113-OR - Oral abstract session: **Is It All About the Food?** Friday Jun 23, 2023 5:30 PM - 6:30 PM

83rd Scientific Sessions

SAN DIEGO, CA / HYBRID | JUNE 23-26, 2023

The OPTIFAST (OP) Total and Partial Meal Replacement Program Improves Cardiometabolic Risk in Adults With Obesity – Secondary and Exploratory Analysis of the OPTIWIN Study

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Nestlé HealthScience

Disclosures, Author Information, and Acknowledgement

Author	Institution	Conflicts of interest
Jamy D Ard, MD	Wake Forest School of Medicine, Winston-Salem, North Carolina, US	Received investigator fee and consulting fee from NHSc
Ian J Neeland, MD	University Hospitals Cleveland Medical Center; Case Western Reserve University School of Medicine, Cleveland, OH, US	Received consulting fees/speaking honoraria from NHSc, Boehringer Ingelheim, Lilly, AMRA Medical
Amy E Rothberg, MD	University of Michigan, Ann Arbor, MI, US	Received investigator fee and consulting fee from NHSc
Robert J Chilton, MD	UTHSCA, San Antonio, TX, US	Received consulting fees/speaking honoraria from Medtronics, Boehringer Ingelheim, Lilly, MSD
Daniel de Luis, MD	Hospital Clinico Universitario Valladolid. Medicine School Dept of Endocirnology and Nutrition	Received investigator fee and consulting fee from Pronokal, a NHSc company
Andrea H Hawkinson	Nestlé Health Science, Bridgewater, NJ, US	Employment NHSc
Sarah S Cohen, MSc	Tox Strategies, Durham, NC, US	Employment Tox Strategis at the time of analysis, who has done analytical work paid by NHSc
Odd Erik Johansen, MD, PhD	Nestlé Health Science, Lausanne, Vaud, Switzerland	Employment NHSc

The study was funded by Nestlé Health Science (NHSc)

We thank all participants and study site personnel involved in this study

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Obesity: risk factor for cardiovascular disease (CVD)

Obesity is a risk factor for the development of cardiovascular disease (CVD) and people with obesity experience CVD events at an earlier age.

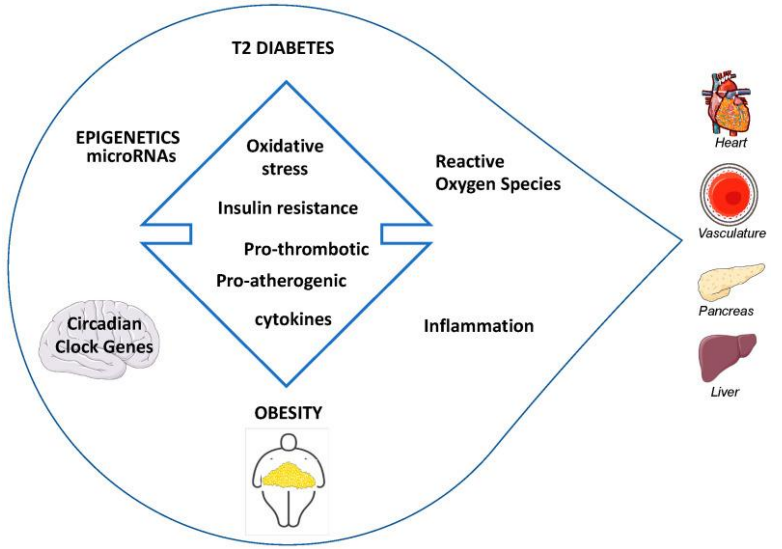
Khan SS, Ning H, Wilkins JT, Allen N, Carnethon M, Berry JD, Sweis RN, Lloyd-Jones DM. Association of body mass index with lifetime risk of cardiovascular disease and compression of morbidity. *JAMA Cardiol*. 2018;3:280–287

In people with type 2 diabetes and obesity, this risk is further aggravated

Fox CS et al, Lifetime Risk of Cardiovascular Disease Among Individuals With and Without Diabetes Stratified by Obesity Status in the Framingham Heart Study. *Diabetes Care* 2008;31:1582–1584.

Driven by multiple pathways, which can exacerbate risk factors such as hypertension and dyslipidemia

- Key goals of obesity management are not only to reduce body weight, but also to mitigate cardiometabolic complications.



La Sala et al. Int J Mol Sci. 2020 Nov; 21(21): 8178

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Weight loss can improve CVD risk factors and CV risk

Regardless of principle, reducing body weight can significantly lower the CVD risk

- Although a modest reduction of 3-5% contributes, greater reductions in body weight are associated with larger reductions in CVD risk

Gregg E, et al. Association of the magnitude of weight loss and changes in physical fitness with long-term cardiovascular disease outcomes in overweight or obese people with type 2 diabetes: a post-hoc analysis of the Look AHEAD randomised clinical trial. Lancet Diabetes Endocrinol 2016;4:913–21

Ryan DH et al. Weight Loss and Improvement in Comorbidity: Differences at 5%, 10%, 15%, and Over. Curr Obes Rep 2017;6:187–94

Use of meal replacement products (MRP) to support weight loss can lead to double-digit reductions

- The use of MRP have been endorsed by multiple guidelines

Guideline[1–6]	Latest update	Recommendations on MRP in adult persons with overweight or obesity
EASO European Association for the Study of Obesity	2023	"In more detail, the previous guidelines stated that "partial meal replacements (replacing one to two meals/day as part of a calorie-restricted intervention) could be used to reduce body weight, wasit circumference, blood pressure and improve glycaemic control," but evidence was graded as level 1a, grade B. The addition of new evidence from literature reviews and meta-analyses indicates that meal replacements could be linked with modest to significant higher weight loss even at 1 year, may indicate a greater role of meal replacements in adult obesity".[1]
anzos australian & new zealand obesity society	2022	Considerations for use as part of a low energy diet (1000-1200 kcal) where MRP substitute one or two meals, or comprehensively as part of a very low energy diet (< 800 kcal/day).[2]
obesity canada	2021	Partial meal replacements are used to replace one to two meals per day as part of a calorie-restricted intervention. These calorie-restricted interventions have been shown to reduce body weight, waist circumference, blood pressure and glycemic control compared with conventional, calorie-restricted weight loss diets. VLCDs using meal replacements include medical supervision and extensive support (nutrition, psychological, exercise counselling) as part of the intervention[3]
American Diabetes Association.	2021	Use of meal replacement plans prescribed by trained practitioners can be beneficial and the use of a partial meal replacement plan was associated with improvements in diet quality and weight loss in the Look-AHEAD trial. Structured very-low-calorie diets, typically 800–1,000 kcal/day utilizing high-protein foods and meal replacement products, may increase the pace and/or magnitude of initial weight loss and glycemic improvements compared with standard behavioral interventions[4]
AACE.	2016	Meal replacements is an option for consideration when discussing meal plans as part of a lifestyle therapy[5]
	2013	VLCD: Comprehensive, high-intensity, on-site lifestyle interventions that include a medically supervised very–lowcalorie diet (often defined as < 800 kcal/d), as provided by complete meal replacement products, produce total weight loss of approximately 14.2 kg to 21.0 kg over 11 to 14 weeks, which is larger than that produced by no intervention or usual care. a. LCD; In overweight and obese women, the use of liquid and bar meal replacements is associated with increased weight loss at up to 6 months, in comparison with a balanced deficit diet using only conventional food[6]

1. Hassapidou, M, et al., Obesity Facts, 2023;16:11-28; 2. Markovic TP, et al. Obes Res Clin Pract 2022;16:353-363; 3: Brown J, et al. Canadian Adult Obesity Clinical Practice Guidelines https://obesitycanada.ca/guidelines/nutrition; 4: American Diabetes Association, Diabetes Care 2021;44 (Suppl 1):S100-S110; 5. Garvey WT, et al. Endocr Pract 2016;22:1-203; 6. Jensen MD, et al. J Am Coll Cardiol 2014;63:2985–3023

Role of Meal Replacement in Weight Management

Sensory specific satiety

- A large variety of foods (stimuli) in a meal is associated with higher calorie intake

Raynor and Epstein. Psychol Bull. 2001 May;127(3):325-41.

- FMRI data suggest that total meal replacement (TMR) may be suppressing pleasure and motivational salience of food by increasing executive control of the dorsolateral prefrontal cortex on ingestive behavior (i.e., decreased hedonic drive)

C.N. Kahathuduwa et al. / Appetite 120 (2018)

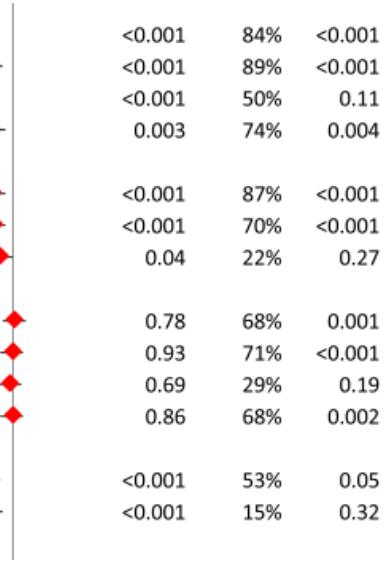
Self-efficacy

- One's sense of confidence about the ability to complete a behavior; for dietary behaviors declines over time in behavioral intervention

Wingo BC et al. J Nutr Educ Behav. 2013 45(4):314-21.

