CoMMiT

Comprehensive Obesity and Metabolism Management and Treatment Program

COLUMBIA UNIVERSITY

Intragastric Balloons

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Division of Digestive and Liver Diseases

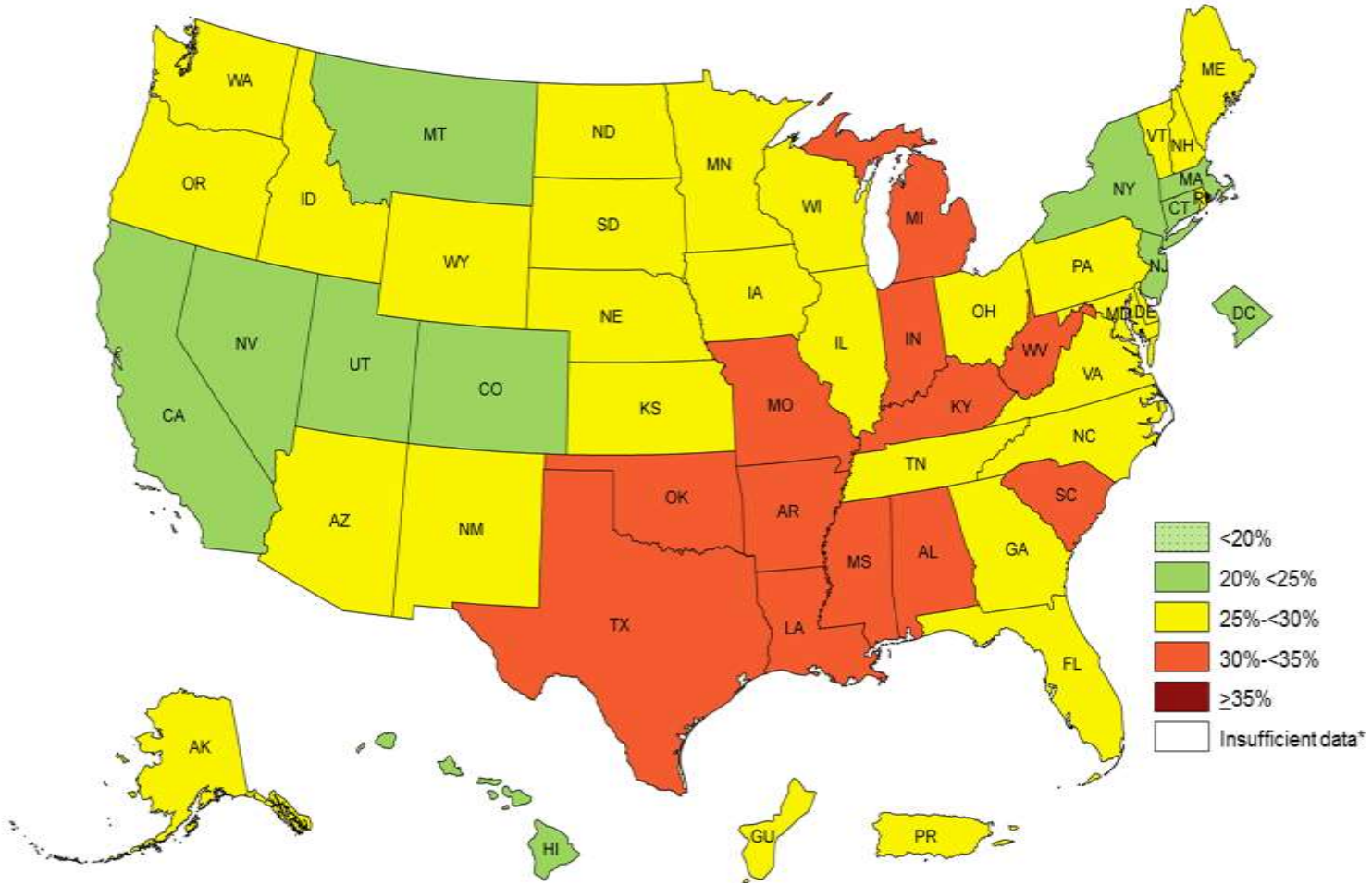
Columbia University

Outline

- Obesity epidemic and the role of endobariatric solutions
- Efficacy of competing therapies and surgery and measures of efficacy
- Current FDA approved Intragastric Balloons
  - Efficacy
  - Complications

Prevalence¶ of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2011

¶ Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.



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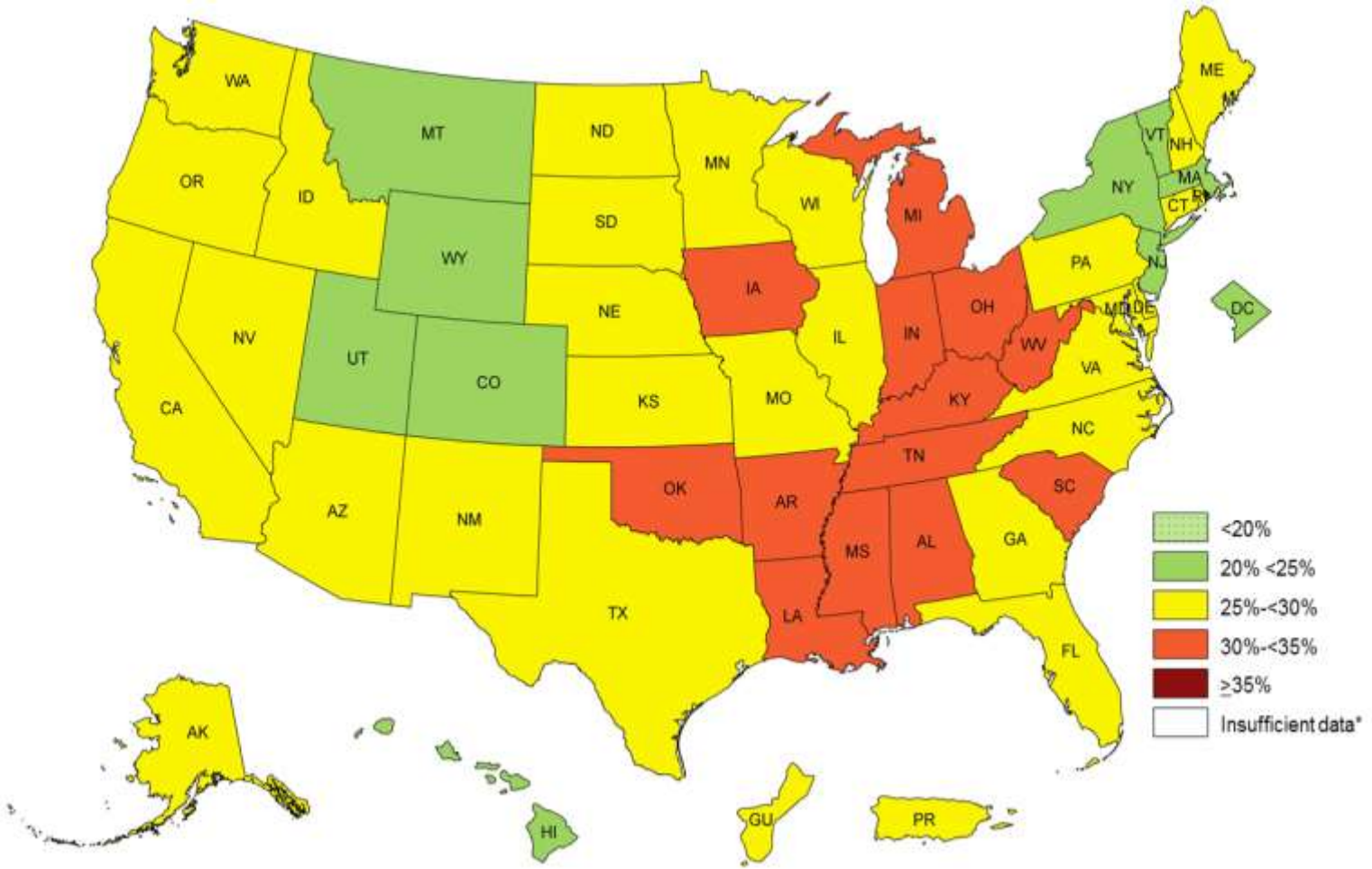

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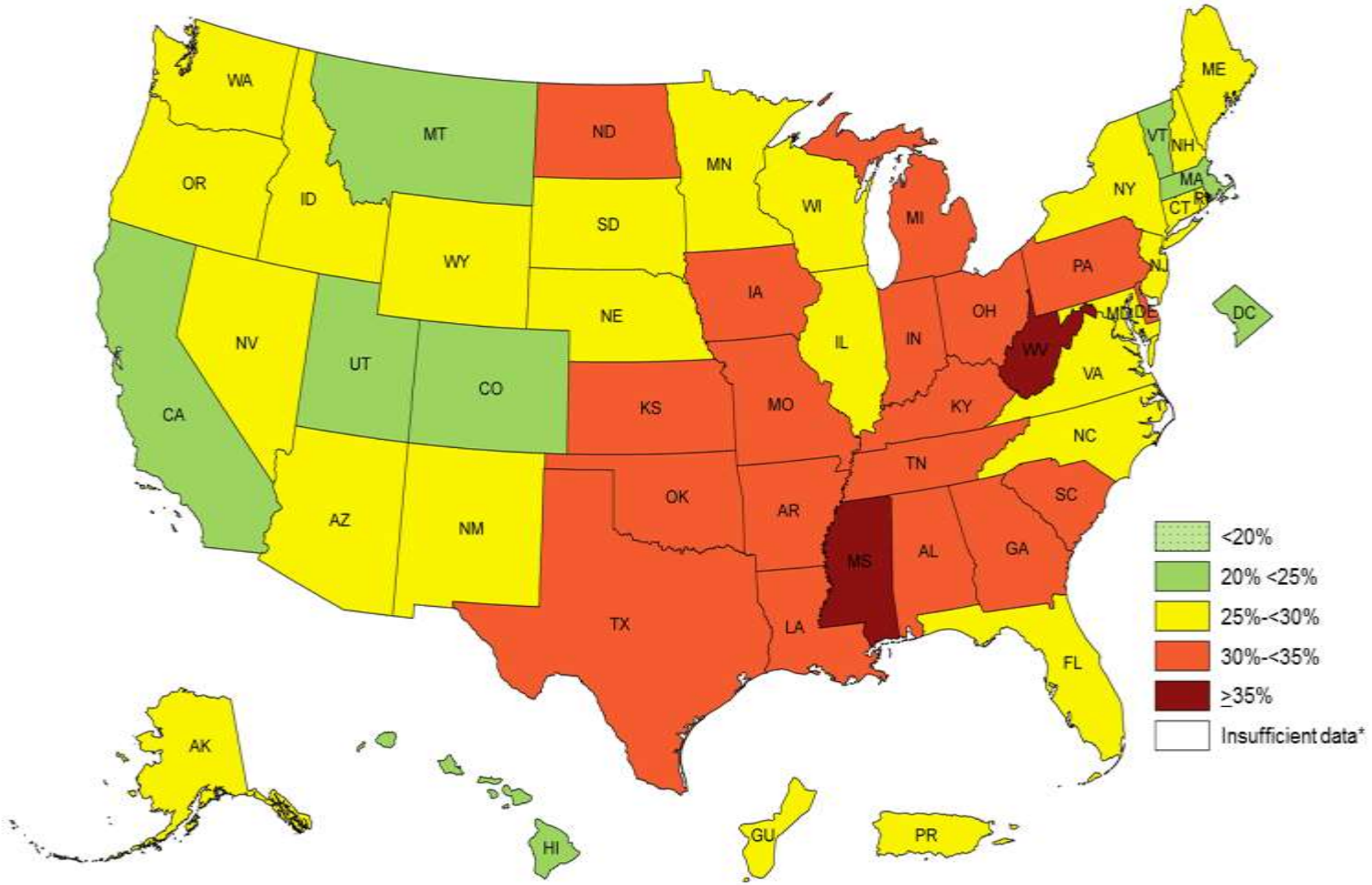

