Medical Management of Obesity:
Diabetes Prevention

How do we treat it

AACE Endocrine University, 2019

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Director, UAB Diabetes Research Center
Treatment Modalities for Patients with Overweight and Obesity

- Lifestyle Intervention
- Medications
- Bariatric Surgery
### Comprehensive Lifestyle Management Is the Foundation of Obesity Treatment

#### Meal Plan
- Reduced-calorie healthy meal plan
- ≈ 500-750 kcal daily deficit
- Many healthy meal plan options\(^a\)
- Meal replacements
- Very-low–calorie diet is an option for selected patients—requires supervision

*Team member/expertise: dietitian, health educator*

#### Physical Activity
- Aerobic activity
  - Goal: > 150 min/wk
  - 3-5 days/wk
- Resistance exercise
  - Major muscle groups
  - 2-3 times/wk
- Reduce sedentary behavior
- Individualized (e.g., preferences, limitations)

*Team member/expertise: exercise trainer, physical activity coach, physical/occupational therapist*

#### Behavior
- Interventionsal package of behavioral methods
- Self-monitoring; goal setting; education; problem-solving; stimulus control; stress reduction; psychological evaluation and treatment; cognitive restructuring; motivational interviewing; social support structures

*Team member/expertise: health educator, behaviorist, clinical psychologist, psychiatrist*

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\(^a\) AACE/ACE guideline lists: Mediterranean, DASH, low-carb, low-fat, volumetric, high protein, vegetarian.

AACE/ACE algorithm for the medical care of patients with obesity.

# Obesity Pharmacotherapy

<table>
<thead>
<tr>
<th>Agents</th>
<th>Action</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Previously available</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phentermine</td>
<td>• Sympathomimetic</td>
<td>• 1959</td>
</tr>
<tr>
<td>Orlistat</td>
<td>• GI lipase inhibitor</td>
<td>• 1997</td>
</tr>
<tr>
<td><strong>Recently Approved</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phentermine/Topiramate ER</td>
<td>• Sympathomimetic/Anticonvulsant (GABA receptor modulation?)</td>
<td>• Approved, Summer 2012</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>• 5-HT(_2)(_C) serotonin receptor agonist</td>
<td>• Approved, Summer 2012</td>
</tr>
<tr>
<td>Naltrexone ER/Bupropion ER</td>
<td>• Dopamine/noradrenaline reuptake inhibitor/Opioid receptor antagonist</td>
<td>• Approved, September 2014</td>
</tr>
<tr>
<td>Liraglutide 3 mg</td>
<td>• GLP-1 receptor agonist</td>
<td>• Approved December 2014</td>
</tr>
</tbody>
</table>

US FDA. Drugs@FDA. http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA.
Actions of Recently Approved Weight-Loss Medications

Phentermine

Naltrexone

Lorcaserin

GLP-1 R

Liraglutide 3 mg

MC4R

Topiramate

Bupropion

5-HT2c

GABA?

Dopamine/NE reuptake

MC4R, melanocortin 4 receptor.
GABA, gamma-aminobutyric acid.
POMC/CART, pro-opiomelanocortin/cocaine- and-amphetamine-regulated transcript.

Courtesy of Dr. W. Timothy Garvey, 2014.
Important Aspects of Obesity Pharmacotherapy

• Adding medication to lifestyle produces more weight loss and keeps weight off for longer duration

• Cessation of medication is followed by weight regain

• Variability in weight loss response – the FDA “off-ramp”

• Consider efficacy, mechanism, side effect profile, warnings, obesity complications, concurrent diseases for optimal selection of medication
Effect of Phentermine/Topiramate ER on Weight Loss in Obese Adults Over 2 Years: SEQUEL Study

<table>
<thead>
<tr>
<th>Time (weeks)</th>
<th>Change in Body Weight (%)</th>
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<tbody>
<tr>
<td>-14</td>
<td>-6.0</td>
</tr>
<tr>
<td>-10</td>
<td>-4.0</td>
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<tr>
<td>-6</td>
<td>-2.0</td>
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<tr>
<td>-2</td>
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<td>66</td>
<td>66.0</td>
</tr>
<tr>
<td>68</td>
<td>68.0</td>
</tr>
</tbody>
</table>

**Liraglutide: 3.0 mg**

- Mean ± SD weight at run-in (week -12): 99.6 ± 21.0 kg

**Placebo:**

- Mean ± SD weight at run-in (week -12): 105.9 ± 22.1 kg

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F = follow-up period; S = screening period.

