"Novel Approaches to Weight Loss"

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Duality of Interests

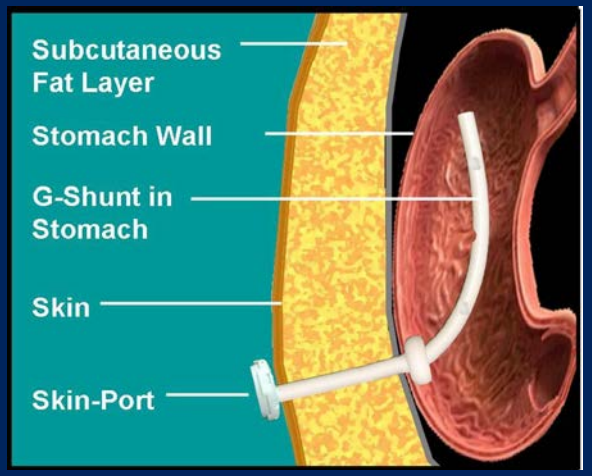
None

Novel Approaches to Weight Loss

- Gastric aspiration
- Endoluminal barrier
- Gastric balloon
- Transoral gastric suturing

Aspiration Therapy Overview

- A-shunt® implantation-outpatient 15-min endoscopic procedure, no general anesthesia
- 30-years experience with PEG tubes; 250,000/yr
- Provides “portion control” at the stomach
- Easy, aspirate stomach contents ~20-min after meal-takes ~ 5-10 minutes
- Removes 25%-30% of consumed calories
- Lowers threshold for achieving successful weight loss which empowers patients
- Provides safe, gradual, and controlled weight-loss, with the patient “in-control” –
- Counting device limited number of aspiration cycles (115), forcing patient back to physician
- Reversible; does not preclude bariatric surgery



Clinical Experience Overview

- **Three trials to date, total of 24 obese patients (BMI 35.5-48.6 kg/m2) treated with Aspiration Therapy:**
  - **3 in proof-of-principle trial in the US**
  - **10 in pilot trial in Mexico**
  - **11 in ongoing randomized controlled feasibility trial in the US.**
- **Safety confirmed by all three trials.**
  - **Careful monitoring for electrolytes, kidney & liver function, vitamins, etc.**
  - **Only serious adverse event reported: buried bumper**
- **Efficacy confirmed by all three trials.**
  - **Percent of patients** losing ≥25% excess weight loss (EWL*) at 52 wks = 94% (50% is FDA guideline)**
  - **Mean** %EWL* at 52 wks = 49.8% (25 % is FDA guideline)**
  - **Mean** %WL at 52 weeks=18.6%**

US Pilot Study

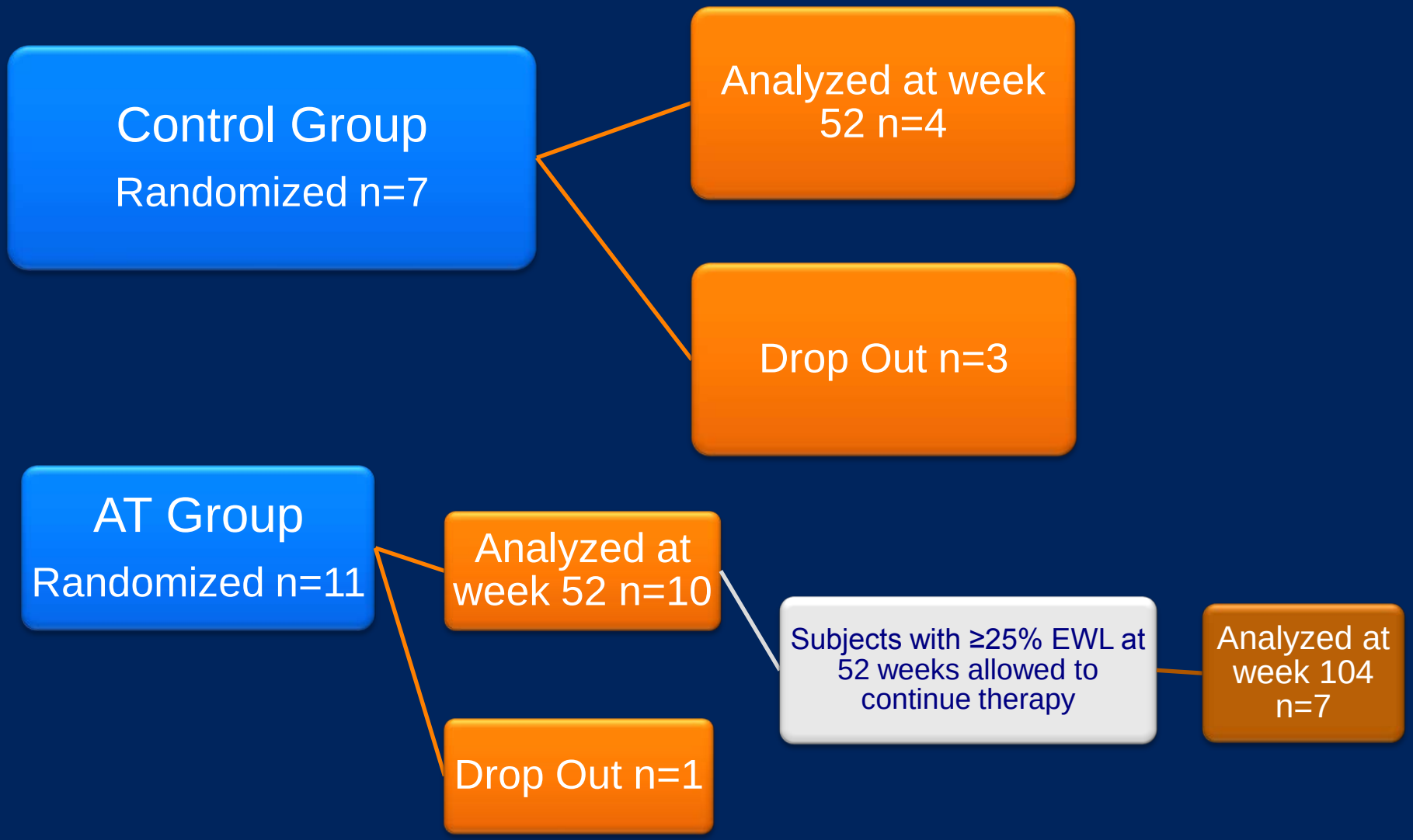
Control Group (12 months)