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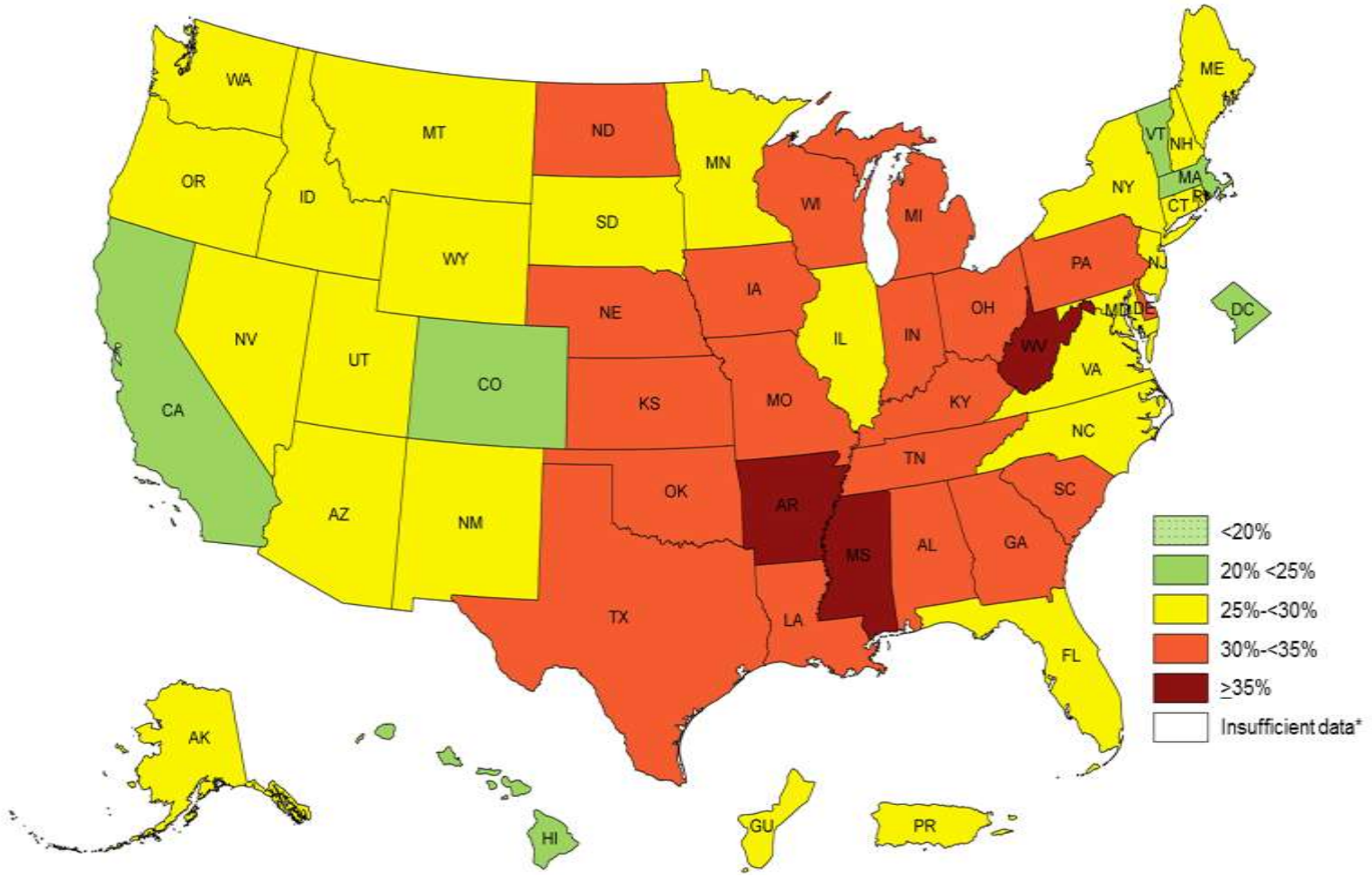

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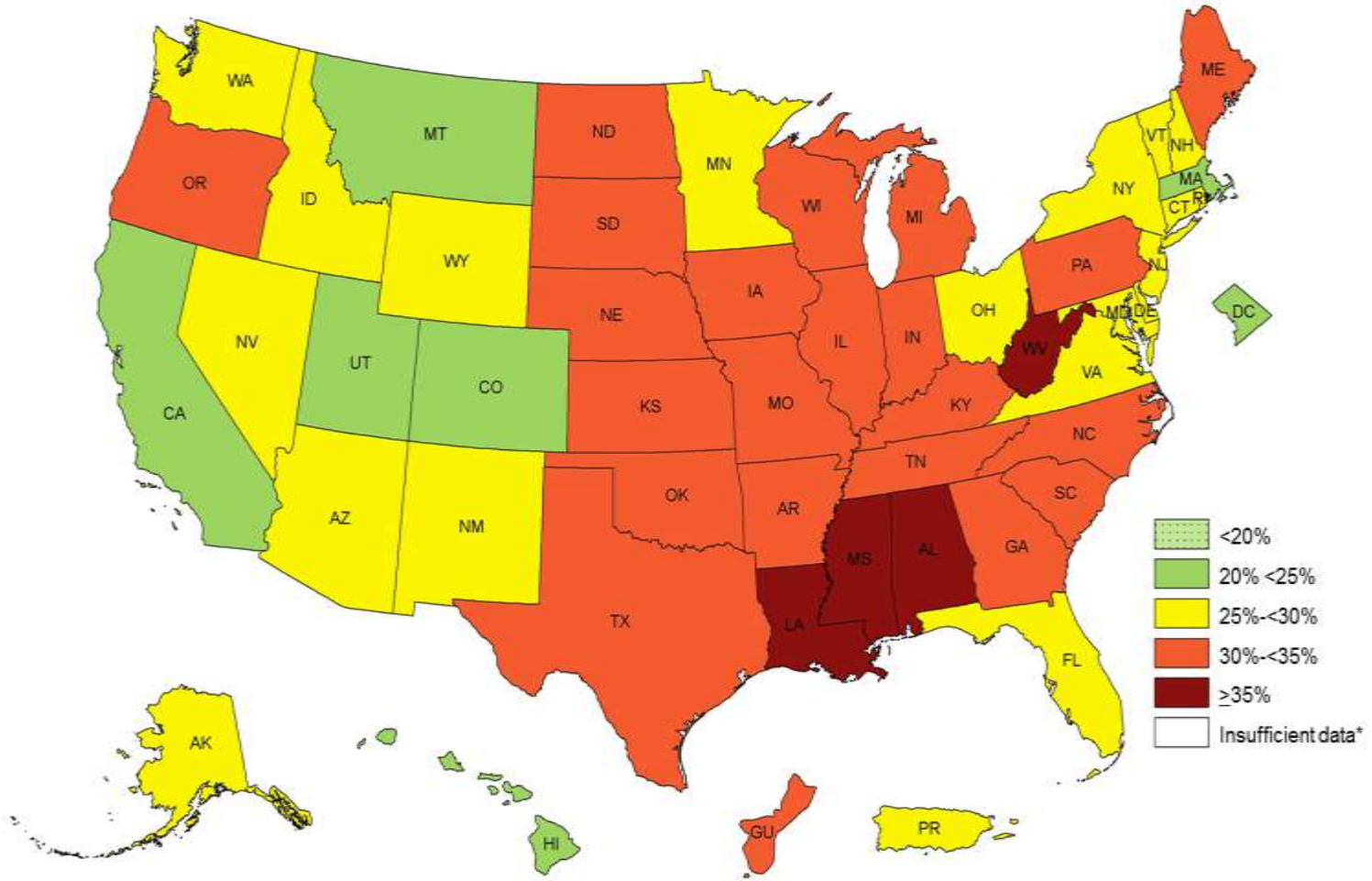

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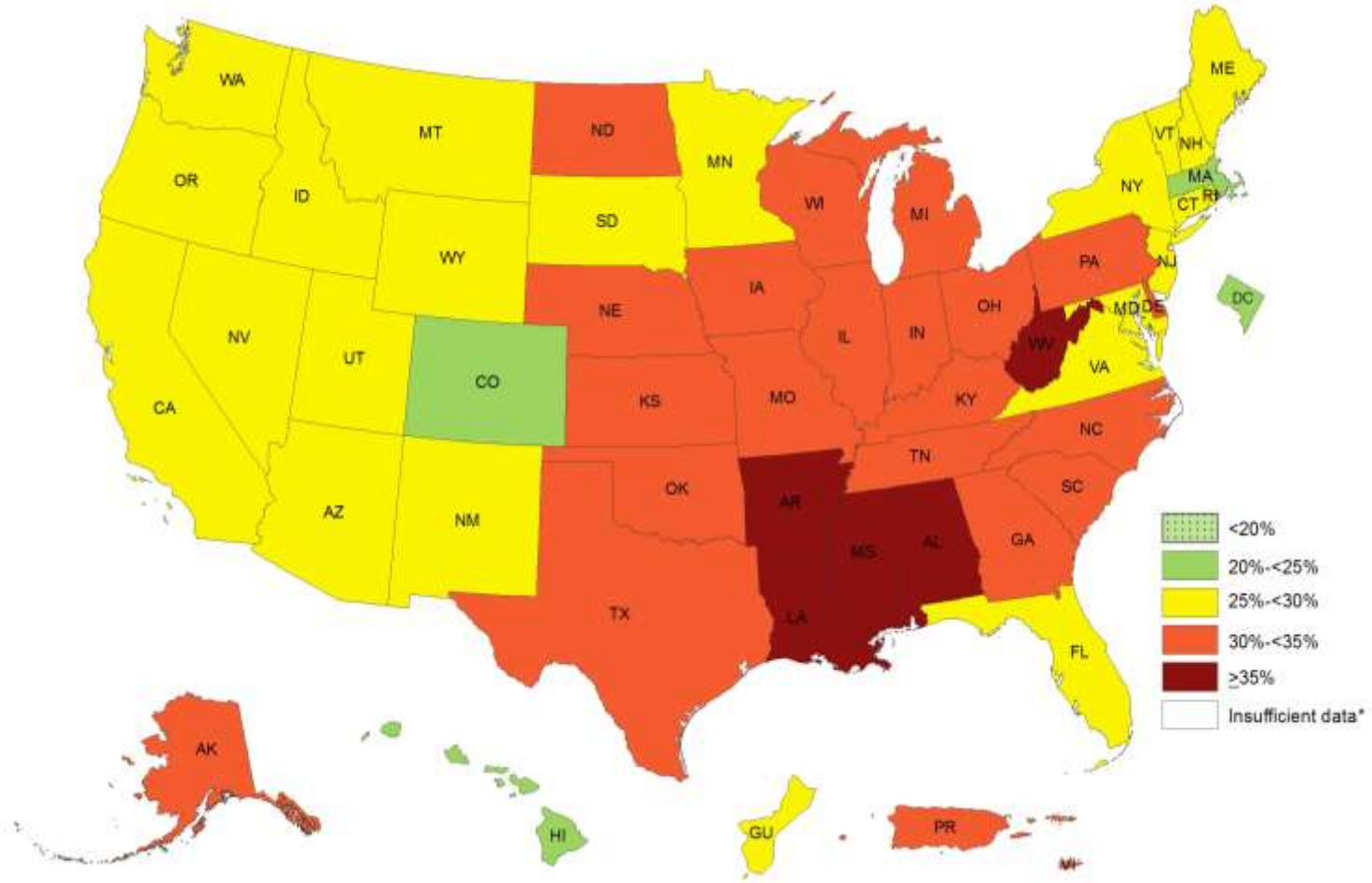

