



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

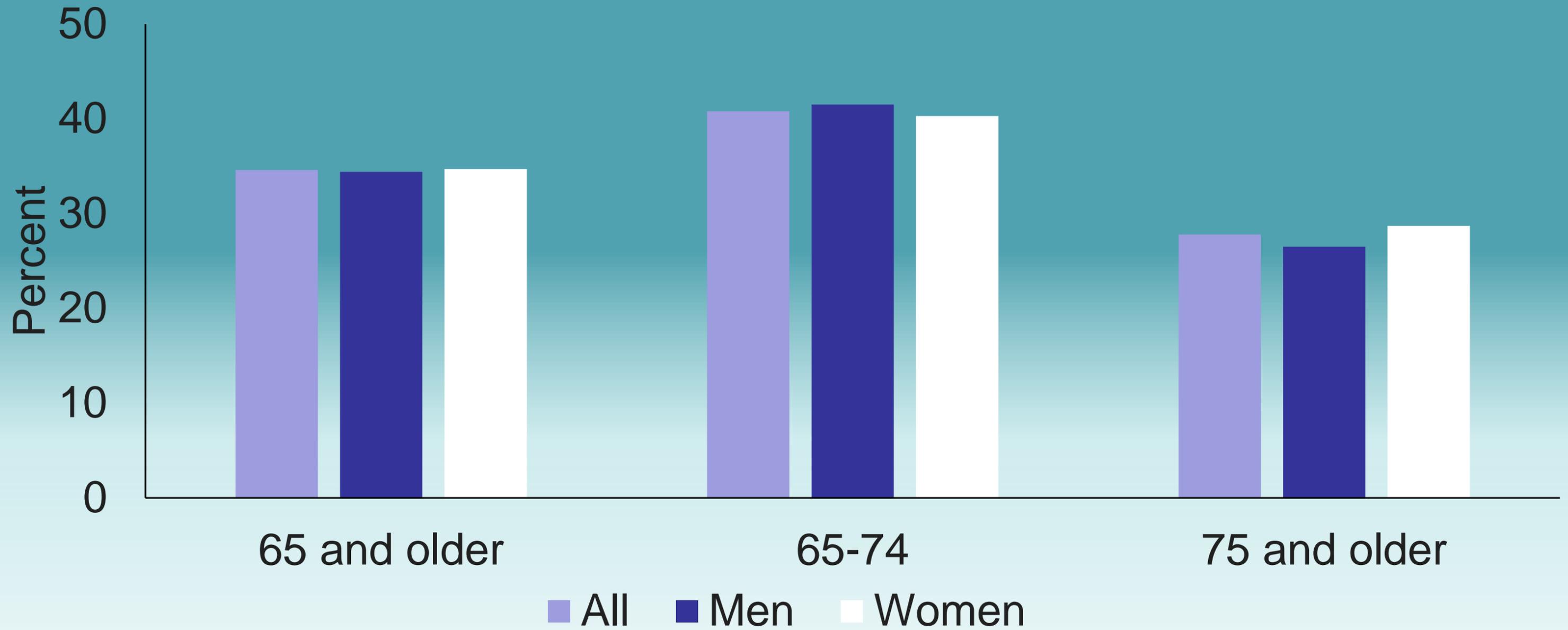
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- Consulting / Employment
 - USGI Medical, EnteroMedics, Obalon, Takeda Pharmaceuticals, Elira Therapeutics, Aspire Bariatrics



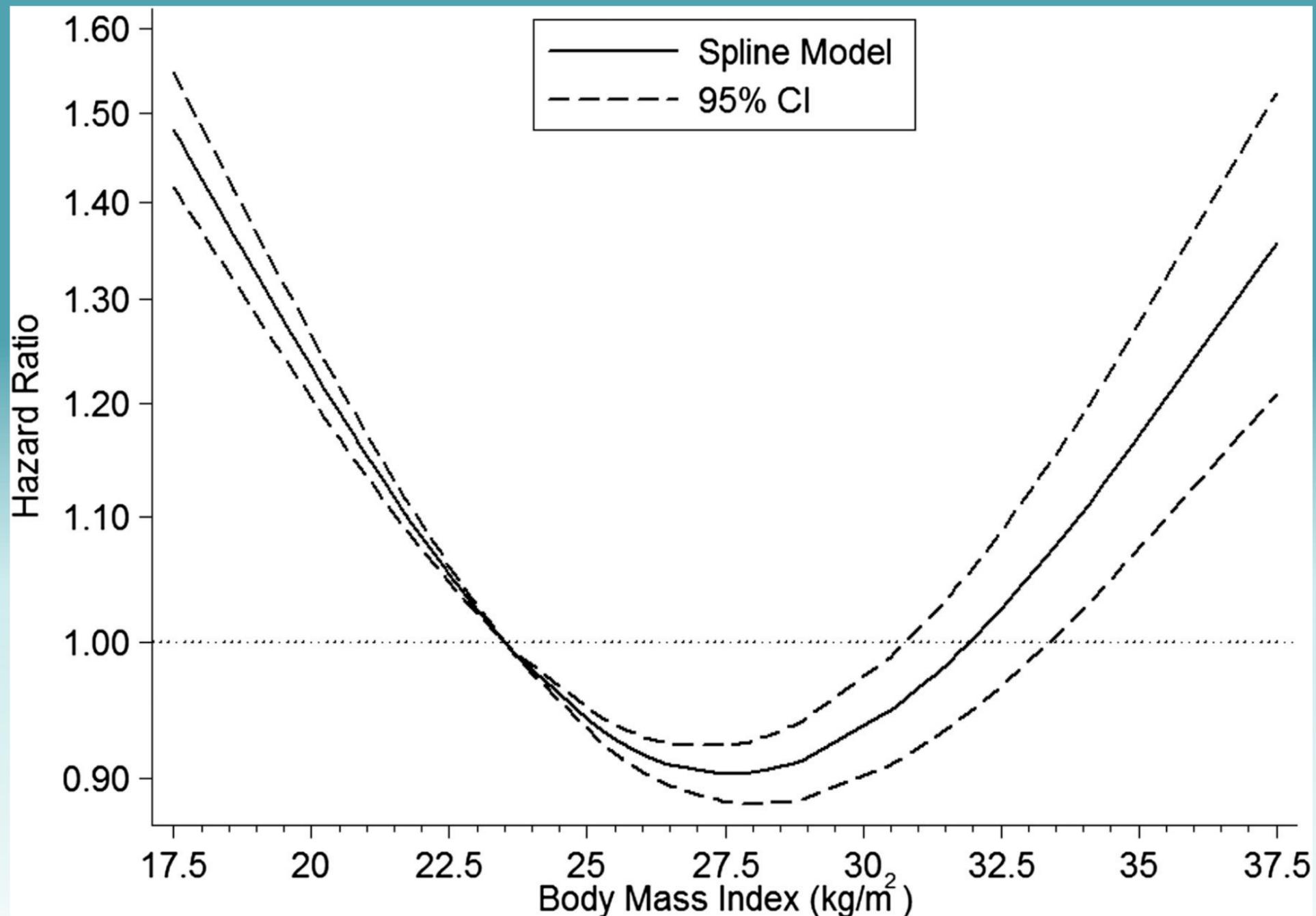
Outline

- 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

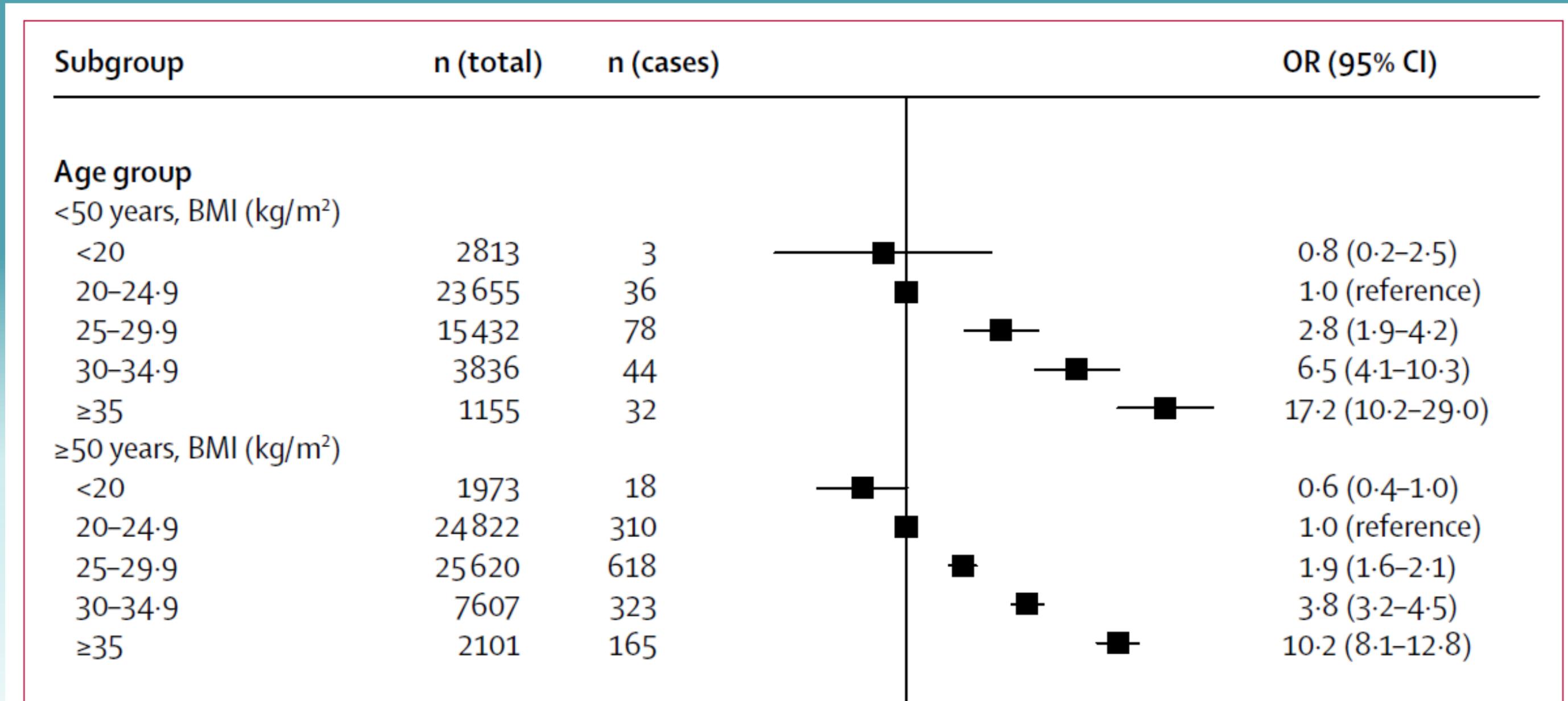
Prevalence of Obesity in Adults Age ≥ 65 years



Obesity Paradox: all-cause mortality according to BMI for men and women aged ≥ 65 y.