Magnitude of effects on CVD risk with MRP: not fully understood

Outcome	No. trials	*N*	MD (95% CI)	Pooled Effect Estimates SMD (95% CI)	P value	Heterogeneity I^2	Heterogeneity P_Q
ADIPOSITY							
Body weight (kg)	9	931	-2.37 [-3.30, -1.44]	-1.66 [-2.32, -1.01]	<0.001	84%	<0.001
BMI (kg/m^2)	8	817	-0.87 [-1.31, -0.42]	-1.35 [-2.04, -0.65]	<0.001	89%	<0.001
Body fat (%)	4	298	-1.66 [-2.17, -1.15]	-3.19 [-4.17, -2.21]	<0.001	50%	0.11
Waist circumference (cm)	5	448	-2.24 [-3.72, -0.77]	-1.33 [-2.21, -0.46]	0.003	74%	0.004
GLYCEMIC CONTROL							
HbA_{1c}	9	931	-0.43 [-0.66, -0.19]	-1.20 [-1.83, -0.53]	<0.001	87%	<0.001
Fasting glucose (mmol/L)	9	891	-0.63 [-0.99, -0.27]	-1.14 [-1.80, -0.49]	<0.001	70%	<0.001
Fasting insulin (pmol/L)	6	586	-11.83 [-23.11, -0.54]	-0.84 [-1.64, -0.04]	0.04	22%	0.27
BLOOD LIPIDS							
LDL-c (mmol/L)	9	891	0.02 [-0.10, 0.14]	0.11 [-0.54, 0.76]	0.78	68%	0.001
HDL-c (mmol/L)	9	891	0.00 [-0.05, 0.04]	0.00 [-0.73, 0.58]	0.93	71%	<0.001
Non-HDL-c (mmol/L)	9	891	-0.02 [-0.11, 0.07]	-0.15 [-0.80, 0.51]	0.69	29%	0.19
Triglycerides (mmol/L)	9	891	-0.01 [-0.17, 0.14]	-0.04 [-0.72, 0.59]	0.86	68%	0.002
BLOOD PRESSURE							
Systolic BP (mmHg)	7	754	-4.97 [-7.32, -2.62]	-1.57 [-2.31, -0.83]	<0.001	53%	0.05
Diastolic BP (mmHg)	7	754	-1.98 [-3.05, -0.91]	-1.37 [-2.11, -0.63]	<0.001	15%	0.32



”MRP in weight loss diets lead to modest reductions in body weight, BMI, and systolic blood pressure, and reductions of marginal clinical significance in body fat, waist circumference, HbA1c, fasting glucose, fasting insulin, and diastolic blood pressure.

More high-quality trials are needed to improve the certainty in our estimates”

Norohna JC et al. The Effect of Liquid Meal Replacements on Cardiometabolic Risk Factors in Overweight/Obese Individuals With Type 2 Diabetes: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Diabetes Care 2019;42:767–776

One reason for heterogeneity in reported effects of MRPs on CVD risk factors could be related to their variability in macro- and micronutrient composition, in particular protein quality and amount

- Protein consumption during diet- and exercise-induced weight loss promotes fat mass loss and lean mass maintenance

Josse, AR, et al., J Nutr, 2011;141:1626-34.

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Aims

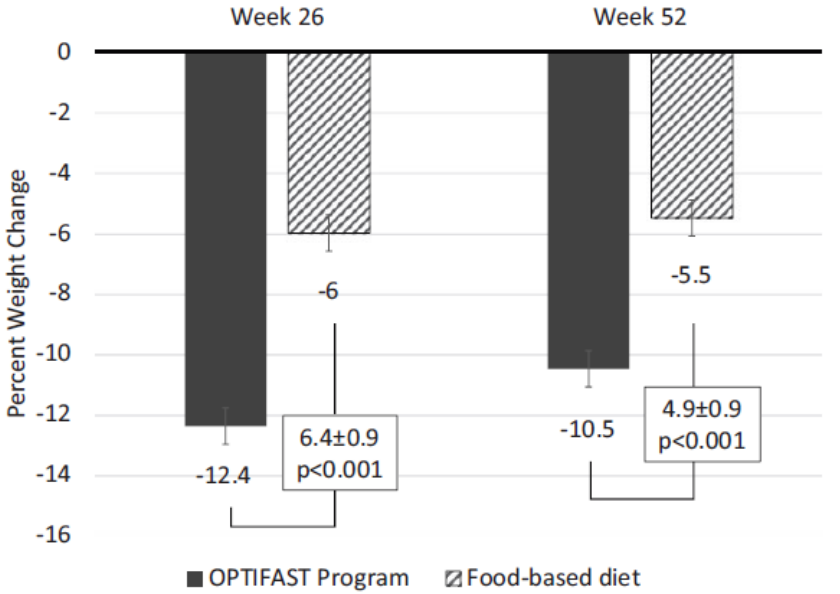
In the randomized controlled OPTIWIN study of 273 individuals (BMI 30-55 kg/m^2; age 18 - 70 years), the use of MRP with Optifast (OP) compared with a low-calorie food-based (FB) dietary plan, in addition to lifestyle intervention (weekly 45-60-min group behavioral sessions and physical activity), resulted in significant weight loss at week (W) 26 (reduction phase) and W52 (maintenance)

Original Article
CLINICAL TRIALS AND INVESTIGATIONS
Obesity

Effectiveness of a Total Meal Replacement Program (OPTIFAST Program) on Weight Loss: Results from the OPTIWIN Study

Jamy D. Ard[1], Kristina H. Lewis[1], Amy Rothberg[2], Anthony Auriemma[3], Sally L. Coburn[4], Sarah S. Cohen[5], Judy Loper[6], Laura Matarese[7], Walter J. Pories[7], and Seletha Periman[8]

Obesity 2019;27:22-29



We wanted to explore if there were differential effects on CVD risk factors and CVD risk with OP vs FB over

- The reduction period (0-26 weeks)
- The reduction period *plus* the maintenance period (0-52 weeks)

Methods

OPTIFAST DIETARY INTERVENTION

Weeks 0-26 – reduction phase

- Typical participant: 5 MRPs/day (800 kcal total) week 0-12
  Gradual reintroduction of food onwards week13-16 through week 26

Weeks 26-52 – maintenance phase

- Calories were gradually increased to achieve weight stability; during this time, participants were advised to use 1-2 MRPs daily.

LOW-CALORIE FOOD BASED DIETARY INTERVENTION

Weeks 0-26 – reduction phase

- Diet followed a modified version of the Diabetes Prevention Program (DPP)
- A calorie-restricted diet (fat 25%-30% of total calories) reduced by 500-750 kcal below estimated total energy expenditure (indirect calorimetry plus an activity factor based on self-reported physical activity)

Weeks 26-52 – maintenance phase

- Calories were gradually increased to achieve weight stability

STATISTICAL APPROACH

- CVD risk factors and CVD risk were analysed as changes over time (mITT) in a modified intention-to-treat dataset
- Least squares (LS) means and LS mean differences calculated
- Linear mixed model with a subject random intercept effect, fixed intervention effect/visit effect/baseline value effect, a treatment-by-visit interaction term, and confounders (age, race, diabetes status)

Endpoints assessed

- CVD risk factors
  - Systolic and diastolic blood pressure (BP)
  - Hemodynamic markers:
    - Heart rate
    - Mean arterial pressure (MAP) ([2 x diastolic BP] + systolic BP)/3)
      - MAP predict CV events (Kodama et al. Am J Cardiol 2014;113:1058-1065)
  - Lipid parameters: total cholesterol (C), LDL-C, HDL-C, triglycerides (TG)

- ASCVD 10-year risk: assessed using American College of Cardiology (ACC)/American Heart Association (AHA) algorithm based on risk factors age, total-C, HDL-C, treated/untreated SBP, current smoker, and diabetes