- 15 session diet and behavioral weight loss program
- Two Town Hall Meetings
- Multivitamin & mineral supplement

AT Group

- A-Tube placed endoscopically
- Tube conversion at 10-14 days post placement
- Subjects instructed on aspiration procedure
- Proton pump inhibitor & potassium
- 15 session diet and behavioral weight loss program
- Two Town Hall meetings
- Multivitamin & mineral supplement

US Pilot Study



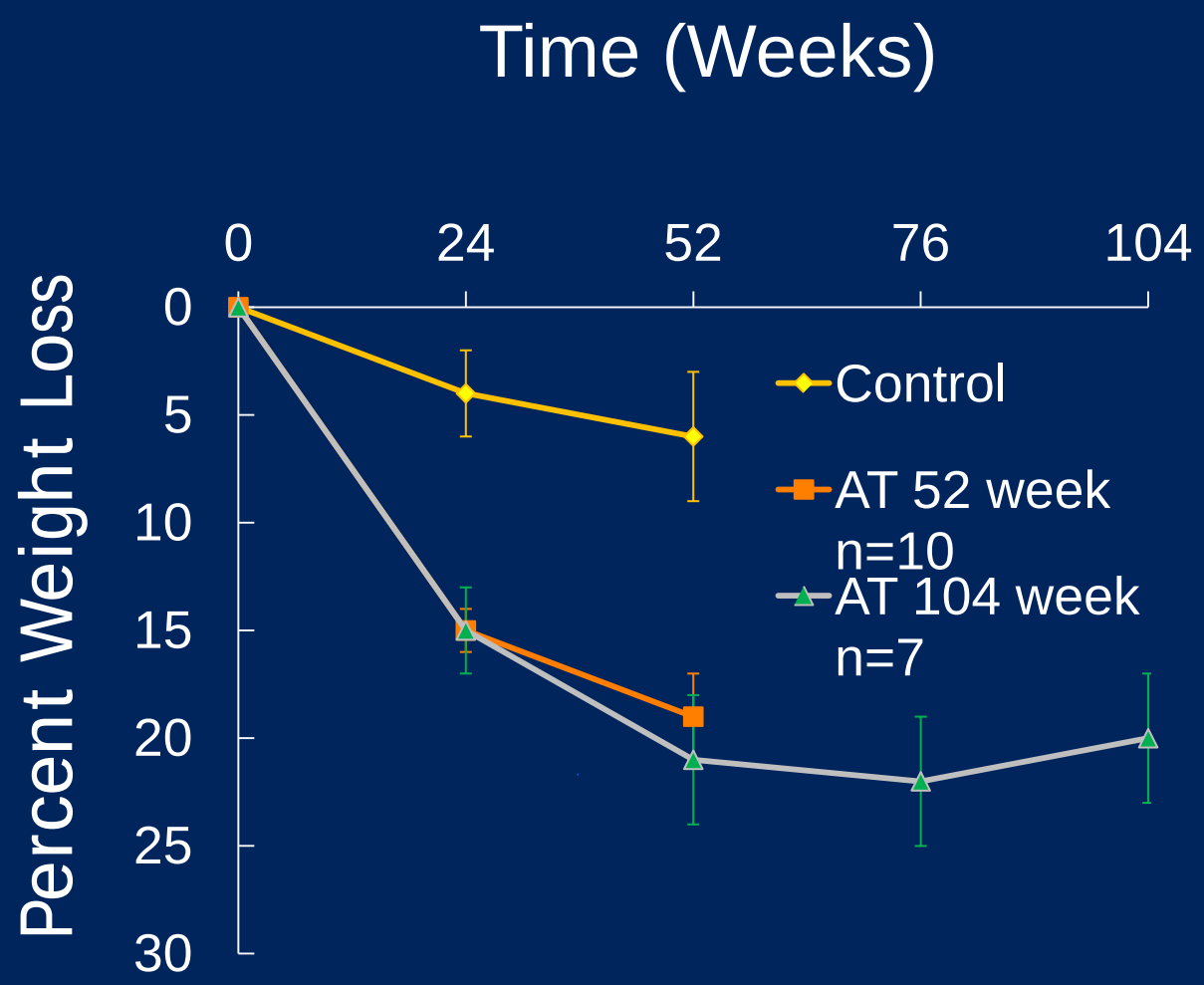
Baseline Characteristics

	Control Group	AT Group
Number (M/F)	4 (1/3)	10 (0/10)
Age (years)	45.3 ± 2.8	38.7 ± 2.3
Weight (kg)	105.3 ± 2.5	112.2 ± 4.6
BMI (kg/m^2)	39.3 ± 1.1	42.0 ± 1.4
Glucose (mg/dL)	86.8 ± 3.4	83.9 ± 1.9
HDL-C (mg/dL)	48.5 ± 4.1	53.6 ± 2.9
LDL-C (mg/dL)	116.0 ± 13.0	112.8 ± 6.9
Triglycerides (mg/dL)	139.3 ± 12.8	113.4 ± 18.8
ALT (IU/L)	26.8 ± 7.3	20.6 ± 2.6
Systolic BP (mmHg)	121.8 ± 6.4	125.8 ± 3.5
Diastolic BP (mmHg)	80.5 ± 3.4	82.6 ± 1.2

