

Obesity and metabolic disorders: role of therapeutic endoscopy

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European Endoscopy Training Centre - Rome

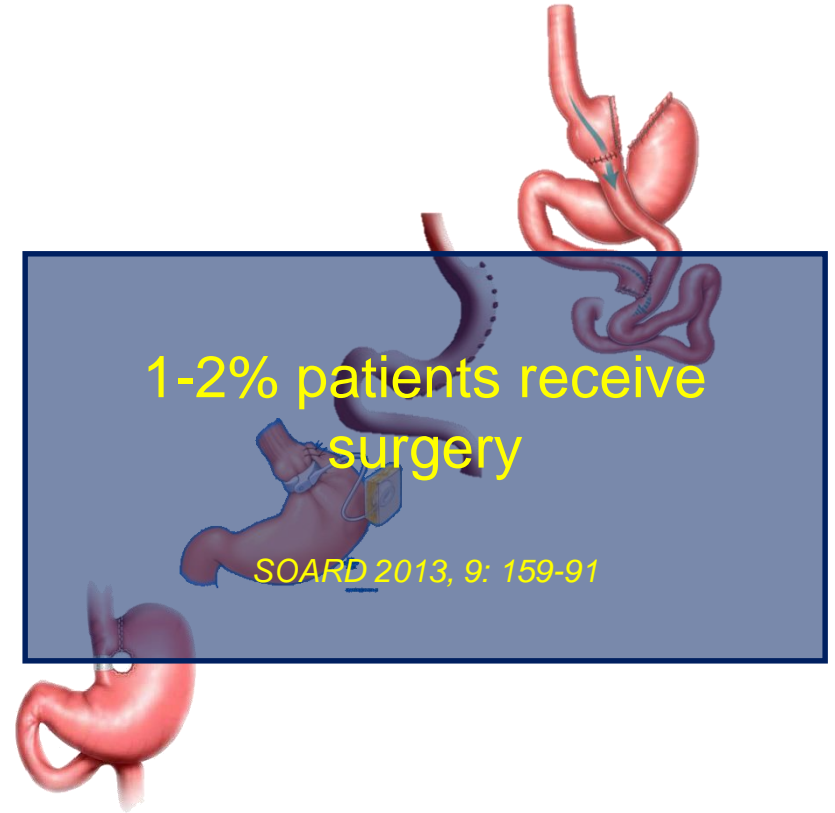
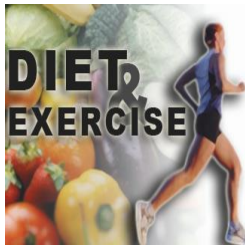
Institut de Chirurgie Guidée par l'Image de Strasbourg



Centre for Endoscopic Research Therapeutics and Training

Treatments for obesity

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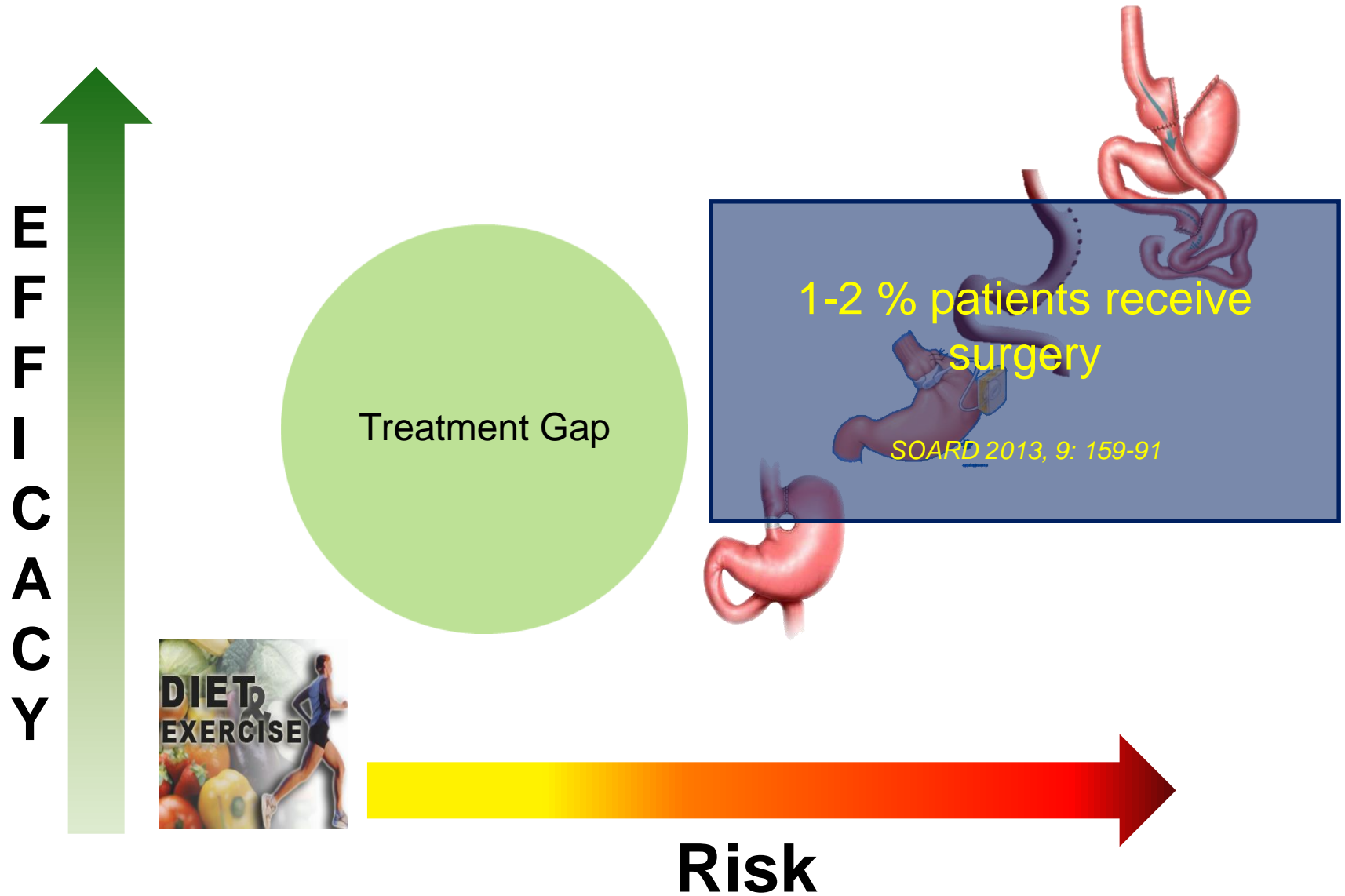


1-2% patients receive surgery

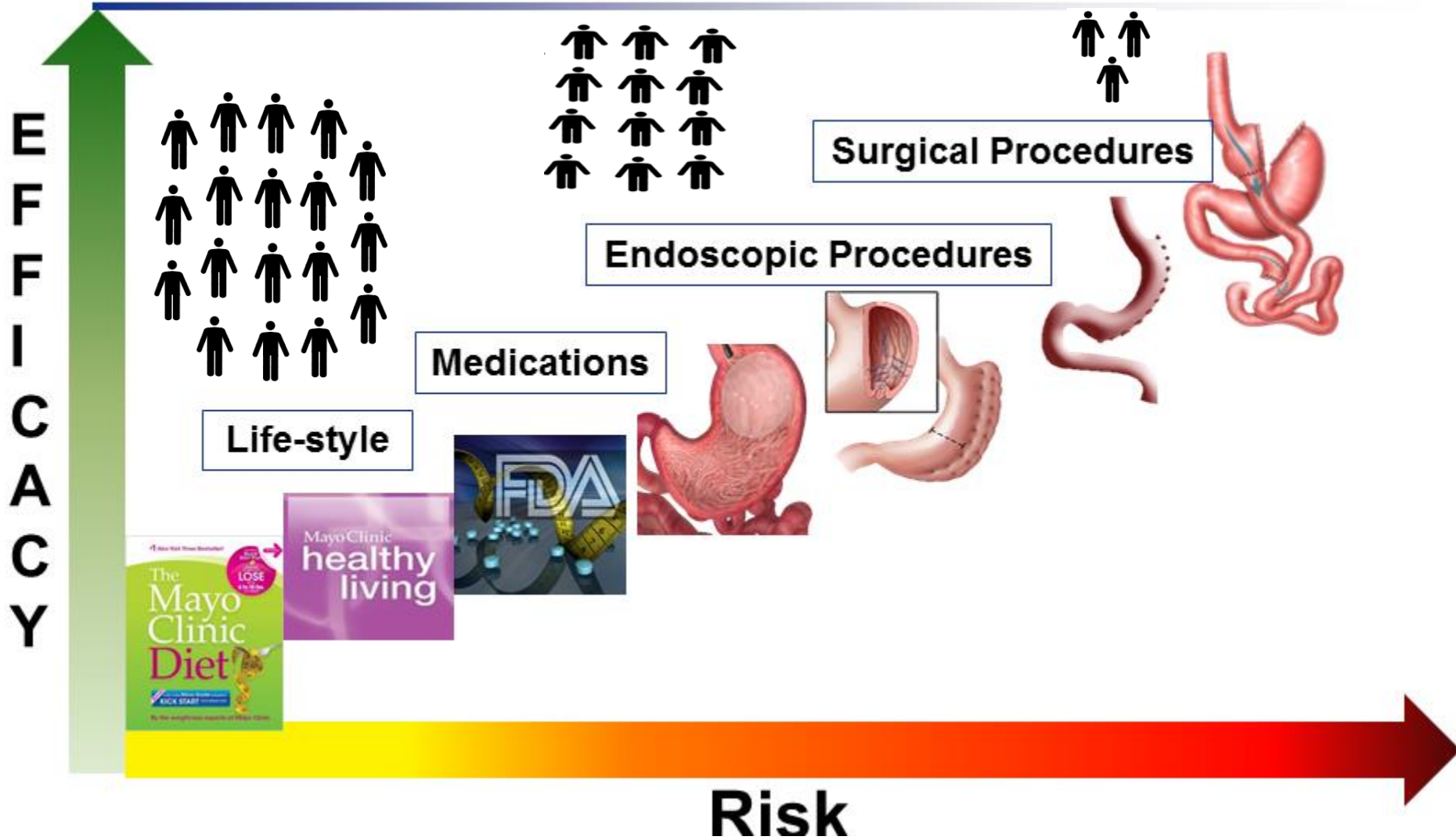
SOARD 2013, 9: 159-91

Risk

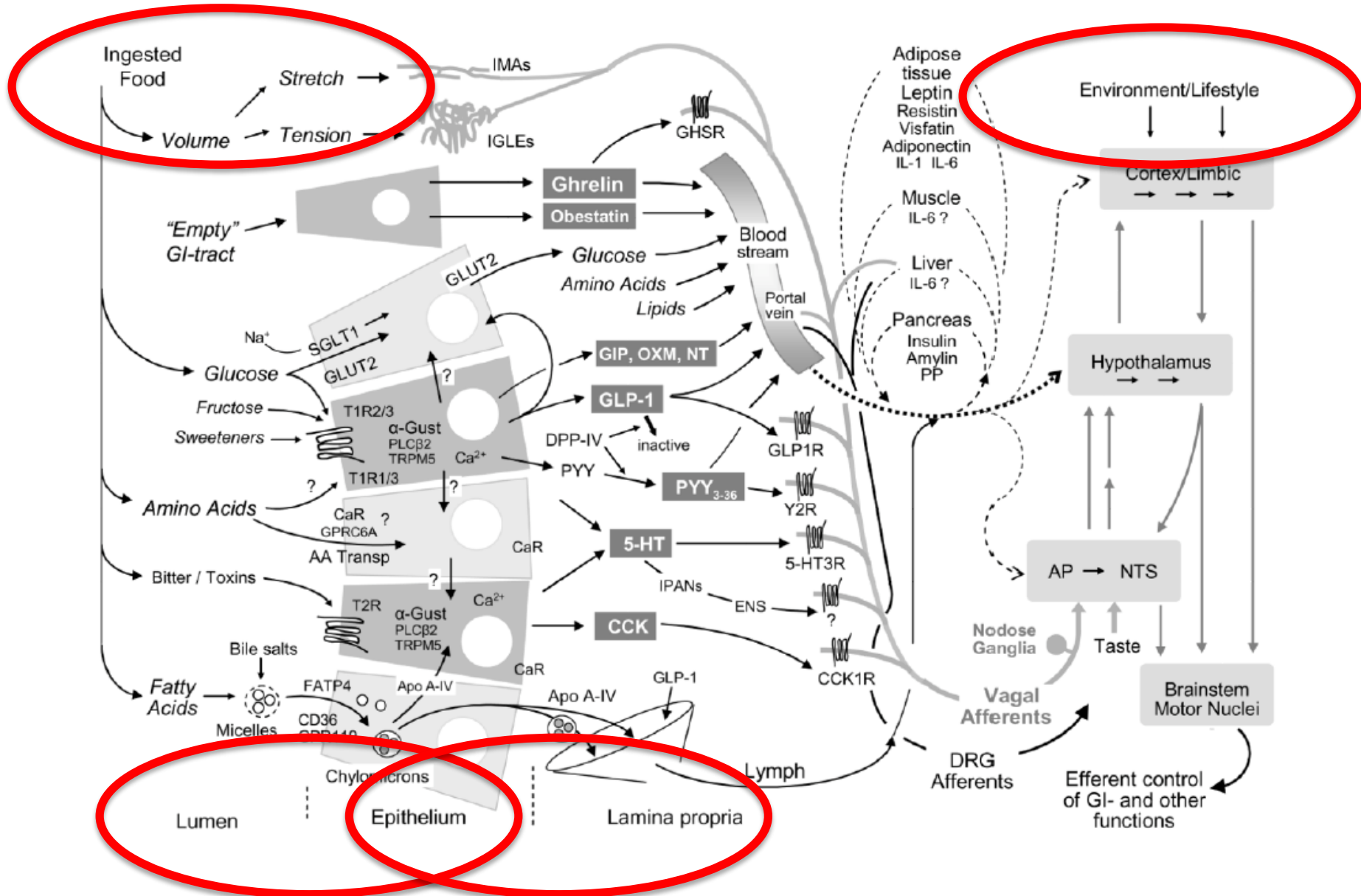
Treatments for obesity



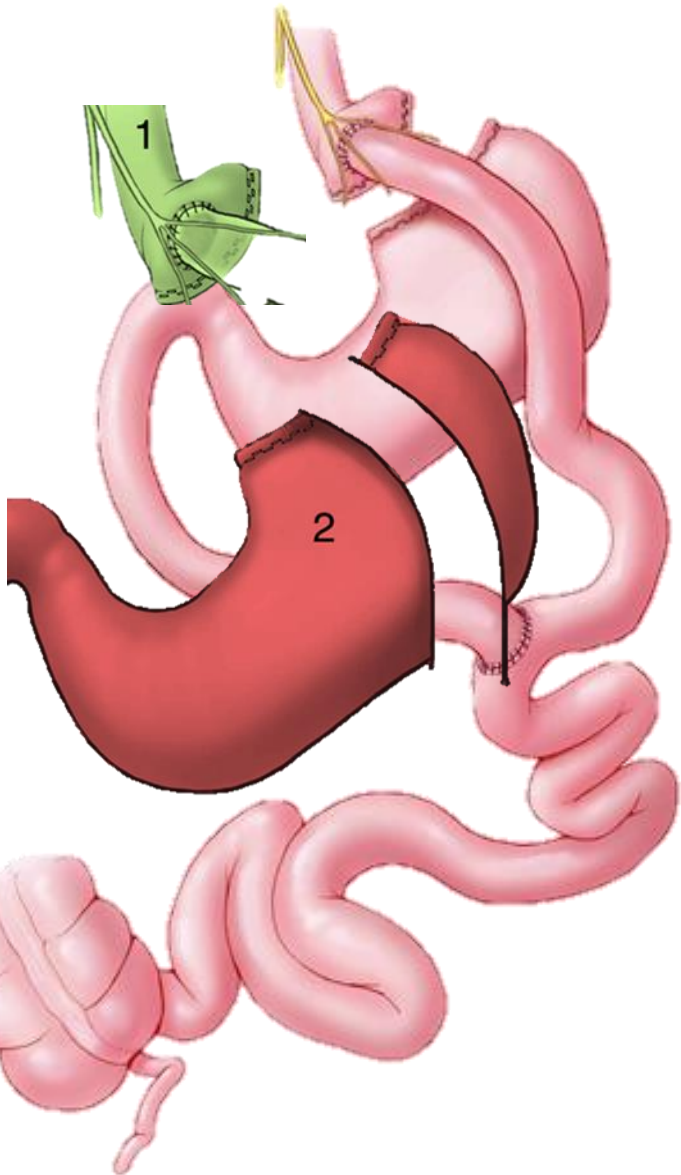
Obesity Continuum



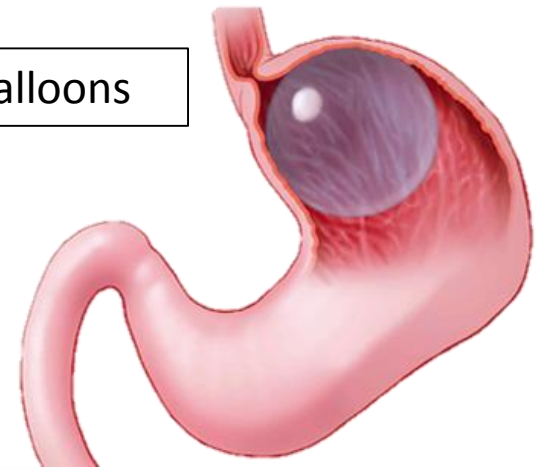
Satiation, Satiety, and the Gut-Brain Axis