### Phentermine/Topiramate ER Effect on Risk Factors: CONQUER Study

<table>
<thead>
<tr>
<th>Variable</th>
<th>PhentermineTopiramate ER 7.5/46 mg</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist (cm)</td>
<td>↓</td>
<td>-7.6</td>
<td>-2.4</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>↓</td>
<td>-4.7</td>
<td>-2.4</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td></td>
<td>-3.4</td>
<td>-2.7</td>
</tr>
<tr>
<td>Triglycerides (%)</td>
<td>↓</td>
<td>-8.6</td>
<td>4.7</td>
</tr>
<tr>
<td>LDL–C (%)</td>
<td></td>
<td>-3.7</td>
<td>-4.1</td>
</tr>
<tr>
<td>HDL–C (%)</td>
<td>↑</td>
<td>5.2</td>
<td>1.2</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>↓</td>
<td>-2.49</td>
<td>-0.79</td>
</tr>
<tr>
<td>Adiponectin (µg/mL)</td>
<td>↑</td>
<td>1.40</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Changes from baseline to week 56 in secondary endpoints

Lorcaserin 10 mg bid: BLOOM Study Weight Change Over Two Years

There is a Variable Response to Weight Loss Therapy: It looks like this.

FDA “Off-Ramp” for Obesity Pharmacotherapy

If patient has not lost at least 5% (lorcaserin, naltrexone ER/bupropion ER, phentermine/topiramate ER) or 4% (liraglutide 3 mg) of baseline weight by week 12 on full maintenance dose, then discontinue

- Lorcaserin: Begin treatment with full dose, 10 mg bid
- Naltrexone ER/bupropion ER: Begin one pill 8 mg/90 mg po q AM for week 1, then one bid for week 2, two q AM one q PM week 3, and 2 po bid week 4
- Phentermine/topiramate ER: one pill 3.75 mg/23 mg po q AM for 2 weeks, then treatment dose 7.5 mg/46 mg po q AM. If <3% weight loss at 12 weeks, proceed to top dose 15 mg/92 mg q AM
- Liraglutide 3 mg: Begin at 0.6 mg q day SQ for 1 week than increase by 0.6 mg q day each week until taking 3 mg q day
Early Response Predicts Long-term Efficacy

Non-Diabetics

**liraglutide 3 mg**

Diabetics

Non-Diabetics

**lorcaserin**

Diabetics

Q7.4. Are there differences in weight-loss drug efficacy and safety?

- **R80.** In selecting the optimal weight-loss medication for each patient, clinicians should consider differences in efficacy, side effects, cautions, and warnings that characterize medications approved for chronic management of obesity, as well as the presence of weight-related complications and medical history; these factors are the basis for individualized weight-loss pharmacotherapy; a generalizable hierarchical algorithm for medication preferences that would be applicable to all patients cannot currently be scientifically justified (Grade A; BEL1).

- **R81.** Clinicians and their patients with obesity should have available access to all approved medications to allow for the safe and effective individualization of appropriate pharmacotherapy (Grade D).

Comparative Efficacy of Weight-Loss Medications

All data placebo-subtracted, maximal dose, ITT-LOCF, 1 year, unless otherwise indicated

