Change in body weight over 2 years

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Xenical® 120 mg</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>–2</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

ITT population: NM14185

STORM: Mean body weight changes during weight loss and weight maintenance phases over 2 years (Observed data)

Top Health Hazards Worldwide
- Underweight
- Unsafe sex
- High blood pressure
- Tobacco
- Alcohol
- Contaminated water, sanitation and hygiene
- Iron deficiency
- Indoor pollution
- High cholesterol
- Obesity

Top Health Hazards in “Rich Countries”
- Tobacco
- High blood pressure
- Alcohol
- High Cholesterol
- Overweight
- Low fruit and vegetable intake
- Inadequate exercise

“Corpulency, when in an extraordinary degree, may be reckoned a disease, as it in some measure obstructs the free exercise of the animal functions; and hath a tendency to shorten life, by paving the way to dangerous distempers.”
- Malcolm Flemyng (1760)

“If morbid and severe obesity is as incurable as it seems to be based on the experience of the last 30 to 40 years, then prevention of weight gain and promotion of healthy weight should become priorities.”
- S Rossner, 1994
It will be “a daunting task to change the course of nations that have become quite comfortable with an effortless lifestyle in which individual consumption is almost unlimited.”

– C Bouchard (1996)

Tools to Reduce Unhealthy Trends in Weight

- Eat regular meals
- Avoid snacking
- Drink water, not caloric beverages
- Reduce dietary fat to 30% or less
- Reduce TV time
- Walk more
- Increase physical education classes
- Increase sports activities, energetic leisure activity
  

The Surgeon General’s Call To Action To Prevent and Decrease Overweight and Obesity

Communication & Education

- Communication
- Research and Evaluation
- Action

- Use an informed, sensitive approach to:
- Change weight-related concerns at all ages
- Educate expectant parents on benefits of breastfeeding
- Educate health care professionals on prevention and treatment of overweight and obesity across the lifespan
- Provide education in schools and communities about healthy eating habits and regular physical activity
RESEARCH

- Improve understanding of causes, prevention, and treatment of overweight and obesity
- Increase research on behavioral and environmental causes
- Increase research and evaluation on prevention and treatment interventions
- Disseminate best practice guidelines
- Increase research on disparities in the prevalence among racial and ethnic, gender, socioeconomic, and age groups
- Identify effective and culturally appropriate interventions

ACTION

- Help people balance healthful eating habits and regular physical activity
- Ensure daily, quality physical education in all school grades
- Reduce time spent watching television and in other sedentary behaviors
- Build physical activity into regular routines and playtime for children and their families
- Create more opportunities for physical activity at worksites
- Make community facilities available and accessible for physical activity for all

References for Obesity


Thank you
Clinical Symposium
Therapeutic Options in Obesity

Richard A Dickey, MD, FACP, FACE
2nd AME Italian Meeting
Associazione Medici Endocrinologi
Joint Meeting with
American Association of Clinical Endocrinologists
Reggio Emilia, Italy - November 8-10, 2002

Options for Weight Excess,
Overweight or Obesity

- Prevention
- When this has failed, use a structured system with a team approach:
  - Patient focused
  - Respectful of patient
  - Compassionate approach
  - Strong patient commitment
  - Long-term support

Options

- Physical and psychological evaluation
- Education of patient
- Initiate changes toward healthy lifestyle and behavior practices
- Motivation and support by:
  - MD
  - Support groups
  - Family and friends

Options

- Reinforcement
- Dietary/nutritional measures
  - Realistic
  - Collaborative with patient
  - Individualized
- Physical activity enhancement/exercise

Options

- When or if these measures fail or are inadequate to satisfactorily reduce risks of and/or ameliorate co-morbid conditions, use:
- Pharmacotherapy in selected patients:
  - As used for hypertension or diabetes, where no ideal therapy is yet at hand either but we still treat
- and/or Surgery in selected patients: e.g. BMI >40
- Long-term follow-up

Long-term follow-up
Pharmacotherapeutic agents

- Should produce:
  - Long-term weight reduction
  - Reduced weight regain
  - Reduced co-morbid conditions
- Should be:
  - Effective
  - Not underutilized
  - Much safer than in the past

Pharmacotherapeutic agents

- Diethylpropion
- Mazindol
- Phentermine
- Sibutramine
- Ephedrine+caffeine
- Orlistat

Causes of Obesity*

- Hereditability (but gene pool fairly constant)
- Cultural practices (explain epidemic)
  - Reduced physical activity
  - Increased snacking
  - Increased fat content of food

* C. Wainee Obesity and Weight Management in Primary Care, 2002
Obesity Associated Increased Risks
Adapted from www.nih.gov/health/nutrit/pubs/statobes.htm

- Premature death
- Type 2 diabetes
- Heart disease
- Stroke
- Hypertension
- Gall bladder disease
- Osteoarthritis
- Asthma
- Breathing problems
- Cancer of:
  - Endometrium
  - Colon
  - Kidney
  - Gall bladder
  - Breast (postmenopausal)
- High blood cholesterol
- Complications of pregnancy
- Menstrual irregularities
- Hirsutism
- Sleep apnea
- Stress incontinence
- Increased surgical risk
- Psychological disorders
- Psychological difficulties due to social stigmatization