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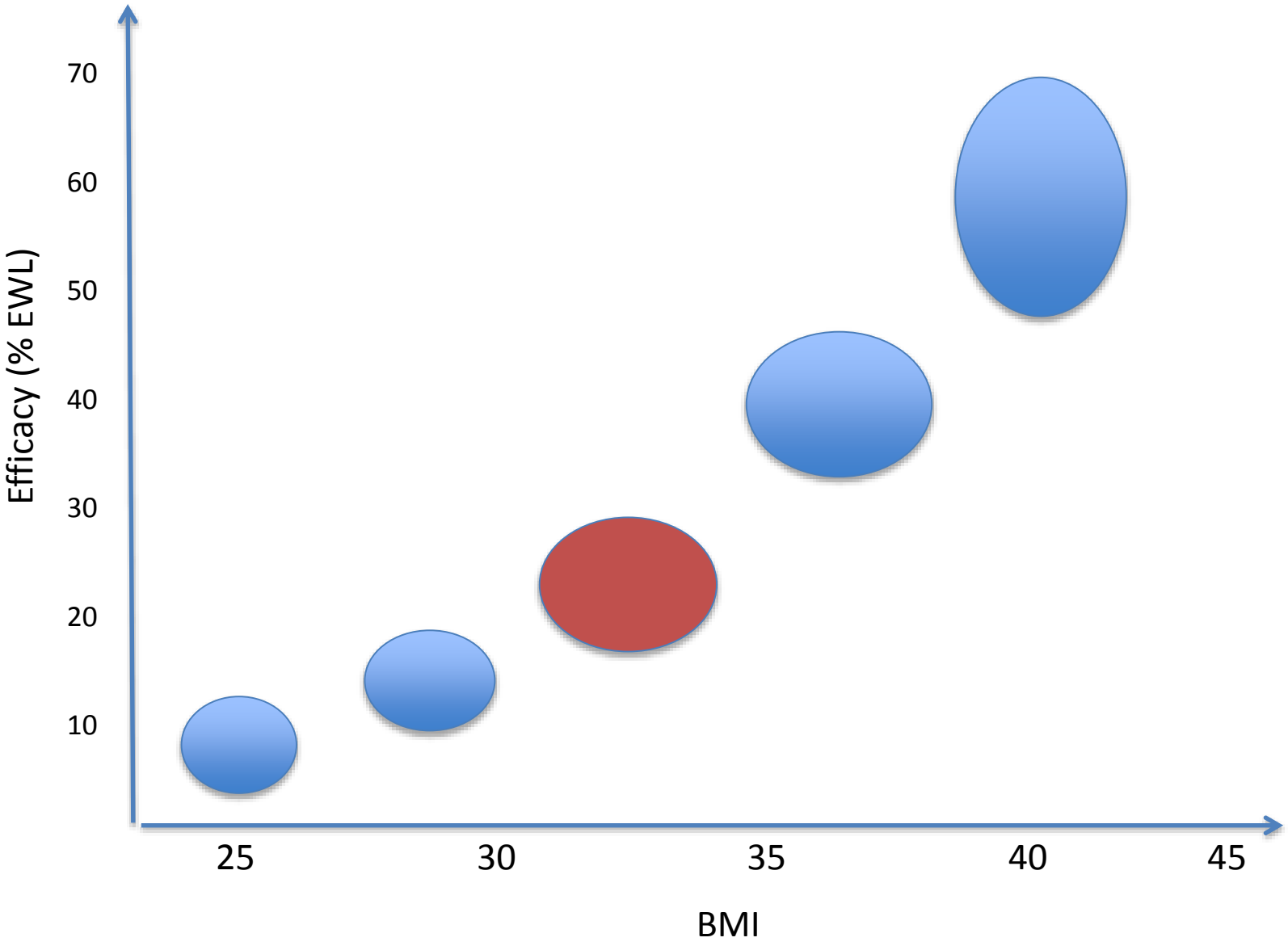
Obesity

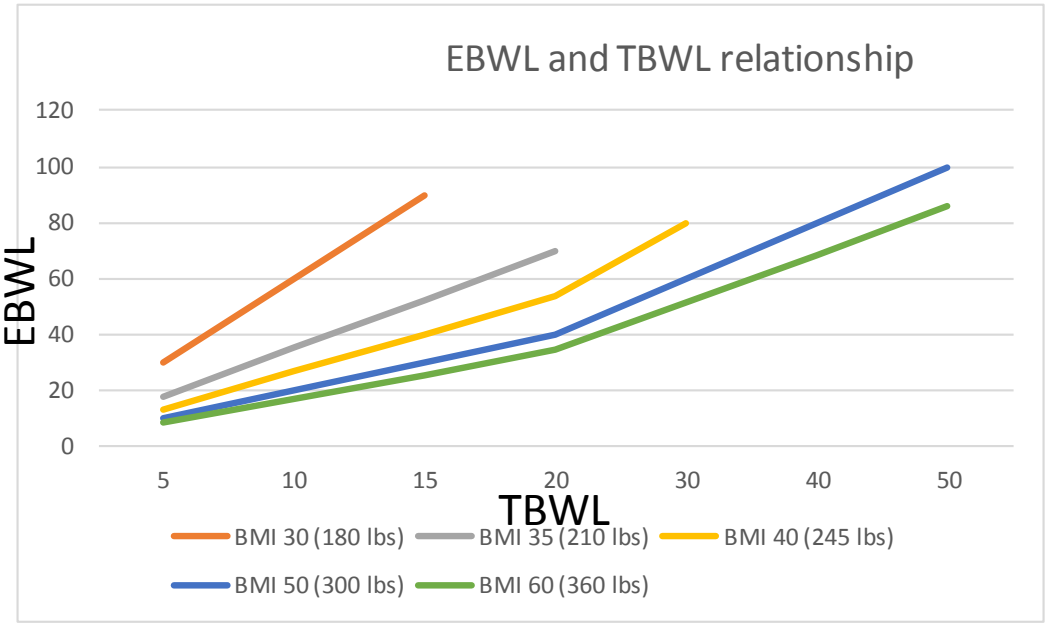
- 35 million obese Americans
- 12 million extremely obese (>BMI 40)
- 170,000 bariatric procedures
- 1:~500 obese individuals get intervention
- 98% do not get intervention

Goal of Endobariatrics: Expand the reach of bariatric therapy by offering a less invasive but effective alternative to surgery


Efficacy (% EWL)
70
60
50
40
30
20
10
25
30
35
40
45
BMI
LIFESTYLE
MEDICAL
ENDOSCOPIC
LAP/SLEEVE
ROUX en Y

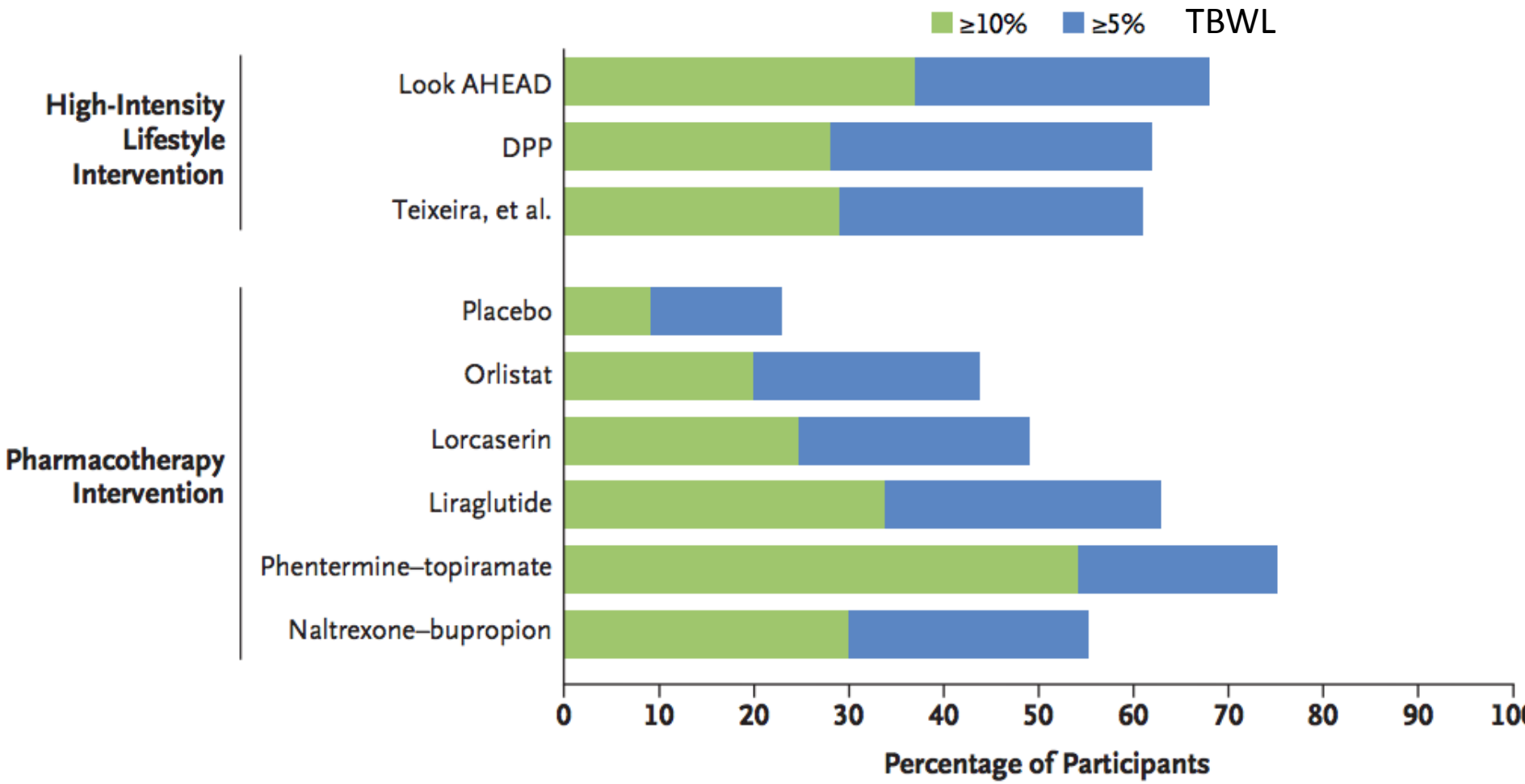
Weight loss measures

- BMI=Weight(Kg)/Height(M^2)
- TBWL (total body weight loss) = preoperative weight-postoperative weight
- EBWL =(TBWL) / (preop weight – ideal weight (at BMI 25)