# Therapeutic Weight Loss Reduces Complications

<table>
<thead>
<tr>
<th>OBESITY COMPLICATION</th>
<th>% weight loss required for therapeutic benefit</th>
<th>Notes</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Prevention</td>
<td>3% to 10%</td>
<td>Maximum benefit 10%</td>
<td>DPP (Lancet, 2009) SEQUEL (Garvey et al, 2013)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5% to &gt;15%</td>
<td>BP still decreasing &gt;15%</td>
<td>Look AHEAD (Wing, 2011)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>3% to &gt;15%</td>
<td>TG still decreasing at &gt;15%</td>
<td>Look AHEAD (Wing, 2011)</td>
</tr>
<tr>
<td>HbA1c</td>
<td>3% to &gt;15%</td>
<td>HbA1c still decreasing at &gt;15%</td>
<td>Look AHEAD (Wing, 2011)</td>
</tr>
<tr>
<td>NAFLD</td>
<td>10%</td>
<td>Improves steatosis, inflammation, mild fibrosis</td>
<td>Assy et al, 2007; Dixon et al, 2004; Anish et al, 2009</td>
</tr>
<tr>
<td>Sleep Apnea (AHI)</td>
<td>10%</td>
<td>Little benefit at ≤ 5%</td>
<td>Sleep AHEAD (Foster, 2009) Winslow et al, 2012</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>5-10%</td>
<td>Improves symptoms and joint stress mechanics</td>
<td>Christensen et al, 2007 Felson et al, 1992; Aaboe et al, 2011</td>
</tr>
<tr>
<td>Stress Incontinence</td>
<td>5-10%</td>
<td></td>
<td>Burgio et al, 2007 Leslee et al, 2009</td>
</tr>
<tr>
<td>GERD</td>
<td>5-10% women 10% men</td>
<td></td>
<td>Singh et al, 2013 Tutujian R, 2011</td>
</tr>
</tbody>
</table>
Direct Meta-Analysis: Likelihood of Discontinuation Due to Adverse Events\(^1\)

**Common Adverse Events\(^2-4, a\)**

- **LIRA 3.0 mg:** hypoglycemia, GI AEs, headache
- **N/B:** GI AEs, headache
- **P/T:** parasthesia, dizziness, distorted taste, insomnia, constipation, dry mouth
- **LOR BID:** hypoglycemia, headache, fatigue
- **ORL:** abdominal pain/discomfort, oily spotting/stool, fecal urgency

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\(^a\) Selected common (defined as incidence > 5%) AEs are noted; refer to medication package inserts and cited references for complete information.
Medications for Chronic Weight Management: Contraindications and Related Precautions

- **Orlistat**
  - Chronic malabsorption syndrome (eg, fat soluble vitamins/medications)
  - Cholestasis

- **Lorcaserin**
  - None other than pregnancy
  - Concomitant SSRIs

- **Phentermine/topiramate ER**
  - Glaucoma
  - Hyperthyroidism
  - During/within 14 days of MAOI use
  - Topiramate: fetal oral clefts (regular pregnancy testing)

- **Naltrexone ER/bupropion ER**
  - Uncontrolled hypertension
  - Seizure disorders; anorexia nervosa or bulimia; abrupt discontinuation of some drugs
  - Use of other bupropion-containing products
  - Chronic opioid use (opioid withdrawal)
  - During/within 14 days of MAOI use

- **Liraglutide 3.0 mg**
  - MEN2, personal/family history of MTC (potential risk of thyroid C-cell tumors—rodent data)

All are contraindicated in pregnancy and generally not recommended for women who are breastfeeding; caution on use of reliable contraception.

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*a For all agents, known hypersensitivity to agent or any component.

*b Alcohol, benzodiazepines, barbiturates, antiepileptic drugs.

*c Relevance in humans has not been determined.

US FDA. Drugs@FDA. http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA.
### Complications
- Prediabetes/Metabolic Syndrome
- Type 2 Diabetes
- NAFLD/NASH
- Hypertension
- PCOS
- Infertility
- CHD
- Sleep Apnea
- Osteoarthritis
- Urinary Stress Incontinence

### Co-Morbidities
- CKD
- Renal stones
- Hepatic Impairment
- Psychoses
- Depression
- Binge eating
- Seizure Disorder
- Pregnancy/breast feeding
- Age > 65 years
- Post-Bariatric Surgery
- Opioid Use

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Garvey WT et al. Endocrine Practice 22(7):842-884, 2016
The Spectrum of Cardiometabolic Disease

