



University of Colorado **Anschutz Medical Campus**

# Endoscopic Bariatric Therapy for Weight Loss in Older Adults: Current Data and Future Directions

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Association for  
Bariatric Endoscopy

A DIVISION OF ASGE

# Disclosures

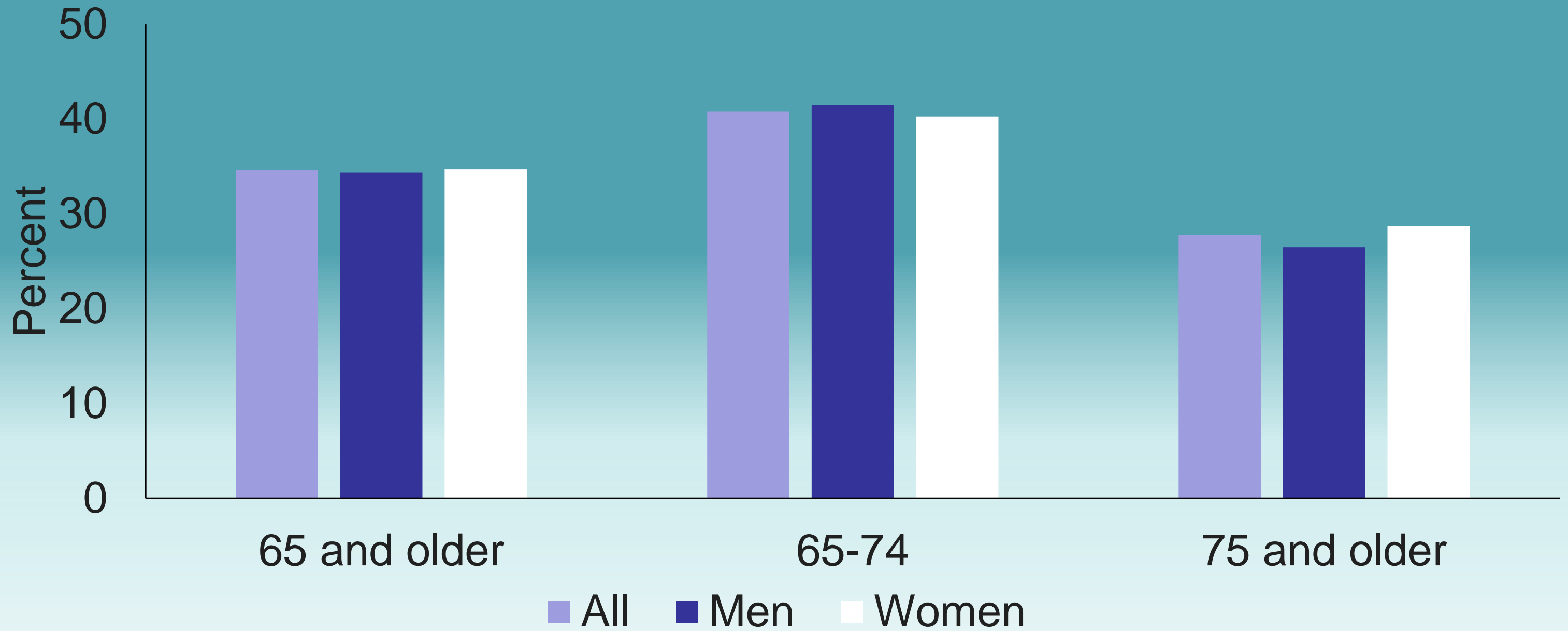
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  - USGI Medical, EnteroMedics, Obalon, Takeda Pharmaceuticals, Elira Therapeutics, Aspire Bariatrics



# Outline

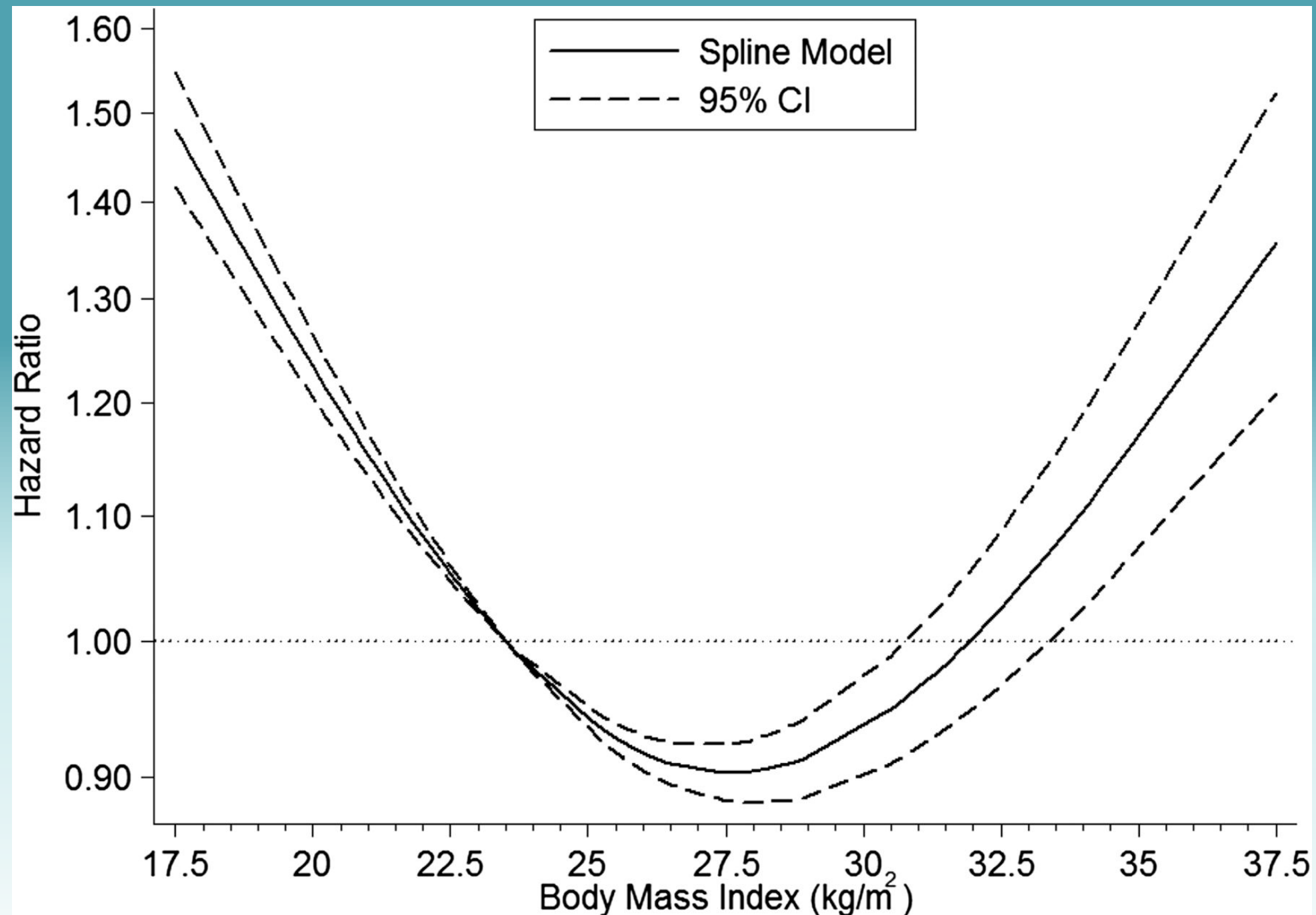
- Obesity and Weight Loss in Older adults
- Evidence behind Endoscopic bariatric therapies
- Mechanisms for acquiring additional safety and effectiveness data of EBTs in older adults