BMI classification	
Underweight	< 18.5
Normal range	18.5 - 24.9
Overweight	⩾ 25.0
Preobese	25.0 - 29.9
Obese	⩾ 30.0
Obese class I	30.0 - 34.9
Obese class II	35.0 - 39.9
Obese class III	⩾ 40.0

Efficacy of non-invasive treatments



Heymsfield SB NEJM 2017

Efficacy of bariatric surgeries

	EBWL	TBWL
LapBand	40-50%	15-20%
Sleeve	60%	25%
RYGB	70%	30%
Duo Switch	80%	>30%

OBESITY COMPLICATION	% wt loss for Rx benefit	Notes	References
T2DM Prevention	3-10%	Maximum benefit at 10%	DPP (Lancet, 2009) SEQUEL (Garvey et al, 2013)
T2DM (HbA1c)	3-15%	HA1c still decreasing at >15%	Look AHEAD (Wing, 2011)
Dyslipidemia (TG/HDL)	3-15%	TG still decreasing at >15%	Look AHEAD (Wing, 2011)
HTN	5-15%	BP still decreasing at >15%	Look AHEAD (Wing, 2011)
NAFLD	10%	Improved steatosis, inflammation, mild fibrosis	Assy et al, 2007; Dixon et at, 2004; Anish et al, 2009
Sleep Apnea	10%	e benefit at ≤ 5%	Sleep AHEAD (Foster, 2009) Winslow et al, 2012
Osteoarthritis	5-10%	Improved symptoms and joint stress mechanics	Christensen et al, 2007 Felson et al, 1992; Aaboe et al, 2011
Stress Incontinence	5-10%		Burgio et al, 2007 Leslee et al, 2009
GERD	5-10% (F) 10% (M)		Singh et al, 2013 Tutujian R, 2011
PCOS	10-15%	Lower androgens, improved ovulation, increased insulin sensitivity	Panidis D et al, 2008 Norman et al, 2002 Moran et al, 2013

Daniel S, Soleymani T, Garvey WT. Curr Opin Endocrinol Diabetes Obes, 20:377-388, 2013.

Endoscopic Interventions
What are the goals?/Where is the bar?

- “minimum threshold of efficacy” (ASGE Task Force)
    - 25% EWL or 15% greater EWL then control arm at 12 months
    - Threshold incidence of complications at 5%
- Improvement in comorbid conditions
    - Less data
    - HTN, DM2, Hyperlipidemia

How can endoscopic interventions "mimic" surgery

Space Occupying/Restrictive

- **Intragastric Balloons**
- Stomach volume reduction
- Outlet obstruction
- Aspiration

Small Bowel Physiology/Bypass

- Small bowel sleeves
- Resurfacing
- Endoscopic anastomoses

FDA approved Intragastric Balloons

ReShape™
Non-Surgical Weight Loss Procedure

OBALON

Orbera™
managed weight loss system

Content	Saline	Air mixture	Saline
Volume	450 x2 *	250 x 3	400-700
Placement	EGD	Non-endosocpic/AXR	EGD
Removal	EGD	EGD	EGD
“Published N”	356	387	>2000 (RCT 300s)

Indications and Contraindications

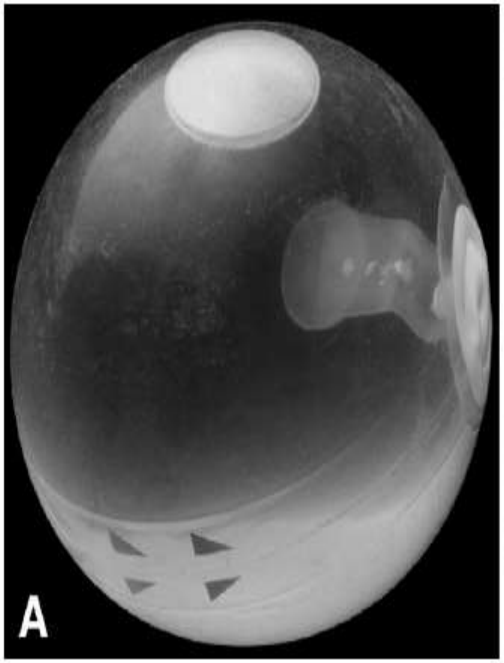
Indications

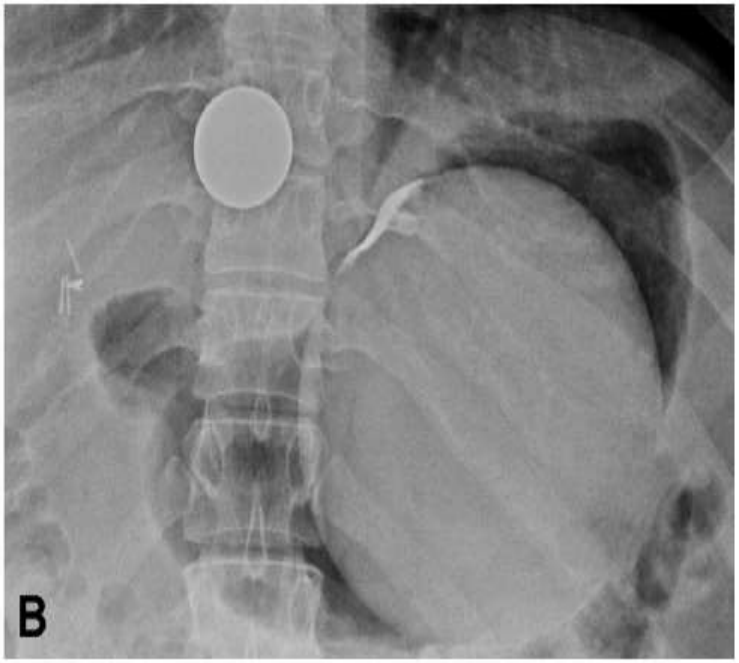
- Obese patients BMI 30-40 who have failed diet and exercise
- (ReShape only) with one obesity associated comorbidity
- (Obalon/Orbera) enrolled in weight loss program

Contraindications

- Large Hiatal Hernia
- Prior gastric surgery
- Inflammatory Bowel Disease
- Bleeding Risk
- Inability to take PPI
- Pregnancy
- Psychiatric Disease

Orbera balloon





Placement: Endoscopic

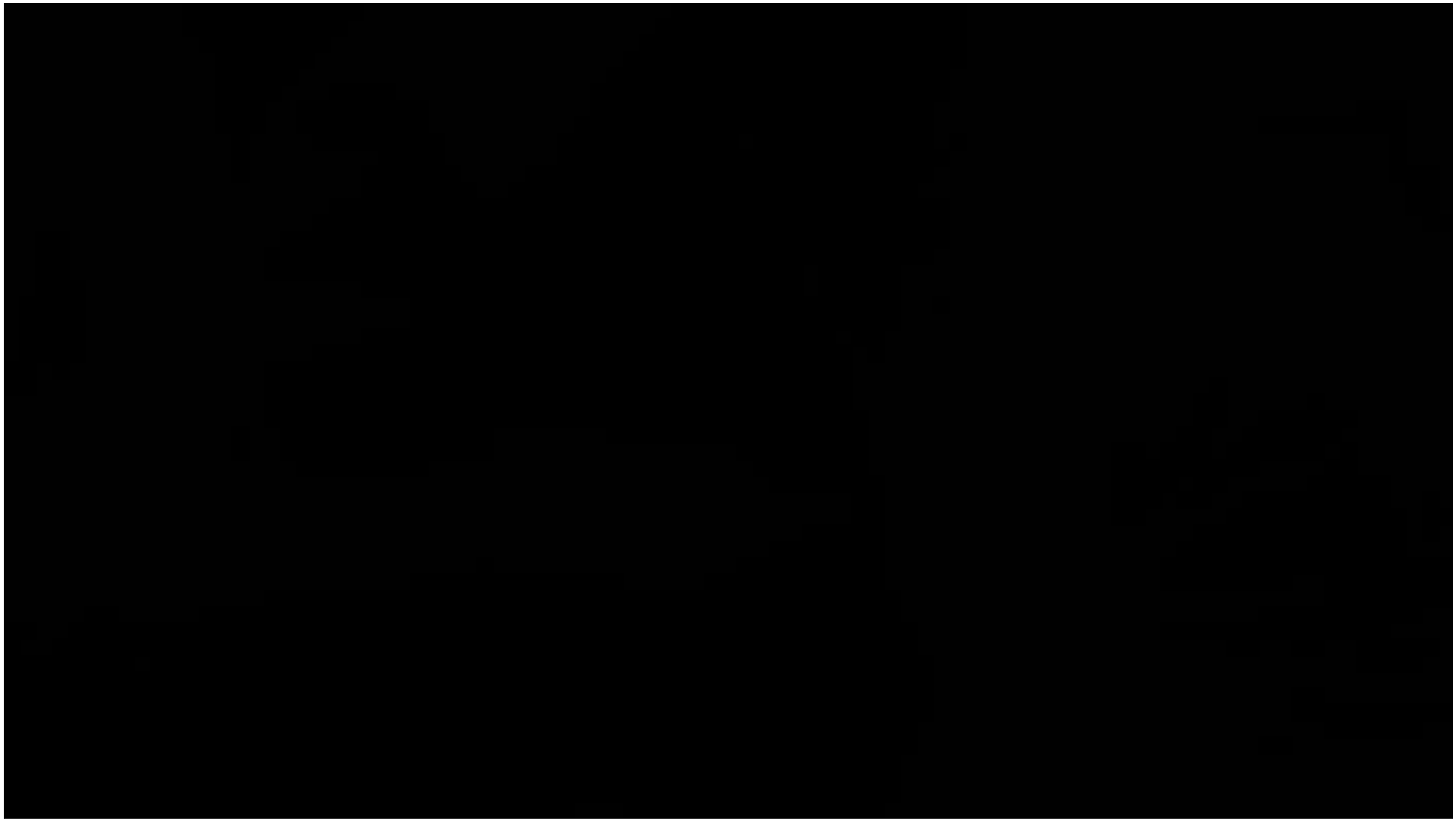
Anesthesia: GA, MAC

Inflation Compound: Sterile Water (methylene blue off label)