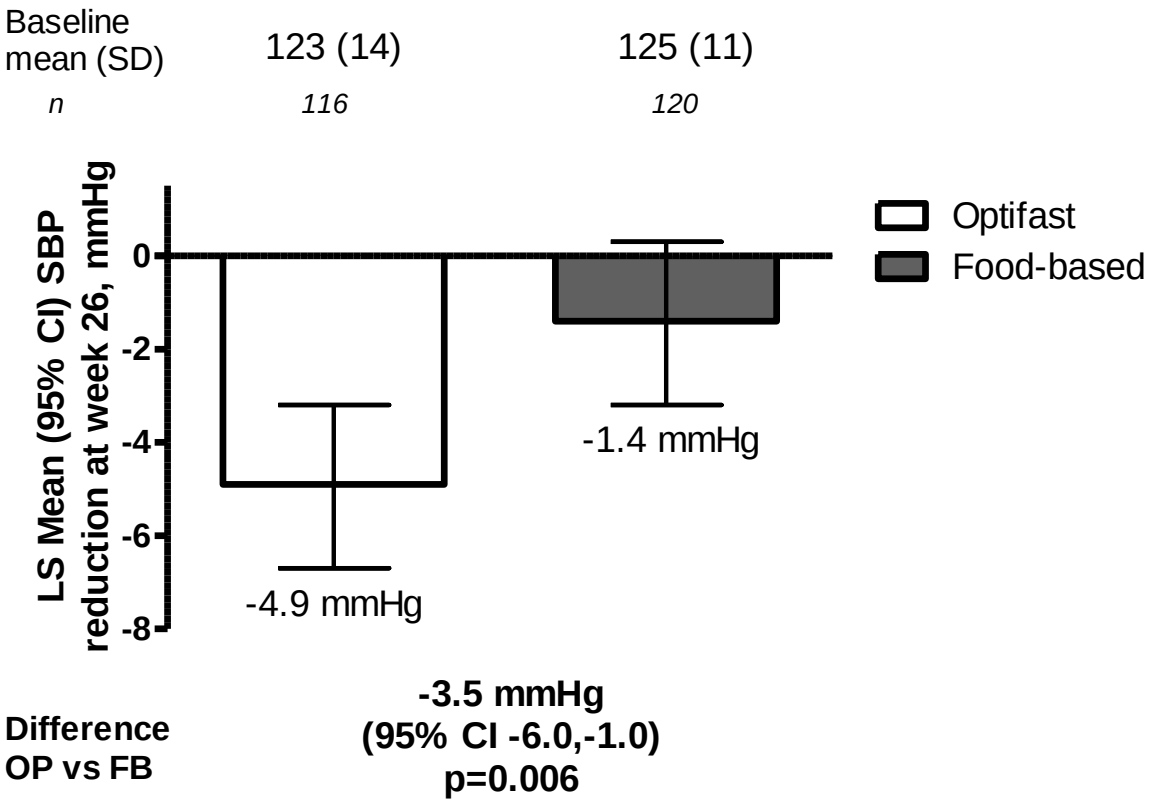
- Subgroup-analysis: Changes in SBP, DBP and ASCVD risk by baseline factors:
  - Systolic BP: < vs ≥ 130 mmHg
  - Sex: female/male
  - Age: < 40, 40-60, ≥ 60 years

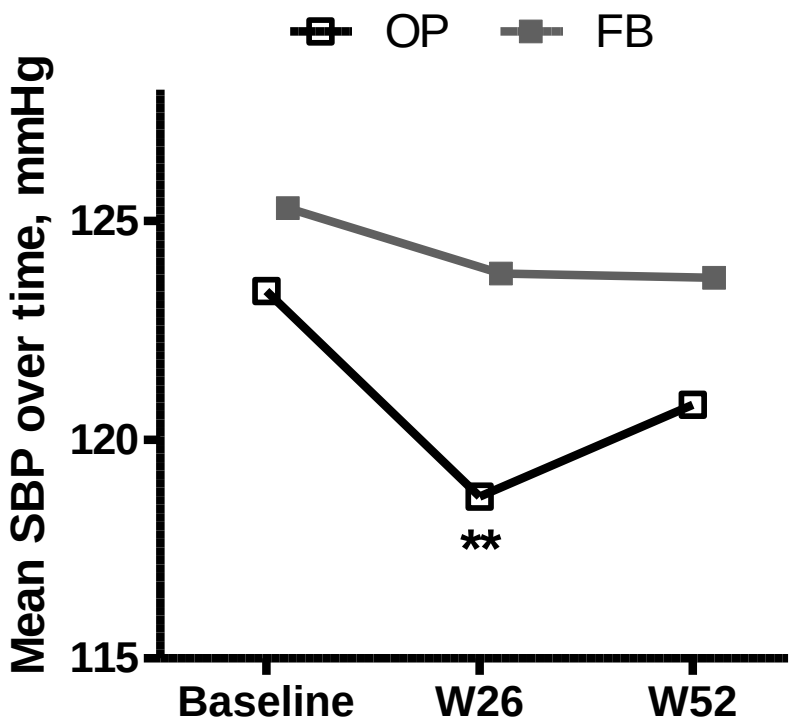
Baseline characteristics, n (%) or mean (SD)

	OP N=135	FB N=138
Age (years)	47.1 (11.2)	47.2 (11.3)
Sex (M/F)	19 (14.1)/116 (85.9)	29 (21.0)/109 (79.0)
Weight (kg)	106.8 (20.8)	109.9 (23.2
BMI (kg/m^2)	38.4 (5.5)	39.2 (6.2)
SBP (mmHg)	123.4 (13.6)	125.3 (11.4)
DBP (mmHg)	77.8 (11.6)	78.0 (10.1)
Heart rate (beats/min)	70.1 (9.2)	73.2 (9.0)
MAP (mean arterial pressure)[1]	93.0 (11.0)	93.8 (9.1)
Lipids		
Total cholesterol (mg/dL)	193.7 (38.6)	187.9 (32.8)
LDL-cholesterol (mg/dL)	122.3 (32.1)	119.7 (30.4)
HDL cholesterol (mg/dL)	51.7 (13.4)	50.9 (14.0)
Triglycerides (mg/dL)	135.9 (123.2)	125.8 (63.0)
Estimated GFR	96.6 (20.7)	92.0 (19.1)
ASCVD risk score, % Mean (SD)	2.6 (3.4)	3.6 (5.1)
Low, <5%	118 (87.4%)	108 (78.3%)
Borderline, 5 to <7.5%	8 (5.9%)	10 (7.2%)
Intermediate, 7.5 to <20%	8 (5.9%)	19 (13.8%)
High, ≥20%	1 (0.7%)	1 (0.7%)
AST (U/L)	26.3 (12.1)	27.2 (12.6)
ALT (U/L)	30.8 (17.8)	32.2 (19.8)

[1][2 x DBP]+SBP)/3 (mmHg)

Systolic BP at W26 and over time





Intensive MR with OP vs a FB-approach led to significant greater SBP reductions with OP at week 26 (-3.5 mmHg), in a population with relatively well controlled BP

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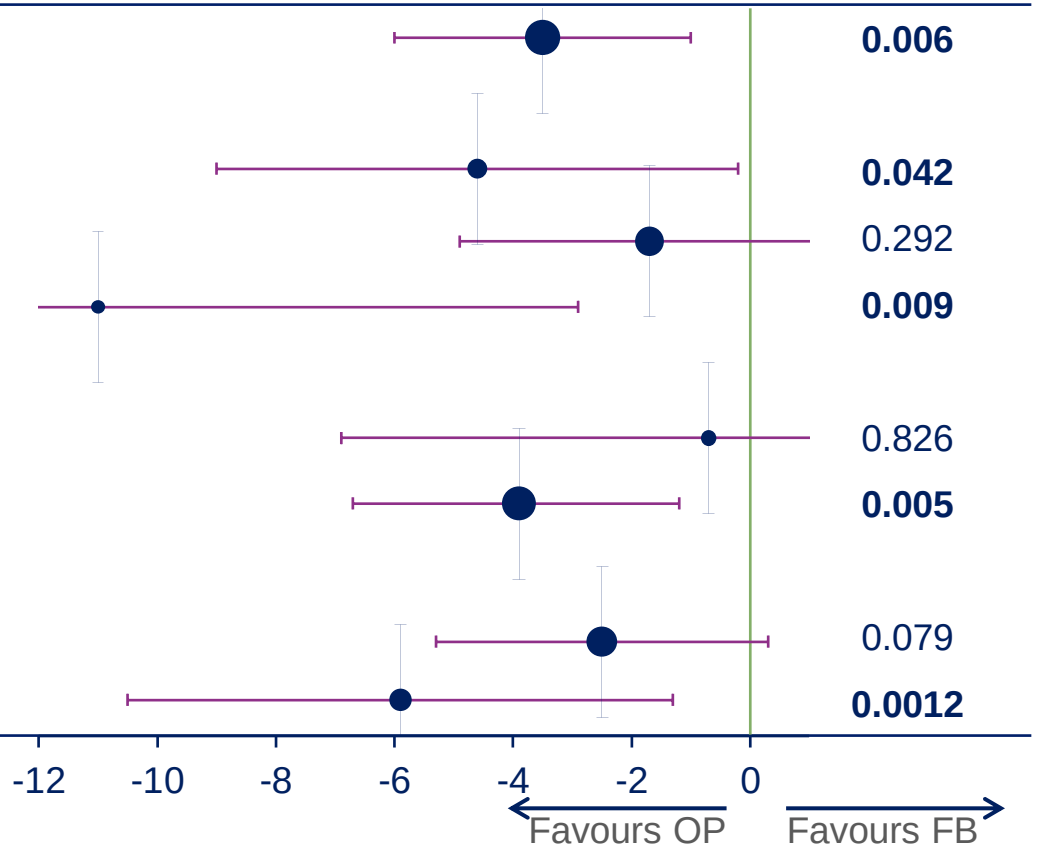
SBP at week 26 overall and by subgroups