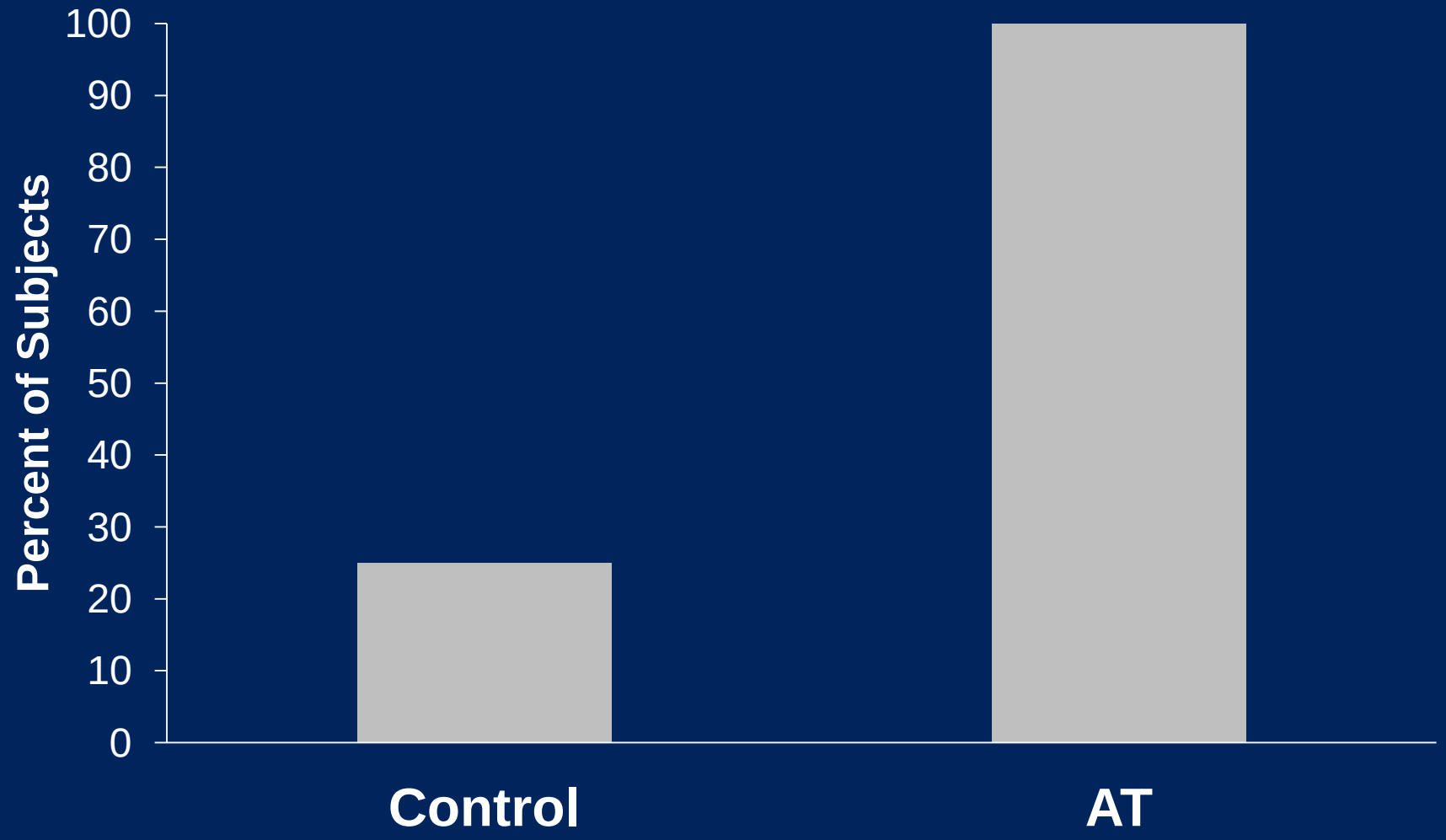
Aspiration Characteristics

Meal	Number of tests	Gastric Aspirate (gm)	Percent of Ingested Calories Aspirated	Aspiration Time (min)
450 kcal, 20 minute wait	6	1747 ± 186	29 ± 4	10.1 ± 1.1
450 kcal, 60 min wait	6	1761 ± 196	18 ± 3	8.5 ± 1.2
800 kcal, 20 min wait	7	2080 ± 240	28 ± 4	9.9 ± 1.1
800 kcal, 60 min wait	7	2034 ± 200	27 ± 5	8.4 ± 1.1

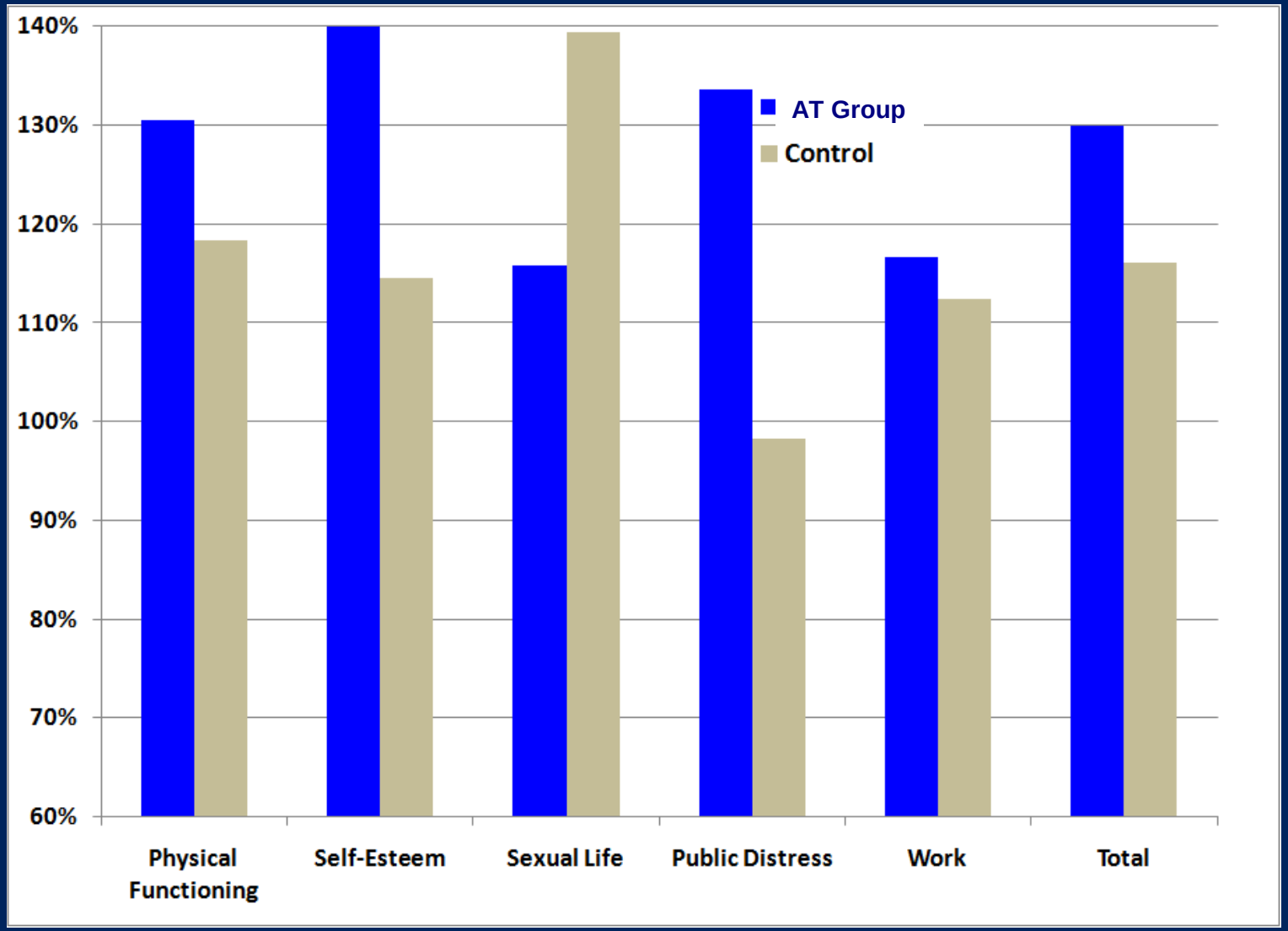
Effect of Aspiration Therapy on Body Weight



