Dietary Analysis with Lipidomics: First Steps toward Objective Dietary Analysis of Macronutrient Intake Using Lipidomics

by

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Dedication

This PhD research allowed me to combine two of my
life-long interests and passions: nutrition and science.
Building on the lessons that I have learned during graduate school,
my career ambition is to continue to objectively know
what people are eating so that we can better
understand the effects that diet has on health.

I dedicate this thesis to my family
who teach me every day that
humility, caring, and passion are virtues that
when applied to life are both important and beautiful.

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Table of Contents

List of Tables

List of Figures

List of Abbreviations

24HR	24 hour dietary recall
ACAR	Acylcarnitine
Actual	Actual Diet
AUC	Area under the curve
BCAA	Branched-chain amino acids
BMI	Body Mass Index
CE	Cholesterol ester
Cer	Ceramide
CHO	Carbohydrate
ChREBP	Carbohydrate-responsive element-binding protein
CL	Cardiolipin
DEXA	Dual-energy X-Ray absorptiometry
DG	Diacylglycerol
EER	Estimated Energy Requirement
EI	Energy Intake
FAO	Fatty Acid Oxidation
FAR1	Fatty Acid Synthase 1
FDR	False Discovery Rate
FFA	Free Fatty Acid
FFQ	Food Frequency Questionnaire
FGF21	Fibroblast growth factor 21
GC-MS	Gas Chromatography-Mass Spectrometry
GIR	Glucose infusion rate
HC	High Carbohydrate Diet
HDL	High density lipoproteins
HF	High Fat Diet
HIEC	Hyperinsulinemic-euglycemic clamp
IDL	Intermediate density lipoproteins
IOM	Institutes of Medicine
IR	Insulin resistant
IS	Insulin sensitive
KNN	K-nearest neighbors
LC-MS	Liquid Chromatography-Mass Spectrometry

LDL	Low density lipoproteins
LEAN	lean control subject
LOOC	Leave one out cross validation
LPC	Lysophosphatidylcholine
LPE	Lysophosphatidylethanolamine
LXRα	Liver X receptor α
m/z	mass:charge ratio
MBDA	Memory-Based Dietary Assessment
MCCV	Monte-Carlo cross validation
MCRU	Michigan Clinical Research Unit at the University of Michigan
MEAL	Metabolomic Analysis of Diet
MetS	Metabolic Syndrome
MNORC	University of Michigan Nutrition and Obesity Research Core
MUFA	Monounsaturated fatty acid
NCC	Nutrition Coordinating Center
NDSR	Nutrition Data System for Research software
NHANES	National Health and Nutrition Examination Survey
NMR	Nuclear Magnetic Resonance
Obese-IR	Obese more insulin resistant
Obese-IS	Obese more insulin sensitive
OGTT	Oral Glucose Tolerance Test
PCOS	Polycystic Ovarian Syndrome
PlsCho	Plasmenyl-Phosphatidylcholine
PlsEth	Plasmenyl-Phosphatidylethanolamine
PA	Physical Activity
PC	Phosphatidylcholine
PCA	Principle component analysis
PCT	Postprandial challenge test
PE	Phosphatidylethanolamine
PG	Phosphatidylglycerol
PI	Phosphatidylinositol
PRO	Protein
PS	Phosphatidylserine
PUFA	Polyunsaturated fatty acid
PUFA/CHO	High Polyunsaturated fatty acid/High Carbohydrate Diet
Reported	Reported Diet
ROC	Receiver Operator Curve
Sat	Saturated fatty acid
SCD-1	Stearoyl-CoA desaturase-1
SS	Steady State during HEIC
SVM	Support Vector Machines

SREBP-1c	Sterol regulator element-binding protein 1c
T2DM	Type-2 Diabetes Mellitus
TCA	Tricarboxylic acid cycle
TG	Triacylglycerol
ULDL	Ultra low density lipoproteins
VLDL	Very low density lipoproteins
WWEIA	What We Eat in America

Abstract

Dietary macronutrients are an important and controllable factor in health. Current research best practices use memory-based dietary assessments (MBDA) to estimate nutrient intake. However, there is evidence of bias in information obtained from MBDA as subjects over or under report energy and macronutrient intake. Metabolomics is a powerful tool to used identify molecular biomarkers of disease risk, not only can provide mechanistic insights into macronutrient metabolism but also can inform our understanding of accuracy and precision of MBDA. Metabolomics uses high throughput profiling to identify small metabolites in an organism. Lipidomics is a subset of metabolomics that primarily identifies lipids. .Here, I describe the use of plasma lipidomic profiling to determine the temporal changes in the plasma lipidome of healthy male and female adult participants provided high fat or high carbohydrate diets and objectively identify dietary macronutrient content.

The PUFA study provided a high polyunsaturated fat diet (40-50% fat, 80% polyunsaturated fats) for 3 weeks followed by a high carbohydrate diet (75% carbohydrates - CHO) to 12 individuals. After 2 days of PUFA, 16% of 480 lipids showed significant changes and 27% changed after 21 days. After switching to CHO, 27% percent of lipids changed after 2 days and 30% after 21 days. This demonstrated that a high PUFA diet produced a rapid turnover of the plasma lipidome. Next, we provided a standard diet for 3 days to 24 individuals then

randomized to a high fat diet (60% fat, HF) or a high carbohydrate diet (75% carbohydrates, HC) for 3 weeks. Fewer lipidomic changes were apparent within group over 21 days, but significant differences between experimental groups were apparent. We identified a set of 'sentinel' lipids comprising mostly plasmalogens and phosphatidylcholines that classified the participants in both studies with 87% predictive value. A significant correlation between macronutrient intake and predictions in lipidomics data from a study of 102 individuals with known diets highlighted the potential use of sentinel lipids to identify dietary intake in free-living population.

In parallel with the MEAL study, we compared known diets of subjects with reported diets during the study. Participants reported kCal intake accurately but over-reported protein intake in all diets. In the high fat diets, fat was under-reported by 6.3% and carbohydrate over-reported by 19.8%. In the high carbohydrate diet, carbohydrate under-reported by 10.8% and fat over-reported by 66%. These results suggest 24HR estimate energy well in controlled feeding studies. However, estimation of extreme macronutrient intakes in the context of a feeding study was poor.

To assess dynamic changes in the metabolome from acute intravenous glucose and insulin, we collected plasma samples from a cohort of obese, metabolically healthy and lean individuals during hyperinsulinemic-euglycemic clamps. Targeted profiles of amino acids, fatty acids and small organic compounds demonstrated changes associated with glucose infusion rate (GIR), rather than obesity. Lean and obese subjects with low glucose infusion rate showed greater suppression of plasma fatty acids and increased levels of branched-chain amino acids

throughout the clamp. Paradoxically, insulin suppressed long chain fatty acids while their cognate acylcarnitines were unchanged but not shorter chained species. This novel finding suggests a clearance difference of acylcarnitines by chain length.

These studies collectively demonstrate the utility of metabolomics and lipidomics to identify macronutrient intake. The development of objective biomarkers of intake could produce complementary diagnostic tools for nutritional studies. The identification of differential dynamic changes due to macronutrient exposures and insulin sensitivity has the potential to identify unknown physiological effects of diet.

Chapter 1: Introduction

The Role of Diet and Nutrition in Health

The rise of chronic diet-related disease due to overconsumption has accelerated greatly in the last century with 40% of adults and 19% of children and youth in the United States classified as obese increasing their risk for heart disease, type 2 diabetes, and some cancers (1). In 2008, the estimated costs of medical treatment of disease related to obesity were $147 billion and per person was $1,429 higher than for normal weight individuals (2, 3). This rise in obesity is indicative of dietary patterns of overconsumption of calories and is evidenced by the under consumption of healthy foods such as fruits and vegetables and overconsumption of added sugars and saturated fats (2).

The Current State of Dietary Analysis

Diet, and in particular macronutrient intake, is an important and controllable factor in health (4). Specifically, over-consumption of calories has been associated with diseases such as cardiovascular disease and type 2 diabetes mellitus (5, 6), though total nutrient intake seems to be more important belied by the preeminence of obesity to the risk of diabetes. In order to provide effective advice about nutrition, nutritional science researchers and epidemiologists require data about dietary intake of individuals that is both valid and unbiased. However,

collecting unbiased dietary intake data proves to be a difficult challenge (7). Current information about macronutrient intake depends on large epidemiological studies that is comprised of data collected using memory-based dietary assessment methods (MBDA) (2, 8-10). The accuracy and precision of the data obtained using MBDA is questionable due to demonstrable underreporting and misreporting of energy and macronutrient intake (11-17).

In 2015, the United States Dietary Guidelines Advisory Committee released the latest dietary guidelines for the country (2). This report contains a dietary component from the National Health and Examination Survey (NHANES) entitled 'What We Eat in America' (WWEIA), which comprises data estimated from memory-based dietary assessment methods such as food frequency questionnaires (FFQ) and 24-hour dietary recalls (24HR) (2, 8). This report informs both national nutritional policy and dietary guidelines (2). FFQ and 24HR are used throughout nutrition research, with perhaps WWEIA being the largest example of the use of MBDA (8, 18).

Collecting dietary intake data proves to be challenging because of the subjective nature of data collection inherent with FFQs, DR, and dietary journals (19). MBDAs do not directly measure nutrient intake but rather require subjects to remember either foodstuffs that are commonly consumed, in the case of FFQs, or food that have been eaten within the last 24 hours in the case of 24HR (8, 20). The strength of FFQs is that they provide glimpses into habitual intake while 24HR typically assess dietary consumption from the most recent days or weeks (19). Research suggests that data obtained using MBDAs exhibit both underreporting and over reporting of caloric and macronutrient intake (8, 21-30).

One difficulty with using MBDA to draw conclusions about actual dietary intake is that there is evidence they do not align well with actual dietary intake (31, 32). MBDAs require a

certain level of subject literacy and are subject to possible recall bias and withholding of information, either intentional or unintentional (8, 33, 34). FFQs tend to have low accuracy, under-report energy intake (EI) and have poor generalizability while 24HR under-reported high intakes and over-reported lower intakes under-estimate carbohydrates, vitamins, and alcohol (12, 22, 33, 35). One criticism of the use of MBDAs is that the range of caloric intake reported are so large that the lower bounds may not be biologically plausible because they would be lower than required for life (36, 37).

Despite the flaws inherent with MBDA, they continue to be widely used for assessing dietary intake and are the best-known source of this information at this point (38). MBDAs are relatively inexpensive to administer, are non-invasive, do not require trained health workers to draw blood, and do not require laboratory analysis (8, 33). There has been a recent call from the Institutes of Medicine (IOM) to fill the knowledge gap in nutritional research through the development of objective biomarkers of dietary intake (7). One suggestion to solve this dilemma would be the merging of data-driven approaches for dietary analysis such as metabolomics with traditional MBDAs such as FFQ and DR (7, 39, 40).

Metabolomics as a Possible Solution

The inaccuracies of nutrient intake based solely on MBDAs has led to a call for objective measures of dietary intake to be developed (41-44). Metabolomics is a promising technology that could provide such measures (41-44). Metabolomics is the comprehensive analytical chemistry approach to provide a global description of all metabolites present in biofluids such as a blood serum and urine (44, 45). The metabolites found in these fluids is defined as the “metabolome” (45, 46) and reflect the downstream products of the genome and proteome and may provide

important information about the biological state of organisms (47). The metabolomic analysis is used to study alterations in metabolism under different conditions or to find correlations between metabolites that might provide insight into biological connections between metabolites (43). Metabolomics primarily uses nuclear magnetic resonance spectroscopy or mass spectroscopy to identify small metabolites in these samples (48). Once samples are analyzed, they produce very large datasets that must be analyzed using advanced statistical methods for high dimensional data (42).

Metabolomics follows a specific pipeline that starts with sample acquisition, followed by sample preparation, sample analysis, and data analysis (43, 46). Sample acquisition in dietary analysis usually involves blood plasma or urine collection (41, 43, 49). The goal of sample preparation is the isolation of metabolites from larger macromolecules such as proteins and larger lipids (46). Sample analysis involves identification of metabolites within the biofluids (50).

Currently, no one technology is best at measuring the entire metabolome. Some analysis techniques may be more appropriate for certain metabolites; for example, GC-MS is most appropriate for polar, easy to volatilize metabolites (45, 46). Often, parallel and/or redundant methods of measurement are used. Nuclear magnetic resonance (NMR) as well as mass spectrometry methods such as gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-mass spectrometry (LC-MS) are the most commonly used techniques currently used to identify metabolites present in biofluids (43, 45). GC-MS and LC-MS rely upon ionization of the gas phase of the sample and then separation of the molecules by mass: charge ratio (m/z) and retention times while NMR does not rely upon separation of the analytes (46). The advantage of using NMR is its reproducibility and simplicity of sample preparation, but

NMR suffers from low sensitivity that limits analysis to only the most abundant metabolites in the sample (50). Conversely, MS methods have higher sensitivity but may be more difficult to quantitate than NMR and suffer from problems from contamination due to this high sensitivity (50).