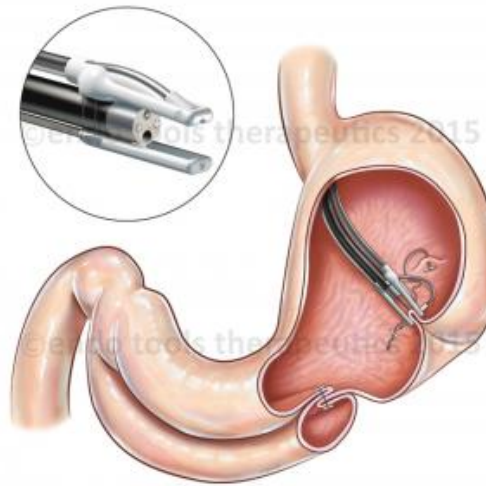
Gastric EBTs



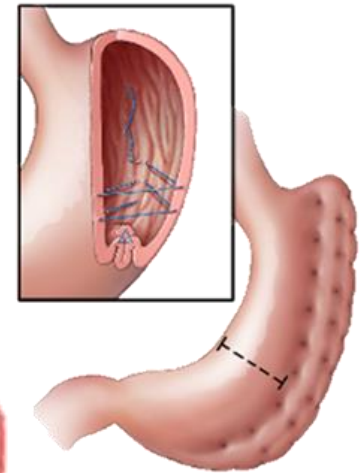
Balloons



Endomina



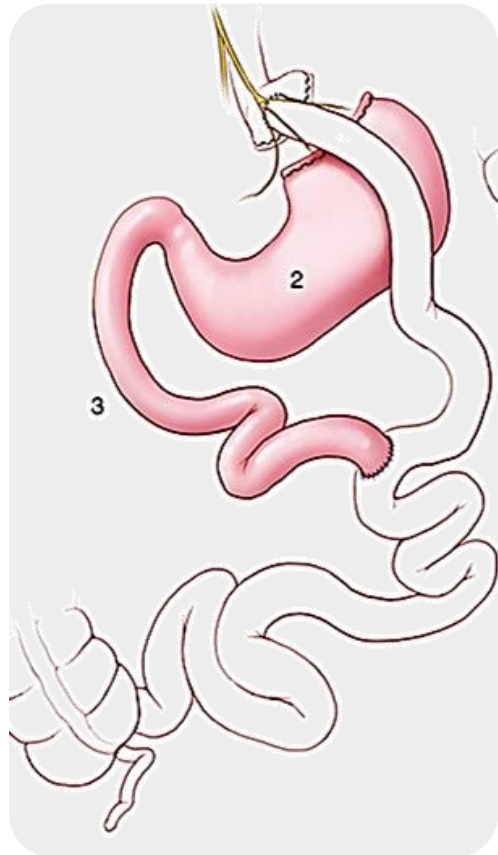
ESG



Others



Small Bowel EBTs



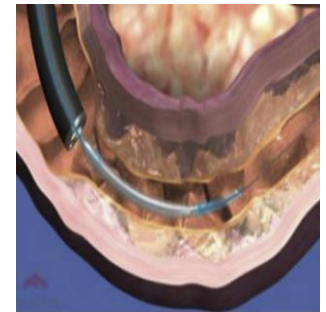
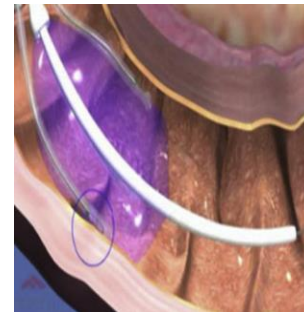
Duodenal Sleeves



Gastroduodenojejunal Sleeves

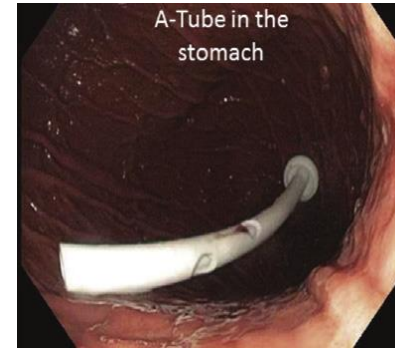
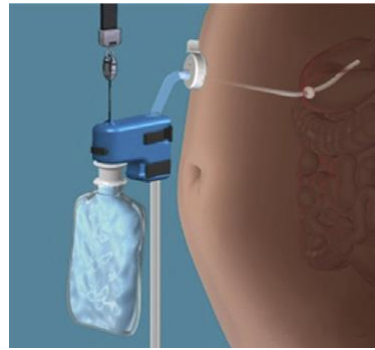


Duodenal Mucosal Resurfacing



Other EBTs

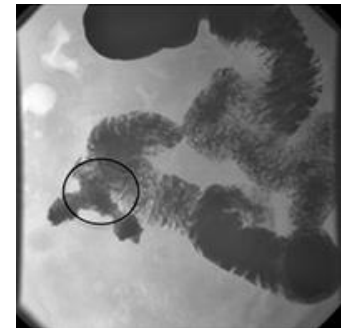
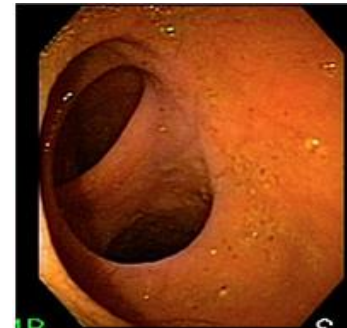
Aspiration Therapy



Full Sense Device

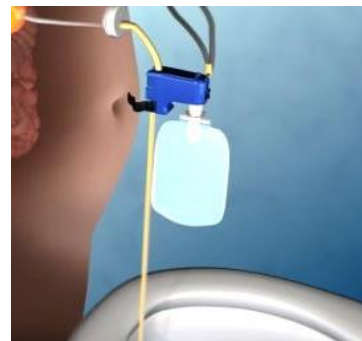
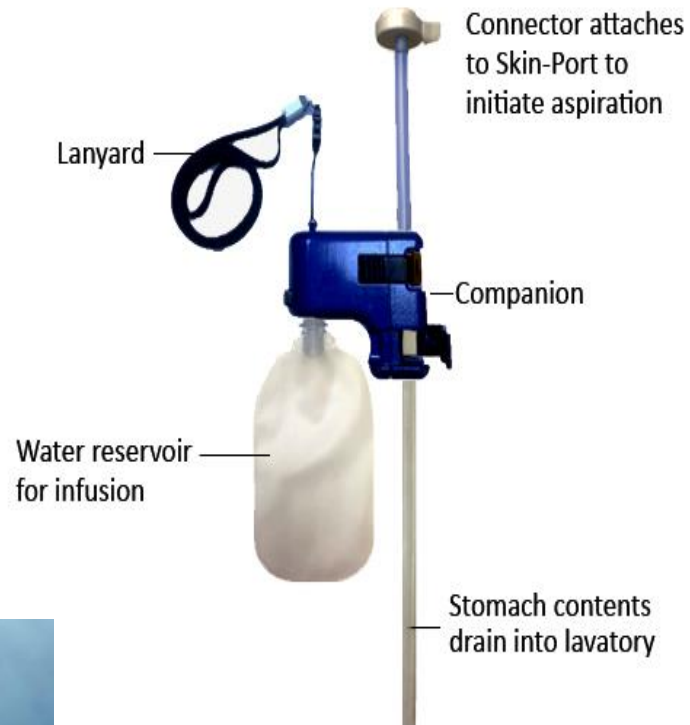
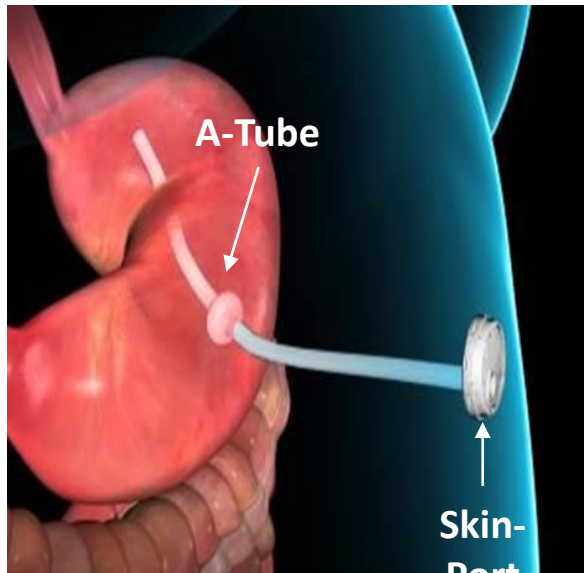


Self-assembling Magnets
for Endoscopy



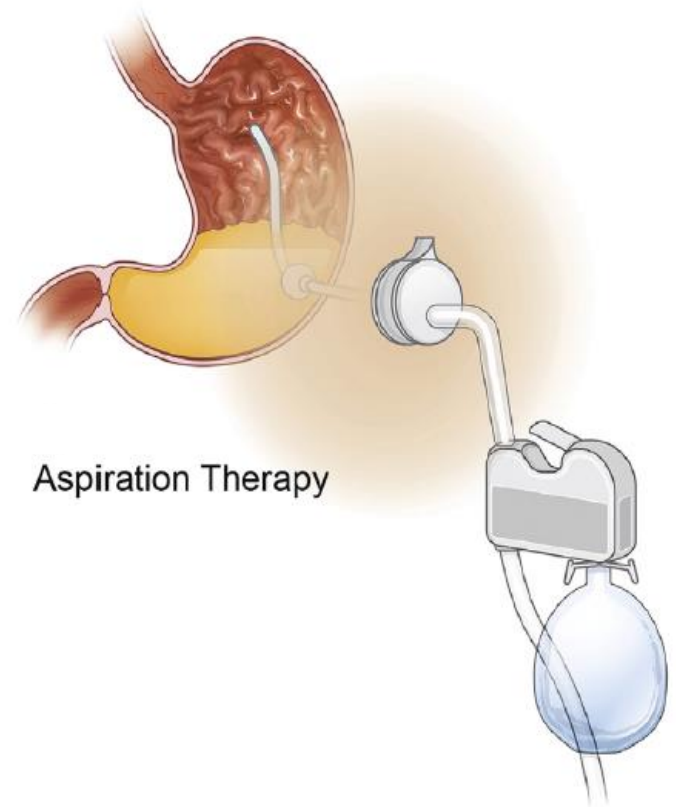
AspireAssist[®] System

Two modes: Drain & Lavage



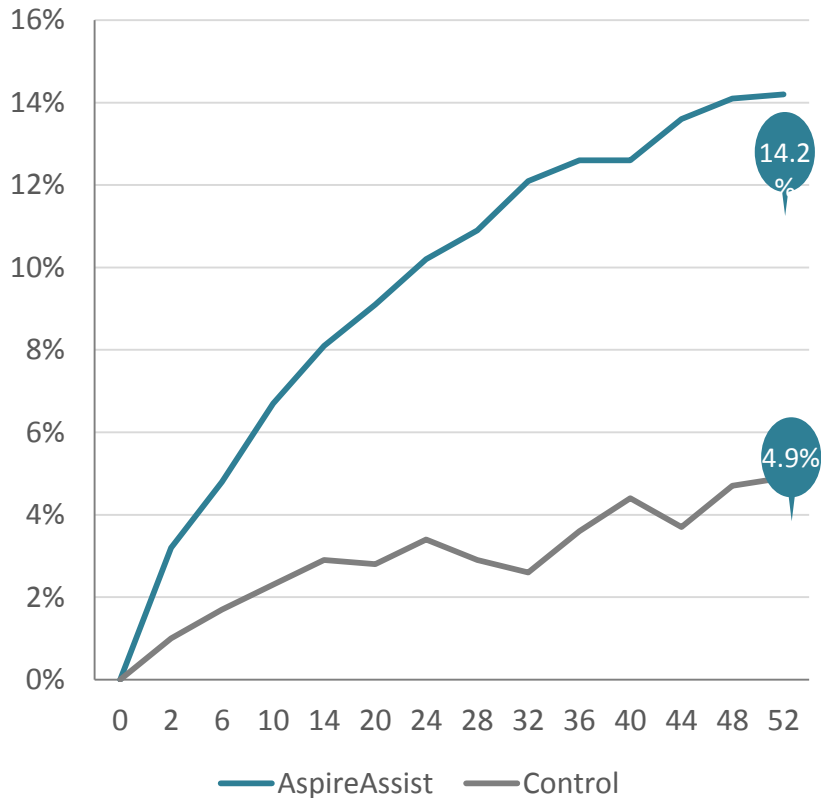
Aspiration Therapy

- ✓ **Indications: BMI 35 - 55 kg/m²**
- ✓ **Partial gastric content removal (30%) through a specific percutaneous gastrostomy**
- ✓ **Aspiration gastric contents 20 -30 minutes after meals**
- ✓ **Together with life style modification it helps in weight loss and its long term managing.**

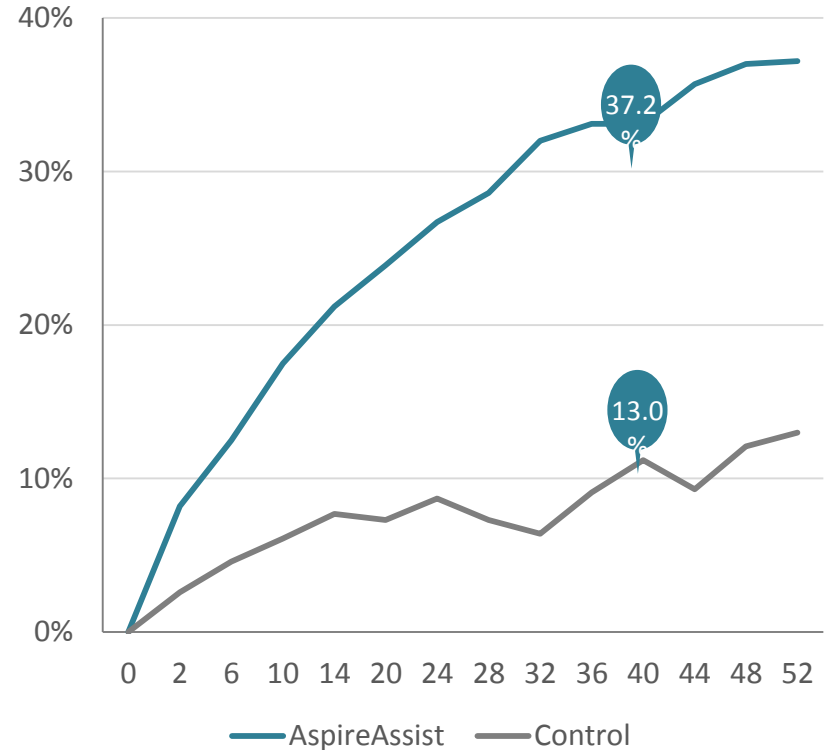


US Clinical Study: Weight Loss Results

Total Body Weight Loss

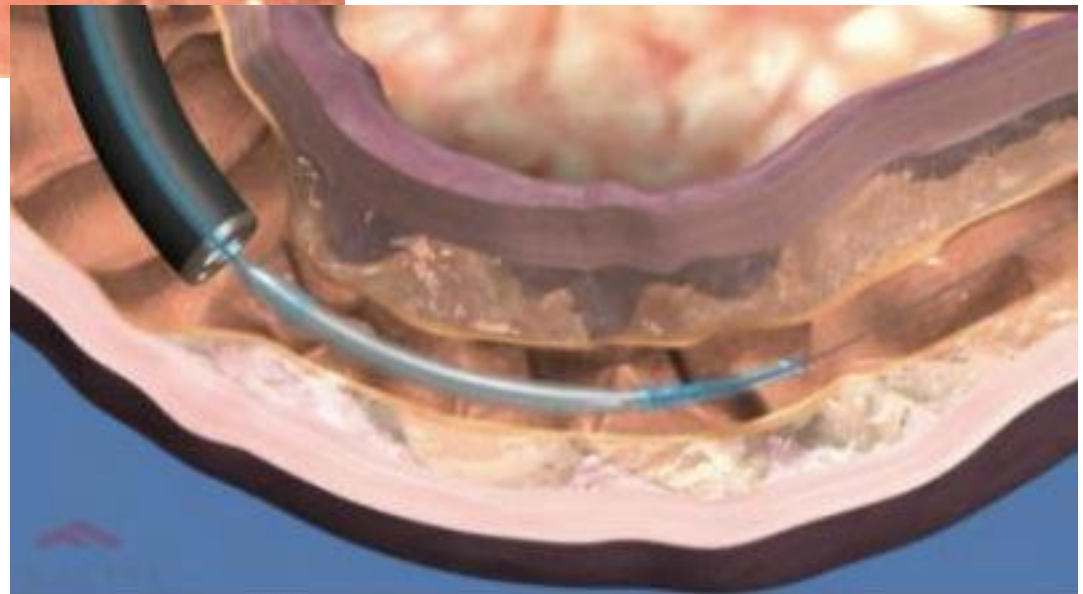
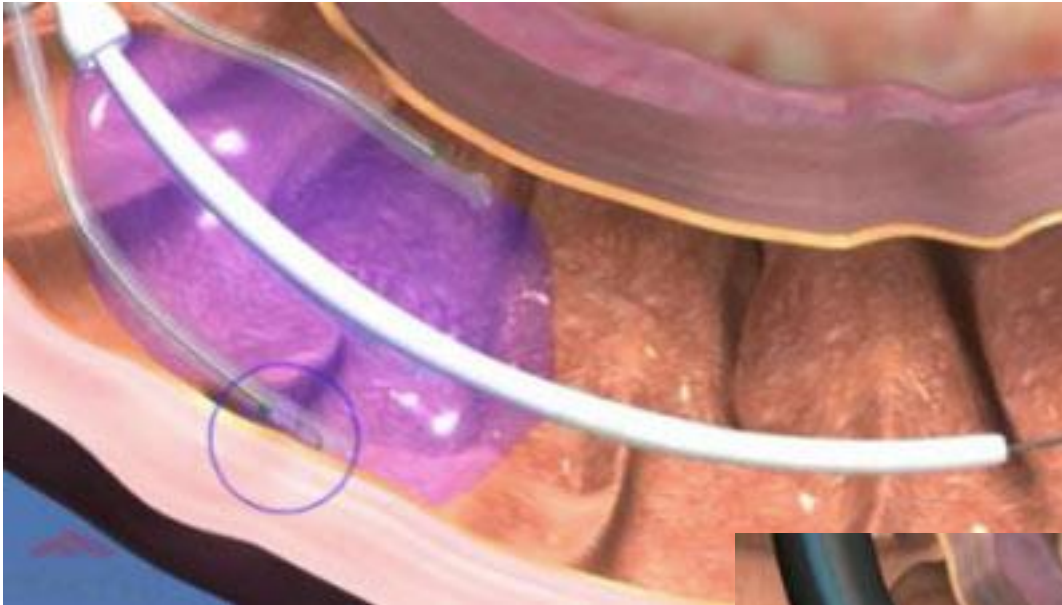