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

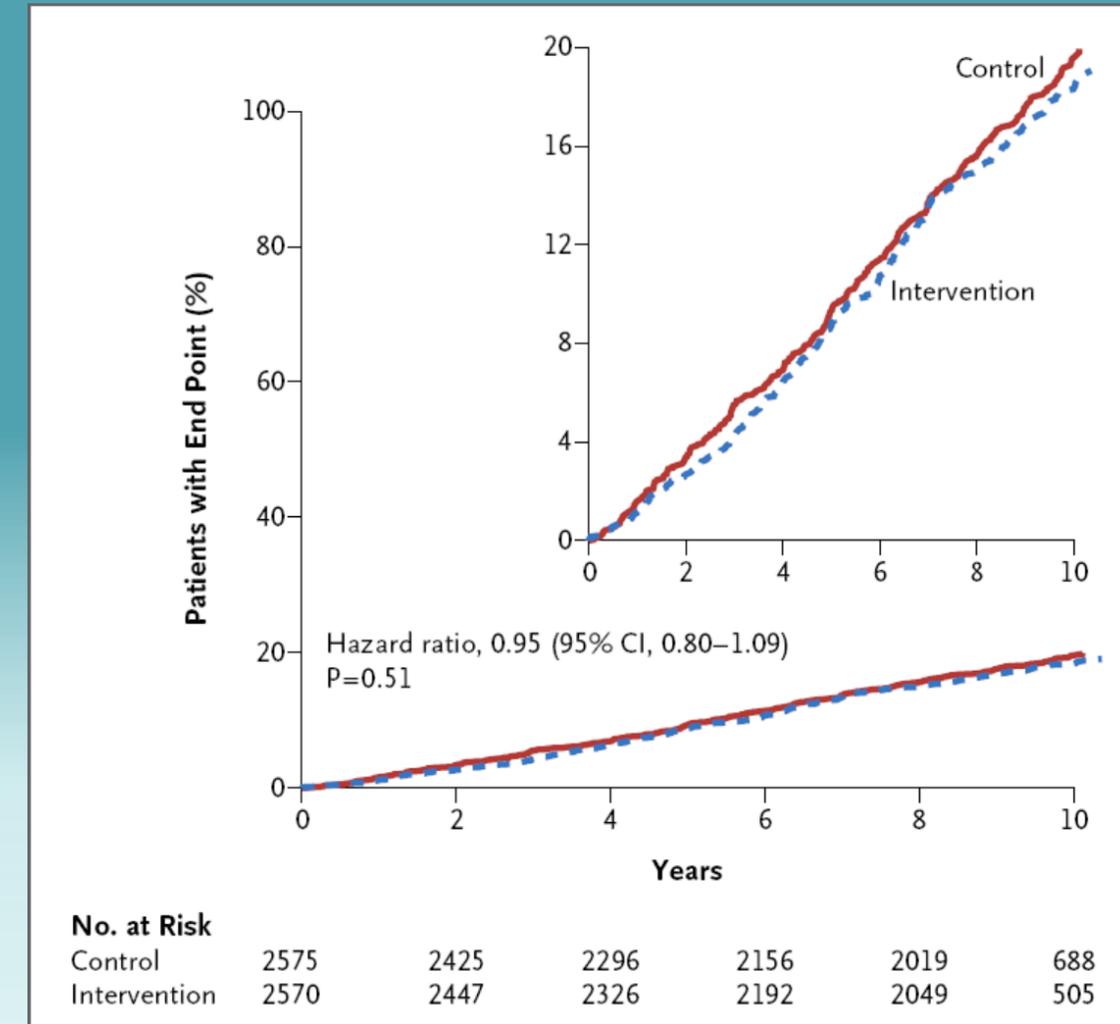
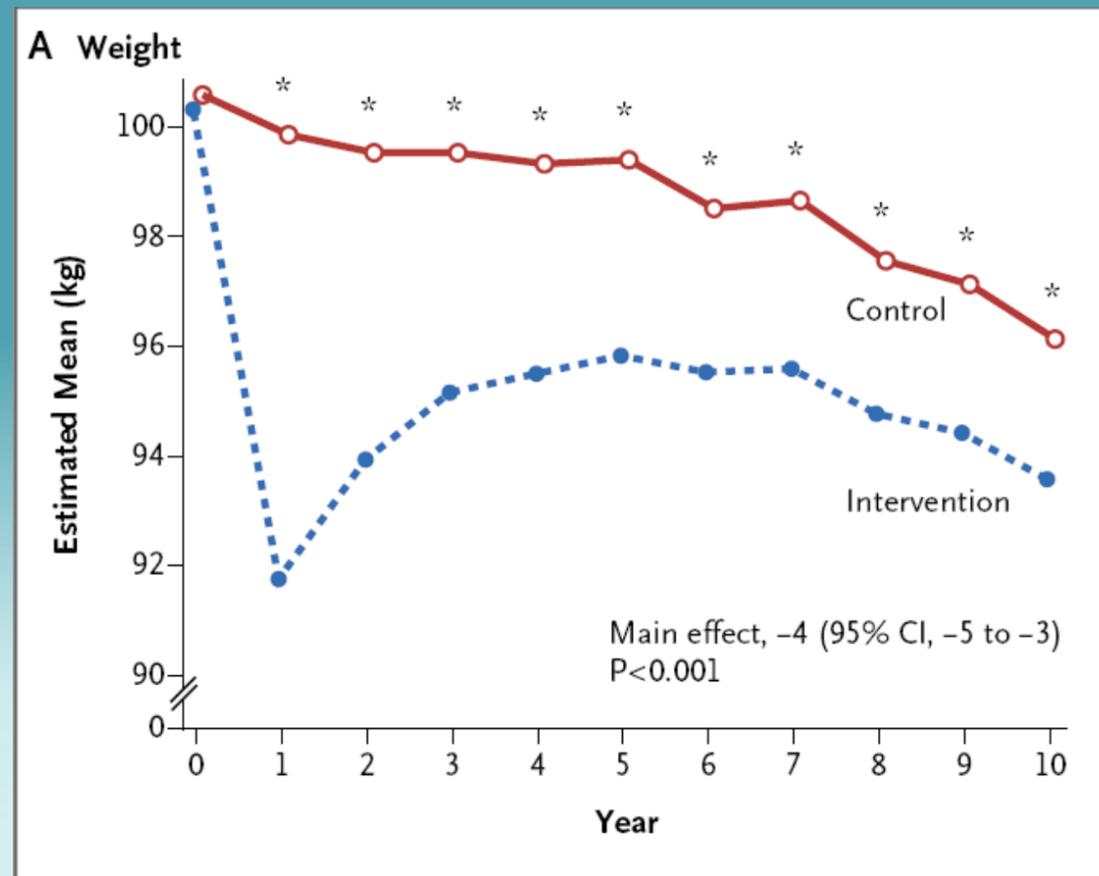