	Optifast	Food based	LS Mean difference (95% CI), mmHg	LS mean diff (95% CI), mmHg	*p*-value OP vs FB
	n	n			
All patients	116	120	-3.5 (-6.0, -1.0)		**0.006**
Age					
<40 years	37	37	-4.6 (-9.0, -0.2)		**0.042**
40 to <60 years	80	82	-1.7 (-4.9, 1.5)		0.292
≥60 years	18	19	-11.0 (-19.0, -2.9)		**0.009**
Sex					
Male	19	29	-0.7 (-6.9, 5.5)		0.826
Female	116	109	-3.9 (-6.7, -1.2)		**0.005**
Systolic BP					
<130 mmHg	89	88	-2.5 (-5.3, 0.3)		0.079
≥130 mmHg	46	50	-5.9 (-10.5, -1.3)		**0.0012**



A consistent pattern of SBP reduction was seen across all subgroups, although the magnitude of effect was largest in people >= 60 years and in those with SBP >= 130 mmHg at baseline

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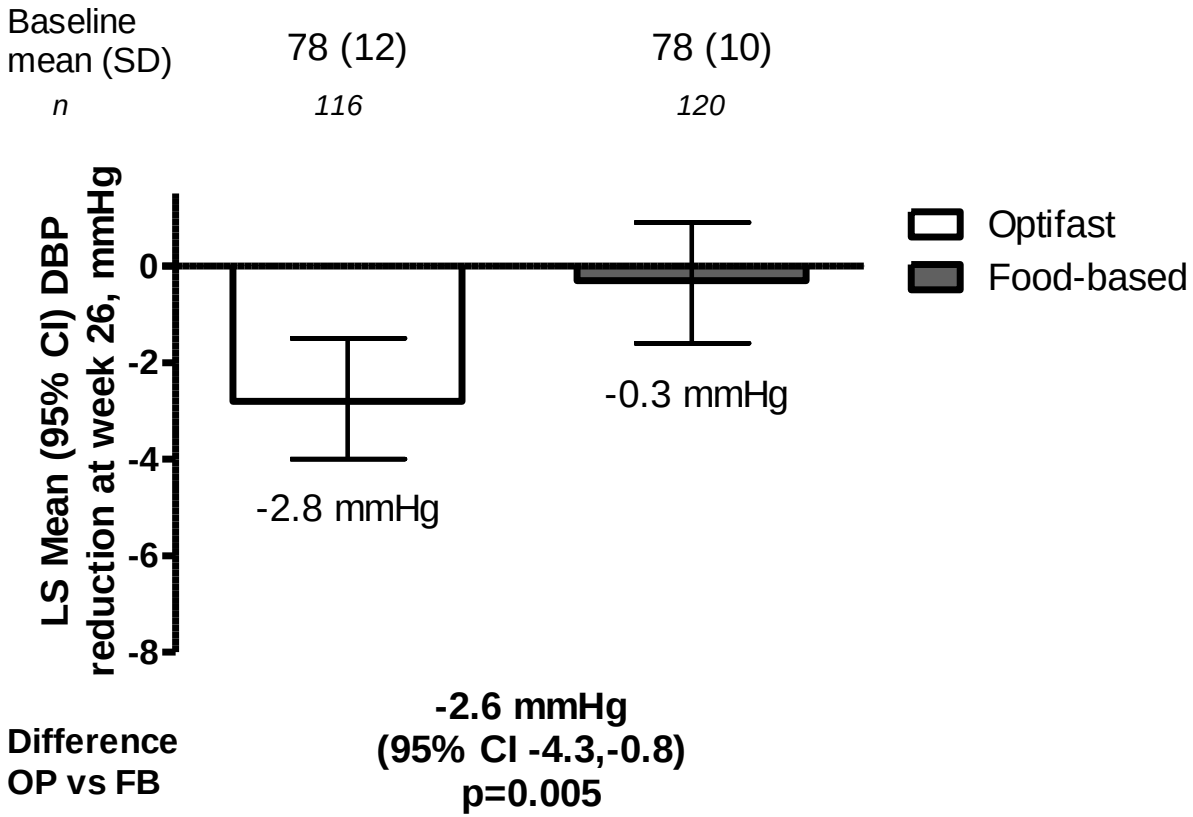
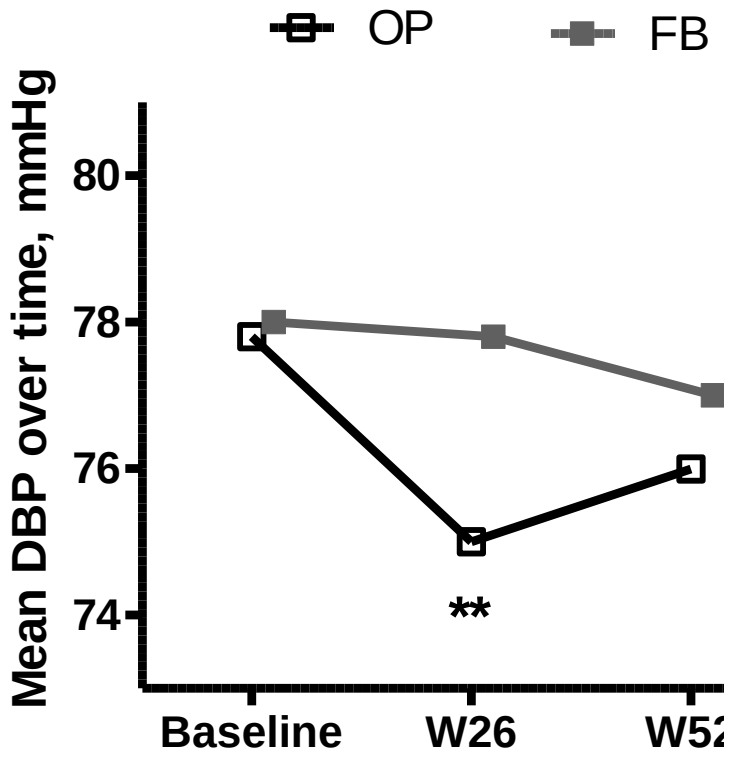
DBP at week 26 and over time

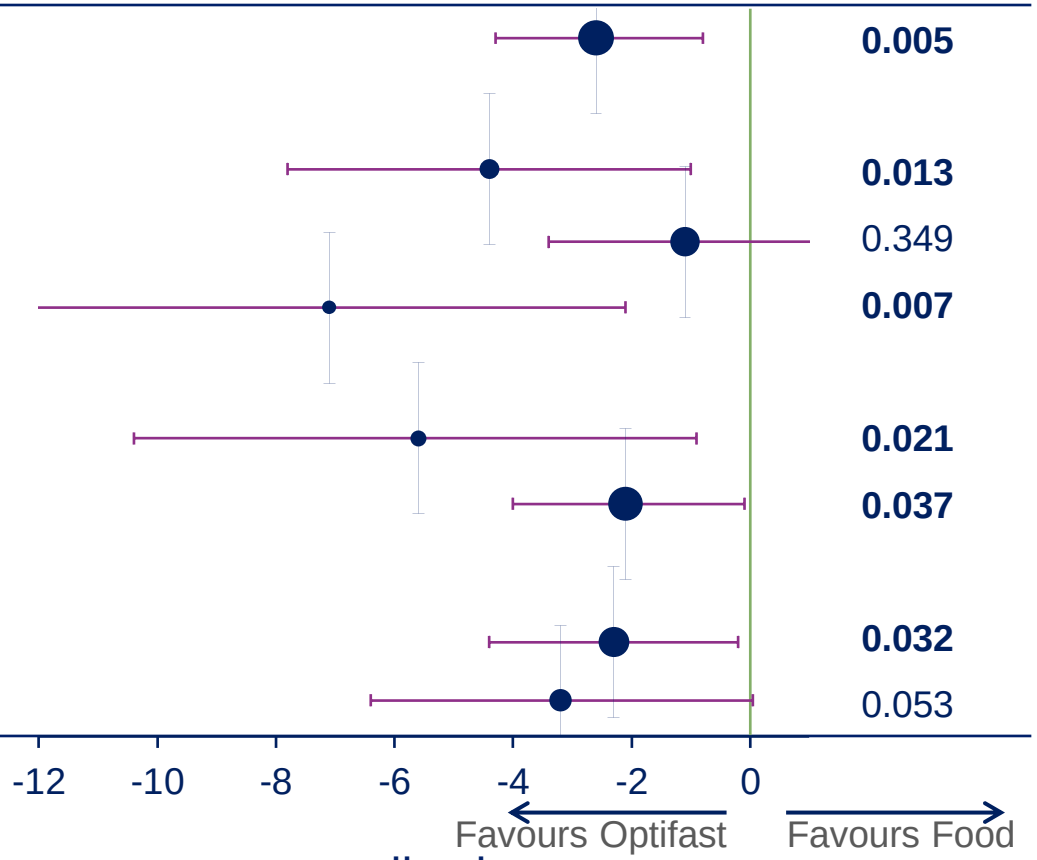




Intensive MR with OP vs a FB-approach led to significant DBP reductions with OP at week 26 (-2.6 mmHg), in a population with relatively well controlled BP