Percent of Subjects Who Achieved ≥25% EWL at week 52



Quality-of-Life: IWQOL



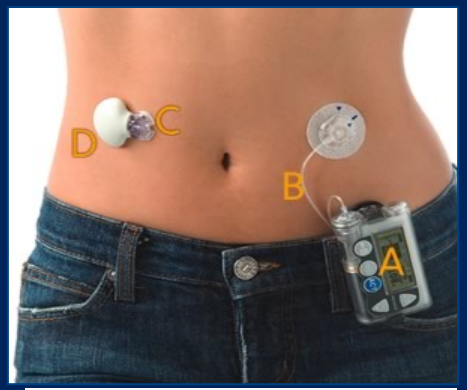
Behavior Outcomes

- **Subject Self-Report**
  - Change in meal-time activities
    - Increased water consumption with meals
    - Increased chewing time
  - Decreased anxiety with meals and eating out
  - Healthier food choices

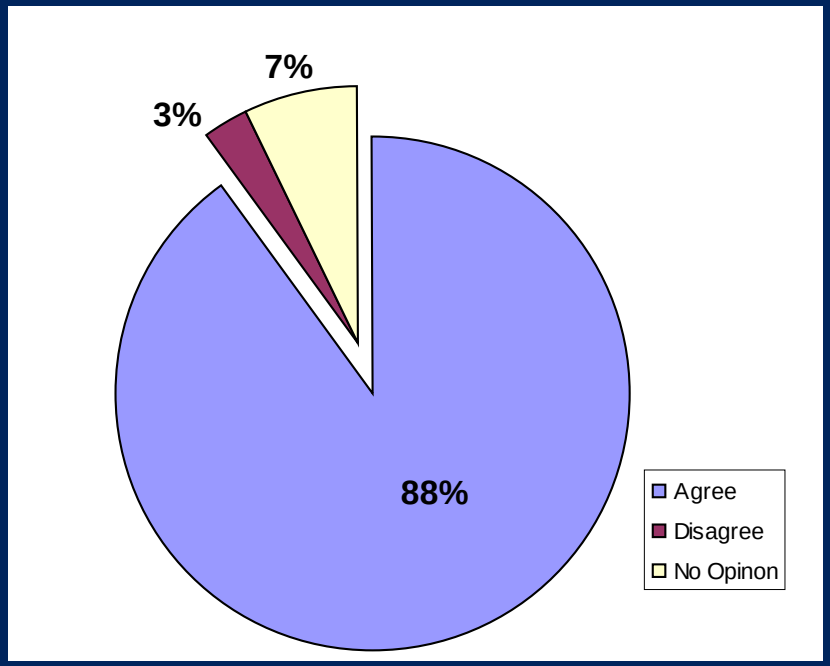
- **Eating Disorders Examination:**
  - No episodes of binging or excessive eating in the AT group
  - No adverse effects on dietary restraint, body image, desired weight and shape

Patient Acceptance

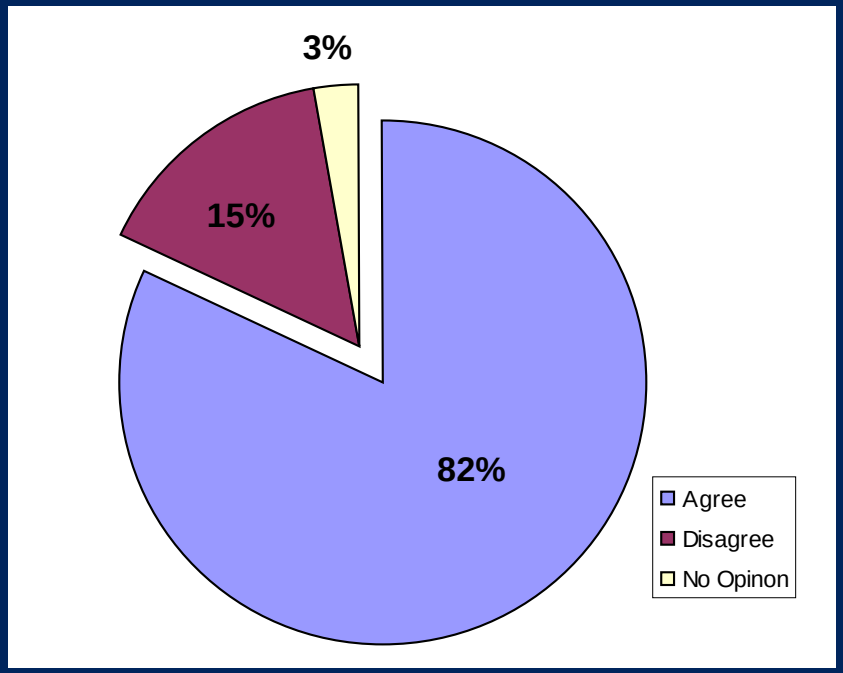
- **AT overwhelmingly accepted by patients**
  - Able to eat normally
  - Minimal invasiveness
  - Reversibility-and no anatomical rearrangement
  - No general anesthesia
  - Discrete/Private
  - Clear mechanism of action
- **Some people dislike having an object attached to their abdomen**
- **Some people fear criticism of therapy**
- **Family acceptance increased over time after weight loss was achieved**



