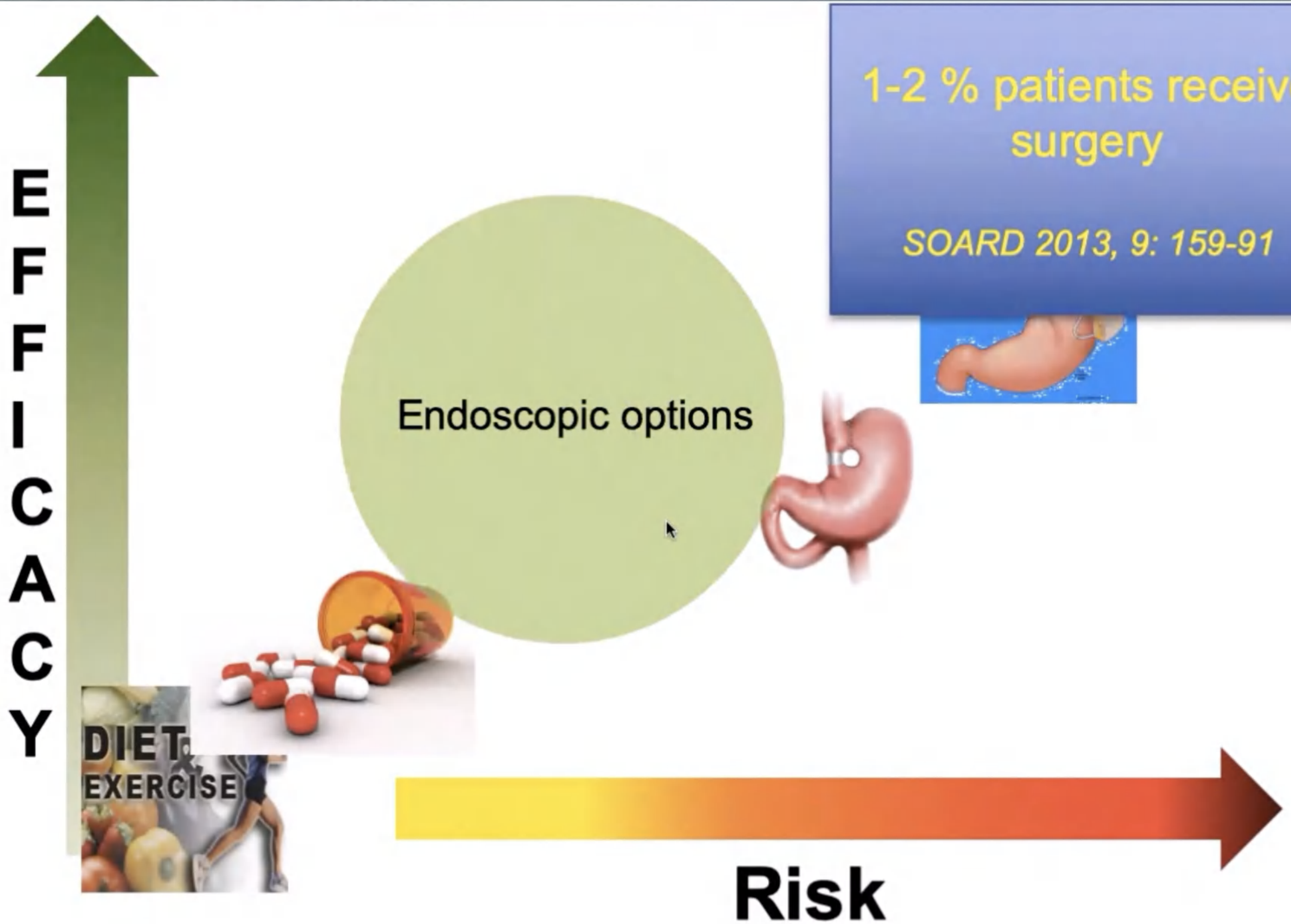


Treatments for obesity

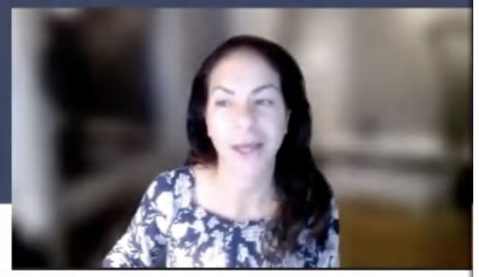


1-2 % patients receive surgery

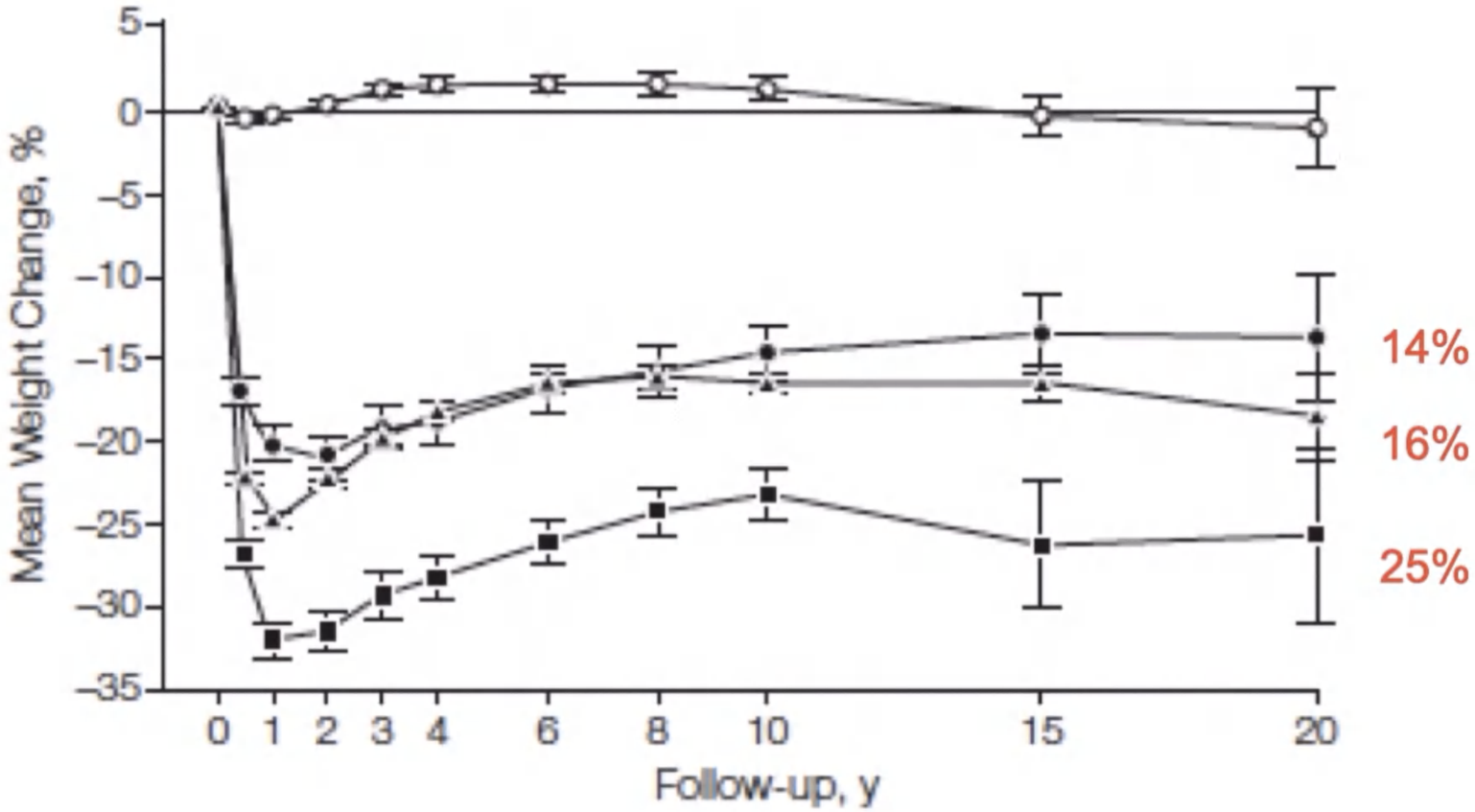
SOARD 2013, 9: 159-91



Bariatric Surgery and Long-term Cardiovascular Events

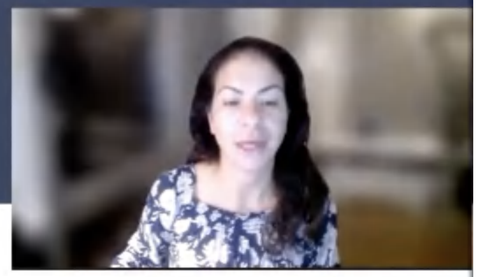


Hazard ratio
Surgical group
0.67 (P<0.001)



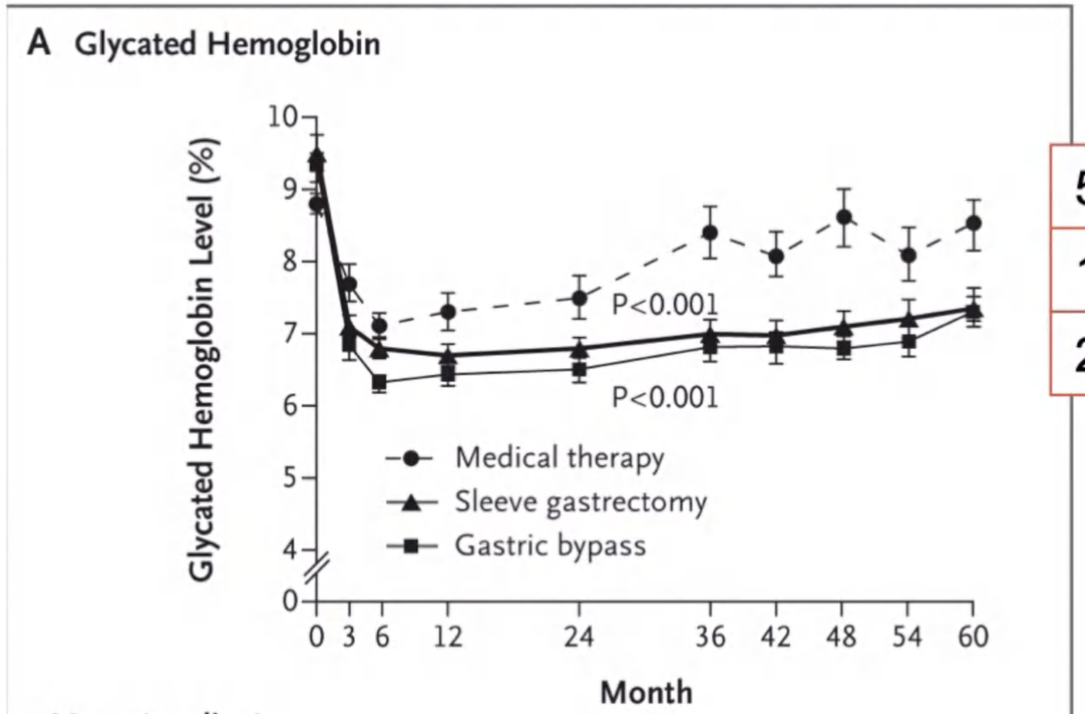
Sjöström, JAMA 2012

Bariatric Surgical Outcomes- Hb A1C



Primary outcome:
Treatment success at 5 years (HbA1c <6%)
Results
- 2% Medical therapy
- 23% SG
- 29% RYGB

A1C reduction Surgery vs Medicine (2.1% vs. 0.3%, P=0.003).



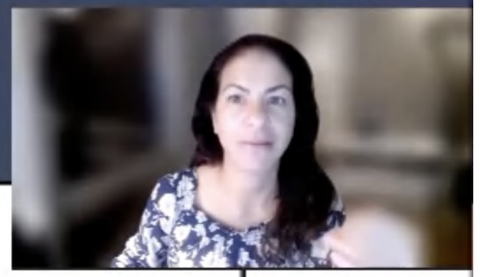
5%
19%
23%

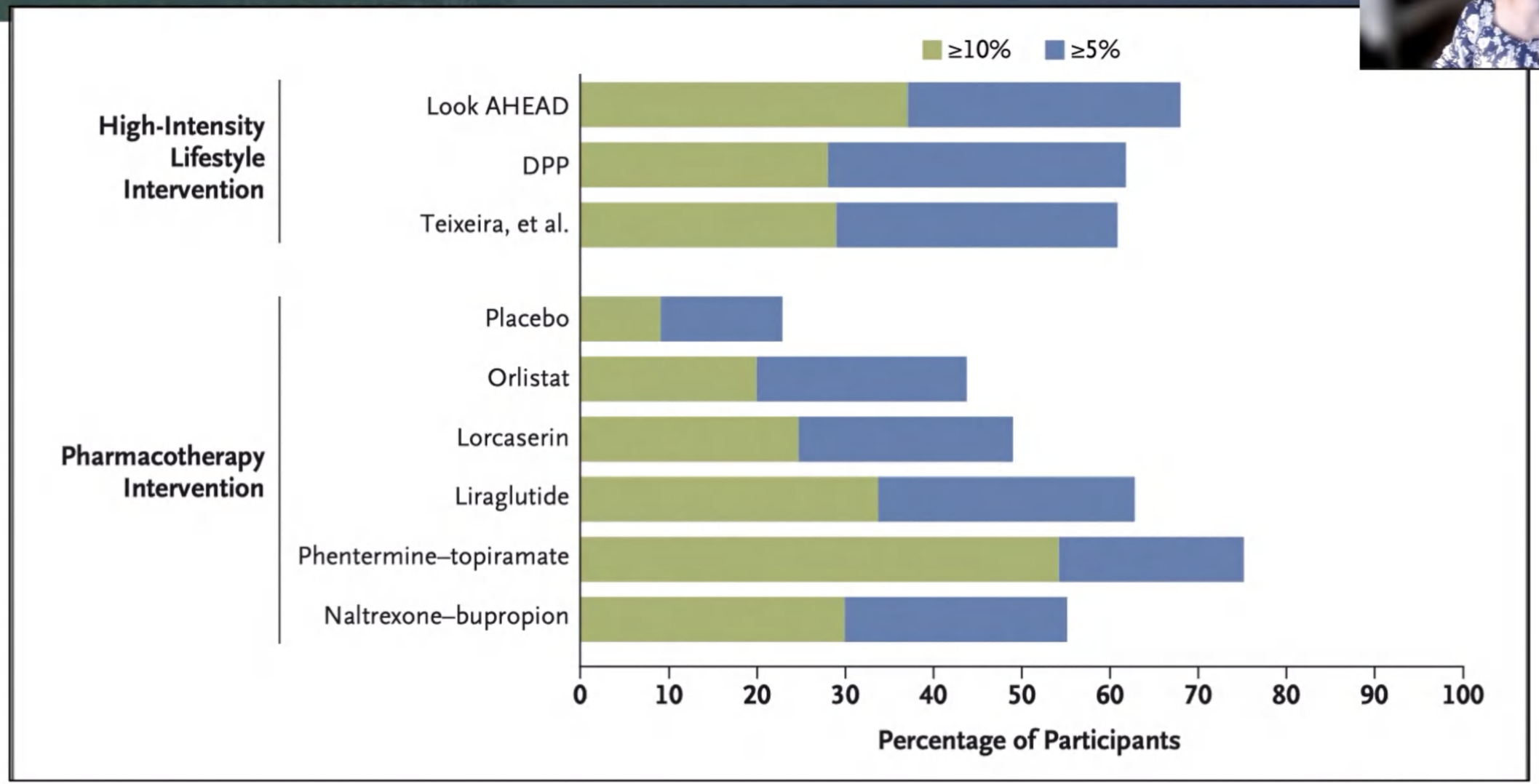
Mean (median) Value at Visit

Medical therapy	8.8 (8.6)	7.3 (6.8)	7.5 (7.2)	8.4 (7.7)	8.6 (8.2)	8.5 (8.0)
Gastric bypass	9.3 (9.4)	6.4 (6.2)	6.5 (6.4)	6.8 (6.6)	6.8 (6.8)	7.3 (6.9)
Sleeve gastrec-tomy	9.5 (8.9)	6.7 (6.4)	6.8 (6.8)	7.0 (6.7)	7.1 (6.6)	7.4 (7.2)

Schauer PR et al. N Engl J Med 2017.

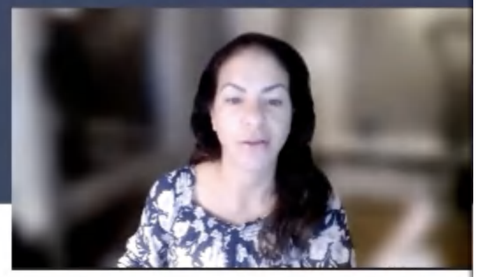
RCT TBWL 5 & 10% TBWL





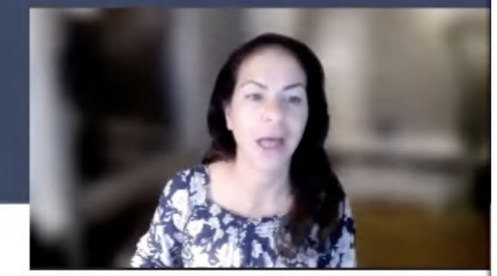
N Engl J Med 2017;376:254-66.

Endoscopic Bariatric Therapies



- Less invasive
- Less cost
- Outpatient
- Repeatability and Reversibility
- Multi purpose
  - Cosmesis
  - Treatment for diabetes
  - Bridge to surgery

Targeted Endoscopic Therapy



Stomach

- Space occupying
- Gastric remodeling
- Outlet obstruction
- Aspiration

Small Bowel

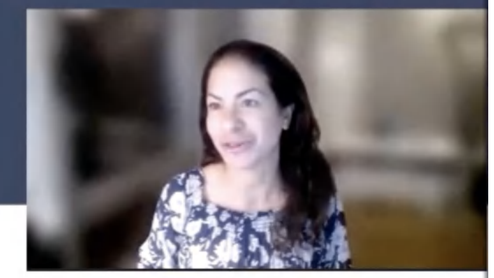
- Sleeves
- Duodenal resurfacing
- Anastomosis
- Flow altering

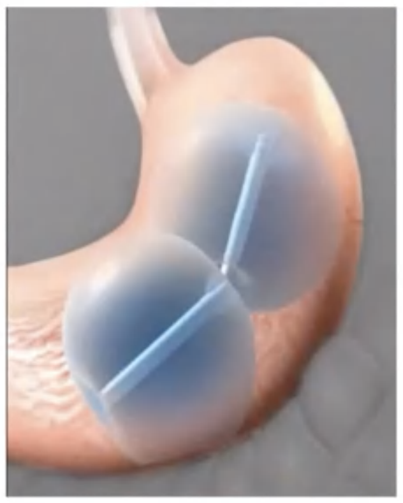
Obesity

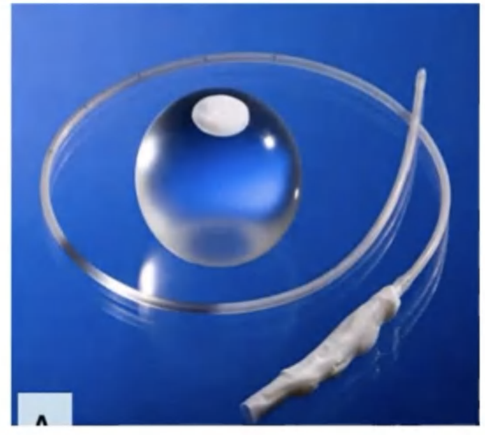
Stronger Antidiabetic and NASH Effect

Courtesy of Chris Thompson

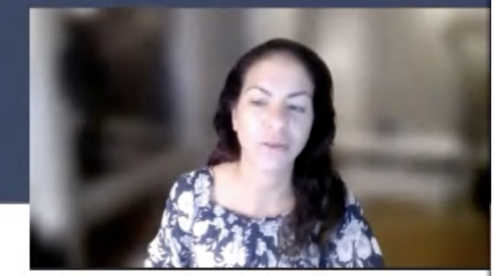
Intragastric Balloons (IGB): Space occupying



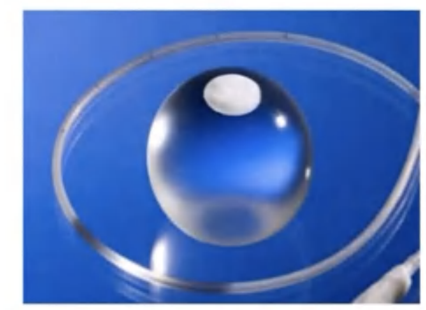




Balloon Data – FDA approved, All met End Points

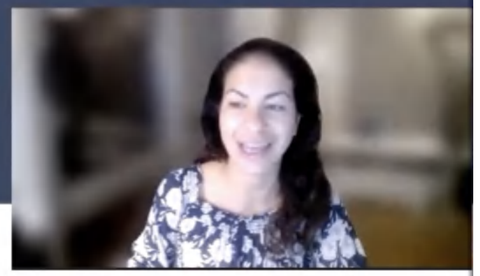


- Reshape
  - Balloon 25% EWL vs 11% (Sham)
- Orbera
  - Balloon 10% TBWL vs 3.9% (Life style)
- Obalon
  - Balloon 6.9% TBWL vs 3.5% (Sham)