DBP at week 26 overall and by subgroups

	Optifast	Food based	LS Mean difference (95% CI), mmHg	LS mean diff (95% CI), mmHg	*p*-value OP vs FB
	n	n			
All patients	116	120	-2.6 (-4.3,-0.8)		**0.005**
Age					
<40 years	37	37	-4.4 (-7.8,-1.0)		**0.013**
40 to <60 years	80	82	-1.1 (-3.4,1.2)		0.349
≥60 years	18	19	-7.1 (-12.3,-2.1)		**0.007**
Sex					
Male	19	29	-5.6 (-10.4, -0.9)		**0.021**
Female	116	109	-2.1 (-4.0,-0.1)		**0.037**
Systolic BP					
<130 mmHg	89	88	-2.3 (-4.4,-0.2)		**0.032**
≥130 mmHg	46	50	-3.2 (-6.4, 0.04)		0.053



A consistent pattern of DBP reduction was seen across all subgroups, although the magnitude of effect was largest in people >= 60 years and in male

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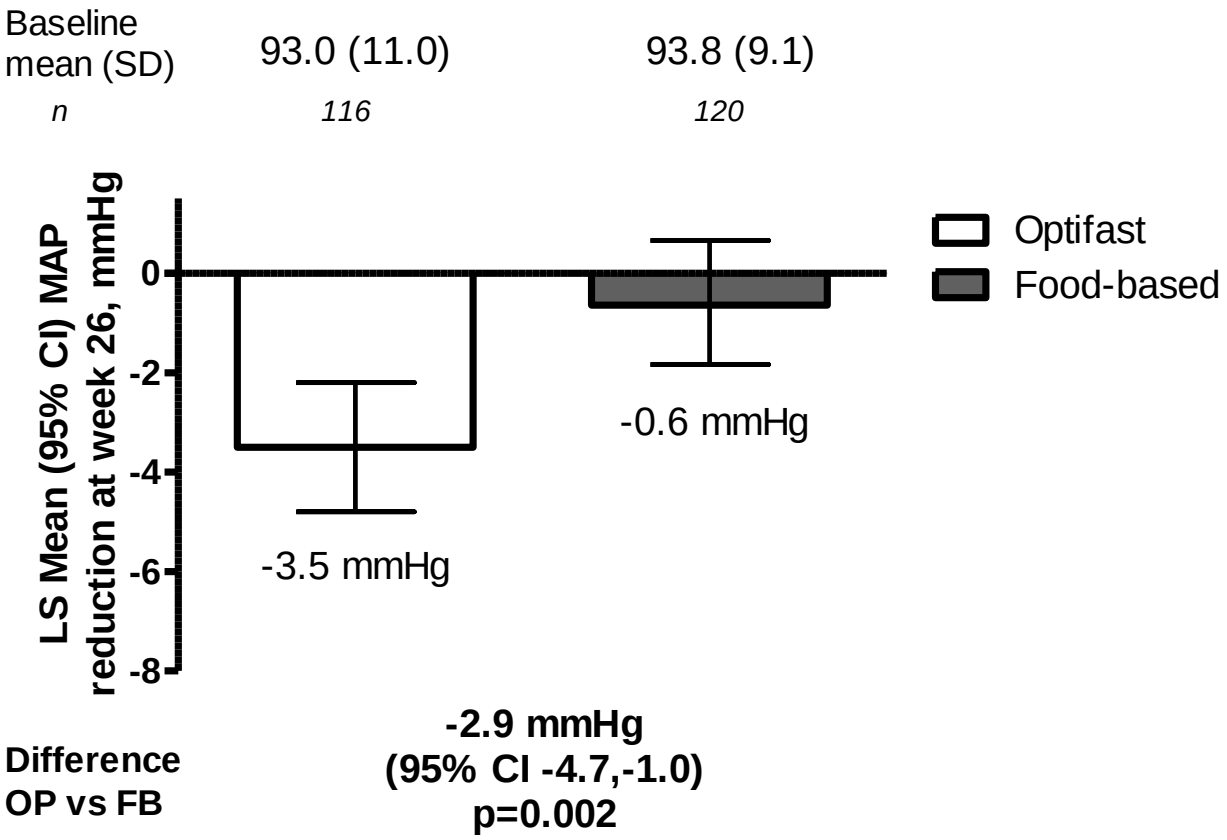
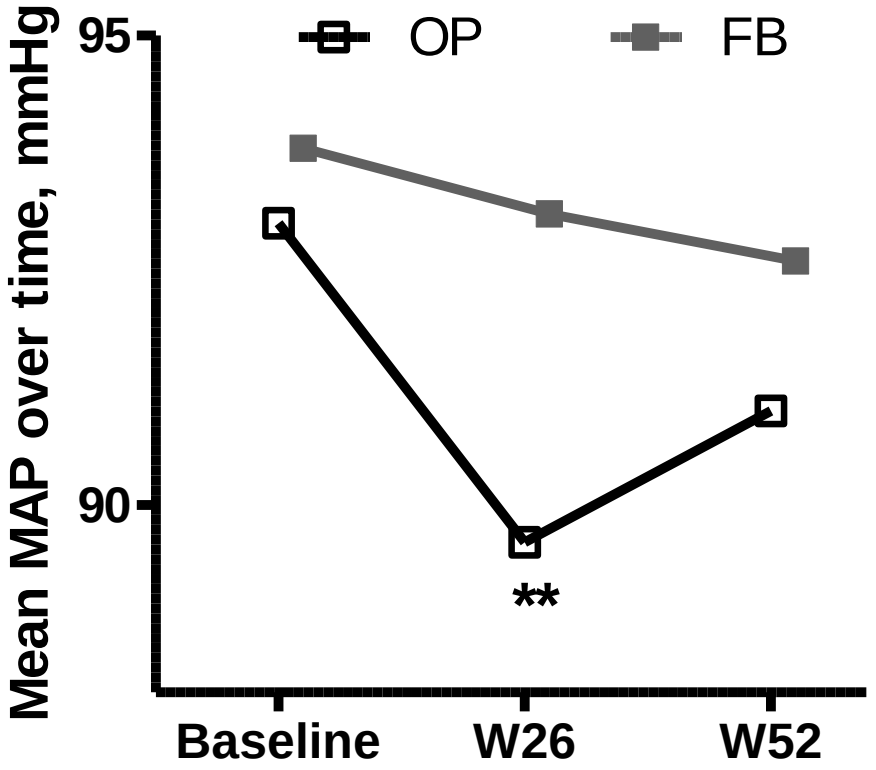
Central hemodynamics (MAP) at week 26 and over time





- Intensive MR with OP vs a FB-approach led to significant reduction in MAP with OP at week 26 (-2.9 mmHg), in a population with relatively well controlled BP.