# Prevalence of Obesity in Adults Age $\geq 65$ years

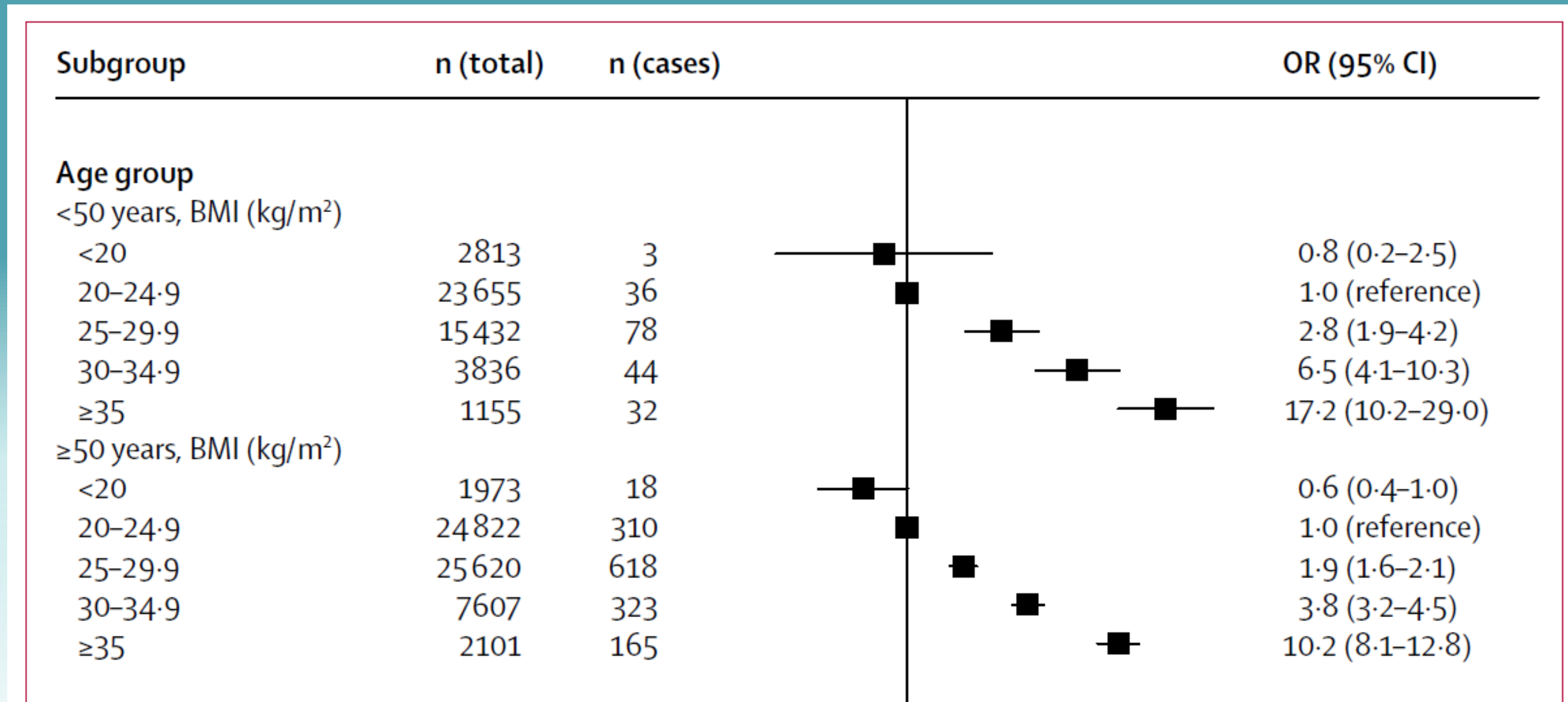




# Obesity Paradox: all-cause mortality according to BMI for men and women aged $\geq 65$ y.



# Effects of Obesity on Developing Cardiometabolic Multi-Morbidity between 1973-2012



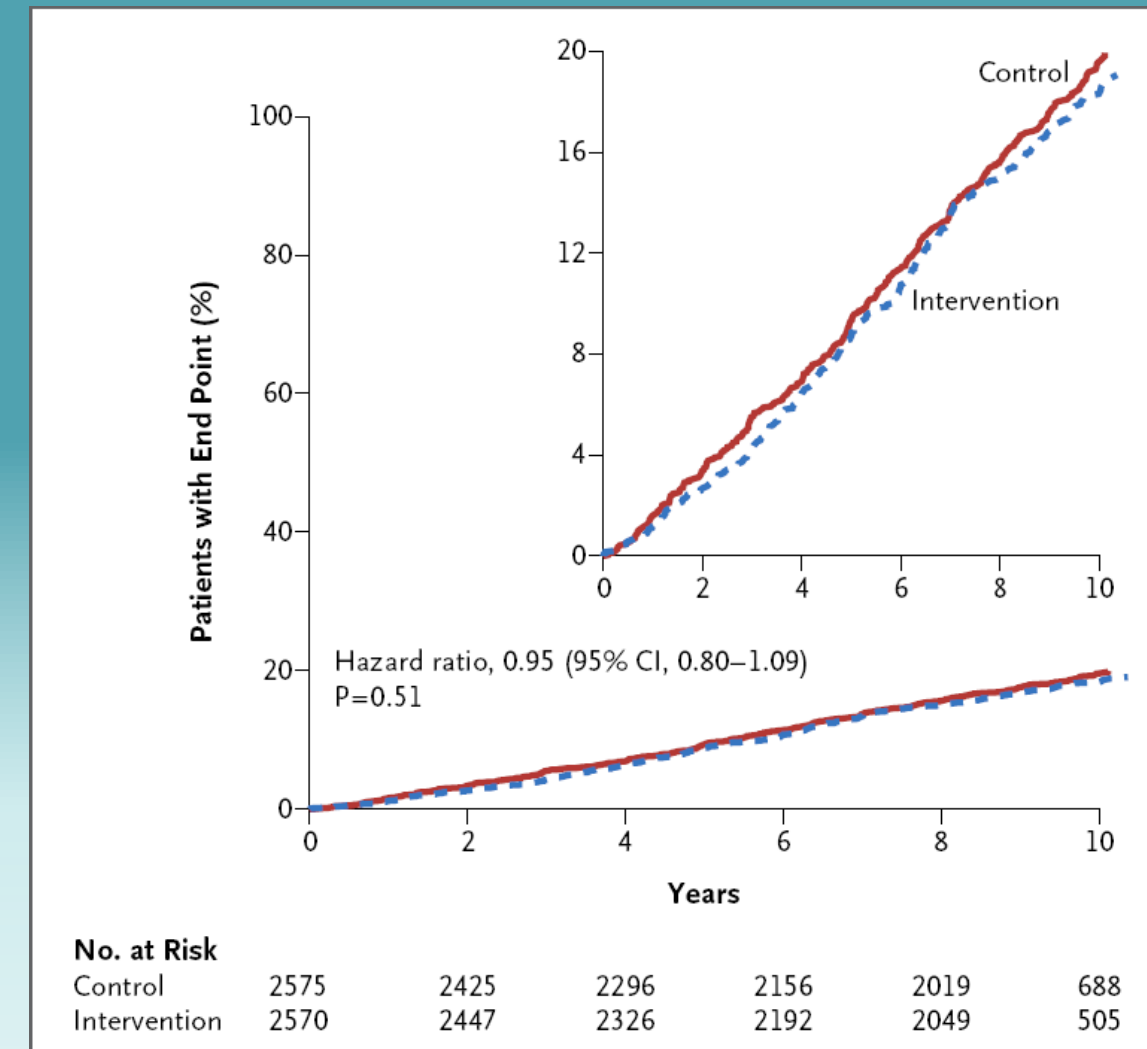
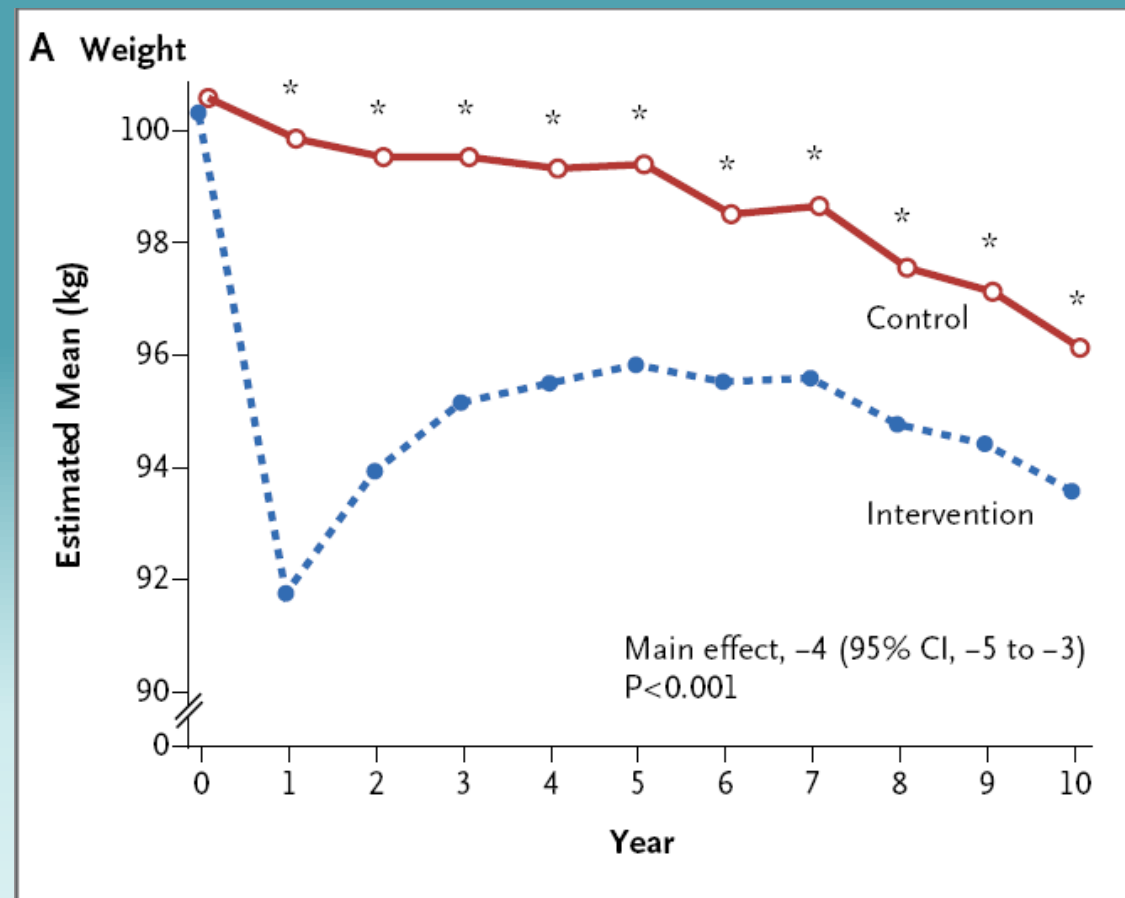
# Weight Loss Effects are Dose Dependent: Progressive Weight Loss Study

Factor	Baseline	5% TBWL	11% TBWL	16% TBWL	Effect of Time (p)
Intrahepatic triglyceride (%)	8.5 (3.9,25.9)	7.4 (3.0,12.5) *	4.1 (1.1,10.2) *	3.0 (1.1,5.2) *	<0.001
Triglycerides (mg/dl)	153 ± 56	130 ± 71	110 ± 59*	97 ± 39*	0.003
Insulin AUC (mU/L·min)	12,365 (9,025,21,012)	12,950 (7,352,17,370)	11,137 (7,965, 17,654)	9,534 (6,548, 14,417)*	0.024
β cell function	6,860 ± 4,808	8,130 ± 3,565	10,607 ± 2,508*	11,107 ± 2,666*	0.003
Glucose Ra suppression (%)†	71 ± 13	77 ± 10*	76 ± 11*	80 ± 6*	0.028
Glucose Rd stimulation (%)	168 (94, 297)	207 (149, 306)*	326 (233, 379)*	311 (248, 388)*	0.009