Acceptability of AspireAssist™



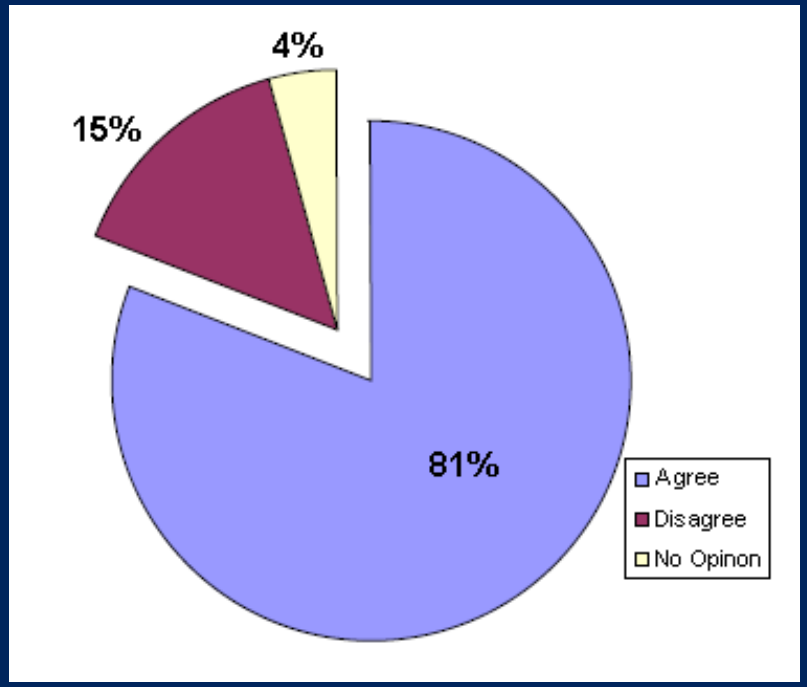
Believe AT will help achieve weight loss



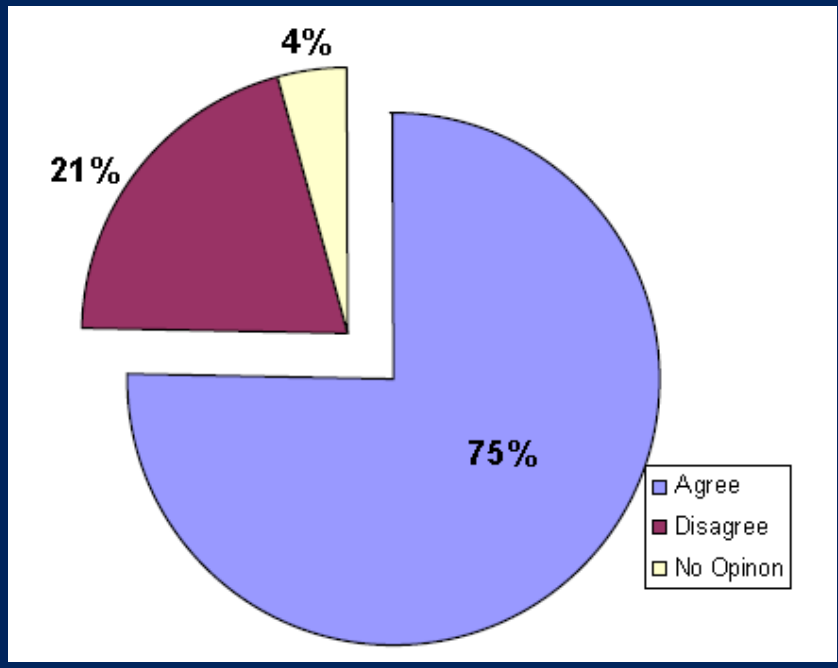
Want to participate in clinical trial

Anonymous survey obtained after Information Session in obese people (N=78) interested in weight loss studies

Acceptability of AspireAssist™



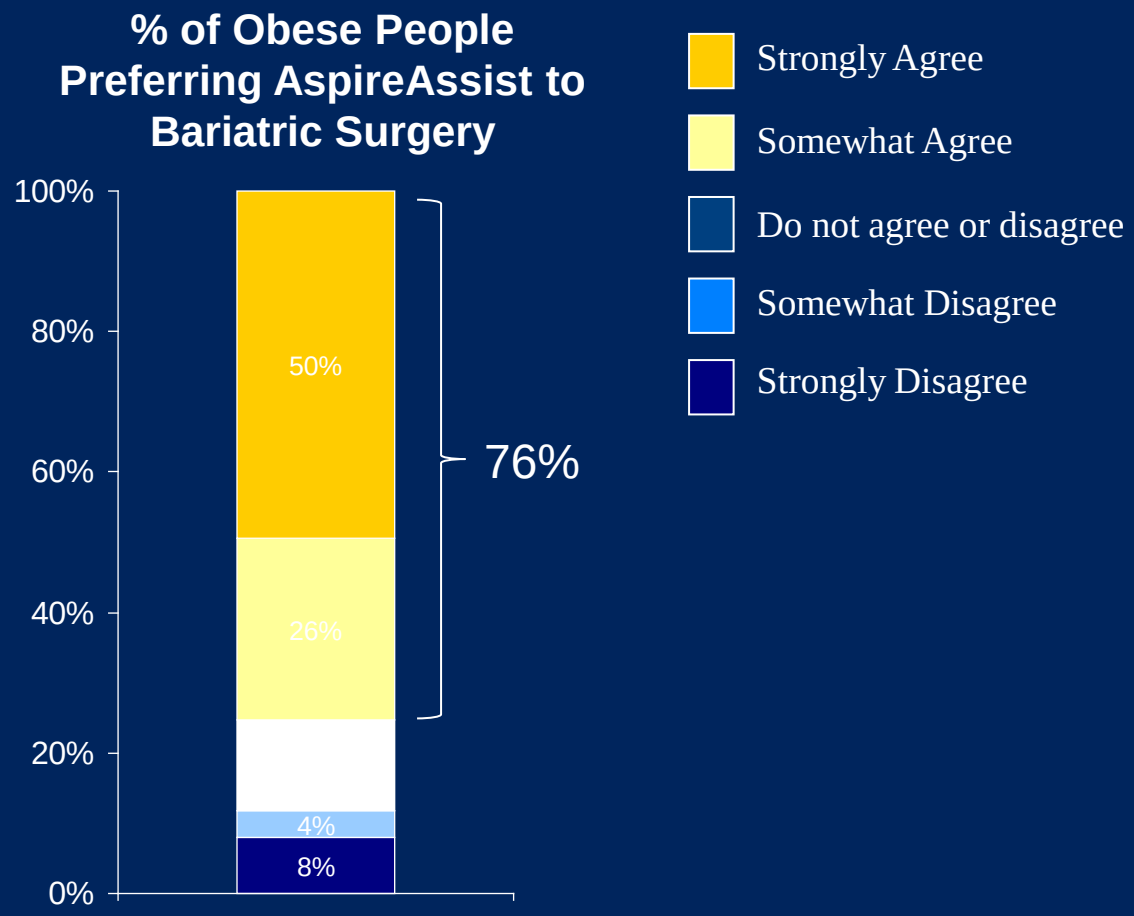
Time spent performing AT is worth it



Permanent Skin-Port is acceptable

Anonymous survey obtained after Information Session in obese people (N=78) interested in weight loss studies

