

The Evidence Base for Effectiveness of Obesity Management Programs: A Comprehensive Review of the Literature

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Agenda

- Project History & Context
- Objectives
- Methods
- Findings
- Future steps

History & Context

- DMAA Obesity with Co-Morbidities Project
 - Supported by Sanofi-Aventis
 - Goals:
 - Expand understanding of co-morbid obesity
 - Develop and disseminate best practices.

Literature review research design

– Objectives:

- Survey clinical interventions for obesity employing diverse mechanisms of action, including:
 - Behavioral,
 - Pharmacologic,
 - Surgical, and
 - Disease Management
 - CDM / Population-based interventions for obesity
- Outcomes of interest:
 - Clinical: Weight reduction and control, recidivism
 - Economic: Cost-effectiveness
 - Humanistic: Quality of life, satisfaction, compliance

Methods

- General **Inclusion** Criteria:
 - Peer-reviewed literature
 - English
 - 2001 – 2007
- General **Exclusion** Criteria:
 - Poor quality study design
 - Outdated (Redundancy)

Main Outcome Measures

- Weight or another indicator of body mass, most other studies excluded. NIH efficacy measure employed.
- Improvement in glucose tolerance, indicating improved diabetes management (2 studies included).
- Improvement in lipid profile, indicating improvement in CVD risk profile.

Obesity Intervention Effectiveness Measure, National Institutes of Health

“10% Weight-loss Threshold”

NIH - National Heart, Lung, and Blood Institute
Obesity Education Initiative

Recommendation: The initial target goal of weight loss therapy is to decrease body weight by 10 percent. If this target can be achieved, consider next step of further weight loss.



Thomas
Jefferson
University

R: National Heart, Lung, and Blood Institute Obesity Education Initiative, Clinical Guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. Bethesda, MD: US Department of Health and Human Services 1998

Primary Findings

- Weight-loss interventions combining two or more mechanisms of action are often effective.
- Pharmacologic and behavior-based interventions not combined with a second mechanism of action are generally not.
- Effectiveness of many promising therapies because studies were flawed.

Results - Behavioral Interventions

- Behavioral interventions may be appropriate for patients who need to lose modest amounts of weight.
(Stevens, 2001)
- American Diabetes Association Guidelines recommends structured behavioral program as first-line intervention.
(ADA, 2007)

Behavior Mechanisms of Action:

- Exercise
- Self-help
- Counseling
- Diet
- Combination of above

Results, review of behavioral studies:

- Most studies short-term (< 1 year)
- Results diminished over time
- Our results verified earlier findings for long-term results of behavioral interventions: average weight loss apx 4 pounds

Behavioral Interventions

Quality Issues in Behavior Studies

- Study periods of less than one-year
- Small sample groups
- Flawed controls
- Objective of study not clearly stated
- High drop-out rates not accounted for in data analysis
- Incomplete descriptions of methods.

Promising Directions for Future Behavioral Weight-Loss Research

- Studies of interventions that can be maintained over significant periods of subjects' life-span
- Studies translating new scientific knowledge of decision-making and behavior change
- Studies of high scientific quality with extended study periods, randomized controls.

Results

Pharmacologic Interventions

1

Obesity Pharmacotherapy Approaches:

1. Acting on central nervous system
2. Acting outside central nervous system



R: 1. Bray G. et al. Medical Therapy for Obesity – Current Status and Future Hopes. Medical Clinics of North America (2007); 2. 1225- 1253<http://images.rxcr.com/boxes/acomplia.jpg>; 3. <http://www.unipharma-sy.com/images/Thumb/MER10EO.jpg>; 4. www.buyalli.org

Central Nervous System Drugs

Primary Central Nervous System Drugs

1. Rimonabant (Acomplia, Zimulti)

- Approved in Europe, not in U.S.
- Antagonist of CB-1 receptor (sweet, tasty food)

2. Sibutramine (Meridia)

1. FDA Approved
2. Originally antidepressant, increases satiety

3. Phentermine



—————> **Focus of presentation; Long-term use**

Peripheral Metabolism Drugs

1. **Orlistat** (Xenical, Alli)

- Reduces intestinal digestion of fat
- FDA approved over-the-counter at reduced dose

Other Drugs (approved for other indications)

1. **Fluoxetine**: anti-depressant, increases serotonin availability
2. **Bupropion**: anti-depressant, smoking cessation
3. **Topiramate**: anti-epileptic, seizure disorders
4. **Metformin**: anti-diabetic

Results – Pharmacologic Interventions

Initial Overview

- Our review confirmed previous findings:
 - No studies of antiobesity medications are associated with $>10\%$, placebo subtracted, weight loss¹
 - Drug combinations may have potential to achieve greater weight loss, further study needed.²



Sources:1: Padwal R.S. Drug Treatments for obesity: orlistat, sibutramine, and rimonabant. Lancet 2007; 2: Bray GA. Medical Therapy for Obesity. Medical Clinics of North America (2007)

Results - Pharmacologic Interventions

Attrition Rates

- Drop-out rates in pharmacotherapy trials high,¹ with average attrition rates of **30-40%**²
- High attrition compromises generalizability
 - Adherence rate in clinical settings?