Weight Loss Effects are Dose Dependent: Progressive Weight Loss Study

| 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

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

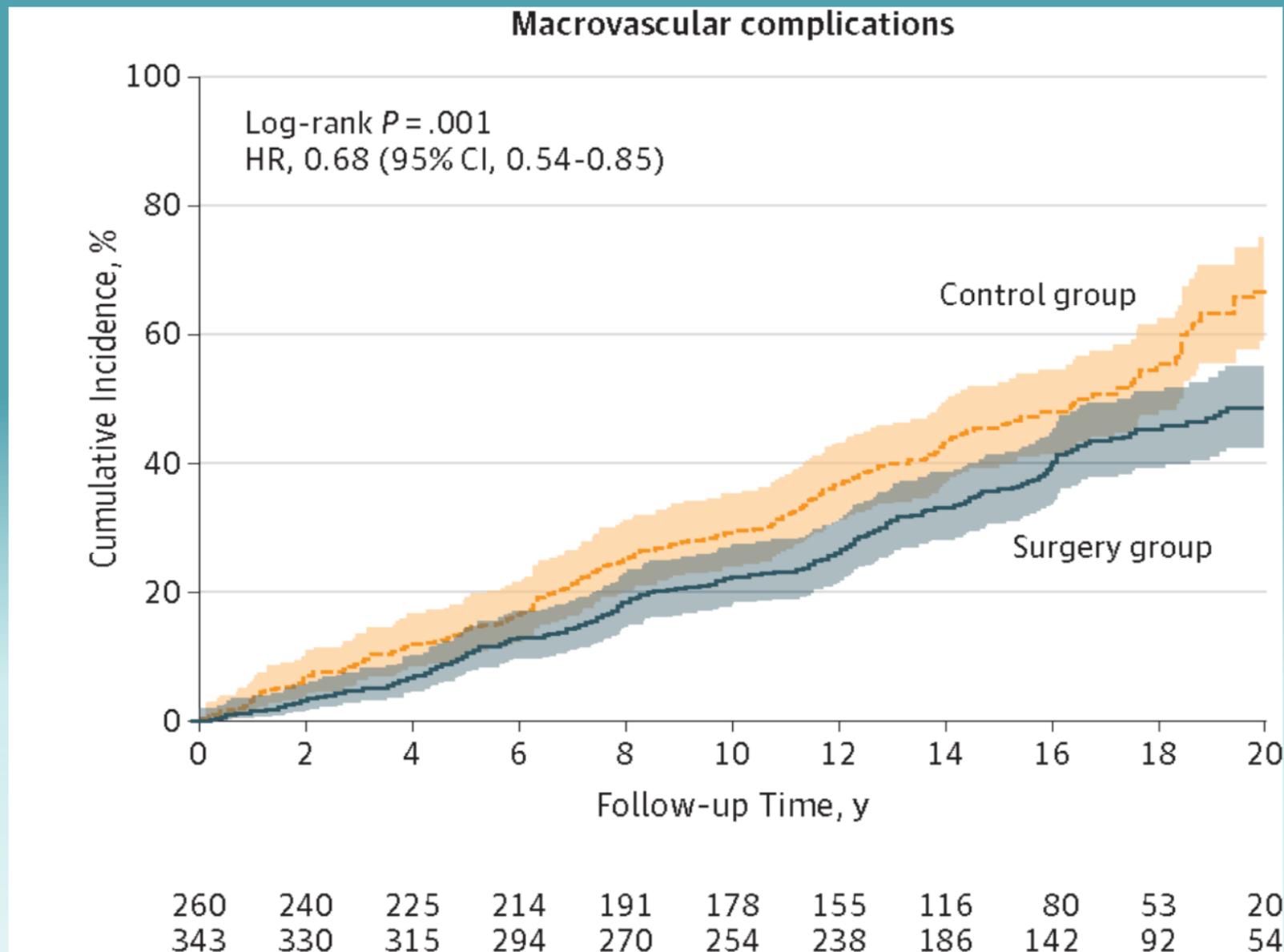


>10% TBWL for Reduction in Cardiovascular Outcomes

| 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 |

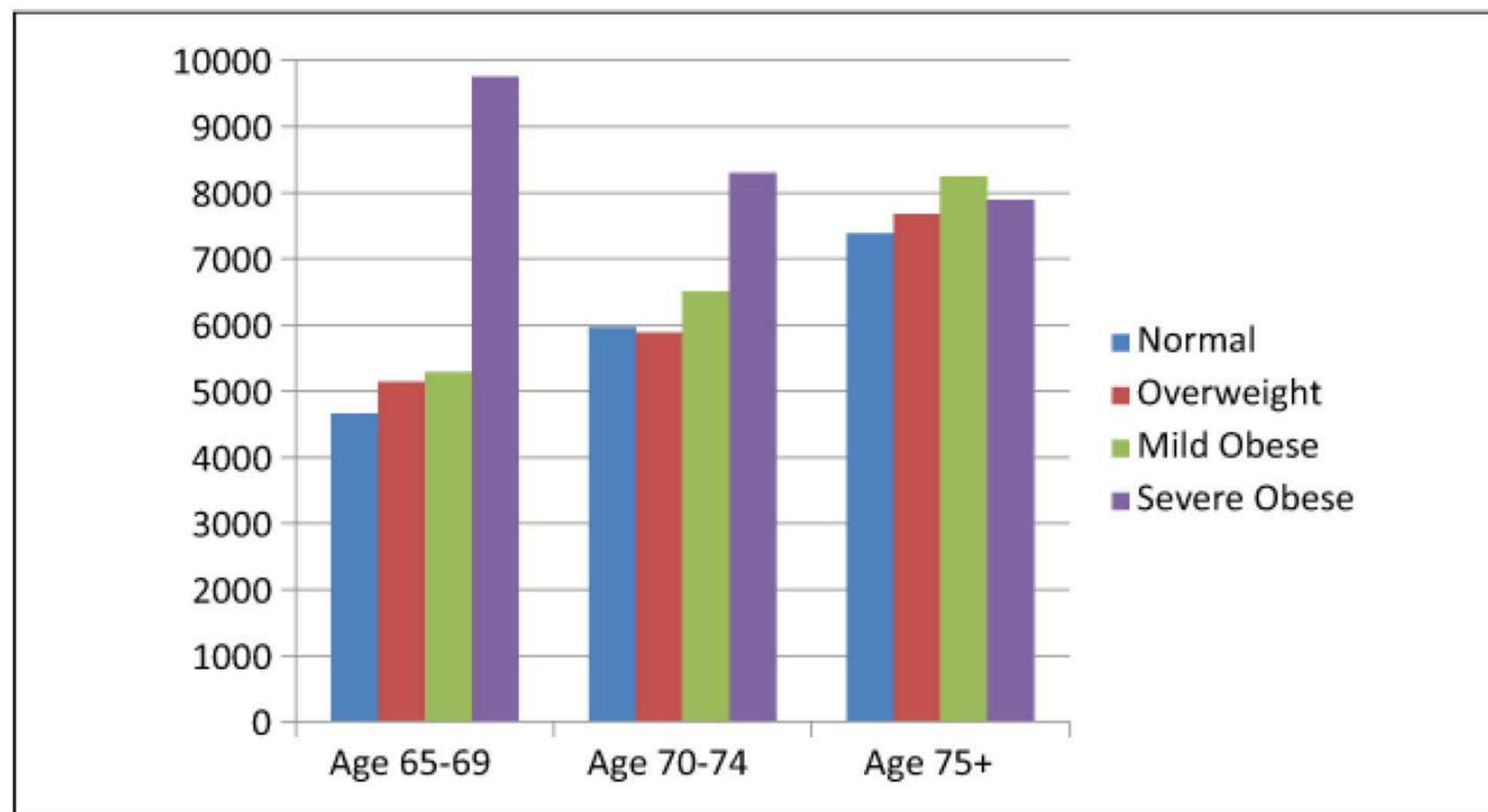
- Look Ahead Trial
- Post-Hoc Analysis
- 4406 subjects in the analysis
- Age 45-76
- Diabetes

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



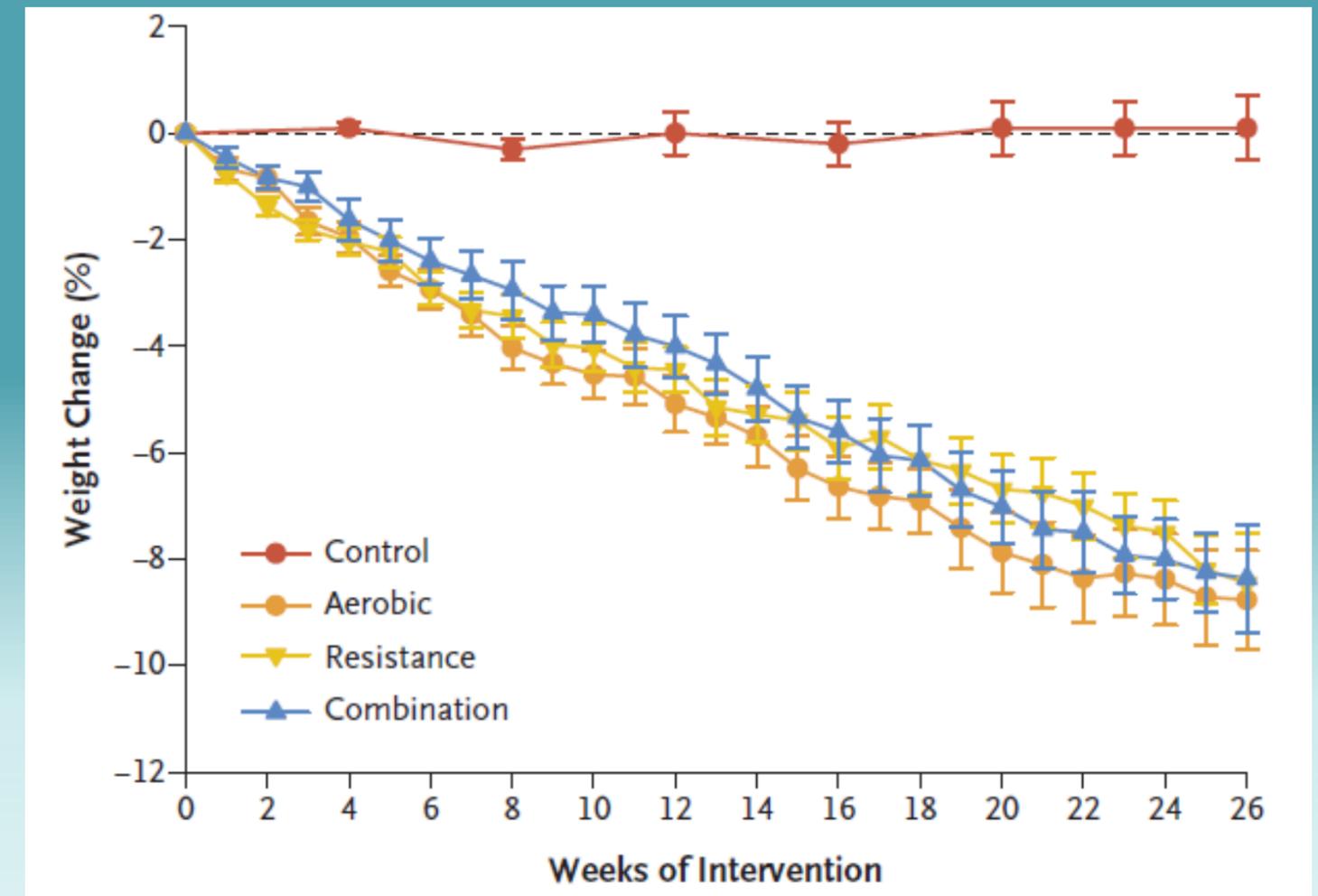
Age Difference and BMI Affects on Medicare Expenditures 1998-2008