1. Prediabetes
   i. IFG
   ii. IGT
   iii. HbA1c

2. Metabolic Syndrome

Type 2 Diabetes

Cardiovascular Disease

Insulin Resistance

Obesity
Incidence of Diabetes

All Participants

- Placebo (n=1082)
- Metformin (n=1073)
- Lifestyle (n=1079)

Risk reduction
31% by metformin
58% by lifestyle

How much weight loss is needed to prevent type 2 diabetes? The DPP experience

For Internal Medical Training Purposes Only – Not for Distribution
Treatment of Patients with Prediabetes with Liraglutide 3 mg/day

Phentermine/Topiramate ER and the Prevention of Diabetes in Patients With Metabolic Syndrome and/or Prediabetes: SEQUEL Study

Cumulative Incidence Rate of Type 2 Diabetes

- Placebo
- PHEN/TPM ER 7.54/46
- PHEN/TPM ER 15/92

Dose-Response for Weight Loss and Diabetes Prevention due to Phentermine/Topiramate ER Treatment: SEQUEL

Garvey et al, Diabetes Care, In Press, 2013
For Internal Medical Training Purposes Only – Not for Distribution
Incidence of Diabetes After Bariatric Surgery

UK Population-Based Matched Cohort Study*

*Matched for BMI, age, gender, index year, and A1C.

BMI = body mass index.

## Cardiometabolic Disease Staging (CMDS)  

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
<th>Rationale</th>
</tr>
</thead>
</table>
| 0     | No Risk Factors | Healthy Obese  
| 1     | 1 or 2 Risk Factors (waist, blood pressure, triglycerides, HDL-c) | Metabolic Syndrome has low sensitivity for CMD, and 1 or 2 risk factors elevates risk of future T2DM and CVD  
| 2     | Metabolic Syndrome OR Prediabetes  
(i) Metabolic Syndrome alone, OR (ii) IFG, OR (iii) IGT | Both Metabolic Syndrome and Prediabetes confer increased risk of T2DM and CVD  
| 3     | Metabolic Syndrome PLUS Prediabetes  
2 or more out of 3: Metabolic Syndrome, IFG, IGT | Risk of future T2DM is double in patients with both Metabolic Syndrome and Prediabetes compared with either alone  
| 4     | End-Stage Cardiometabolic Disease  
Type 2 Diabetes and/or CVD | T2DM is CVD risk equivalent  
Cardiometabolic Disease Staging: Cumulative Diabetes Incidence as a Function of Increasing CMDS Risk Stage: CARDIA Study Cohort

Number needed to treat to prevent one case of T2D as a function of baseline weighted cardiometabolic disease staging

<table>
<thead>
<tr>
<th>CMDS score</th>
<th>Number needed to treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–29</td>
<td>258</td>
</tr>
<tr>
<td>60+</td>
<td>18</td>
</tr>
</tbody>
</table>

CMDS, Cardiometabolic Disease Staging; T2D, type 2 diabetes

What if there was a treatment for T2D that:

1. Reduced HbA$_1c$ by 0.5–1.6% while other diabetes medications were reduced in dosage or eliminated
2. Led to a 5–10% decrease in body weight
3. Reduced blood pressure
4. Lowered triglycerides and raised HDL-c
5. Was renal protective – decreasing albuminuria
6. Improved sleep apnea
7. Improved mobility and decreased pain
8. Improved quality of life

This is the therapeutic profile of weight loss in T2D

Look AHEAD study references. Phase 3 trials for weight loss meds
Reduction in initial weight (%)

ILI, intensive lifestyle intervention; DSE, diabetes support and education.

Retention at 4 years:
ILI = 94.1%
DSE = 93.1%

Diabetes support and education
Intensive lifestyle intervention

P<0.0001
Effect of Weight Loss in T2DM on CV Risk Factors and Diabetes Measures

Look AHEAD Trial  (N=5145)

<table>
<thead>
<tr>
<th>At 1 year</th>
<th>DSE</th>
<th>ILI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss (%)</td>
<td>-0.7</td>
<td>-8.6</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>-0.14</td>
<td>-0.64*</td>
</tr>
<tr>
<td>FPG (mg/dL)</td>
<td>-7.2</td>
<td>-21.5*</td>
</tr>
<tr>
<td>% on diabetes medications</td>
<td>2.2</td>
<td>-7.8*</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>-2.8</td>
<td>-6.8*</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>-1.8</td>
<td>-3.0*</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>-5.7</td>
<td>-5.2</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>1.4</td>
<td>3.4*</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>-14.6</td>
<td>-30.3*</td>
</tr>
</tbody>
</table>

*P≤0.001, †P=0.01 vs customary support.