Inflation Volume: 500-700 ml

Duration of Therapy: 6 months

Removal: Endoscopic



Orbera balloon

Short term efficacy

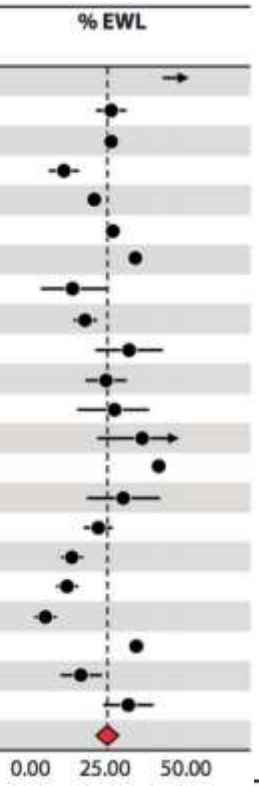
Reference	No.	Starting BMI, kg/m^2	Fill volume, mL	Weight loss at 3 mo, kg	Weight loss at 6 mo, kg	% of weight loss at 3 mo
Bonazzi et al,[22] 2005	12	38.5	700	12.4	14.4	86
Fuller et al,[37] 2013	31	36.0	450-750	10.5	14.4	73
Mathus-Vliegen and Tytgat,[38] 2005	19	43.3	500	12.9	16.7	77
Mathus-Vliegen and Eichen,[26] 2014	19	43.0	500	13.1	16.4	80
Peker et al,[39] 2010	31	41.8	600	12.17	15.04	81
Stimac et al,[40] 2011	171	41.9	600	12.8	16.9	76
Totte et al,[41] 2001	126	37.7	500	13.7	15.4	89
Total	409					
Weighted mean ± weighted SD				12.9 ± 0.8	16.0 ± 0.9	80 ± 6

Short term efficacy – prospective RCT

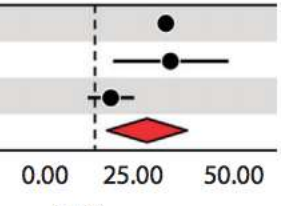
IGB device	IGB treatment time (wks)	Number of subjects		% EWL	*p* value
		N (total)	Study arm		
Orbera*	12	32	16 (IGB + diet arm)	34 ± 4.8	$p < 0.001$
Genco et al. [15]			16 (sham + diet arm)	2.1 ± 1	
Orbera*	24	66	31 (IGB + behavioral modification)	50.3	$p < 0.001$
Fuller et al. [68]			35 (behavioral modification alone)	16.9	
Orbera*	24	114	60 (IGB)	44.6 ± 23.9	$p < 0.01$
Majanovic et al. [69]			54 (cognitive behavioral therapy)	24.3 ± 16.0	
Orbera*	24	32	16 (IGB)	39.3	$p = 0.189$
Peker et al. [56]			16 (lap band)	32.3	

Does Orbera balloon meet ASGE PIVI threshold?

Study name	Subgroup within study	Statistics for each study			
		Mean	Lower limit	Upper limit	Total
Sallet 2004	Orbera	50.900	44.777	57.023	85
Herve 2005	Orbera	27.000	21.747	32.253	100
Angrisani 2006	Orbera	27.100	25.001	29.199	82
Ganesh 2006	Orbera	10.900	5.559	16.241	16
Genco 2007	Orbera	21.300	17.900	24.700	129
Crea 2008	Orbera	27.400	26.616	28.184	138
Genco 2009	Orbera	35.100	33.961	36.239	80
Ohta 2009	Orbera	14.000	2.913	25.087	8
Al Kahtan 2009	Orbera	18.000	13.680	22.320	137
Mui 2010	Orbera	32.900	21.325	44.475	68
Genco 2010	Orbera	25.100	17.838	32.362	50
Nikolic 2011_1	Orbera	27.800	15.300	40.300	19
Nickolic 2011_2	Orbera	37.400	22.437	52.363	24
Kotzampassi 2012	Orbera	43.000	41.127	44.873	384
Bozkurt_1_2012	Orbera	30.900	18.248	43.552	15
Bozkurt_2	Orbera	22.500	17.509	27.491	68
Bozkurt_3	Orbera	13.500	9.917	17.083	57
Boskurt_4	Orbera	12.300	8.741	15.859	62
Boskurt_5	Orbera	4.700	0.667	8.733	18
Farina 2012	Orbera	34.900	31.495	38.305	14
Dogan 2013	Orbera	16.700	9.743	23.657	50
Fuller 2013	Orbera	32.700	23.900	41.500	31
	Random	25.441	21.457	29.426	



Study name	Statistics for each study				Sample size	
	Difference in Mean	Lower limit	Upper limit	P	IGB	Control
Genco 2006	31.900	29.498	34.302	0.000	16	16
Fuller 2013	33.400	17.627	49.173	0.000	31	35
Mohammed 2014	17.300	10.560	24.040	0.000	84	44
Random	26.956	15.666	38.246	0.000		



Abu Dayyeh et al GIE 2015

Orbera – benefits in comorbid conditions

- HTN, DM, hyperlipidemia

Comparison	Odds ratio	95% CI	No. of studies (subjects)	I^2	*P*-value
Diabetes resolved	1.4	1.3, 1.6	9 (4,232)	0%	<0.001
Diabetes improved or resolved	9.3	7.6, 11.4	6 (3,556)	0%	<0.001
Hypertension resolved	2.0	1.8, 2.2	8 (3,961)	0%	<0.001
Hypertension improved or resolved	9.1	5.5, 15.2	6 (3,556)	71%	<0.001
Dyslipidemia resolved	1.7	1.2, 2.6	6 (3,101)	84%	<0.001

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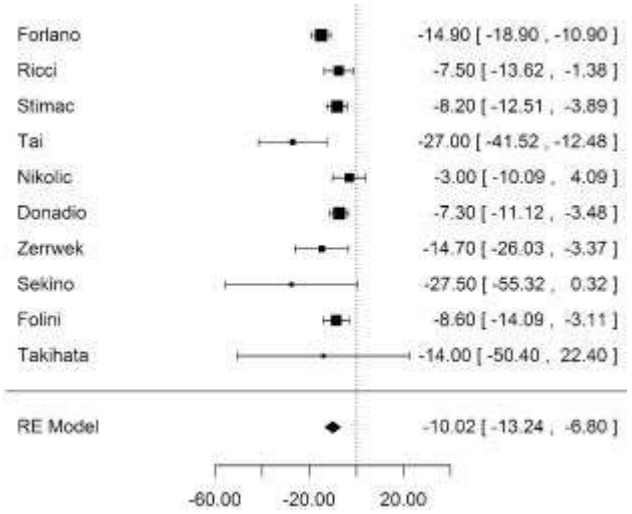
- Non-alcoholic fatty liver disease (NAFLD)

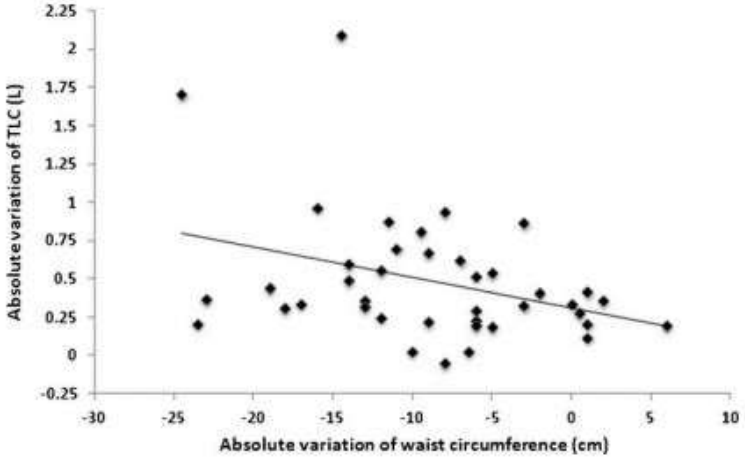


Popov VB et al Am J Gastro 2017
Popov VB Dig Dis Sci 2016

Orbera – benefits in comorbid conditions

- Lung function

	Baseline	After 6 months	*p* value[a]
Weight (kg)	111 (95.5–119.8)	93.8 (80.2–108.7)	0.0001
BMI (kg/m^2)	39.1 (35.7–44.2)	34.5 (30.2–40)	0.0001
FVC (L)	3.21 (2.86–3.83)	3.38 (3.06–4.02)	0.0001
FEV_1 (L)	2.75 (2.35–3.14)	2.88 (2.57–3.26)	0.0001
FEV_1/FVC (%)	85 (82.5–88.8)	81 (79–84)	0.0001
MIP (cm H_2O)	68 (51.3–114.5)	68.5 (38.8–116.0)	0.21
MEP (cm H_2O)	85.5 (70.5–102.8)	74.5 (65–121)	0.91
TLC (L)	4.42 (3.83–4.87)	4.68 (4.17–5.60)	0.0001



Mafort TT et al Obes surg 2014

- Obstructive Sleep apnea

Sleep study	Before	After (BIB x 6 months)
Obstructive apneas, No.	277 ± 105	90 ± 120§
Central apneas, No.	7 ± 17	1 ± 1
Mixed apneas, No.	16 ± 17	1 ± 1
Hypopnea, No.	116 ± 83	36 ± 55‡
AHI, events/h	59.3 ± 18.1	14.0 ± 12.4§
ESS score	11.2 ± 5.2	4.7 ± 2.3†

Busetto L et al Chest 2005

Real life US experience w/ Orbera

- Multicenter, registry study
- 6, 9 and 12 months follow up
- 316 patients
- Average BMI 37.9
  - 16% diabetics
  - 19% dyslipidemia
- Procedural issues at placement: 4/316 failures
- Complications:
  - <2% early removal rate
  - Ulcers – 0.3% pre and 0.5% post placement
  - Esophagitis 3 pre and 8% post placement

