

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Wadden TA, Volger S, Sarwer DB, et al. A two-year randomized trial of obesity treatment in primary care practice. *N Engl J Med* 2011;365:1969-79. DOI: 10.1056/NEJMoa1109220.

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### **A Two-Year Randomized Trial of Obesity Treatment in Primary Care Practice**

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Online Supplementary Table 1. Estimated mean weight loss, percent reduction in body weight, and change in body mass index (BMI) over a 24-month period in the modified intention-to-treat population (ITT), excluding sibutramine-treated participants.

	Usual Care (N=130)	Brief LC (N=131)	Enhanced LC (N=85)	P values for Pairwise Comparisons		
				Brief LC vs. Usual Care	Enhanced LC vs. Usual Care	Enhanced LC vs. Brief LC
<b>Weight (kg)</b>						
Month 6	-2.0 ± 0.5*	-3.5 ± 0.5	-5.7 ± 0.6	0.023	<0.001	0.005
Month 12	-2.3 ± 0.6	-3.4 ± 0.6	-6.1 ± 0.8	0.208	<0.001	0.007
Month 18	-1.9 ± 0.7	-3.0 ± 0.7	-5.4 ± 0.8	0.210	<0.001	0.027
Month 24	-1.7 ± 0.7	-2.9 ± 0.7	-4.3 ± 0.8	0.230	0.015	0.170
<b>Weight loss (%)</b>						
Month 6	-1.8 ± 0.5	-3.5 ± 0.5	-5.6 ± 0.6	0.004	<0.001	0.002
Month 12	-2.1 ± 0.6	-3.5 ± 0.6	-6.0 ± 0.7	0.078	<0.001	0.004
Month 18	-1.7 ± 0.6	-3.1 ± 0.6	-5.4 ± 0.8	0.100	<0.001	0.016
Month 24	-1.6 ± 0.6	-2.9 ± 0.6	-4.5 ± 0.8	0.130	0.003	0.106
<b>BMI (kg/m<sup>2</sup>)</b>						
Month 6	-0.7 ± 0.2	-1.3 ± 0.2	-2.0 ± 0.2	0.014	<0.001	0.008
Month 12	-0.8 ± 0.2	-1.3 ± 0.2	-2.1 ± 0.3	0.150	<0.001	0.012
Month 18	-0.7 ± 0.2	-1.1 ± 0.2	-1.9 ± 0.3	0.151	0.001	0.042
Month 24	-0.6 ± 0.2	-0.9 ± 0.2	-1.5 ± 0.3	0.270	0.015	0.147

\* All values in columns 2-4 are model-based estimates of the mean  $\pm$  standard error. Model-based estimates include all randomized participants in the modified ITT population.

Note: Brief LC = Brief Lifestyle Counseling; Enhanced LC = Enhanced Lifestyle Counseling.

Online Supplementary Table 2A. Estimated mean changes in cardiovascular disease risk factors over a 24-month period in the intention-to-treat (ITT) population.

	Usual Care (N=130)	Brief LC (N=131)	Enhanced LC (N=129)	P values for Pairwise Comparisons		
				Brief LC vs. Usual Care	Enhanced LC vs. Usual Care	Enhanced LC vs. Brief LC
<b>Waist circumference (cm)</b>						
Month 6	-2.7 ± 0.6*	-4.9 ± 0.6	-6.6 ± 0.6	0.002	< 0.001	0.013
Month 12	-3.2 ± 0.6	-4.6 ± 0.6	-7.5 ± 0.6	0.089	< 0.001	< 0.001
Month 24	-2.3 ± 0.7	-4.0 ± 0.7	-5.5 ± 0.7	0.056	< 0.001	0.077
<b>Triglycerides (mg/dl)</b>						
Month 6	-13.7 ± 5.7	-21.6 ± 5.8	-25.9 ± 5.6	0.290	0.096	0.554
Month 12	-16.5 ± 5.4	-22.9 ± 5.5	-38.6 ± 5.4	0.353	0.002	0.024
Month 24	-21.6 ± 6.0	-29.7 ± 6.1	-33.4 ± 6.0	0.312	0.137	0.635
<b>Total cholesterol (mg/dl)</b>						
Month 6	-11.4 ± 3.2	-11.2 ± 3.2	-7.7 ± 3.1	0.971	0.374	0.397