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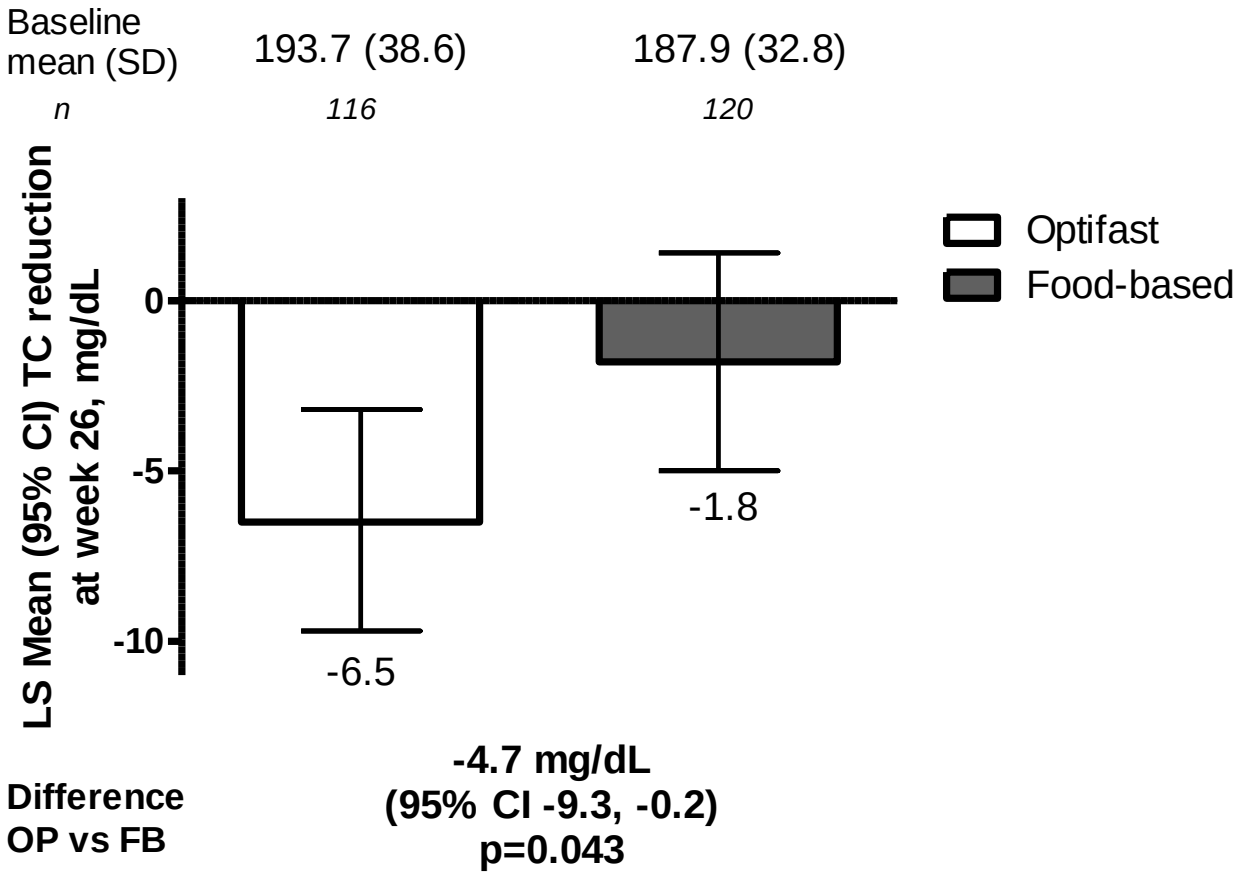
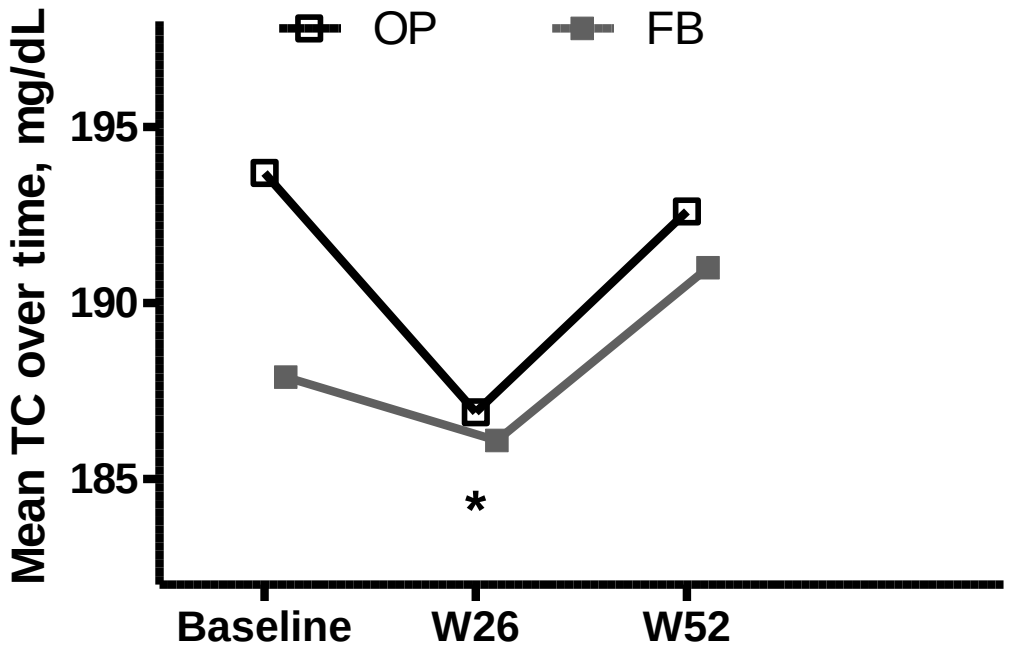
Total cholesterol (TC) at W26 and over time





Intensive MR with OP vs a FB-approach led to significant TC reduction at week 26 (-4.7 mg/dL), in a population with relatively well controlled TC

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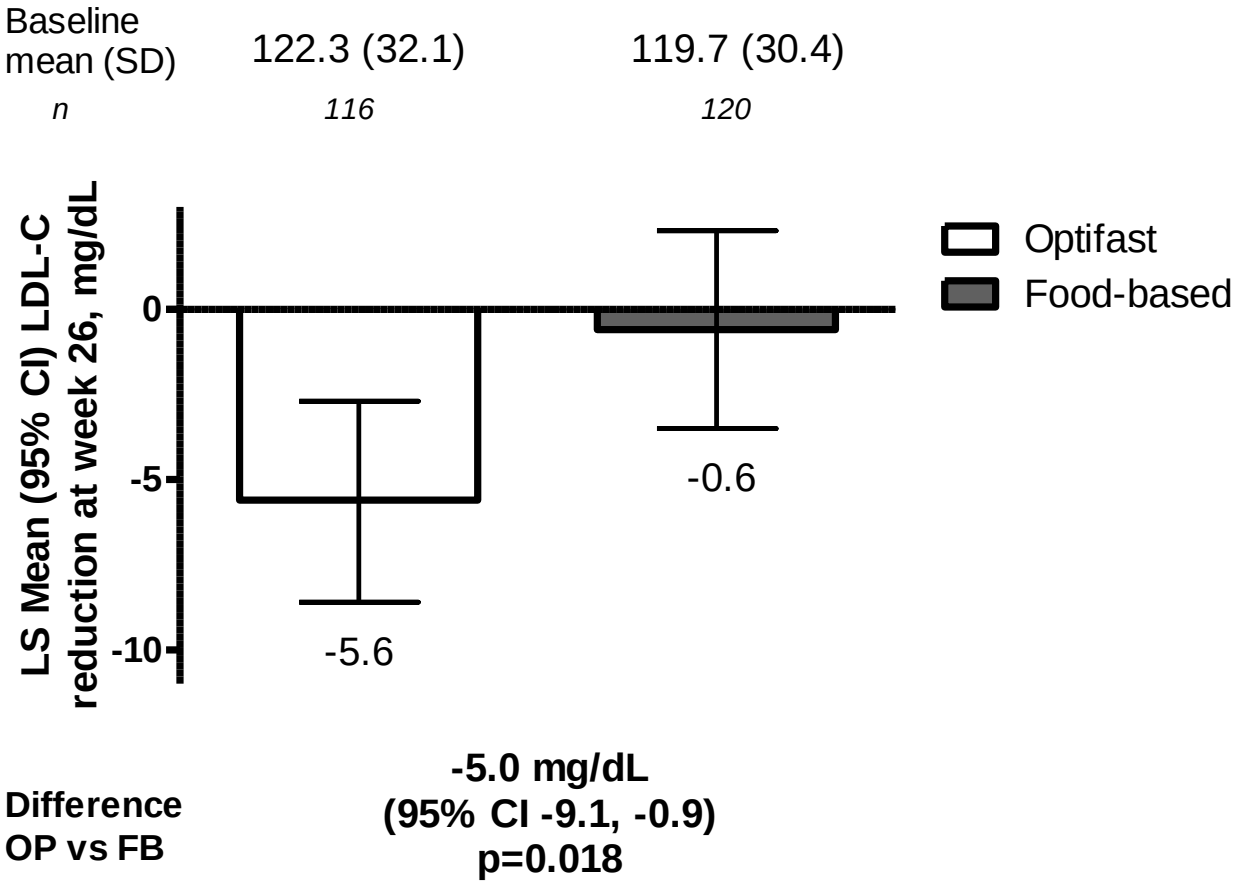
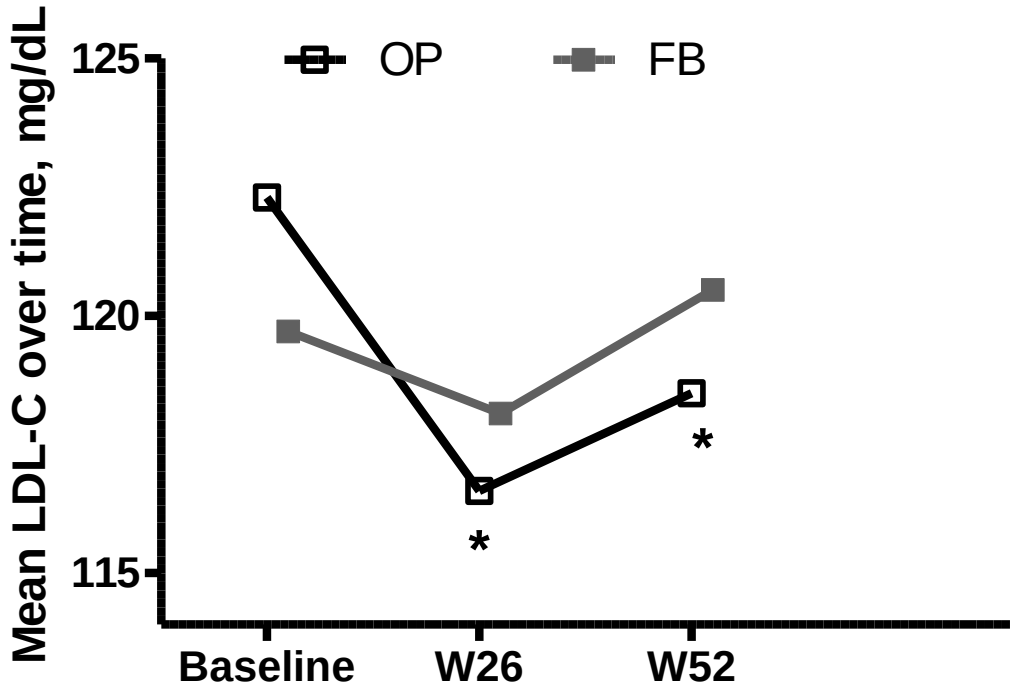
LDL cholesterol (LDL-C) changes at W26 and over time





Intensive MR with OP vs a FB-approach led to significant LDL-C reduction at week 26 (-5.0 mg/dL)