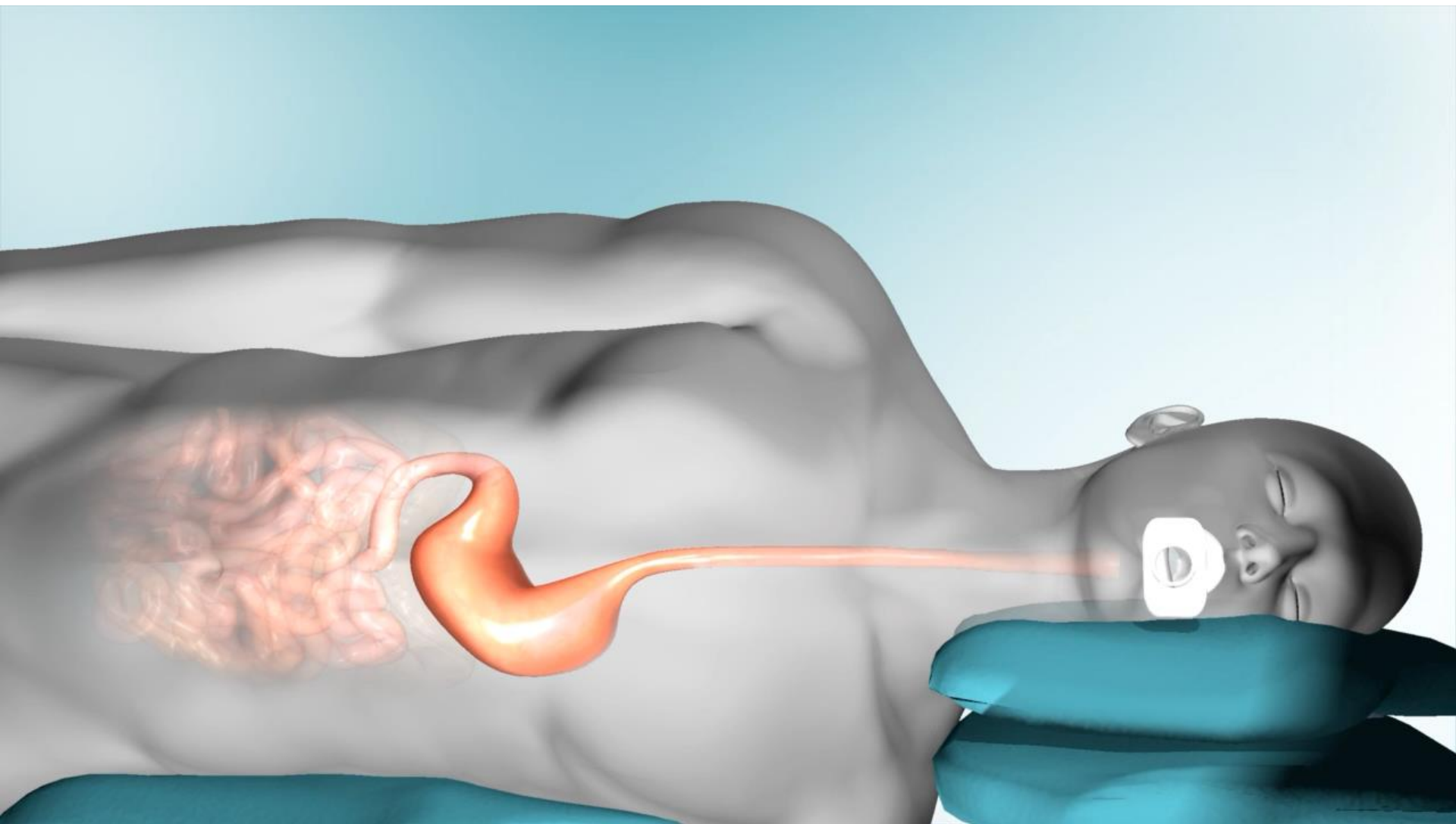
Excess Weight Loss



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.

REVITA Duodenal mucosal resurfacing

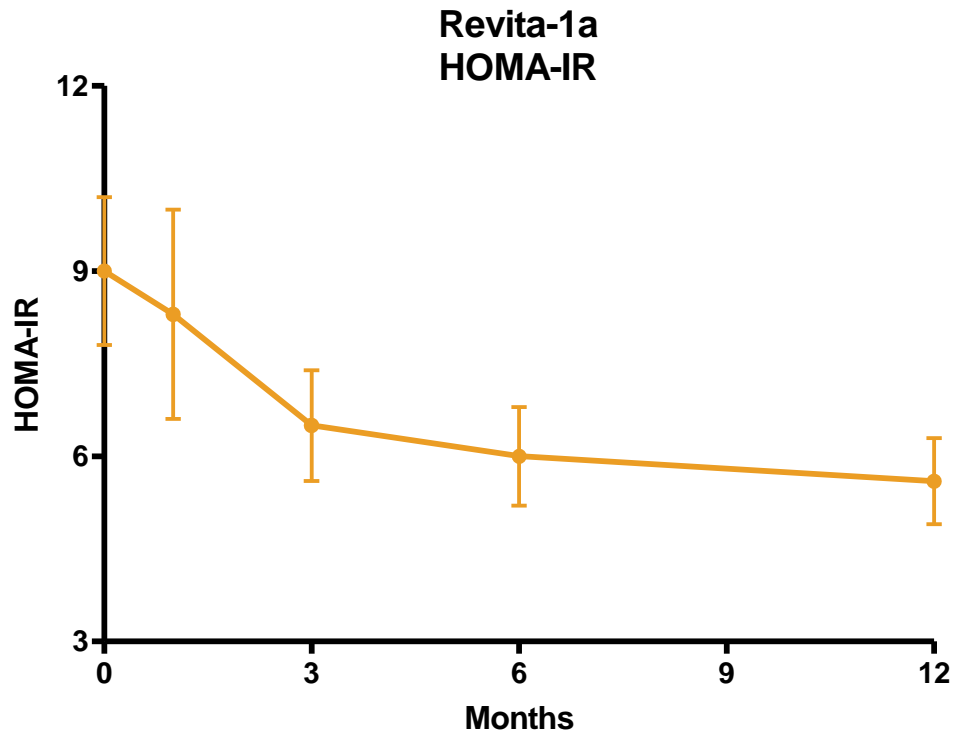




DMR Safety and Tolerability

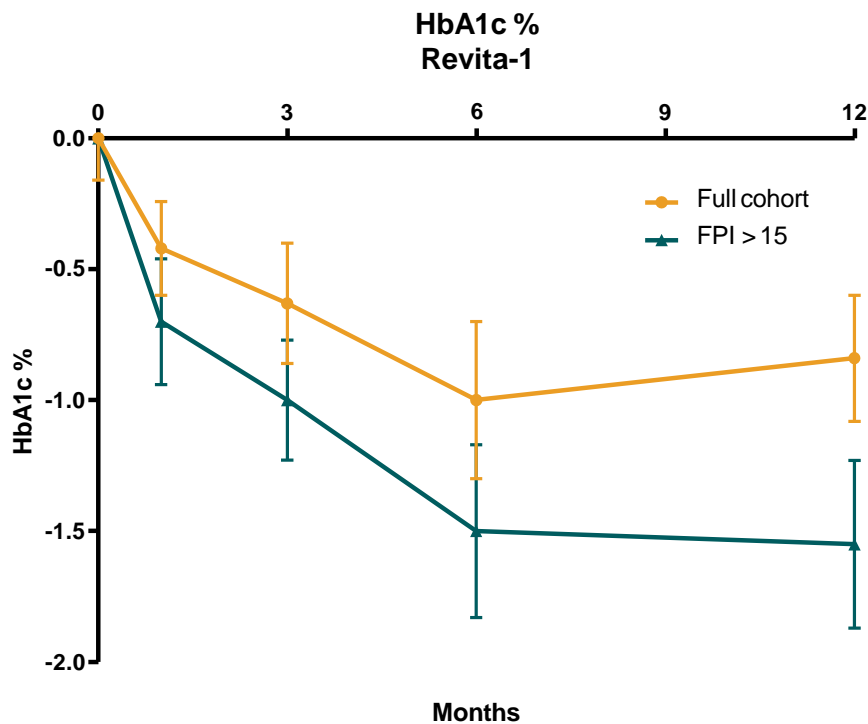
- Total ~100 cases in early First-in-Human (“FIH”) and ongoing multicenter Revita-1 study
- Post-procedure: favorable tolerability profile with minimal GI symptoms
- Three duodenal stenoses in early FIH experience → each successfully treated with single non-emergent balloon dilation and no later sequelae
- One small bowel perforation SAE in recent use
- No other device/procedure related SAEs No apparent hypoglycemic risk
- No evidence of malabsorption
- No late adverse events observed (60+ patients >12 months)

Revita-1 Trial Key Finding: Durable Lowering of HOMA-IR

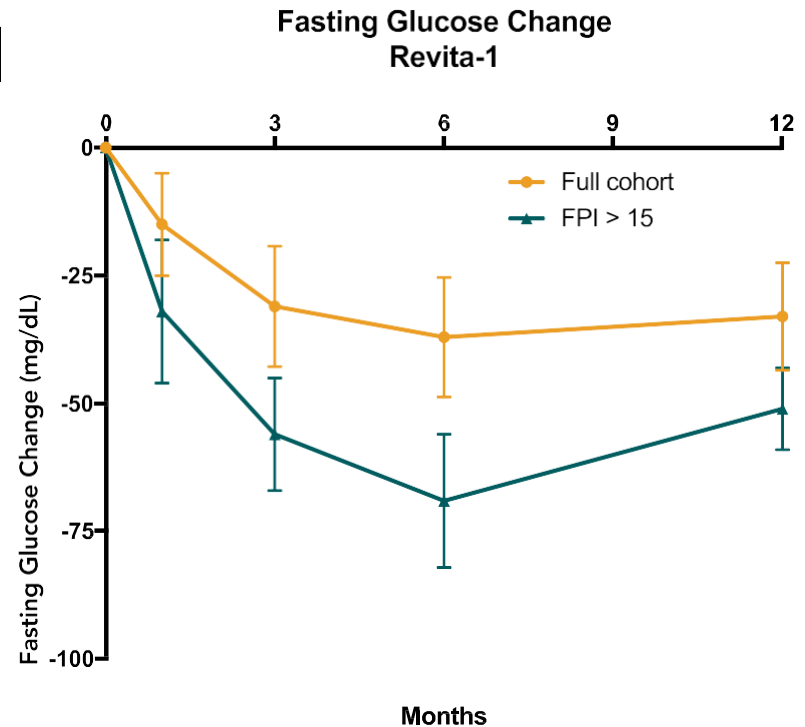


- Durable reductions in insulin
- resistance (HOMA-IR) - highlights our mechanism of action
- Reductions seen in both glucose levels and insulin levels
- Weight loss independent of metabolic improvement
- No lifestyle intervention in the study
- Consistent with observations from duodenal bypass surgery
- 27 patients at study entry & 23 patients at 12 month follow up

Revita-1 Trial: Blood Glucose



e1



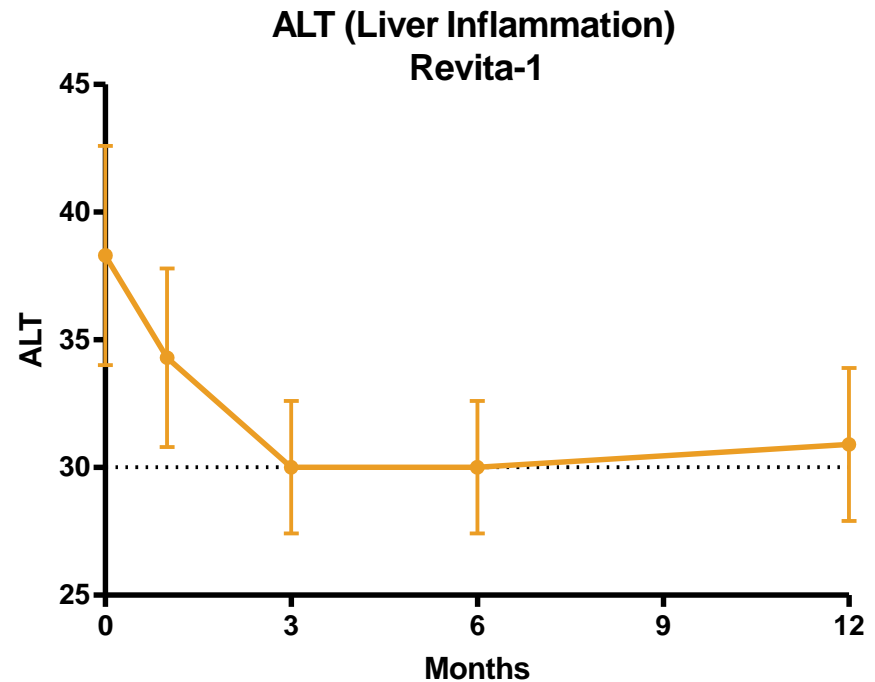
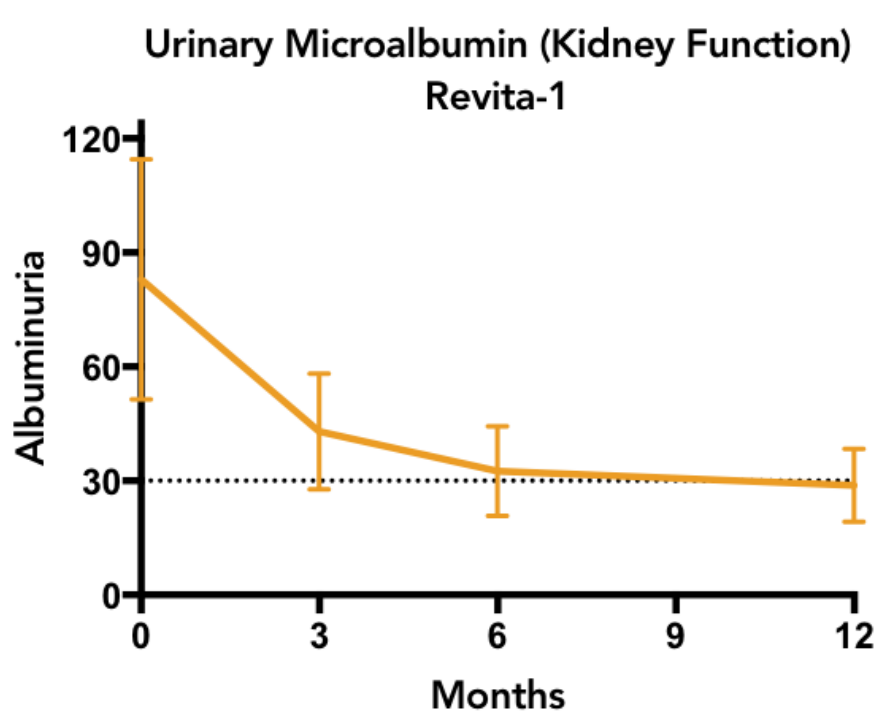
- 12 month data shows durable improvements in blood sugar
- Baseline pancreatic function at baseline can be used to identify those patients most likely to respond, as seen with bariatric surgery²⁻⁴

DATA ON FILE; FRACTYL LABS

¹ Nannipieri *et al* JCEM 2011 ² Souteiro *et al* Obes Surg 2016

³ Aarts *et al* Obes Surg 2013 ⁴ Lee *et al* Obes Surg 2012⁵

Revita-1 Trail: Lowering of Microalbuminuria and Hepatic Transaminase



- Reduction in abnormal microalbuminuria – a marker of heart attack and stroke risk¹
- Normalization of ALT - a marker of NAFLD-NASH²
- Both valuable surrogate markers of insulin resistance and broader cardiometabolic risk

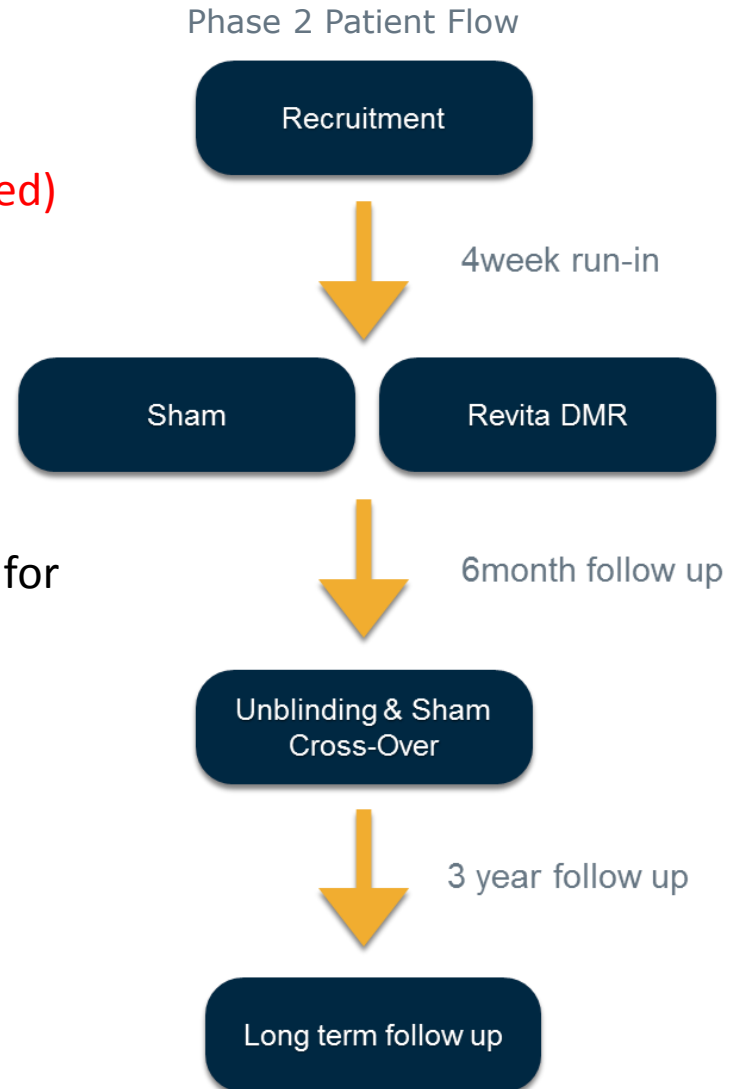
DATA ON FILE; FRACTYL LABS

¹ *Diab Med* Volume 20, Issue 4 April 2003 Pages 277–282

² *Ann Intern Med.* 2016;165(5):305-315.