Vargas E et al DDW 2017

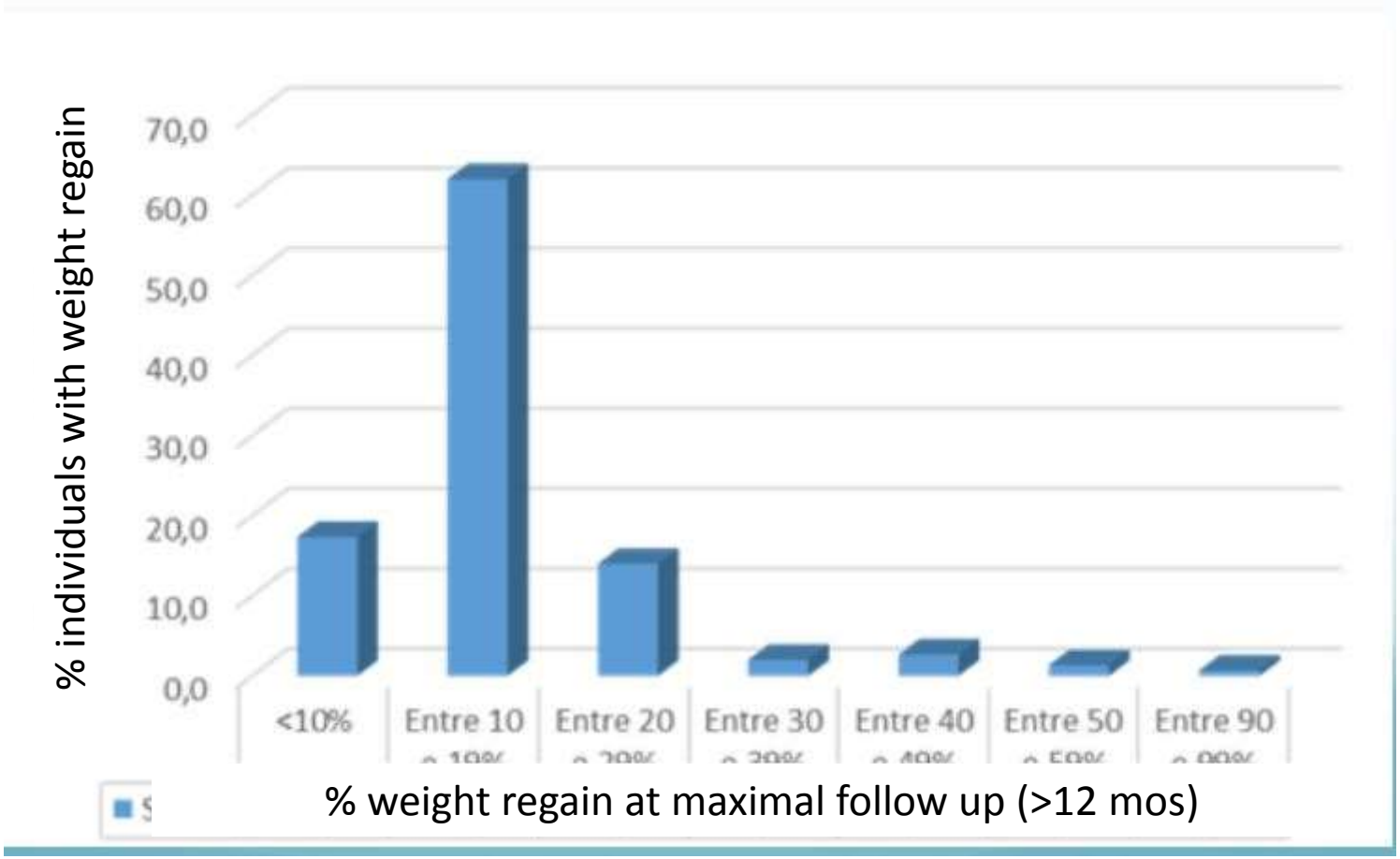
Real life US experience w/ Orbera

- Weight loss
  - 7,10,13% TBWL at 3,6,9 mos
  - 84% achieved >5% TBWL
  - 56% achieved >10%TBWL
- A1C declined from 6.1 to 6.9 % (although therapy may have changed in interval)
- SSRI use had an inverse association with weight loss

Benefits beyond 12 months

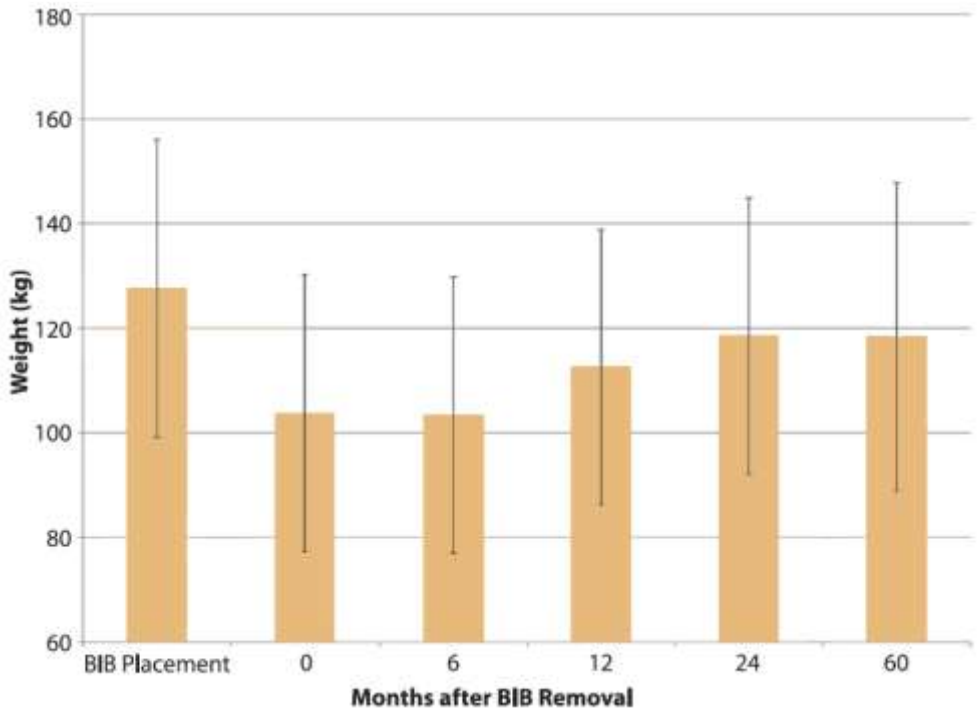
- Observation study of 224 patients up to 5 years after IGB placement
- 6 months outcomes: 66% EWL
- Between 2 and 5 years 67% of patients regained weight
- 79% of patients regained less then 20% of weight

Benefits beyond 12 months



Vargas E et al DDW 2017

Benefits beyond 12 months



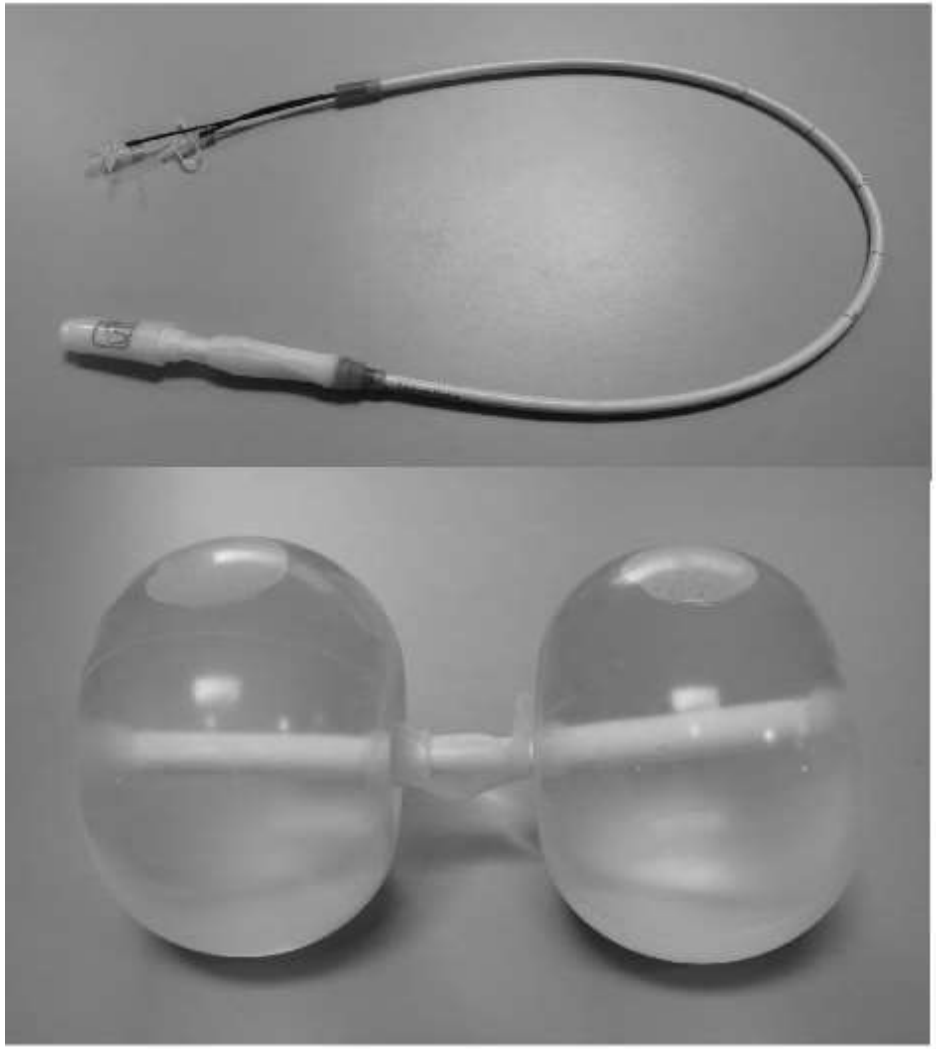
AbuDayyeh GIE 2016

Extended IGB treatment beyond 6 months

- Repeated balloon placement (N=19)
  - Lower EWL with second balloon (30 vs 49%)

  (Dumencau et al)
- Orbera balloon for 12 months
  - Compared to LapBand greater EWL at 12 mos (70% vs 53 %)
  - Additional EWL between 6 and 12 months was 12%

ReShape balloon



ReShape Balloon

Placement: Endoscopic

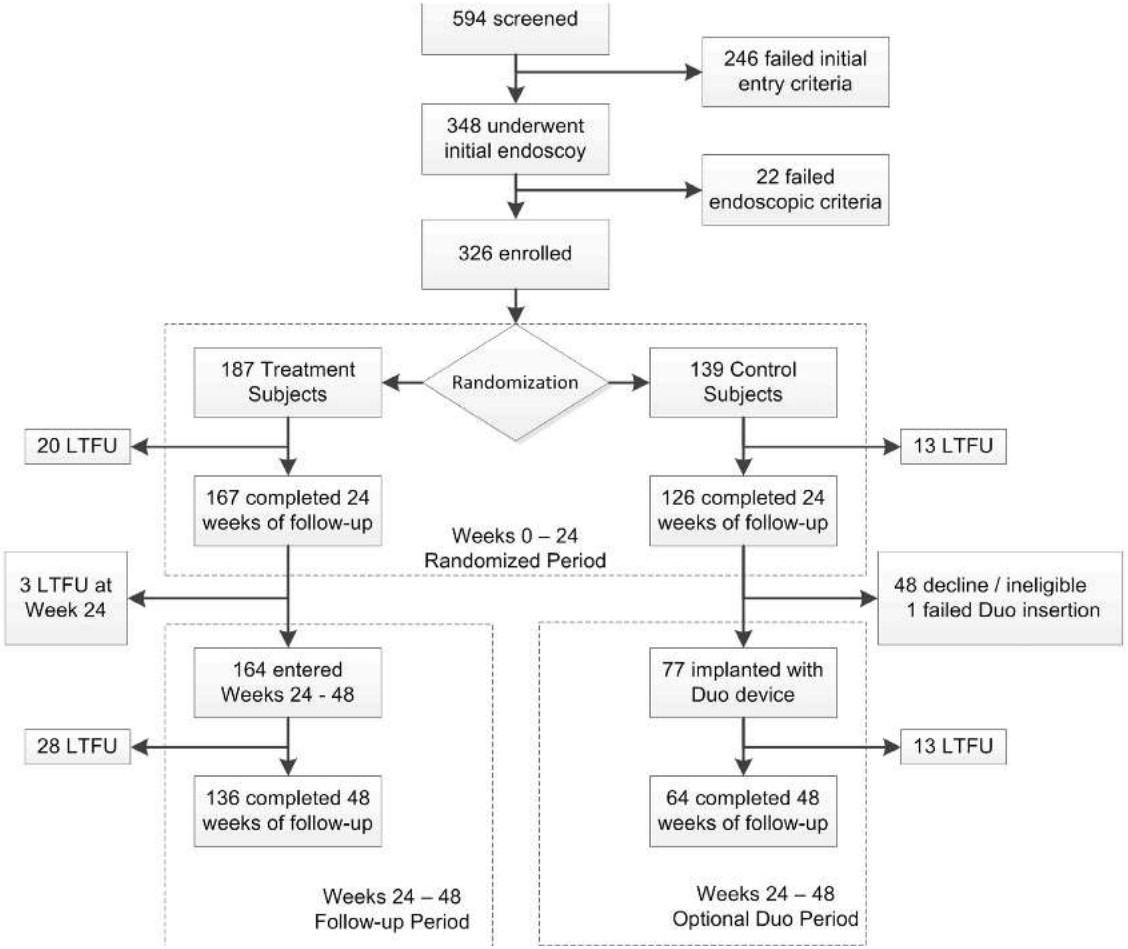
Anesthesia: GA

Inflation Compound: Saline

Inflation Volume:
750-900 ml (reduced for small stature)