Month 12	-11.1 ± 3.1	-10.1 ± 3.2	-9.3 ± 3.1	0.801	0.665	0.857
Month 24	-14.3 ± 3.3	-16.6 ± 3.3	-6.9 ± 3.3	0.597	0.087	0.025
HDL cholesterol (mg/dl)						
Month 6	-0.4 ± 0.7	-0.0 ± 0.7	-0.5 ± 0.7	0.703	0.937	0.643
Month 12	-0.2 ± 0.7	-0.8 ± 0.7	1.4 ± 0.7	0.502	0.085	0.017
Month 24	0.5 ± 0.8	0.7 ± 0.8	3.0 ± 0.8	0.851	0.016	0.026
LDL cholesterol (mg/dl)						
Month 6	-8.5 ± 2.8	-7.1 ± 2.9	-2.3 ± 2.8	0.717	0.095	0.195
Month 12	-7.9 ± 2.8	-5.0 ± 2.8	-3.4 ± 2.8	0.428	0.225	0.674
Month 24	-11.5 ± 2.8	-11.6 ± 2.9	-4.1 ± 2.8	0.972	0.046	0.042
Glucose (mg/dl)						
Month 6	-0.0 ± 2.6	-8.1 ± 2.7	-3.1 ± 2.6	0.023	0.376	0.156
Month 12	1.4 ± 2.2	-3.8 ± 2.2	-5.9 ± 2.2	0.069	0.011	0.461
Month 24	0.5 ± 3.1	-0.0 ± 3.1	-4.8 ± 3.1	0.899	0.196	0.247
Systolic blood pressure (mm Hg)						
Month 6	-0.7 ± 1.3	0.3 ± 1.3	-0.1 ± 1.2	0.567	0.717	0.825

Month 12	1.2 ± 1.3	0.8 ± 1.3	0.2 ± 1.2	0.849	0.570	0.708
Month 24	1.5 ± 1.6	1.5 ± 1.6	-1.1 ± 1.6	0.998	0.244	0.243
Diastolic blood pressure (mm Hg)						
Month 6	-0.3 ± 0.9	-0.2 ± 0.9	-0.5 ± 0.8	0.941	0.846	0.788
Month 12	-0.5 ± 0.8	-0.8 ± 0.8	-1.4 ± 0.8	0.828	0.458	0.602
Month 24	0.2 ± 0.9	-0.2 ± 0.9	-0.8 ± 0.9	0.974	0.452	0.434

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\* All values in columns 2-4 are model-based estimates of the mean ± standard error. Model-based estimates include all randomized participants in the ITT population.

Note: Brief LC = Brief Lifestyle Counseling; Enhanced LC = Enhanced Lifestyle Counseling.

Online Supplementary Table 2B. Estimated mean changes in cardiovascular disease risk factors over a 24-month period in the modified intention-to-treat (ITT) population (excluding sibutramine-treated participants).

	Usual Care (N=130)	Brief LC (N=131)	Enhanced LC (N=85)	P values for Pairwise Comparisons		
				Brief LC vs. Usual Care	Enhanced LC vs. Usual Care	Enhanced LC vs. Brief LC
<b>Waist circumference (cm)</b>						
Month 6	-2.8 ± 0.6*	-4.9 ± 0.6	-6.3 ± 0.6	0.002	<0.001	0.084
Month 12	-3.2 ± 0.6	-4.6 ± 0.6	-7.0 ± 0.7	0.085	<0.001	0.010
Month 24	-2.4 ± 0.7	-4.0 ± 0.7	-5.5 ± 0.8	0.063	0.002	0.137
<b>Triglycerides (mg/dl)</b>						
Month 6	-13.9 ± 6.0	-21.6 ± 6.1	-25.0 ± 7.1	0.323	0.200	0.700
Month 12	-16.8 ± 5.5	-23.0 ± 5.7	-40.2 ± 6.6	0.375	0.003	0.031
Month 24	-21.8 ± 6.3	-29.6 ± 6.4	-36.3 ± 7.5	0.350	0.118	0.467