REVITA-2 Multi-Center Study

- Two-Phased Multi-Center Study in Europe
 - ☞ Phase 1: Non-randomized (completed)
 - ☞ Phase 2: Double blind, sham control (completed)
- Inclusion Criteria
 - T2DM < 10 years
 - 28-75 years old
 - BMI 24-40
 - HbA1c 7.5 -10%
 - At least one oral glucose lowering medication for at least 3 months
 - No injectable medication
- Endpoints
 - Procedural safety
 - HbA1c improvement at 6 months
 - Long term follow up for safety



Endoscopic Sleeve Gastroplasty (ESG)

Surgical Gastric Sleeve
80% stomach removed to leave 'sleeve'



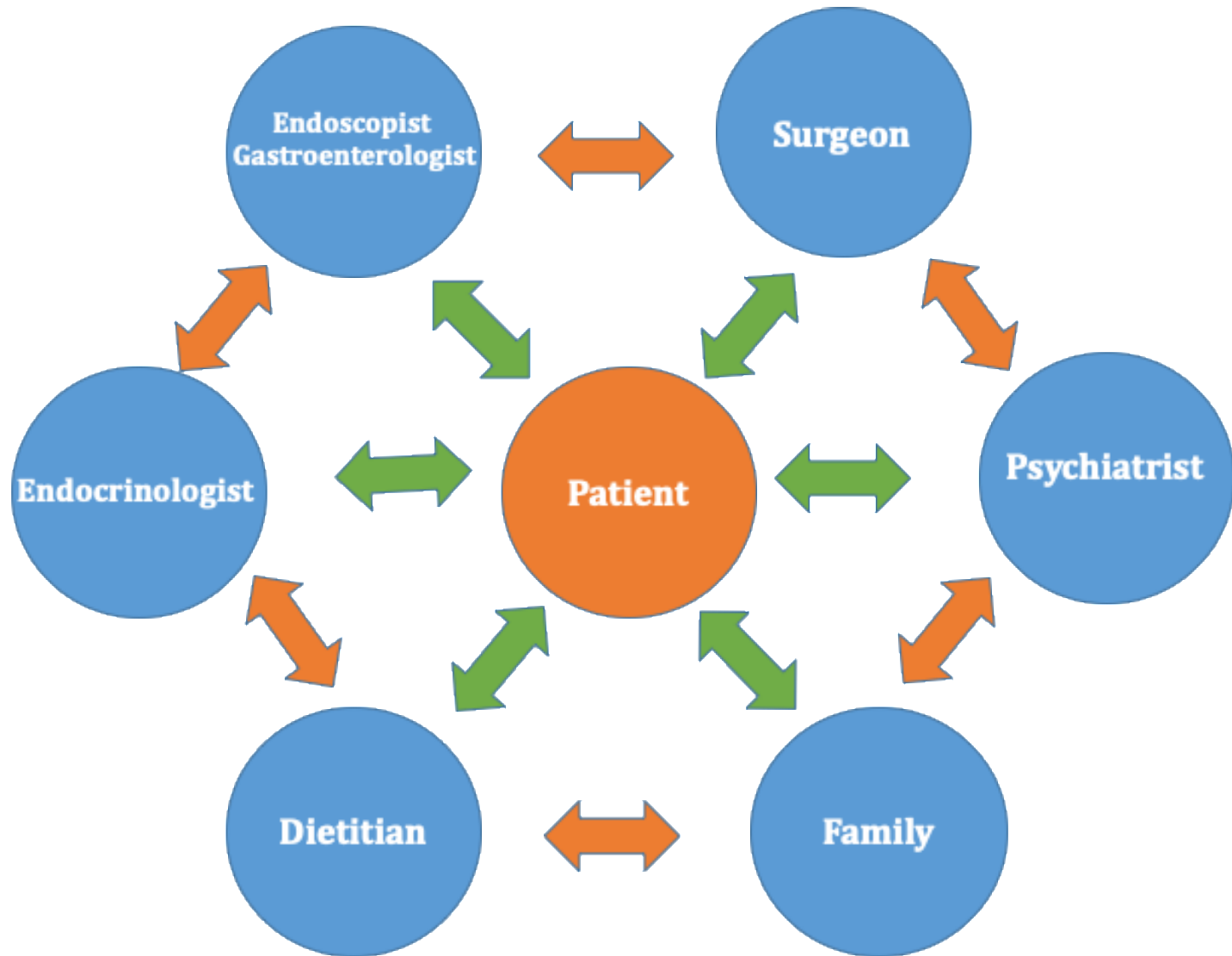
Endoscopic Sleeve Gastroplasty (ESG)
Stomach left intact, stitched to form 'sleeve'

Indications

- BMI > 40 kg/m²
- BMI > 35 kg/m² with diabetes not controlled by medical therapy
- BMI > 30 kg/m² with comorbidities

*Wentworth JM et al. Lancet Diabetes
Endocrinol 2014
Parikh M et al. Ann Surg 2014
Musella M et al. Obes Surg 2016*

Multidisciplinary approach



Devices

Apollo Overstitch (Apollo Endosurgery)

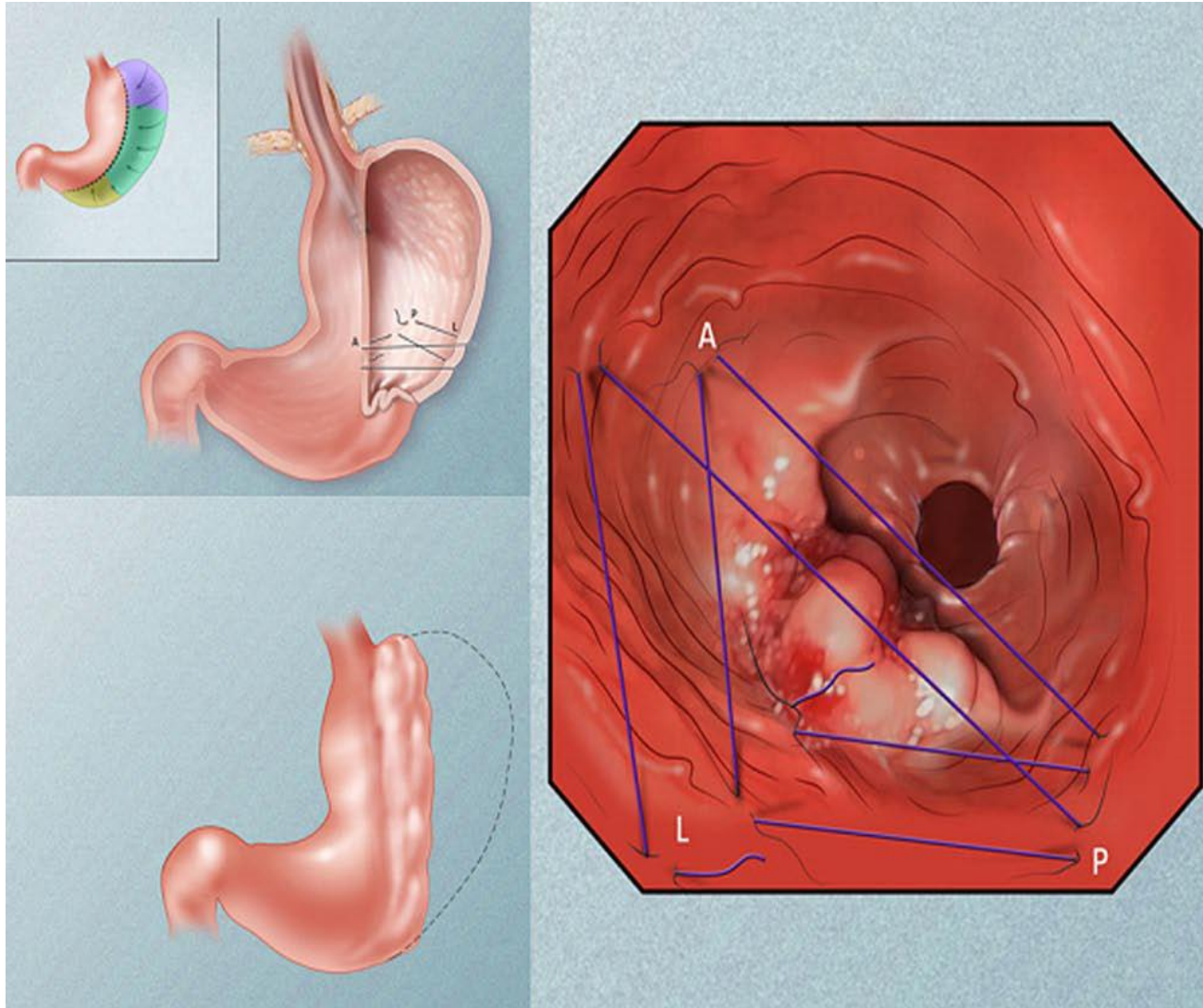
Endomina (Endotools)

Pose (USGI Medical) (?)

Endoscopic Sleeve Gastroplasty with Apollo Overstitch



Endoscopic sleeve gastropasty



Endoscopic sleeve gastropasty



Real life



Study	Patients N	Mean BMI	6 Mo TWL	12 Mo TWL	24 Mo TWL
Sharaiha RZ, 2015	25	38,5 ± 4,6	NA	18,7 ± 10,7	NA
Kumar N, 2015	126	36,2	NA	20 ± 3,8	NA
Lopez-Nava G, 2016	25	35,5	17.8 ± 7.5	18.7 ± 10.7	NA
Abu Dayyeh BK, 2017	10	45,2	33	NA	NA
Lopez-Nava G, 2017	248	37.8 ± 5.6	15.2	NA	18.6
Sartoretto A, 2018	112	37,9 ± 6,7	16.4 ± 10.7	NA	NA

Reported complications 2%

Short-term outcomes of endoscopic sleeve gastroplasty in 1000 consecutive patients

Aayed Alqahtani^{1*}, MD, FRCSC, FACS; Abdullah Al-Darwish¹; Ahmed Elsayed Mahmoud¹, MD; Yara A. Alqahtani¹, MD; MD; Mohamed Elahmedi¹, MBBS

¹Obesity Chair, Department of Surgery, College of Medicine, King Saud University, Riyadh, Saudi Arabia.

Gastrointest Endosc. 2018

Single-Surgeon Registry



N=1,000

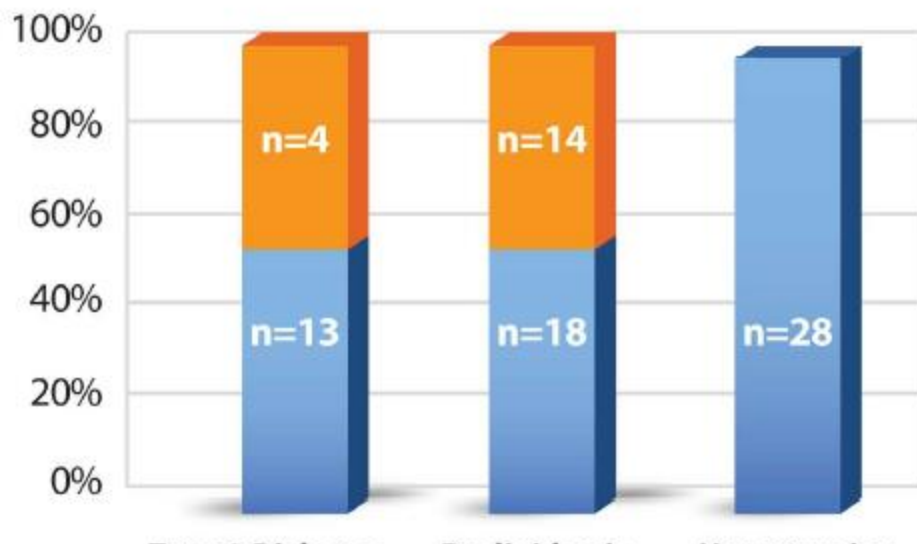
BMI=33.3 ± 4.5kg/m²

Age=34.4 ± 9.5 years

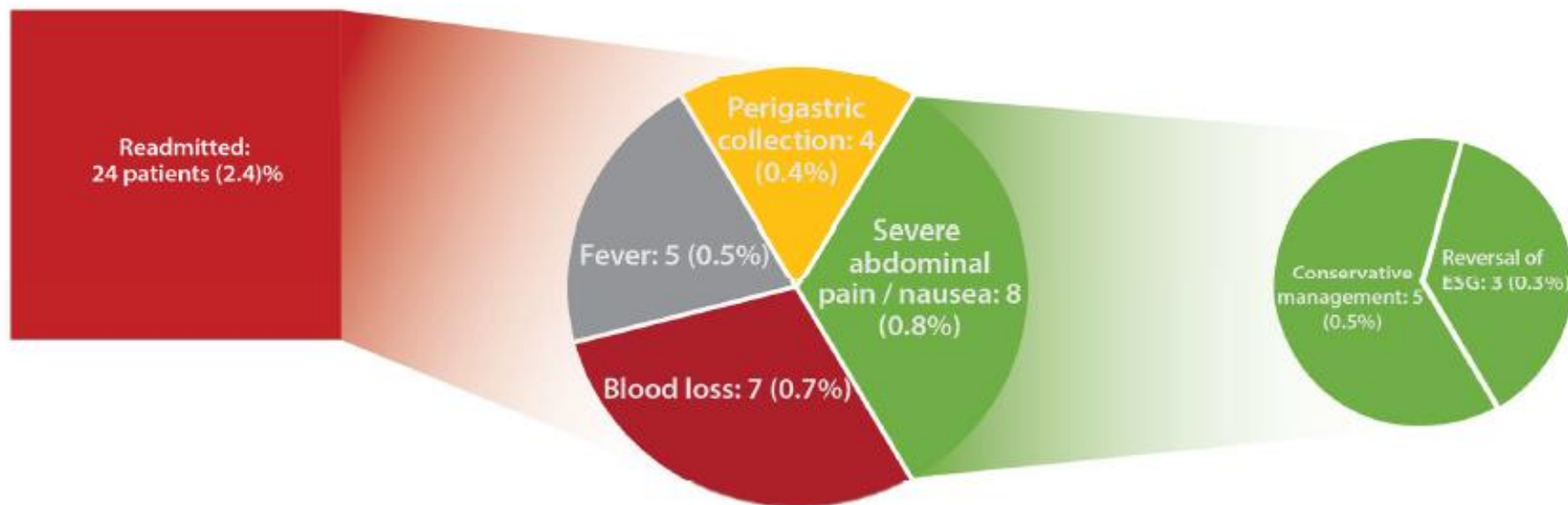
% Excess Weight Loss after ESG



Change in Co-morbidities after ESG



Readmissions after ESG



Endoscopic Sleeve Gastroplasty with ENDOMINA



Devices are designed to be compatible with most endoscopes and surgical tools

- Single use
- Assembled within the stomach to avoid orifices size limitation
- Adds triangulation to endoscope
- Universal (i.e. can be used with any endoscope and endoscopy tools), limiting upfront costs
- Easy to use (3h initial training, learning curve 5-7 patients)
- Deeper suture than any other device on the market (key for long lasting tissue apposition)



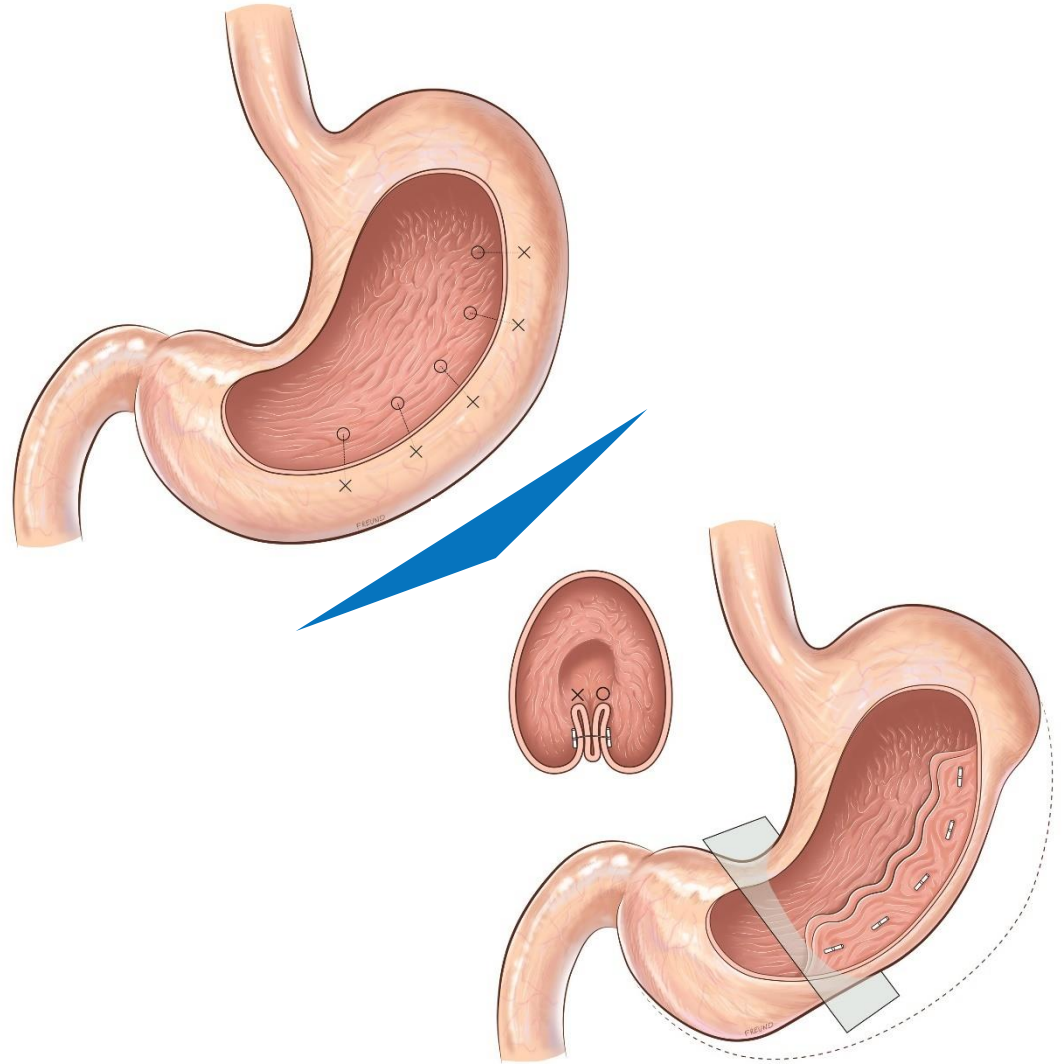
Procedure for bariatric surgery

Restrictive surgery on the stomach


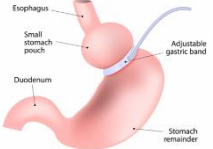
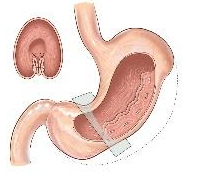
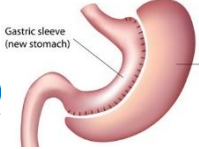
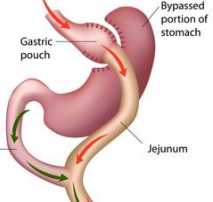
- Reduces size of the stomach
- Limits distensibility of the stomach
- 5-10 tissue approximations

Target impact (under clinical trial) :

- Long lasting tissue approximation
- Volume restriction lower than surgery
- Improved quality of life vs surgery
- Highly reduced rate of complications



Clinical results confirm endoscopic techniques positioning between temporary treatment and surgery (>180 patients; 2 papers published)

Procedure	Follow-up	Excess weight loss	SAE rate	Ref.
Balloon 	6 months	28 %	N/A	[1]
Gastric band 	1 year	34 %	8 %	[2, 3]
Endoscopic Treatment (with endomina) 	1 year	ASGE guideline is 25% 30-40 %	0 %	No serious adverse event so far (N>180)
Sleeve gastrectomy 	1 year	51 %	9 %	[2, 3]
Gastric bypass 	1 year	63 %	12 %	[2, 3]

Endoscopic gastric reduction with an endoluminal suturing device: a multicenter prospective trial with 1-year follow-up.