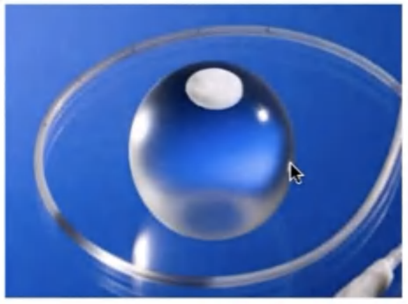


Ponce J et al. Surg Obes Relat Dis 2015 11:874-81
Courcoulas A et al. Int J Obesity 2017
Sullivan et al Surg Obes Relat Dis. 2018

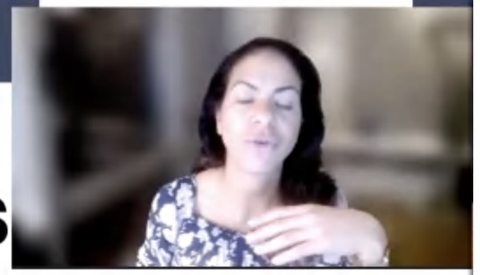
Balloon Data – FDA approved, All met End Points



- Reshape
  - Balloon 25% EWL vs 11% (Sham)
- Orbera
  - Balloon 10% TBWL vs 3.9% (Life style)
- Obalon
  - Balloon 6.9% TBWL vs 3.5% (Sham)



Ponce J et al. Surg Obes Relat Dis 2015 11:874-81
Courcoulas A et al. Int J Obesity 2017
Sullivan et al Surg Obes Relat Dis. 2018



Liquid-filled Intragastric Balloon Systems Letter to Healthcare Providers - Potential Risks

[Posted 08/10/2017]

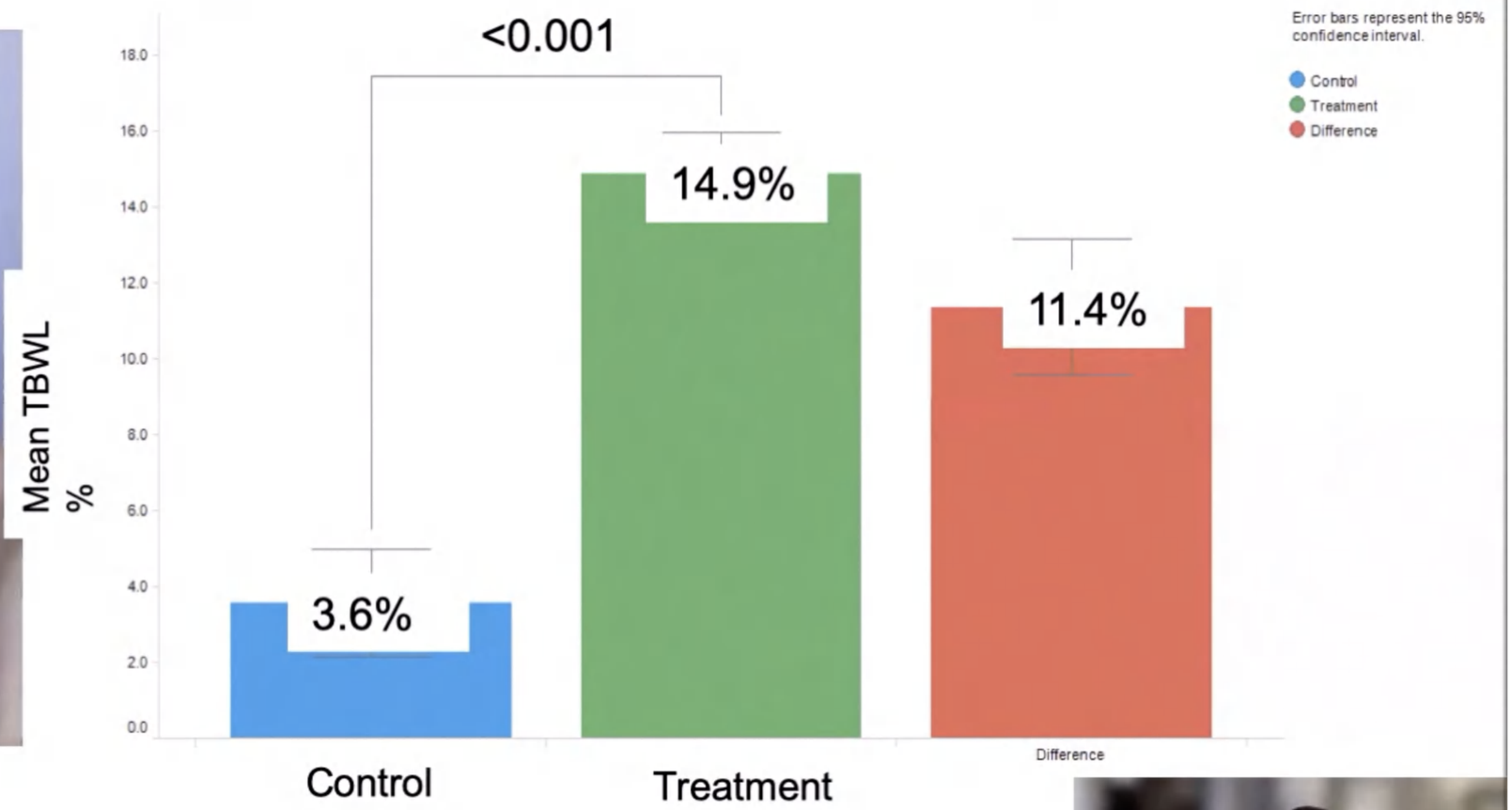
AUDIENCE: Surgery, Gastroenterology, Health Professional

ISSUE: FDA is issuing an update to alert health care providers of five reports of unanticipated deaths that occurred from 2016 to present in patients with liquid-filled intragastric balloon systems used to treat obesity. Four reports involve the Orbera Intragastric Balloon System, manufactured by Apollo Endo Surgery, and one report involves the ReShape Integrated Dual Balloon System, manufactured by ReShape Medical Inc.

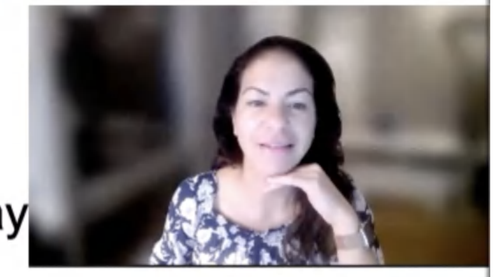
All five reports indicate that patient deaths occurred within a month or less of balloon placement. In three reports, death occurred as soon as one to three days after balloon placement. At this time, we do not know the root cause or incidence rate of patient death, nor have we been able to definitively attribute the deaths to the devices or the insertion procedures for these devices (e.g., gastric and esophageal perforation, or intestinal obstruction). The Agency has also received two additional reports of deaths in the same time period related to potential complications associated with balloon treatment (one gastric perforation with the Orbera Intragastric Balloon System and one esophageal perforation with the ReShape Integrated Dual Balloon System).

The FDA continues to work with Apollo Endo-Surgery and ReShape Medical Inc. to better understand the issue of unanticipated death, and to monitor the potential complications of acute pancreatitis and spontaneous over-inflation.

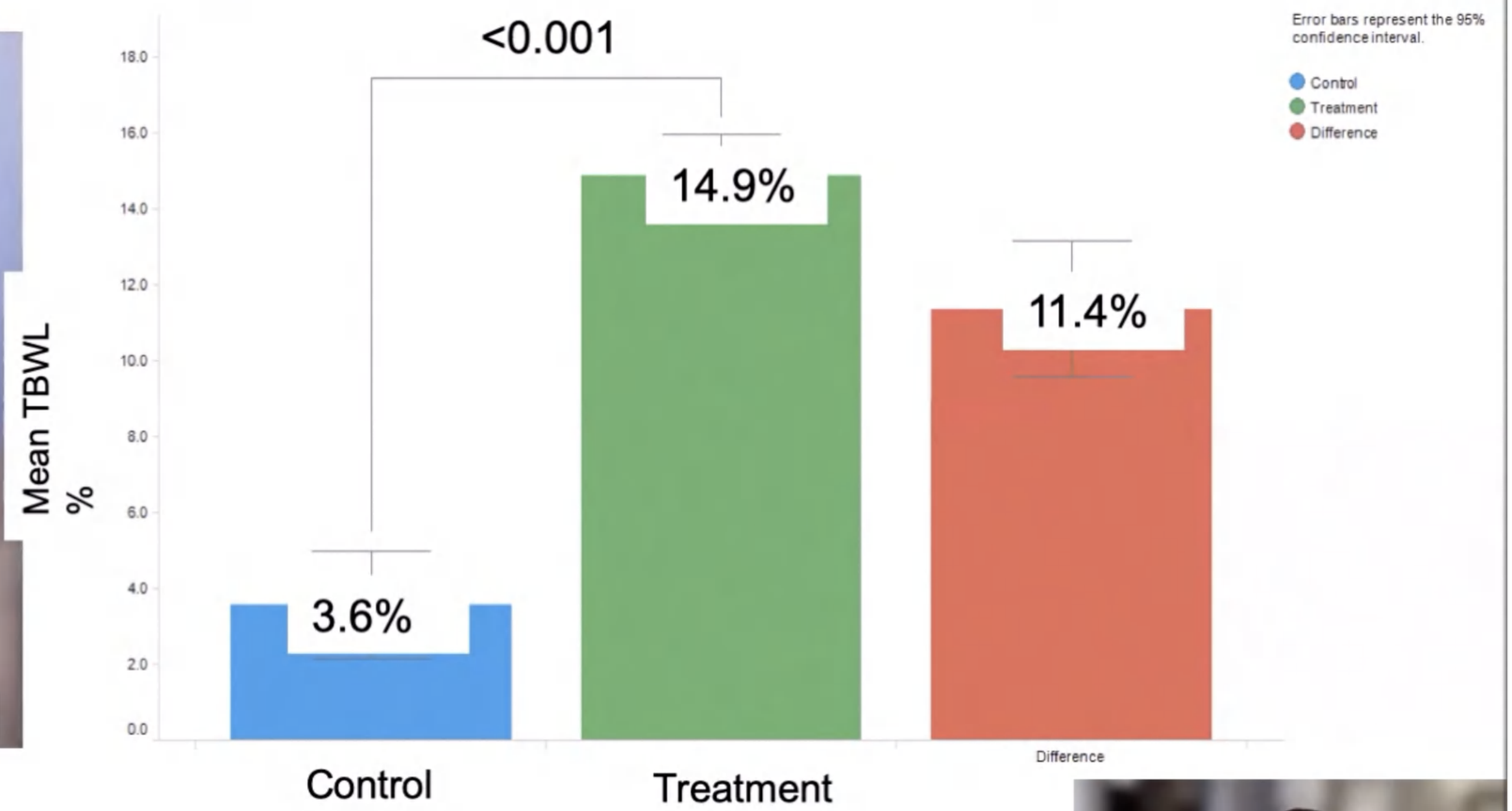
Open-label RCT of an adjustable IGB system plus lifestyle therapy compared with lifestyle therapy alone for weight loss in 288 participants (187 device and 101 control).



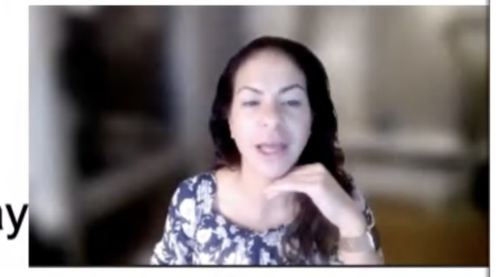
Abu Day



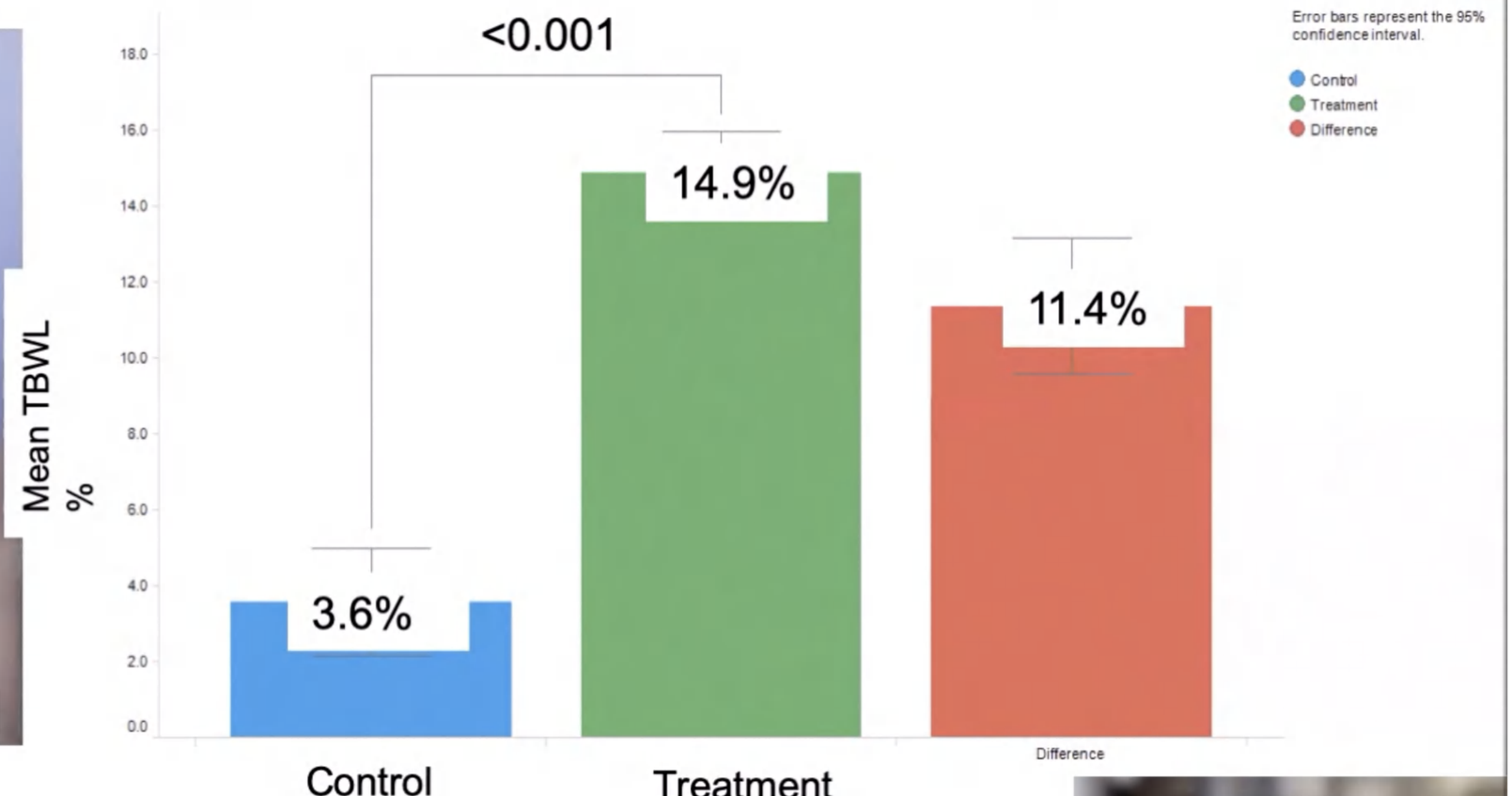
Open-label RCT of an adjustable IGB system plus lifestyle therapy compared with lifestyle therapy alone for weight loss in 288 participants (187 device and 101 control).



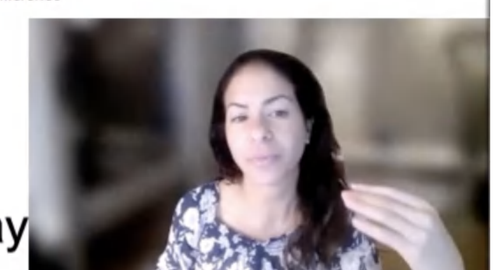
Abu Day



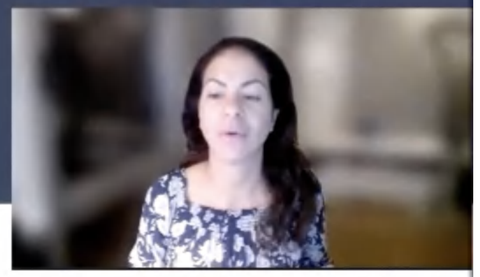
Open-label RCT of an adjustable IGB system plus lifestyle therapy compared with lifestyle therapy alone for weight loss in 288 participants (187 device and 101 control).



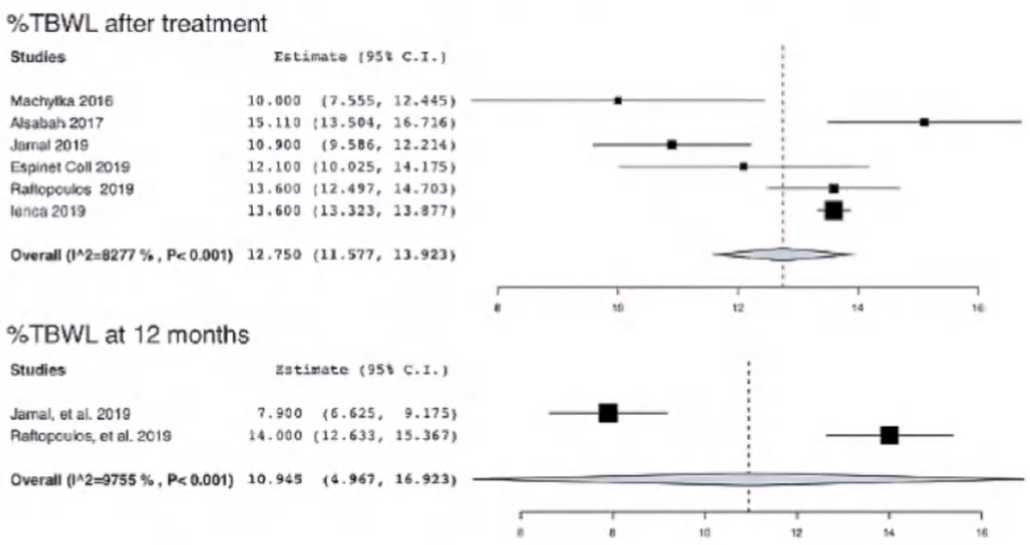
Abu Day

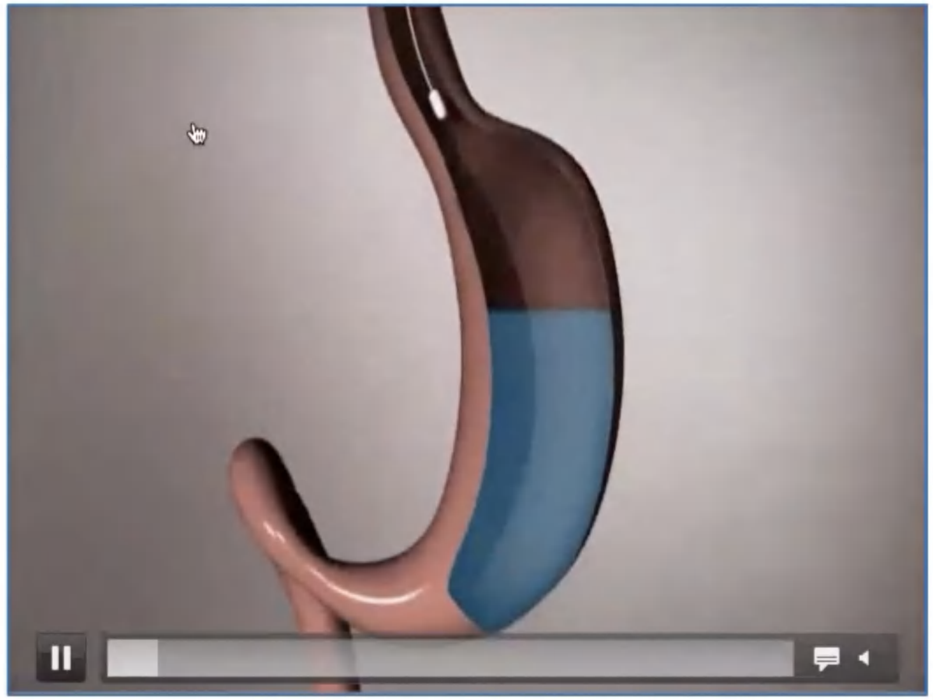


The Efficacy and Safety of a Procedureless Gastric balloon: A Systemic Review and Meta-analysis