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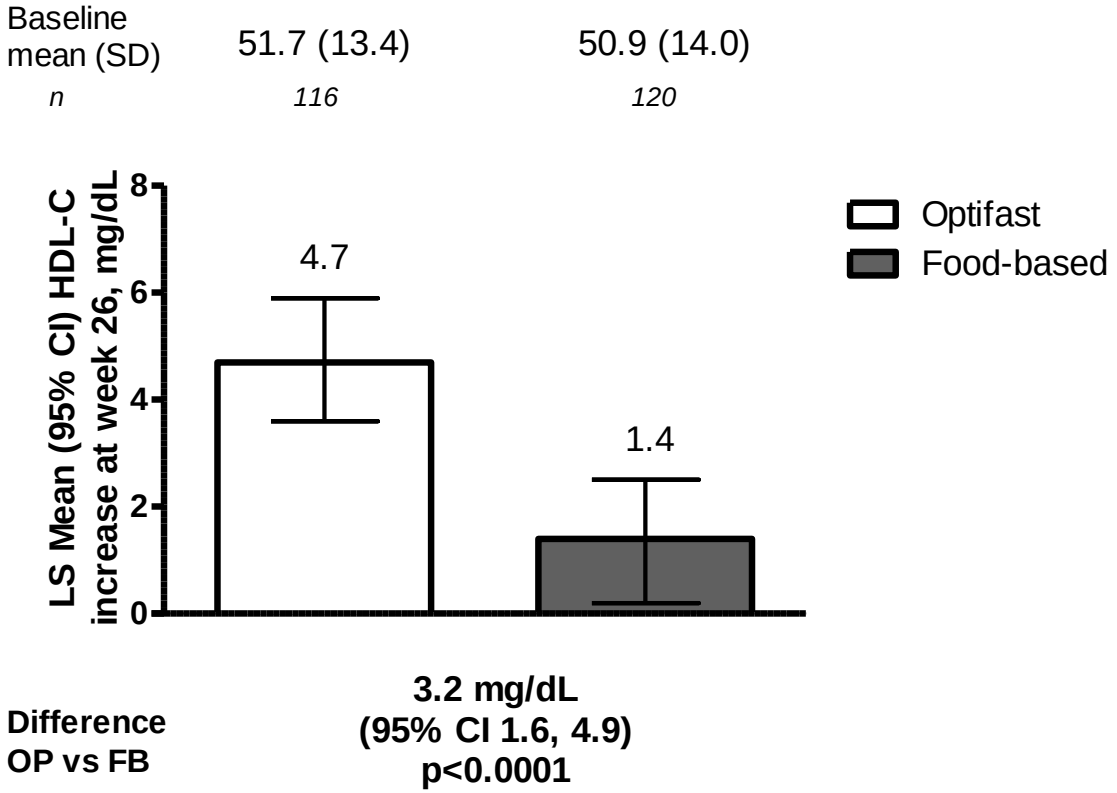
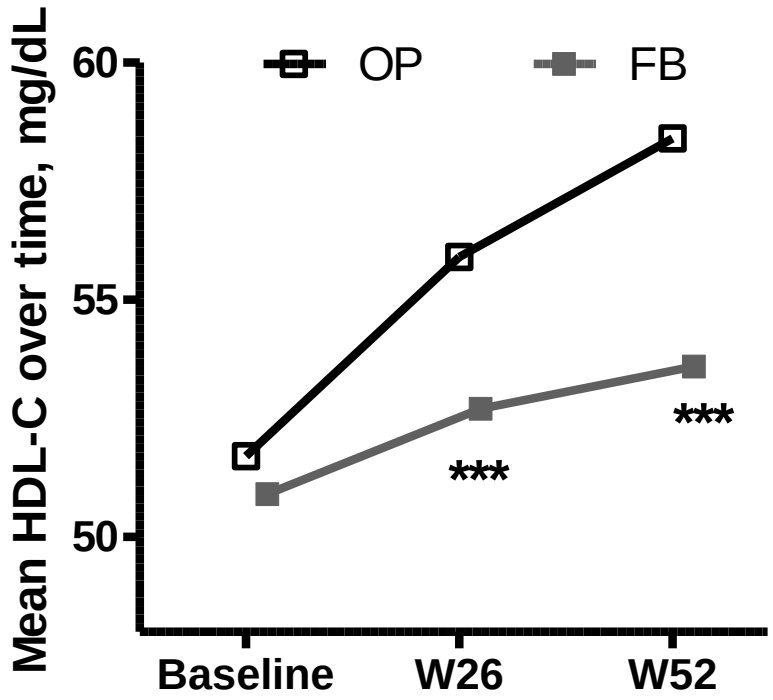
HDL cholesterol (HDL-C) at W26 and over time





Intensive MR with OP and a FB-approach led to significant HDL-C increase at week 26, but a significantly greater increase was seen with OP (3.2 mg/dL)

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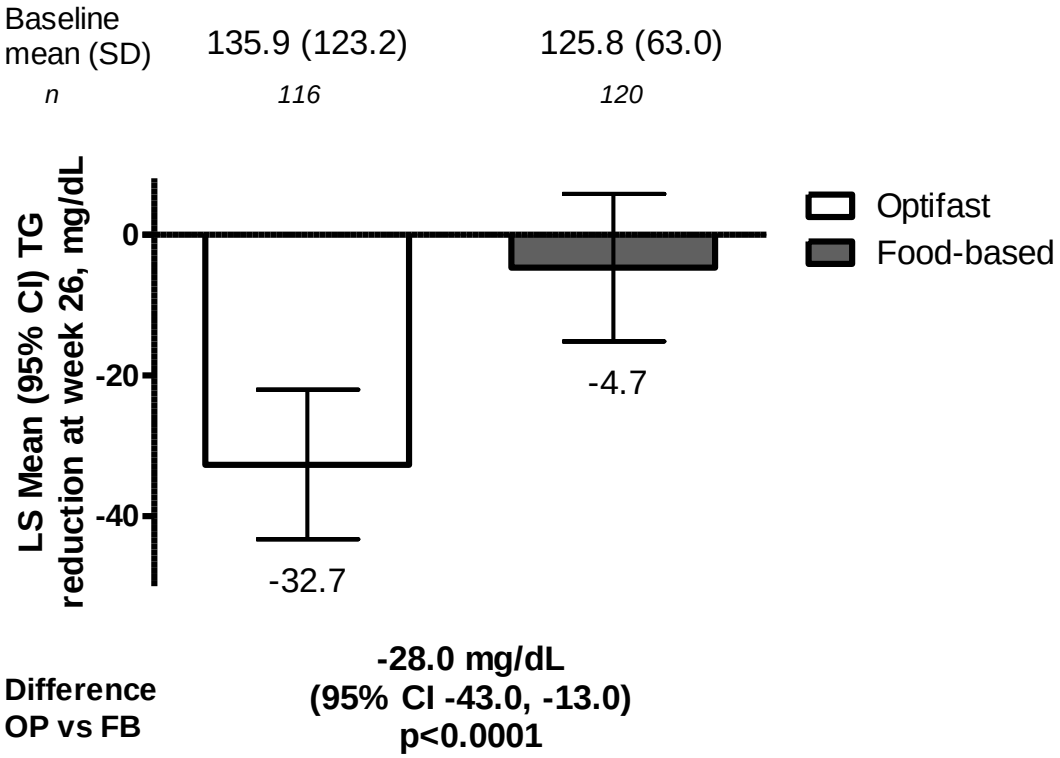
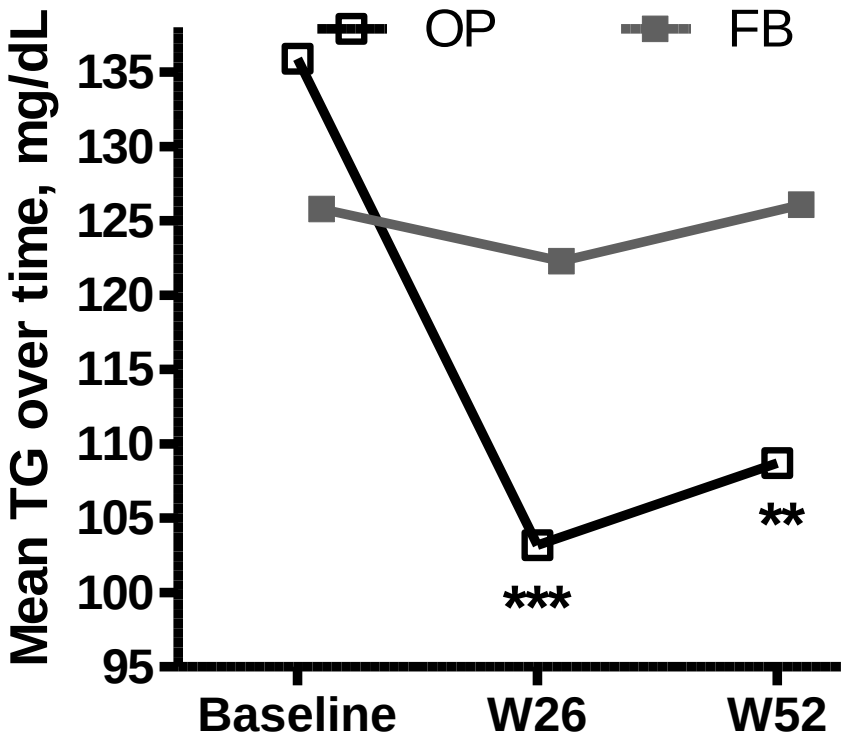
Triglycerides (TG) at W26 and over time