BP, blood pressure; CV, cardiovascular; DSE, diabetes support and education; ILI, intensive lifestyle intervention; T2DM, type 2 diabetes mellitus.

Week 28 marked the end of the OB-202 Study and the baseline for the DM-230 Study. †P, 0.0001 for PHEN/TPM ER groups vs. placebo at all time points except week 0. ‡P, 0.05 vs. placebo.

Garvey WT et al, Diabetes Care, 37(12):3309-3316, 2014
Effects of Phentermine/Topiramate ER in T2DM

Achieving HbA1c Targets

- Placebo (n=55)
- PHEN/TPM ER 15/92 (n=75)

Change in Dose/Number of Diabetes Meds

- Decreased No. of Antidiabetic Medications
- Increased No. of Antidiabetic Medications

**HbA1c ≤ 7.0%** (≤ 53 mmol/mol)

- Placebo: 40%
- PHEN/TPM ER: 53%

**HbA1c ≤ 6.5%** (≤ 48 mmol/mol)

- Placebo: 16%
- PHEN/TPM ER: 32%

Garvey WT et al, Diabetes Care, 37(12):3309-3316, 2014

*P < 0.05 vs. placebo
GLYCEMIC CONTROL ALGORITHM

**INDIVIDUALIZE GOALS**

*A1C ≤ 6.5%* For patients without concurrent serious illness and at low hypoglycemic risk

*A1C > 6.5%* For patients with concurrent serious illness and at risk for hypoglycemia

**LIFESTYLE THERAPY** (Including Medically Assisted Weight Loss)

**Entry A1C < 7.5%**

**MONOTHERAPY**

- Metformin
- GLP1-RA
- SGLT2i
- DPP4i
- TZD
- AGi
- SU/GLN

If not at goal in 3 months proceed to Dual Therapy

**Entry A1C ≥ 7.5%**

**DUAL THERAPY**

- MET or other 1st-line agent
- GLP1-RA
- SGLT2i
- DPP4i
- TZD
- Basal Insulin
- Colesevelam
- Bromocriptine QR
- AGi
- SU/GLN

If not at goal in 3 months proceed to Triple Therapy

**Entry A1C > 9.0%**

**TRIPLE THERAPY**

- MET or other 1st-line agent + 2nd-line agent
- GLP1-RA
- SGLT2i
- DPP4i
- TZD
- Basal Insulin
- Colesevelam
- Bromocriptine QR
- AGi
- SU/GLN

If not at goal in 3 months proceed to or intensify insulin therapy

**SYMPTOMS**

**NO**

*DUAL Therapy* OR *TRIPLE Therapy*

**YES**

*INSULIN ± Other Agents*

**ADD OR INTENSIFY INSULIN**

Refer to Insulin Algorithm

**LEGEND**

- ✔️ Few adverse events and/or possible benefits
- 🚫 Use with caution

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1. Order of medications represents a suggested hierarchy of usage; length of line reflects strength of recommendation
2. Certain GLP1-RAs and SGLT2is have shown CVD and CKD benefits—preferred in patients with those complications
3. Include one of these medications if CHD present
Thank You
COMPLICATIONS-CENTRIC MODEL FOR CARE OF THE PATIENT WITH OVERWEIGHT/OBESITY

**STEP 1**

**EVALUATION FOR COMPLICATIONS AND STAGING**

**CARDIOMETABOLIC DISEASE** | **BIOMECHANICAL COMPLICATIONS**

<table>
<thead>
<tr>
<th>BMI &lt;25</th>
<th>NO COMPLICATIONS</th>
<th>BMI ≥25</th>
<th>COMPLICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO OVERWEIGHT OR OBESITY</td>
<td>OVERWEIGHT OR OBESITY</td>
<td>MILD TO MODERATE</td>
<td>SEVERE</td>
</tr>
</tbody>
</table>