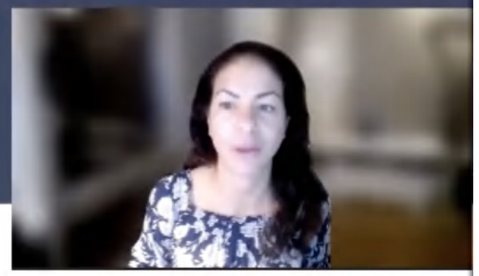
- A total of 160 studies were identified
- 3 - Bowel obstruction. (0.2% SAE)





PIVOTAL Trial Completed under review with FDA

The Procedureless Elipse Gastric Balloon Program: Multicenter Experience in 1770 Consecutive Patients



- 1770 Consecutive patients
- mean age 38.8 ± 12
- mean weight 94.6 ± 18.9 kg
- Mean BMI 34.4 ± 5.3 kg/m^2

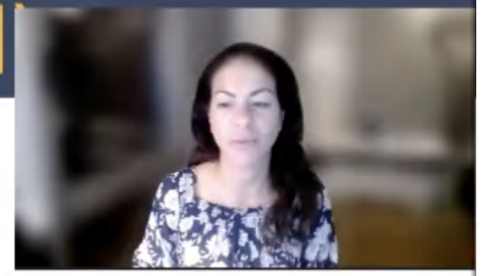
	Mean (SD).
Wl (kg)	13.5 ± 5.8, $p < 0.0001$ (from baseline)
%TBWL	14.2 ± 5.0, $p < 0.0001$ (from baseline)
%EWL	67.0 ± 64.1, $p < 0.0001$ (from baseline)
BMIL (kg/m^2)	4.9 ± 2.0, $p < 0.0001$ (from baseline)

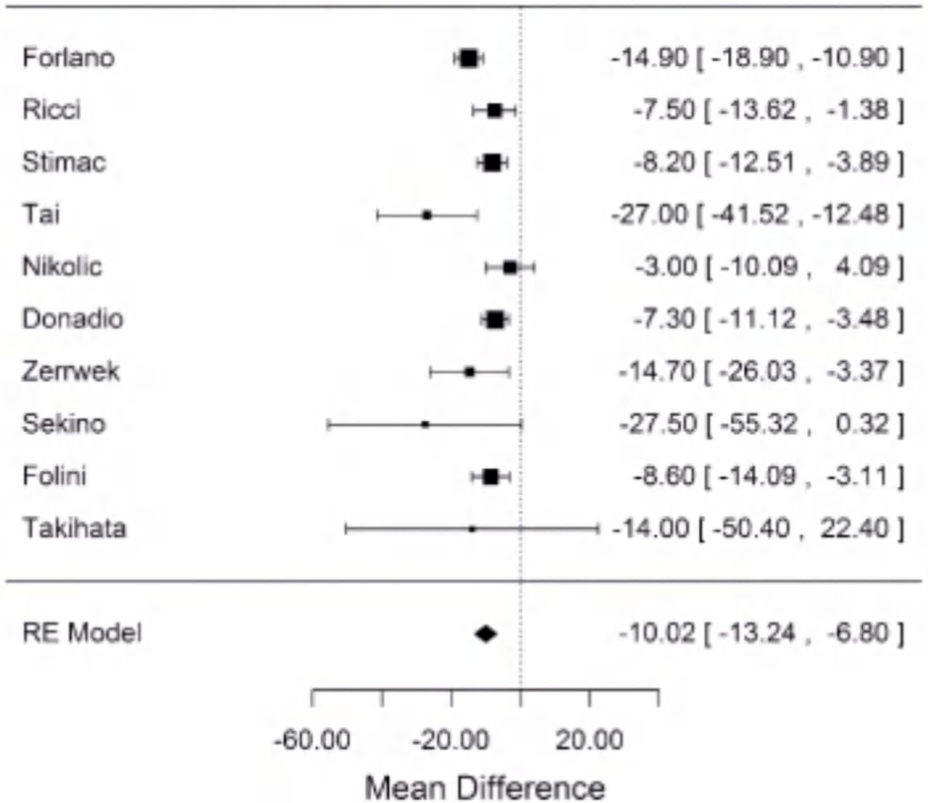
- Fifty-two (2.9%) intolerance requiring balloon removal.
- Eleven (0.6%) balloons deflated early.
- 3 small bowel obstructions requiring laparoscopic surgery

Improvement in A1C and LDL, TG @ 4 months

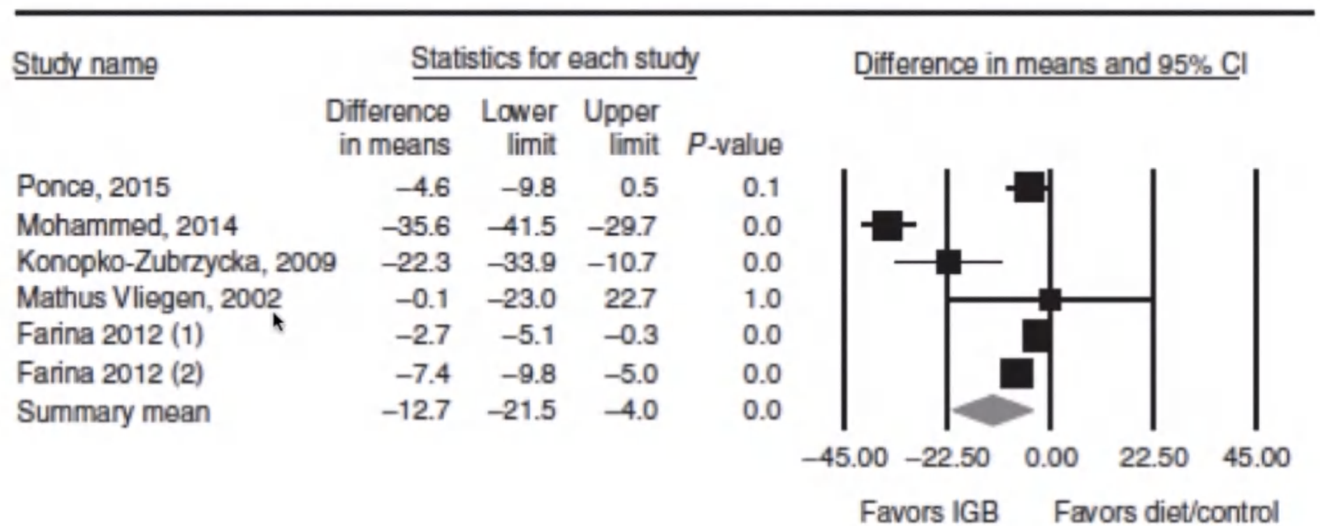
Ienca et al. Obes Surg. 2020

Balloons Improve Comorbidities (NASH and DM)



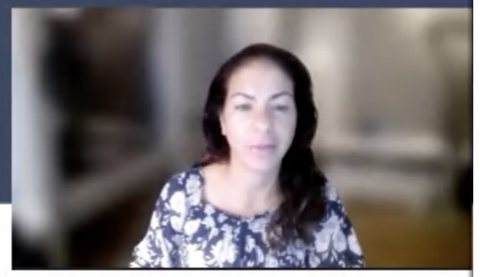


Forest plot of mean difference in **ALT** baseline to 6 months of intragastric balloon



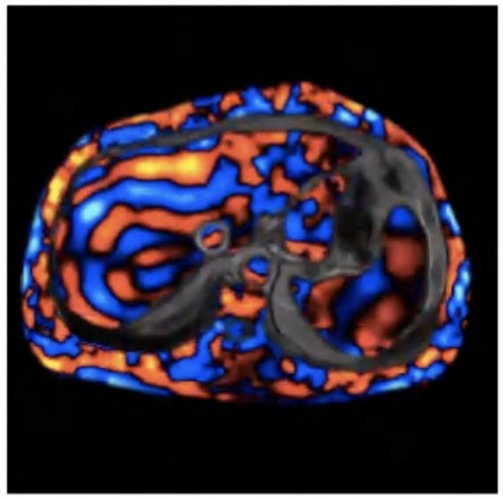
Popov et al. A m J Gastroenterol 2017
Popov et al. Dig Dis Sci (2016)

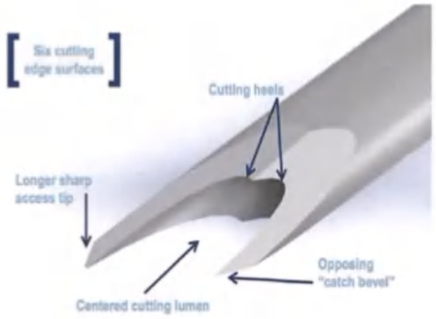
Impact of Balloon on liver biopsy

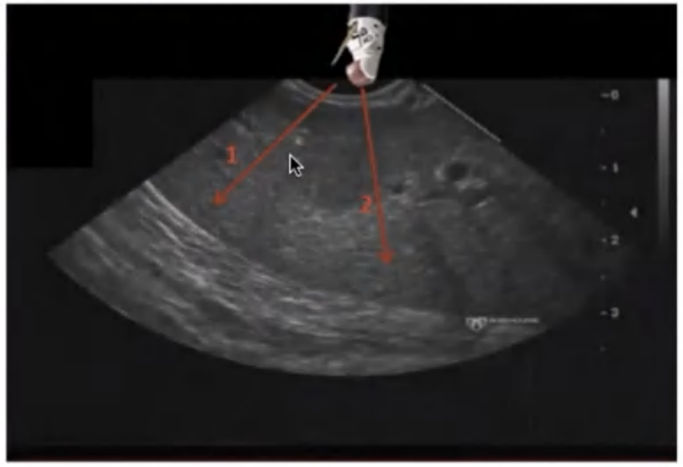


- Study the impact of the Orbera IGB on NAS and liver fibrosis in a prospective cohort of noncirrhotic patients. FDA approved protocol.

- Accomplished via paired EUS guided biopsies and MR elastography/spectroscopy at the time of placement and removal after six months.

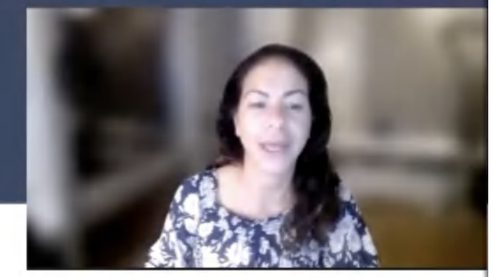


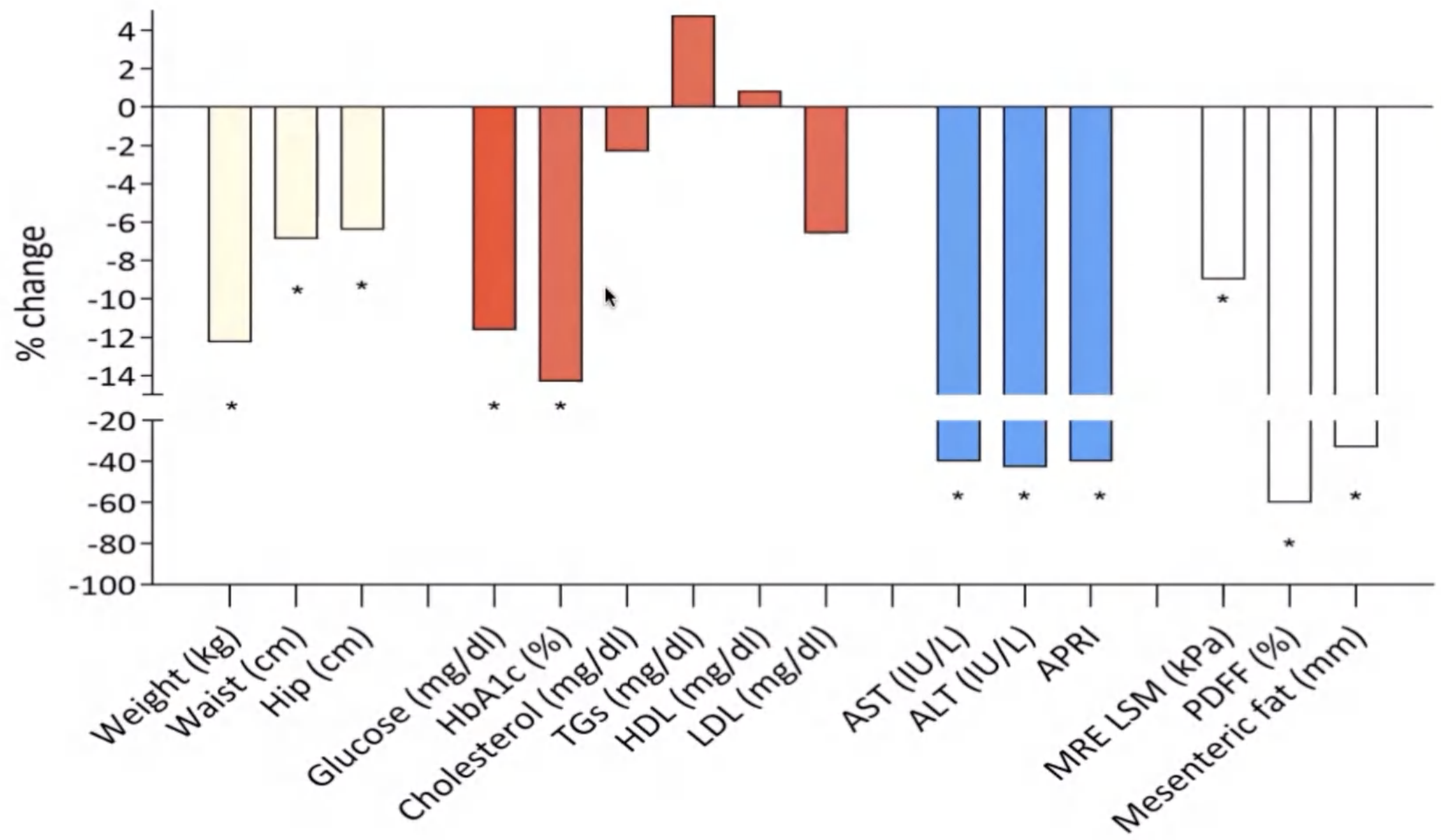




CGH 2021

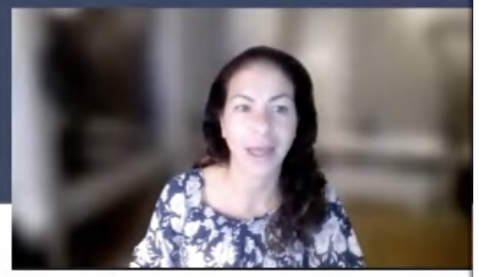
% Δ in Studied Variables





CGH 2021

Steatofibrosis Results Summary



Fibrosis regressed

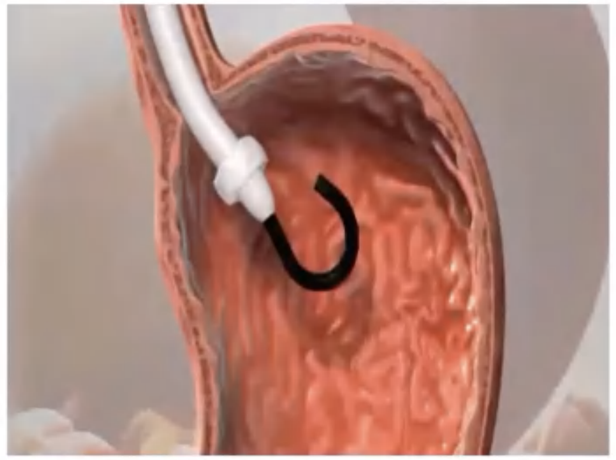
- Per biopsy in 15% (by an average of 1.16 stage)
- 10% of patients are at stage 0 post intervention
- Per MRE LSM median Improved in 75% ($p < 0.05$) an average of 0.70 kPa

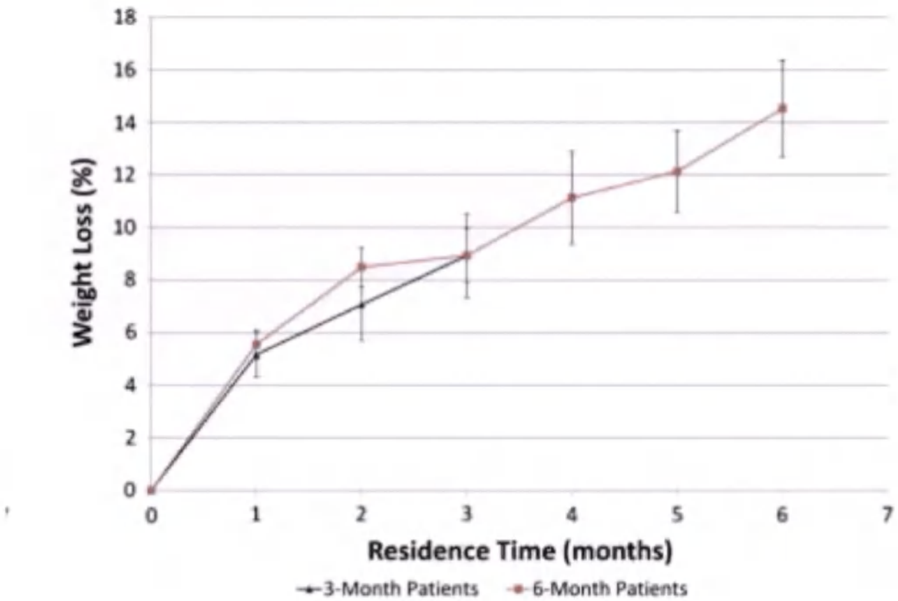
NAS improved

- 95% of patients (average decrease of 2.6 points)
- 80% decreased by at least 2 points
- 65% complete resolution of steatohepatitis

CGH 2021

BAROnova- FDA Approved





ENDObesity II Trial

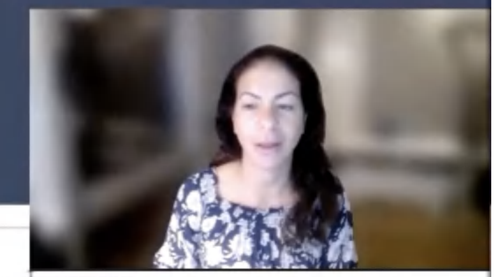
Multi-center randomized double-blind sham-controlled trial
270 subjects randomized 2:1
12 month device implantation
BMI 30-40 kg/m^2
- BMI 30-34.9 kg/m^2: one obesity co-morbidity
- BMI 35-40 kg/m^2: no co-morbidity required

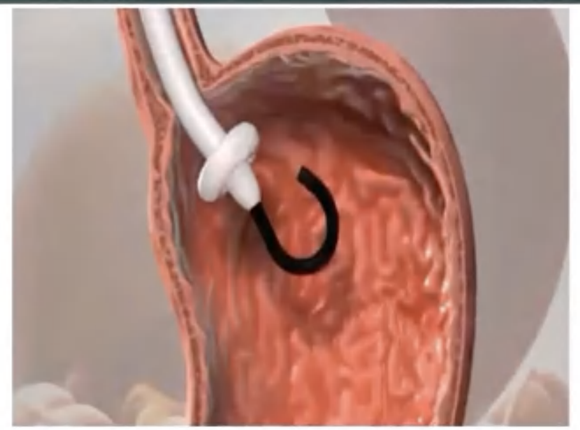
Lifestyle therapy visits: 7 in person, 4 phone call
Endoscopies at 2 and 6 months for ulcer surveillance