Huberty V¹, Machytka E², Boškoski I³, Barea M¹, Costamagna G⁴, Deviere J¹.

+ Author information

Abstract

BACKGROUND: Obesity is the pandemic disease of this century. Surgery is the only effective treatment but cannot be offered to every patient. Endoscopic sutured gastroplasty is a minimally invasive technique that may potentially fill the gap between surgery and behavioral therapy. In this study, we prospectively investigated the efficacy and safety of a novel suturing device.

METHODS: After a pre-bariatric multidisciplinary work-up, class 1 and 2 obese patients were included. Using a simple triangulation platform, transmural sutures with serosa-to-serosa apposition were performed in the gastric cavity. Patients were followed according to the same routines as those performed for bariatric procedures.

RESULTS: Between November 2015 and December 2016, 51 patients were included across three European Centers. Mean body mass index at baseline was 35.1 kg/m² (SD 3.0). Excess weight loss and total body weight loss at 1 year were 29% (SD 28) and 7.4% (SD 7), respectively, for the whole cohort (45 patients). At follow-up gastroscopy, 88% of sutures were still in place (30 patients). No severe adverse events were observed.

CONCLUSIONS: Endoscopic sutured gastroplasty using this novel device is safe and achieved weight loss results in line with criteria expected for these endoluminal techniques. Further prospective studies vs. placebo or nutritional support are needed.

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PMID: 29906810 DOI: [10.1055/a-0630-1224](https://doi.org/10.1055/a-0630-1224)

Up to date trials – Endomina v2 for Endoscopic Sutured Gastroplasty (ESG)

T1 – Feasibility study

- **12** patients between April and July 2015
- BMI 34.6 kg/m² SD 2.2
- 1 patient excluded
- 8 women / 4 men
- *Gastrointestinal Endoscopy* 2017 85, 833-837 (6-months results)
- Light follow-up, similar to routine balloon follow-up
- GE visit : 1, 3, 6, 9 and 12 months
- Dietician visit : 1, 3, 6, 9 and 12 months
- ClinicalTrials.gov
NCT02534662

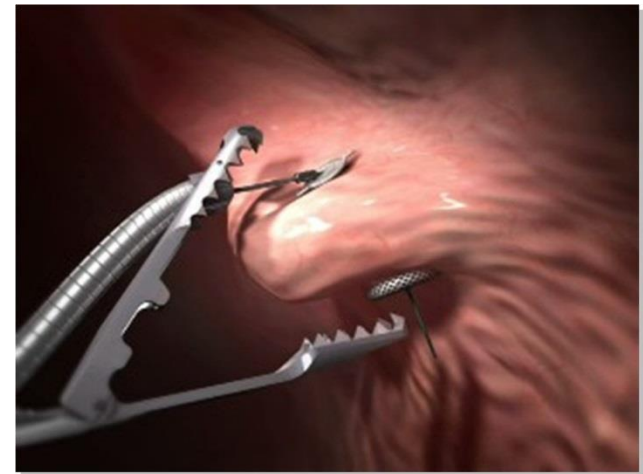
T2 – Multicentric efficacy study

- **51** patients in Brussels / Rome / Ostrava between February and December 2016
- BMI 33,5 kg/m² SD 2.6
- 0 patient excluded
- 24 women / 2 men
- Same follow-up
- ClinicalTrials.gov
NCT02582229

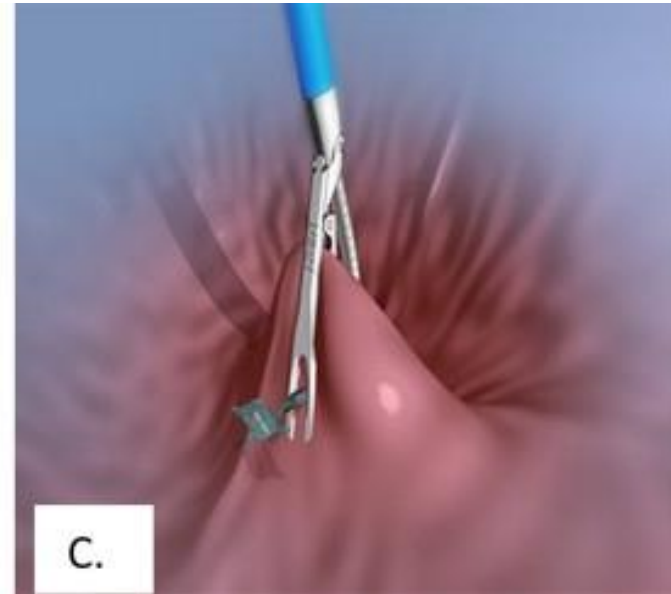
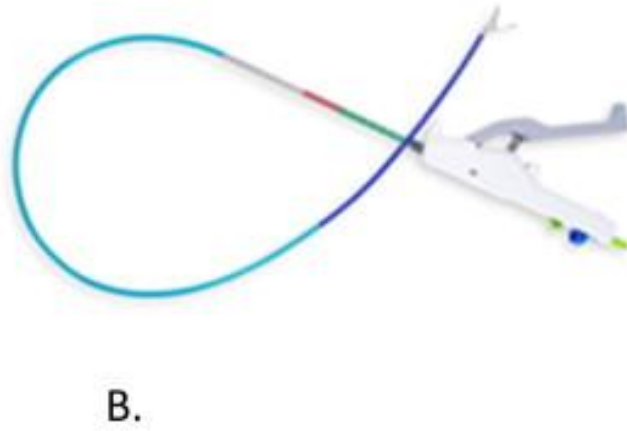
T3 – Randomized Control Trial

- **70** patients planned, starting September 2017, ongoing
- 3 centers Erasme (Brussels), APHM (Marseille), Gemelli (Rome)
- 0 patient excluded so far
- Procedure versus diet
- **47** patients in active arm
- **23** patients in control arm
- Control arm = diet for 6 months then crossover
- ClinicalTrials.gov
NCT03255005

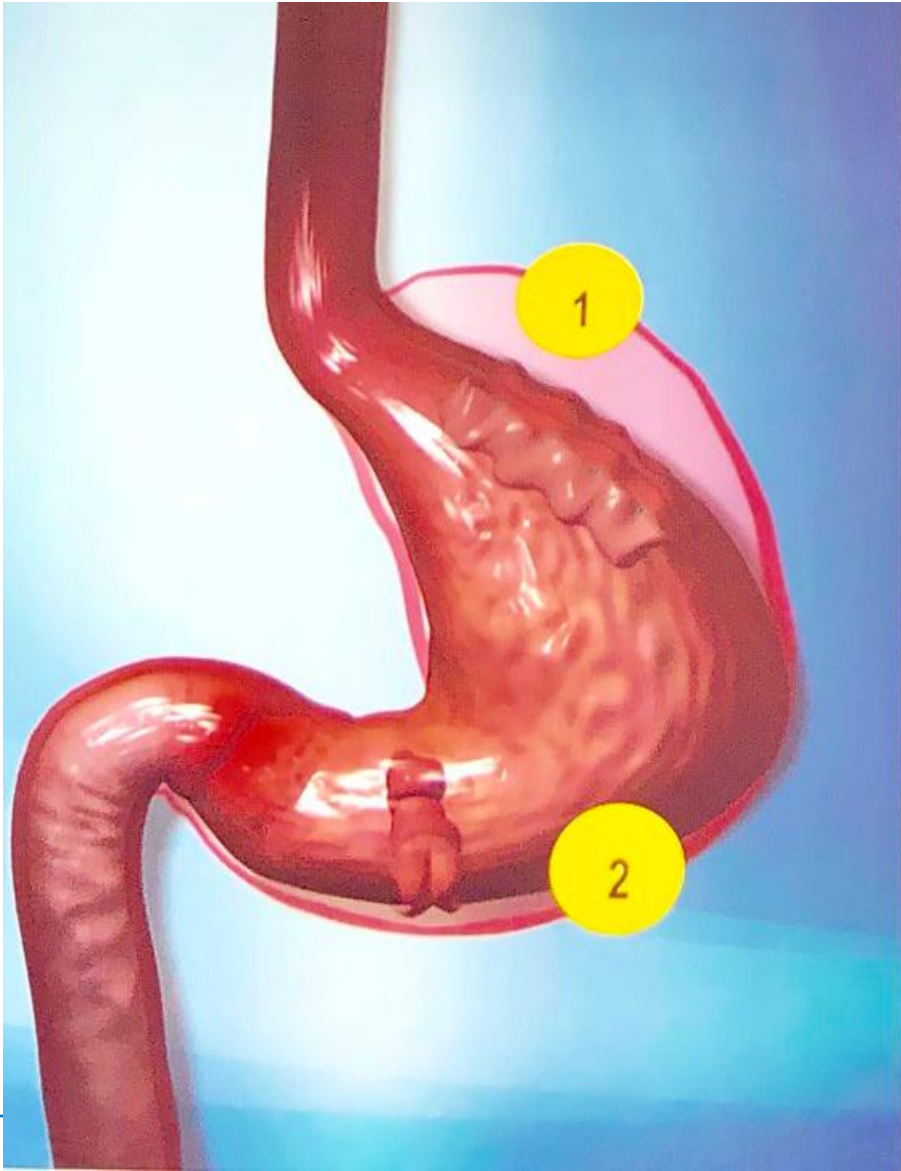
Endoscopic Sleeve Gastroplasty with POSE



POSE Procedure



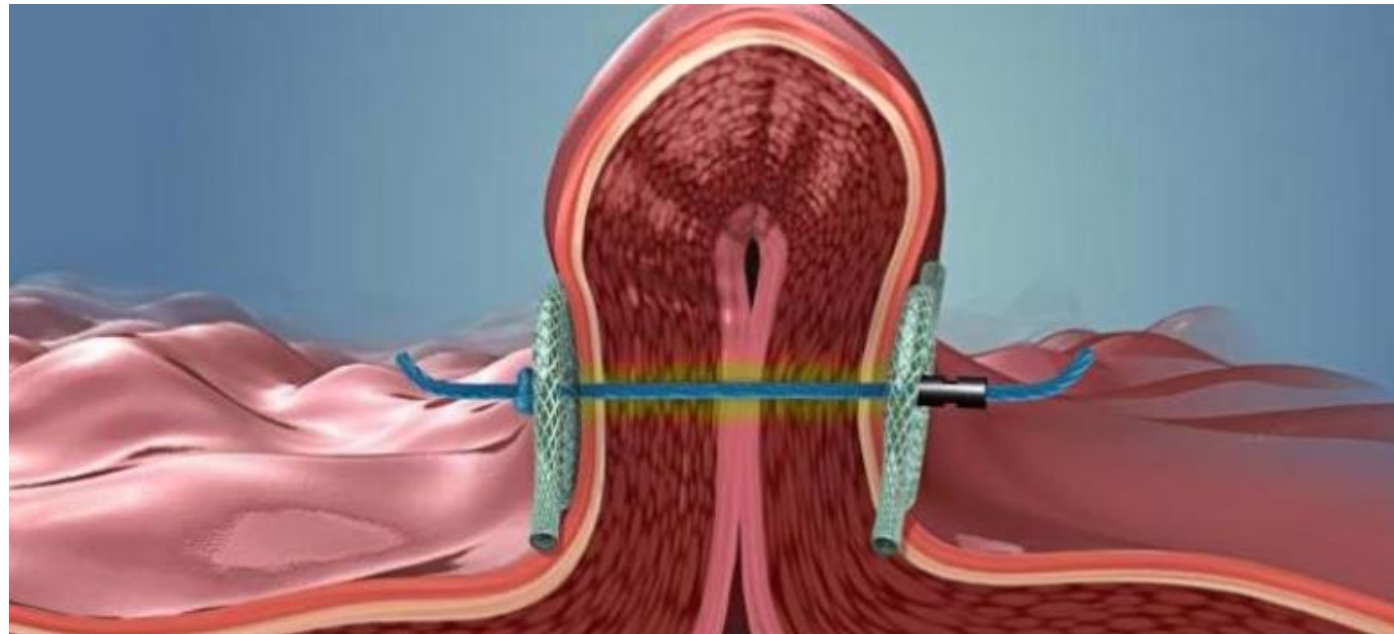
Mechanisms of action of POSE procedure



1. Invaginate the Fundus Completely
 - No reservoir for food – decreases functional capacity for meal
 - Speeds food to antral mill: physiologic fullness rapidly
2. Plical Antral Inlet
 - Dysmotility delays total gastric emptying time
 - Prolongs fullness, delays onset of hunger

New pattern for POSE procedure

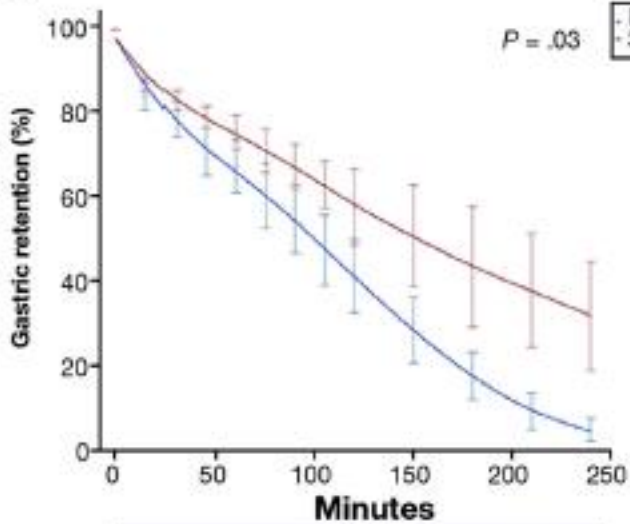
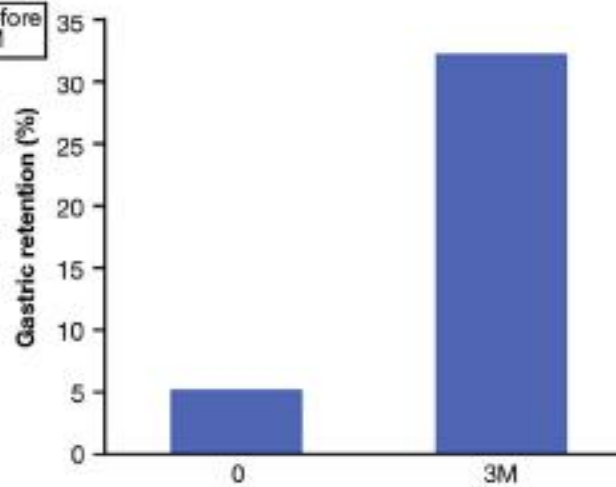
Endoscopic Gastroplasty



Mechanisms of Action

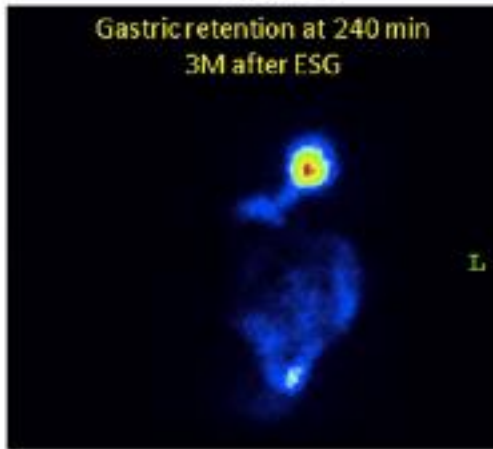
2 mechanisms of action:

- Gastric volume reduction
- Delayed Gastric Emptying

A**B**

(A) Changes in gastric emptying of solids before and 3 months after ESG.

(B) Percent gastric retention of a solid meal at 240 minutes before and 3 months after ESG.

C**D**

(C) Gastric scintigraphy image at 240 minutes after a solid meal ingestion depicting retained solid meal in a small gastric fundus cap after ESG.

(D) Upper gastrointestinal series with a radiopaque contrast demonstrating a sleeve effect with a small fundus cap.

The future is bright!