%TBWL: % Total Body Weight Loss, \*Different from Baseline

Magkos F. Cell Metabolism. 2016;23:591-601

# Look Ahead Trial: Long-term cardiovascular effects of weight loss in obese persons with Type 2 Diabetes

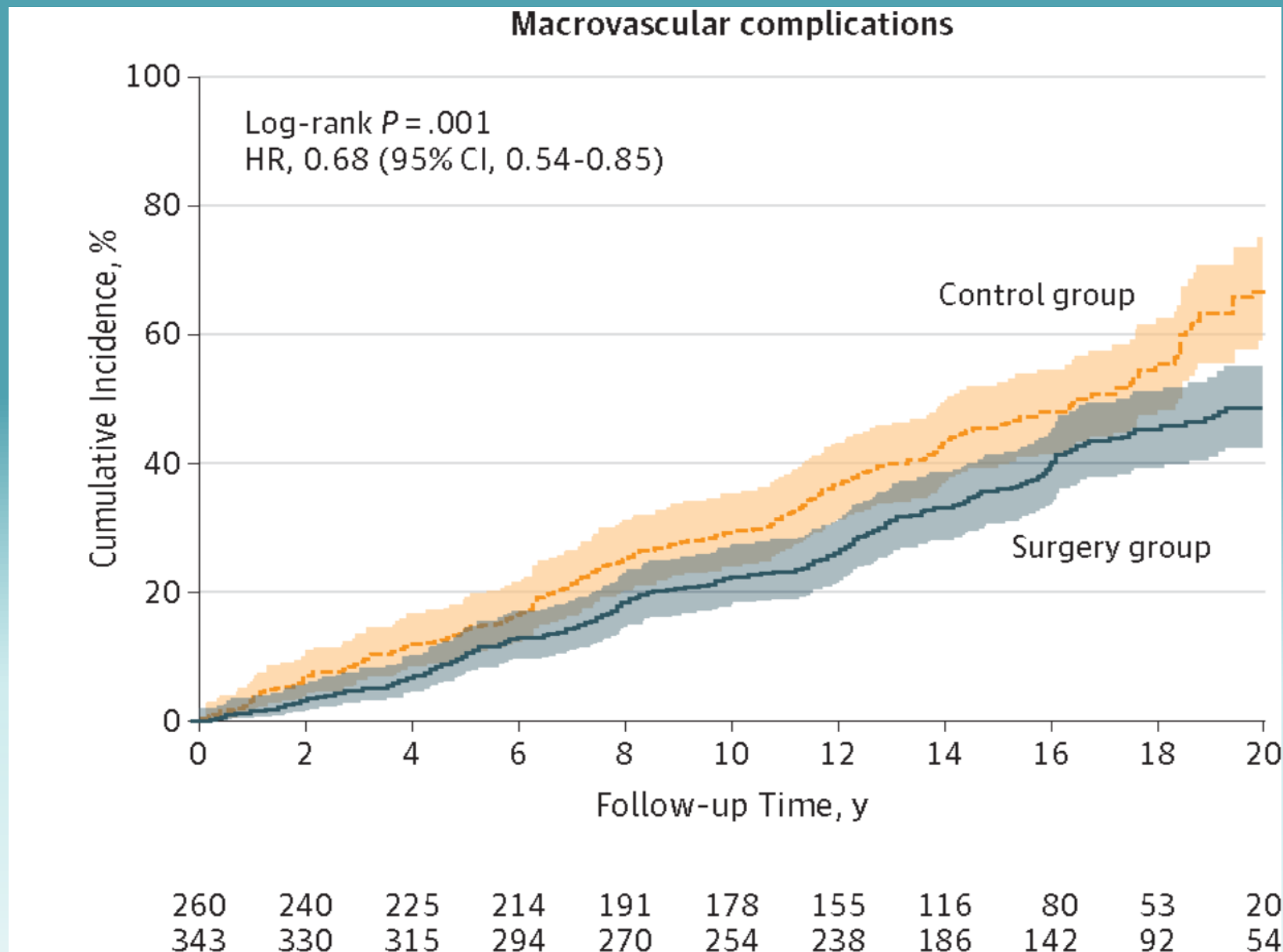


# >10% TBWL for Reduction in Cardiovascular Outcomes

Outcome	Control Group (Reference)	<2% Loss or Weight Gain	Small Loss (≥2-<5%)	Medium Loss (≥5-<10%)	Large Loss (≥10%)
Primary Adjusted Hazard Ratio (95% CI)	1.00	1.29 (0.96-1.72)	1.04 (0.80-1.36)	1.15 (0.92-1.43)	0.80 (0.65-0.99) p=0.039
Secondary Adjusted Hazard Ratio (95% CI)	1.00	1.28 (1.01-1.64) p=0.045	1.19 (0.96-1.47)	1.02 (0.84-1.23)	0.79 (0.66-0.95) p=0.011

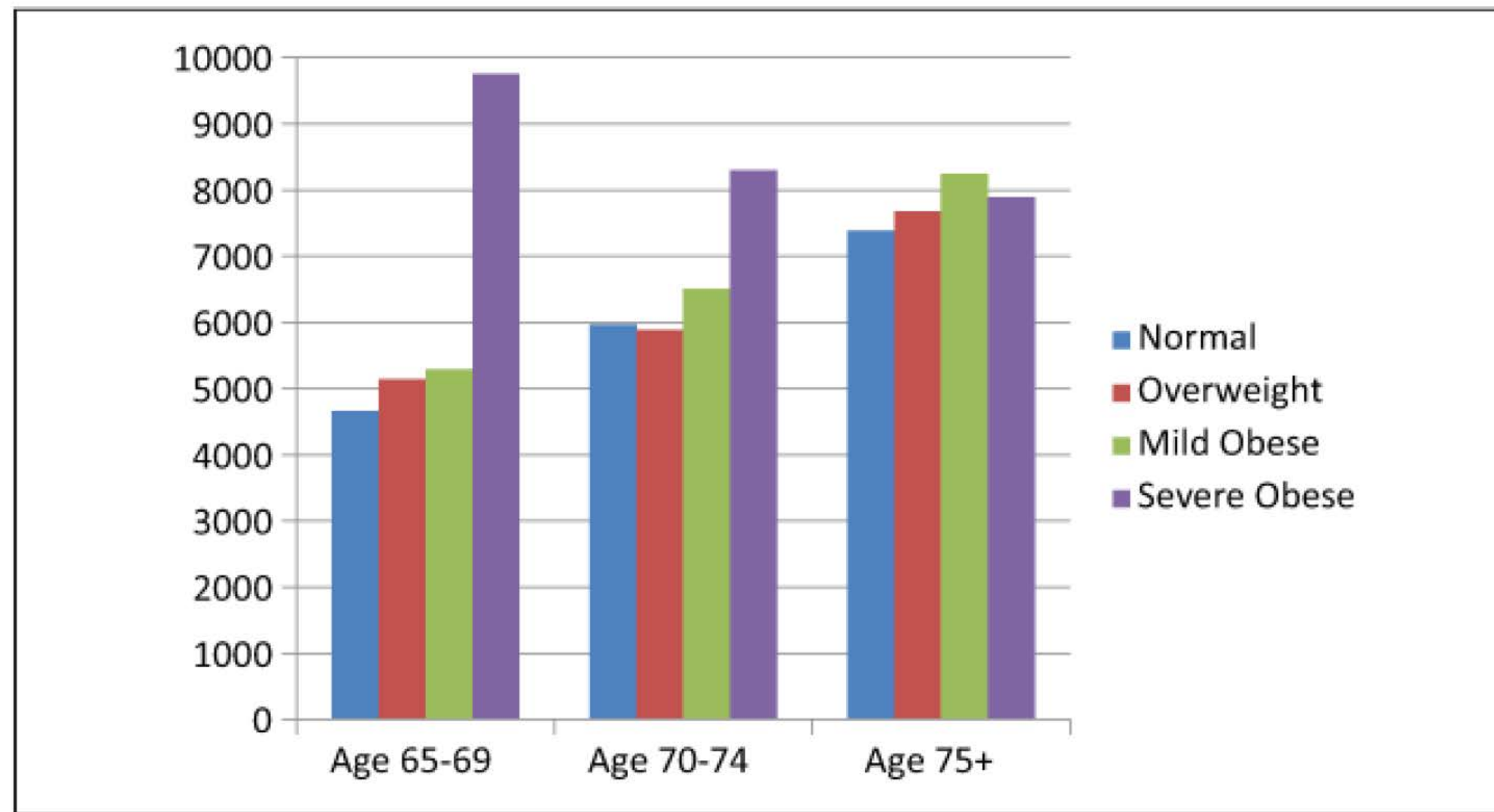
- Look Ahead Trial
- Post-Hoc Analysis
- 4406 subjects in the analysis
- Age 45-76
- Diabetes

# Bariatric Surgery and Macrovascular Complications of Diabetes



- Weight loss
  - Year 2
    - Control 2.4% TBW
    - Surgery 21% TBW
  - Year 10
    - Control 3.6% TBW
    - Surgery 18.0% TBW
- Diabetes remission at 2 years
  - Control: 16.4%
  - Surgery: 72.3%
- Macrovascular endpoints:
  - CVD, Stroke, Lower Extremity Vascular disease

# Age Difference and BMI Affects on Medicare Expenditures 1998-2008





# Age Difference and BMI Affects on Medicare Expenditures 1998-2008

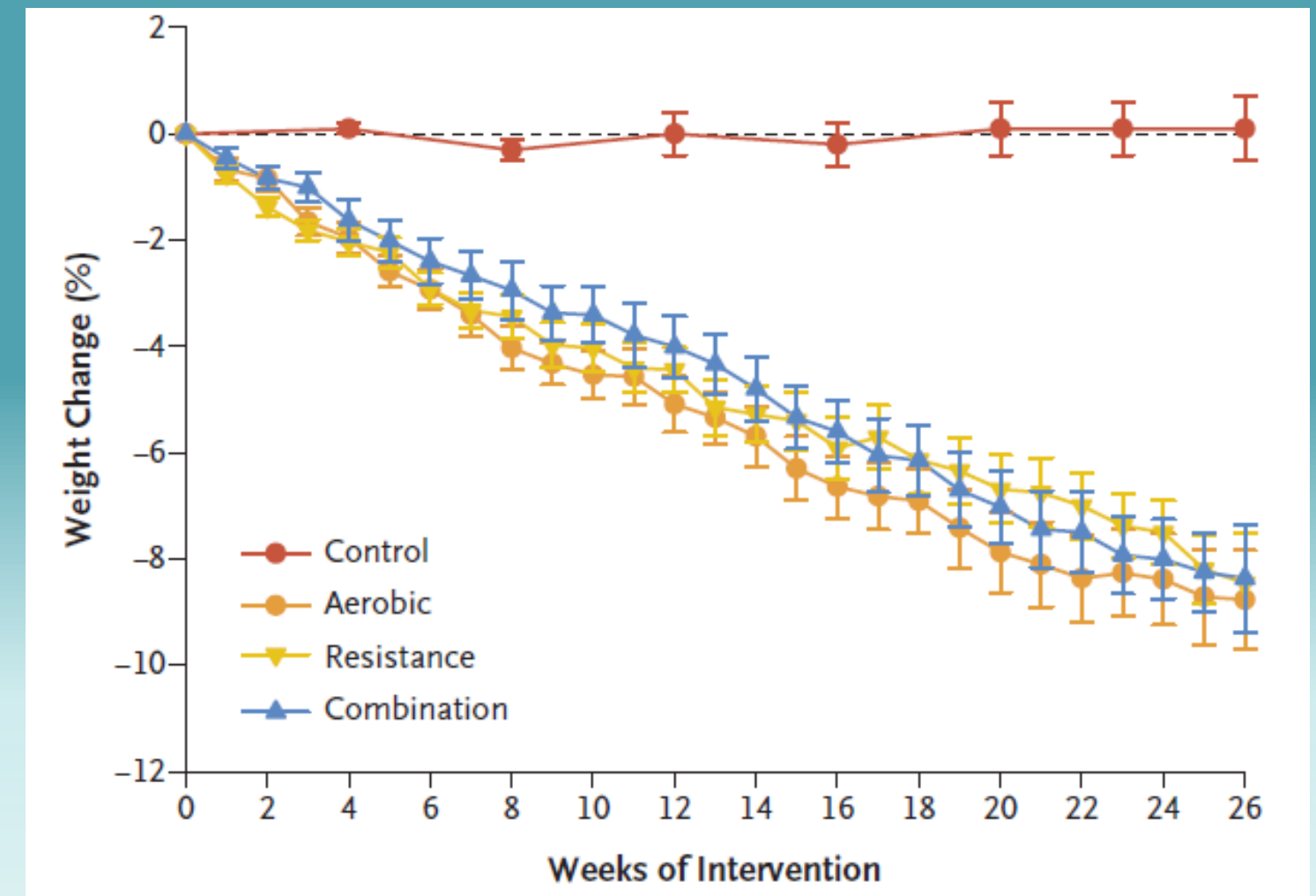
- Adjusted for age, gender, ethnicity, education, and smoking history:
  - Normal weight age 65-69: \$4,663
  - BMI  $\geq 35$  kg/m<sup>2</sup> age 65-74: \$9,751
  - Cost of class II obesity in older adults age 65-69: \$25,440
- Significantly higher rate of Hypertension, CHF, Diabetes and arthritis
- When adjusted for chronic illness, these costs remain higher
  - Durable medical equipment
  - Home health and Nursing home
  - Emergency department, inpatient, and outpatient

\*Frailty with disability contributes to increased Medicare expenditures in patients with a BMI  $\geq 35$  kg/m<sup>2</sup> age 65-74