	TPS	Control	P value
>5 % TBL	67.0 %	29.3 %	<0.0001
>10% TBL	39.5 %	14.0 %	0.0001

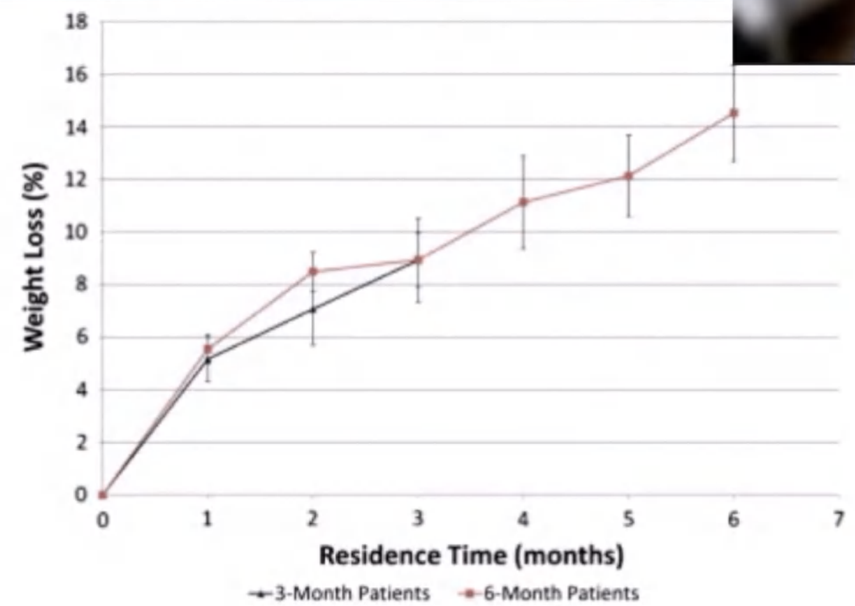
Rothstein et al. Obesity Week 2018

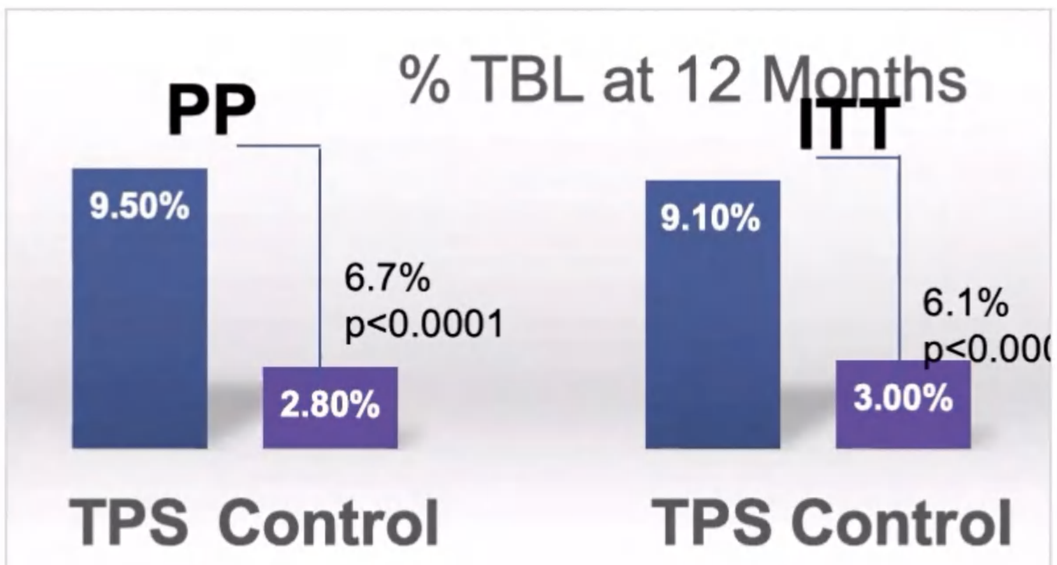
BAROnova- FDA Approved





ENDObesity II Trial

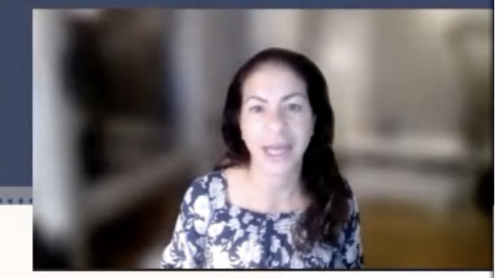




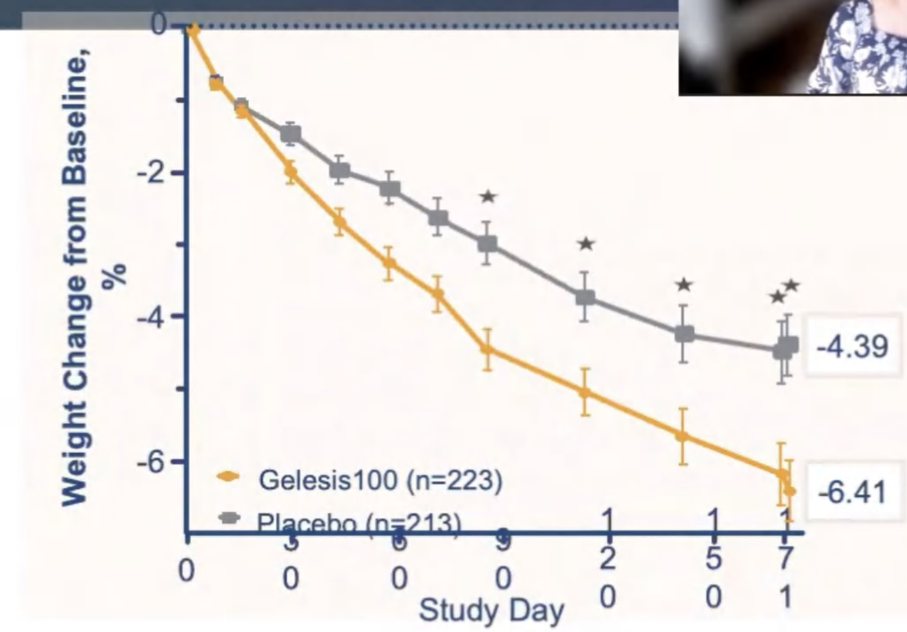
Gastric ulcers 10.3% - responded to PPI and sucralfate
Improvement in HTN, insulin, HOMA IR, cholesterol in TPS compared to control group ($p < 0.05$)

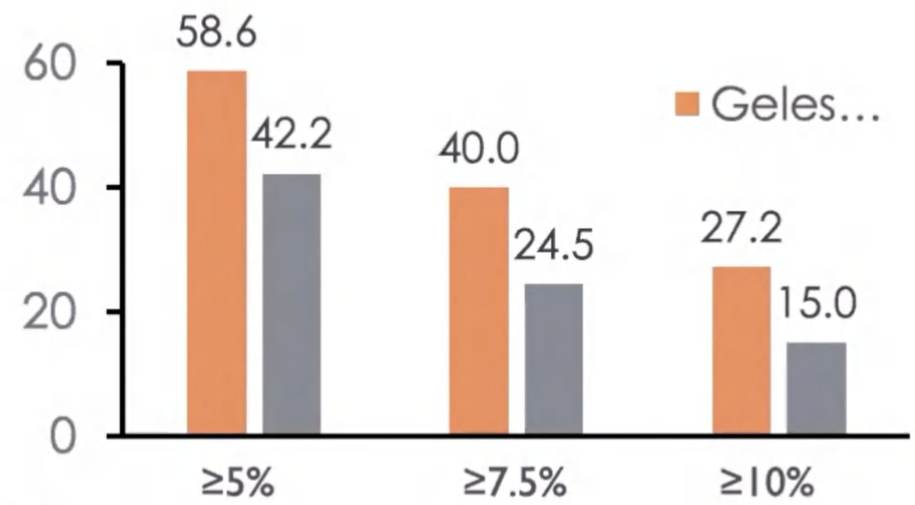
Rothstein et al. Obesity Week 2018

Gelesis100: FDA Approved



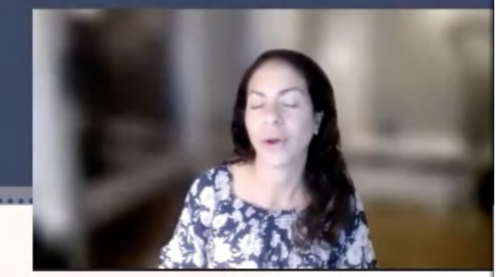
24-week, multicenter, randomized, doubleblind
BMI ≥ 27 and ≤ 40 kg/m2



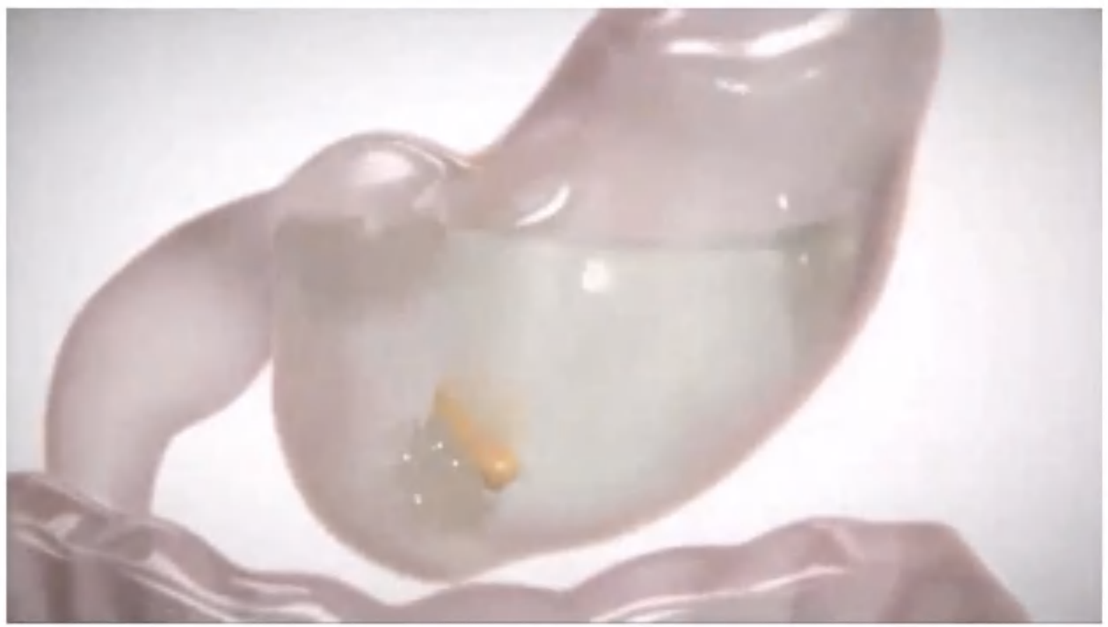


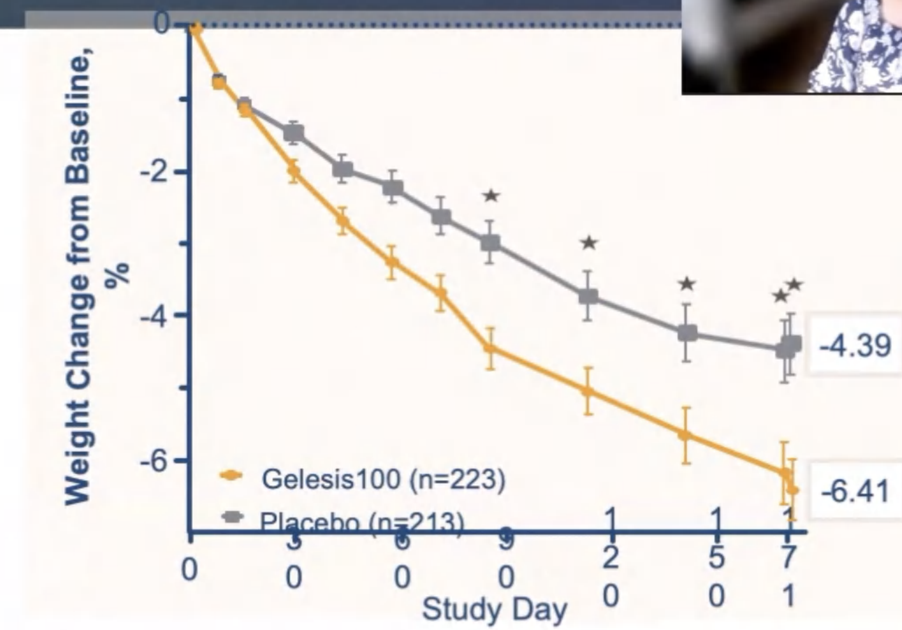
Obesity (2019) 27, 205-216.

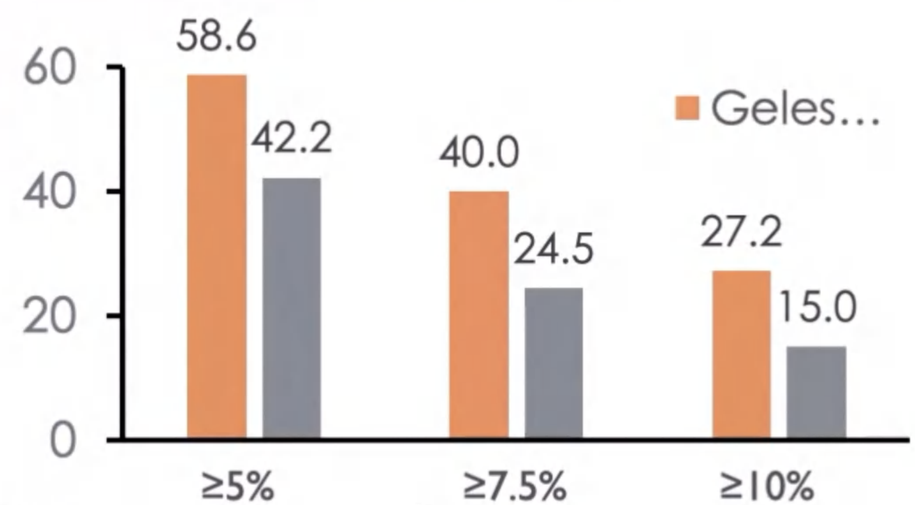
Gelesis100: FDA Approved



24-week, multicenter, randomized, doubleblind
BMI ≥ 27 and ≤ 40 kg/m2

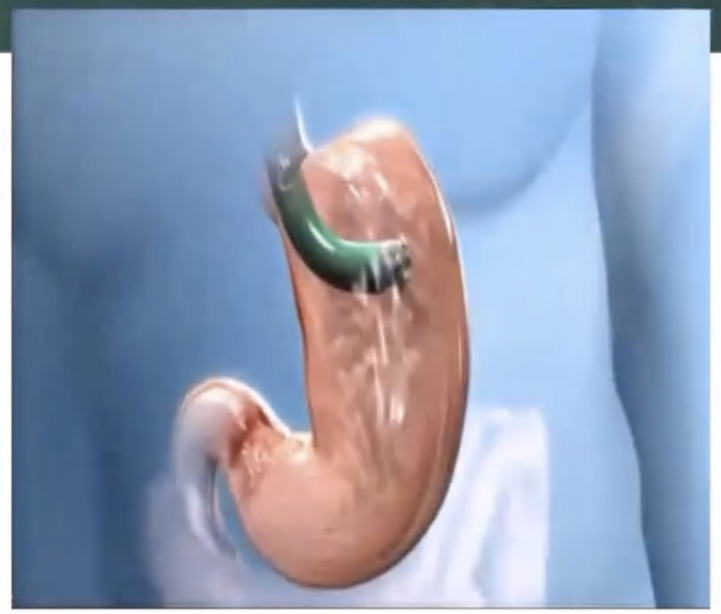


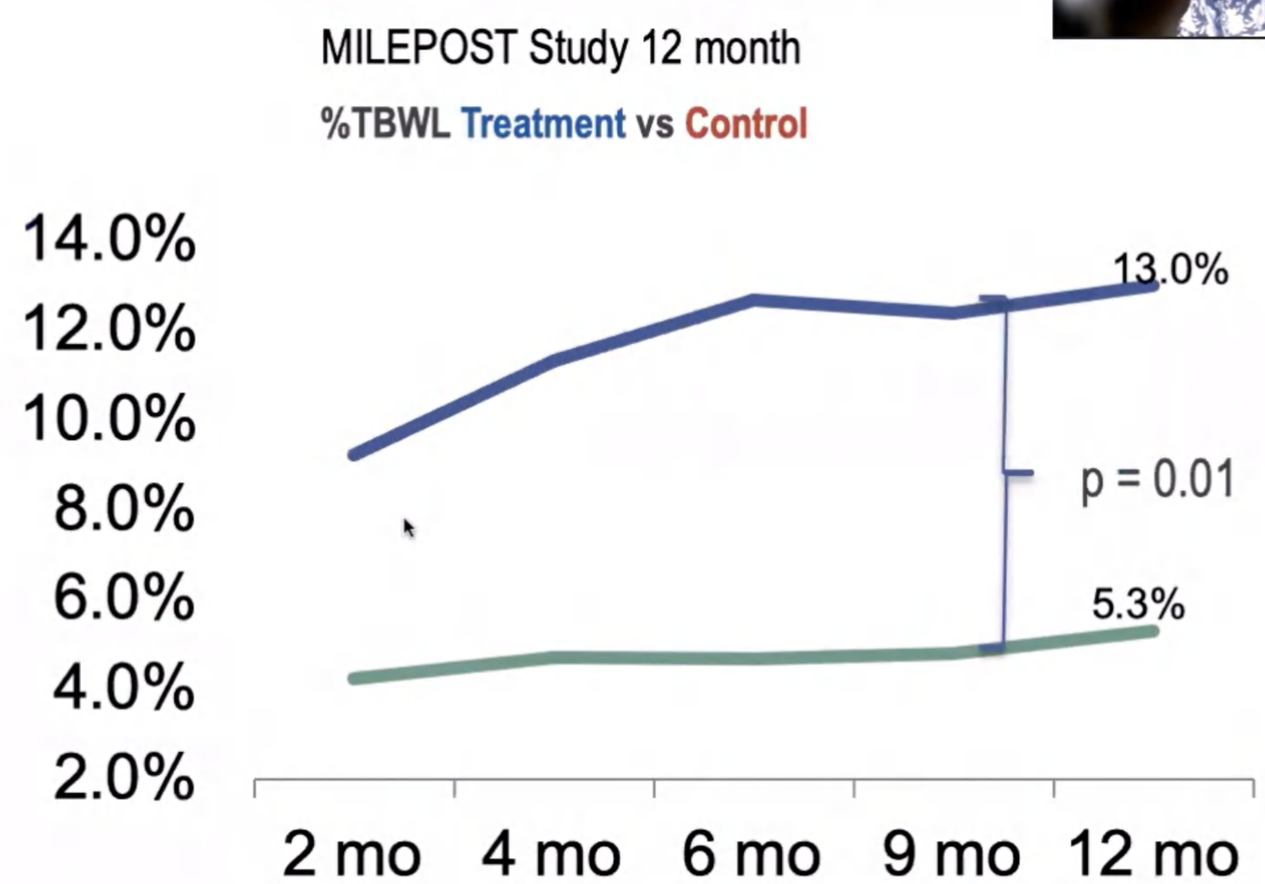




Obesity (2019) 27, 205-216.