Robotic Endoscopists

MASTER (Singapore)

ISIS/Stras (Strasbourg)

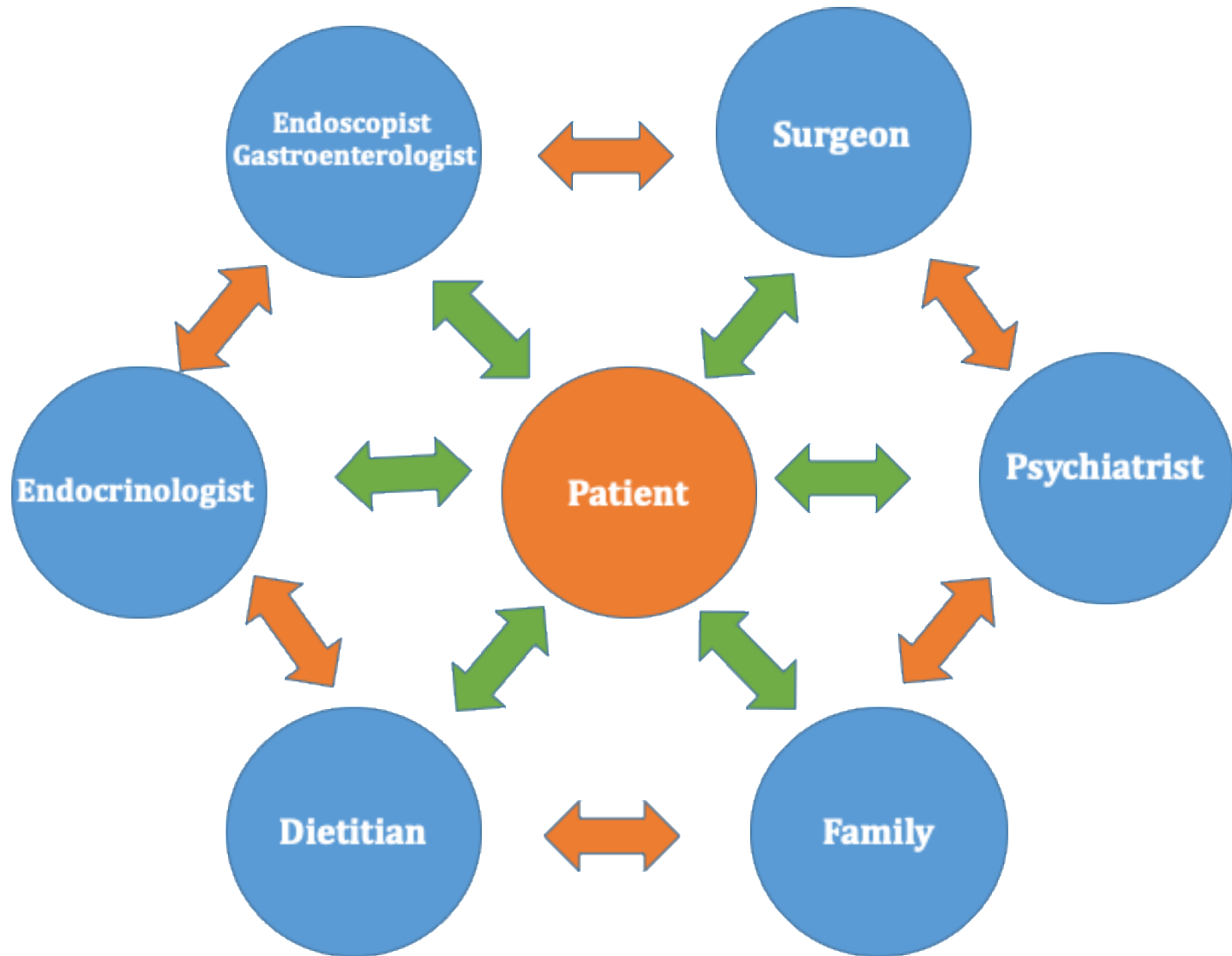
ENDOSAMURAI (Tokyo)

.....

From January 2018 : 71 ESG

Results and Follow-up (54 pts)				
	WL (Kg)	%EWL	%TBWL	BAROS
Follow-up 1 mo	9.2 (range -6 – 17)	17.9 (range -9 – 30.4)	8.1 (range -5 – 12.8)	2.6 (range -2 – 5.25)
Follow-up 3 mo	15.9 (range 5 – 27)	30.1 (range 7.5 – 49.1)	13.7 (range 3.8 – 21.4)	3.9 (range 0.5 – 6.5)
Follow-up 6 mo	18.4 (range -5 – 37)	33.8 (range -7 – 83.7)	15.5 (range -4 – 32.5)	3.9 (range -2 – 9)

Multidisciplinary approach



40 pts (2017 pre-MA) vs. 54 pts (2018 post-MA)

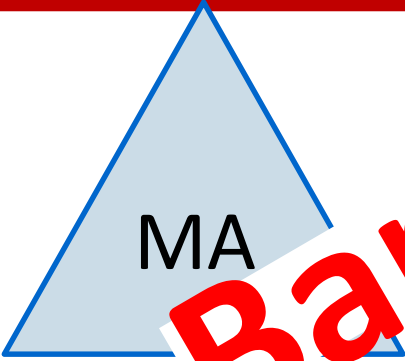
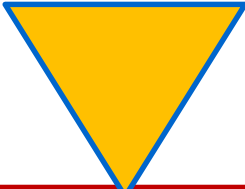
	WL (Kg)		%EWL		%TBWL		BAROS		
	pre-MA	post-MA	pre-MA	post-MA	pre-MA	post-MA	pre-MA	post-MA	p
1 month follow-up	5.7	10.7	11.5	20.5	5.2	9.2	1.4	3.25	<0.01
3 months follow-up	12.1	18.1	23.7	33.9	11	15.3	2.3	4.8	0.02
6 months follow-up	14.1	28	26.5	47.5	14.7	21.8	2.5	7	n.a.

WL = Weight Loss; EWL = Excess Weight Loss (%EWL); TBWL = Total Body Weight Loss; na = non available

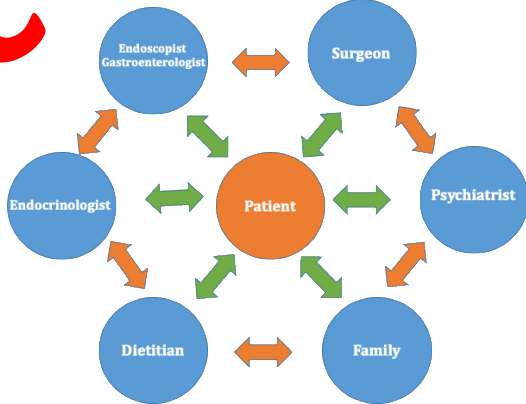
BAROS = Bariatric Analysis and Reporting Outcome System.

Bariatric Endoscopy

intervention

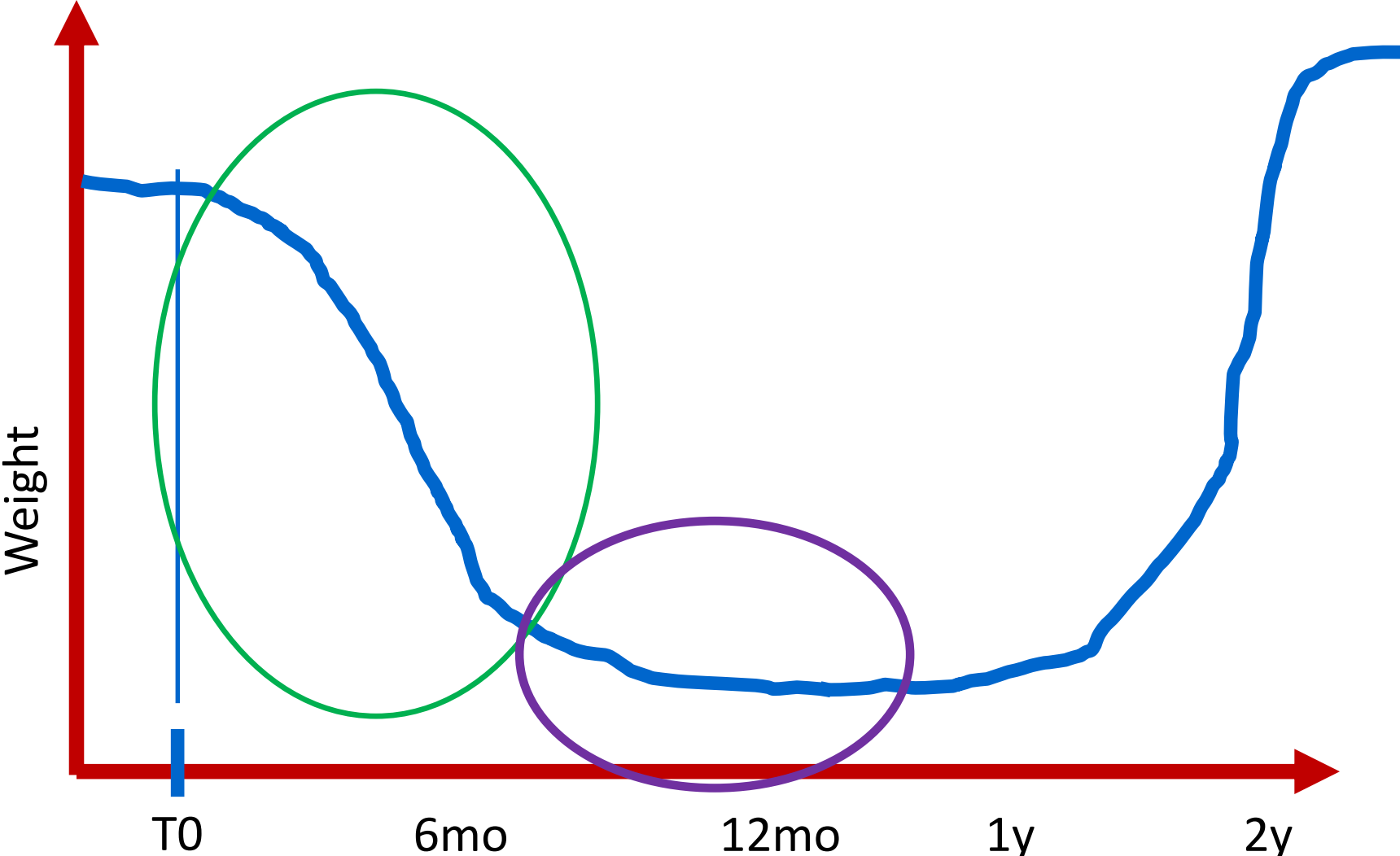


Bariatric Endoscopy

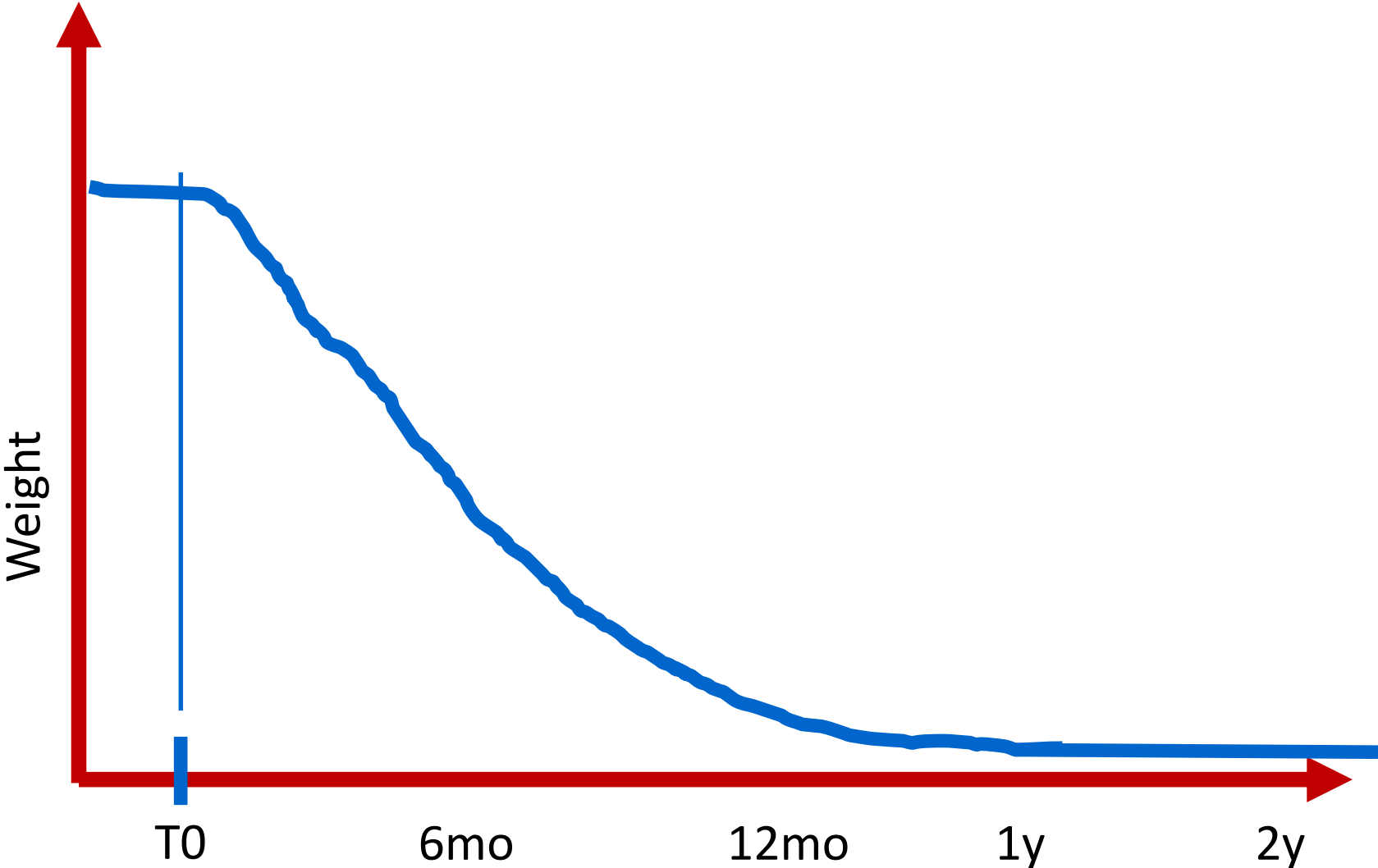


Family

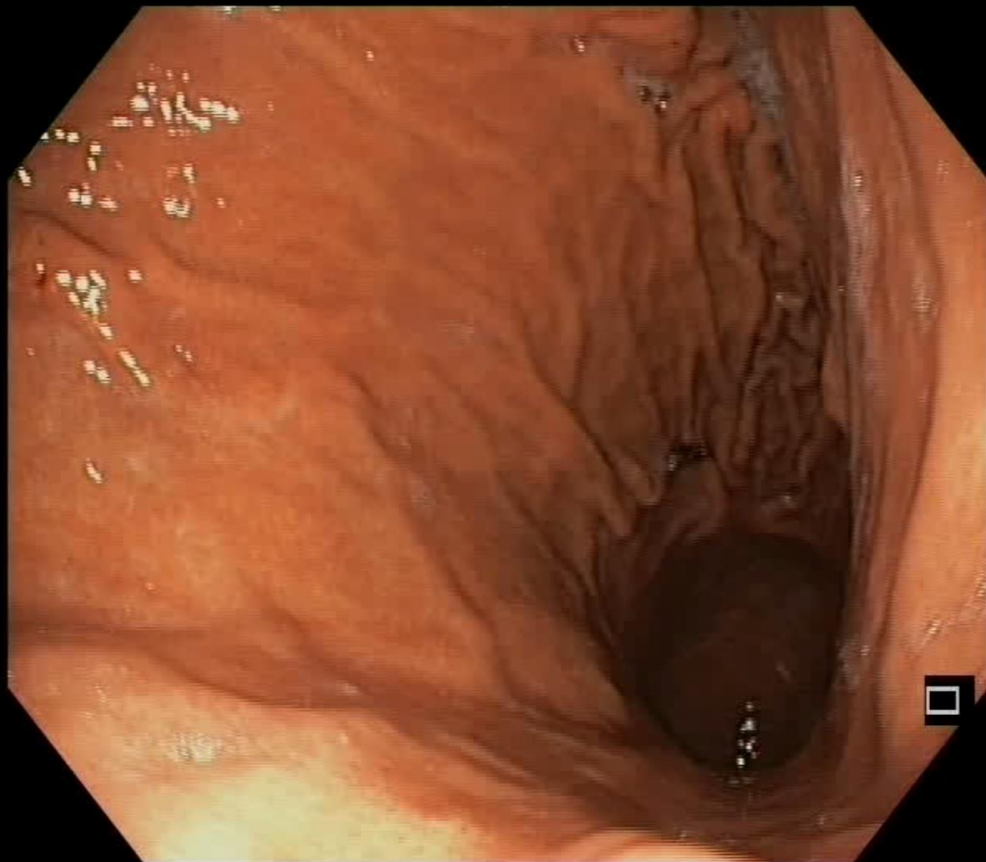
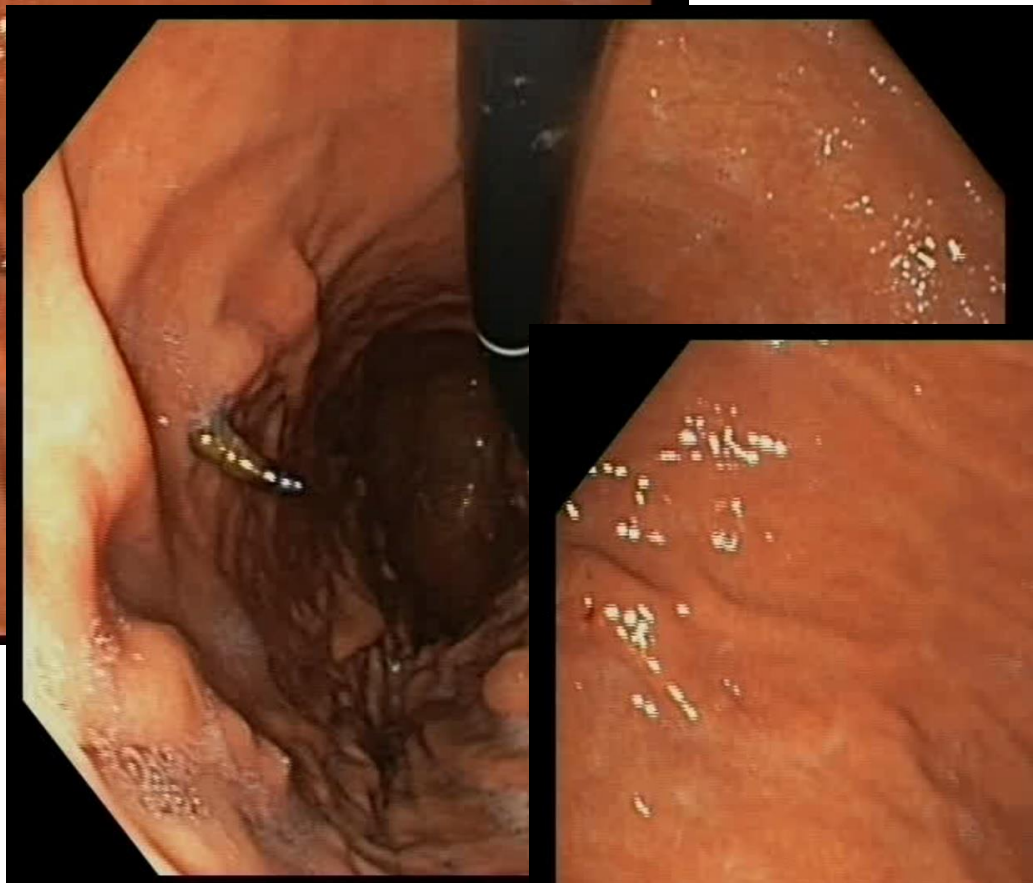
Maintainence