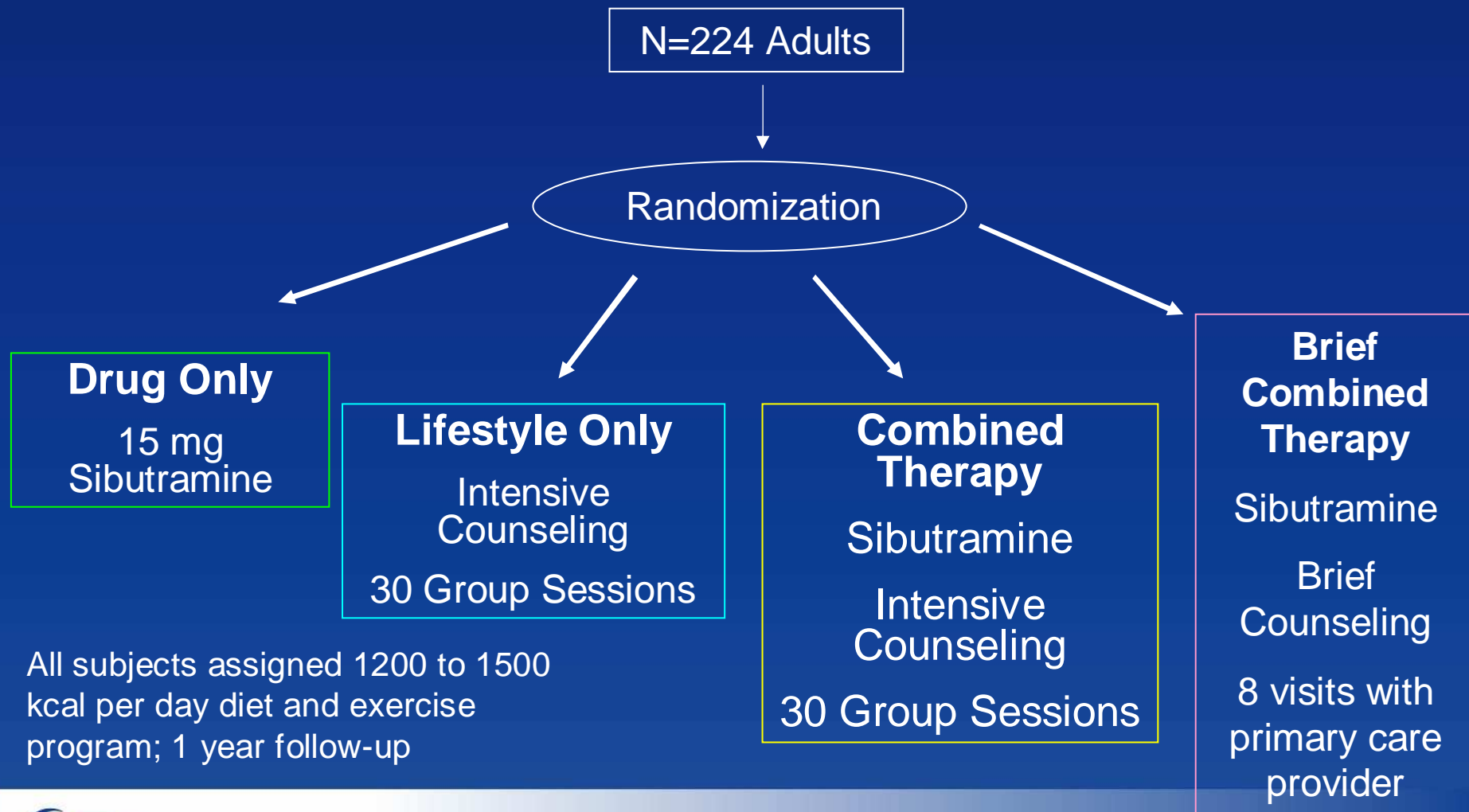


Sources: 1. Padwal R.S. Drug Treatments for obesity: orlistat, sibutramine, and rimonabant. *Lancet* 2007; 2: Rucker, Padwal et al. Long term pharmacotherapy for obesity and overweight: updated meta-analysis. *BMJ* 2007 Dec 8;335(7631):1194-9. Epub 2007 Nov 15; 3: Blue L. Time Magazine "Obesity Drugs Work-Modestly". Thursday, Nov. 15 2007