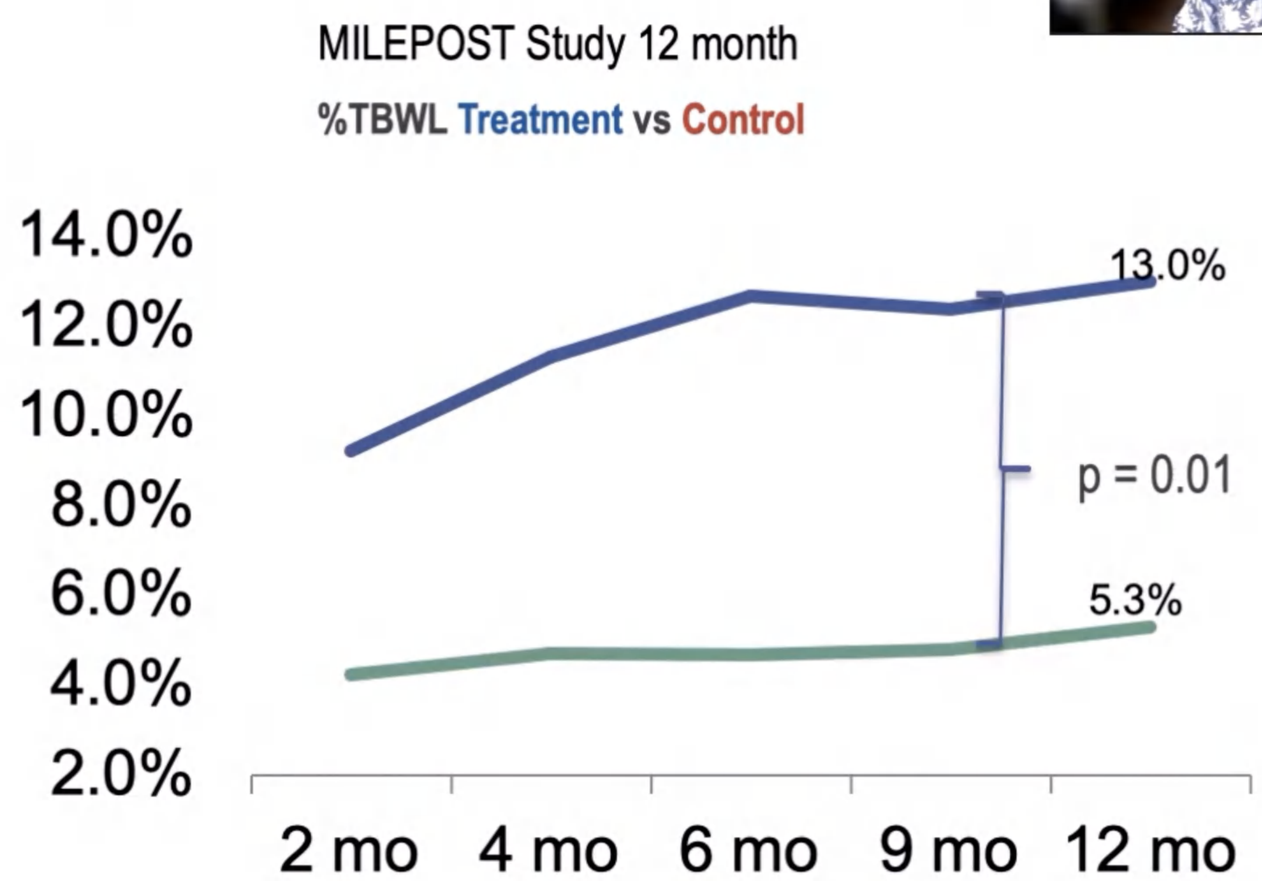
The Primary Obesity Surgery Endolumenal (POSE) procedure: one-year patient weight loss and safety outcomes



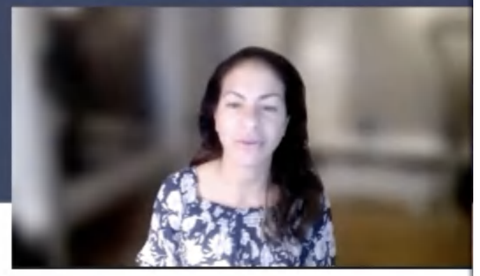


Miller, K et al. Obesity Surgery; 2016 doi:10.1007/s11695-016-2295-9

The Primary Obesity Surgery Endolumenal (POSE) procedure: one-year patient weight loss and safety outcomes



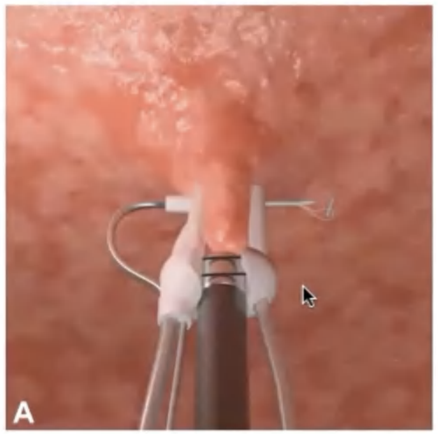
Miller, K et al. Obesity Surgery; 2016 doi:10.1007/s11695-016-2295-9

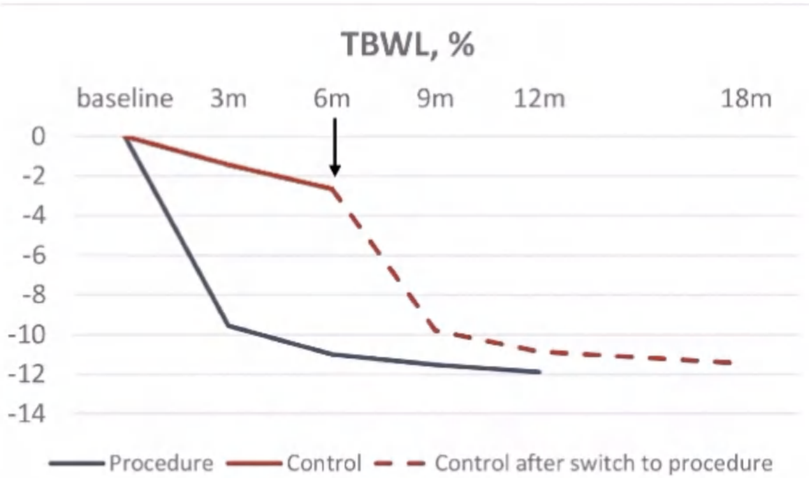


ORIGINAL RESEARCH

Endoscopic sutured gastroplasty in addition to lifestyle modification: short-term efficacy in a controlled randomised trial

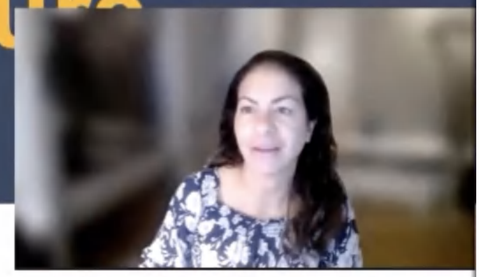
- BMI 20-40
- Randomisation 2:1 ratio
- 71 patients included
- EWL 45%





Huberty et al Gut 2020

Endoscopic sutured gastroplasty: procedure evolution from first-in-man cases through current technique.



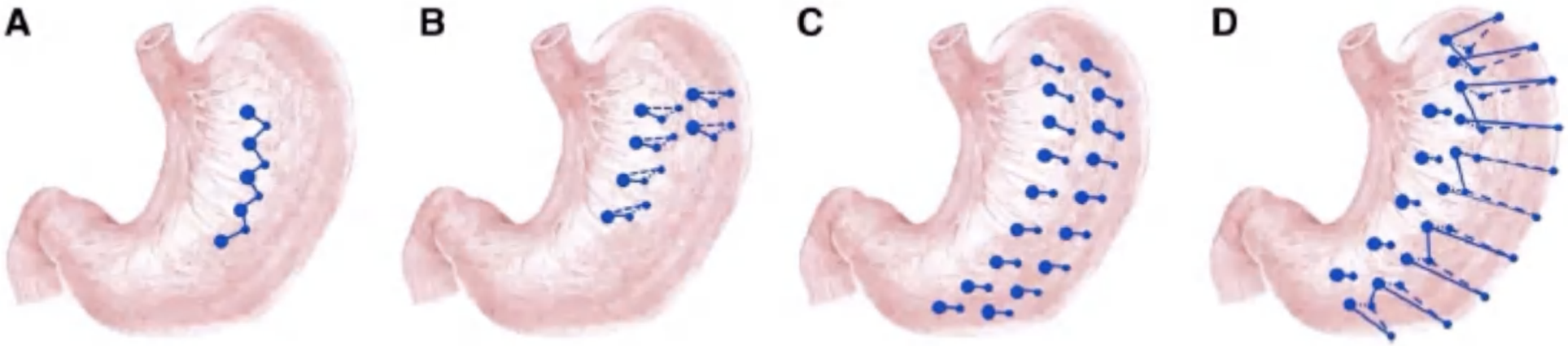
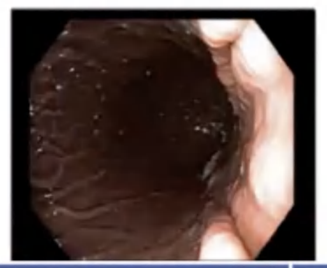


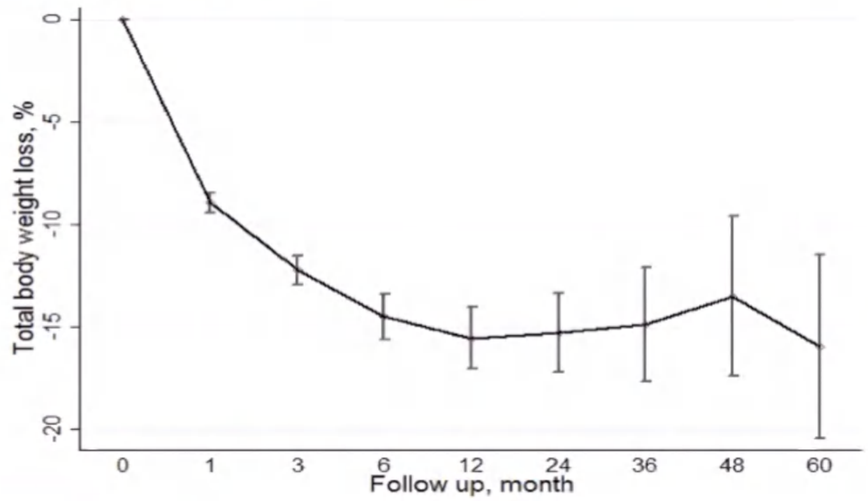
Table 1 Overall weight loss, Phases II and III

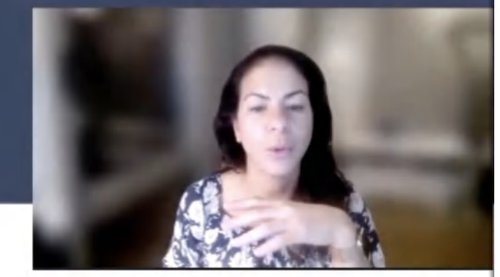
	Weight change (kg)	Total weight loss (%)
6 months	−16.3±0.8	16.2±0.7
12 months	−17.9±1.3	17.4±1.1

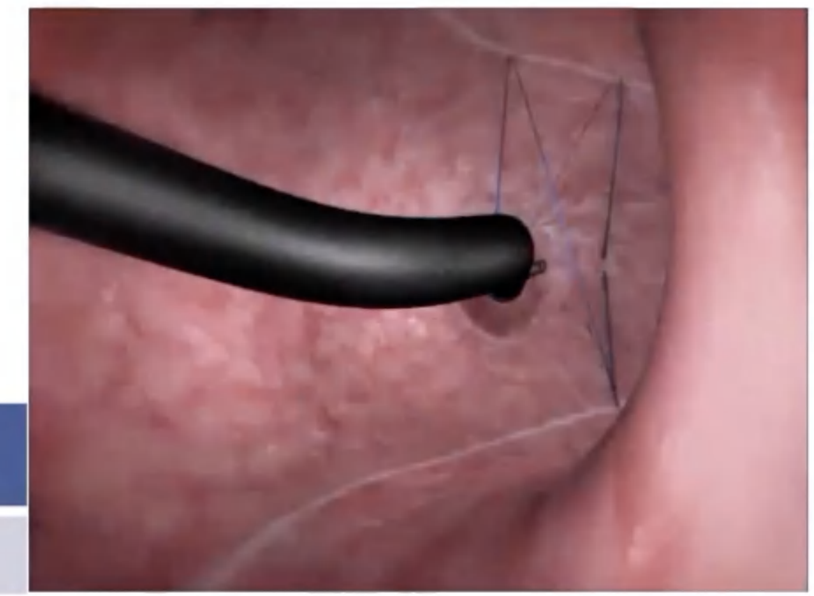
Kumar et al. Surgical Endoscopy Oct 20

Endoscopic Suturing, Durable





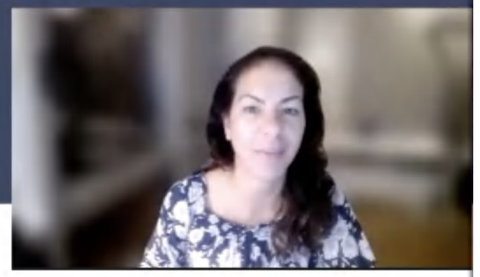




Follow up, month	TBWL% (95%CI)	P-value	TBWL≥10%, n(%)
12	15.6 (14.1-17.1)	<0.0001	(77)
24	15.3 (13.4-17.2)	<0.0001	(72)
36	14.9 (12.1-17.7)	<0.0001	(63)
48	13.5 (9.6-17.4)	<0.0001	(67)
60	15.9 (11.7-20.5)	<0.0001	(61)
Weight loss% at nadir weight	16.7 (15.6-17.7)	<0.0001	(80)

Sharaiha et al 2020 CGH

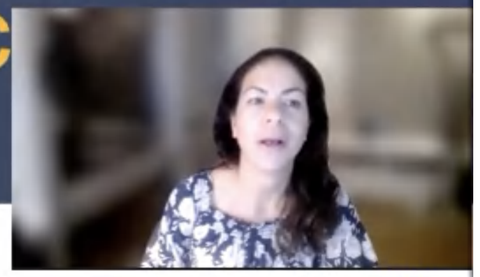
Impact on Comorbidities



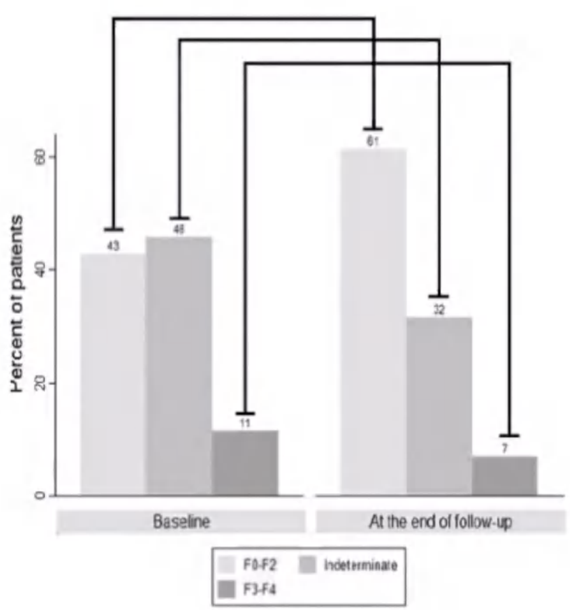
	Prior to ESG, mean (SD)	12months after ESG, mean (SD)	p-value
HgbA1c, % (all patients)	6.1 (1.1)	5.5 (0.48)	0.05
HgbA1c, % (only diabetics and prediabetics)	6.6(1.2)	5.6 (0.51)	0.02
Waist circumference, cm	119.66 (14.05)	92.75 (5.85)	<0.001
Systolic blood pressure, mmHg	129.02 (13.44)	122.23 (11.69)	0.023
LDL, mg/dL	121.62 (38.61)	124.27 (27.82)	0.786
TG, mg/dL	131.84 (83.19)	92.36 (39.43)	0.017
ALT (mg/dL)	32.28 (16.43)	20.68 (11.44)	<0.001

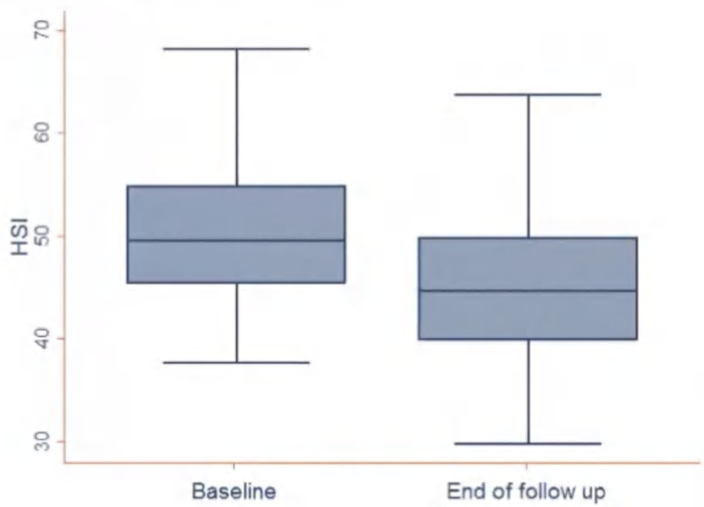
Sharaiha et al. Clin Gastroenterol Hepatol. 2017 Apr;15(4):504-510.

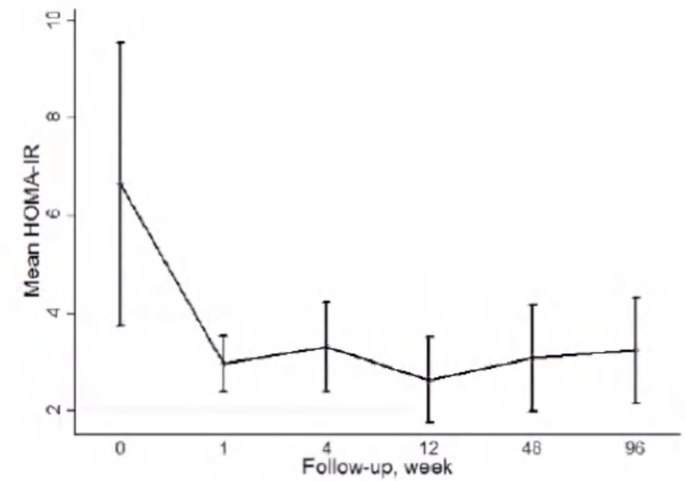
Impact on Fatty liver: Improvement in hepatic steatosis index (HIS) after ESG



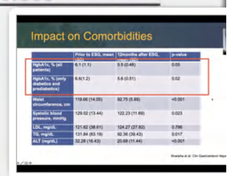
- 118 patients who underwent ESG
- Patients were screened for NAFLD using Hepatic Steatosis Index
- (HSI=8 ~ (ALT/AST ratio) + BMI (+2, if female; +2, if diabetes mellitus)
- NAFLD ➔HSI score>36





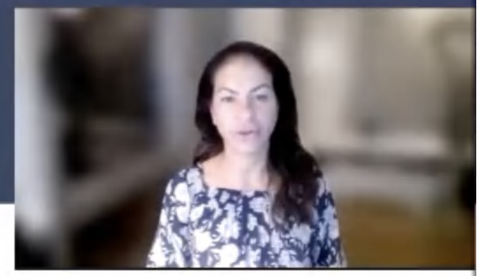


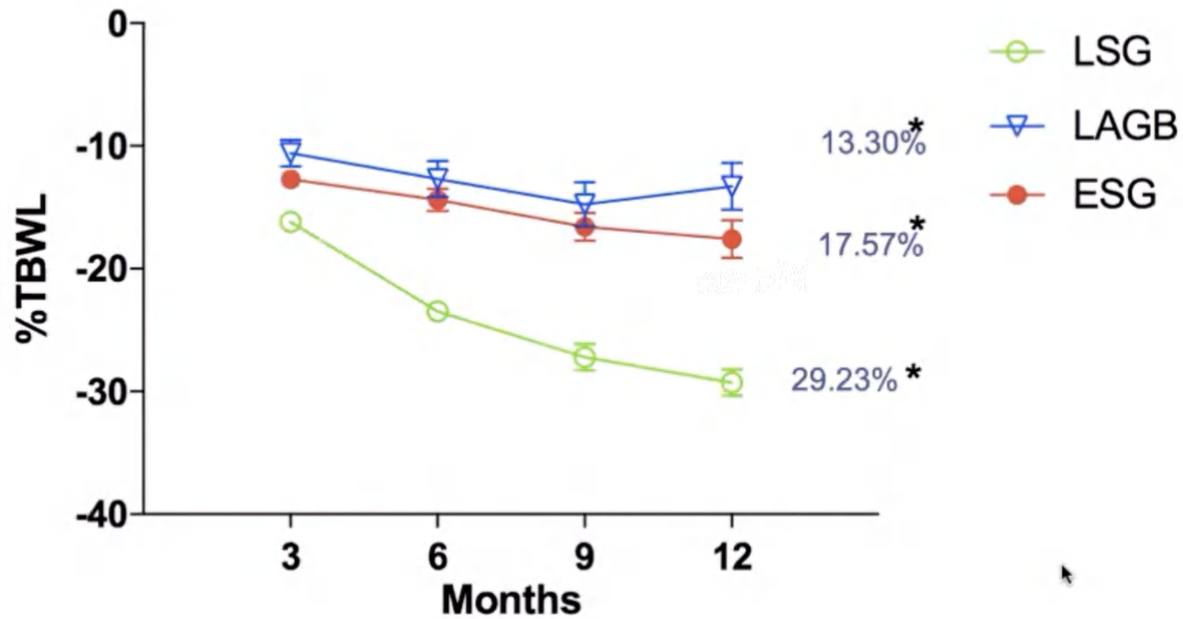
Variable	Absolute change per year	95% CI	Pvalue for linear trend
ALT^, U/L	-5	-3 to -7	<0.001
AST^, U/L	-3	-2 to -4	<0.001
HSI* score	-4	-3 to -4.4	<0.001
NAFLD fibrosis score‡	-0.3	-0.02 to -0.6	0.034
Hemoglobin A1C, %	- 0.2	-0.1 to -0.3	<0.001
HOMA-IR†	-1.7	-0.2 to -3.2	0.029
Leptin, ng/mL	-3.8	-1.6 to -5.9	0.001



Hajifathalian et al. GIE 2020

Comparing ESG to Surgery

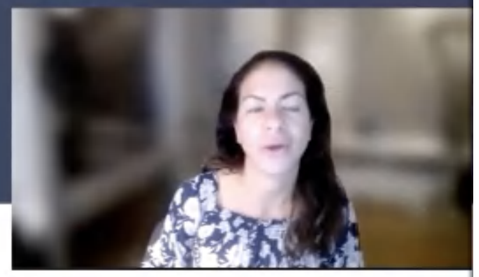




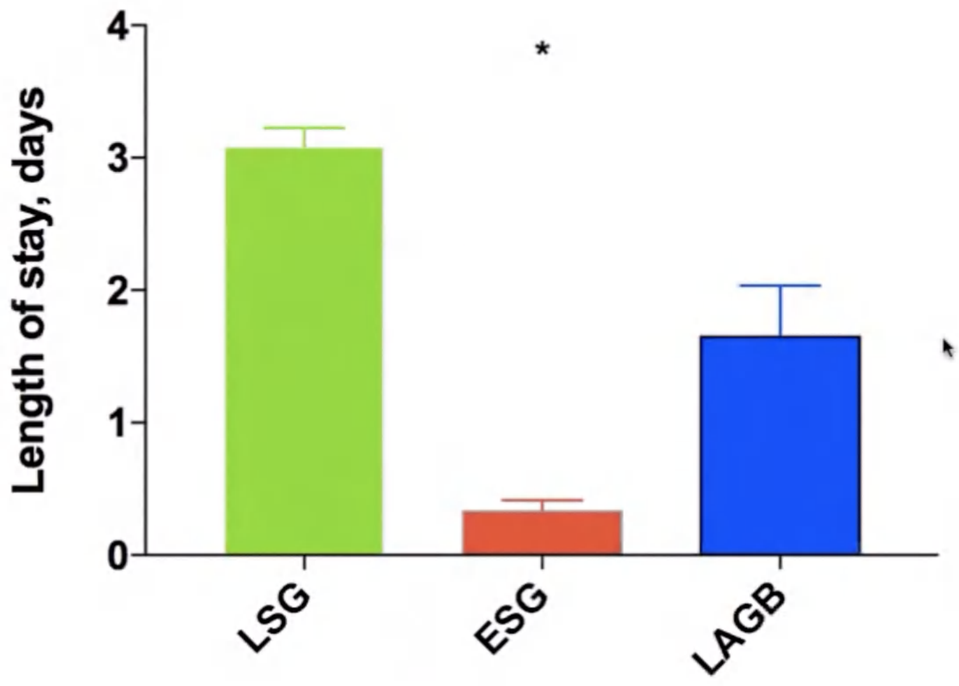
Stratified by BMI <40	Coefficient	p-value
Procedure type		
LSG	Ref	
ESG	-0.053	0.2
LAGB	-0.117	0.1
Age	0.000	0.9
Gender		
Female	Ref	
Male	0.004	0.9
ASA class	0.071	0.1

Novikov et al. J Gastrointest Surg. 2018 Feb;22(2):267-273.