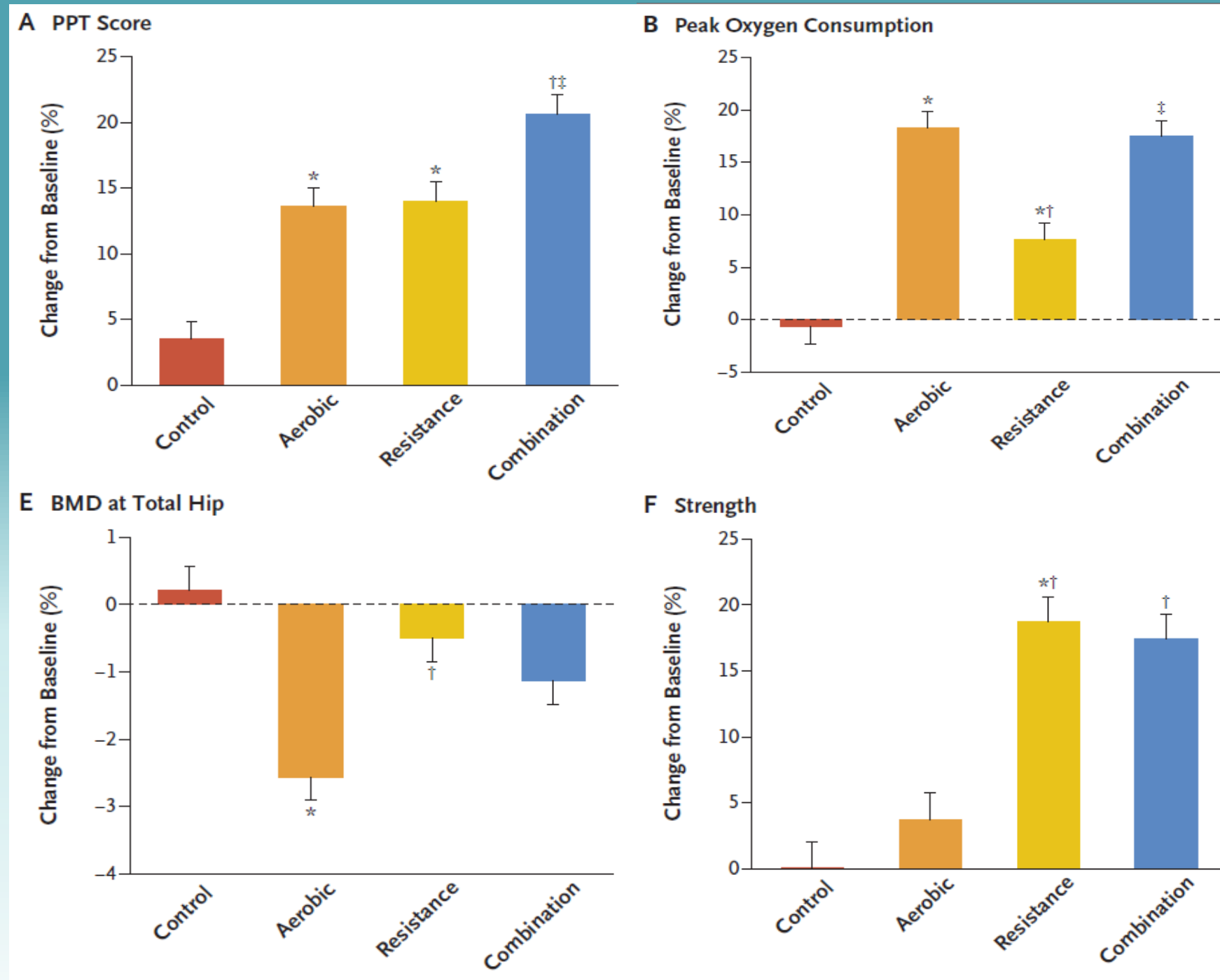


# Weight Loss in Older Adults

- 160 older adults with obesity
- Randomized to:
  - Control
  - Aerobic Exercise + Wt Loss
  - Strength Training + Wt Loss
  - Aerobic and Strength Exercise + Wt Loss
- 26 weeks
- 141 participants completed the study



# Measures of Physical Function, Lean Mass, and Bone Mineral Density



- PPT Score: Physical Performance Test
  - 36 point scale
  - Moderately frail at baseline on average
  - Change in Combination group = increase to not frail on average

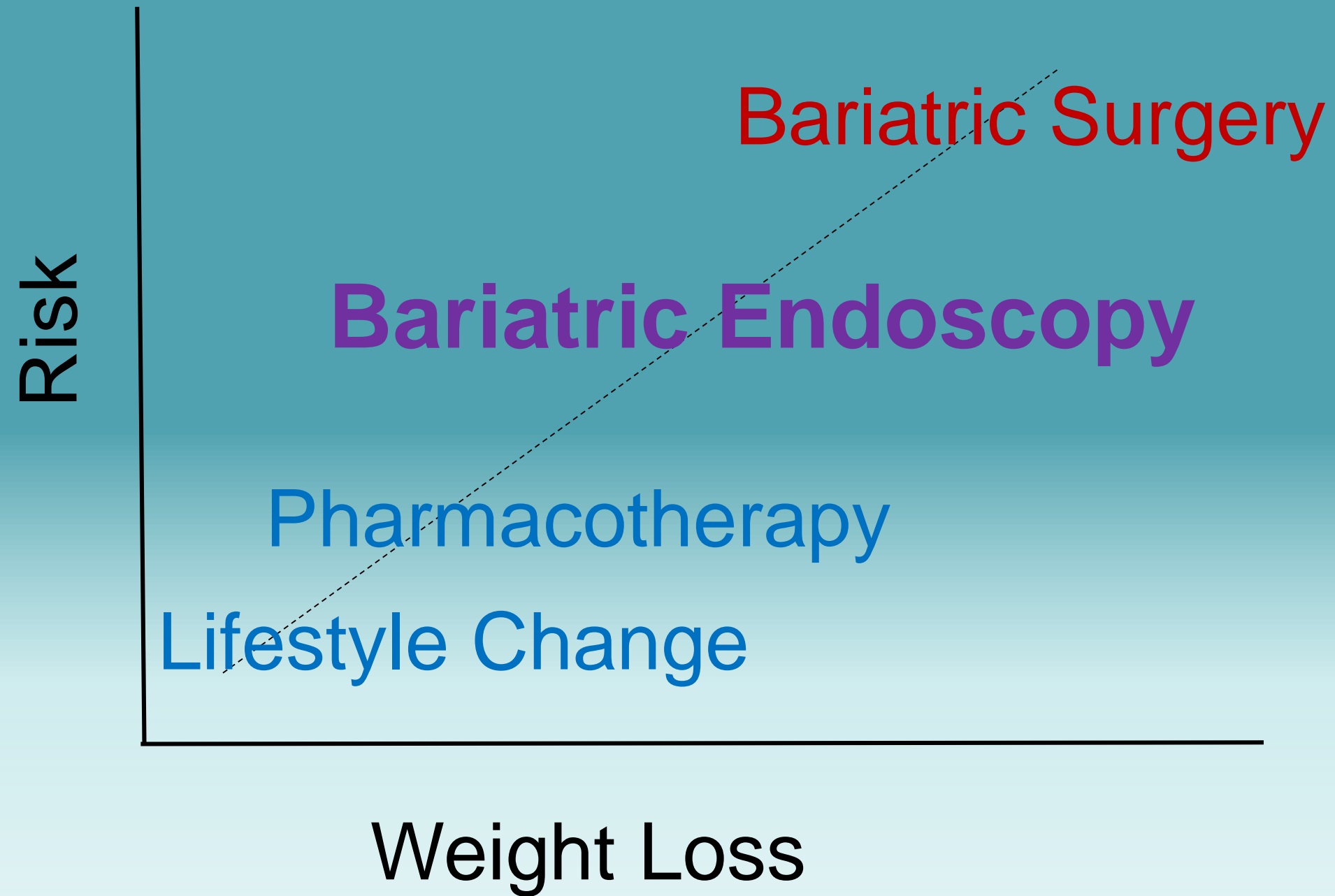
# Obesity and Weight Loss in Older Adults

- Over 1/3 of older adults have obesity
- Obesity, in particular BMI  $\geq 35$  kg/m<sup>2</sup> is associated with:
  - Cardiometabolic co-morbidities
  - Disability
  - Double Medicare annualized expenditures
- Weight loss
  - improves cardiometabolic factors and body composition in dose dependent fashion
  - improvement in cardiovascular endpoints likely requires  $\geq 10\%$  TBWL
- To decrease risk of cardiovascular disease and metabolic disease in addition to prevent/improve frailty, weight loss programs should be accompanied by exercise programs with combination aerobic and strength training

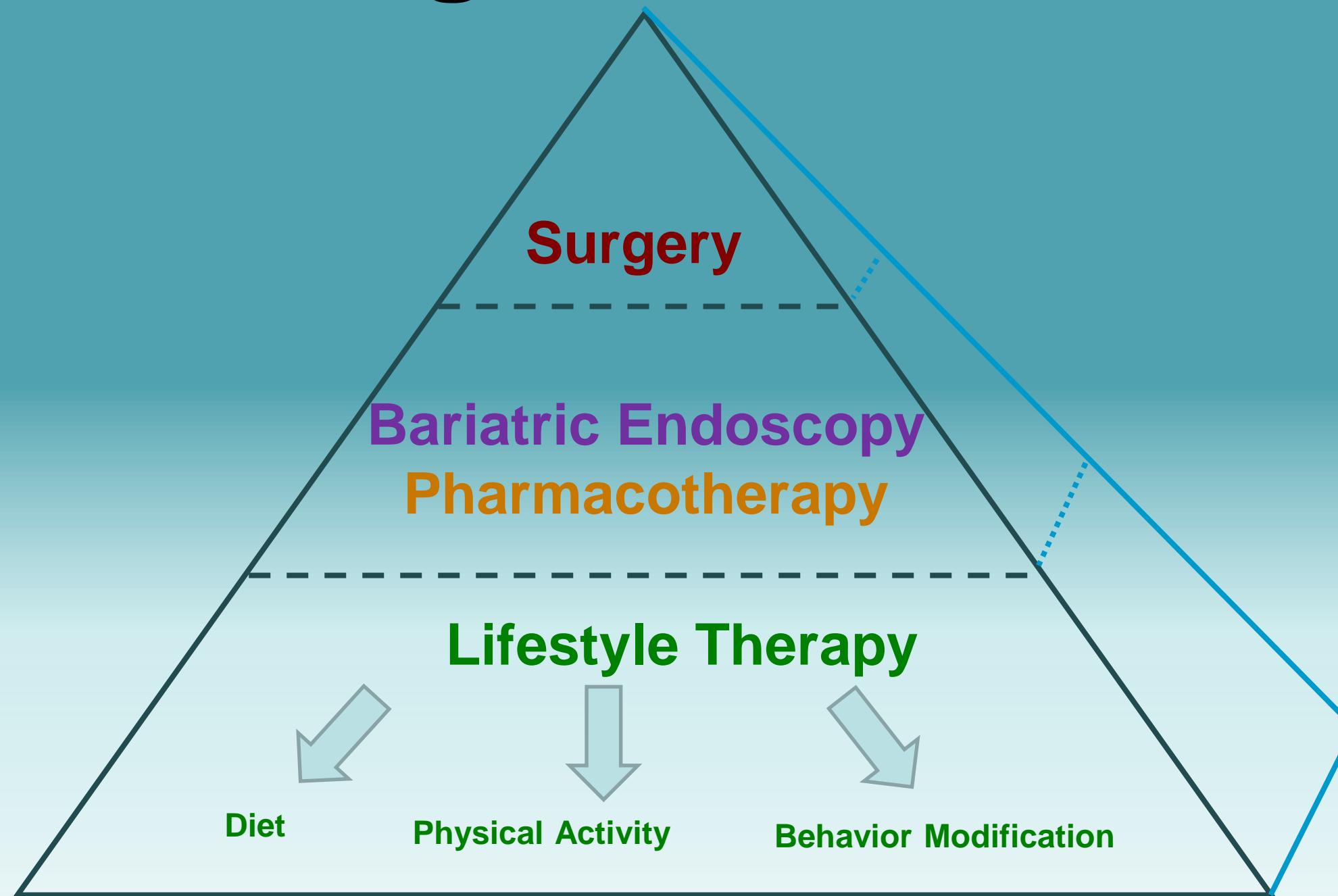
# Outline

- Obesity and Weight Loss in Older adults
- Evidence behind Endoscopic bariatric therapies
- Mechanisms for acquiring additional safety and effectiveness data of EBTs in older adults