Lifestyle Component Intensity: A Significant Variable Associated with Efficacy

- Association independent of pharmaceutical agent under study
- What Sampsel and May called the “bidirectional, mutually beneficial relationship”¹

Example – Wadden, Berkowitz, et al. 2005 NEJM



Incremental Cost-Effectiveness (Pharmacologic)

- Malone DC, et al 2005 – Payer perspective
- Cost-effectiveness of adding Sibutramine to Weight Management Program (1 year)
- \$1,279 increase in healthcare costs in Sibutramine group compared to \$271 in WMP alone group
- Increased total cost by **\$44 per additional pound of weight loss**



Malone DC. Cost-effectiveness of sibutramine in the LOSE Weight Study: evaluating the role of pharmacologic weight-loss therapy within a weight management program. *Journal of Managed Care Pharmacy*. 2005 Jul – Aug;11(6):458-68

Cost-Effectiveness

- Incremental Cost per Quality Adjusted Life Year (QALY) compared to diet and lifestyle alone
- European evaluations translated to US Dollars
- Orlistat:
 - Lacey (2005): 2 American, 3 European Trials: **\$25,036 per QALY**
 - Ruof (2005): 7 Randomized Controlled Trials: **\$20,674 per QALY**
- Sibutramine:
 - Brennan (2006): Published RCTs: : **\$20,239 per QALY**
- Pharmacotherapy considered cost-effective

Results – Pharmacologic Interventions

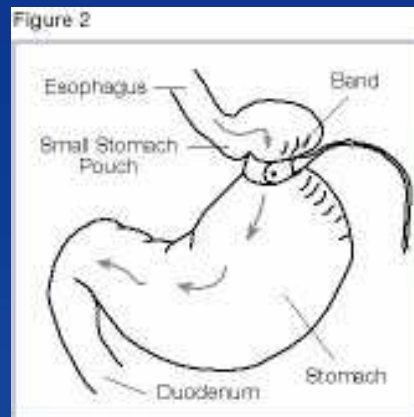
Summary

- Data in the literature does not decisively show one pharmacologic treatment to be superior in effectiveness to another
 - Intensity of accompanying lifestyle, behavioral component significantly impacts results
- No drugs produce placebo-subtracted weight-losses of 10% or more (NIH)
- Best results achieved when intensive lifestyle intervention is coupled with therapy.

Results - Surgical Interventions

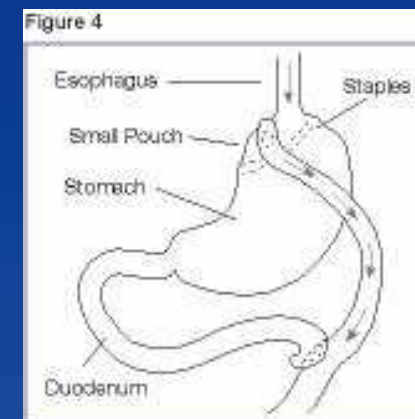
- **Restrictive**

- Restricts stomach capacity, reducing food intake
- Adjustable Gastric Banding, Vertical Banded Gastroplasty



- **Combined Restrictive / Malabsorptive**

- Restricts stomach and amount of nutrients, calories absorbed
- Gastric Bypass, Bileopancreatic Diversion



Results - Surgical Interventions

Trends in Bariatric Surgery (1988-2004)

- Increased number of surgeries (13,000 to 121,000)
- Decreased mortality rate (.9% to .2%)
- Total US cost for bariatric surgery increased (\$147 m to \$1.3 b)
- In 2002, 11.5 million patients met clinical criteria for surgery; 0.6% actually received surgery.¹
- Gastric bypass, BPD more common in US
- Gastric banding more common in Europe, Australia



R: 1. Powers KA. Financial Impact of Obesity and Bariatric Surgery. Med Clin N Am 91 (2007)321-338. 2. Livingston EH. Hospital costs associated with bariatric procedures in the United States. Am J Surg. 190 (2005) 816-820; 2. AHRQ HCUP Statistical Brief #23, January 2007

Preferred Surgical Methods

- The US stands alone.
- Gastric bypass, BPD more common in US
- Gastric banding accepted as standard of practice in Europe, Australia

Reduction in Co-Morbidities (All Surgeries)