**STAGE 0**

- Therapeutic targets for improvement in complications

**STAGE 1**

- Treatment modality

**STAGE 2**

- Treatment intensity based on staging

**STEP 2**

**SELECT:**

<table>
<thead>
<tr>
<th>Lifestyle Therapy</th>
<th>Physician/RD counseling, web/remote program, structured multidisciplinary program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Therapy (BMI ≥27):</td>
<td>Individualize care by selecting one of the following based on efficacy, safety, and patients’ clinical profile: phentermine, orlistat, lorcaserin, phentermine/topiramate ER, naltrexone/bupropion, liraglutide 3 mg</td>
</tr>
</tbody>
</table>

| Surgical Therapy (BMI ≥35): | Gastric banding, sleeve, or bypass |

**STEP 3**

If therapeutic targets for complications not met, intensify lifestyle, medical, and/or surgical treatment modalities for greater weight loss. Obesity is a chronic progressive disease and requires commitment to long-term therapy and follow-up.
ASCVD RISK FACTOR MODIFICATIONS ALGORITHM

DYSLIPIDEMIA

LIFESTYLE THERAPY (Including Medically Assisted Weight Loss)

LIPID PANEL: Assess ASCVD Risk

STATIN THERAPY
If TG >500 mg/dL, fibrates, Rx-grade omega-3 fatty acids, niacin

If statin-intolerant
Try alternate statin, lower statin dose or frequency, or add nonstatin LDL-C-lowering therapies
Repeat lipid panel; assess adequacy, tolerance of therapy
Intensify therapies to attain goals according to risk levels

RISK LEVELS

<table>
<thead>
<tr>
<th>RISK LEVELS</th>
<th>HIGH</th>
<th>VERY HIGH</th>
<th>EXTREME</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C (mg/dL)</td>
<td>&lt;100</td>
<td>&lt;70</td>
<td>&lt;55</td>
</tr>
<tr>
<td>Non-HDL-C (mg/dL)</td>
<td>&lt;130</td>
<td>&lt;100</td>
<td>&lt;80</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>&lt;150</td>
<td>&lt;150</td>
<td>&lt;150</td>
</tr>
<tr>
<td>Apo B (mg/dL)</td>
<td>&lt;90</td>
<td>&lt;80</td>
<td>&lt;70</td>
</tr>
</tbody>
</table>

If not at desirable levels: Intensify lifestyle therapy (weight loss, physical activity, dietary changes) and glycemic control; consider additional therapy

To lower LDL-C:
To lower Non-HDL-C, TG:
To lower Apo B, LDL-P:
To lower LDL-C in FH:**
Intensify statin, add ezetimibe, PCSK9i, colesveleam, or niacin
Intensify statin and/or add Rx-grade OM3 fatty acid, fibrate, and/or niacin
Intensify statin and/or add ezetimibe, PCSK9i, colesveleam, and/or niacin
Statin + PCSK9i

Assess adequacy & tolerance of therapy with focused laboratory evaluations and patient follow-up

* EVEN MORE INTENSIVE THERAPY MIGHT BE WARRANTED ** FAMILIAL HYPERCHOLESTEROLEMIA

HYPERTENSION

GOAL: SYSTOLIC <130, DIASTOLIC <80 mm Hg

ACEi or ARB
For initial blood pressure >150/100 mm Hg:
DUAL THERAPY
ACEi or ARB + 
Calcium Channel Blocker ✓
β-blocker ✓
Thiazide ✓

If not at goal (2-3 months)
Add calcium channel blocker, β-blocker or thiazide diuretic

If not at goal (2-3 months)
Add next agent from the above group, repeat

If not at goal (2-3 months)
Additional choices (α-blockers, central agents, vasodilators, aldosterone antagonist)

Achievement of target blood pressure is critical

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Effects of Naltrexone/Bupropion ER on weight and HbA1c in Patients with Type 2 Diabetes