Maintainence

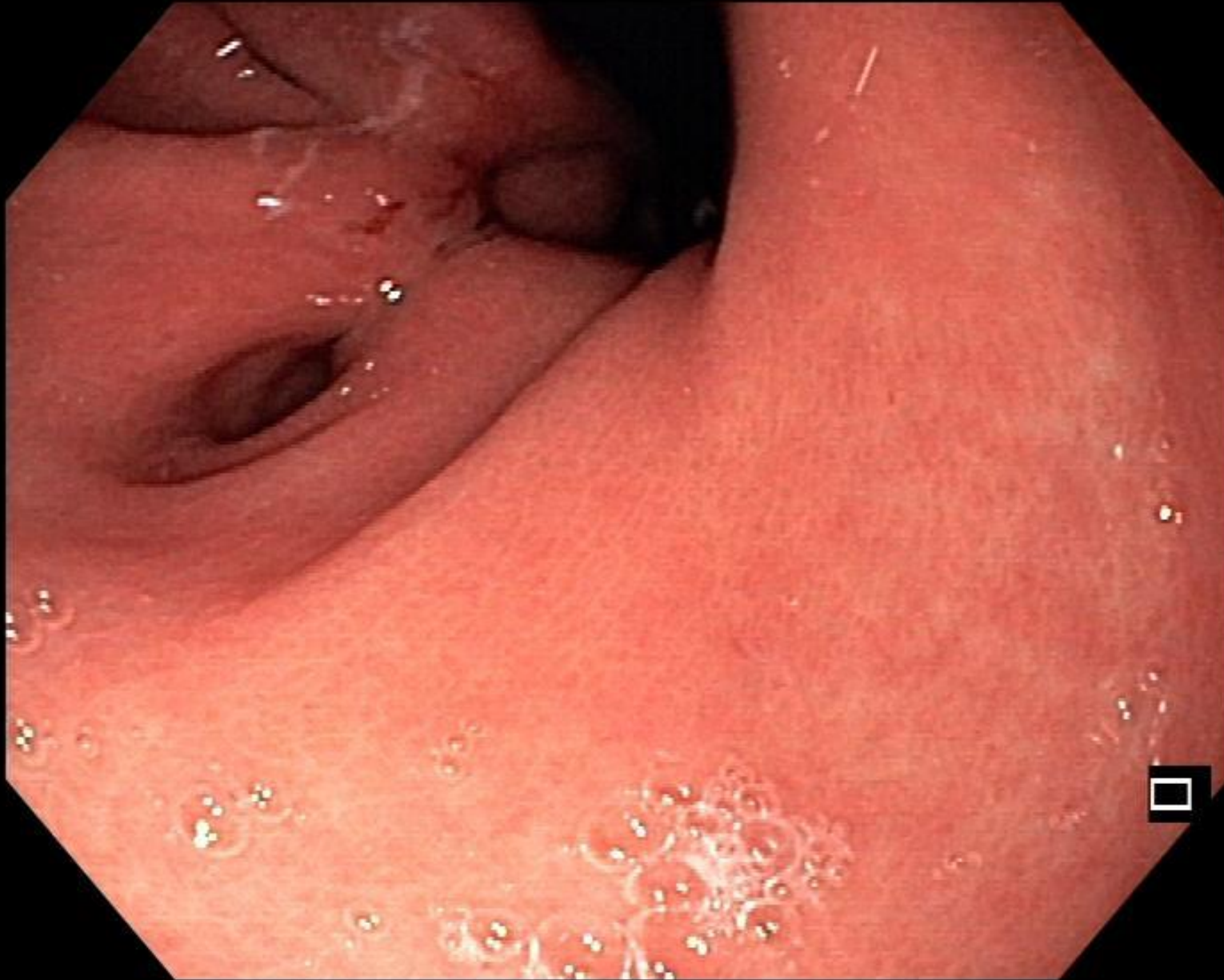


- In 2016 had ESG with Apollo Overstich (BMI 39) with hypertension
- All follow-up visits OK, lost 35 Kg, is following diet and physical activity, patient is HAPPY
- November 2018 M.C. has epigastric pain and «burning», no other symptoms, OK with PPIs, still EGD is planned



So ????????

- ESG was successful!
- Patient changed his lifestyle!

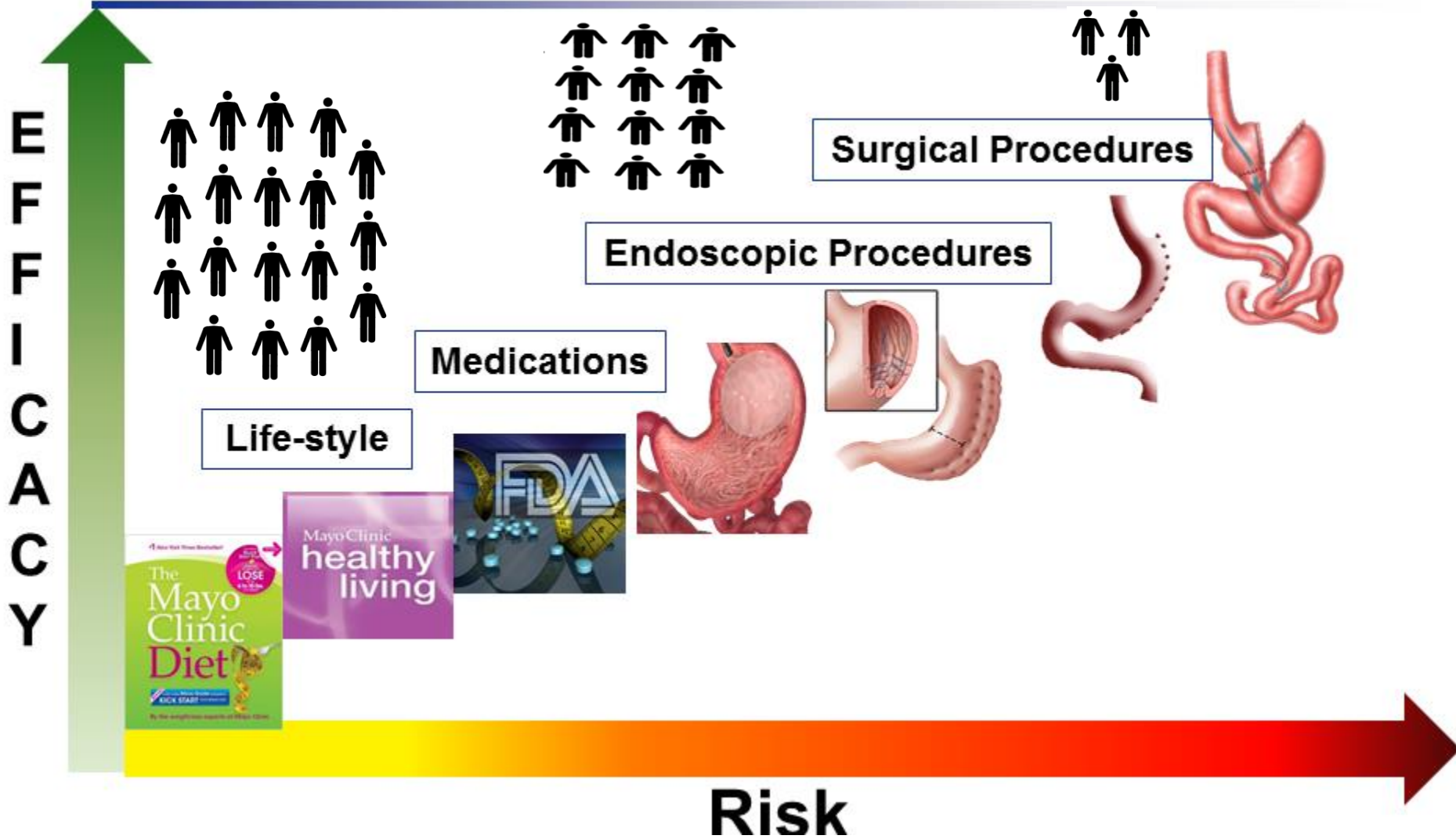


Conclusions

- ✓ Endoscopy plays a pivotal role in the multidisciplinary management of morbid obesity
- ✓ New bariatric endoscopic technologies and techniques mimicking surgery are expected
- ✓ Combination of techniques and “hybrid” approaches will be developed

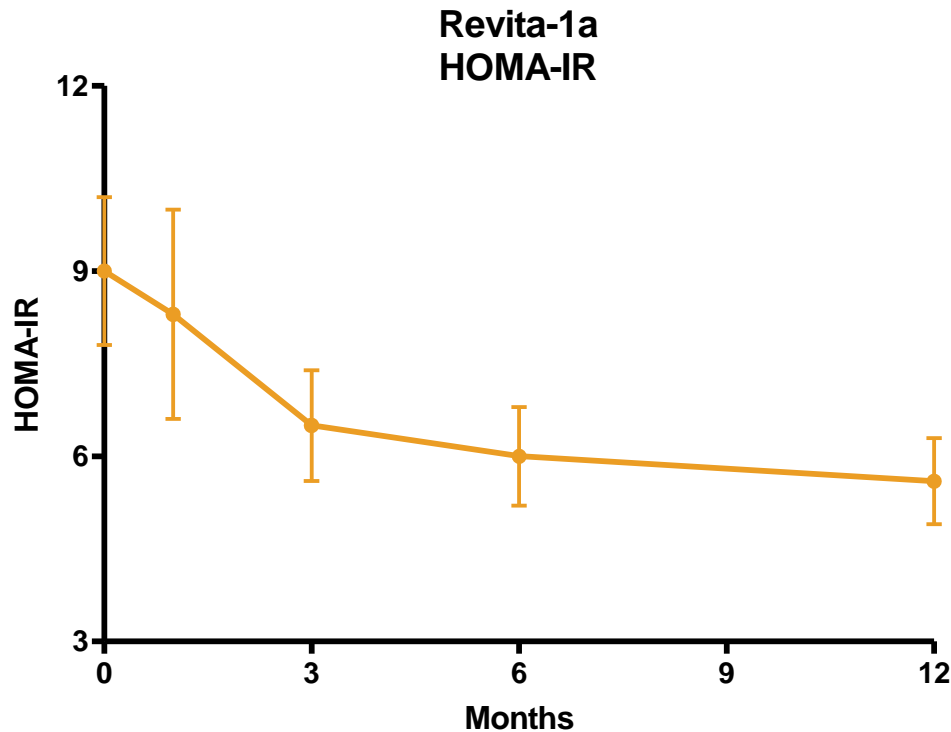
Obesity Continuum

1



Revita-1 Trial Key Finding: Durable Lowering of HOMA-IR

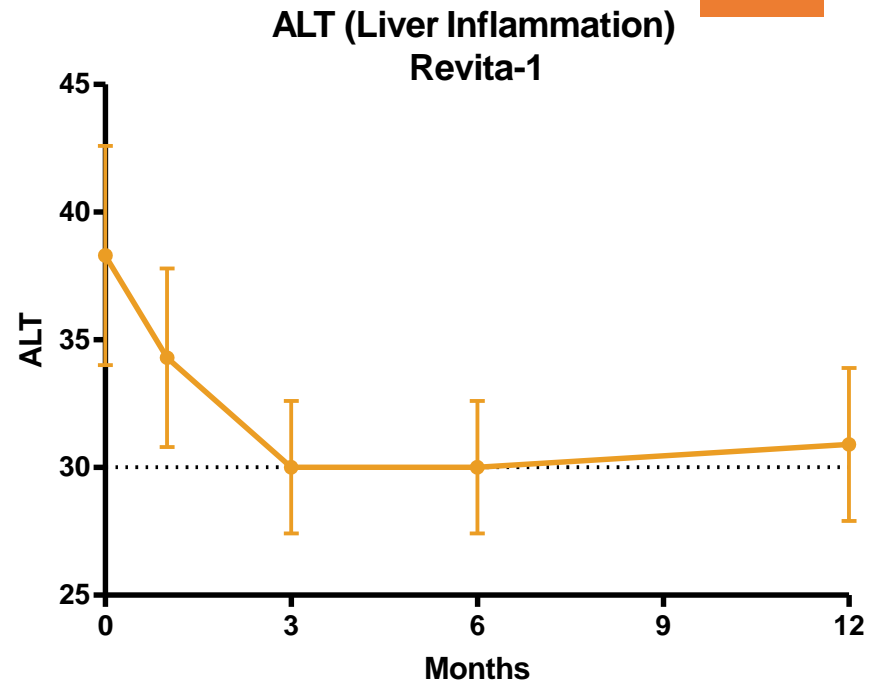
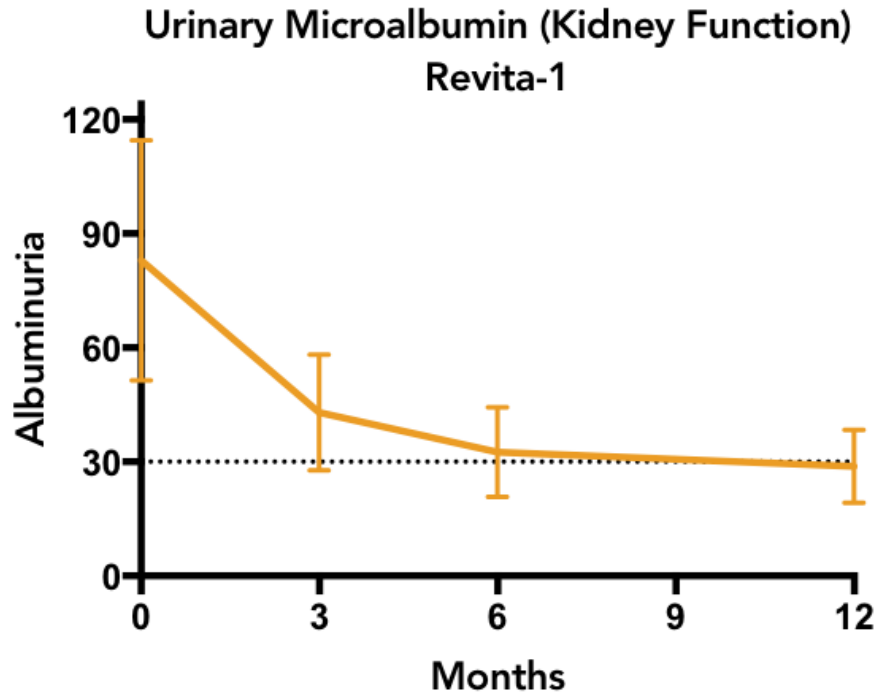
2



- Durable reductions in insulin resistance (HOMA-IR) - highlights our mechanism of action
- Reductions seen in both glucose levels and insulin levels
- Weight loss independent of metabolic improvement
- No lifestyle intervention in the study
- Consistent with observations from duodenal bypass surgery
- 27 patients at study entry & 23 patients at 12 month follow up

Revita-1 Trail: Lowering of Microalbuminuria and Hepatic Transaminase

3



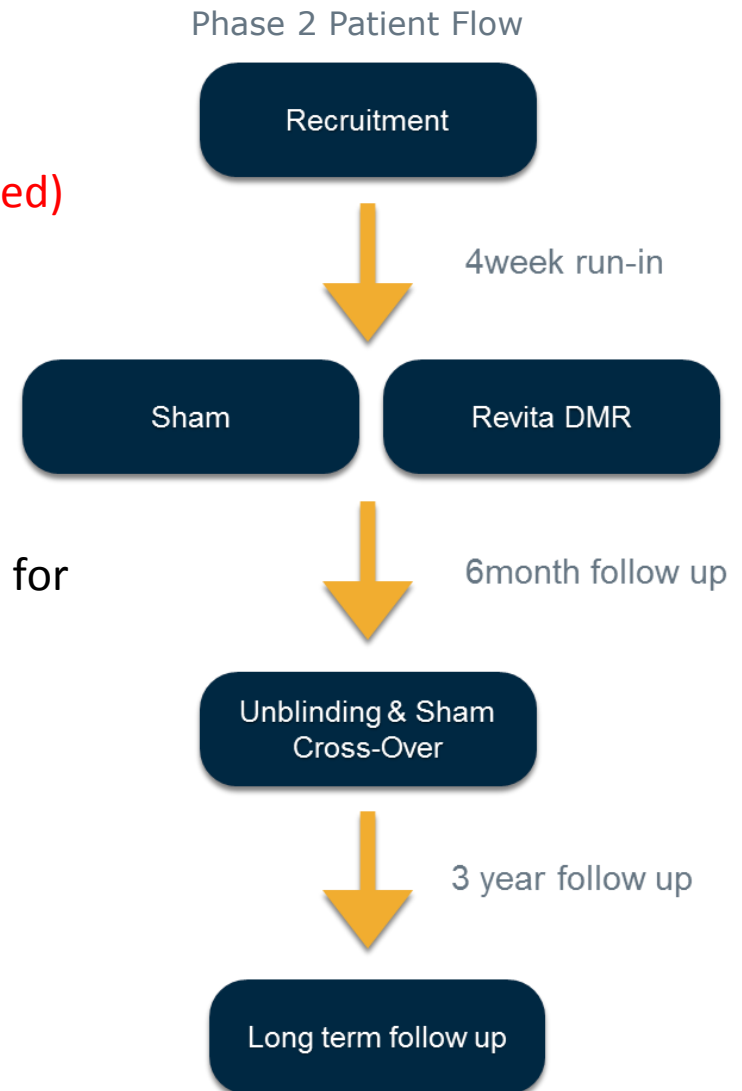
- Reduction in abnormal microalbuminuria – a marker of heart attack and stroke risk¹
- Normalization of ALT - a marker of NAFLD-NASH²
- Both valuable surrogate markers of insulin resistance and broader cardiometabolic risk