- Adjusted for age, gender, ethnicity, education, and smoking history:
 - Normal weight age 65-69: \$4,663
 - BMI ≥ 35 kg/m² 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

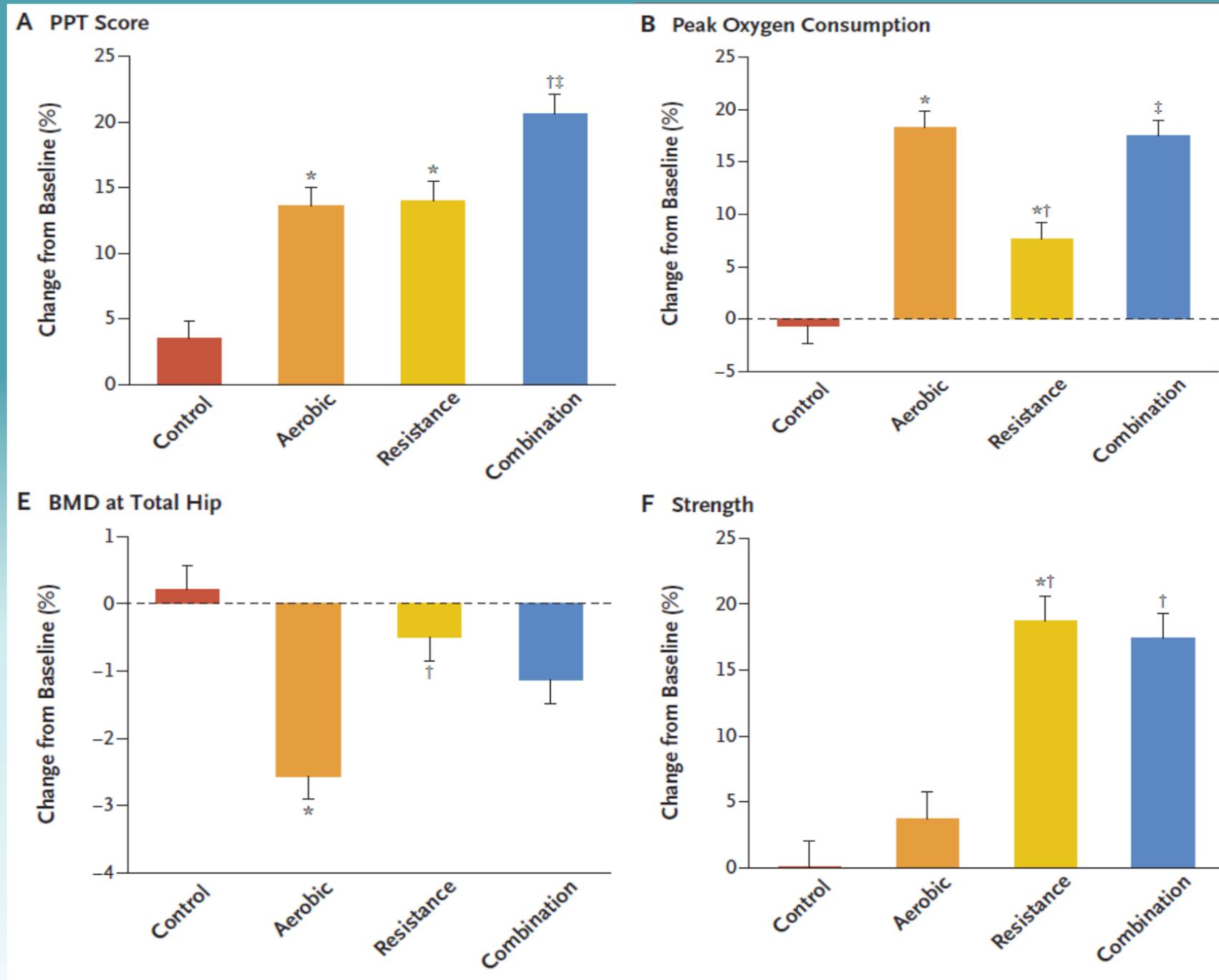
*Frailty with disability contributes to increased Medicare expenditures in patients with a BMI ≥ 35 kg/m² age 65-74

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

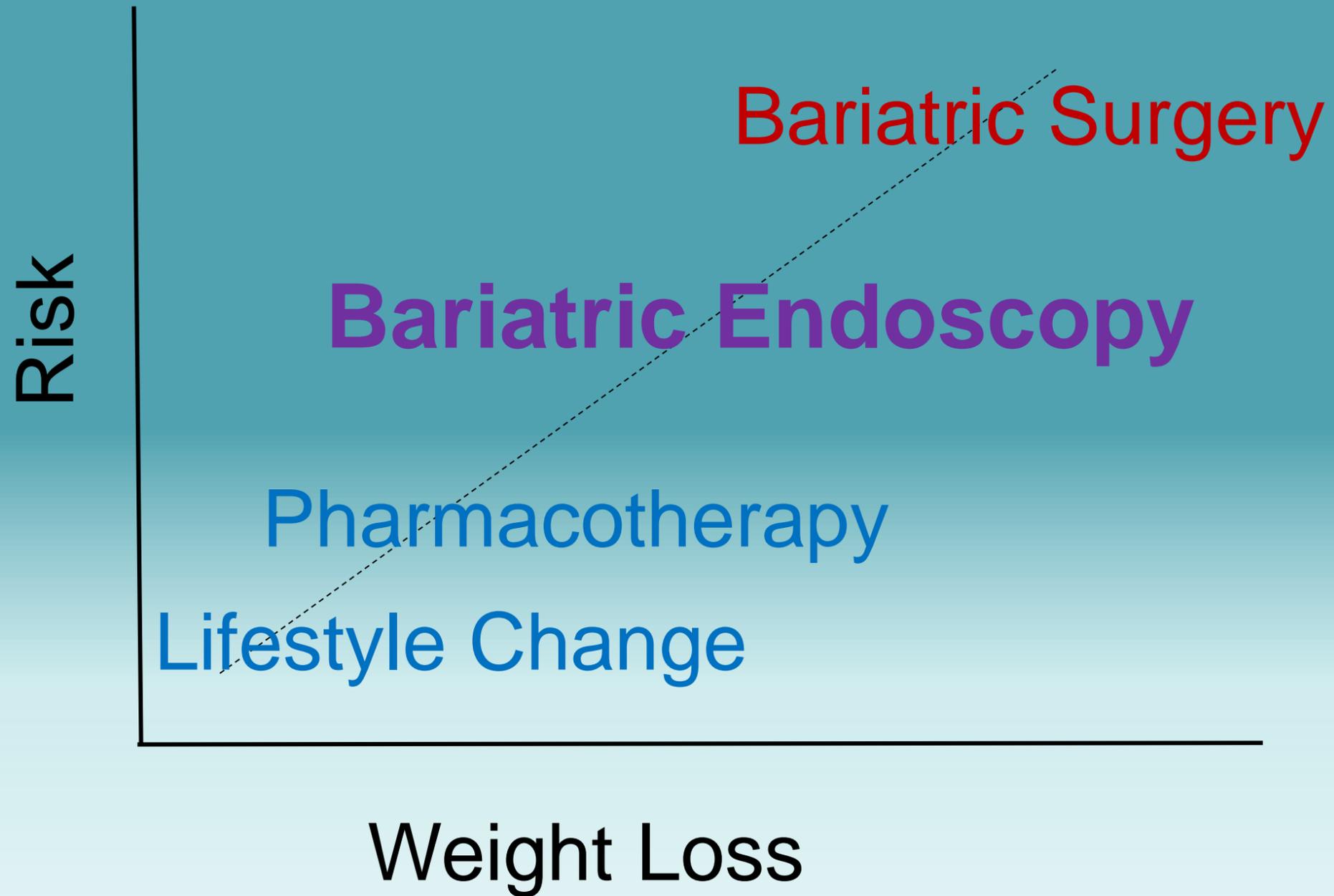
Obesity and Weight Loss in Older Adults

- Over 1/3 of older adults have obesity
- Obesity, in particular BMI ≥ 35 kg/m² 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