Removal: Endoscopic

REDUCE trial

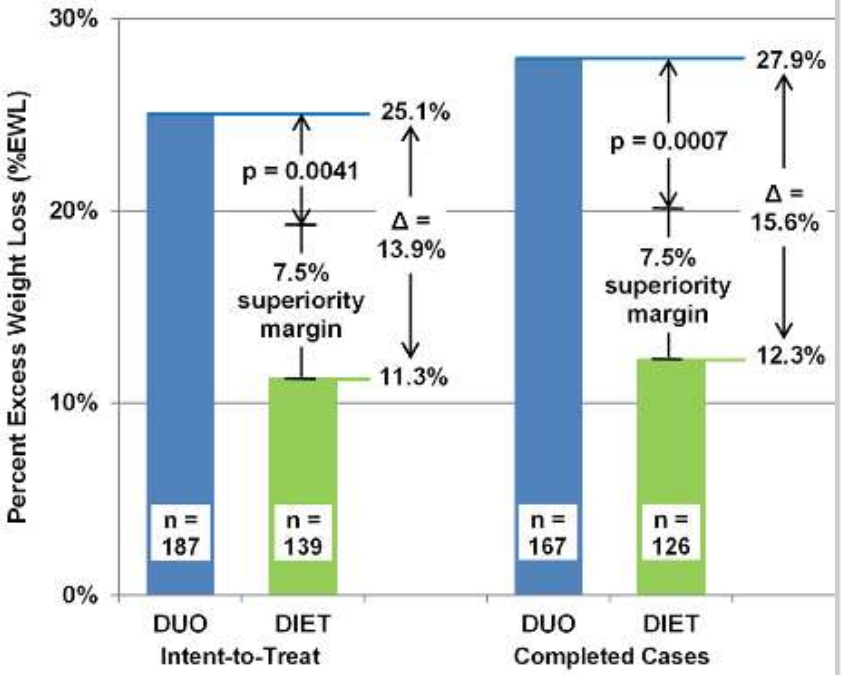


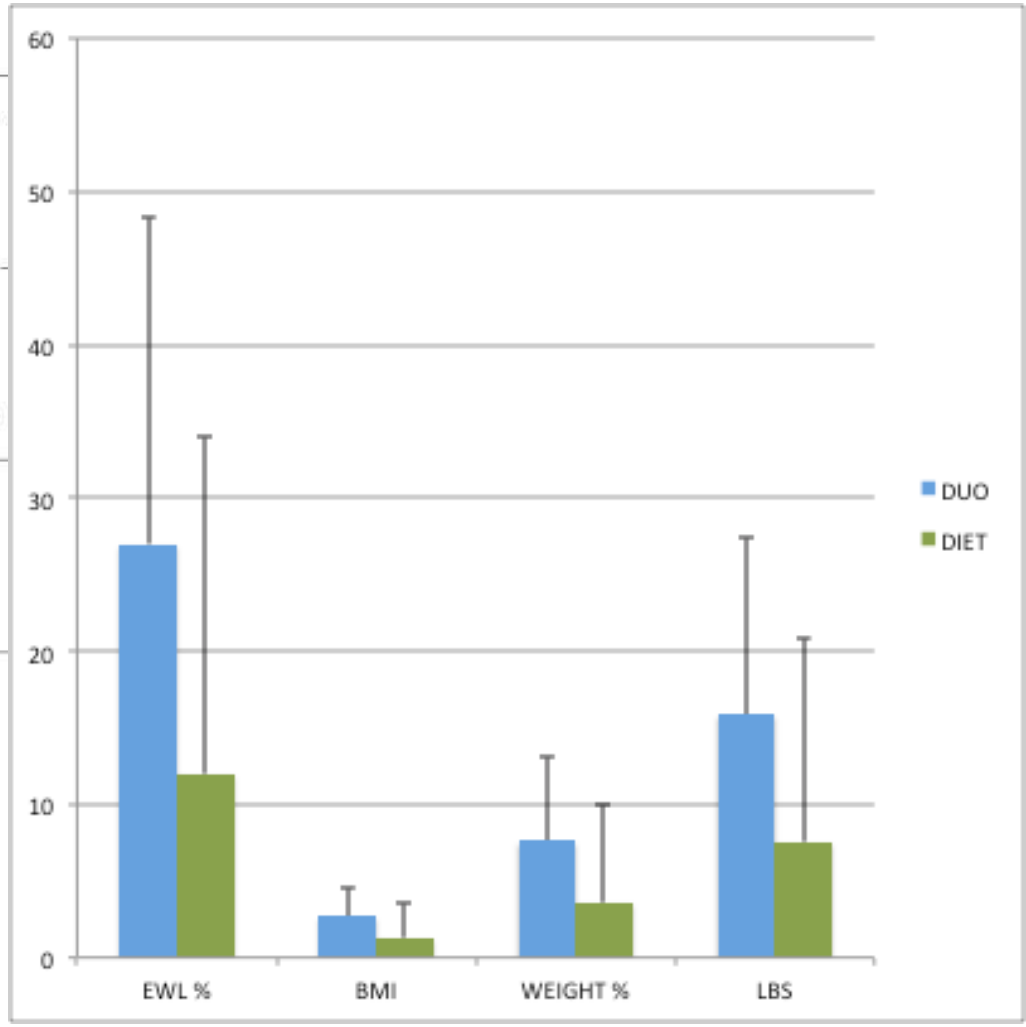
REDUCE trial

Baseline subject characteristics

Physical parameter	DUO (N = 187) Mean ± SD	DIET (N = 139) Mean ± SD
Age (years)	43.8 ± 9.5	44.0 ± 10.2
Weight (lb)	209.2 ± 25.8	213.2 ± 25.5
BMI (kg/m^2)	35.3 ± 2.8	35.4 ± 2.6
Waist circumference (in)	43.4 ± 4.4	43.2 ± 4.4
Hip circumference (in)	47.1 ± 3.5	47.7 ± 2.9
Systolic BP (mm/Hg)	130.4 ± 13.9	133.2 ± 14.0
Diastolic BP (mm/Hg)	81.8 ± 10.1	82.8 ± 10.2
Heart rate (beats/min)	78 ± 11.2	79 ± 12.7
Hemoglobin A1 c (%)	5.7 ± .7	5.7 ± .88
Cholesterol	200 ± 38	196 ± 40
Triglycerides (mg / dL)	141 ± 87	137 ± 88

REDUCE





Ponce J et al Surg Obesity and Related Disease 2015

ReShape – comorbid conditions and longer term outcomes

DUO Patients Laboratory Values	Value at Baseline	Change from Baseline at:			
		Week 12	Week 24	Week 36	Week 48
		During DBS Treatment		After DBS Treatment	
Glucose	93.2	−1.0	0.3	−1.5	0.9
Insulin	17.8	**−4.8**	**−3.8**	−0.7	−1.0
HbA1 c	5.7	**−0.1**	**−0.2**	**−0.3**	**−0.2**
TG	140.9	**−17.9**	**−15.7**	−6.7	−9.0
HDL	52.0	−0.9	1.0	**1.6**	**1.9**
LDL	121.0	−3.0	**−4.1**	**−6.8**	**−4.6**
Systolic BP	130.4	**−8.2**	**−8.3**	**−9.3**	**−6.6**
Diastolic BP	81.8	**−2.7**	**−4.3**	**−4.3**	**−4.4**

Ponce J Surg Obesity 2015

Procedural Notes for Endoscopic Placement and Removal

- Pre-procedural Preparations
  - PPI x 7 days and pre-procedural instructions and prescriptions
- Placement (Orbera, ReShape)
  - Preplacement endoscopy
  - MAC
  - Post-procedural hydration, antiemetics
- Removal
  - Liquid diet 24 hours before
  - MAC vs GA (perhaps depending on initial assessment by EGD) – GA capable setting???

Obalon Balloon

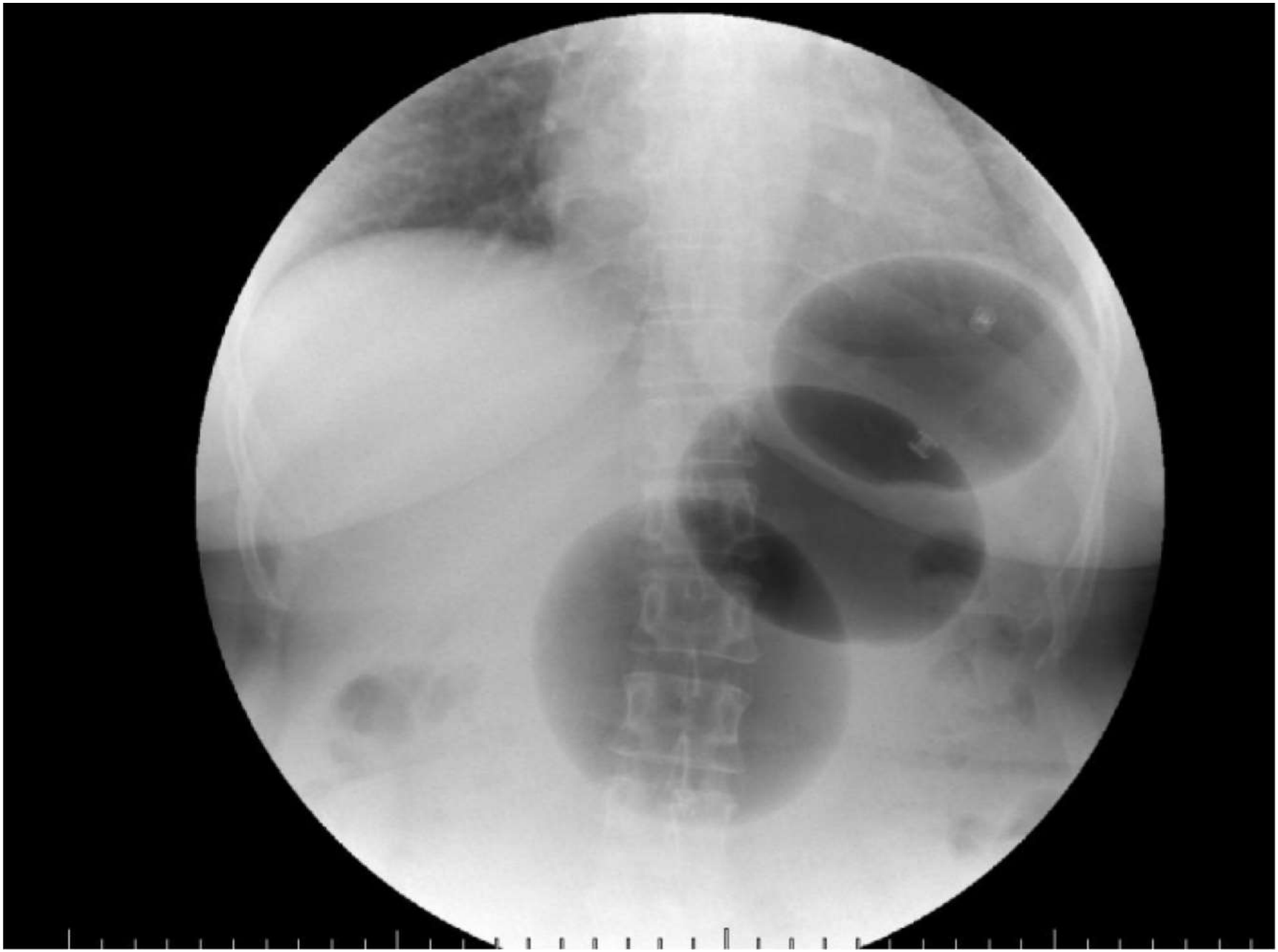
Obalon Balloon & Inflation System

(Obalon, San Diego, CA)