Total cholesterol (mg/dl)

Month 6	-11.2 ± 3.2	-11.1 ± 3.3	-8.4 ± 3.8	0.990	0.550	0.560
Month 12	-10.9 ± 3.2	-10.0 ± 3.3	-8.6 ± 3.9	0.824	0.624	0.770
Month 24	-14.2 ± 3.3	-16.4 ± 3.4	-12.0 ± 4.0	0.598	0.661	0.365

HDL cholesterol (mg/dl)

Month 6	-0.3 ± 0.7	0.0 ± 0.8	-0.9 ± 0.9	0.730	0.604	0.410
Month 12	-0.1 ± 0.7	-0.7 ± 0.7	0.9 ± 0.9	0.489	0.322	0.111
Month 24	0.6 ± 0.8	0.8 ± 0.8	2.3 ± 1.0	0.853	0.137	0.187

LDL cholesterol (mg/dl)

Month 6	-8.4 ± 2.9	-7.1 ± 3.0	-2.7 ± 3.5	0.736	0.180	0.301
Month 12	-7.7 ± 2.9	-4.9 ± 2.9	-1.8 ± 3.5	0.453	0.166	0.470
Month 24	-11.4 ± 2.9	-11.5 ± 3.0	-7.4 ± 3.5	0.980	0.344	0.331

Glucose (mg/dl)

Month 6	-0.2 ± 2.8	-8.2 ± 2.9	-2.9 ± 3.3	0.030	0.510	0.198
Month 12	1.2 ± 2.3	-3.9 ± 2.4	-8.0 ± 2.8	0.083	0.007	0.228
Month 24	0.4 ± 3.2	-0.2 ± 3.3	-5.5 ± 3.9	0.910	0.232	0.279

Systolic blood pressure (mm Hg)

Month 6	-0.7 ± 1.3	0.4 ± 1.3	-1.4 ± 1.6	0.570	0.740	0.400
Month 12	1.2 ± 1.3	0.8 ± 1.3	-0.4 ± 1.6	0.863	0.450	0.548
Month 24	1.5 ± 1.6	1.5 ± 1.6	-1.9 ± 2.0	0.990	0.183	0.180

Diastolic blood pressure (mm Hg)

Month 6	-0.3 ± 0.9	-0.2 ± 0.9	-1.3 ± 1.0	0.927	0.464	0.415
Month 12	-0.5 ± 0.9	-0.8 ± 0.9	-2.2 ± 1.0	0.825	0.220	0.304
Month 24	0.2 ± 1.0	0.2 ± 1.0	-1.4 ± 1.2	0.972	0.315	0.301

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\* All values in columns 2-4 are model-based estimates of the mean ± standard error. Model-based estimates include all randomized participants in the modified ITT population.

Note: Brief LC = Brief Lifestyle Counseling; Enhanced LC = Enhanced Lifestyle Counseling.

Online Supplementary Table 3. Serious Adverse Events by Intervention Group.

Event	Usual Care	Brief LC	Enhanced LC	Total
<b>Cardiac disorders</b>				
Angina pectoris	1	5	2	8
Atrial fibrillation	2	3	3	8
Congestive heart failure	2	0	0	2
Myocardial infarction	1	0	0	1
Transient ischemic attack	0	0	1	1
<b>Other</b>				
Atrial flutter	0	1	0	1
Syncope	0	1	0	1
<b>Blood and lymphatic system disorders</b>				
Chronic Lymphocytic Leukemia	1	0	0	1
<b>Gastrointestinal disorders</b>				
Appendicitis	0	0	1	1
Clostridium difficile	0	1	0	1
Colitis	1	0	0	1
Colon cancer with hemicolectomy	0	0	1	1
Colon resection	0	1	0	1
Crohn's disease	0	0	1	1
Diverticulitis	0	1	2	3