# Endoscopic Bariatric Therapy



# Comprehensive Weight Loss Program



# Endoscopic Bariatric and Metabolic Therapies

## Gastric Therapies

- Intragastic Balloons (IGB)
  - ReShape Intragastic Dual Balloon System (ReShape Medical)
  - Orbera Balloon System (Apollo Endosurgery)
  - Obalon Balloon System (Obalon Therapeutics)
- Suturing and Plication procedures
  - Endoscopic Sleeve Gastroplasty (Overstitch, Apollo Endosurgery)
  - Primary Obesity Surgery Endoluminal (Incisionless Operating Platform, USGI Medical)
- Aspiration Therapy (Aspire Bariatrics)
- Transpyloric Shuttle (BARONova)

Weight loss with metabolic effects dependent on weight loss







## Small Bowel Therapies

- Bypass liners
  - Duodenojejunal Bypass Liner: EndoBarrier (GI Dynamix)
  - Gastroduodenojejunal Bypass Liner: ValenTx Endoluminal Bypass (ValenTx Inc)
- Intestinal bypass: Incisionless Anastomosis System (GI Windows)
- Duodenal Mucosal Resurfacing: Revita DMR (Fractyl Laboratories Inc)

Metabolic effects independent of weight loss, but some weight loss may be seen



# FDA Approved Intragastic Balloons

Device	Device Image	Characteristics	FDA Status
<b>ReShape Dual Balloon System</b> ReShape Medical, San Clemente, CA	 	<ul style="list-style-type: none"> <li>Two medical grade silicone spheres joined by a flexible shaft</li> <li>each balloon filled with 375 ml to 450 ml of saline dyed with methylene blue</li> <li>Endoscopically placed and removed</li> </ul>	<ul style="list-style-type: none"> <li>Approved July 28, 2015</li> <li>BMI 30-40kg/m<sup>2</sup> with one obesity related co-morbidity</li> <li>6 Months</li> </ul>
<b>Orbera Intragastic Balloon</b> , Apollo Endosurgery, Austin, TX		<ul style="list-style-type: none"> <li>Medical grade silicone sphere, filled with 400-700 ml of saline</li> <li>Endoscoically placed and removed</li> </ul>	<ul style="list-style-type: none"> <li>Approved August 5, 2015</li> <li>BMI 30-40kg/m<sup>2</sup></li> <li>6 Months</li> </ul>
<b>Obalon Balloon System</b> Obalon Therapeutics, Carlsbad, CA	  	<ul style="list-style-type: none"> <li>Thin polymer elipse shape</li> <li>filled with 250 ml of a nitrogen mix gas</li> <li>3 balloons administered over 8 to 12-week period</li> <li>Swallowed and endoscopically removed</li> </ul>	<ul style="list-style-type: none"> <li>Approved September 8, 2016</li> <li>BMI 30-40kg/m<sup>2</sup></li> <li>6 Months from first administration</li> </ul>



# Comparison of Intragastric Balloon

## Pivotal Trial: 6 Month Data

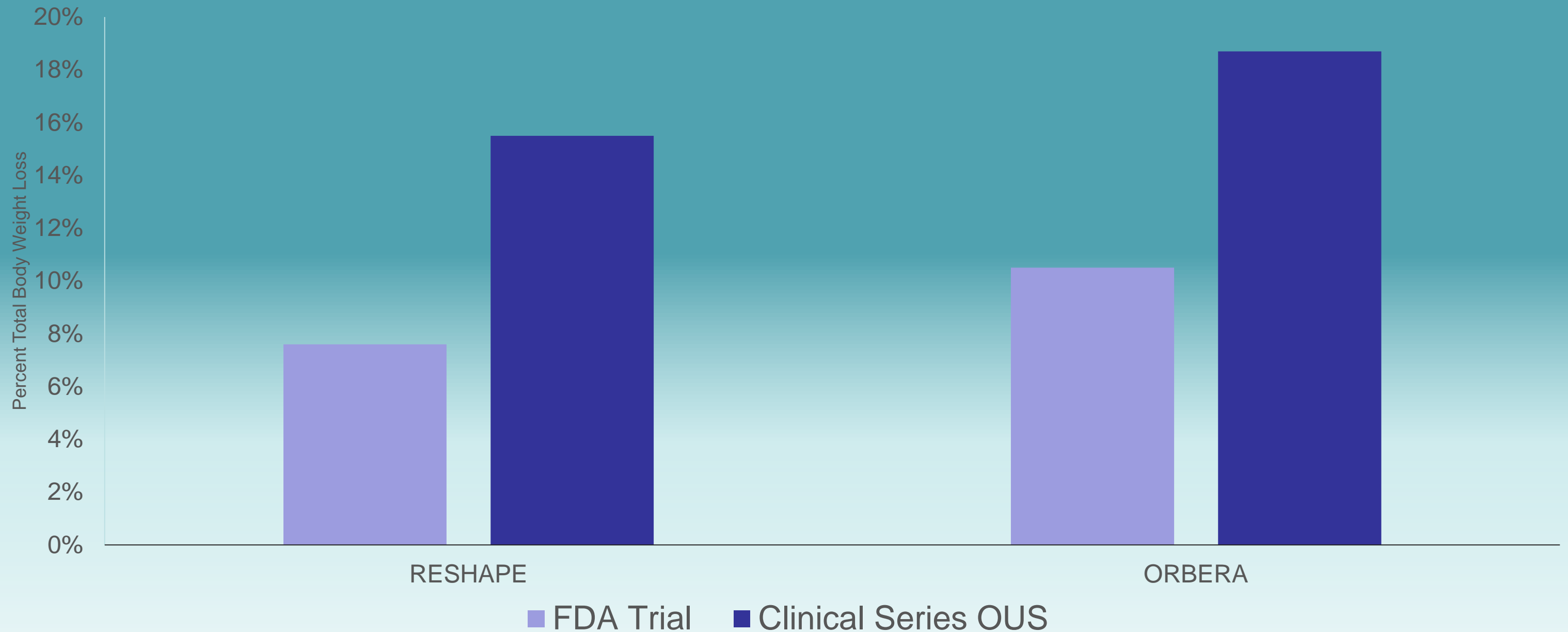
Device	Number of subjects		Body Mass Index (kg/m <sup>2</sup> )		Percent total Body Weight loss		Active Group Responder rate	Serious Adverse Event Rate
	Control Group	Active Group	Control Group	Active Group	Control Group	Active Group		
Orbera	130	125	35.4±2.7	35.2±3.2	3.3±5.0%	10.2±6.6%	79.2%	10%**
Reshape	139	187	35.4±2.6	35.3±2.8	3.3%	6.8%	48.8%*	10.6%**
Obalon	189	198	35.4±2.7	35.1±2.7	3.4±5.0%	6.6±5.1%	62.1%	0.5%

\*ReShape responder rate based on Excess Weight Loss of 25%

\*\*Majority of SAE's were due to accommodative symptoms

Ponce J. *Surgery for Obesity and Related Diseases*. 2015;11(4):874-881  
Sullivan S. *Gastroenterology*.2016;150(4) S1267  
FDA. Summary of Safety and Effectiveness Data (SSED) ORBERA Intragastric Balloon System. In: FDA, ed, 2015:1-32

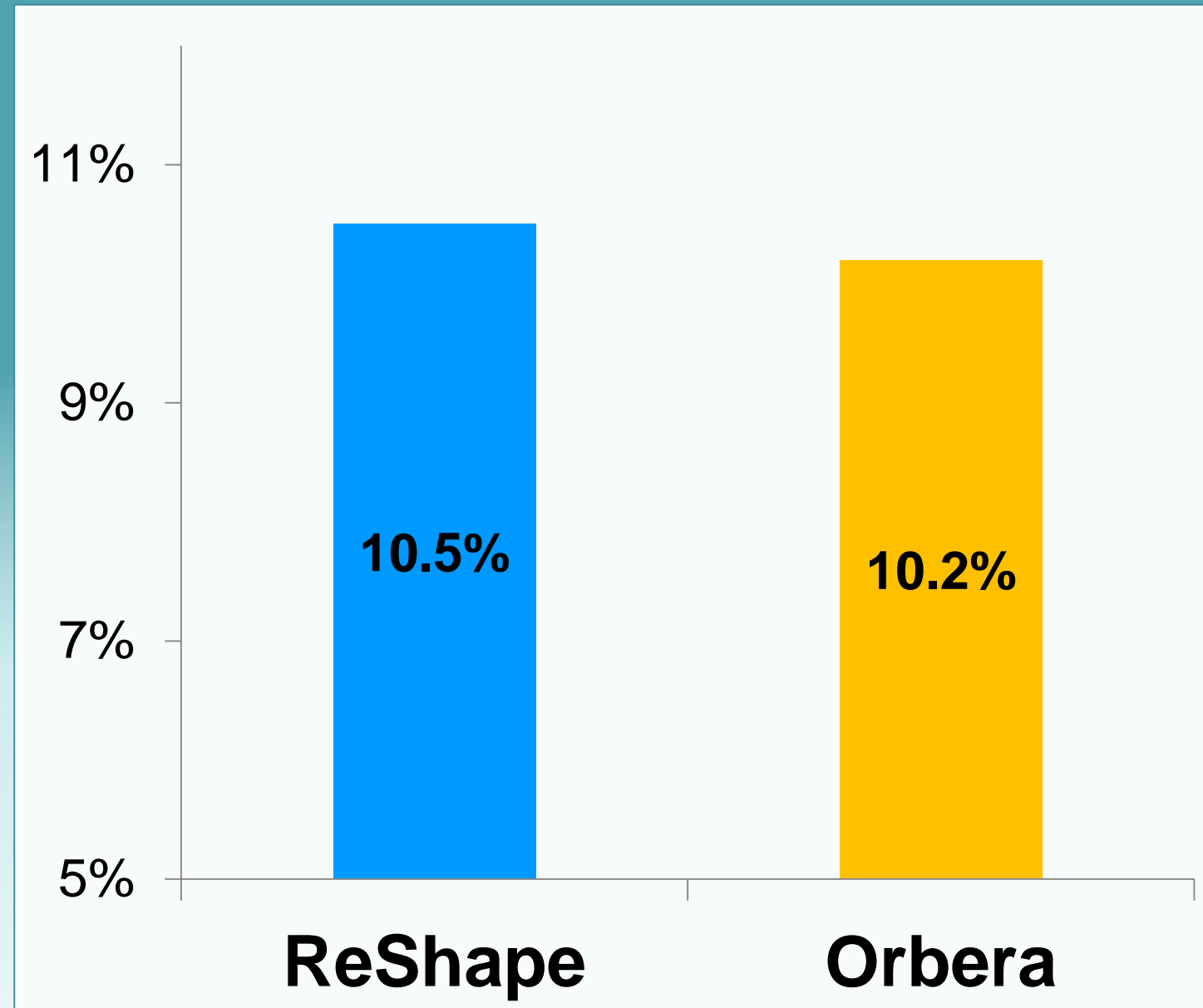
# Intragastric Balloon: Higher Effectiveness in Clinical Practice