Assessment of plasma samples using metabolomics is performed one of two basic profiling methods, either a targeted or an untargeted profiling. Targeted profiling uses a small group of predefined metabolites chosen for analysis while untargeted profiling obtains a broader picture and identifies all metabolites within the sample (41, 51). Untargeted profiling produces a much larger metabolome picture and is often used as a hypothesis-generating approach while targeted profiling uses known information or assumptions about metabolism and is regarded as a more hypothesis-driven approach (46). Depending on the research question, strategies for metabolite analysis may include selection of either targeted metabolomics, untargeted metabolomics, or both (43). With the advent of metabolomics as a reliable and commonly used technology, and problems with the reliability of MBDAs, there have been calls to exploit this technology to assess dietary exposure (42).

Processing of most MS and NMR data begins initially with software specific to each machine or manufacturer for analysis or with freely available software for peak detection and integration (52). Targeted metabolomics uses isotope-labeled authentic standards, so processing is straightforward. Untargeted metabolomics requires that software is capable of peak selection, evaluation, and relative quantification (52). After peak detection, researchers conduct library searches for presumptive peak identification (53, 54). Missing data is not often a problem with small sample sets or experiments, especially in a targeted approach, however in untargeted

metabolomics missing data must be imputed using statistical procedures such as a nearest neighbor procedure or imputing the minimum detection level (51, 52).

Lipidomics

While metabolomics is the systematic study of metabolites produced during biological processes, lipidomics is a subset of metabolomics which focuses on lipids as the metabolites of interest (55). Lipidomics, more than just characterizing the complete lipidome, is the complete understanding of how lipids influce biological systems (47). Initially thought only as storage molecules and membrane constituents, lipids have proven to have important physiological roles including cell signaling, protein modification, and membrane anchoring (47).

Lipids have classicaly been defined as biological molecules which are generally hydrophobic and usually soluble in organic solvents and the presence of long hydrocarbon chains (47, 56). Some lipids, such as phosphoinositol, are often soluble in water and steroids do not posess the typical hydrocarbon chains (47). Recent work has attempted to develop a comprehensive classification and nomenclature system for lipids (47, 56, 57). These lipids have been divided into 8 classes: 1) fatty acyls (FA), 2) glycerolipids, 3) glycerophospholipids, 4) sphingolipids, 5) sterol lipids, 6) prenol lipids, 7) saccharaolipids, and 8) polyketides (56, 57). Recent clarification of naming glycerophospholipids has also added nomenclature to identify specific head group moeties including phosphatidylcholines (PC), phosphatidylethanolamines (PE), phosphatidylinositol (PI), phosphatidylserine (PS), phosphatidylglycerols (PG), cardiolipins (CL) (57). Furthermore, nomenclature to identify the monoglycerphospholipids may use a lyso- prefix for identificiation (i.e. lysophosphatidylcholine uses LPC) and the plasmalogen forms of these are identified with an O- prefix to identify the ether bonded to the sn-1 alkenyl

group (PlsCho or PlsEth) (57, 58). Finally, two numbers separated by a colon indicate the total hydrocarbon length and total number of double bonded carbons in that chain (56, 57). For example, a phosphatidylcholine with 36 carbons and two double bonds would be indicated by PC 36:2.

Because of their hydrophobic nature, lipids are not readily transported in the blood throughout the body. Instead, they are bound into lipoproteins which are protein/lipid complexes which allow transport of the hydrophobic lipids in the aqueus blood plasma (59). There are 5 types of lipoproteins named according to the density of their lipid constituents: chylomicrons (ultra low density lipoproteins; ULDL), very low density lipoproteins (VLDL), intermediate density lipoproteins (IPL), low density lipoproteins (LDL), and high density lipoproteins (HDL) (60). These lipoproteins all have interiors containing hydrophobic lipids with surface monolayers consisting of the hydrophilic heads of phosopholipids and cholesterols (60). Various lipid binding apolipoprotein serve to stabilize lipoproteins and act as interact with lipoprotein receptors on organelles and cells for uptake and transport (60, 61).

Lipidomics has been used recently to understand the dysregulation of lipid metabolism in diseases such as diabetes (62) and hypertension (63). Hu et al. found that PC and Triacylglycerol (TG) were elevated in hypertensive while CE were decreased (64). Lipidomics has also been used to find biomarkers of disease such as pre-eclampsia (65). A recent study has shown that metabolomics can be effectively used to monitor the dietary intake of phenylalanine in individuals with phenylketonuria (66). The work of this dissertation seeks to use lipidomics to find biomarkers of dietary intake.

Statistical Challenges with High Dimensional Metabolomics Data

Because thousands of metabolite features are produced after analysis with LC-MS and GC-MS identification of metabolites which are associated with each feature is challenge and often require the use of advanced statistical methods to analyze (46, 51). The number of features produced using metabolomics can number in the thousands with many being redundant or adducts of known metabolites. Pearson's correlations overlap between metabolites detected in positive and negative mode, and database searching can help to eliminate redundant features and limit the size of the data (52). Feature lists are compared to known databases to help identify metabolites, but some metabolites may remain unknown (53, 54). False discovery rate (FDR) and family-wise error rate methods are used to decrease feature redundancy (52).

To compare two separate metabolomes, for example a treated group compared to a control group, univariate methods such as student's t-tests (parametric), rank sums (nonparametric), and ANOVA (parametric, multiple classes) can be used (51, 52). However, the effect of potential confounding variables such as sex, BMI, and age are not taken account by these methods and multivariate methods should be used instead (51). Multivariate methods take into account all of the metabolomic features simultaneously and are useful at identifying relationship patterns between these features (51). Unsupervised methods, such as principal component analysis (PCA) and partial least squares discriminant analysis (PLS-DA) are used in many studies of metabolomics to identify patterns of metabolite differences between groups (43, 51, 67-69). Other unsupervised methods such as hierarchical clustering analysis (HCA) have been used with metabolomic data to identify non-linear relationships not always discovered with PCA (51). In these studies we use univariate methods (student's t-tests and ANOVA),

multivariate methods (linear and non-linear regression), and unsupervised methods (PCA and machine learning)

Dynamic Change in the Metabolome

Measuring metabolomic differences at several time points during a study allows for the identification of dynamic changes in the metabolome. Variations in the metabolome can be particularly important for understanding the etiology of both short-term and long-term changes due to diet. The dynamics of the metabolome, and lipidome, have only recently been studied. Dynamic changes have been used to understand metabolite trajectories associated with early life growth between the ages of 6 months and 4 years in humans (69). In this study, 30 children provided urine samples which were analyzed using NMR (69). Higher levels of trimethylamine N-oxide (TMAO) and betaine were found at the 6 month time period (69). Glycine and glutamine were decreased after 6 months along with increases in creatine and creatinine (69).

With regard to diet, targeted metabolomics has been useful in defining metabolite signatures associated with high fat diet (70), the 'prudent diet' (71), and the "Western diet" (71). In the Krug et al. study, 15 healthy male participants provided several time course plasma and urine samples for targeted metabolomics (191 metabolites). Participants' metabolomes were analyzed using NMR to reflect several physiological tests: 1) a single day fast, 2) consumption of a standard liquid diet, 3) during an oral glucose tolerance test (OGTT), and 4) physical exercise. The finding of this study was that these physiological challenges provided many interindividual differences despite physiological similarities (70).

Changes in the metabolome due to circadian cycles under different nutritional challenges, specifically a high fat diet and high carbohydrate diet, have also been identified (72). Participants (8 males) were randomized and consumed one day of a standard diet, a high fat diet (HFD), and a high carbohydrate diet. Untargeted plasma metabolomics were analyzed with ultra-high-performance liquid chromatography-tandem MS at two time points, 8 am and 7 pm. The results of the study show differences in metabolomics due to time of day in all subjects (72).

Dynamic changes in the metabolome have been identified using nutritional challenges used to measure insulin resistance such as the hyperinsulinemic-euglycemic clamp (HEIC) (73). In this study, 12 women with polycystic ovarian syndrome (PCOS) and 10 age matched controls underwent an 8 week exercise program at 60% VO_2max. Participants underwent a hyperinsulinemic-euglycemic clamp (HEIC) to assess insulin resistance before and after the intervention. Plasma samples were provided at three points: before the HEIC, 120 minutes after saline drip, and after the HEIC. Metabolomics was assessed using LC-MS/MS (Triple Q) in an targeted fashion (163 targets). A decrease in several amino acids (leucine/isoleucine, glutamate, methionine, ornithine, phenylalanine, tyrosine, and proline) in PCOS subjects which was not seen in control subjects. The were no differences in amino acid profiles between controls and subjects after exercise, suggesting that exercise can normalize insulin resistance (73).

Current Uses of Metabolomics in Dietary Analysis

The use of high-throughput profiling of metabolites in biological fluids has emerged as a potential method to provide an objective measure of dietary intake and could supplement MBDA in dietary research (19, 41, 43, 44, 74). Multiple studies have identified relationships between MBDAs and blood metabolites levels (75, 76). Recent studies using metabolomics to analyze

data fall into two basic groups, epidemiological studies using large data sets, and controlled feeding studies. The epidemiological studies use large cohort studies to identify specific biomarkers of dietary intake while the controlled feeding studies use feeding trials to identify biomarkers of intake (44).

A few epidemiological studies have identified metabolomics patterns that correspond with specific dietary patterns. Bouchard-Mercier et al. were able to identify an increase in plasma amino acids and short-chain acylcarnitines (ACAR) in subjects who eat a Western diet when compared to those that eat a Prudent diet composed of high levels of fruits, vegetables, and lean meats and low in fat and cholesterol (77). McCullough et al. found identified biomarkers for 4 healthy dietary patterns in post-menopausal woman in the United States were associated with consumption of fish (78). Peré-Trepat et al. using an FFQ found that individuals who reported eating an animal-based food diet had higher concentrations of lysine, arginine, glutamine and glutamate, threonine, aspartate and asparagine, citrate, and polyol compounds in plasma when compared to individuals who report a plant-based diet (79). An epidemiological study by Floegal et al. used cross-sectional data to identify metabolites from serum showing habitual intake of butter (acylcarnitines, acyl-alkyl-phosphatidylcholines, lysophosphatidylcholines, and hydroxy-sphingomylines), red meat, and fish (hexose and phosphatidylcholines) using a targeted profiling approach (80). Habitual potato, dairy product, and corn flake ingestion was identified by this study (80). Habitual citrus intake indicated by the metabolite proline betaine when compared to FFQs by Heinzmann et al. in 2010 (81). One particular interesting study looked at dietary exposures based upon habitual diets (vegan, vegetarian, and omnivorous) then used metabolomic data obtained from 1-H-nuclear magnetic resonance to predict habitual intake of meat and other animal products (82).

While these epidemiological studies are thought provoking and provide evidence that metabolomics can be a useful tool for identifying biomarkers of habitual intake, their reliance on MBDAs draws into question the accuracy and precision of effect estimates of associations. Controlled feeding trials in conjunction with metabolomics could be a potentially be used to understand and increase the validity and reliability of MBDAs, especially 24HR (83, 84). Metabolomics is used with controlled feeding trials to identify specific biomarkers of dietary intake. These fall into three categories: acute feeding trials, short term feeding trials, and habitual feeding trials.

Heinzmann et al. fed 7 subjects a standardized diet for 6 days with different standardized meals fed each day (85). The urine metabolome was assessed at 4 points in each day (85). A clear metabolite profile exists for fruit and wine ingestion (tartrate, proline betaine, hippurate, and 4-hydroxyhippurate (85). Metabolome patterns between subjects also shifted in conjunction from diet to diet (85). Metabolite profiles have been identified following acute consumption of cocoa (metabolites of cocoa-phytochemicals, alkaloid derivatives, polyphenol metabolites and processing-derived products such as diketopiperazines) (86), sugar sweetened beverages (formate, citrulline, taurine, and iso-citrate) (49), tea extract (hippuric acid, 4-hydroxyhippuric acid, and 1,3-dihydroxyphenyl-2-O-sulfate) (87), salmon (trimethylamine-N-oxide and 1-methylhistidine) (88), raspberries (ascorbate, sulphonated caffeic acid and sulphonated methyl-epicatechin) (88), broccoli (ascorbate) (88), coffee (dihydrocaffeic acid-3-O-sulfate and feruloylglycine) (89), polyphenols (hesperetin, quercetin, & naringenin) (90), and red meat (2-aminoadipic acid, β-alaninine, and 4-hydroxyproline) (91).