- Substantial reduction in **obesity comorbidities**
 - Diabetes resolved in 76.8% of patients²
 - Hypertension resolved in 61.7% of patients²
 - Sleep Apnea resolved in 85.7% of patients²
 - Hyperlipidemia improved in 70% of patients²
- Reduction of **chronic conditions** compared to controls:¹
 - Risk of cancer reduced 76%¹
 - Risk of cardiovascular disease reduced 82%¹
 - Risk of musculoskeletal problems reduced 59%¹
 - Risk of respiratory conditions reduced 76%¹
 - Risk of digestive conditions **increased** 48%¹



R: 1. Christou NV. Surgery Decreases Long-Term Mortality, Morbidity, and Health Care Use in Morbidly Obese Patients. *Annals of Surgery*. Vol. 240 No. 3 Sep. 2004; 2. Buchwald H. Bariatric Surgery A Systematic Review and Meta-Analysis. *JAMA* Oct. 13, 2004. Vol. 292. No. 14

Adverse Events (Bypass, Banding)

- Most invasive intervention --> more benefits, more risks¹
 - GI / Surgical / Nutritional
-
- Bypass Adverse Events:²
 - 19% Surgical (anastomotic leak, bleeding, re-operation)
 - 17% GI (Vomiting, Dumping)
 - 16.9% Nutritional (mineral and vitamin deficiencies)
 - Banding Adverse Events:²
 - 13% Surgical (Band erosion, slippage, re-operation)
 - 7% GI (Vomiting, Reflux)

Adverse Events / Readmissions

- 2,522 surgeries at 308 hospitals²
 - 22% complication rate during initial surgical stay²
 - Increases to 40% at 180 days after discharge²
 - 7% readmitted to hospital²
 - 18% have post-operative hospital visit (ER, hospital readmission, outpatient visit)²

- Bypass Surgeries in California '95 – '04¹
 - 1st year: 20.2% readmission rate¹
 - 2nd year: 18.4% readmission rate¹
 - 3rd year: 15% readmission rate¹



R: 1. Eninosa W. Healthcare Utilization and Outcomes After Bariatric Surgery. Medical Care Vol. 44, No. 8 Aug. 2006.; 2. Zingmond D. Hospitalization Before and After Gastric Bypass Surgery. JAMA Oct. 19, 2005. Vol. 294, No. 15

Readmissions and Costs

- Mean, risk adjusted healthcare payments for surgery and first 6 months after surgery with **NO readmissions: \$27,125**
- Mean cost for patients **readmitted at least once** in first 6 months: **\$65,031**



Economic Outcomes of Surgery

- 23 economic outcomes studies
- Insurer Perspective:
 - High up front cost, long-term cost-savings
 - Reduction in obesity-related medication costs, complications
- Employer Perspective:
 - High upfront cost, return on Investment
 - Increased productivity
 - Decreased disability, absenteeism
 - Decreased presenteeism

Summary- Surgical Interventions

- The evidence for efficacy is well-established.
- Only intervention that meets NIH standards for weight-loss. Not appropriate for all patients.
- Effectiveness hindered by post-operative complications, costly readmissions.
- Costs, insurer perspective: high costs up front, savings over time secondary to reduced co-morbidities.
- Mean ROI for employers is 6 years, with reduced absenteeism, increased productivity.

Disease Management

Best Practices for Obesity

- Disease Management (DM) programs for obesity are still in the beginning phases²
- Employers, Payers, and DM vendors are moving in this direction²
- Primary barrier to progression of DM for obesity is lack of evidence on return on investment¹



R: 1. Sidorov J. Obesity Disease Management Opportunities and Barriers. *Obesity*. Vol. 14. No. 4. April 2006; 2. May J. The Role of Disease Management in the Treatment and Prevention of Obesity with Associated Comorbidities. *Disease Management*. Volume 10. No. 3, 2007

Disease Management Approaches

- Health Plans: implement “best practices,” merging:¹
 - Provider incentives
 - Nutritional counseling
 - Physical activity goals
 - Patient-customized intervention
 - Community education and planning
- Employers: diverse approaches
 - wellness plans, including support for weight loss
 - penalizing unhealthy behaviors
 - rewarding healthy lifestyles



Overall Results

- **Not Effective:**
 - Behavioral or medication interventions administered independently
 - Surgical intervention without behavior change
- **Effective:**
 - Medical OR Surgical interventions WITH:
 - strong pre and post-behavioral intervention,
 - personal commitment of individual patient,
 - provided in context of population-based initiative, creating environmental reinforcement

Future Directions

- Innovative strategy combinations: clinical intervention, disease management, population education initiatives.
- Science of weight-loss matures: higher quality studies measure medical outcomes over significant portions of the life-course.
- New generation of cost-effectiveness studies create evidence-base for payer support.
- Long-term studies that yield genuine evidence, ie, rigorously designed, three-year behavior trial reported NEJM 7/2008.