Ponce J. *Surgery for Obesity and Related Diseases*. 2015;11(4):874-881  
Lopez-Nava G. *Obesity Surgery*. 2015;25:2263-2267

Courcoulas A. *Int J Obes*. 2017;41:427-433  
Mathus-Vliegen EM. *Endoscopy*. 2015;47: 302-307

# Comparison of Intragastric Balloons in Clinical Practice at 20 weeks



## Baseline Characteristics

	ReShape	Orbera	p value
Number placed	26	14	
Female	22 (85%)	14 (100%)	0.28
Age (years)	48.3±2.0	52.2±4.0	0.34
Weight (pounds)	225±9	248±11	0.13
BMI (kg/m <sup>2</sup> )	36.5±1.2	40.8±1.8	0.05

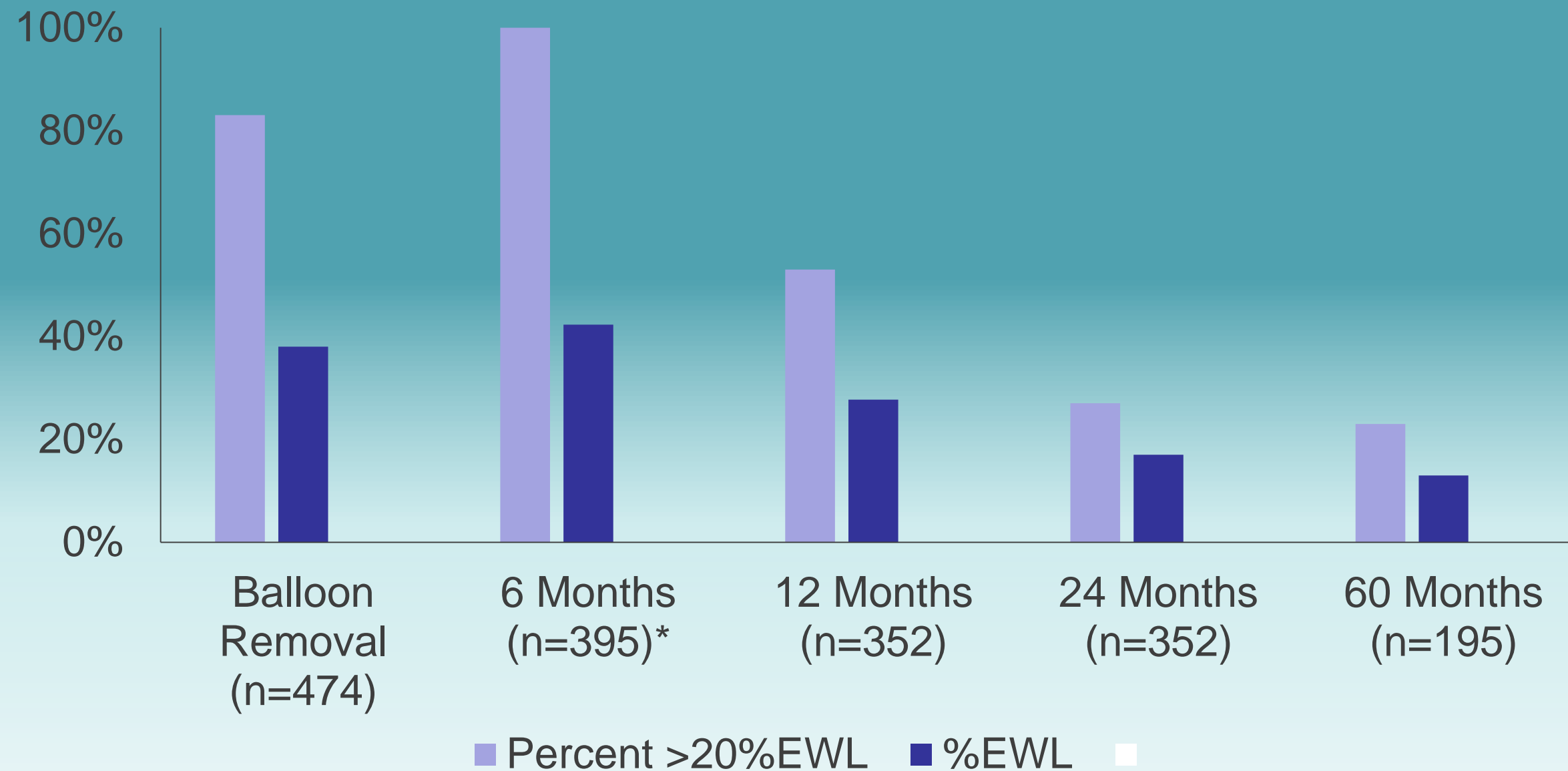
- No difference in nausea, vomiting, reflux, or abdominal pain

# ASGE Bariatric Endoscopy Task Force Systematic Review and Meta-analysis Assessing the ASGE PIVI Thresholds for Adopting Endoscopic Bariatric Therapies

- 1638 patients average percent excess weight loss (%EWL) at 12 months (6 months after balloon removal): 25.44[95% CI 21.47-29.41]
- Average total body weight loss:
  - 3 months after removal:12.3% [95% CI 7.9 – 16.73]
  - 6 months after removal:13.16% [95% CI 12.37 – 13.95]
  - 12 months after removal:11.27% [95% CI 8.17 – 14.36]
- Three randomized controlled trials the difference in %EWL between active and control patients: 26.9%

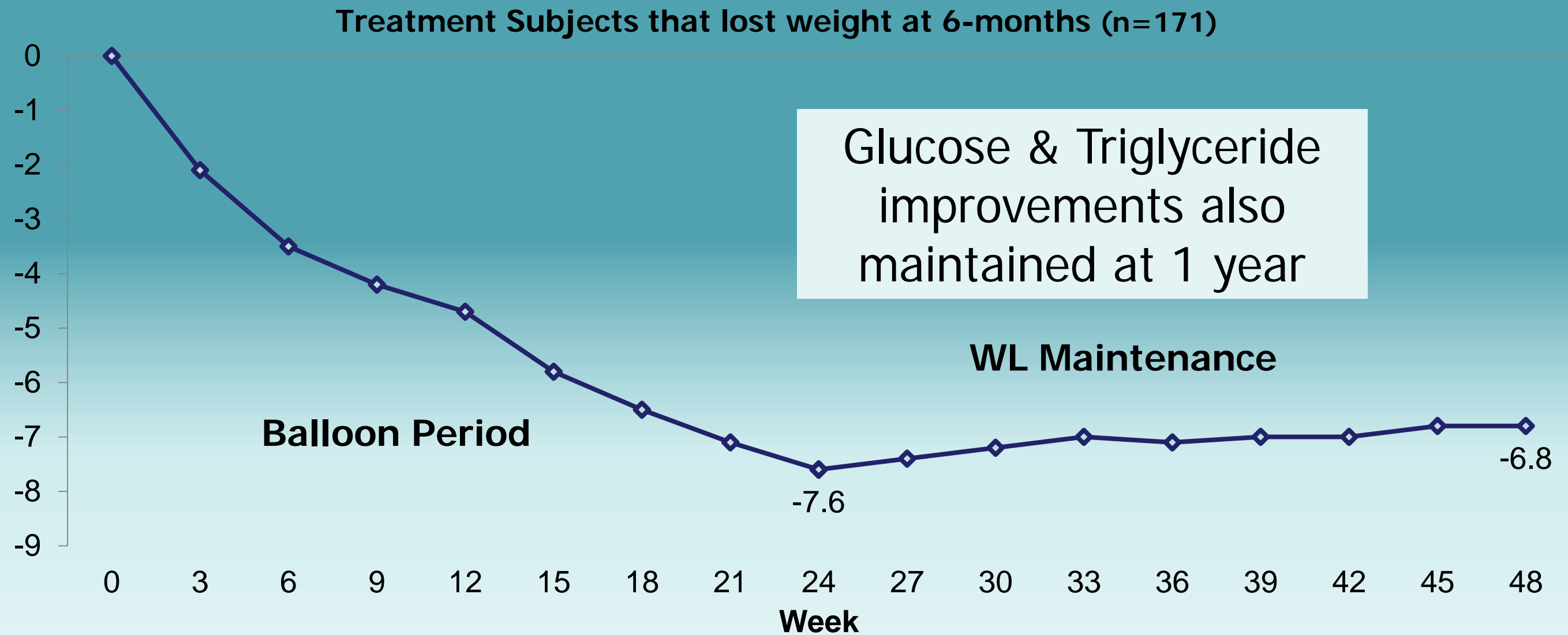
# IGB Long-Term Weight Loss

Percent of Patients Successful and %EWL



# 1 Year Weight Loss Maintenance:

## 89.5% Mean %TWL Maintained



# FDA Approved IGB Non-Serious Adverse Events

Adverse Event	ReShape (%)	Orbera (%)	Obalon (%)
Vomiting	86.7	86.8	17.3
Nausea	61.0	75.6	56.0
Abdominal Pain	54.5	57.5	72.6
Gastric Ulcer	35.2*	0	0.9
Dyspepsia	17.8	21.3	16.9‡
Eructation	16.7	24.4	9.2
Abdominal Discomfort	13.3	6.3	0
Abdominal distension	11.0	17.5	14.6
Erosive Gastritis	9.1	0.6	7.1†
GERD	6.8	30.0	(see dyspepsia)
Erosive Esophagitis	0.4	0.6	1.8
Constipation	5.3	0	2.7
Diarrhea	3.0	13.1	8.3

\*After design modification of the distal tip of the ReShape Balloon, the ulcer rate decreased to 10%.