GERD	0	0	1	1
Lower GI bleed	0	0	1	1
Endocrine disorders				
Adrenalectomy	1	0	0	1
Pancreatitis	1	0	0	1
Right parathyroidectomy	0	0	1	1
Respiratory disorders				
Asthma	1	1	0	2
Bronchiectasis	0	0	3	3
Pneumonia	0	0	1	1
Psychiatric disorders				
Bipolar II, general anxiety disorder	0	1	0	1
Major depression	0	1	0	1
Renal and urinary disorders				
Kidney stones	0	0	1	1
Nephrolithiasis	1	0	0	1
Hepatobiliary disorders				
Liver abscess	0	1	0	1
Cholecystitis	1	0	0	1
Cholecystectomy	1	3	0	4
Musculoskeletal disorders				
Knee replacement	0	4	1	5
Leg pain	0	0	1	1

Reproductive and breast disorders				
Breast cancer	0	1	0	1
Hysterectomy	1	1	3	5
Myomectomy	1	0	0	1
Ovarian mass	1	0	0	1
Prostate cancer	1	0	0	1
Spontaneous abortion, anembryonic	1	0	0	1
Infections and Infestations				
Cellulitis	1	0	0	1
Injuries				
Motor vehicle accident	1	0	0	1
General disorders				
Syncope	0	0	1	1
Chest pain	0	0	1	1
Total	21	26	26	73

## Captions for Online Supplementary Figures

Online Supplementary Figure 1. The figure shows estimated mean ( $\pm$ SEM) reduction in initial weight (in kg) over 24 months for the Enhanced Lifestyle Counseling participants (N=129) in the intention-to-treat population who, at baseline, chose to use meal replacements (N= 67), sibutramine (N=38), and orlistat (N=24). Analyses that were based on participants' original choice of enhancements showed estimated mean weight losses at Month 24 of  $3.9\pm 1.0$ ,  $5.5\pm 1.3$ , and  $4.6\pm 1.7$  kg, respectively, with no significant differences among groups. At Month 6, sibutramine-treated individuals lost  $9.3\pm 1.1$  kg, greater than the losses associated with meal replacements ( $5.6\pm 0.8$  kg,  $P=0.008$ ) and orlistat ( $4.8\pm 1.4$  kg,  $P<0.001$ ), with no differences between the latter groups. At Month 12, sibutramine losses of  $10.4\pm 1.4$  kg were greater than those produced by meal replacements ( $5.9\pm 1.0$  kg,  $P=0.009$ ) and orlistat ( $4.3\pm 1.8$  kg,  $P=0.008$ ), with no differences between the latter groups. At Month 18, mean losses for these three groups were  $8.1\pm 1.4$ ,  $4.9\pm 1.1$ , and  $4.4\pm 1.8$  kg, respectively, with no significant differences among groups.

Online Supplementary Figure 2: Percentage of participants achieving different categorical weight losses. Panel A shows the percentage of participants in the modified intention-to-treat population (which excluded sibutramine-treated participants) in each group who were at or below their baseline weight at months 12 and 24. (Participants with missing weights were assumed to be above baseline.) Significant differences between groups are shown by P values, with the absence of a bracket linking two groups indicating no significant difference between the two groups. Panels B and C show the percentages of participants in the three groups who lost  $\geq 5\%$  and  $\geq 10\%$  of initial weight, respectively, at months 12 and 24. The percentage of participants who lost  $\geq 5\%$

includes the percentage who lost  $\geq 10\%$ . Brief LC = Brief Lifestyle Counseling; Enhanced LC = Enhanced Lifestyle Counseling.