DATA ON FILE; FRACTYL LABS

¹ *Diab Med* Volume 20, Issue 4 April 2003 Pages 277–282

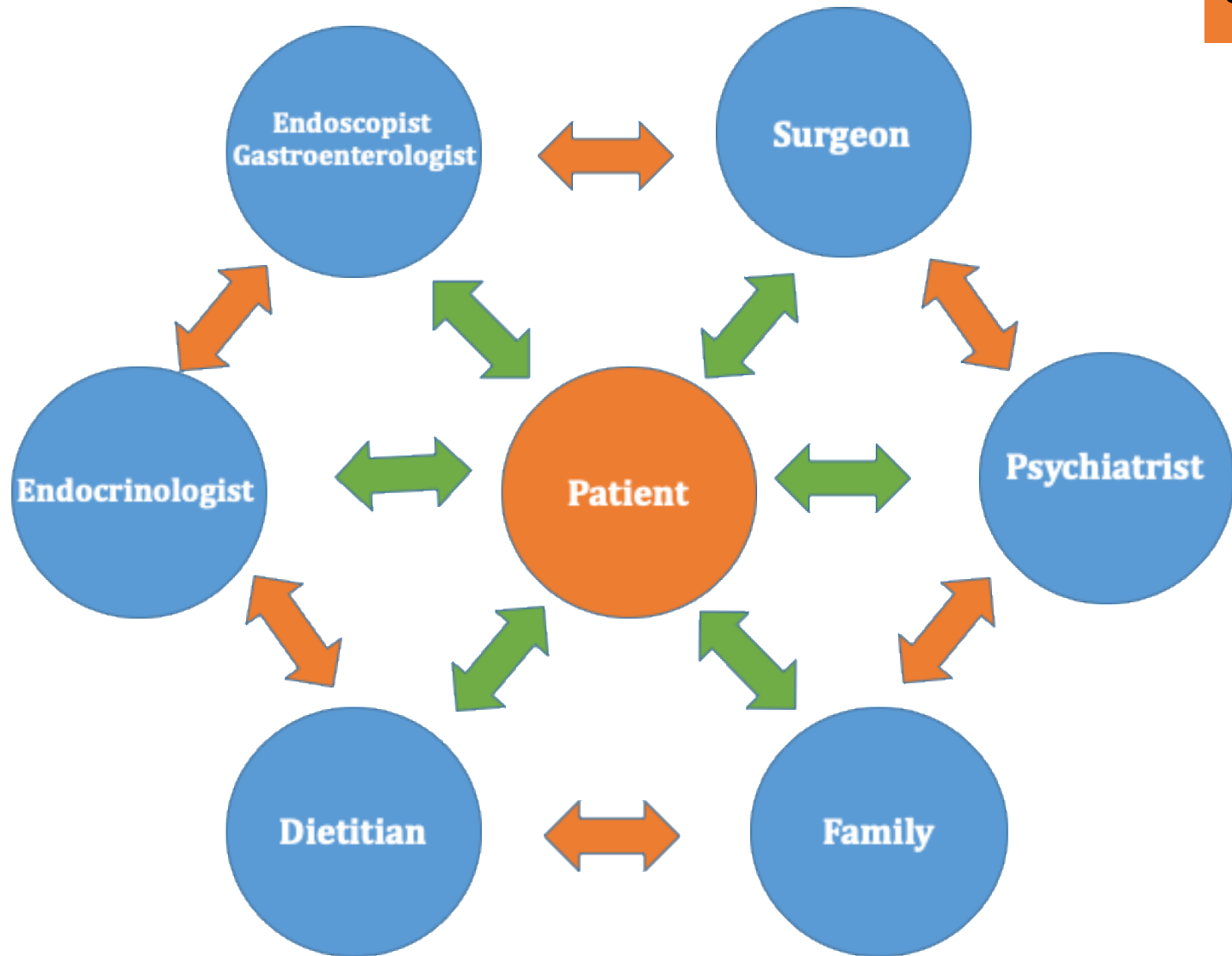
² *Ann Intern Med.* 2016;165(5):305-315.

- Two-Phased Multi-Center Study in Europe
 - ☞ Phase 1: Non-randomized (completed)
 - ☞ Phase 2: Double blind, sham control (completed)
- Inclusion Criteria
 - T2DM < 10 years
 - 28-75 years old
 - BMI 24-40
 - HbA1c 7.5 -10%
 - At least one oral glucose lowering medication for at least 3 months
 - No injectable medication
- Endpoints
 - Procedural safety
 - HbA1c improvement at 6 months
 - Long term follow up for safety



Multidisciplinary approach

5



T1 – Feasibility study

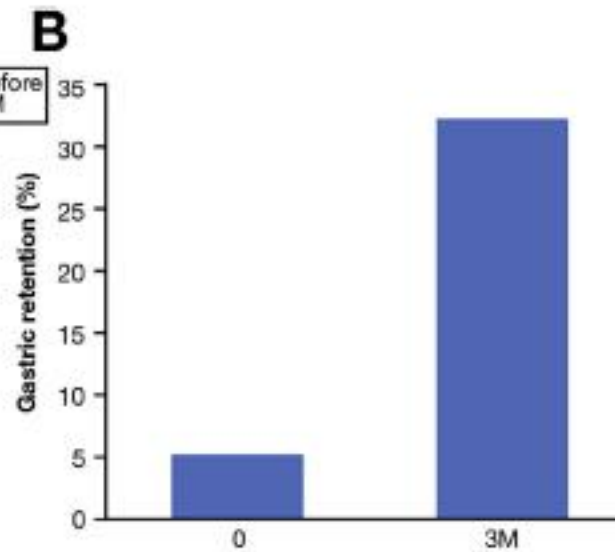
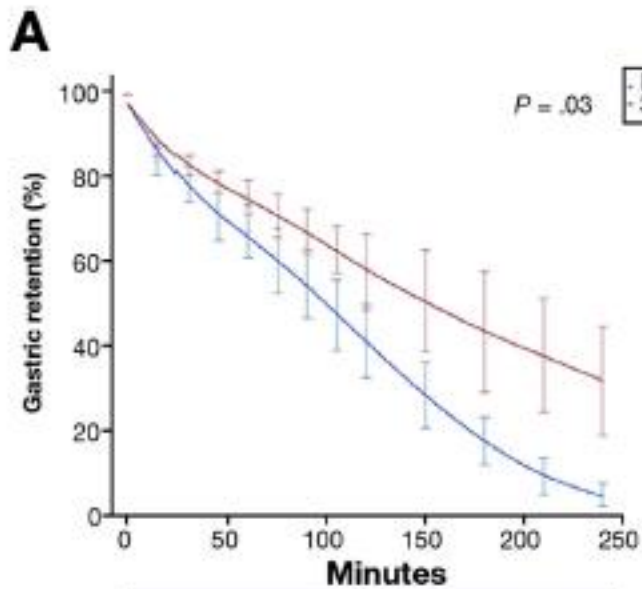
- **12** patients between April and July 2015
- BMI 34.6 kg/m² SD 2.2
- 1 patient excluded
- 8 women / 4 men
- *Gastrointestinal Endoscopy* 2017 85, 833-837 (6-months results)
- Light follow-up, similar to routine balloon follow-up
- GE visit : 1, 3, 6, 9 and 12 months
- Dietician visit : 1, 3, 6, 9 and 12 months
- ClinicalTrials.gov
NCT02534662

T2 – Multicentric efficacy study

- **51** patients in Brussels / Rome / Ostrava between February and December 2016
- BMI 33,5 kg/m² SD 2.6
- 0 patient excluded
- 24 women / 2 men
- Same follow-up
- ClinicalTrials.gov
NCT02582229

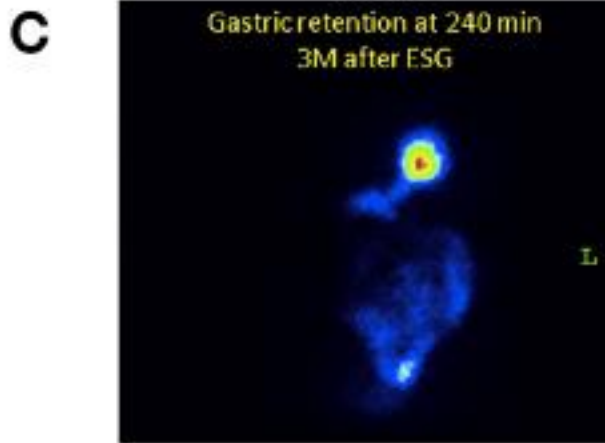
T3 – Randomized Control Trial

- **70** patients planned, starting September 2017, ongoing
- 3 centers Erasme (Brussels), APHM (Marseille), Gemelli (Rome)
- 0 patient excluded so far
- Procedure versus diet
- **47** patients in active arm
- **23** patients in control arm
- Control arm = diet for 6 months then crossover
- ClinicalTrials.gov
NCT03255005



(A) Changes in gastric emptying of solids before and 3 months after ESG.

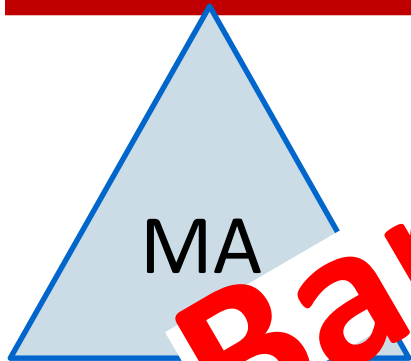
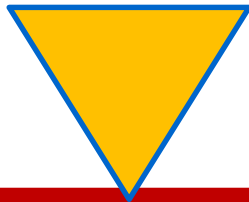
(B) Percent gastric retention of a solid meal at 240 minutes before and 3 months after ESG.



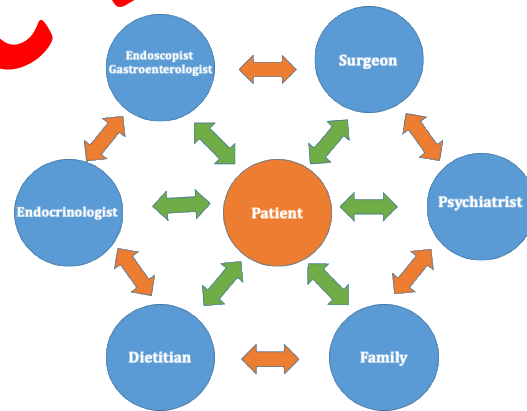
(C) Gastric scintigraphy image at 240 minutes after a solid meal ingestion depicting retained solid meal in a small gastric fundus cap after ESG.

(D) Upper gastrointestinal series with a radiopaque contrast demonstrating a sleeve effect with a small fundus cap.

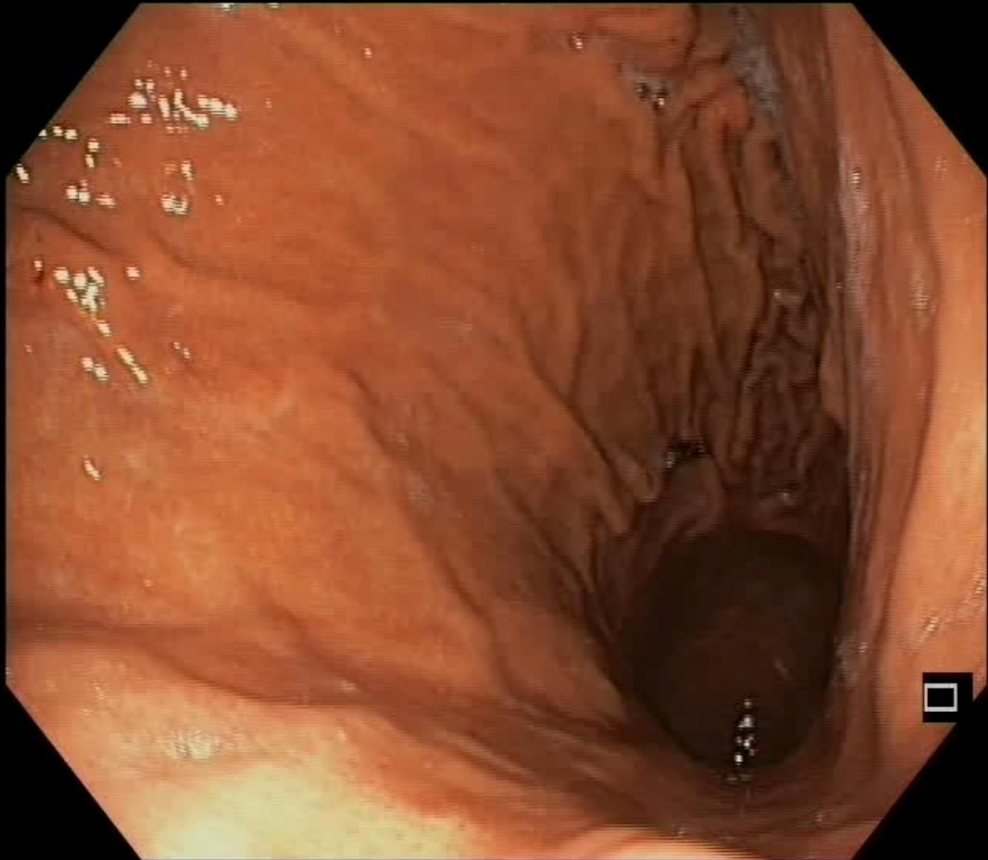
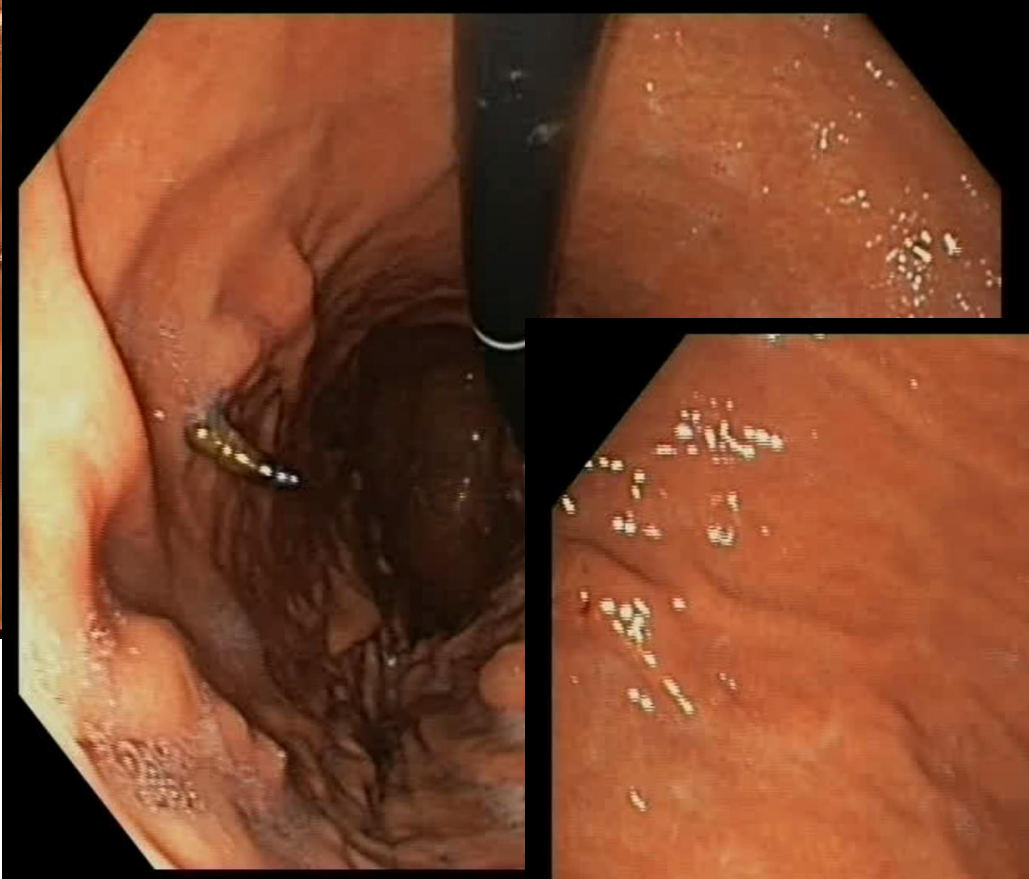
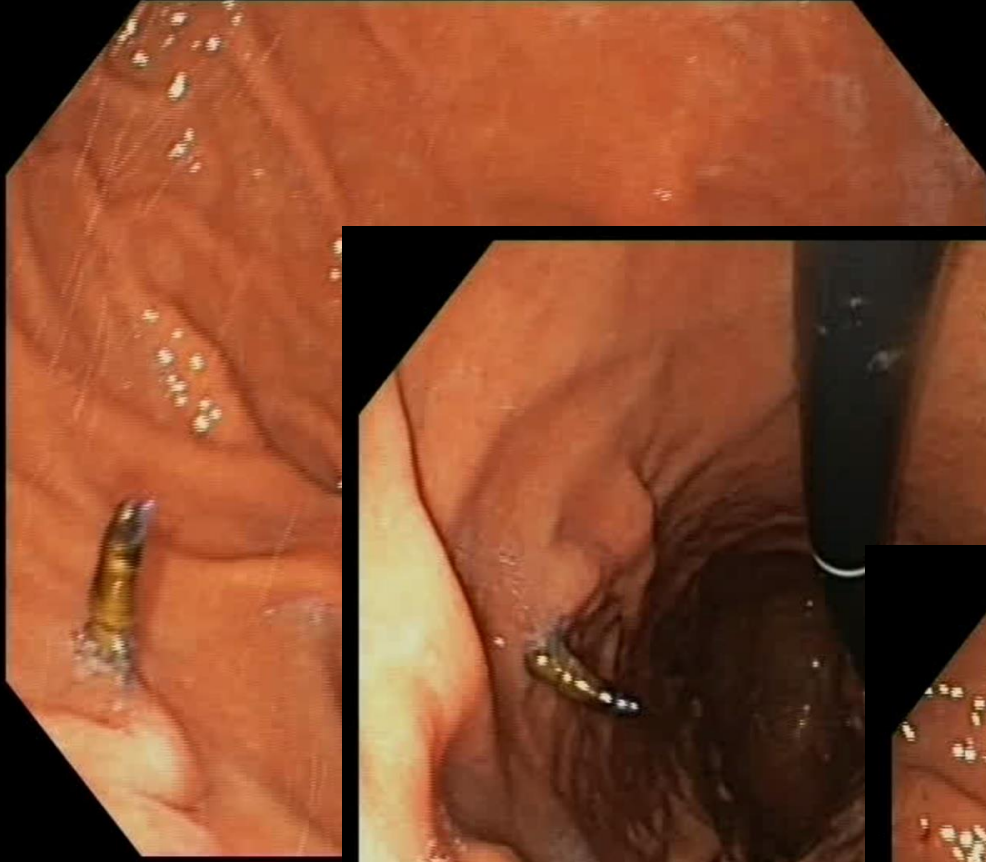
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ENDOLIVE ROMA



INTERNATIONAL CONFERENCE ON:

**Live demonstration workshop on
GI ENDOSCOPY**