Intensive MR with OP vs a FB-approach led to a significant TG reduction at week 26 (-28 mg/dL)

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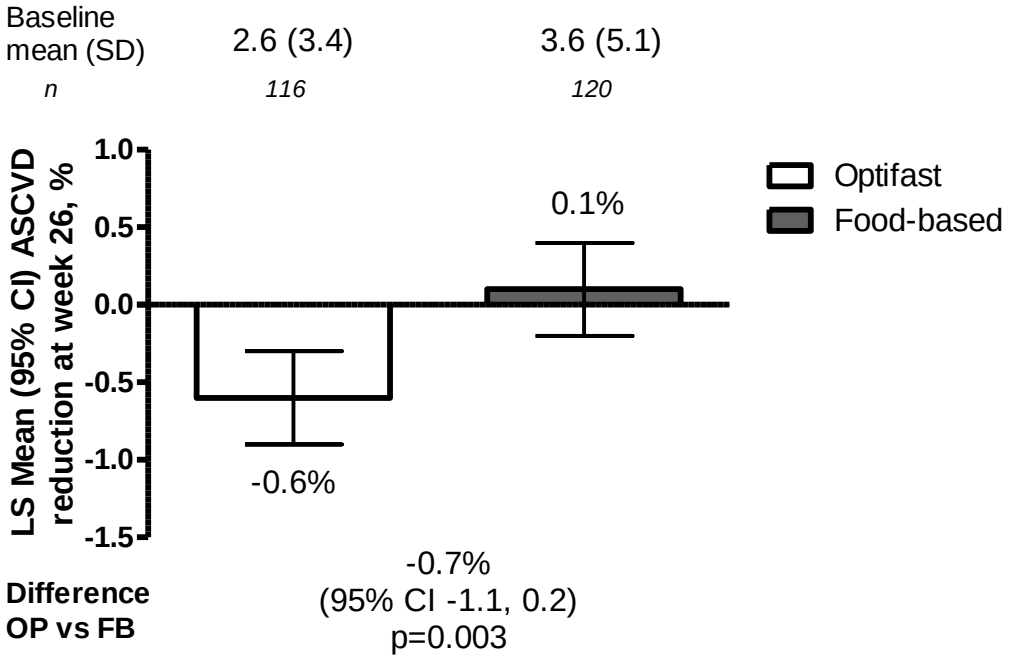
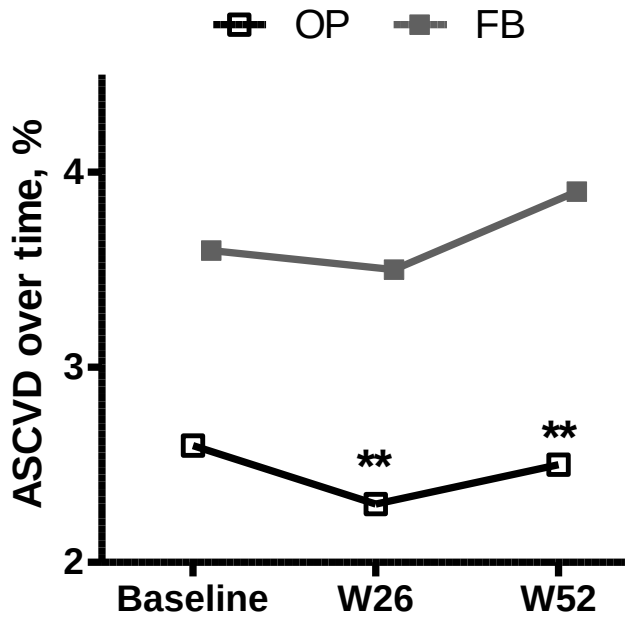
Effects on predicted ASCVD risk at week 26 and over time

- Generally the population average risk was low (OP 2.6%; FB 3.6%)
- Among participants, the majority were in the low (<5%) ASCVD risk category (OP 87.4%, FB 78.3%), with 11.8%/21.0% of the OP/FB in the borderline-intermediate risk group (5-<20%) and only one person (0.7%) in each group in the high risk (>= 20%) category.
- The mean predicted score was significantly reduced with OP at week 26, by -0.6%-point, and increased by 0.1%-point in the FB-group (difference -0.7% (95% CI -1.1, 0.2), p=0.003).





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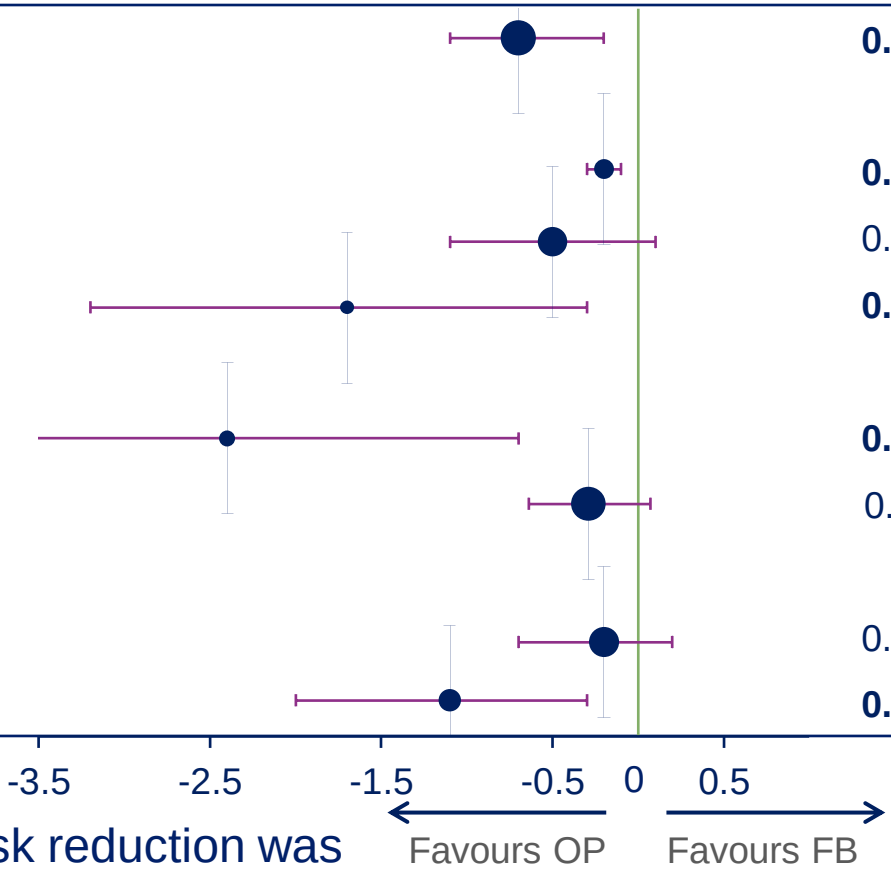
Difference in ASCVD risk at week 26 between Optifast and Food based at Week 26

	Optifast	Food based	LS Mean difference (95% CI)	LS mean diff (95% CI)	*p*-value OP vs FB
	n	n			
All patients	116	120	-0.7 (-1.1, -0.2)		**0.003**
Age					
<40 years	37	37	-0.2 (-0.3,-0.1)		**0.002**
40 to <60 years	80	82	-0.5 (-1.1,0.1)		0.091
≥60 years	18	19	-1.7 (-3.2,-0.3)		**0.020**
Sex					
Male	19	29	-2.4 (-4.1, -0.7)		**0.007**
Female	116	109	-0.3 (-0.6,0.1)		0.111
Systolic BP					
<130 mmHg	89	88	-0.2 (-0.7, 0.2)		0.293
≥130 mmHg	46	50	-1.1 (-2.0,-0.3)		**0.007**



A consistent pattern of ASCVD risk reduction was seen across all subgroups, although the magnitude of effect was largest in people >= 60 years and in male

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Conclusions

- In OPTIWIN, total or partial use of MRP with OP vs a food-based program for 26 weeks:
  - Significantly reduced SBP and DBP without affecting heart rate, where the magnitude of effect was generally larger in people being older (> 60 years of age) and in those with a baseline SBP above > 130 mmHg
  - Improved all blood lipid parameters measured (TC, LDL-C, HDL-C, TG)
  - Improved 10 year ASCVD risk, where the magnitude of effect that was generally larger in people being older (> 60 years of age) and in those with a baseline SBP above > 130 mmHg.
- **Following a transition from a total MRP program to a maintenance phase with partial MRP for an additional 26 weeks, the benefits on CV risk factors were sustained for weight, and lipid-parameters, but less pronounced for BP and vascular parameters. The reduction in ASCVD risk remained significant.**

These results support that weight loss induced with MRP using OP, significantly improves CVD risk factors and CVD risk, with the largest magnitude of effect in people > 60 years, and with SBP > 130 mmHg at baseline