Short-term feeding trials tend to be longer than 24 hours but are still controlled feeding trials. Using short term feeding, biomarkers for soy feeding, specifically isoflavones have been

identified (92). A 12-week feeding trial in individuals with metabolic syndrome of mixed nuts was able to identify discernable difference between those who ingested nuts and those who did not (93). An 8-week feeding trial of milk and meat protein was able to identify a specific metabolic profile in individuals who were given milk but not in those who were fed meat (94). Whey protein was found to produce distinct metabolic profiles compared to gelatin protein in women with type 2 diabetes over an 8-week weight loss program (95). Another 12-week study found specific biomarkers of cheese and butter intake in 23 subjects (96). Cruciferous vegetables (97) and dark chocolate (98) consumption biomarkers have been identified using short term feeding trials and metabolomics. Several studies have also identified biomarkers of meat intake using short term feeding trials and metabolomics (99, 100). Animal studies have shown identifiable metabolic changes after 12-week high-fat diets (101).

Metabolomic Response to Standard Diet

While biomarkers of specific food intake have been identified using metabolomics, there is a gap in the literature in which controlled feeding studies identify dynamic changes in the metabolome. A few acute or short-term feeding trials have elucidated convergence of metabolomics patterns. Heinzmann et al. performed a study in which subject's metabolomics patterns shifted in parallel relative to different standardized diets (85). Winnike et al. fed 10 healthy volunteers a standardized diet for 2 weeks and found that both urine and serum metabolite patterns were most diverse on the first day and converged significantly over time (76). The metabolome convergence was most pronounced after day 1 and much less so over time (76). In a more acute feeding study of standard diet, Favé et al. fed subjects a standardized meal the night before a standard breakfast and collected urine up to 4 times (102). It was found that

the metabolomics patterns of all subjects converged to a similar pattern soon after the test breakfast (102).

Habitual feeding studies using metabolomics tend to focus on drawing together information from MBDAs and combining that with GC-MS, LC-MS and/or NMR to identify dietary patterns in larger populations and/or over longer periods (44). These studies have applied metabolomics to samples using food diaries (43, 103), FFQs (44, 104), and 24HR (104). These studies have identified metabolite profiles among habitual cocoa drinkers (105, 106). Habitual fat intake has been associated with specific lipidomic profile (107). Specifically, habitual saturated fat intake is identifiable through detection of phospholipids (108). Habitual milk ingestion is associated with specific biomarkers, specifically uridine and trimethyl-N-aminovalerate, in a large twin study in the UK (109).

In one very large study comparing Western diets (United States and United Kingdom) with Asian diets (Japan and China) metabolomic profiling was able to identify a Western diet from an Eastern diet using urine metabolites (67). Holmes et al. conducted a particularly large study using a metabolomics approach and was able to distinguish Eastern Asian diet consumers from UK and USA Western diet consumers based upon their blood serum metabolite profiles (67). This study involved 4630 participants from the INTERMAP epidemiological study from 17 populations from China, Japan, UK, and the USA (67). Four 24HRs were conducted to establish eating patterns as well as metabolomics profiling of two 24hr urine specimens (67). Using hierarchical cluster analysis (HCA) of metabolites, there appeared two clear dietary patterns which were grouped into Western (UK and USA) and Asian (Japan and China) (67). These HCA results were then confirmed using principal components analysis (PCA) (67).

The TwinsUK cohort is a large epidemiological study involving 3262 monozygotic female twins and has been used to establish dietary patterns using urinary metabolomics which were used to be modeled using regression analysis and structural equation modelling (112-114). Teucher et al. found that dietary patterns determined using FFQs showed a strong heritable component for food choice (113). This was followed by a targeted metabolomic analysis of these same subjects and it was found that dietary pattern was able to be statistically modeled using regression analysis and structural equation modeling (112). In a recent study by Pallister and Jennings et al. habitual food intake of this same population was determined using FFQ and then 71 reported food groups were assessed against 601 identified metabolites (114). This study identified 180 significant associations with 39 food groups that contained 106 different metabolites (114). Ergothioneine was found to be a biomarker for mushroom intake, trans-4-hydroxyproline for red meat, and 3-phenypropionate, indoleproprionate, and threitol for fruit intake (114). Recently, this same group also found trimethyl-N-aminovalerate, hydroxyphingomyelin, and diacylphosphatidylcholine 28:1 are associated with milk intake with this same group of subjects (109).

Recent work has proven that metabolomics holds promise for use in dietary recall. Metabolomic profiles successfully classified subjects according to their diets with very high accuracy (115). Urinary metabolites have been used to classify individuals into “healthy” or “unhealthy” dietary patterns based on metabolomics patterns (49). Lipidomic pattern dynamics in a high fat diet following a high carbohydrate diet has recently been investigated by feeding 46 heathy, non-obese pair twins (116). In this study, subjects were given a high carbohydrate diet (15% protein, 30% fat, 55% carbohydrate) for six weeks followed by six weeks of a high fat diet (15% protein, 45% fat, 40% carbohydrate) (116). Lipidomic analysis revealed five distinct lipid

patterns, a) no reaction, b) a monotonous increase, c) an acute increase followed by plateau, d) stable concentration for one week followed by a delayed reaction, and e) a counter regulation with an acute response in one direction for one week followed by a rebound in the opposite direction after this (116).

Nutritional metabolomics has been able to identify specific foods biomarkers for dietary intake (41-44, 110, 111). However, with the exception of studies in habitual fat intakes (107, 108), little has been reported on metabolite changes due to controlled changes in macronutrient content of food. The Holmes study which identified subjects who consumed either a Western or an Eastern diet based upon their metabolome is promising because of the inherent difference in these diets (67), but this study was not a controlled feeding study. This leads us to a particular gap in the literature. We were not able to find many studies using metabolomics to identify specific differences in the metabolome that used a feeding study in which the macronutrient content of diet was identified and well controlled.

The Use of Metabolomics during the Hyperinsulinemic-euglycemic Clamp

Metabolomics elucidated differences in metabolism between insulin resistant and insulin sensitive individuals. Several studies have identified changes in plasma levels of amino acids, TCA cycle intermediates, and fatty acids (117, 118). Metabolomic analysis has shown that that circulating branched-chain amino acids (BCAA) correlate negatively with insulin sensitivity and T2DM due to obesity when compared to lean, healthy individuals (119). Metabolomic analysis identified elevations in plasma BCAAs, aromatic amino acids, 2-aminoadipic acid, and lipids of lower carbon number and double bond content as predictors of diabetes in healthy individuals (120-124).

These findings highlight the use of metabolomics to enhance our knowledge and understanding of metabolic disorders like insulin resistance and T2DM and their causes (118, 125-128). Recent metabolomics studies have identified biomarkers and metabolites associated with cardiovascular disease, type 2 diabetes mellitus, and metabolic syndrome. The phospholipid phosphatidylcholine 34:2 has a positive correlation in patients with metabolic syndrome (MetS) and comorbidities such as waist circumference, plasma glucose, free fatty acid and triglyceride levels (129). The BCAA isoleucine positively correlates with MetS while lysine is negatively correlated (130). It has long been known that insulin resistance is positively correlated with the BCAAs, tyrosine, phenylalanine and negatively correlated with glycine (131), but recent work using the more sensitive metabolomics methods has identified a glutamine (positive correlation) and glutamate (negative correlation) as potential identifiers of insulin resistance (132). To strengthen these findings, a recent large population study of Finnish men identifies nine amino acids are associated with insulin resistance and T2DM (133); these were phenylalanine, tryptophan, tyrosine, alanine, isoleucine, leucine, valine, aspartate, and glutamate.

This dissertation utilized high throughput metabolomic and lipidomic methodologies to understand dynamic changes in the metabolome and lipidome due to changes in dietary intake using two modalities. First was a 24-day feeding study of a standard diet followed by very high carbohydrate and very high fat diets. Second, we compared the plasma metabolomic profiles of individuals collected during a hyperinsulinemic-euglycemic clamp (HEIC) which involved intravenous glucose administered over the course of an hour.

In the study of insulin resistance, the use of metabolomics is new and provides great promise both in finding predictive biomarkers as understanding the physiological implications and actions of the disease (118, 134). Metabolomics elucidates differences between insulin

resistant and insulin sensitive individual's levels of amino acids, TCA cycle intermediates, and fatty acids (117, 118). Acylcarnitines have been implicated, through metabolomic profiling, as a possible cause of insulin resistance (135). Acylcarnitines are thought to be incompletely oxidized through muscle fatty acid ß-oxidation and could play a role in muscle insulin resistance (136). Incomplete fatty acid oxidation (FAO) outpacing the tricarboxylic acid cycle could result in the accumulation of excess acylcarnitines that interferes with insulin sensitivity (135). However, whether insulin sensitivity is caused by an increase in acylcarnitines or results in an increase in acylcarnitines is not understood (137).

In a metabolomics study during an oral glucose tolerance test (OGTT), medium chain acylcarnitines, CAR 10:0 and 12:0, were found to be associated with insulin resistance in a large (n=470) study of older men (age 70.6±0.6) while these associations were not found in longer chained and shorter chained acylcarnitines (138). While metabolomics has used to study dynamic changes in the metabolome during glucose tolerance test, these dynamics are poorly studied in the HEIC. This is of interest because the HEIC is considered the gold standard in the measurement of insulin resistance. One study did find that insulin stimulation lowered most medium- and long-chained acylcarnitines compared to basal levels in healthy individuals and that leucine, isoleucine, and lysine negatively correlate with insulin sensitivity (139).

One aim of this dissertation work is to elucidate the dynamic changes in metabolite profiles using metabolomics during the HEIC. In particular, obese metabolically healthy individuals were studied who were either more or less insulin sensitive based on their glucose infusion rate. We also used lean participants as negative controls.

Summary

Currently in nutritional research, dietary intake of both individuals and populations is established using MBDAs. However useful, the validity of estimates of dietary intake based solely on MBDAs is in question (140). Metabolomics has emerged as a tool that could provide an objective measurement of dietary intake (43, 74, 141). With the emergence of metabolomics and subsequent use in nutritional analysis, there has been significant use in the identification of biomarkers of specific food intake. There has also been much of use of metabolomics to identify both dietary patterns as well as biomarkers of intake using MBDAs. However, because both reliability and validity of MBDAs has come into question, there is a significant gap in the literature and the science in using metabolomics as an indicator of objective macronutrient intake. Furthermore, there has been a recent call for the merging of data-driven approaches for dietary analysis such as metabolomics with traditional MBDAs such as FFQ and DR (39, 40). Secondly, there have been several acute and short term controlled feeding trials using metabolomics that determined biomarkers of dietary intake of specific nutrients (141). Despite, this there has been little work done on changes in metabolomics patterns using controlled feeding trials of macronutrient intake.

Study Population

This study utilized four distinct adult study populations. The first feeding study population was a group of 12 healthy controls in a high polyunsaturated fat (PUFA)/high carbohydrate (CHO) feeding study. The second feeding study population was a group of 23 healthy individuals who took part in a 24-day high fat/high carbohydrate feeding study (MEAL). A third population of subjects tested against the training populations of the PUFA/CHO and MEAL and was a group of 46 healthy controls in a bipolar feeding study. This population came

from the community as a whole and we refer to as the Community population (Community). The final population was for the hyperinsulinemic-euglycemic clamp study and involved 18 subjects.

The PUFA/CHO study was initially designed to look at the efficacy of a high PUFA diet to change the viral load in individuals with hepatitis C. Here, we analyze the data from the 12 healthy controls recruited for the study. The subjects were fed a high PUFA diet for three weeks followed by an immediate switch to a high CHO diet for three weeks. Plasma samples were collected from these subjects for comparison at baseline and then on days 2, 7, and 21 of each experimental diet for a total of 7 samples.

The high carbohydrate/high fat study (MEAL) was designed to identify dynamic changes in the metabolome of subjects during a 24-day feeding study. 23 subjects (11 ♀/12 ♂) were fed a standard diet (12% protein/ 35% fat/ and 50% CHO) for 3 days followed by either a high CHO diet (15% protein/ 10% fat/ 75% CHO) or a high fat (15% protein/60% fat/25% CHO) for 21 days following the standard diet. Plasma samples were collected at baseline, after the standard diet, and at 4 points during the experimental diet for a total of 6 time points.