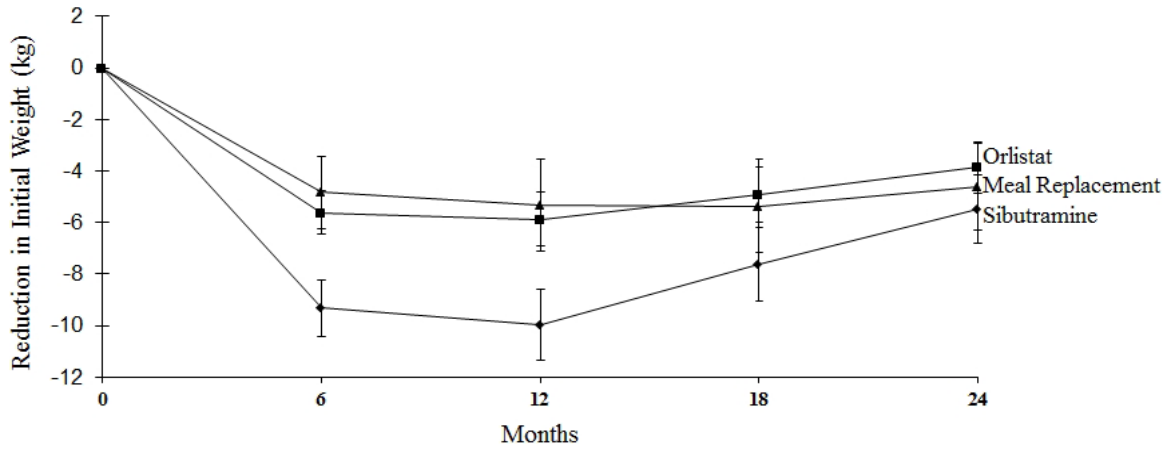
Online Supplementary Figure 3: Relationship between treatment attendance and weight loss.

Panel A shows percent reduction in initial weight at Month 24 for participants in the three interventions, based upon a median split analysis of participants' attendance of their PCP visits.

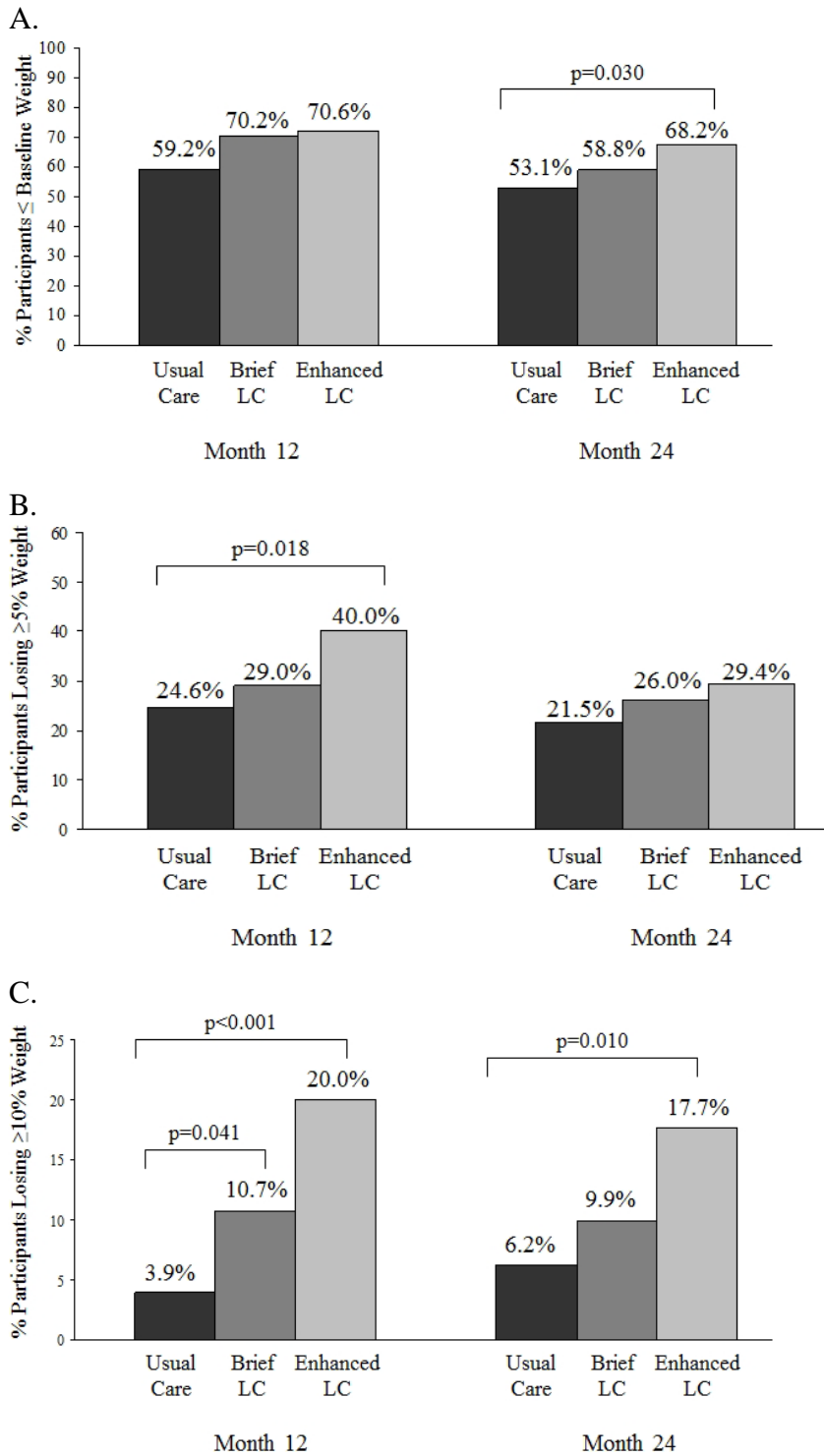
The values inside the bars show the percentage of possible visits attended for low and high attenders within each treatment group. Panel B shows similar findings based upon a median split analysis of participants' attendance of lifestyle coaching visits. Analyses are provided for all participants in Enhanced LC, as well as excluding the 44 participants who received sibutramine.