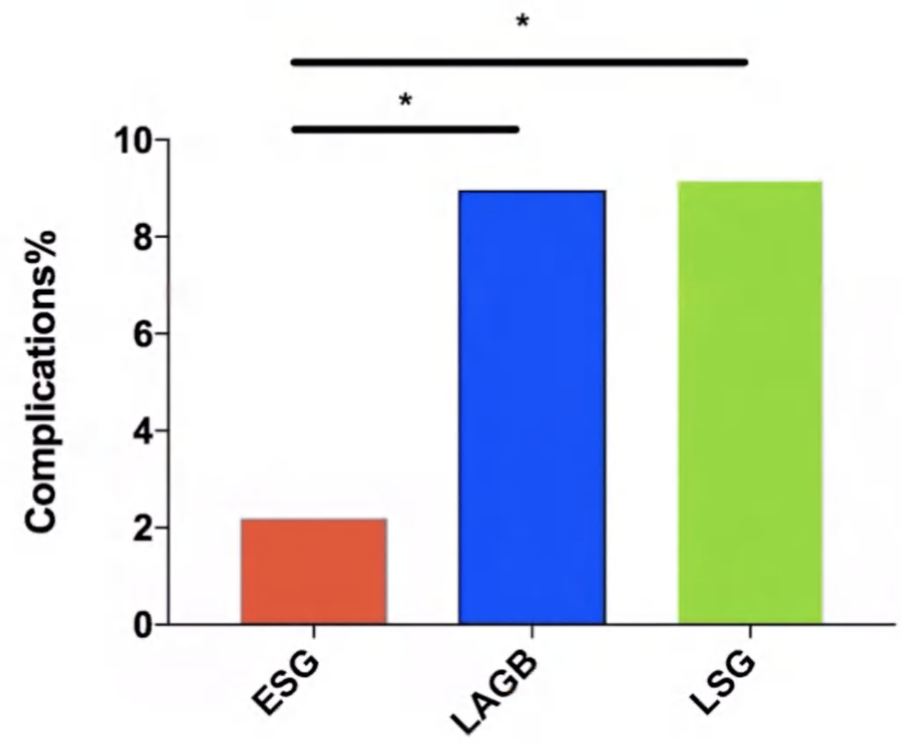
Comparing ESG to Surgery



Hospital Length of Stay

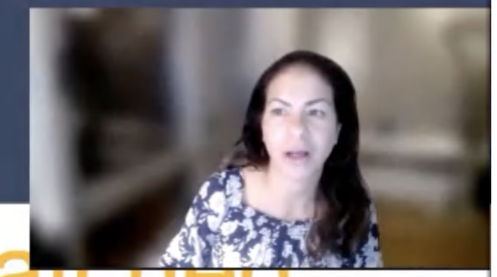


Adverse Events



Novikov et al. J Gastrointest Surg. 2018 Feb;22(2):267-273.

Less GERD
Endoscopic sleeve gastroplasty versus laparoscopic sleeve gastrectomy: a case-matched study

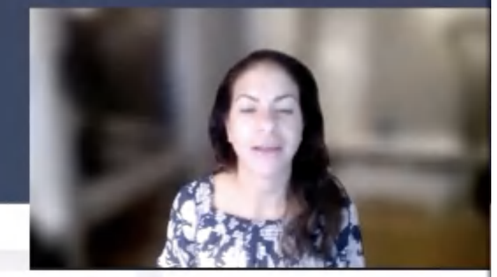


- 54 ESG
- 83 LSG

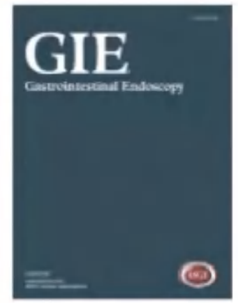
- TBWL 6 months
  - 17.1% vs 23.6% $P < .01$
- Lower rate of new onset GERD
  - 1.9% vs 14.5%, $P < .05$

Fayad et al GIE 2019

Comparison between Diet and Exercise

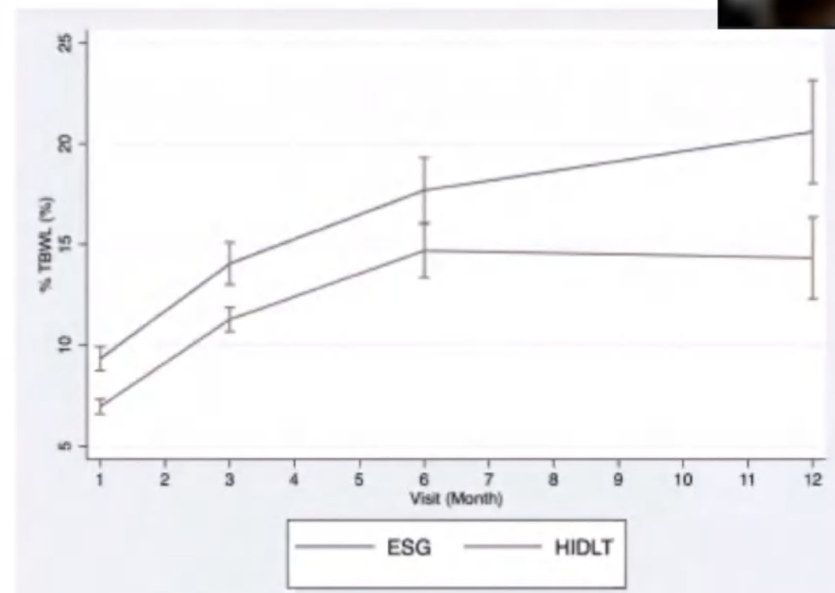


Journal Pre-proof



Endoscopic sleeve gastroplasty versus high-intensity diet and lifestyle therapy: a case-matched study

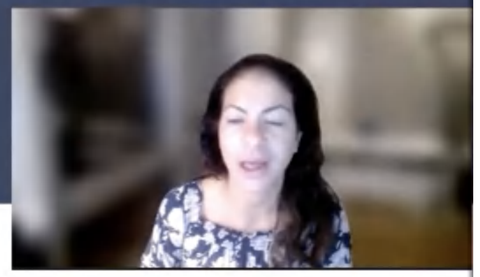
Lawrence J. Cheskin, Christine Hill, Atif Adam, Lea Fayad, Margo Dunlap, Dilhana Badurdeen, Kristen Koller, Linda Bunyard, Robin Frutchey, Haitham Al-Grain, Scott Kahan, Abdellah Hedjoudie, Mouen A. Khashab, Anthony N. Kalloo, Vivek Kumbhari

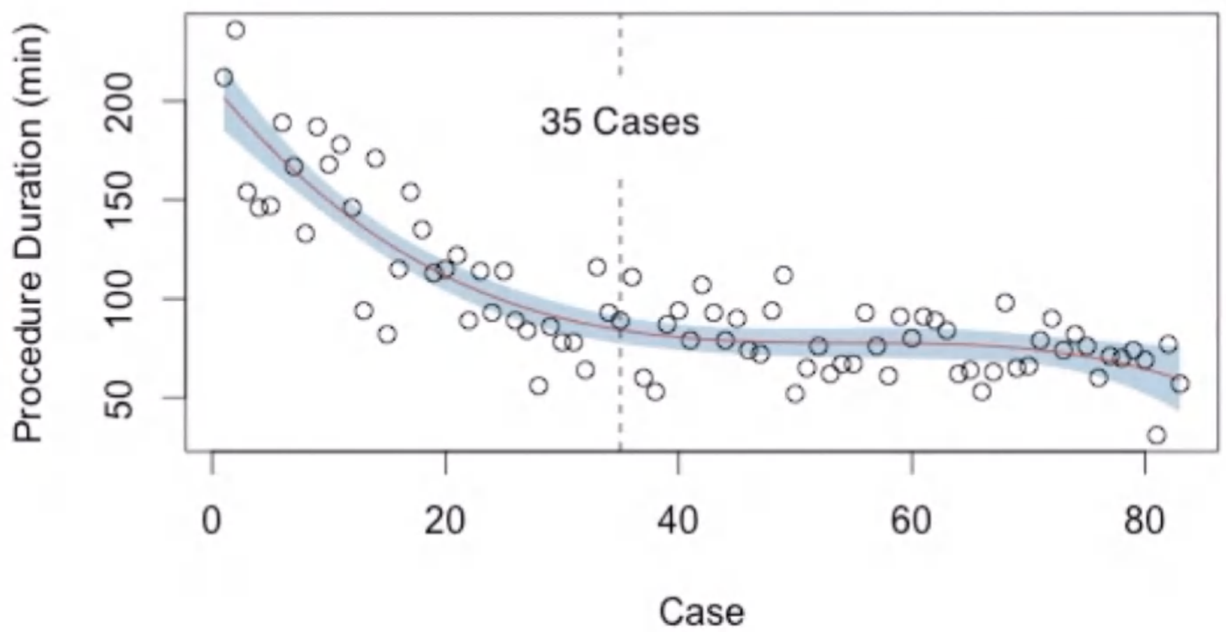


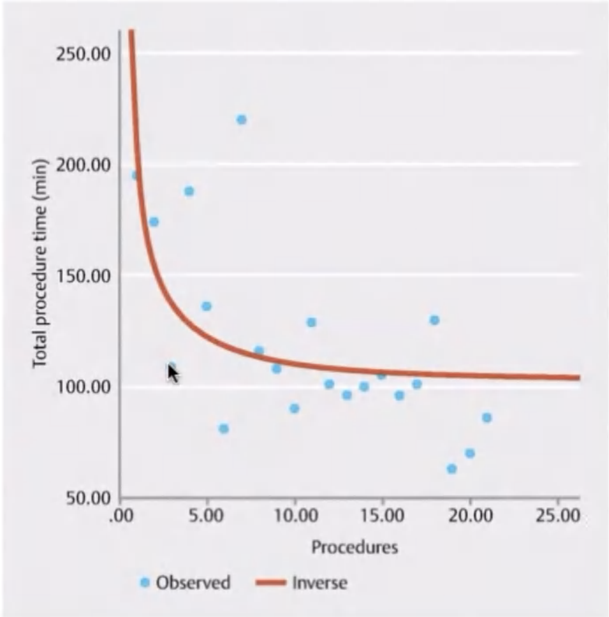
	ESG (n)	% of ESG patients*	HIDLT (n)	% of HIDLT patients*	*P* value
>5% TBWL at 12 months	41	95.35%	219	77.9%	0.008
>10% TBWL at 12 months	39	90.70%	143	50.9%	<0.001
>20% TBWL at 12 months	24	55.81%	31	11.0%	<0.001

Cheskin et al 2019

Learning Curve



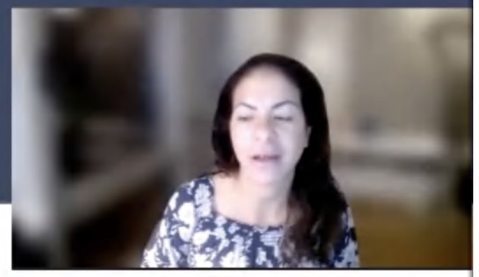




Saumoy et al Gastrointest Endosc. 2017 Aug 24
Hill et al Endosc Int Open. 2017
Sharaiha et al. Clin Gastroenterol Hepatol. 2017

Obesity Surgery (2020) 30:1696–1703
https://doi.org/10.1007/s11695-019-04370-w

ORIGINAL CONTRIBUTIONS



Safety and Feasibility of a Novel Endoscopic Suturing Device (EndoZip TM) for Treatment of Obesity: First-in-Human Study

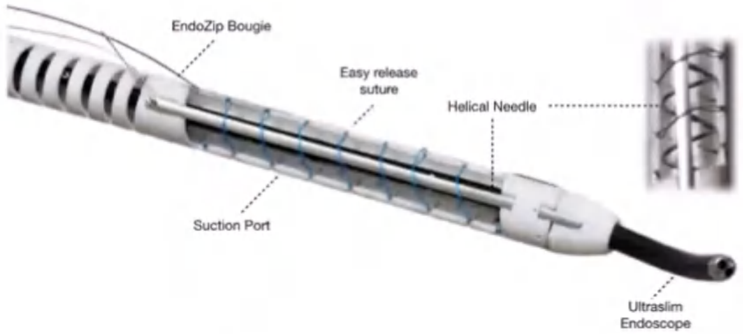
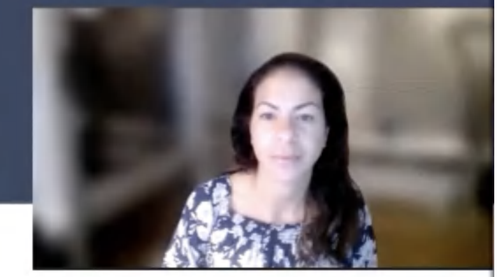


Table 1 Clinical characteristics of the patients

	Patients ($n = 11$)
Age ± SD, years (range)	42.7 ± 5.6 (30–51)
Male (n)	7 (64%)
Mean ± SD initial weight (kg)	111.1 ± 12.3 (81–127)
Mean ± SD initial BMI (kg/m$^{2)}$	36.9 ± 2.8
Mean ± SD procedure time (min)	54.6 ± 23.9 (23–100)
Technical success	11 (100%)
Median sutures placed (range)	3 (2–4)
Length of stay (days)	1
Completed 6 months follow-up	11 (100%)

Lopez-Nava G. et al. Obesity Surg. 2020

Aspiration Therapy, FDA approved & Durable



At least 50% of AT group achieves 25 %EWL or more at 52 Weeks

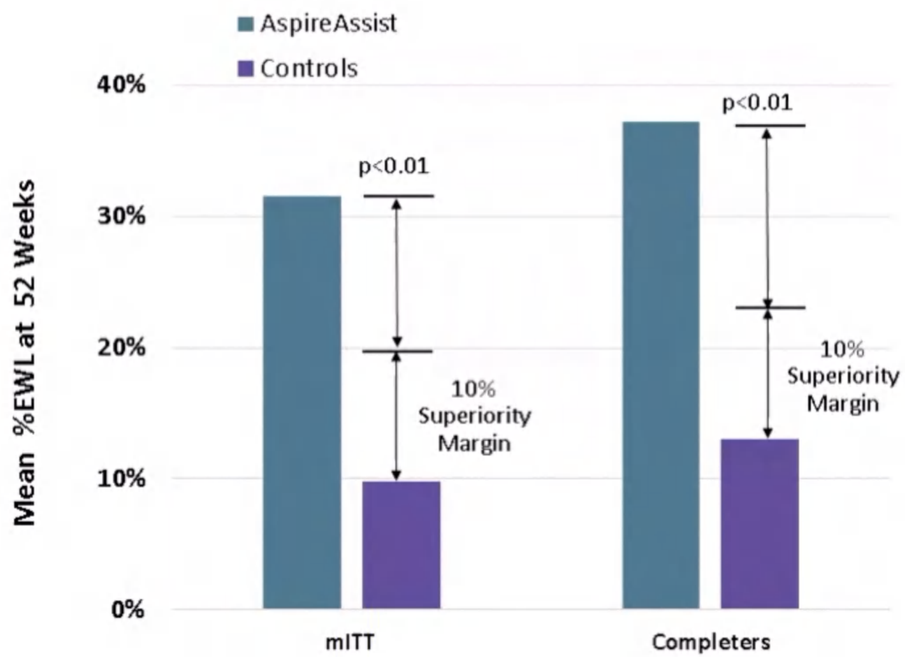


Table 3. Summary of Meta-A ount of Weight Loss Following Aspiration Therapy

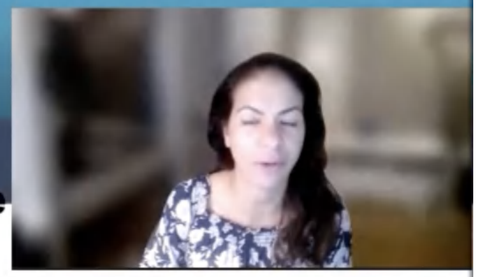
Duration of aspiration	No. of studies (No. of subjects)	Amount of weight loss	*p*-value
Total weight loss (%)			
1 yr	4 (296)	17.8 (15.0, 20.7)	<0.0001
2 yr	4 (174)	18.3 (15.7, 20.9)	<0.0001
3 yr	2 (46)	19.1 (14.5, 23.7)	<0.0001
4 yr	2 (27)	18.6 (13.9, 23.4)	<0.0001

Jirapinyo P. et al. Clin endosc 2020

Thompson CC et al. Am J Gastroenterol. 2016

Nyström M. et al. Obes Surg. 2018 Feb 1.

Standard PEG "Pull" Gastrostomy



Transillumination *is* ***required**

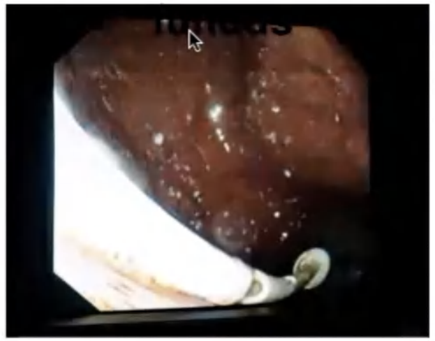
Discrete finger indentation

Standard "pull" technique

Intragastric "tail" on Aspire tube

External bolster for recovery

A-Tube curls into



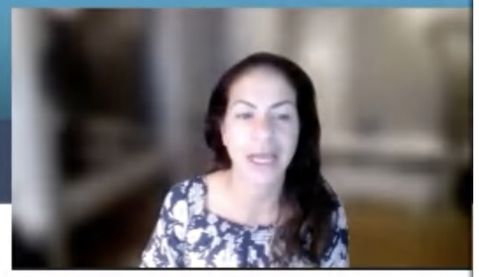
Transillumination successfully achieved

Note: In one patient, inadequate transillumination on first attempt, but successful transillumination on second

How Does AspireAssist Work?