AspireAssist™ vs. Bariatric Surgery



Anonymous survey obtained after Information Session in obese people (N=78) interested in weight loss studies

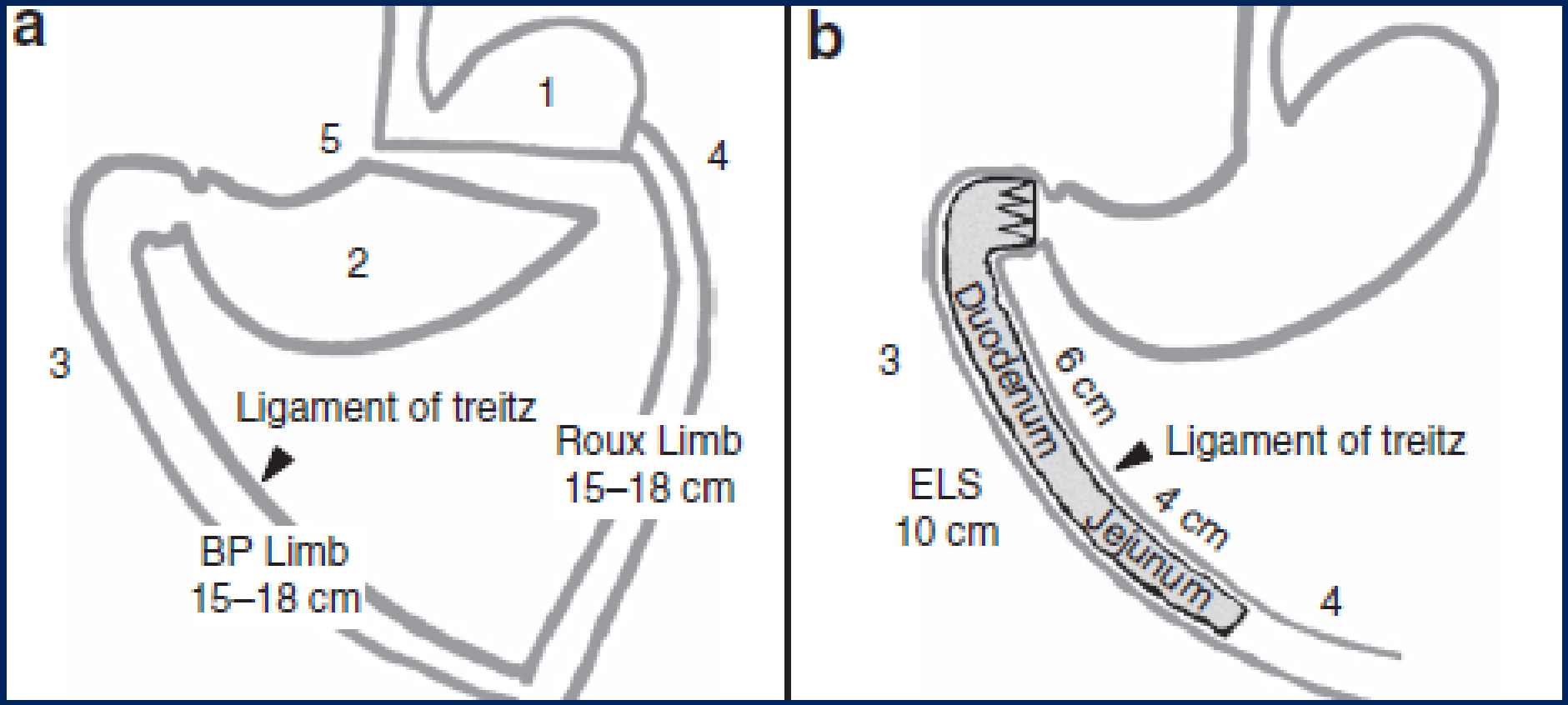
Conclusions

- Aspiration Therapy results in successful long-term weight loss
- No evidence of abnormal eating behaviors, attitudes towards eating, or perceived hunger/satiety (some psychological and eating behaviors improved)
- No compensation for decreased calorie absorption by increasing food intake.
- Psychosocial factors are important drivers of food intake in obese people (not a physiological signal for more calories or drive to meet a set point). Removing food contents after eating allowed subjects to satisfy their drive to eat without the consequence of excessive energy absorption.
- Patient acceptance of therapy is very high

EndoBarrier Gastrointestinal Liner: GI Dynamics

Majumder S & Birk J. *Surg Endosc* 27:2305, 2013

Endoluminal Barrier



Aguirre V et al, *Obesity* 10:1038, 2008

Surg Endosc (2013) 27:2305–2311
DOI 10.1007/s00464-012-2765-7

A review of the current status o
as a primary approach to obesity man

Shounak Majumder · John Birk

Received: 18 September 2012 / Accepted: 4 December 2012 / Published online: 24 January 2013

The duodenojejunal bypass sleeve mimics the physiology of intestinal bypass and shares the metabolic advantages of intestinal diversion. A high rate of premature device withdrawal has been its major limiting factor.