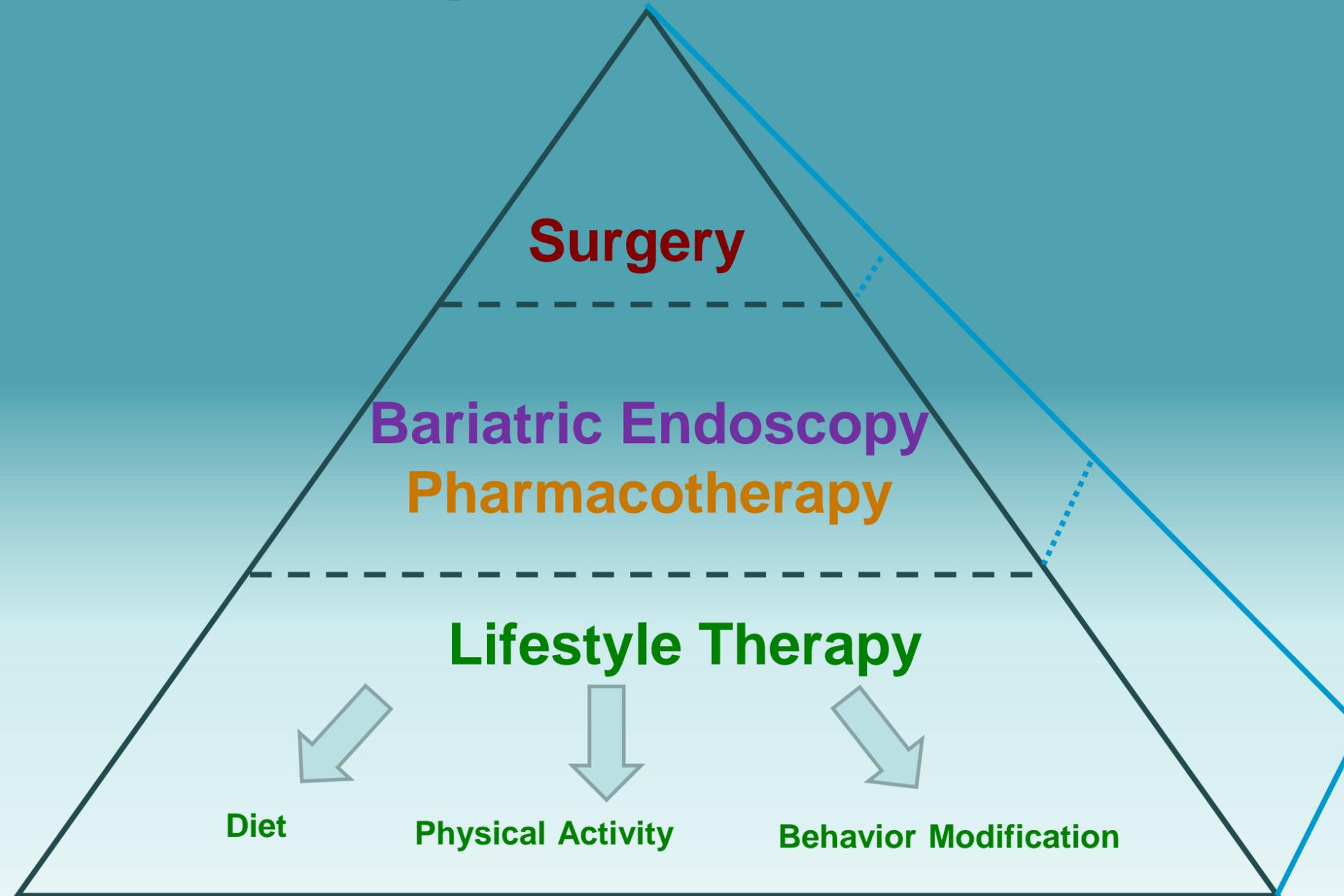
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Endoscopic Bariatric Therapy



Comprehensive Weight Loss Program



Endoscopic Bariatric and Metabolic Therapies

Gastric Therapies

- Intra-gastric Balloons (IGB)
 - ReShape Intra-gastric 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 |
|--|--|--|---|
| <p>ReShape Dual Balloon System ReShape Medical, San Clemente, CA</p> |  | <ul style="list-style-type: none"> • Two medical grade silicone spheres joined by a flexible shaft • each balloon filled with 375 ml to 450 ml of saline dyed with methylene blue • Endoscopically placed and removed | <ul style="list-style-type: none"> • Approved July 28, 2015 • BMI 30-40kg/m² with one obesity related co-morbidity • 6 Months |
| <p>Orbera Intra-gastric Balloon, Apollo Endosurgery, Austin, TX</p> |  | <ul style="list-style-type: none"> • Medical grade silicone sphere, filled with 400-700 ml of saline • Endoscoically placed and removed | <ul style="list-style-type: none"> • Approved August 5, 2015 • BMI 30-40kg/m² • 6 Months |
| <p>Obalon Balloon System Obalon Therapeutics, Carlsbad, CA</p> |  | <ul style="list-style-type: none"> • Thin polymer elipse shape • filled with 250 ml of a nitrogen mix gas • 3 balloons administered over 8 to 12-week period • Swallowed and endoscopically removed | <ul style="list-style-type: none"> • Approved September 8, 2016 • BMI 30-40kg/m² • 6 Months from first administration |

Comparison of Intragastic Balloon Pivotal Trial: 6 Month Data

| Device | Number of subjects | | Body Mass Index (kg/m ²) | | 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%

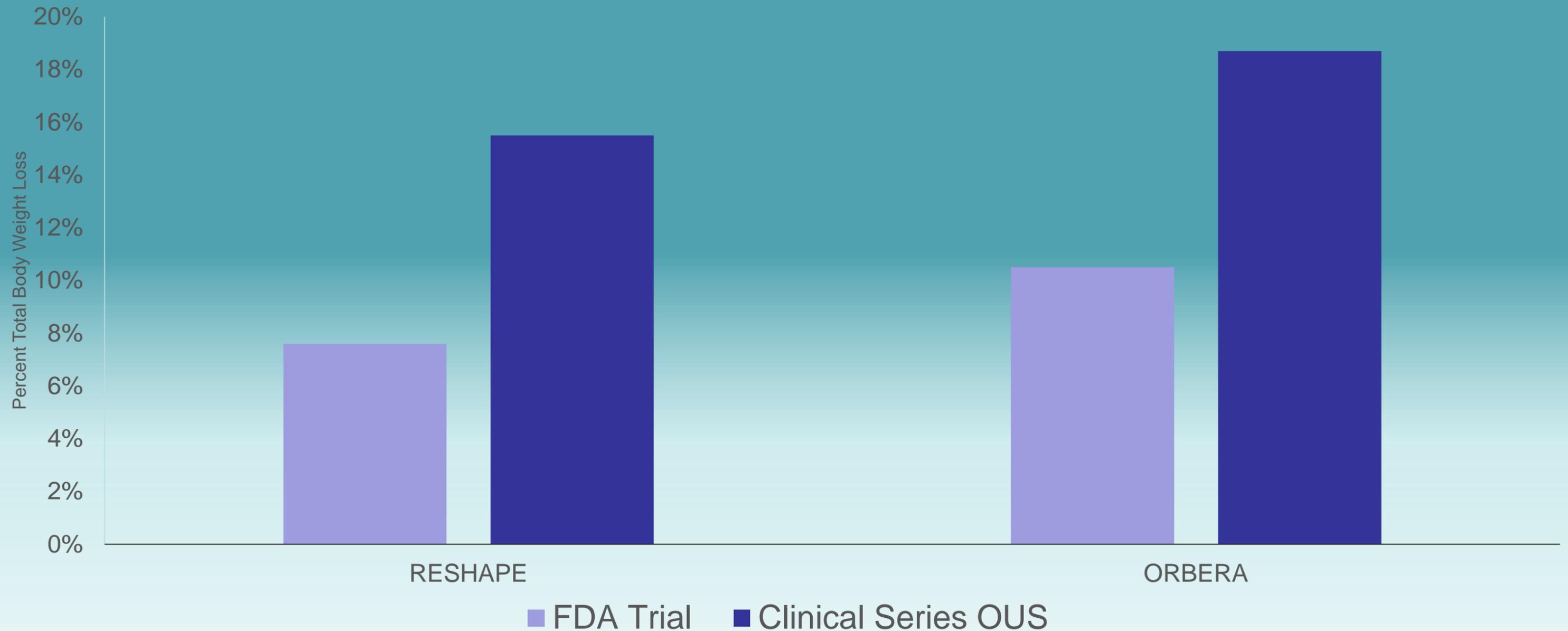
**Majority of SAE's were due to accommodative symptoms

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 Intragastic Balloon System. In: FDA, ed, 2015:1-32