DUAL MECHANISM OF ACTION

for *effective* and *sustainable* weight loss



Lifestyle Therapy and AspireAssist reinforce one-another

1

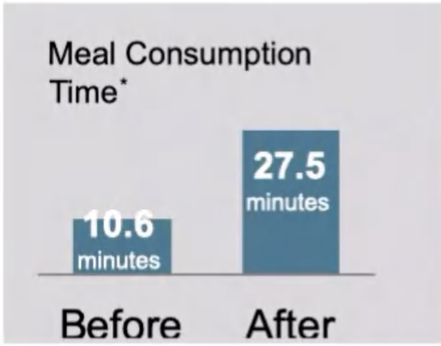
REDUCES CALORIC ABSORPTION*

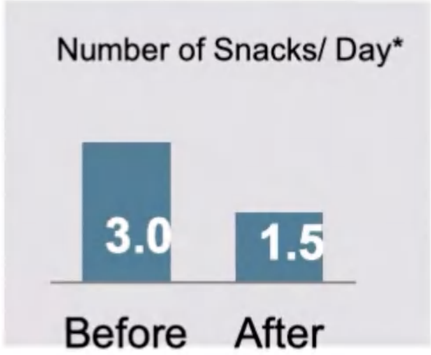
Up to 30% of calories drained by AspireAssist

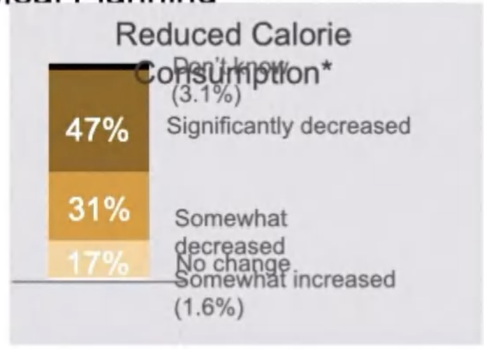
2

IMPROVES EATING BEHAVIOR

Thorough chewing/ slower eating
Increased water consumption
Less snacking
Mindful Eating
Meal Planning



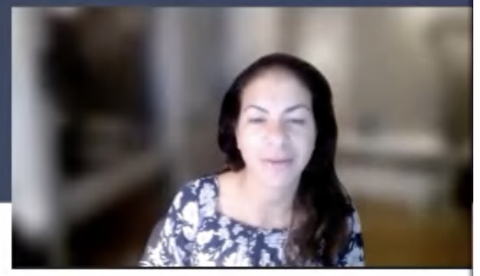




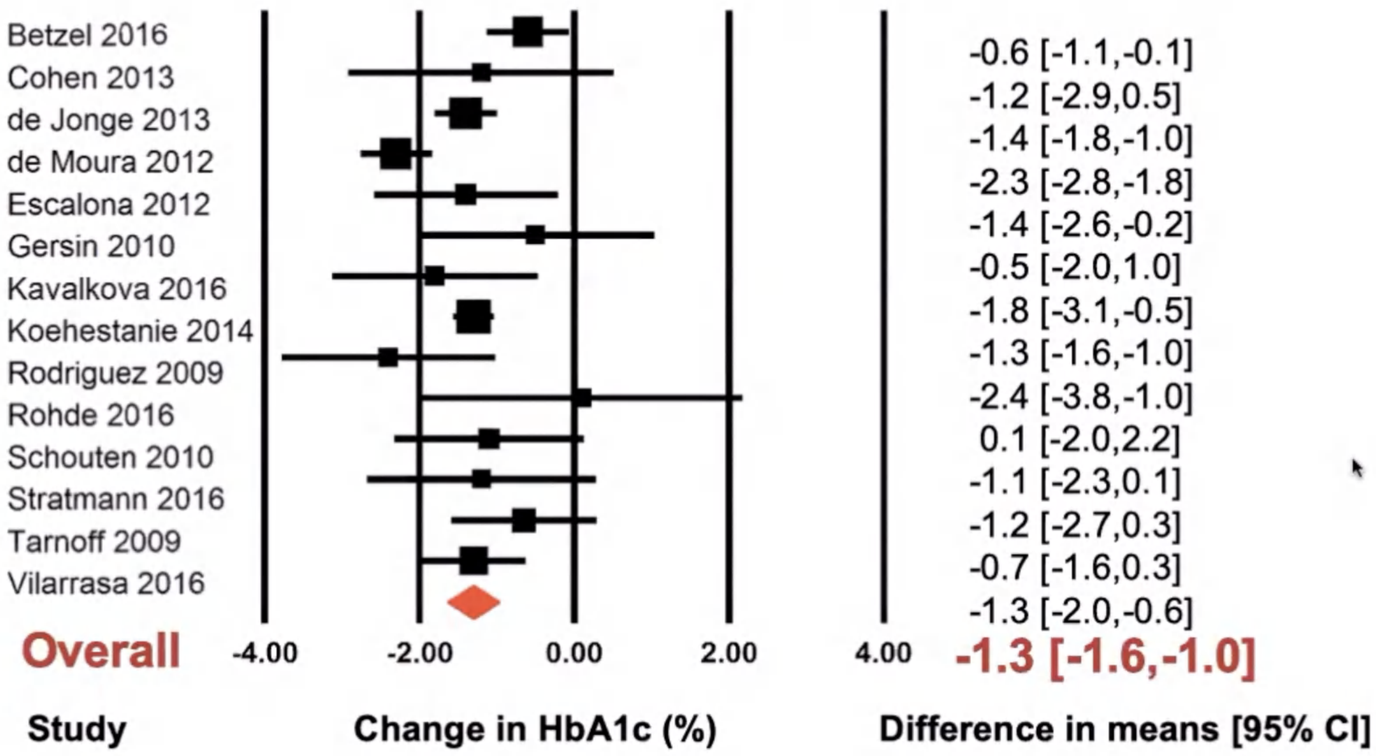
Since beginning therapy with the AspireAssist, I believe the number of daily calories I eat has:

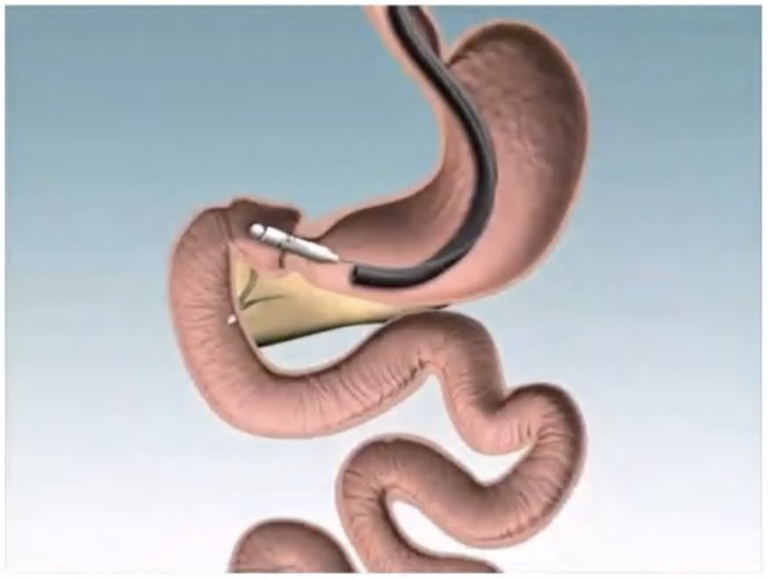
Thompson CC et al. Am J Gastroenterol. 2016

Duodenal-Jejunal Barrier Sleeve



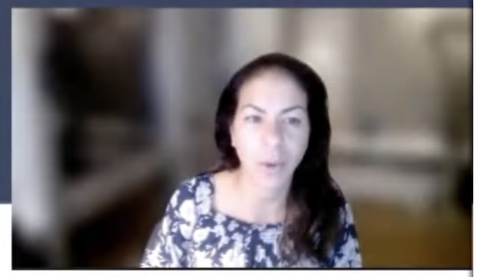
- **Explant HbA1c decreased by 1.3 [1.0,1.6] % (p<0.0001)**



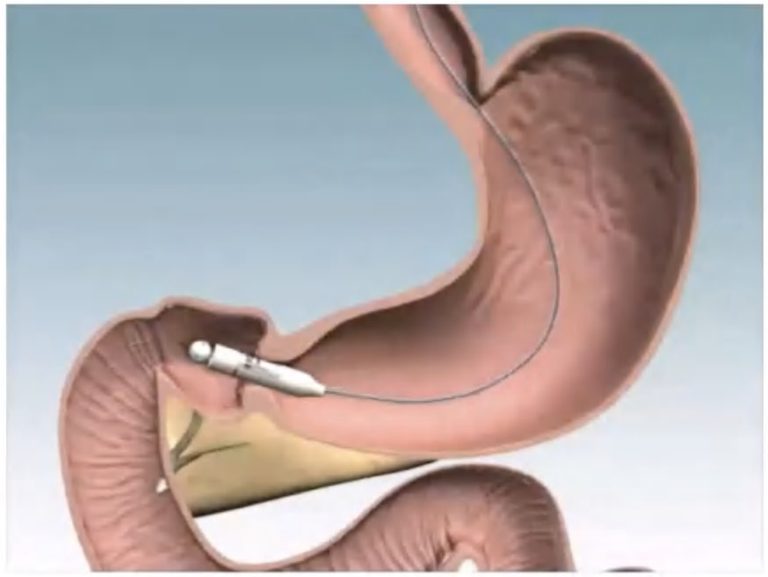


Jirapinyo et al. Diabetes Care 2018

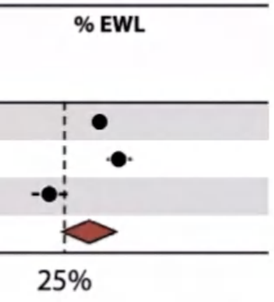
Duodenal-Jejunal Barrier Sleeve



- Metaanalysis
  - 9.5% TWL
  - HbA1C decreased by -1.5 ($p < 0.001$)
  - SAE
    - Migration 4.9%
    - Bleeding 3.9%
    - Obstruction 3.4%
    - Liver abscess 0.13%
    - Esophageal perforation 0.13%
    - Cholangitis 0.13%
- FDA trial on hold because of hepatic abscesses 3.5%

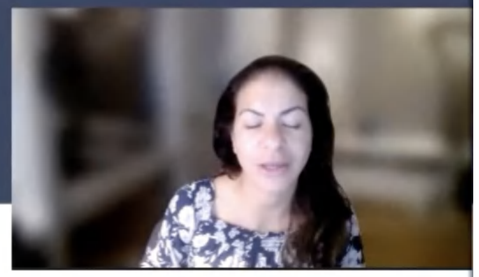


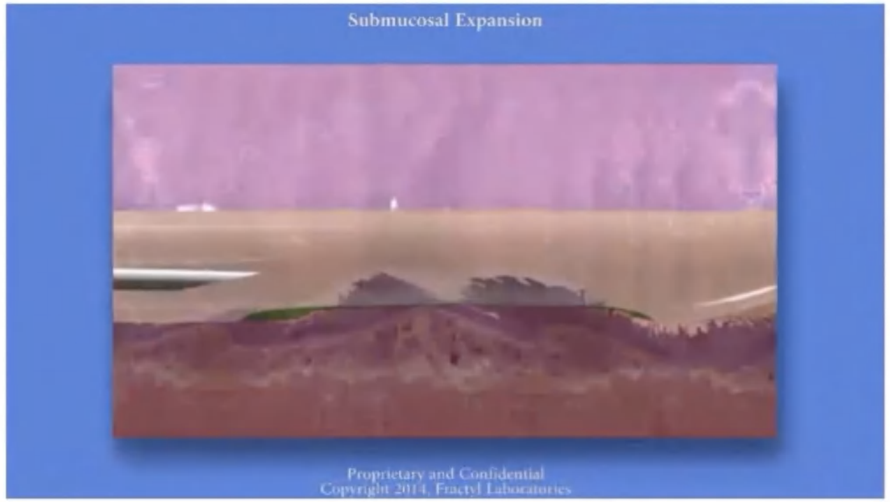
Study name	Subgroup within study	Statistics for each study			
		Mean	Lower limit	Upper limit	Total
de Moura 2012	EndoBarrier	39.000	36.880	41.120	13
Munoz 2014	EndoBarrier	46.000	41.483	50.517	61
Koehestanie 2014	EndoBarrier	19.800	12.830	26.770	31
	Random	35.387	24.658	46.116	

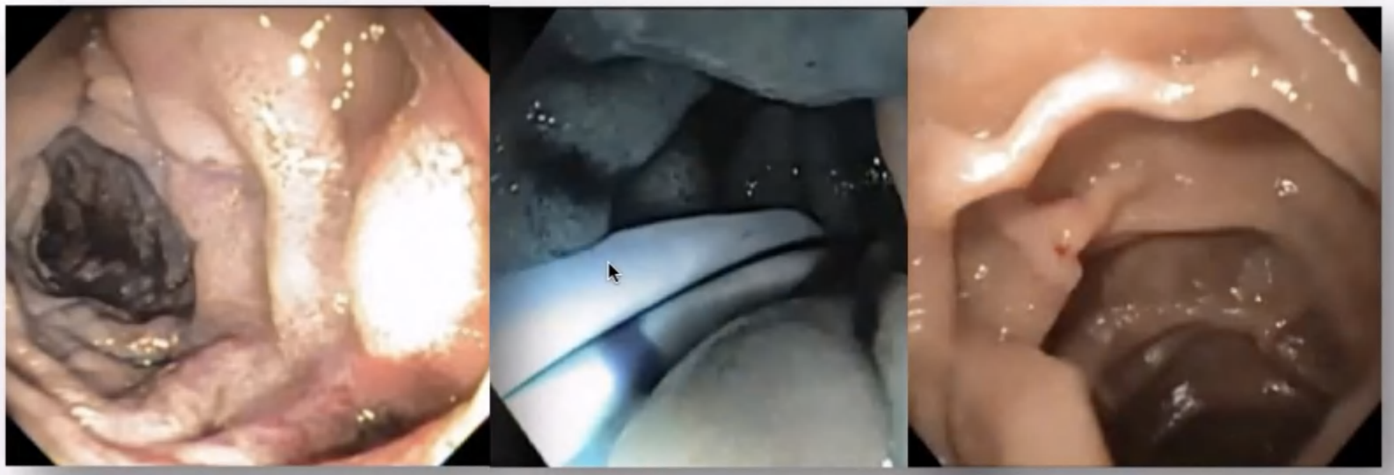


GIE 2015

Duodenal Mucosal Resurfacing – Improvement in comorbidities (NASH and DM)





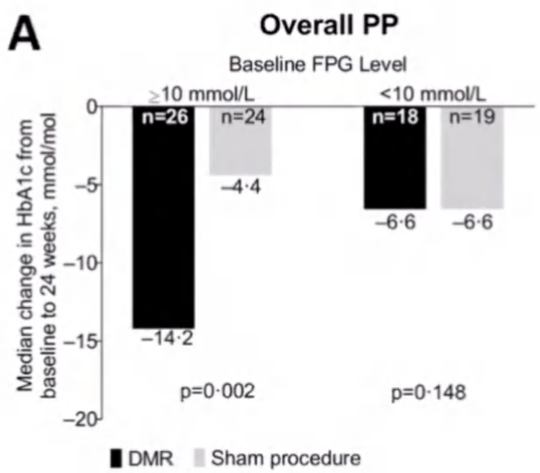


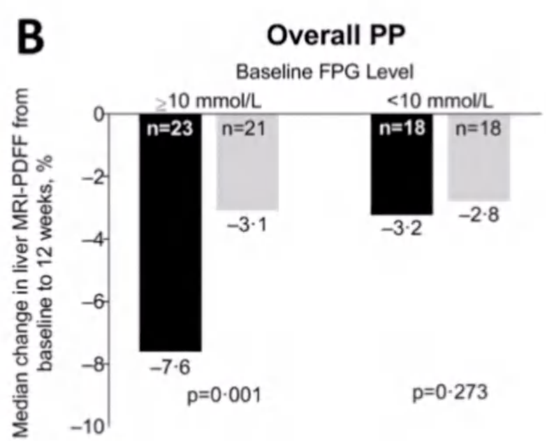
Rajagopalan, H, et al., Diabetes Care, 2016

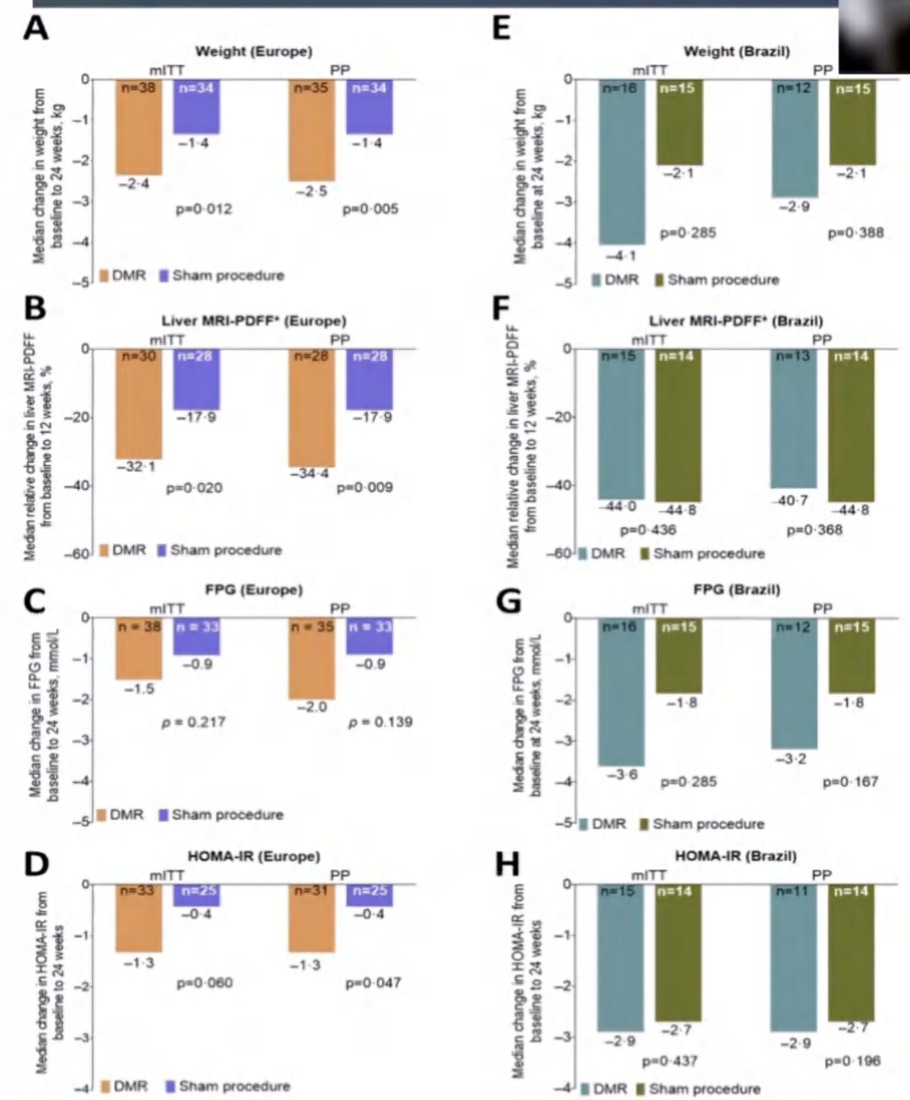
van Baar, A.C.G. et al presented at EASD 2017

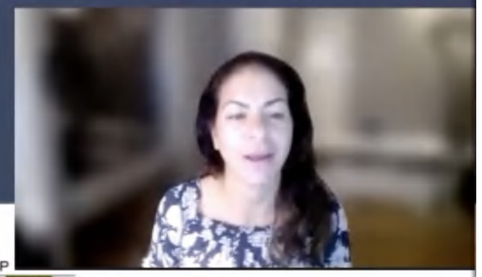
Van BAAR, et al., GUT 2020

Safety and efficacy of hydrothermal duodenal mucosal resurfacing in patients with type 2 diabetes: the randomised, double-blind, sham-controlled, multicentre REVITA-2 feasibility trial