In the Community population, 43 healthy control subjects from a bipolar study were selected. These individuals were not bipolar. These individuals gave one plasma sample at the end of one week in which their diets were ascertained with 7 consecutive days of dietary journals.

In the hyperinsulinemic-euglycemic clamp study, there were 18 individuals; 6 lean controls, 6 metabolically healthy obese individuals who were more insulin sensitive, and 6 metabolically healthy obese individuals who were less insulin resistant. These subjects all took part in a larger study conducted by the lab of Dr. Jeffrey F. Horowitz at the University of

Michigan. Each underwent a hyperinsulinemic-euglycemic clamp with 7 plasma samples taken during the clamp and analyzed for metabolomic differences between groups.

Thesis Aims

This leads us to the specific aims of this dissertation work: 1a) determine dynamic changes in the lipidome due to high carbohydrate and high fat diet. 1b) identify diet as either high fat or high carbohydrate based on biomarkers determined using lipidomics. 2) Compare the recalled macronutrient intake with the actual macronutrient intake of subjects in a controlled feeding study. 3) Compare the metabolomic profiles of a) obese but metabolically healthy individuals who are more insulin sensitive, b) less insulin sensitive, and c) lean control (fig. 1.1).

Thesis Overview

Chapter 2 identifies dynamic changes in the lipidome due to high fat and high carbohydrate diets. Furthermore, 54 lipid classifiers (Sentinel lipids) were used to successfully classify subjects as either high carbohydrate or high fat eaters. Lastly, “real-world” diets were successfully classified as either high fat or high carbohydrate based using these sentinel lipids.

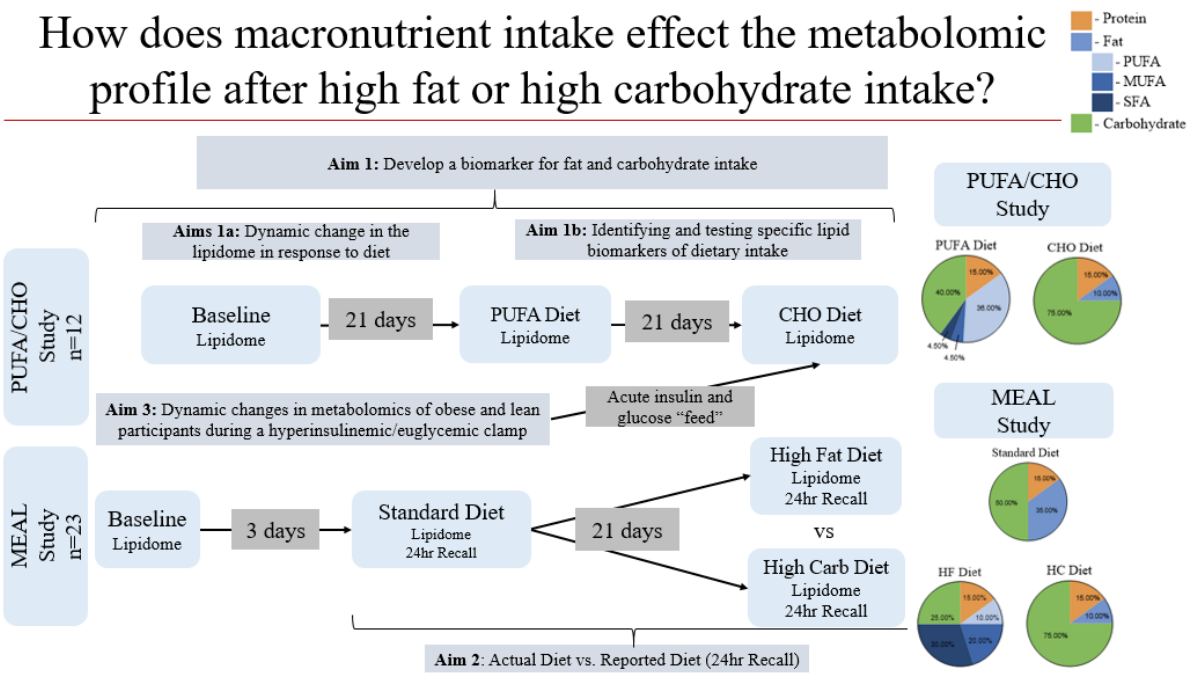
Chapter 3 compared recalled diet using 24-hour recalls (24HR) with provided diet for the 23 subjects in the MEAL study. The goal of chapter 3 is to ascertain the reliability of 24HR in a controlled feeding.

Chapter 4 investigated the metabolomic changes in metabolically healthy obese individuals and lean control individuals who were either more insulin sensitive or resistant.

Chapter 5 summarizes the work of this dissertation and offers recommendations and future directions for research on expanding the scope of this research to increase the generalizability of the results from these small studies to the larger population.

Figures

Figure 1.1 *Overview of the aims of this dissertation.*



Schematic overview of the aims of this dissertation. The overall research question is: "How does macronutrient intake effect the metabolomic profile after high fat or high carbohydrate diet?" The PUFA/CHO and MEAL studies' macronutrient proportions are indicated on the right with protein, fat (PUFA/MUFA/SFA) and carbohydrate. Aim 1 focuses on development of a biomarker that differentiates between high fat and high carbohydrate diet. Aim 1a focuses on the dynamic changes in the lipidome and Aim 1b on identifying and testing biomarkers that differentiate between high fat and high carbohydrate intake. Aim 2 compares actual diet and 24HR reported macronutrient and EI. Aim 3 identifies dynamic metabolomic changes during the HEIC in lean and metabolically healthy obese participants.

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Chapter 2: Towards Unbiased Assessment of Nutrient Intake: Dynamic Response of the Plasma Lipidome to Macronutrient Intake in Humans

Abstract

Introduction:

Nutrition researchers use several forms of memory based dietary analysis (MBDA) to estimate dietary intake. However, dietary intake information that comes from MBDAs is flawed as subjects misreport both energy intake and macronutrient intake. Given these limitations, developing lipidomics as a tool to assess objective dietary intake would provide a significant addition to epidemiological studies in assessing diet and understanding dynamic changes in lipidome as a risk for chronic diseases.

Objective:

The first aim of this study was to elucidate the dynamic changes in the lipidome in humans on a very high fat and very high carbohydrate feeding diet. The second aim was to identify lipidomic biomarkers that would discriminate high fat and high carbohydrate diets and to validate these biomarkers in a free-living population.

Methods:

We used two controlled diets in this study. The first was a 21-day PUFA/21-day CHO study with 12 subjects. The second study fed 24 subjects a standard diet for 3 days followed by 3 weeks of either a very high fat (HF) or very high carbohydrate diet (HC). We conducted plasma lipidomic analysis on samples from these studies to identify lipid differences and similarities. Statistical analysis identified 12 “Sentinel Lipids” which were significantly different between PUFA/CHO and HF/HC. Support Vector Machine learning (SVM) produced ROC curves using Monte-Carlo cross validation, identify important features, and produce predictive probabilities of a validation test set.

Results:

We elucidated dynamic changes in the lipidome of the PUFA/CHO study and HF/HC study. In the PUFA/CHO, we observed rapid changes in lipid levels with 41% changing after 2 days of changing to a PUFA diet and 64% within 2 days of changing of a CHO diet. Plasmalogens, LPCs, and LPEs changed in a slower fashion. Approximately 200 lipids were statistically different between CHO and PUFA at tested days. After 3 days of a standard diet, variation in the lipidome decreased significantly in the MEAL study. The MEAL study showed similar patterns to PUFA/CHO but with much less significant differences. After ROC analysis, selected important features were able to discriminate between plasma samples of high fat and high carbohydrate with an AUC of 0.873.

Conclusion:

The lipidome is very responsive to diet. Variation decreased after 3 days of a standard diet highlighting the need for feeding studies to begin a standard diet to normalize the lipidome.

Several lipids showed an adaptive response to feeding which demonstrates that lipids change quickly after a HC or HF feeding, but this difference is blunted (but still significant) over 3 weeks. Several lipids also showed a monotonous and stable response providing evidence that finding an objective measure of macronutrient intake is possible. We also identified a small panel of lipids that discriminate between very high fat and very high carbohydrate diets. While quite preliminary, and limited by small sample size, these sentinel lipids perhaps hold promise for identification of macronutrient intake in free-living populations.

Introduction

Diet, and in particular macronutrient intake, is an important and modifiable lifestyle behavior (1). Specifically, macronutrient intake has been associated with cardiovascular health and type 2 diabetes mellitus (2, 3). Current recommendations about energy and macronutrient intake are based on large cross-sectional studies such as What We Eat in America which utilizes data from the National Health and Nutrition Examination Survey (NHANES) (4, 5). Several forms of memory based dietary analyses (MBDA), such as food frequency questionnaires, 24-hour recalls, and food diaries are routinely used to estimate actual food intake (4, 5).

Despite their widespread use, there is abundant evidence that dietary intake information obtained from surveys and recalls are biased as subjects misreport both energy and macronutrient intake (6-12). As a result, epidemiological studies use well-established methods of adjustment to account for these inconsistencies (13-16). Associations between diet and disease in the context of nutritional intake are often drawn from information obtained via MBDAs (17, 18). The use of biased dietary information could potentially lead to inaccurate estimation of the effects of diet on

health (19-23). Despite the known limitations with MBDAs, they remain the primary approach to estimate dietary intake (4, 5, 11).

Metabolomics is an emerging technology that could be used in conjunction with epidemiological studies to provide an objective method for measuring dietary intake and relating it to chronic risk for disease (24-27). Current uses of metabolomics in dietary research tend to fall into two basic categories, epidemiological studies that rely on large data sets and controlled feeding studies. Epidemiological studies use large cohorts to identify specific biomarkers of intake and relate these biomarkers to health outcomes (28), while the smaller feeding trials use controlled feeding trials to identify biomarkers of intake of specific foods (29). For example, a diet characterized by higher intakes of red meat and lower intake of whole-grain bread and tea was identified in the large EPIC-Potsdam cohort was associated with hexose and PCs in serum (30). Wellington, et. al., used metabolomics to successfully identify human dietary patterns, specifically "Western" and "Prudent" dietary patterns (31). Another study identified the association of the blood metabolite betaine with citrus fruit consumption in a feeding study and validated these findings in a larger cohort (32). A few studies have identified relationships between blood metabolites and MBDA data (33, 34).

Research into dynamic time course changes in the metabolome following diet have also been examined in a handful of studies (31, 35, 36). The first study by Pellis, et. al., performed metabolomic and proteomic analysis following a postprandial challenge test (PCT) comprised of 59% lipids, 30% carbohydrates, and 12% protein as a percentage of total kCal (35). Thirty-six overweight subjects were given a PCT before and 5 weeks after following an anti-inflammatory supplement mix in a crossover design. These authors were able to identify differences in metabolites associated with amino acid, oxidative stress, inflammation, and endocrine

metabolism before and after supplementation (35). In a study involving 46 healthy, non-obese twin pairs, Frahnow, et. al., performed lipipomic profiling on subjects at baseline, after 1 week, and after 5 weeks after switching from a low fat to high fat eucaloric diets. They found that lipid profiles diverged after only 1 week of the change to a high fat diet and further after 5 weeks (36). In the final study, 42 subjects were provided a eucaloric Prudent or Western diet for 2 weeks and targeted and untargeted metabolomic profiling was performed on both plasma and urine (31). Several small metabolites were identified which were associated with consumption of these diets including linoleic acid, α-linoleic acid, and linoelaidic acid (Western diet) and ketoleucine, ketovaline, nad hydroxypipecolic acid (Prudent diet) (31).

The aim of this study was three-fold: 1) Description of dynamic metabolomic changes that occur after a 3-day diet followed by 3-week high fat or high carbohydrate diet, 2) identification of lipidomic patterns which differentiate between very high carbohydrate diets and very high fat diets and development of a training set of metabolites, 3) classification of subjects on "typical" or "normal" diets as either high carbohydrate or high fat using patterns based on metabolites identified in aim 2.

Methods

Controlled Feeding studies:

Two controlled feeding studies and one cross-sectional study were used to conduct this research. The first was a high polyunsaturated fatty acid diet (PUFA) followed immediately by a high carbohydrate diet (CHO) and is referred to as the PUFA/CHO study. The second controlled feeding study was a standard diet followed by either a high fat (HF) or a high carbohydrate (HC) diet and is referred to as the MEtabolomic AnaLysis of Diet study (MEAL). The test study (Community) was a cross-sectional study of control subjects from another study of healthy

controls from the community who were taking part in a study of bipolar disorder. Subjects in the Community study completed 7 consecutive days of dietary journals so their diets are relatively well characterized.