nature publishing group

ARTICLES

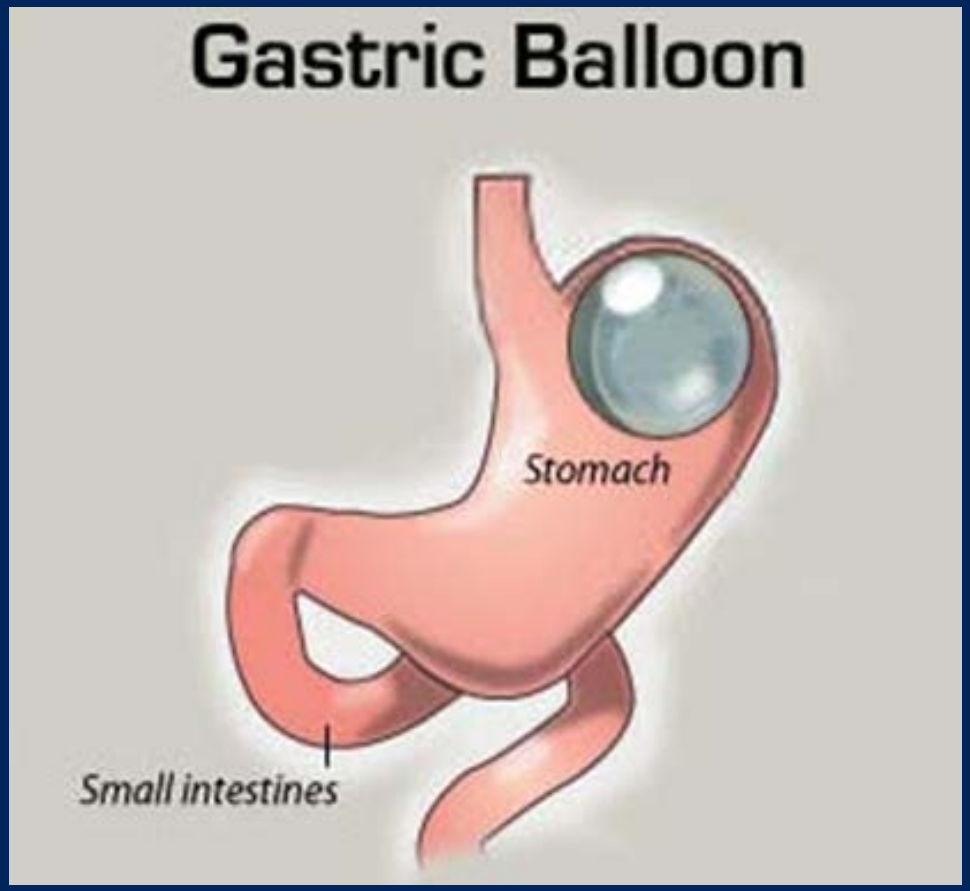
INTEGRATIVE PHYSIOLOGY

An Endoluminal Sleeve Induces Substantial Weight Loss and Normalizes Glucose Homeostasis in Rats with Diet-Induced Obesity

Vincent Aguirre[1], Nicholas Stylopoulos[1], Ronit Grinbaum[1] and Lee M. Kaplan[1]

To investigate the contributions of two surgical gut manipulations—exclusion of the proximal intestine from alimentary flow and exposure of the jejunum to partially digested nutrients—to body weight regulation and metabolism, we have developed a rat model of an investigational device, the endoluminal sleeve (ELS). The ELS is a 10 cm, nutrient-impermeable, flexible tube designed for endoluminal implantation. ELS devices were surgically implanted in the duodenal bulb of rats with diet-induced obesity. Body weight, food intake, stool caloric content, and glucose homeostasis were subsequently evaluated. ELS-implanted rats demonstrated a 20% reduction of body weight compared to sham-operated (SO) controls. ELS-treated animals consumed an average of 27% fewer kcal/day than SO, and there was no evidence of malabsorption. ELS treatment improved fasting glycemia and glucose tolerance after oral and intraperitoneal (IP) administration. ELS treatment enhanced insulin sensitivity, as demonstrated

Gastric Balloon



Gastric Balloon

- Soft silicon sac placed in stomach
- Not a surgical procedure
  - Placed by endoscopy
  - Filled with 500-700 ml of normal saline
- Rapid transition from liquid to soft ot normal diet
- Inflated to produce a sensation of satiety
- Remove at 6 months

Gastric Balloon Results: Italian Multicenter Study

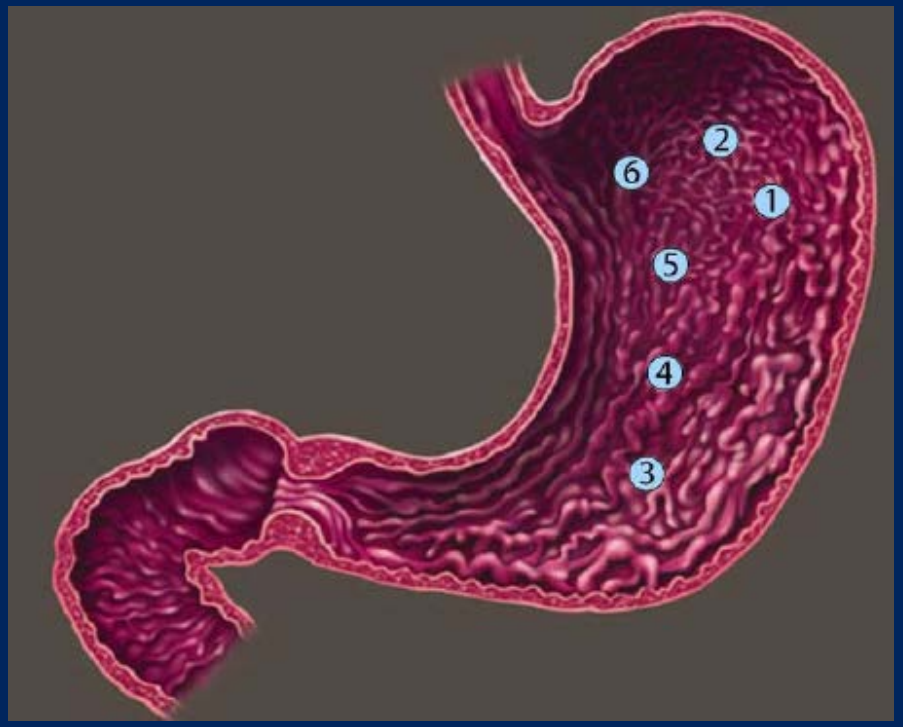
- January 2005 to December 2009
- n = 1357 patients
- BMI: 44. 9 $\pm$ 8.4 kg/m^2 (range 29-82.5)
- At 6 months 39.4 $\pm$ 7.3 kg/m^2
- Intragastric balloon results also predicted 3 and 5 year benefit from LAP band procedure to follow.