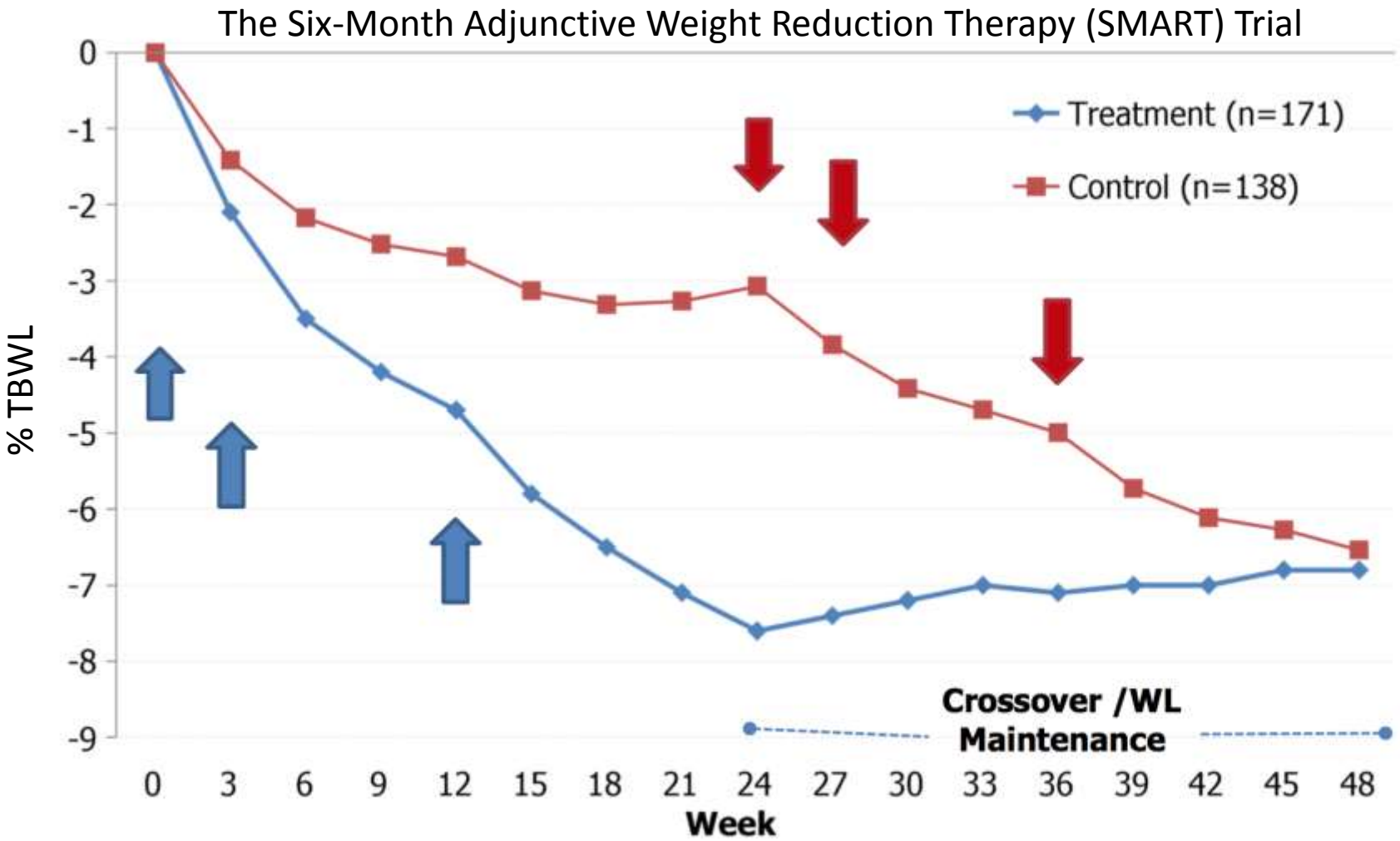
Swallowable Capsule

EzFill Inflation System

Gas-Filled Balloon



Obalon outcomes



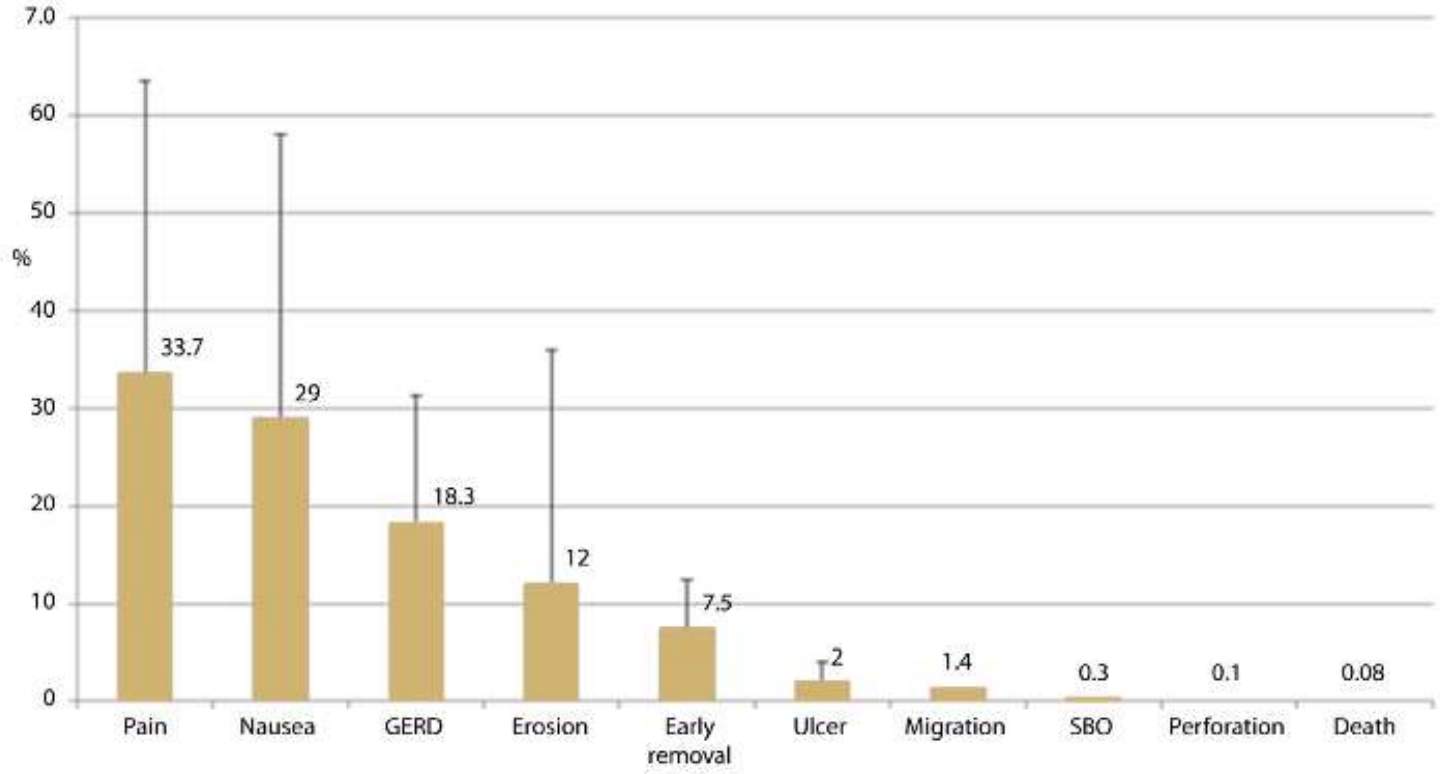
Pryor AD et al DDW 2017/Obesity 2016

Balloon side effects

	Orbera (BIB)	ReShape Duo	Obalon
Minor complications			
Abdominal pain	12.6–57.5	3.9–11.6%	60.8%—mild 11.6%—moderate 0.1%—severe
Nausea and vomiting	32.8–86.9	14.9–34%	56% nausea 17.3% vomiting
Reflux symptoms/erosive esophagitis	1.27–30	6.8%	1.8% (esophagitis)
Eructation	4.8–24.9	16.7%	9.2%
Dyspepsia	4.4–21.3	17.8%	16.9%
Major complications			
Gastrointestinal ulceration	0.02–2.6	10%*	0.9%
Dehydration	0.2–1.25	1.5%	NR
Luminal obstruction	0.2–76	NR	0%
Esophageal or gastric perforation	0.19–1.25	1.6%	0%
Deflation	0.9–4.5	6%	0.1%
Early removal	7.6–18.75	7.7%*	1.8%

Laing P et al Dig Dis Sci 2017

Balloon side effects and complications



FDA warning regarding deaths following IGB placement – Aug 2017

BALLOON	LOCATION	YEAR	CAUSE OF DEATH	TIME AFTER PLACEMEMNT	DEVICE MALFUNCTION
Orbera	Brazil	2016	MI	10 days	Not suspected/known
Orbera	USA	2016	Unknown	1 month	Not suspected/known
Orbera	Brazil	2016	Gastric perforation	3 days	Gastric wall ischemia, perforation, intact balloon
Orbera	GB	2016	Sepsis, aspiration?	3 days	Second balloon, no known malfunction
Orbera	Mexico2015	2017	Cardiogenic shock	3 days	NO evidence of balloon malfunction
ReShape	US	2017	Shock, ?aspiration	2 days	Not known

Number of Orbera balloon placed to date (2016): 270,000+; reported incident rate <0.01%

Other Balloons

- Adjustable Balloon
  - Spatz

- Procedure- free balloons
  - Allurion Technologies
  - Intragastric balloon
  - Requires no procedure for implantation or explantation; self passing

  - PlenSat Digestible Balloon
  - Balloon swallowed in

  a capsule and broken down by stomach

Summary

- Intragastric Balloons
  - Consistent efficacy for short term weight loss
  - Possible benefits in comorbid conditions
  - Possible durable benefits
  - Studies to look out for
    - Long term data (weight loss , comorbid conditions)
    - Sequential IGBs
    - Less invasive placement and removal strategies
    - Cost effectiveness
    - Personalized approach to choosing balloons
  - Best done as part of a comprehensive obesity management program

CoMMiT

Comprehensive Obesity and Metabolism Management and Treatment Program

Your Health, Our CoMMiTment