Recruitment and Ethics:

The Michigan Institutional Review Board approved all procedures involved in this study (HUM00006248, HUM000110543 and HUM00045653) and we obtained informed consent forms from all participants before beginning any portion of the study. All recruitment of participants for each of the studies described used umclinicalresearch.org and local advertisements.

PUFA/CHO Study:

The first controlled feeding study used a longitudinal paired study design without crossover involving 12 (6 male, 6 female) subjects. These subjects consumed a very high PUFA diet (10-15% Protein, 25-50% carbohydrate, & 40-50% fat; 10% MUFA, 10% SFA) for 21 days immediately followed by 21 days of a high carbohydrate diet (10-15% protein, 70-80% carbohydrate, & 10-15% fat; <10% SFA) (Figure S2.1). Recruitment criteria were between the ages of 19 and 50, no history of metabolic disorders, no recent changes in weight, and no current use of metabolism altering medications. There was no washout period between diets. On the initial day (Day 0), subjects were consented, weighed and measured, and provided with food for the first 2 days. Subjects returned to the metabolic kitchen twice per week during the study to receive meals for consumption.

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Blood collection:

We collected 7 overnight-fasted blood samples in 10.0 mL EDTA treated vacutainers (www.bd.com) on days 0, day 2 of the PUFA diet (P2), P7, P21, day 2 of the CHO diet (C2), C7, and C21. Samples were immediately inverted 7 times and placed on ice to be processed in ≤1 hr. Plasma was frozen at -80^{0}C for later LC/MS analysis.

MEAL Study:

The MEAL study used a parallel randomized block design blocked by sex and involved 23 participants randomized to 2 experimental diets, high fat (HF) and high carbohydrate (HC), 13 HC (7 male, 6 female) & 10 HF (5 male, 5 female) (Figure S2). Recruitment criteria included subjects between the ages of 19 to 40, BMI 18.5 to 25, no history of metabolic disorders, no recent change in weight, and no use of metabolism altering medications. Initial protocol called for 24 subjects. One HC participant was removed for non-adherence to the assigned diet that was recognized in the data and was confirmed by a post-study questionnaire administered to the participants. This reduced the total number of subjects in the analytic sample to 23.

Study design summary and randomization scheme:

Participants completed baseline assessments, consumed a 'standard' diet for 3 days, and randomly assigned to experimental diet groups for the following 21 days (Figure S2). We randomized subjects into study groups based upon date of consent and blocked by sex. A random number generator (Microsoft Excel 2016) was used to assign subjects into diet groups.

Participants returned to the study location every 2-4 days for repeated assessments and to pick-up food.

Body composition and anthropometry:

Baseline height was measured in duplicate to the nearest 0.5 cm using a wall-mounted stadiometer (Easy-Glide Bearing Stadiometer, Perspective Enterprises, Portage, MI). Weight was measured in light clothing to the nearest 0.1 kg using a calibrated electronic scale (Scale-Tronix Model 6002, White Plains, NY). At each food pick-up current weight was measured. If body weight fluctuated more than 1 kg, the total kcal provided were adjusted to maintain baseline body weight.

Blood collection:

Fasted blood samples were collected in EDTA treated vacutainers ((www.bd.com)) on days -3, 0, 2, 7, 14 and 21. Samples were immediately inverted 7 times and placed on ice and processed in ≤1 hr. Plasma aliquots were frozen at -80^{0}C. **Lipidomics:**

Untargeted LC/MS-based shotgun lipidomics was performed on -80^{0}C frozen, once-thawed, and single-aliquot plasma samples in a manner detailed in Afshinnia et al (37), including sample extraction and preparation on plasma samples. Mass spectroscopy data acquisition for each sample was performed in both positive and negative ion mode using a TripleTOF 5600 equipped with a DuoSpray Ion Source as performed earlier by Kregel, et. al. (38). 605 lipids and 563 lipids combined in positive and negative mode were annotated for the PUFA/CHO and MEAL studies respectively. Lipidomics data were normalized to remove batch and run order effects. Each lipid was normalized individually, without the use of internal standards. Positive and Negative modes were treated separately, until the final step of removing redundant duplicate lipids.

Pooled samples were derived from combining of small aliquots of experimental samples and were dependent on each experiment (PUFA/CHO, MEAL, or Community). Lipids missing more than 30% of data from either the pooled samples or the experimental data were removed. Robust regression on the pooled data was used to calculate an adjustment ratio between batches within each experiment; this ratio was then used to remove batch effects. For each lipid *i*, we calculate a batch-adjustment factor βi. If there were two batches, this adjustment factor was the slope from the robust regression of one batch on the other, without an intercept. If there were more than two batches, one batch was selected as the reference, and all other batches were regressed against the reference batch individually. We calculated the adjustment ration between batches using the lmrob function from the R package robustbase. Once the adjustment factors were calculated, missing data were imputed using the knn function from the R pamr package. Imputation considers the batch number, run order and sample label. Loess smoothing was used to remove the remaining effects of run order. Once all batch and run order effects had been adjusted, data from positive and negative modes were combined and redundant lipids removed. If a lipid was present in only one mode, but with multiple ions, the ion with lowest variability as measured by relative standard deviation (RSD) was retained. If a lipid was present in both modes, we picked the mode that had the most lipids of that lipid's class and kept the ion w/ the lowest RSD within that mode. If a lipid is present in both modes with identical number of ions/lipids present, we retained the ion with the lowest RSD across both modes. After normalization and the elimination of duplicates, there remained 480 lipids in the PUFA/CHO study, 571 in the MEAL study, and 549 in the Community study (Supplemental Tables S2.1 to S2.7).

For each subject in both PUFA/CHO and MEAL, we calculated log2 fold difference from baseline and between time points using Microsoft Excel 2016 as the log2 (resultant lipid

AUC/initial lipid AUC) (Redmond, WA, USA). We calculated fold difference for the time intervals 0 to P2, P2 to P7, P7 to P21, & 0 to P21 in the PUFA/CHO study and for 0 to 2, 2 to 7, 7 to 14, 7 to 21, and 0 to 21 in the MEAL study. Statistical significance between time points was determined using an FDR correction of 0.1 (Figures 2.1 & 2.2). Because these samples were from 2 different studies, extracted at different times, and run on LC/MS at different times, all lipids were median scaled to the MEAL samples, which contained the greatest number of lipids. Median scaling involved multiplying all lipids by a ratio of the median of pooled samples for each lipid (MEAL pooled lipid/Pooled lipid). The average AUC for all studies was more abundant in the MEAL study so we used the MEAL study lipids as the numerator.

Analysis of Variation of Lipids between Days:

To demonstrate the reduction of variation in all lipids after a standard diet, we calculated the variance in each lipid during each day in the MEAL study. For each day in the MEAL studies mean, standard deviation and variance in z-scores for each lipid was calculated using Microsoft Excel. Using SAS 9.4 software one-way analysis of variance (ANOVA) with Tukey's post-hoc analysis was used to determine differences in variance between days with a Bonferroni-Hochman correction for all lipids. Mean variance scores for each day were plotted for each day of the MEAL study (Figure 2.2D) (SAS Institute Inc., Cary, NC, USA). Principle component analysis (PCA) to help explain the unsupervised variance in the dataset was performed using the statistical analysis feature in Metaboanalyst (http://metaboanalyst.ca) (39, 40) for each day in the PUFA/CHO and MEAL study (fig. S2.3). All data was normalized using log transformation and auto-scaling. There were only significant differences during experimental days for both PUFA/CHO (days 2,7,21) and MEAL (days 2,7,14,21) so principal component 1 was compared to principle compenent 2 (fig. S2.3).

Sentinel Lipids:

From lipids identified in the PUFA/CHO and MEAL studies, Metaboanalyst (http://metaboanalyst.ca) (39, 40) was used to determine significant differences between diet groups (PUFA/CHO and HC/HF) at any experimental time point using Student's t-tests (FDR<0.1) and which overlapped between the MEAL and PUFA/CHO studies. From an initial 480 lipids in PUFA/CHO and 571 lipids in MEAL, a total of 311 and 82 were significantly different at any experimental time point, respectively. The overlap of significantly different lipids between datasets produced 54 initial sentinel lipids. (Figure 2.3).

Sentinel Lipid classification of macronutrient intake in PUFA/CHO and MEAL Subjects:

The predictive power of the MEAL and PUFA/CHO was determined using the 12 sentinel lipids. The biomarker analysis feature of Metaboanalyst was used to produce ROC curves for identifying discriminating biomarkers (Figure 2.4A). Missing features in all datasets the data were imputed using K-nearest neighbors (KNN). Linear support vectors machines (SVM) was used as a machine learning classification method and feature ranking method to rank features from most discriminating to least discriminating (Figure 2.4D). A natural break occurred at 60% selection frequency and the 12 lipids with the highest selection frequency were used to generate multivariate ROC using Monte-Carlo cross validation (MCCV) using balanced sub-sampling (Figure 2.3).

For each MCCV, 2/3 of the samples were used to evaluate the discriminating features and tested on the other 1/3 of sample; this process was iterated 100 times to improve performance. (39). Confusion matrices were produced, and sensitivity and specificity were calculated using high carbohydrate consumption as positive and high fat as negative (Figure 2.4B&2.4C). Sensitivity was calculated as the number of HC eaters who were identified as HC/total number of

HC eaters and specificity was calculated as the number of HF eaters who were positively identified/total number of HF eaters. Accuracy was calculated as (true carbohydrates + true fat)/(true carbohydrate + true fat + false carbohydrate + false fat). Plots of lipid changes over the course of the study were produced in GraphPad Prism 8 for Windows version 8.1.1 (220) (San Diego, CA). A correlation matrix of all sentinel lipids with one another was produced in an in-house R package called Coolmap and presented as a heat map (Figure S2.5).

Community Study:

Subjects for the Community study wear comprised of 43 healthy control subjects and 59 euthymic subjects from the Heinze C. Prechter Longitudinal Study of Bipolar Disorder (41). Subjects were between the ages of 25 and 60. All bipolar subjects were not expressing bipolar systems (euthymic) for several weeks before and during the study period.

Application of Sentinel lipids in estimating dietary intake:

Lipidomics profiles from the Community study were generated using fasting blood samples. Blood samples were taken following an overnight fast of at least 8 hours. All subjects provided 7 consecutive dietary journals to the registered dietitians at the Michigan Nutrition and Obesity Center. Nutrition Data System for Research software (NDSR), version 2016 developed by the Nutrition Coordinating Center (NCC), University of Minnesota, Minneapolis, MN (42), was used to estimate the energy, macronutrient and micronutrient content of the reported diet. A ratio of %carbohydrate: %fat was used to classify subjects as either high fat reporters (>1.43) or high carbohydrate reporters (<1.43). The value 1.43 was selected as a cut-off because this was the ratio of % carbohydrate: % fat in the MEAL standard diet (50% cho: 35% fat). Plasma samples were also obtained from these subjects on the last day of their dietary journals. Plasma was extracted and frozen in the same manner and the same lab as the PUFA/CHO and MEAL

samples. Lipidomics analysis was performed in the same manner as the PUFA/CHO and MEAL samples and median scaling performed as described earlier. Using the subset of 12 discriminating from the 54 sentinel lipids as a test set and the MEAL & PUFA/CHO experimental days as a training set a predicted diet score was produced. A score of 0 to 0.5 indicated a prediction of HC and a score of 0.5 to 1.0 indicated a prediction of HF. Scores farther away from 0.5 are indicative of higher confidence. Predicted scores were plotted against reported CHO:Fat in GraphPad Prism 8 for Windows version 8.1.1 (220) (San Diego, CA). Linear regression was also calculated in Prism with a calculation for significance of a slope of non-zero. (Figure 2.5).

Results

To create a potential objective blood marker of carbohydrate and fat macronutrient intake in people, we performed two independent controlled feeding studies in healthy subjects. Dietitians designed and provided custom meals with known macronutrient composition to healthy volunteers. Weight was monitored and total energy intake adjusted every 2-3 days to maintain the subjects' starting weight.

PUFA/CHO study

To provoke a significant change in the lipidome, participants were initially provided a eucaloric diet high in polyunsaturated fatty acids for 3 weeks followed immediately by a high carbohydrate diet (70-80% CHO) for an additional 3 weeks (Figure 2.S2.1). We performed plasma lipidomics profiling after an overnight fast at baseline and on days 2, 7 and 21 days (PUFA) and days 23, 28 and 42 (CHO). Subject weights varied less than 1% over the course of the study (Table 2.1A).