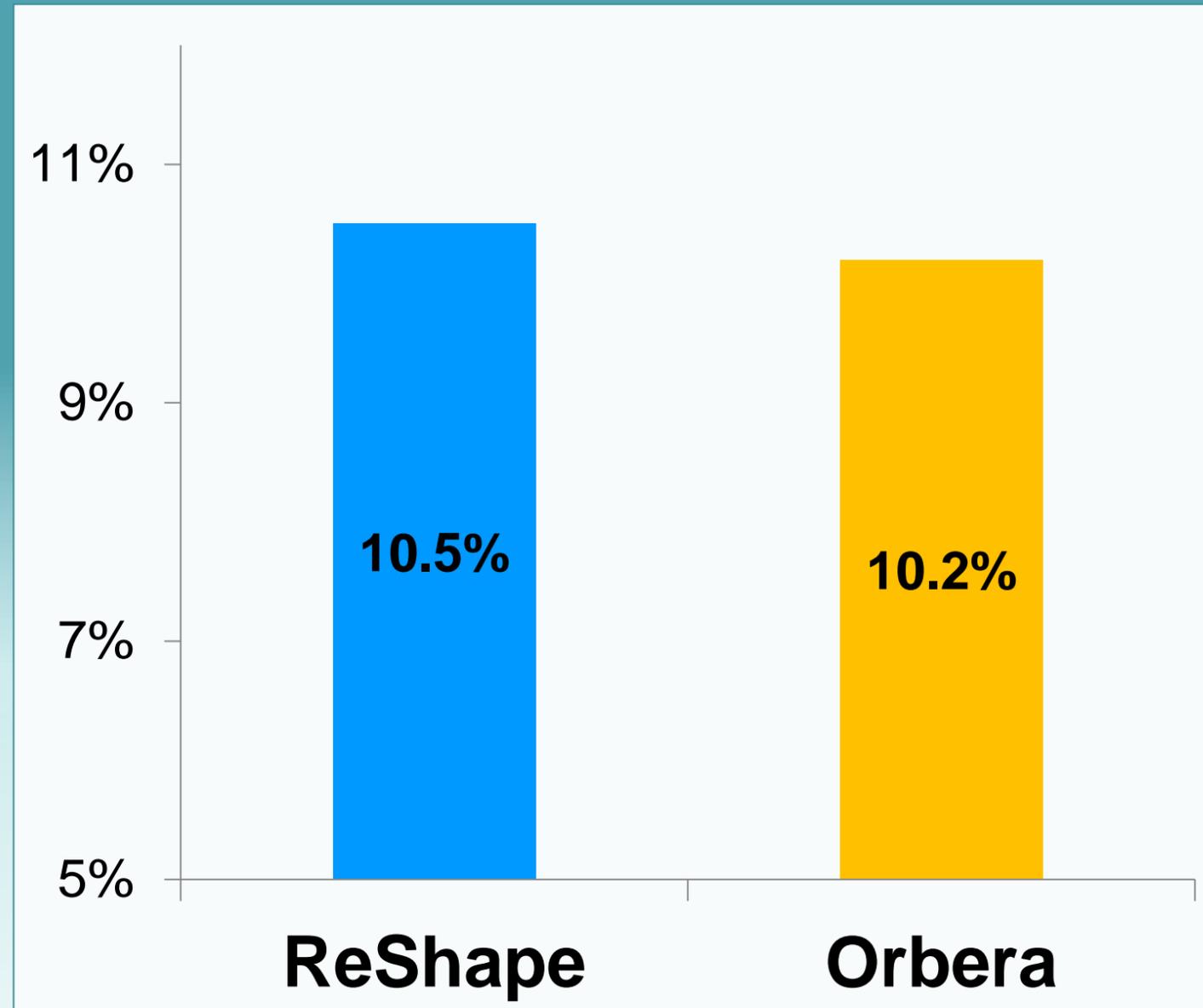
Intragastric Balloon: Higher Effectiveness in Clinical Practice



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/m²) | 36.5±1.2 | 40.8±1.8 | 0.05 |

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

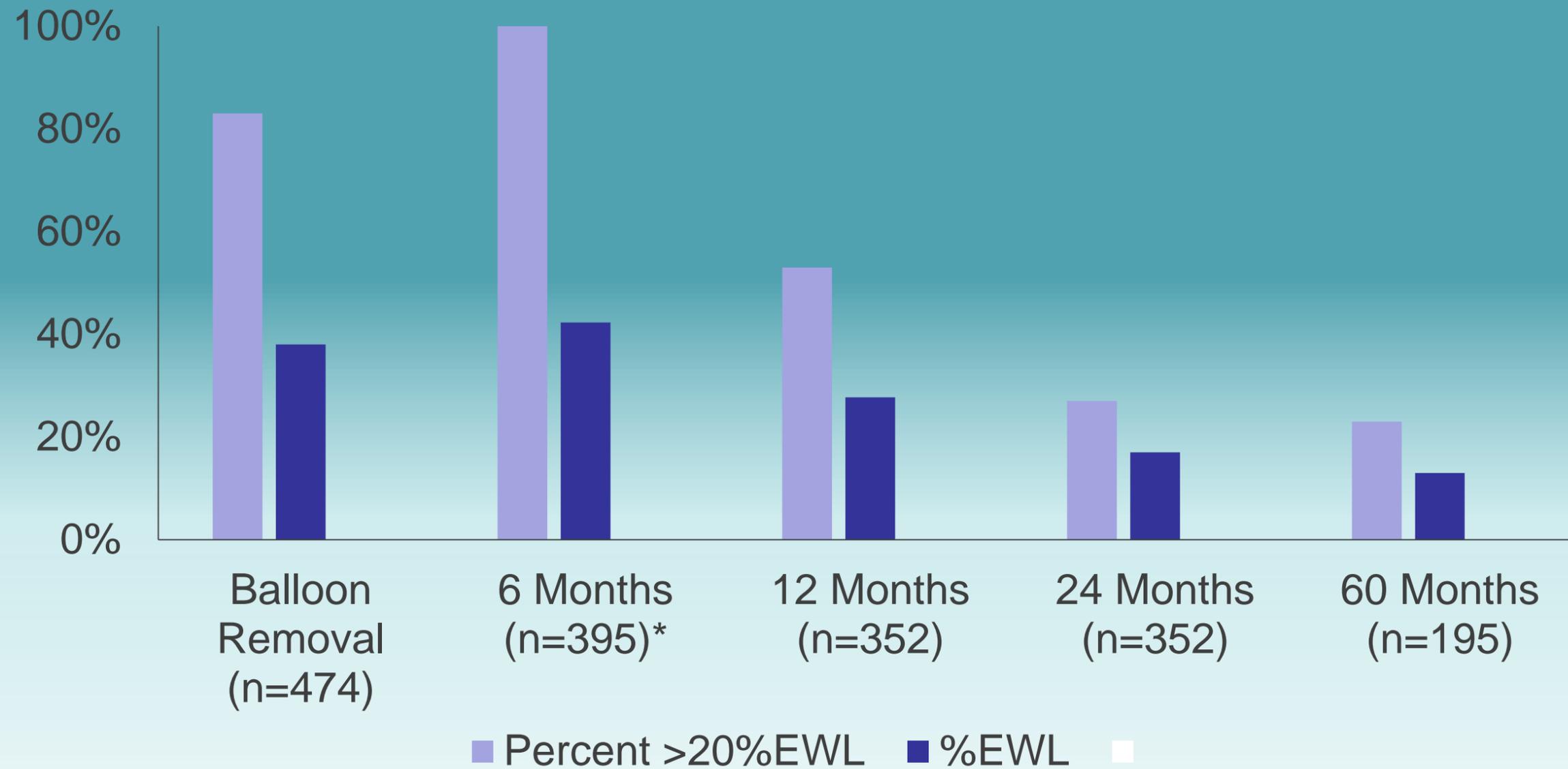
ASGE Bariatric Endoscopy Task Force Systematic Review and Meta-analysis Assessing the ASGE PIVI Thresholds for Adopting Endoscopic Bariatric

Therapies

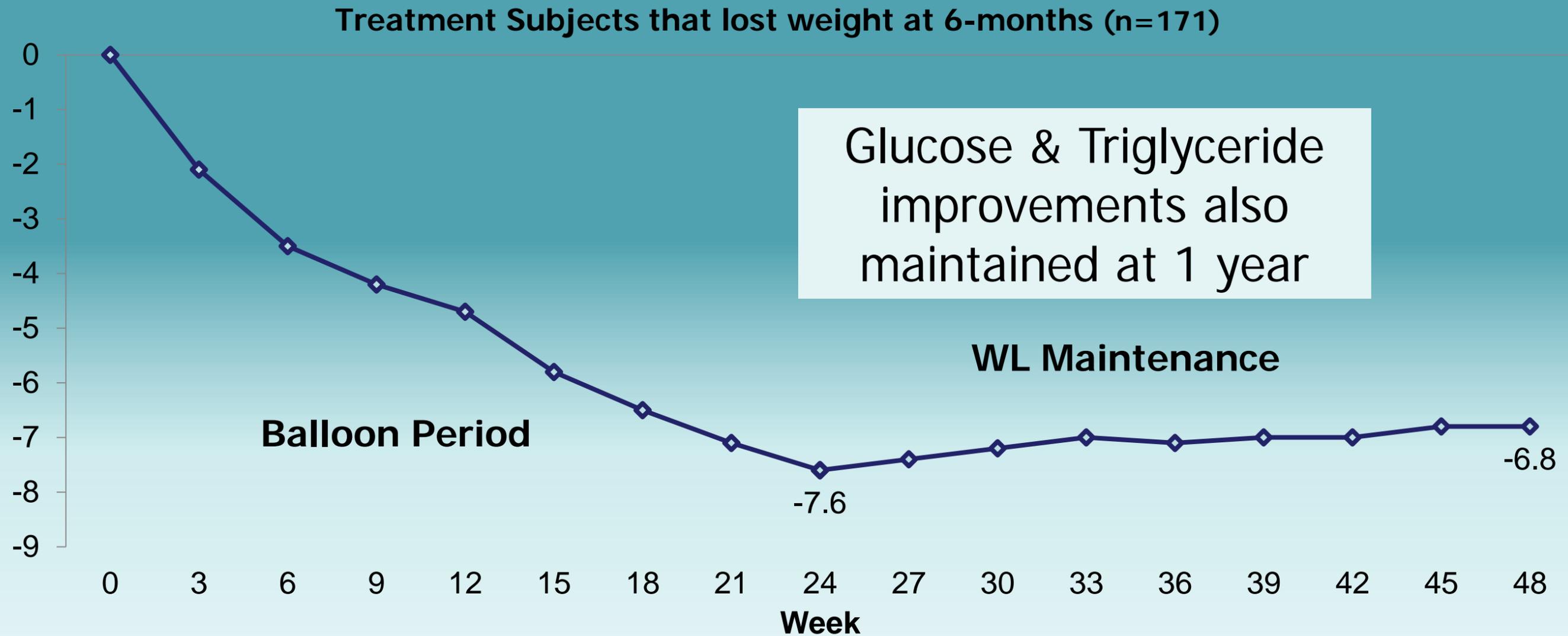
- 1638 patients average percent excess weight loss (%EWL) at 12 months (6 months after balloon removal): 25.44[95% CI 21.47-29.41]
- Average total body weight loss:
 - 3 months after removal:12.3% [95% CI 7.9 – 16.73]
 - 6 months after removal:13.16% [95% CI 12.37 – 13.95]
 - 12 months after removal:11.27% [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