†Composite of Erythema, Erosion, inflammation, or polyp

‡Composite of Dyspepsia and GERD

# Orbera Meta-Analysis Adverse Events

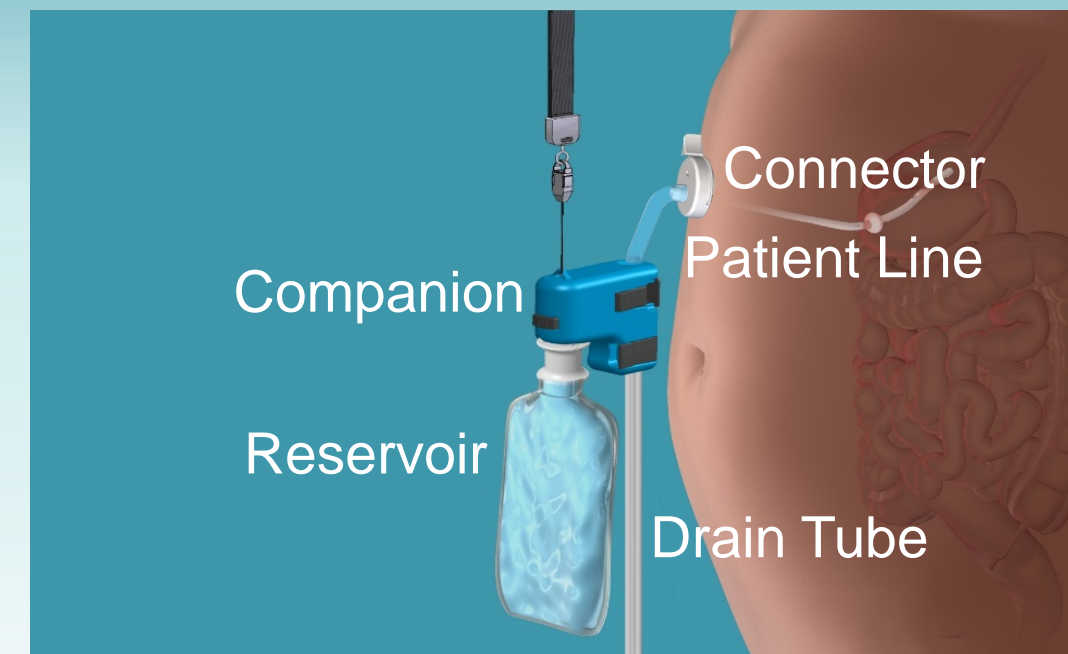
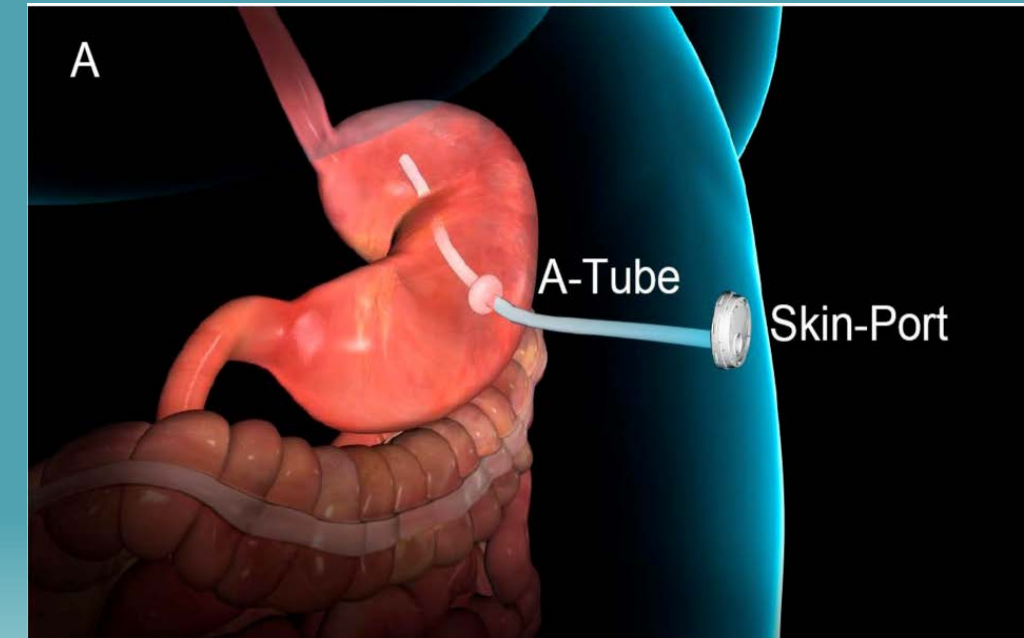
- Eighty Studies including 8506 patients
- Early Removal: 7.5%

Side-Effect	Rate (%)
Pain	33.7
Nausea	29
GERD	18.5
Gastric Erosions/Ulcers	12/2
Migration	1.4
Small Bowel Obstruction	0.3
Perforation	0.1
Death	0.08



# AspireAssist System (Aspire Bariatrics, King of Prussia, PA)

- Similar in concept to a percutaneous endoscopic gastrostomy tube
  - Known SAE rate of 2%
- Aspirate gastric contents ~20 minutes after meals 2-3 x/day
- Removes 25-30% of calories consumed at that meal
- Accounts for 50-80% of weight loss – lifestyle and mealtime behaviors reduce overall food intake
- Food choices improve anecdotally



# A-tube and Skin Port Placement

- A-Tube Placement:  
Standard pull  
technique using a pull  
PEG kit
  - 15 minute procedure
  - Monitored anesthesia  
care for most patients
  - 60 minute recovery
- Skin Port conversion 1  
week after A-Tube  
placement



# BMI 35-55 kg/m<sup>2</sup>

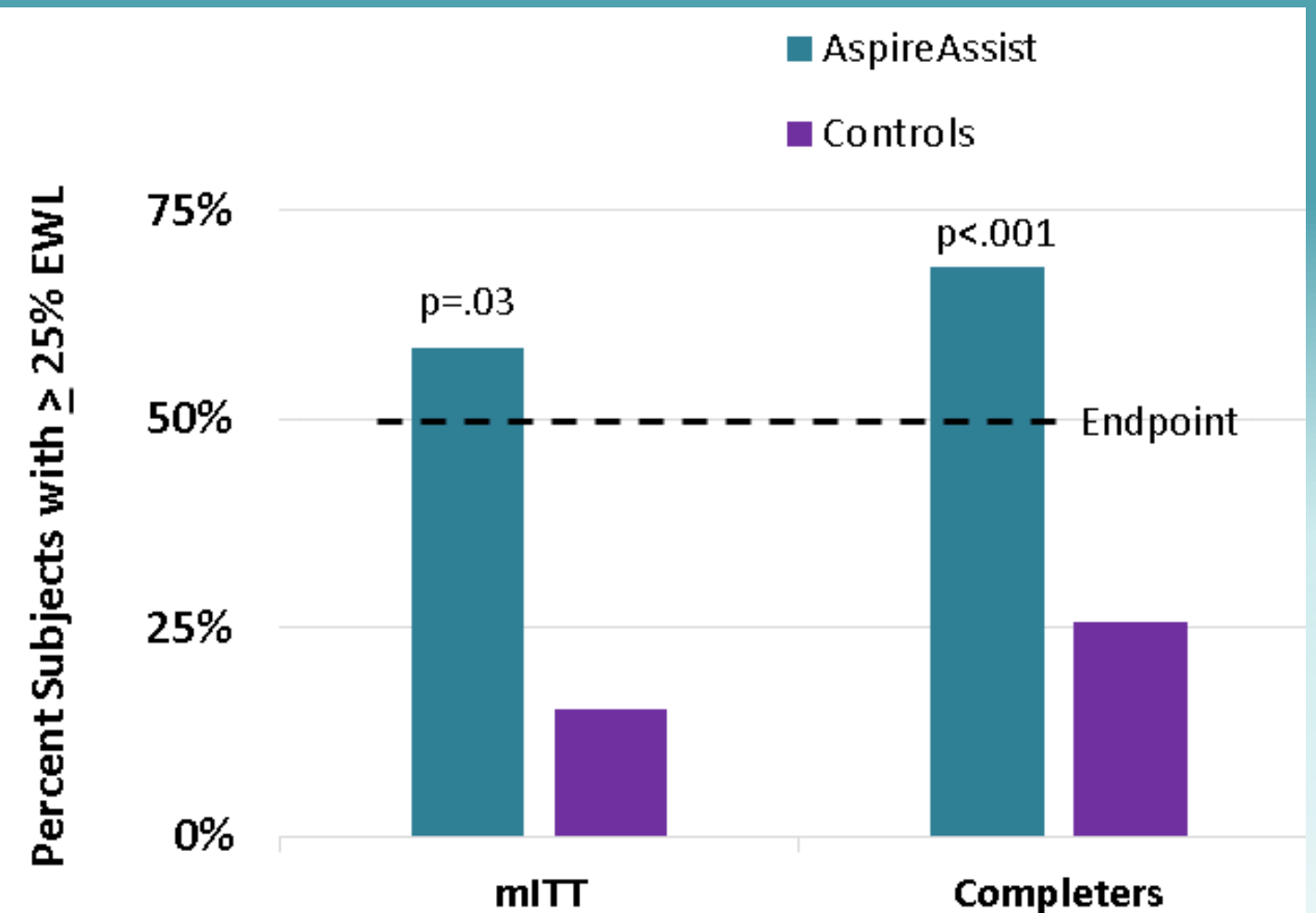
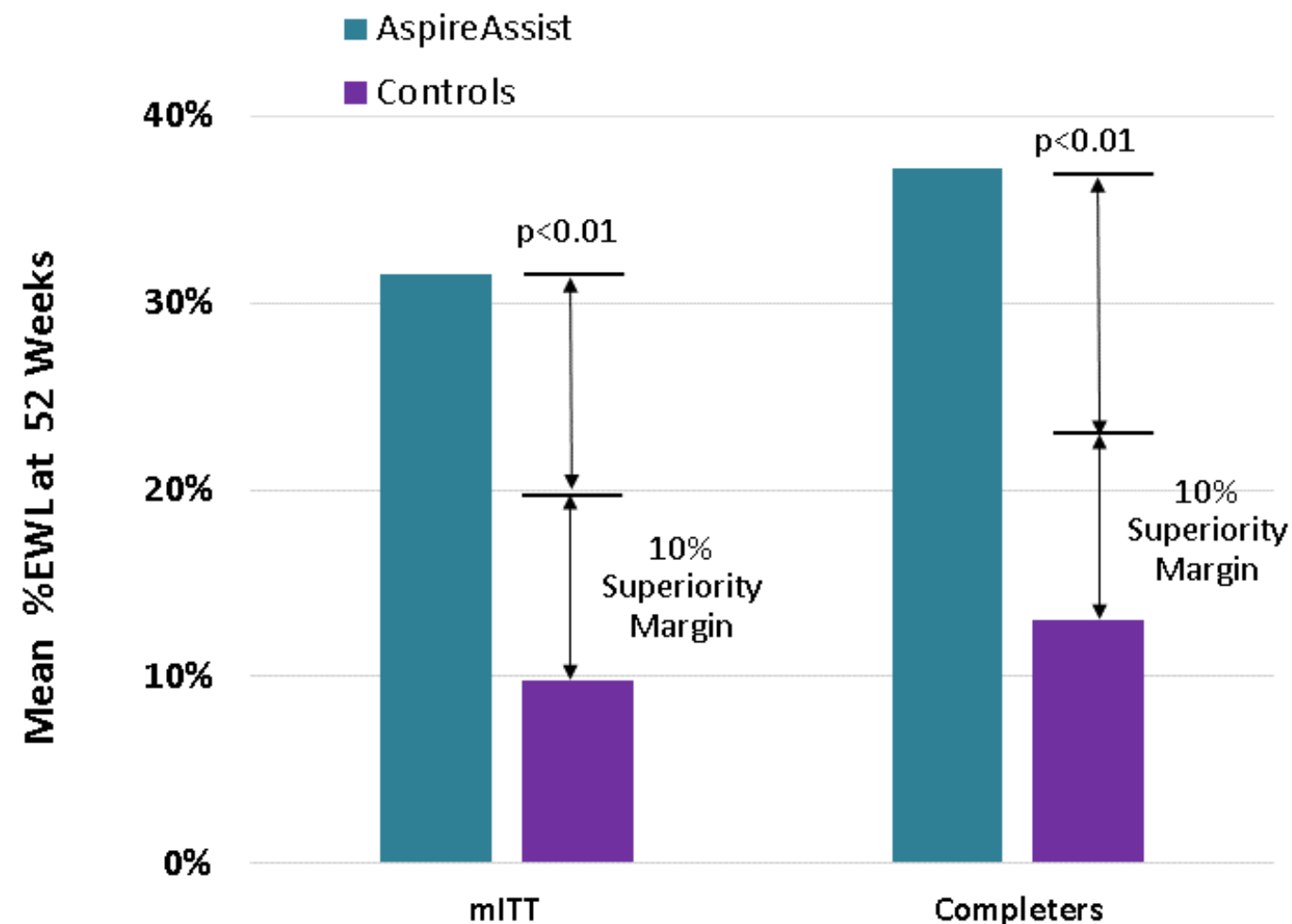
## Two Co-Primary Endpoints