A significant proportion of the 480 annotated lipids showed robust changes and were observed across most of the 23 lipid classes (Table 2.S2.1-S2). At Day 21 of PUFA, 128 lipids exhibited statistically significant changes (FDR adjusted p-value < 0:1) compared to Baseline and 145 lipids changed at Day 42 (CHO) compared to Day 21 (Figure 2.1A and 2.2B, Table S2A to 2.S2.4A). Of the 85 lipid species that showed reciprocal changes. These lipids were largely decreased at Day 21 compared to baseline and increased to Day 42 (n=81). Not surprisingly, lipid species comprised of saturated fatty acids fell following the PUFA diet and rose following the CHO diet.

Lipid change rapidly after 21 days following either diet with 52 of 128 lipids (41%) changing after 2 days of PUFA and 93 of 145 (64%) changing after 2 days of CHO diets ('Fast", Figure 2.1C). LPC and LPEs composed of polyunsaturated fatty acids showed a slower change following PUFA diet but was rapid after a CHO diet. This is likely due to the greater variety of fatty acids entering the pool following PUFA as compared to relatively restricted fatty acid species (saturated and monounsaturated fatty acid) in the CHO dietary period. Plasmalogens also showed relatively slow changes following dietary change (Figure 2.1A). Finally, we note that the TGs with lipids containing fatty acids with the longest chains and most double bonds showed significant increases 2 days following consumption of either the PUFA or CHO diet, but rapidly returned to baseline and mostly did not differ between the diets at 21 days.

To identify lipids that could potentially discriminate macronutrient intake, we assessed the differences in the levels of lipids at each time point following dietary changes (Figure 2.1B & Tables S2 to 2.S2.4). Approximately 200 lipids at each time point showed differential expression but distinct patterns appear. Plasmenyl-PCs and plasmenyl-PEs stood out, showing significant differences at day 2, with only a subset showing differences between , suggesting that these

lipids, which are primarily found in membranes (43-45), adapt to dietary changes (Figure 2.1 & Tables S2 to 2.S2.4). This is similar to the pattern seen in TG with long chain polyunsaturated fatty acid, described above. Approximately half of the lipid species (218) were not significantly different between PUFA and CHO at any time point (Tables S2 to 2.S2.4), suggesting that these lipids turn over slowly, have high variability or may be under control.

MEAL Study

The high polyunsaturated fatty acid diet allowed us to assess lipid turnover and showed a rapid divergence in the levels of lipid species (Figure 2.1 & Tables S2A to 2.S2.4A). However, the polyunsaturated fatty acid levels used in the PUFA/CHO study were more abundant than in the typical ranges consumed in US adults. The metabolites which show differences may not be useful to objectively assess macronutrient intake in a population consuming lower amounts of polyunsaturated fatty acids. For this reason, we performed a second controlled feeding study to assess the effect of a more representative mixture of fatty acid intake in 12 men and 12 women (data from one woman was dropped due to admission of dietary non-adherence) using a different feeding paradigm (Figure S2).

Age, weight change, caloric intake, BMI, total mass, and DEXA measurements did not reach statistical difference between groups ($p<0.05$). Energy consumed was similar between both study groups. Study participants weight was stable during the 24-day feeding study, showing less than 1 kg in weight change from baseline.

In plasma samples, 571 lipids were identified. At Baseline and after Standard Diet, no significant differences were seen in the lipidome between the individuals randomized to either HF or HC

diets (Figure 2.2B, Tables S2.3 – S2.5). As was the goal, the metabolite variability decreased from Baseline to Standard Diet (Figure 2.2D).

There were very few statistically significant changes within each group following either the HF or HC interventions (Figure 2.2A, Tables 2.S2.5 to 2.S2.7). These results were expected because the HF, compared to the PUFA diet did not supply large amounts of PUFA to the lipidome. When CHO diet group was compared to the PUFA diet group here were significant changes in the levels of lipids species between groups (Figure 2.2B, Tables 2.S2.5 to 2.S2.7). At Day 2, 22 lipids were differential in their plasma concentrations, and this increased to 58 lipids showing expression changes by Day 21 (Figure 2.2B, Tables 2.S2.5 to 2.S2.7). As with the PUFA/CHO study, at day 7 there appears to be an adaptation to diet change as only 5 lipids are differentially expressed. As seen in the PUFA/CHO results, the differentially expressed lipids were enriched in O-PCs, O-PEs as well as SM and TGs with Cer species showing differential expression in the MEAL study group.

Identification of lipids that discriminate dietary intake:

As described in methods, we identified a subset of 54 initial sentinel lipids that fulfilled the criteria of significant change in any experimental time point in both the PUFA/CHO and MEAL study, of those we used the 12 with the highest selection frequency to discriminate between high fat and high carbohydrate diets as sentinel lipids. In order to show the ability of these sentinel lipids (Figure 2.4) to predict unknown diets, we classified all samples from both diets as either high fat (PUFA & HF) or high carbohydrate (CHO & HC).

ROC curves were generated from all experimental days of the PUFA/CHO and MEAL studies (days 2, 7, 14, & 21). Using the 12 sentinel lipids, ROC area under the curve was estimated to be 0.873, which indicates excellent discrimination (Figure 2.4A). Of 70 HC subjects, 55 were classified as high carb which produced a sensitivity of 0.753 (0.639 – 0.847) while 59 of the 77 high fat subjects were classified as which is a specificity of 0.797 (0.688 – 0.882) (Figure 5C & D). Predictive accuracy was also determined to be excellent at 0.776 (0.699 – 0.840) (Figure 2.4D). To illustrate that this score was similar during all experimental days, AUC's from ROCs were calculated by day x diet (Figure 2.4C) and were comparable to the overall ROC. This indicates that these sentinel lipids may be relatively agnostic to short-term dietary changes.

Next to further illustrate the power of the sentinel lipids to separate HC and HF diets, principal component analysis (PCA) was performed on both the PUFA/CHO diet and the MEAL diet separately. PC1 vs PC2 graphs on the PUFA/CHO illustrate separation which is most clear after day 2 and may diminish slightly by day 21 (Figure S2.3). This pattern is similar in the MEAL study, but PCA analysis also included baseline and standard measurements (day -3 and day 0) which shows no separation, followed by clear separation on days 2 through 21 (Figure S2.3).

Testing Sentinel Lipids using the Community Study

Finally, to test and demonstrate the predictive power of the sentinel lipids on a "real world" population we used the biomarker analysis on the subjects from the Community study. Lipidomics analysis from this group identified 527 lipid species. The 102 individuals (Table 2.1A) provided diet journals over 7 consecutive days and average ratio of carbohydrate to fat was calculated (Table 2.1B) (see methods). These values were then regressed with predictive probabilities generated using the sentinel lipids and resultant assigned class scores (either HC or HF) (Figure 2.6). When compared to the reported CHO/FAT ratio of these test subjects (n=102),

linear regression showed linearity and a significant negative slope ($p<0.05$) which is indicative of correct predictions (Figure 2.6). This is despite the narrow range of reported dietary intake that is closer to the standard diet than to the HC or HF diets (Figure 2.6).

Discussion

Dynamic response of the lipidome to diet:

Food provides a complex mixture of organic and inorganic materials that are digested into constituent metabolites, exposing cells to a constant supply of nutrients. Alterations in the ability to effectively metabolize ingested nutrients can lead to a wide variety of diseases. Indeed, diet is likely the primary environmental factor in gene-environment interactions that increases risk of the major diseases of modern times (47). Allelic variations across the genome are associated with changes in an array of blood metabolites and contribute to variation in the metabolome (48) as well as a proportion the risk attributable for different diseases (49). As accumulating evidence demonstrates that blood metabolite levels can potentially enhance the prediction of a variety of diseases (50-53), determining the effect of diet on metabolites is a necessary step in order to disentangle diet and genetics while moving towards individualized intervention with diet therapy.

Effects of a standard diet:

It is important to note that the MEAL study utilized a standard diet, while the PUFA/CHO study did not. In the MEAL study we found that the lipidome of subjects at baseline, entering the study on their habitual diets, were had more variability between subjects than after just 3 days of consuming a standard diet (Figure 2.5B). Winnike, Busby, Watkins, and O'Connell performed a similar study (n=10) and found normalization occurring in both urine and serum metabolomics

occurring after one day of a standardized diet (33). Similarly, Favé et al found that subjects fed a standardized meal the night before an experimental diet protocol clustered together when analyzed by PCA indicating a standardized diet is necessary and sufficient to draw subject's metabolomes together at the beginning of a feeding study (54). Our results are further supported by the lack of significant differences between HC and HF subjects at baseline and after the standard diet, but many differences after just two days of experimental diets (Figure 2.2). Our results, along with those of Winnike and Favé highlight the importance of a standard diet to "wash out" lipid differences in plasma between subjects and normalize all subjects lipidome profiles at the beginning of feeding studies (33, 54).

Adaptive response of the lipidome after a diet change:

Plasma lipidomics appear to be a useful platform to classify individuals according to their relative intake of carbohydrates and fat, irrespective of the amount of polyunsaturated fatty acids in the diet. While the lipidome is diverse, polyunsaturated fatty acids are derived from dietary intake while saturated and monounsaturated fatty acids and others are derived from both dietary and endogenous production through de novo lipogenesis. Through the administration of a very high polyunsaturated fat diet, induced changes in about 30% of lipids after two days (Figure 3.1A, Tables 3.S2 to S2.4). There is adaptation to the high PUFA diet with as about a 1/3 of lipids which were significantly changed after Day 2 of PUFA were not different at Day 21. This indicates a homeostatic adaptive response to high PUFA intake. This indicates a homeostatic adaptive response to high PUFA intake. This may be due to reduction in elongase and desaturase enzyme activity which are regulated transcriptionally by carbohydrate-responsive element-

binding protein (ChREBP) (55, 56) liver X receptor α (LXRα) (57) and sterol regulator element-binding proteins 1c (SREBP-1c) (58), each of which are suppressed following high fat feeding.

The adaptive response pattern seen in lipids could potentially be due to a lagged increase in SCD-1 activity. SCD-1 is an endoplasmic reticulum enzyme that catalyzes one of the rate limiting steps in the formation of monounsaturated fatty acids such as oleate (FFA 18:1) and palmitoleate (FFA 16:1) from 18:0-CoA and 18:1-CoA (59, 60). SCD-1 is necessary for endogenous MUFA synthesis from saturated fatty acids (61). Increased SCD-1 and de novo lipogenesis activity has been associated with high carbohydrate diets, such as the HC and CHO diets in the MEAL and PUFA/CHO studies (62-64) whereas high PUFA diets are associated with suppression of the transcription of the SCD-1 gene (64). This PUFA intake mediated repression of hepatic SCD1 and MUFA synthesis may have evolved as a mechanism to maintain cellular unsaturated fatty acid balance (63). Additionally, diets high in cholesterol upregulate SREBP-1c expression that overrides the PUFA mediated SCD-1 suppression (58). It is also been shown that, in humans, a high carbohydrate diet will increase free fatty acid synthesis (65), potentially through an increase in SCD-1 activity and increased insulin (62, 63). One possibility for the adaptive response pattern that we are seeing in lipids (Figures 1 & 2) is due to an acute increase in SCD-1 that is blunted over longer-term high fat/high carbohydrate feedings.

The significant rise in longer, polyunsaturated fatty acid containing lipid species after Day 2 of CHO diet in DG and TG could be due to several reasons: increased oxidation of carbohydrate with sparing of fatty acid oxidation (66), rapid induction of elongases and desaturases (67), and an increase in the levels of shorter chain, saturated and monounsaturated derived from de novo lipogenesis, competing for oxidation of polyunsaturated fatty acids (68). The amount of lipids produced by hepatic de novo lipogenesis may also be playing a role in the rise we see in PUFA

containing lipid species; Wilke et al. (69) found that after a 3-day higher-fat diet, healthy subjects had higher rates of de novo lipogenesis than those on a lower-fat diet.

Differences between dynamic responses in the PUFA/CHO and MEAL studies:

The MEAL study showed a smaller number of significant changes to the overall metabolome within each diet group (Figure 1A & 1C). However, as seen in the PUFA/CHO diet, there were more lipids significantly different at day 2 than at day 7 (Figure 2B), again suggesting an adaptation to the diet in these individuals. Another feeding study has found a similar adaptive response in sterols and DGs (36) while we found it other species as well. The MEAL study perhaps identified more adaptive responsive lipids because we collected plasma in much smaller intervals (2 days, 7 days, 14 days, & 21 days) while the former study was collected 5 weeks apart

Discriminatory power of the sentinel lipids:

We identified a small subset of the lipids that showed the ability to classify the individuals consuming high fat or high carbohydrate diet (Figure 2.3 & 2.44). These sentinel lipids were primarily composed of phosphatidylcholines, and ethanolamine-containing plasmalogens (Figure 2.3). The discriminating sentinel lipids tended to change slower and in general, increased following a high carbohydrate diet, despite the fact that most of them showed increased unsaturation in their fatty acid side chains. Within class, the lipids tended to be correlated across subjects and time (Figure S2.4), but across classes, there was lower correlation.