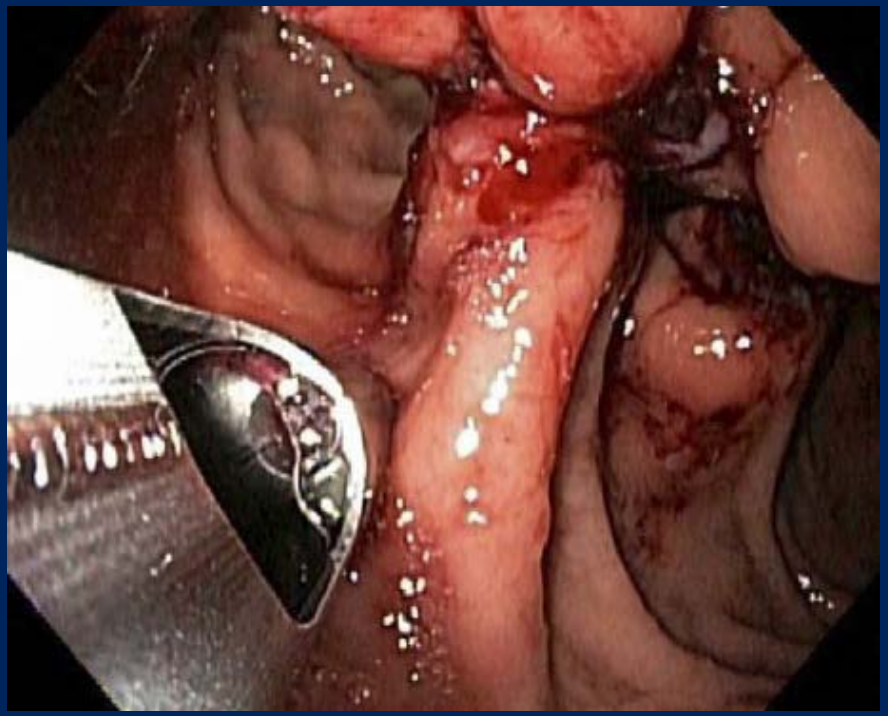
Genco A et al, *Surg Obes Related Dis* 10:474, 2014

Transoral Gastric Suturing

Brethauer SA et al, *Surg Obes Related Dis* 6:689, 2010

Transoral Gastric Suturing





Brethauer SA et al, *Surg Obes Related Dis* 6:689, 2010

Transoral Gastric Suturing: Effect at 12 Months

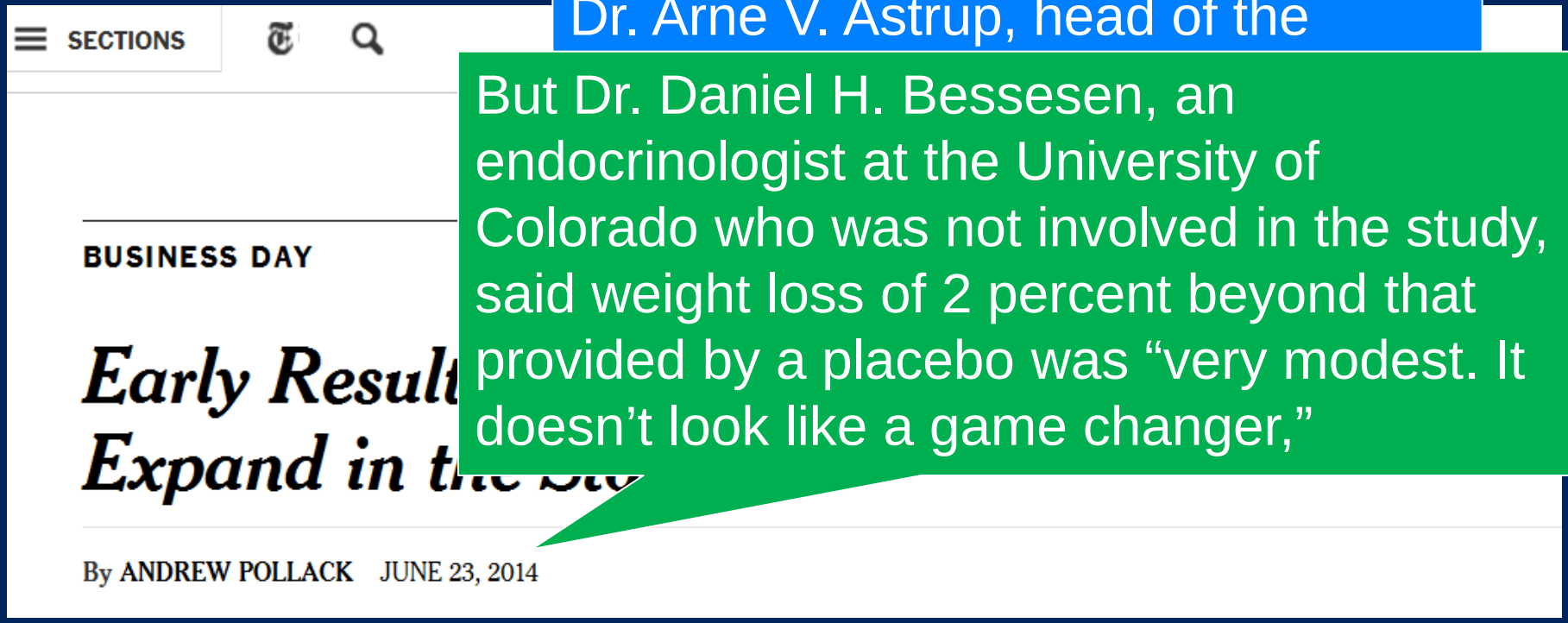
Mean Age – 40 years, BMI 38 kg/m^2,

Δ Wt	Δ BMI	Δ WC	Δ EWL	Δ Syst BP	Δ Diast BP
-11.0 ± 10.0 kg	-4.0 ± 3.5 kg/m^2	-12.6 ± 9.5 cm	-27.7 ± 21.9%	-15.2 mm	-9.7 mm

Brethauer SA et al, *Surg Obes Related Dis* 8:296, 2011

And too good to be true?

I'm definitely impressed, absolutely," Dr. Arne V. Astrup, head of the



But Dr. Daniel H. Bessesen, an endocrinologist at the University of Colorado who was not involved in the study, said weight loss of 2 percent beyond that provided by a placebo was "very modest. It doesn't look like a game changer,"

So What Have We Learned Here?

- Have we really changed ***body weight regulation*** by these novel approaches?
  - Aspiration seems to create a CNS-mediated mechanism. **YES**
  - The endoluminal barrier also resembles the metabolic benefits of surgery. **Likely**
  - The gastric balloon by restricting food intake, more resembles the LAP band. **No**
  - Transoral gastric suturing (plication) might mediate effects by modifying blood supply to the greater curvature – data from pigs.
    - Cells that produce ghrelin. **Perhaps**


Thank You!