Brief LC = Brief Lifestyle Counseling; Enhanced LC = Enhanced Lifestyle Counseling.

Online Supplementary Figure 1

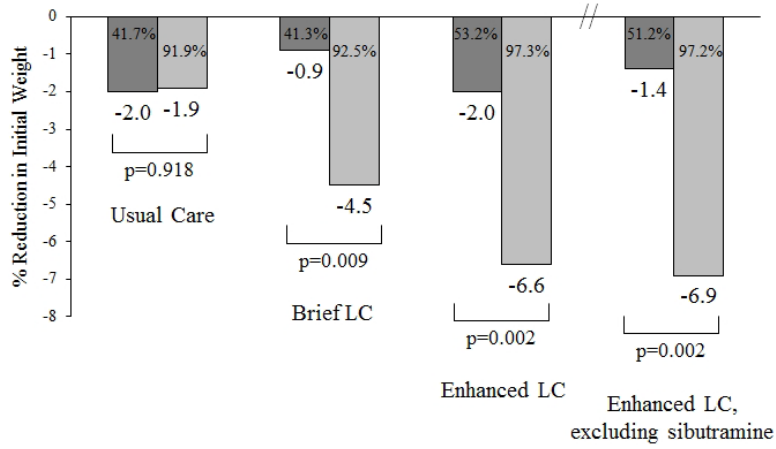


Online Supplementary Figure 2.