Plasmalogens are a major subclass of choline and ethanolamine glycerophospholipids that have a long chain fatty alcohol attached at the sn-1 position through a vinyl ether bond. These lipids can compose up to 20% of lipids in plasma membranes (44, 45) and are ascribed to act as antioxidants (43). Ethanolamine-containing plasmalogens (PlsEth) have other activities. These

lipids are synthesized initially in peroxisomes with the final, rate-limiting step is by the enzyme Fatty Acid Synthase 1 (Far1) which attached to the outer membrane of the peroxisome. The levels of PlsEth in cells appear to be strictly regulated by modulating the stability of the rate-limiting enzyme Far1; low levels of PlsEth (but not choline containing plasmalogens (PlsCho) increase the stability of the Far1 protein and higher levels stimulation degradation of Far1 (70). PlsCho which are also increased following carbohydrate diets are thought to be synthesized through the hydrolysis of PlsEth and condensation of the alkenylglycerol with phosphocholine (43). The levels of PlsEth and PlsCho are highly correlated (Figure 2.S2.4). We speculate that in the presence of higher levels of saturated fatty acids in PlsEth synthesis may be increased as these lipids prefer polyunsaturated fatty acids in the sn2 positon of the lipid (71).

Another, non-physiological possibility is that subjects became less compliant in consuming the provided diets over the course of the study. Noncompliance in the MEAL diet is unlikely as we report in chapter 3 using dietary recall from this study; our data indicates that subjects were very compliant throughout the study.

Strengths/Limitations

This study has several strengths. First, we used state of the art high throughput targeted lipidomic techniques which provided an objective measure of lipidomic changes due to diet. Using 2 longitudinal well-controlled feeding studies elucidates dynamic changes in the lipidome due to high fat and high carbohydrate diet. Further, the use of a 3-day standard diet in the MEAL study demonstrated the rapid change in the lipidome due to diet and convergence of the lipidomes of our participants. Unsupervised machine learning techniques allow for unbiased prediction of as well as identification of biomarkers of dietary intake. Finally, use of the Community study which

relied upon 7-day dietary diaries provides insight into the value of our sentinel lipids for identifying macronutrient intake in free-living populations.

Findings also must be interpreted in light of certain limitations. First, we used extreme test diets which provided ~+/-3SD carbohydrate and fat intake compared to adults' dietary intake reported in NHANES (46). While the experimental protocol produced a set of lipids that discriminated between the test diets, our assessment was based on the dietary recall of these participants. Future tests on diets which are less extreme and closer approximate the reported habitual intake of the population by NHANES should be conducted to probe and hone the discriminatory ability of the sentinel lipids to identify macronutrient intake.

Secondly, the populations used in this study were fairly small. Further testing with larger populations could inform the generalization of these findings to the population as a whole. Also, these controlled feeding studies and Community group were conducted in healthy, mainly Caucasian individuals, but did include both women and men. Confirmation of the performance of the sentinel lipids to identify macronutrient intake will need to be done in populations with more diversity in terms of age, ethnicity, and health status. . Finally, protein levels were held constant when deriving the sentinel lipids. The average protein intake reported in the Community study was similar the PUFA/CHO and MEAL studies, but had a much larger standard deviation. (Table 2.1B). Perhaps better discriminators may be identified in controlled feeding studies across a broader range of protein intake.

Conclusions

In our studies, the lipidome was highly responsive to diet with but is also able to adapt to significant increases in fatty acid and carbohydrate intake (Figures 1 & 2). This suggests that using lipidomics profiles to assess individual differences in metabolism not directly related to

diet, it may be prudent use a short intervention with a standard diet to achieve greater homogeneity in the lipidome prior to initiating the study and to keep the diet consistent during the study. These caveats should be added to circadian changes in the lipidome (72) in designing lipidomics studies. Finally, we developed a panel of “sentinel” lipids and in particular, a subset of 12 lipids that do an excellent job of discriminating between very high fat and very high carbohydrate diets (Figure 3).

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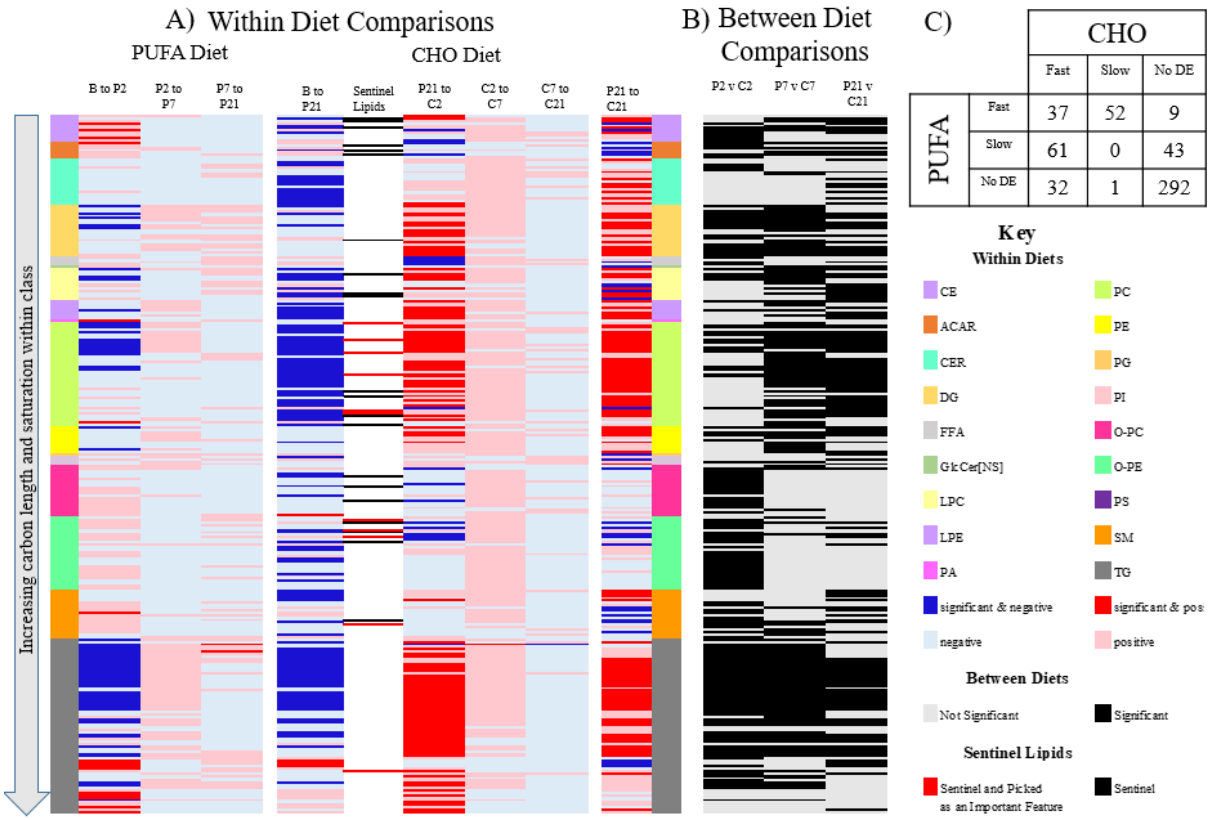
2) The Dr. Robert C. and Veronica Atkins Foundation
3) Michigan Clinical Research Unit supported by grant UL1TR002240
4) MNORC: This work utilized Core Services supported by grant DK089503 of NIH to the University of Michigan.

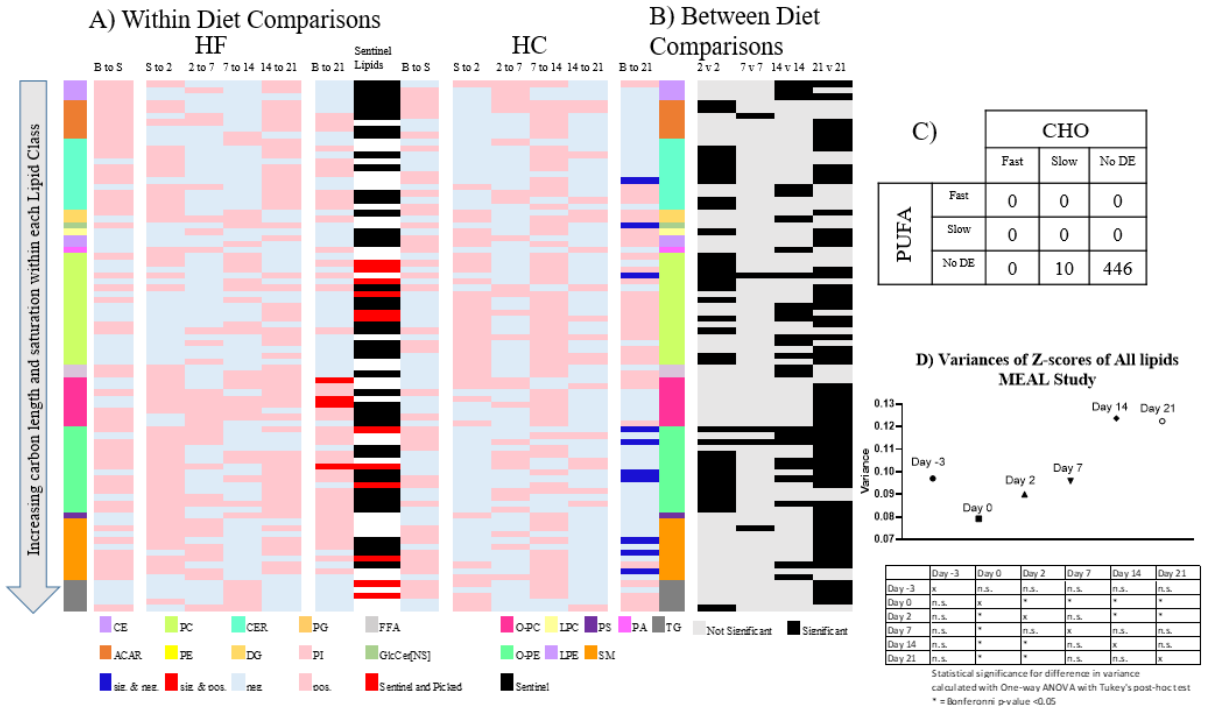
Tables and Figures:

Figure 2.1*(A-C). PUFA/CHO study Log2 differences within and between diet comparisons.*



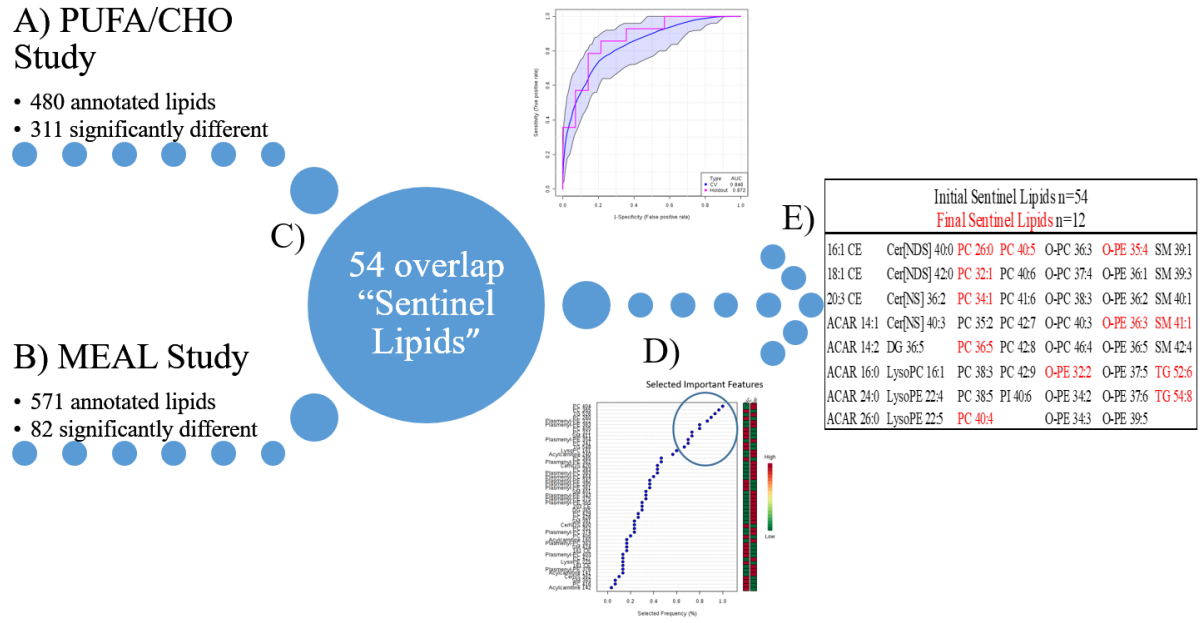
Here we show only lipids significant within or between diets at any time point. Lipids are organized from the top to bottom from shortest chain length and most saturated to longest chain length and least saturated within each lipid class. A) Data represented as Log2 difference of area under the curve (AUC) within each diet. For PUFA this is in the time course between Baseline (B) to day 2 PUFA diet (P2), P2 to P7, P7 to P21, & B to P21 that represents the total change during the course of the PUFA diet. This pattern repeated for the CHO diet starting with P21 (P21 to C2, C2 to C7, C7 to C21, & P21 to C21). Light blue represents a decrease and pink an increase, dark blue and red are significant (FDR <0.1). Black bars between PUFA and CHO data indicate Sentinel Lipids with red indicating Sentinel Lipids chosen as the 12 Selected Important Features by SVM ROC analysis. B) Black is significant (FDR <0.1) between PUFA and CHO at corresponding diet days (P2 v C2, P7 v C7, and P21 v C21). Grey is not significant. C) This matrix is representative of the rapidity of significant lipid changes. Fast is a significant change at day 2 PUFA or CHO and a significant difference at B to P21 or P21 to C21. Slow is a significant change at day 21 and again at B to P21 or P21 to C21. No dietary effect (No DE) is representative of no significant change at B to P21 or P21 to C21.