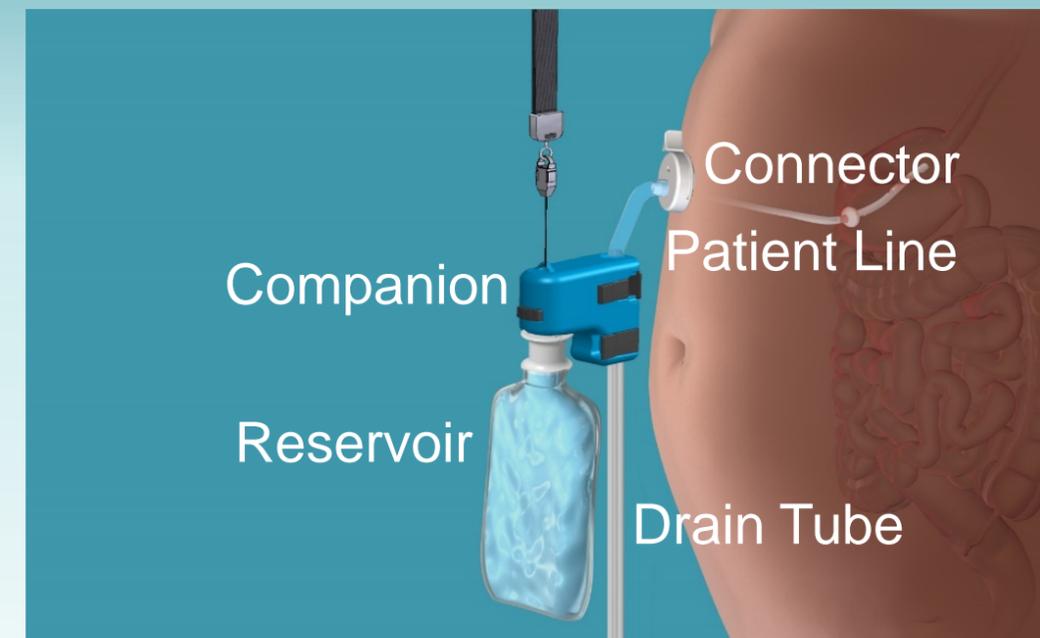
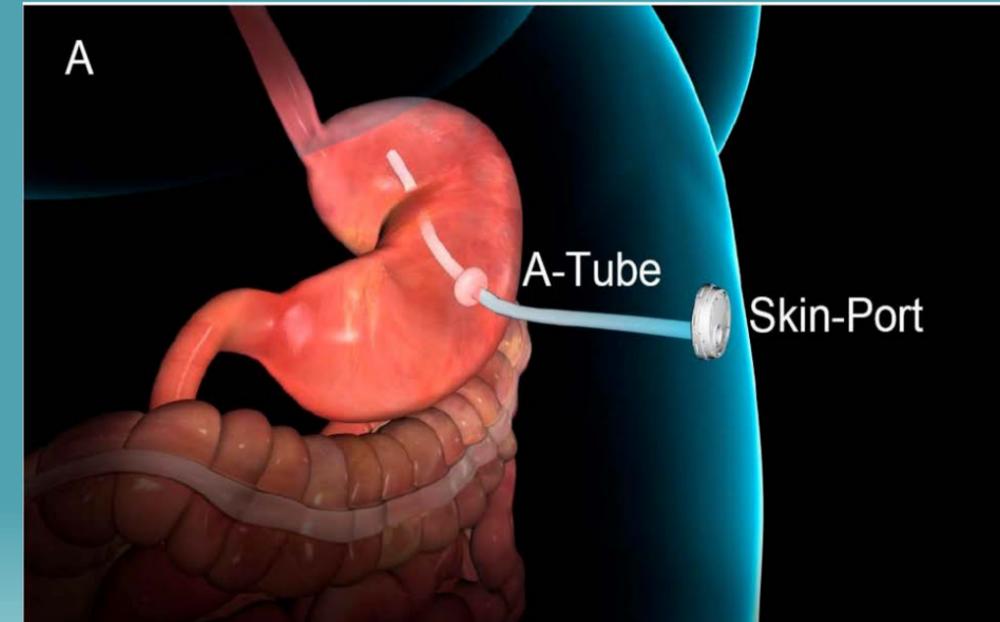
Orbera Meta-Analysis Adverse Events

- 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 |

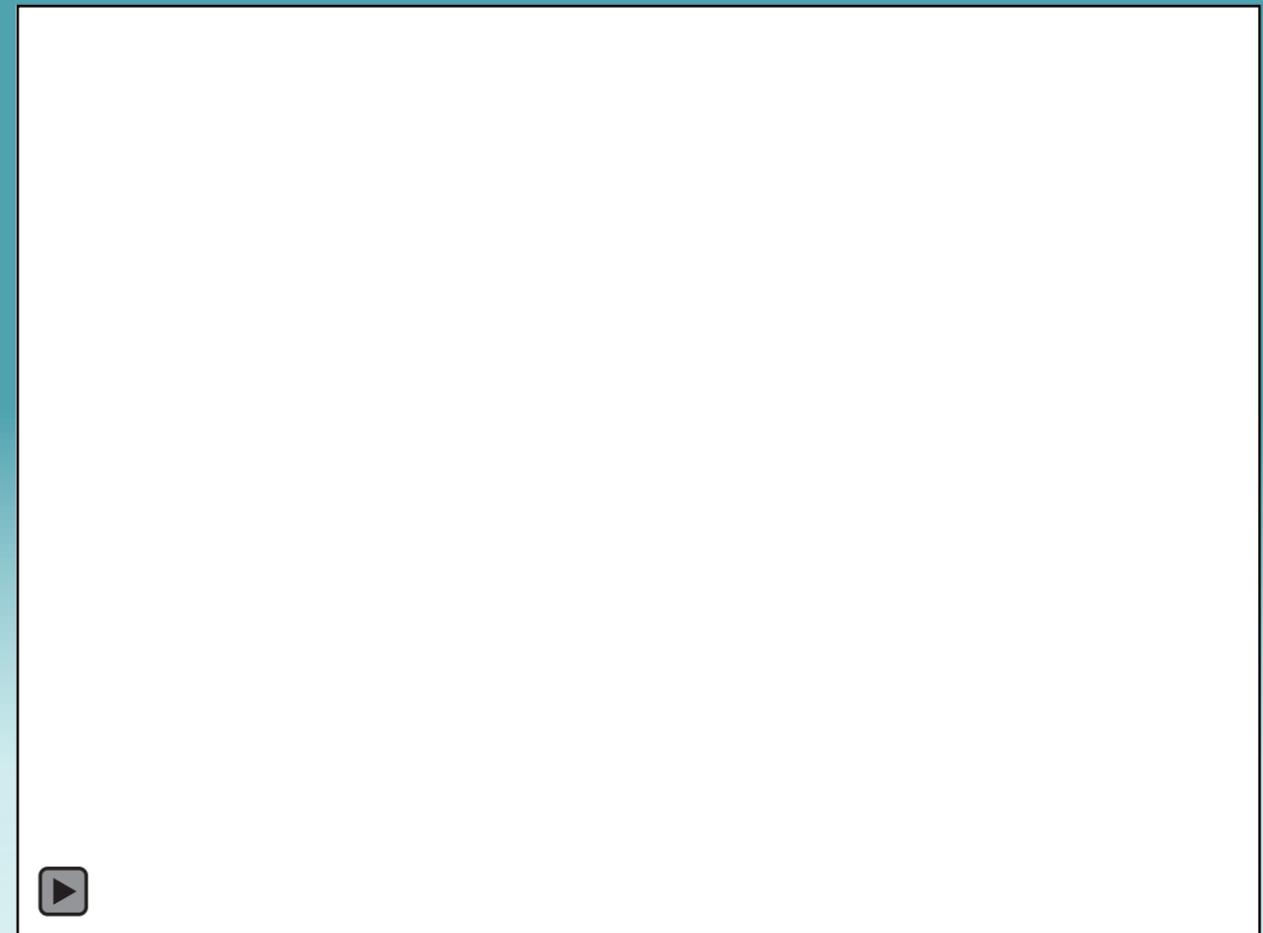
AspireAssist System (Aspire Bariatrics, King of Prussia, PA)