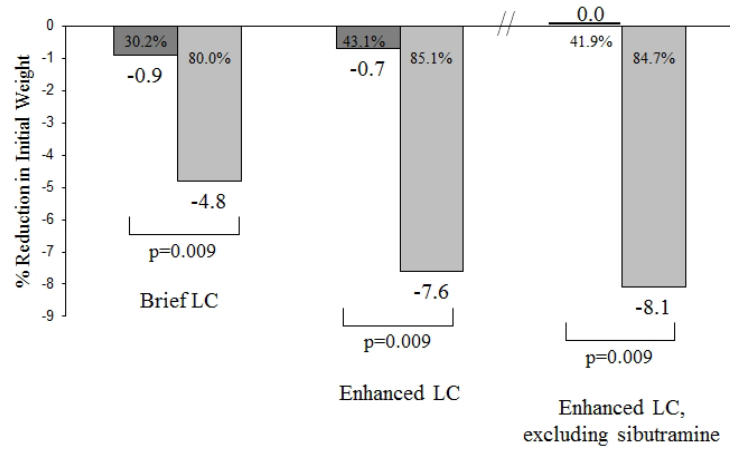


Online Supplementary Figure 3.

A.



B.



Features of the Three Treatment Conditions

Treatment Component	Usual Care	Usual Care + Brief Lifestyle Counseling	Usual Care + Enhanced Brief Lifestyle Counseling
Quarterly Visits with Primary Care Provider	√	√	√
NHLBI Handouts: “Aim for a Healthy Weight”	√	√	√
Dietary goal: 1200-1500 kcal/d if <250 lb (113.4 kg) 1500-1800 kcal/d if ≥250 lb (113.4 kg)	√	√	√
Exercise goal: ≥ 180 min/week of moderate intensity activity	√	√	√
Record Food Intake and Activity		√	√
Brief Monthly Counseling Sessions with Auxiliary Health Care Provider (primarily medical assistants)		√	√
DPP Lifestyle Modification Curriculum		√	√
Meal Replacements*			√
FDA-Approved Weight Loss Medication*			√

\* Participants in this group will select the use of meal replacements or medication

Summary of PCP Quarterly Visits

<b>Month</b>	<b>Visit</b>	<b>Handout</b>	<b>Source</b>
0	1	How to Lose Weight and Maintain It	NHLBI “Aim for a Healthy Weight” Booklet, pp. 5-8
3	2	Fat Matters but Calories Count	NHLBI Booklet, p. 9
6	3	Physical Activity	NHLBI Booklet, pp. 25-26
9	4	Keep an Eye on Portion Size	NHLBI Booklet, p. 12
12	5	Moving Forward	NHLBI Booklet, pp. 30-31
15	6	Dining Out – How to Choose	NHLBI Booklet, pp. 19-20
18	7	How You Can Fit Activity Into Your Schedule	NHLBI Booklet, pp. 27-28
21	8	Low Calorie, Lower Fat Alternatives	NHLBI Booklet, pp. 10-11
24*	9	Weight Loss Program Graduation	NHLBI Booklet, pp. 33-34.

\* No PCP counseling was provided at session 9. This was a farewell, graduation visit at the Month 24 assessment.

## Summary of Lifestyle Coach Sessions

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Visit #		Topic
1	Week 0	Welcome to the POWER-UP Program
2	Week 2	Keeping Track and Counting Calories
3	Month 1	Eating Healthy
4	Month 2	Increasing Physical Activity
5	Month 3	Monitoring Fat Intake
6	Month 4	Triggers for Overeating
7	Month 5	The Eating Environment
8	Month 6	Jump Start Activity
9	Month 7	Problem Solving
10	Month 8	Making Social Cues Work for You
11	Month 9	Stress Management
12	Month 10	Talk Back to Negative Thoughts
13	Month 11	The Slippery Slope of Lifestyle Change
14	Month 12	Beginning Year Two
15	Month 13	The Ins and Outs of Energy Balance
16	Month 14	Stepping Up Physical Activity
17	Month 15	Structuring Eating for Success
18	Month 16	Staying Positive
19	Month 17	Controlling Hunger
20	Month 18	Preventing Relapse
21	Month 19	Becoming a Weight Loss Maintenance Pro
22	Month 20	Essentials for Eating Out
23	Month 21	Supermarket Smarts
24	Month 22	Preparing for What is Next
25	Month 23	The Year Ahead
26*	Month 24	Graduation Visit

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\* No Lifestyle Coaching was provided at Month 24. This was a farewell, graduation visit at the Month 24 assessment.

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