Health Problems Associated with Obesity in Developed Countries
Relative risk = 1 to 2

- Cancer
  - Endometrium
  - Colon
  - Breast (postmenopausal)
- Reproductive hormone abnormalities
- Polycystic ovarian syndrome
- Impaired fertility
- Low back pain from obesity
- Increased anesthetic risk
- Fetal defects from maternal obesity

Health Problems Associated with Obesity in Developed Countries
Relative risk = 2 to 3

- Coronary heart disease
- Osteoarthritis of knees
- Hyperuricemia and gout
- Congestive heart failure

- WHO 1997

Health Problems Associated with Obesity in Developed Countries
Relative risk = >3

- Diabetes type 2
- Gall bladder disease
- Hypertension
- Dyslipidemia
- Insulin resistance
- Breathlessness
- Sleep apnea

- WHO 1997
Reaven Syndrome
Metabolic Syndrome
Dysmetabolic Syndrome

ATP III: The Metabolic Syndrome*

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal obesity</td>
<td></td>
</tr>
<tr>
<td>(Waist circumference)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&gt;102 cm (&gt;40 in)</td>
</tr>
<tr>
<td>Women</td>
<td>&gt;88 cm (&gt;35 in)</td>
</tr>
<tr>
<td>TG</td>
<td>≤150 mg/dL</td>
</tr>
<tr>
<td>HDL-C</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>≥40 mg/dL</td>
</tr>
<tr>
<td>Women</td>
<td>≥50 mg/dL</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>≥130/85 mm Hg</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>≥110 mg/dL</td>
</tr>
</tbody>
</table>

*Diagnosis is established when ≥3 of these risk factors are present.


Consequences of the Metabolic Syndrome

- Insulin Resistance
  - Hyperinsulinemia
  - Insulin Resistance
  - Glucose Intolerance
  - Increased Triglycerides
  - Decreased HDL Cholesterol
  - Increased Blood Pressure

- Increased PAI-1
- Small, Dense LDL
- Increased Microvascular Disease—e.g., Coronary Heart Disease
- Increased Mortality
- Depression

Cardiovascular Diseases
- Hyperinsulinemia
- Myocardial Infarction
- Sudden Death
- Stroke
- Renal Failure

Endocrine Metabolic Disorders
- Diabetes Mellitus
- Dyslipidemia
- Hyperuricemia
- Hypertension
- Left Ventricular Hypertrophy
- Myocardial Infarction
- Comparative Heart Failure

Gastrointestinal Disorders
- Colon Polyps
- Colon Cancer
- Endometrial Cancer
- Ovaries

Neoplastic Disorders
- Lung Cancer
- Breast Cancer
- Colon Cancer
- Prostate Cancer

Respiratory Disorders
- Sleep Apnea
- Pneumonia
- Corticosteroids

Musculoskeletal Disorders
- Arthritis
- Joint Pain
- Bone Fracture

Psychosocial Disorders
- Depression
- Anxiety
- Stress

Case Presentation
Case Presentation

When patient first seen in 1992

- 58 y/o Caucasian female RN administrator
- History of repetitive miscarriages from age 20 to 25
- Hypothyroidism diagnosed and treated
- Four full-term pregnancies thereafter
- TAH and BSO at age 40

- Cholecystectomy at age 48
- Progressive weight gain from age 30 to 58
- BMI 37 (Ht 63.5"; Wt 212 lb)
- BP 120-150/80-90 mm Hg

- Family history:
  - Father died at age 48; Hx of hypertension
  - Mother died at age 72; Hx of hypertension, MI
  - MGF, Hx type 2 DM
  - MGM, hypertension and MI
  - PGF died of MI

- Cholesterol 230 mg/dL; HDL 52 mg/dL; TG 141 mg/dL; calc LDL 150 mg/dL
- Levothyroxine 0.1 mg beginning at age 25 to present
- TSH now 0.8 μIU/mL; TT4 10.7 μg/dL; T3U 1.01%; T3 125 ng/dL
- Antithyroid Abs negative

- Levothyroxine discontinued
- TSH rose to 6.0 μIU/mL in 2-3 wk; 2 months later, TSH and TT4 normal

When seen in 1996

- Patient now 62 y/o; RN administrator
- History: persistent obesity
- BMI 41 (Ht 63"; Wt 230 lb; waist circumference 42.5")
- BP 160/106 mm Hg
- 1000 calorie diet
- Support group
- Regular aerobic physical activity
- Rx phentermine-fenfluramine; April 1996 to July 1997
- Weight fell from 230 to 145 lb
- BMI fell from 41 to BMI 26

- Aug 1997: Wt 145 lb; Rx dexfenfluramine
- Sept 1997: Wt 156 lb; Rx phentermine
- Sept 1998: Wt 182 lb; ramipril to control BP; then Rx sibutramine
- July 1999: Wt 186 lb; Rx orlistat
- March 2000: Wt 181 lb; Rx phentermine for 3 months on, 3 months off
- June 2001: Wt 174 lb

Thank you