- 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/m²

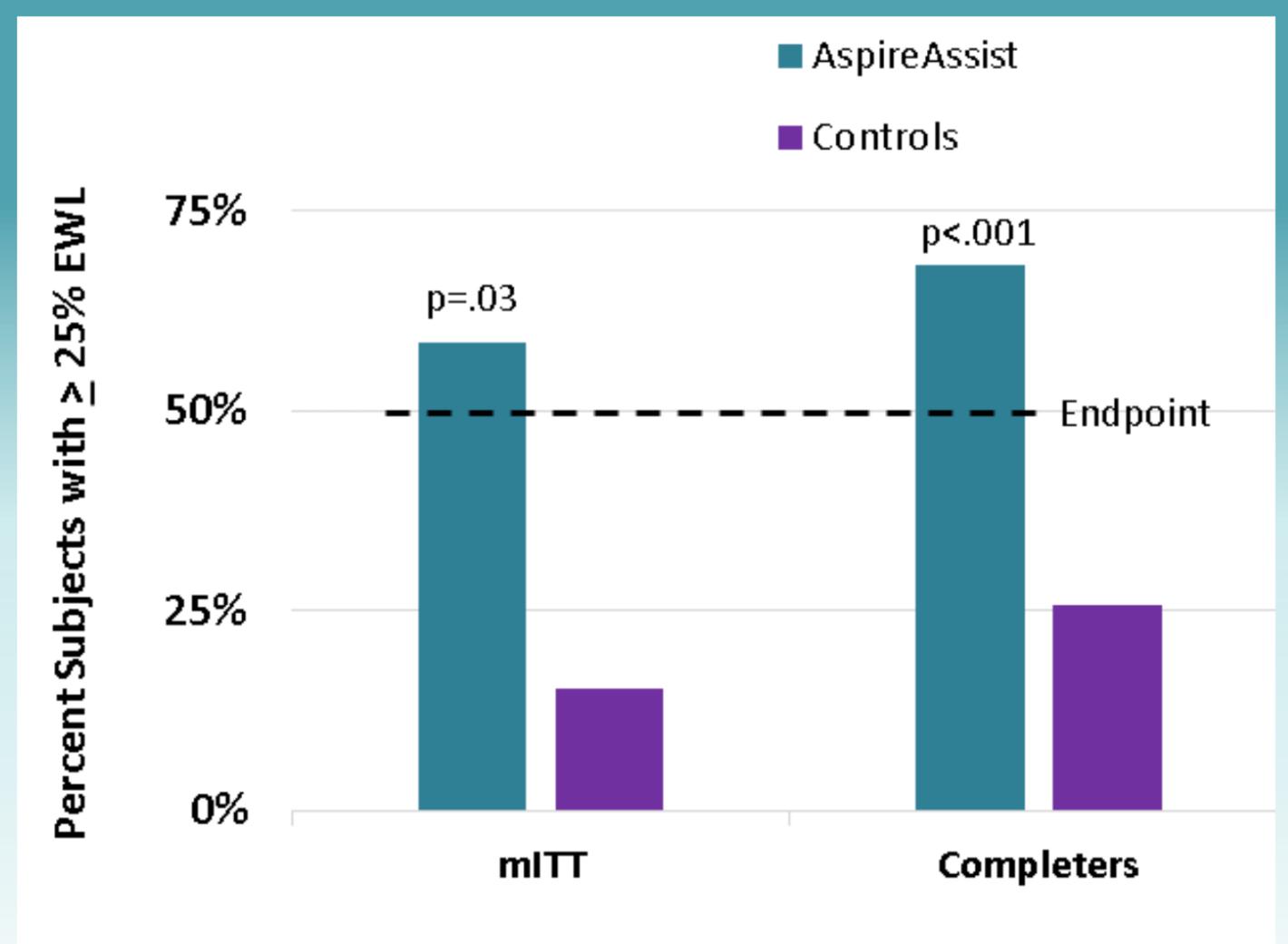
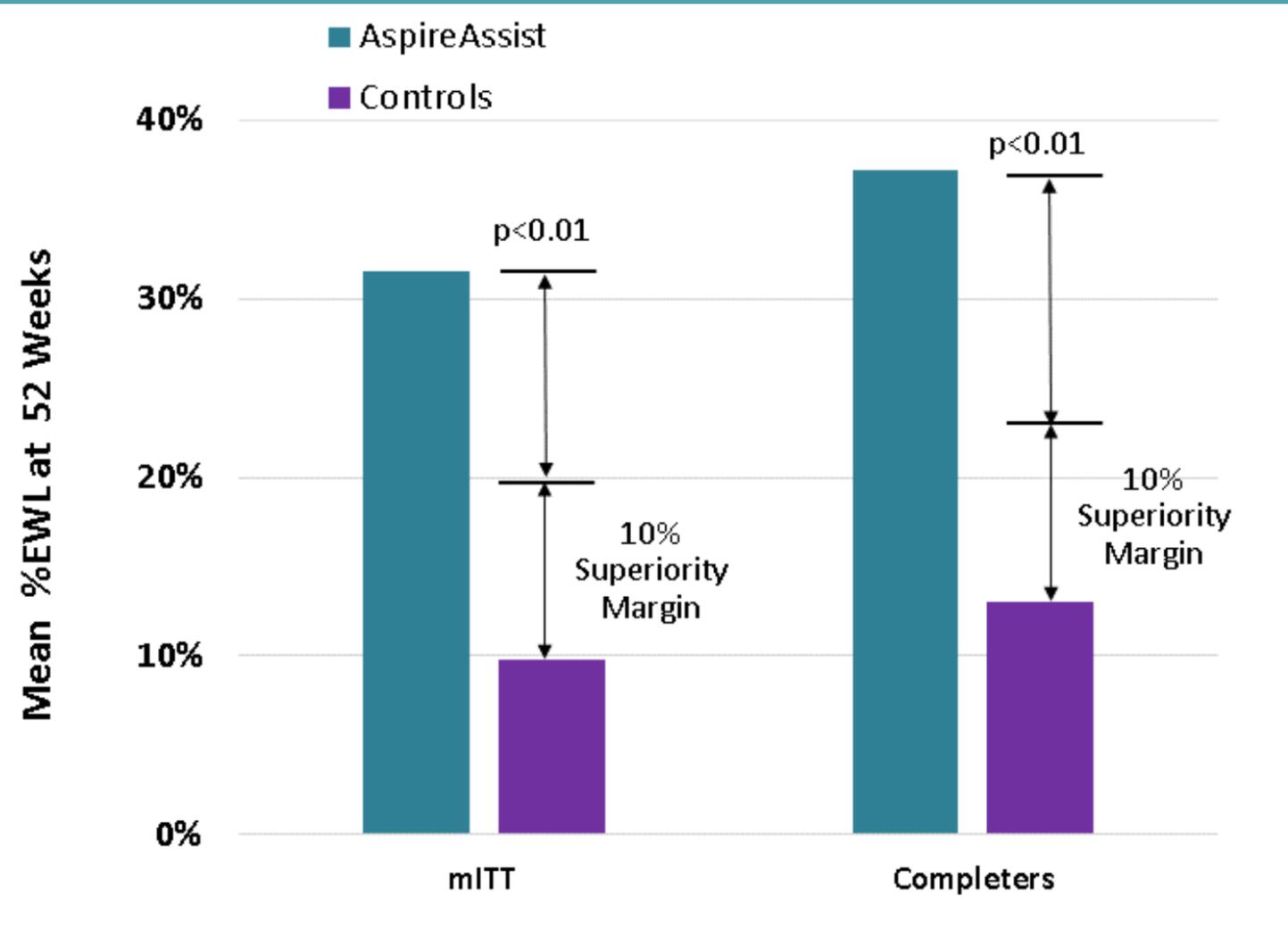
Two Co-Primary Endpoints

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:

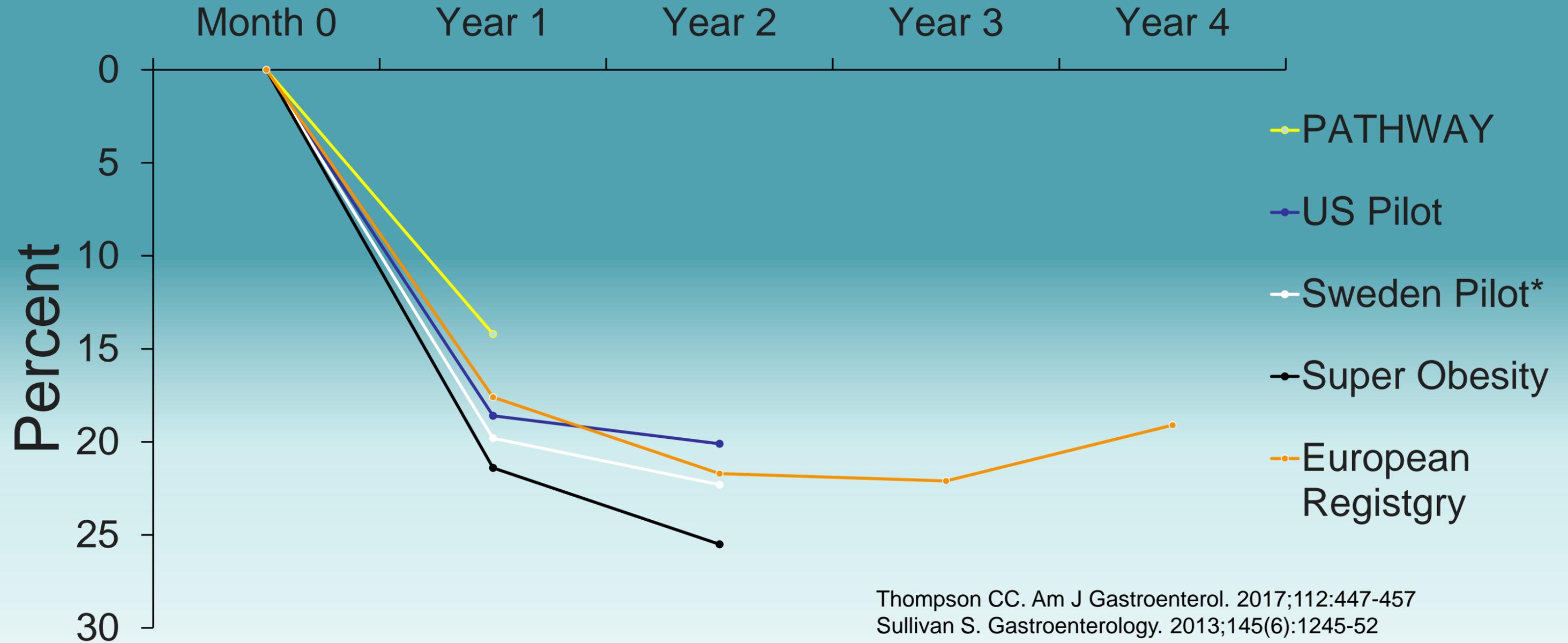
- 91% of patients reported strongly agreeing/somewhat agreeing to increased chewing
- 78% reported significantly/somewhat decreased calorie consumption

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 ± 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