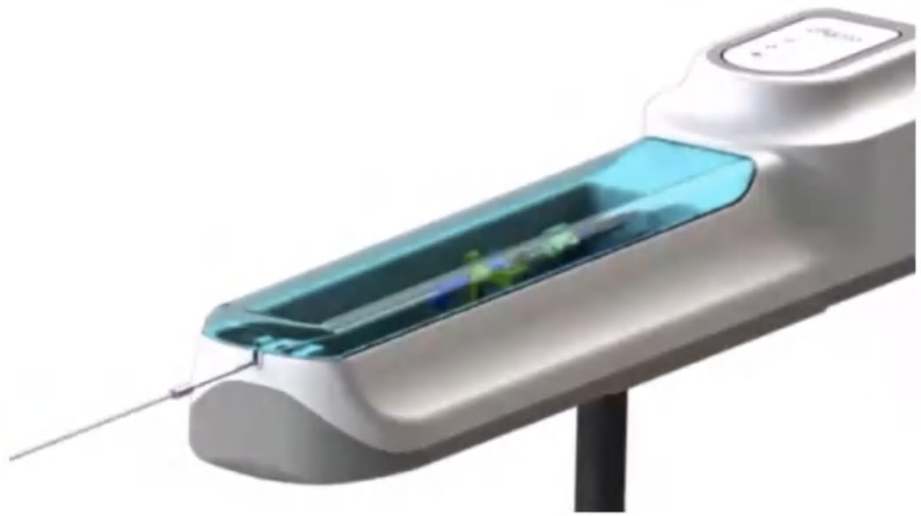






Mingrone Gut 2021

Targeted Ablation in the Duodenum: Diagone (Digma Medical)



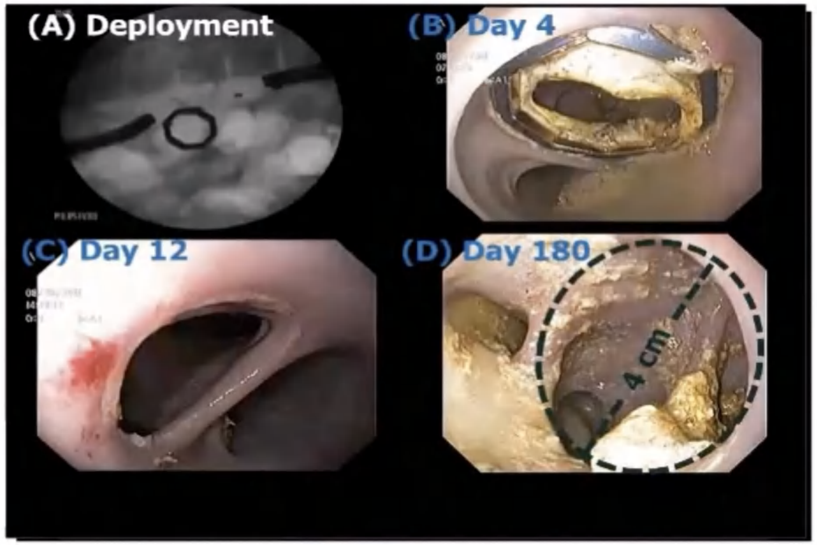
- Targets the submucosal neural plexi with a laser (30 min procedure)
- First in Human
  - N=9
  - BMI 34.0 ± 4.6 kg/m2
  - T2DM on metformin

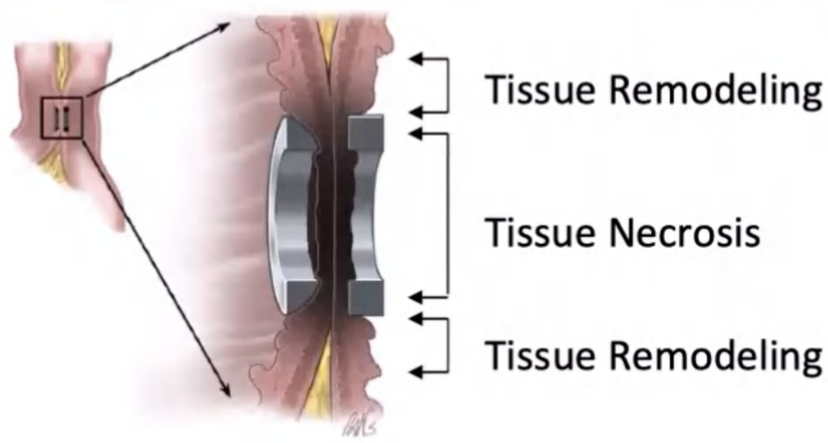
Factor	Baseline	3 Months	6 months
HbA1c mmol/mol (% HbA1c)	78.3± 13.3 (9.3 %)	64.9 ± 6.4 (8.1%)	64.8 ± 7.1 (8.1%)
FPG Mmol/l (mg/dl)	12.4 ± 3.5 (223)	9.5 ± 2.0 (171)	9.7 ± 2.7 (174)
Glucose AUC during mixed meal test	43,435	34,096	
Insulin	Only reported as no change from baseline		

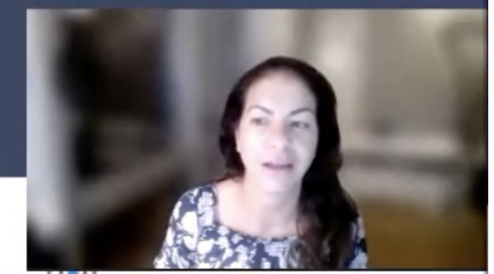
Mraz. M. Diabetes 2019 Jun; 68(Supplement 1)

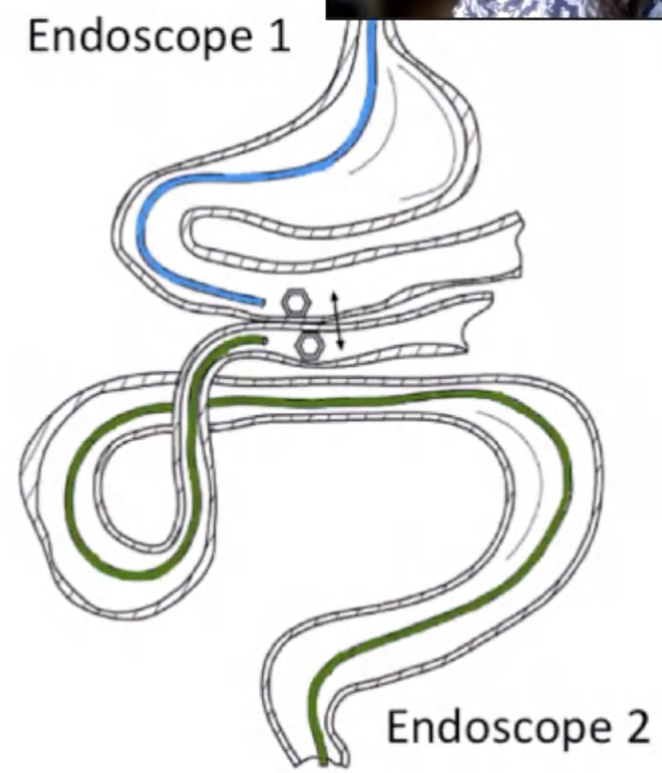
Endoscopic Anastomosis

Incision-less Anastomosis System (IAS)







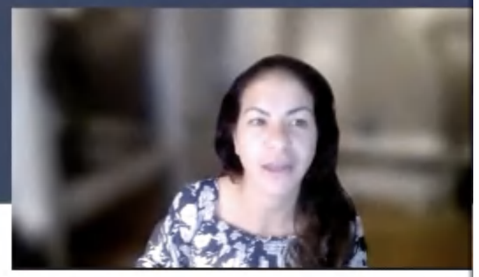


Small Bowel Bypass

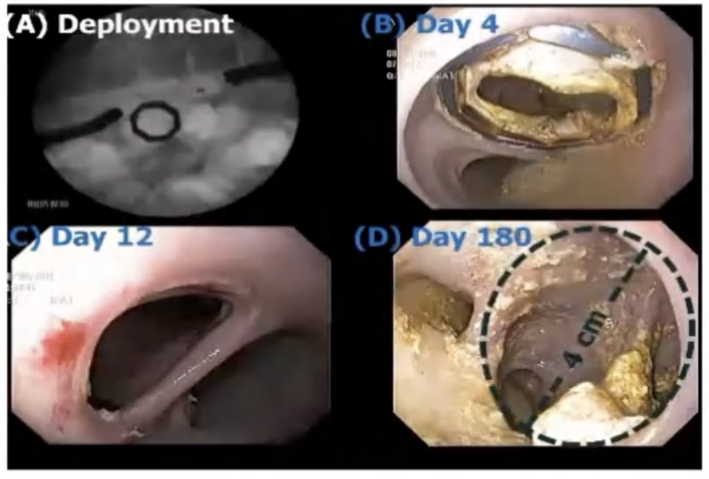
Ryou M, et al. Gastrointest Endosc. 2011 Feb;73(2):353-9

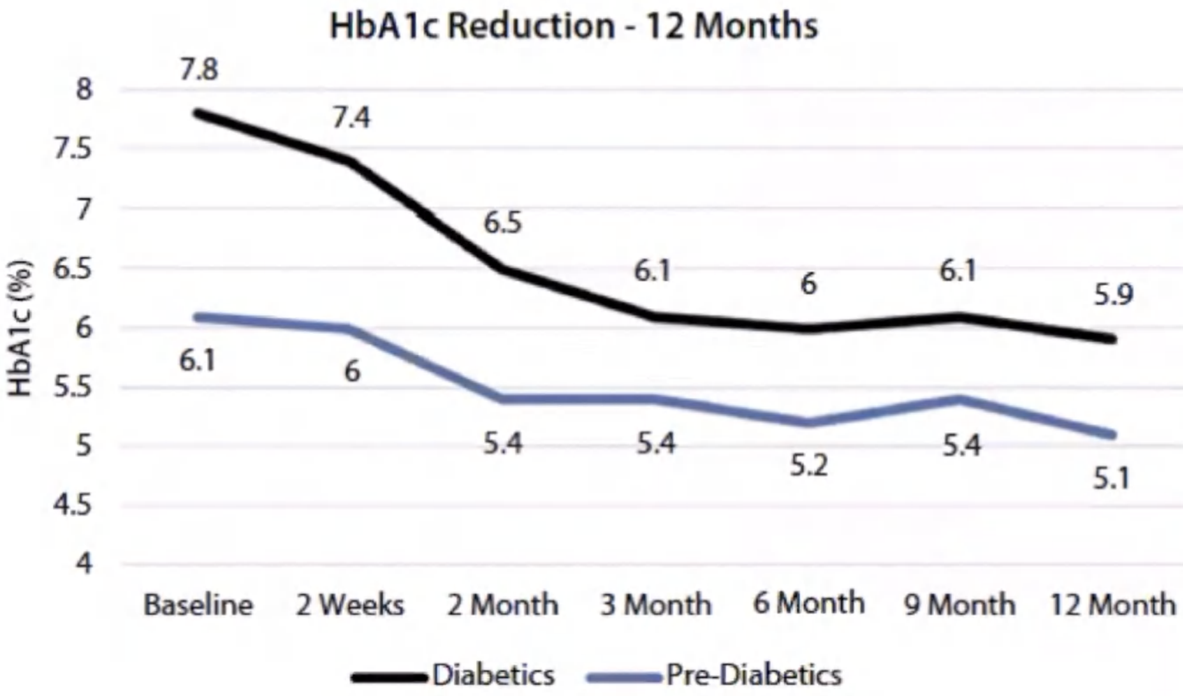
Gonzales KD, et al. J Pediatr Surg. 2012 Jun;47(6):1291-5

Incision-less Anastomosis System (IAS) Improvement in Weight and Diabetes



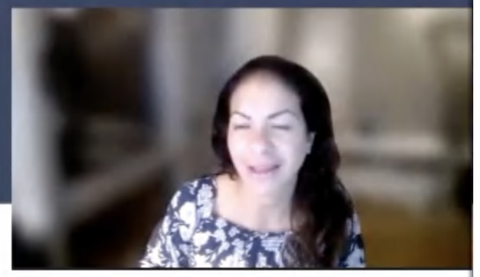
- 6 month weight loss of 12.9Kg
  - 10.6% TWL
  - 28.3% EWL



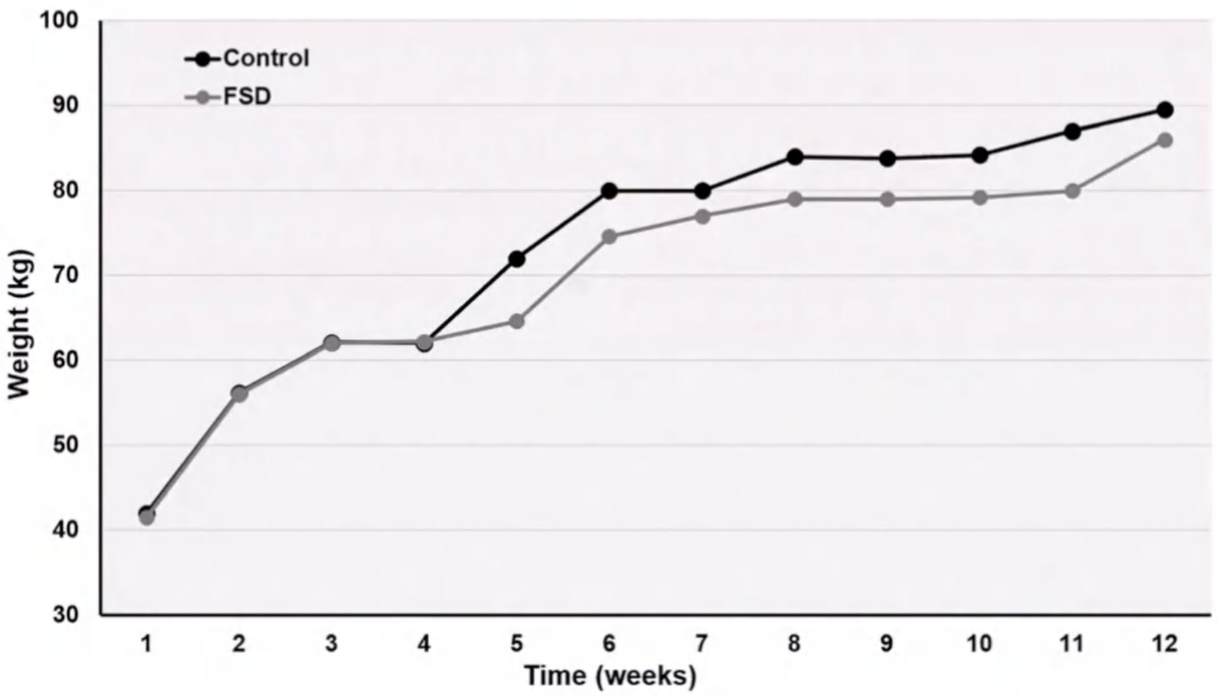


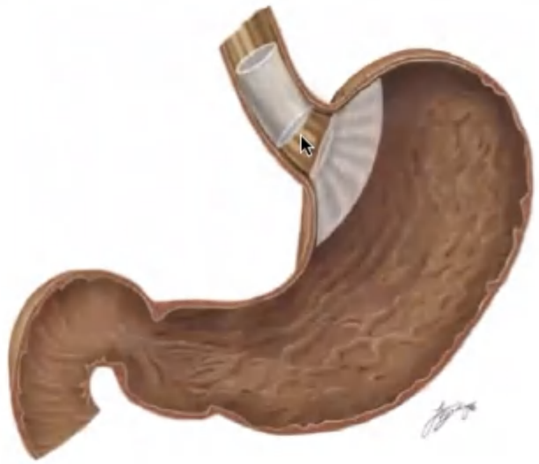
Machytka E Gastrointest Endosc. 2017 Nov;86(5):904-912.

Other space occupying lesions and future devices



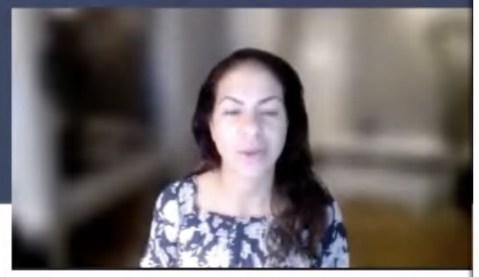
Full Sense device





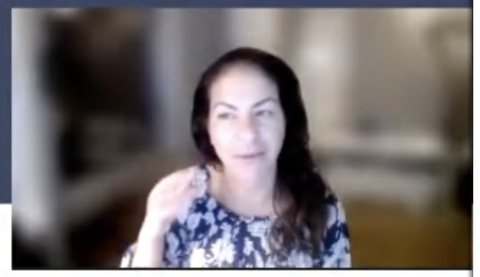
Park et al. Obes Surg. 2019

Importance of a multidisciplinary program



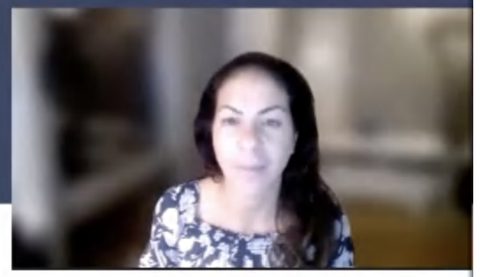
- Add medications for inadequate weight loss or weight regain
- Convert to another endobariatric procedure
  - Remember no balloon if ESG or POSE
- Convert to surgery
- Ensure compliance with nutrition
- Ensure that patients understand tool concept of weight loss

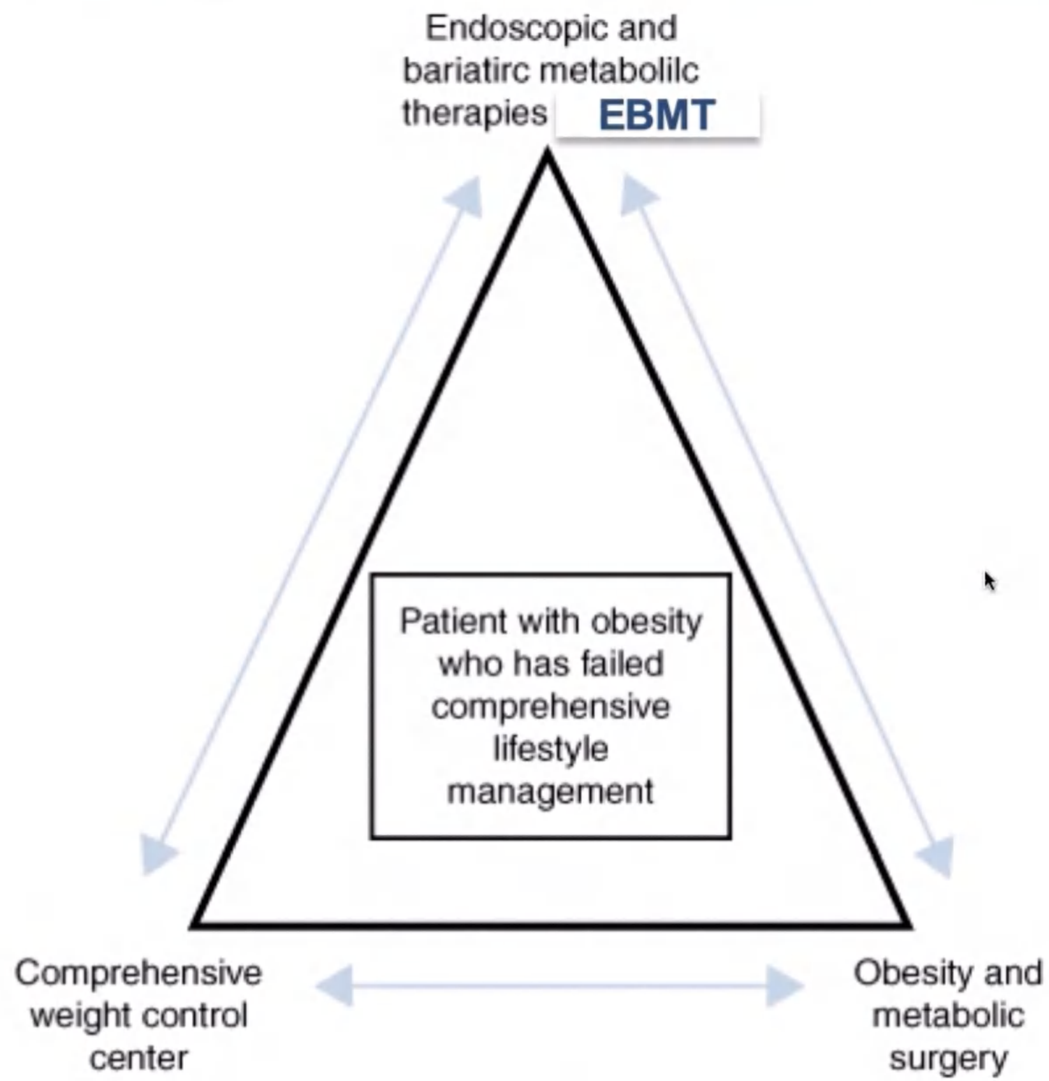
New Paradigms in Obesity



- Risk / benefit ratio
- Procedures viewed as tools to help manage a chronic condition, not as the ‘cure’
- Repeatability

Setting Up An Endobariatric Weight Loss Program





Shah, Aronne, Sharaiha Am J Gastroenterol. 2018