### Co-Primary Endpoint #1

Mean %EWL at 52 Weeks of AT Group  
at least 10% greater than Control Group

### Co-Primary Endpoint #2

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



# Eating Behaviors

Subjects assessed for binge-eating, bulimia, & night-eating syndrome

- Eating Behavior Assessment: Questionnaire on Eating and Weight Patterns-Revised and the Eating Disorder Examination
- Assessments at Baseline, Week 14 (AT subjects only), Week 28, and Week 52
- 1 Control subject developed binge-eating syndrome at Week 28 and was removed from study
- No AT subject showed any evidence of worsening eating behaviors

Frequency of aspiration monitored by Connector counts

- No evidence of any subject excessively aspirating

Self-reported eating behaviors:

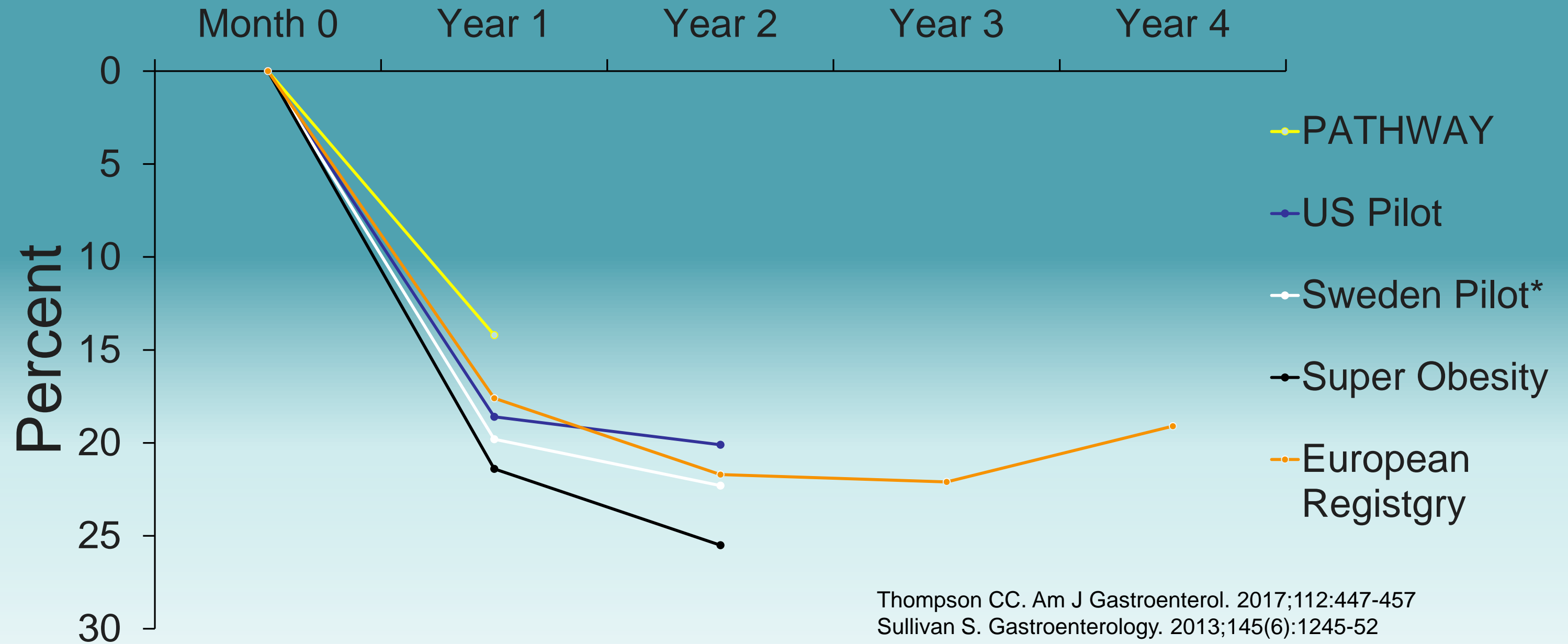
- 91% of patients reported strongly agreeing/somewhat agreeing to increased chewing
- 78% reported significantly/somewhat decreased calorie consumption

# Adverse Events >5%

Adverse events	No. of Subjects (%)	No. of Subjects, Perioperative*	No. of Subject, Postoperative**
Peristomal granulation tissue	45 (40.5%)	0	45
Abdominal pain $\leq$ 4 weeks after A-tube placement*	42 (37.8%)	41	1
Nausea/vomiting	19 (17.1%)	15	4
Peristomal irritation	19 (17.1%)	2	17
Intermittent abdominal discomfort	18 (16.2%)	16	2
Possible or definite peristomal bacterial infection	15 (13.5%)	13	2
Abdominal pain >4 weeks after A-tube placement*	9 (8.1%)	0	9
Dyspepsia (acid reflux, heartburn, hiccups, belching)	7 (6.3%)	1	6
Peristomal inflammation	6 (5.4%)	4	2

5 SAEs in 4 subjects, all resolved (3.6% SAE rate)

# Aspiration Therapy Percent Total Body Weight Loss



Thompson CC. Am J Gastroenterol. 2017;112:447-457  
Sullivan S. Gastroenterology. 2013;145(6):1245-52  
Noren E. BioMed Central Obesity. 2016;3:56  
Machytka E. Gastroenterology 2016;150:S822-S823  
Machytka E presenting at IFSO. London. 2017

# Endoscopic Bariatric Therapies in Older Adults: Limited Data

- Orbera Balloon (n=20) and Spatz Balloon (n=10)
  - Safety: 3 early removals, one for deflation and migration into the small bowel
- Weight Loss:
  - Both groups: median  $20 \pm 3$  kg

# Endoscopic Bariatric Therapies

- Intragastric Balloons
  - Weight Loss
    - 10% or more TBWL in clinical practice at 1 year
    - limited data on weight loss at >2 years after removal, but limited data suggests weight loss maintenance in some patients at 5 years
  - Safety
    - Low serious adverse event rates
    - Low early removal rate
- Aspiration Therapy
  - Weight loss: 14-21% TBWL at 1 year with weight loss maintenance at 4 years in a small number of patients
  - Safety
    - Low serious adverse event rate
    - Known complication rates from similar procedures (PEG tubes)



# Outline

- Obesity and Weight Loss in Older adults
- Evidence behind Endoscopic bariatric therapies
- Mechanisms for acquiring additional safety and effectiveness data for EBTs in older adults

# Proposal for Expedited Evaluation of EBT in Older Adults

- CMS coverage for older adults age 65-74
  - Requires reversal of NCD for Endoscopic Bariatric Therapies
  - Consider registry to acquire larger data set
- Physician Benefits
  - CMS coverage of procedures, complications, and program costs
- Physician requirements
  - Ability to perform endoscopic bariatric therapies
  - Comply with all program components

# Program Components

- EBT
  - FDA Approved therapies
    - IGBs
    - Aspiration Therapy
- Lifestyle Intervention
  - Based on cardiac rehabilitation model
    - Physical therapy, exercise tolerance, and nutrition evaluations
    - Registered Dietitian visits
    - Exercise sessions
  - Follow-up visits can be done in group model to reduce the cost

# Non-Procedure Program Costs

Component	Practitioner	HCPCS	Cost
Initial Medical Evaluation	Physician	99204	\$150
Follow-up	Physician	99213 (4 units)	\$326
Initial Nutrition Evaluation	Registered Dietitian	G0447 (2 units)	\$58
Barriers to Exercise Evaluation	Physical Therapist	97163	\$91
Initial Fitness evaluation	Exercise Trainer	97110	\$36.39
Group Nutrition and Behavioral Therapy	Registered Dietitian, trained behavioralist	G0473 (12 units)	\$108
Group Exercise Sessions	Exercise Trainer	97150 (208 units)	\$464

Physician Fee Schedule: <https://www.cms.gov/apps/physician-fee-schedule/search/search-results.aspx?Y=0&T=0&HT=0&CT=1&H1=97163&C=16&M=5>

# Total EBT Costs

- Vary with procedure
- All current therapies require 1-2 endoscopic procedures
  - Anesthesia support
  - Usual procedure time 30 minutes
- Current range of cash pay program price (without exercise sessions):
  - IGBs: \$6,000-\$12,000
  - Aspiration Therapy: \$7,500-\$14,000

# Conclusions

- Weight loss is beneficial for older adults
  - $\geq 10\%$  TBWL likely needed for reduction in risk of cardiovascular events
  - Improvement in multiple markers of frailty likely requires exercise with weight loss
- EBTs have Level 1 evidence for safety and efficacy as well as increased weight loss in clinical practice in short-term studies
  - Small amount of data weight loss outcomes out to 4 years
  - Only one case series in older adults with IGB treatment

# Suggestions

- Advise CMS to reverse the NCD on IGBT on the basis of extensive level 1 evidence in adults
  - Last Revised 9/1987
  - <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=111&ncdver=1&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyWord=balloon&KeyWordLookUp=Title&KeyWordSearchType=And&generalError=Invalid+Email+Document.&bc=gAAAACAAAAAAAAAA%3d%3d&>
- Advise CMS to cover FDA approved EBT's with lifestyle therapy (including exercise) in the Medicare population to reduce chronic disease, disability, and annualized expenditures.
- If it is felt that additional data on the efficacy of EBT's in the Medicare population is needed, ASGE/ABE will work with other medical societies and CMS to establish a Medicare EBT registry to allow patient treatment and data collection.



# Thank you



**Association for  
Bariatric Endoscopy**  
A DIVISION OF ASGE