***Figure 2.2(A-D)**. MEAL study Log2 differences within and between diet comparisons.*



Here we show only lipids significant within or between diets at any time point. Lipids are organized from the top to bottom from shortest chain length and most saturated to longest chain length and least saturated within each lipid class. A) Data represented as Log2 difference of area under the curve (AUC) within each diet. On the left are subjects on the HF diet from B to S, S to 2, 2 to 7, 7 to 14, 14 to 21, & B to 21 that represents the total difference during the experimental diet. This pattern repeats for the HC. Light blue represents a decrease and pink an increase, dark blue and red are significant (FDR <0.1). Black bars between HF and HC data indicate Sentinel Lipids with red indicating Sentinel Lipids chosen as the 12 Selected Important Features by SVM ROC analysis. B) Black is significant (FDR <0.1) between PUFA and CHO at corresponding diet days (2v2, 7v7, 14v14, and 21v21). Grey is not significant. C) This matrix is representative of the rapidity of significant lipid changes. Fast is a significant change at day 2 HF or HC and a significant difference at B to 21 in each diet. Slow is a significant change at day 21 and again at B to 21. No dietary effect (No DE) is representative of no significant change at B to 21. D) Variances were computed for all lipid measures in both groups at each experimental day, ANOVA with a Tukey's post-hoc assessment indicated significant differences ($p<0.05$).

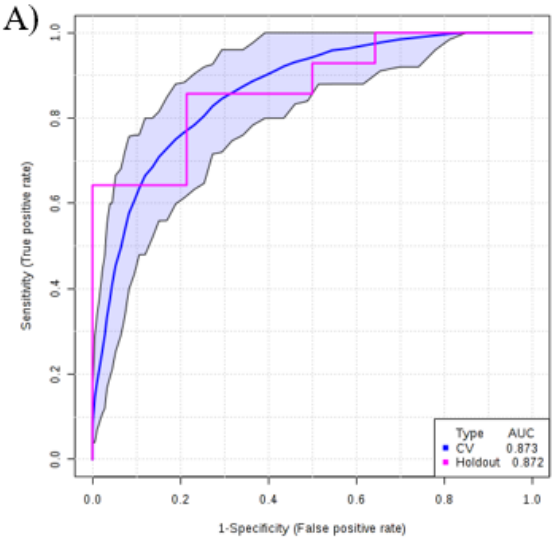
Figure 2.3 *(A-E) Description of determination of Sentinel Lipids*



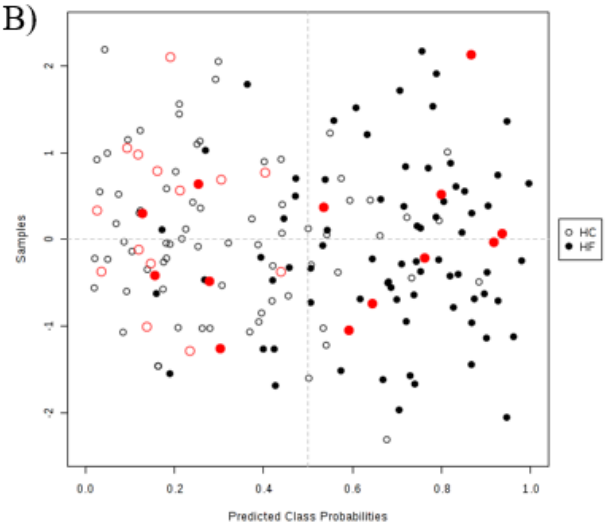
Sentinel lipids were determined using the following method. A) 480 annotated in lipids in the PUFA/CHO study were compared and 311 which were significantly different at any experimental time point (P2, P7, P21, C2, C7, or C21) between PUFA and CHO diets. B) 571 annotated lipids in the MEAL study compared and 82 were significantly different at any experimental time point (2, 7, 14, or 21). (FDR <0.1). C) Of the significantly different lipids, 54 overlapped between studies and selected as Sentinel Lipids. D) SVM machine learning used as a classification method using the sentinel lipids. There was a natural break point above the 60% selection criterion with 12 were chosen as E) 54 initial sentinel lipids with lipids highlighted in red determined to be discriminating sentinel lipids.

Figure 2.4 (A-D). ROC analysis using Sentinel Lipids on the MEAL and PUFA dataset.

A)



B)



C)

AUC of ROC By Day:
Day 2 – 0.803 (0.589 – 0.938)
Day 7 – 0.838 (0.577 – 1.0)
Day 21 – 0.781 (0.675 – 0.887)

D) Training Samples

Actual \ Predictions	HC	HF
HC	55	15
HF	18	59

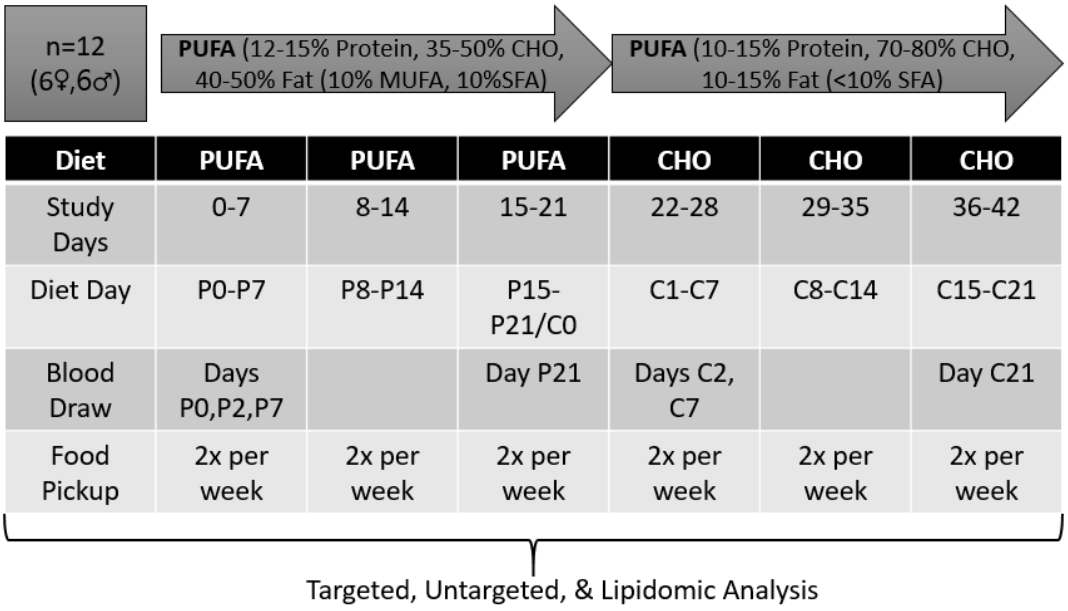
Holdout Samples

Actual \ Predictions	HC	HF
HC	14	4
HF	0	10

	Training Samples	Holdout Samples
Sensitivity =	0.753 (0.639-0.847)	1.0 (0.768 – 1.0)
Specificity =	0.797 (0.688-0.882)	0.714 (0.419 - 0.916)
Accuracy =	0.776 (0.699-0.840)	0.857 (0.673 - 0.960)

A) ROC graph plotting sensitivity (true positive rate) against 1-specificity (false positive rate) for PUFA/CHO and MEAL samples (blue line). AUC indicated as 0.873 which indicates excellent discrimination by the 12 Selected Important Features from the Sentinel Lipids. This data also includes 14 randomly selected and balanced holdout samples for validation (purple line) which had a comparable AUC of 0.872. B) Shows predicted class probabilities for each sample (black filled circles are HF and open are HC) using 12 Selected Important Features. Red circles are holdout samples. C) AUCs from ROC analysis for each day shows good discrimination by day and as such identifies these features as agnostic by day. D) Confusion matrices for training and holdout samples along with sensitivity, specificity, and accuracy calculations.

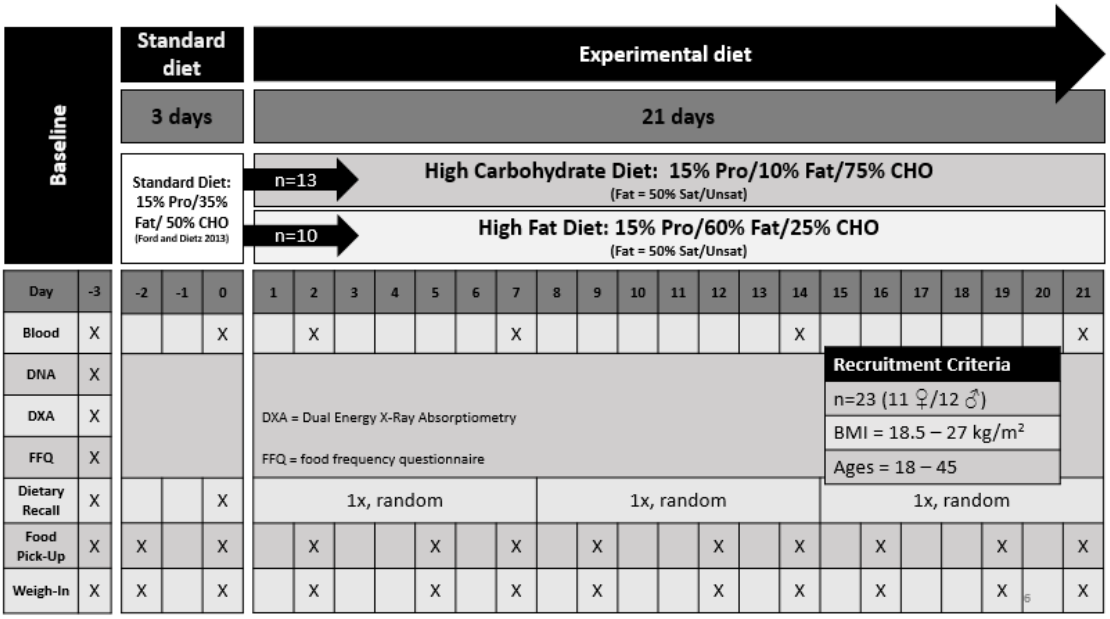
Figure S2.1. Study design for the PUFA/CHO Study



Diet	PUFA	PUFA	PUFA	CHO	CHO	CHO
Study Days	0-7	8-14	15-21	22-28	29-35	36-42
Diet Day	P0-P7	P8-P14	P15-P21/C0	C1-C7	C8-C14	C15-C21
Blood Draw	Days P0,P2,P7		Day P21	Days C2, C7		Day C21
Food Pickup	2x per week	2x per week	2x per week	2x per week	2x per week	2x per week

The PUFA/CHO study was a 42-day longitudinal paired study design without crossover involving 12 subjects (6♀, 6♂). A high polyunsaturated diet provided for the first 21 days immediately followed by 21 days of a high carbohydrate diet. Days labeled as P0, P2, P7, P21, C2, C7, & C21.

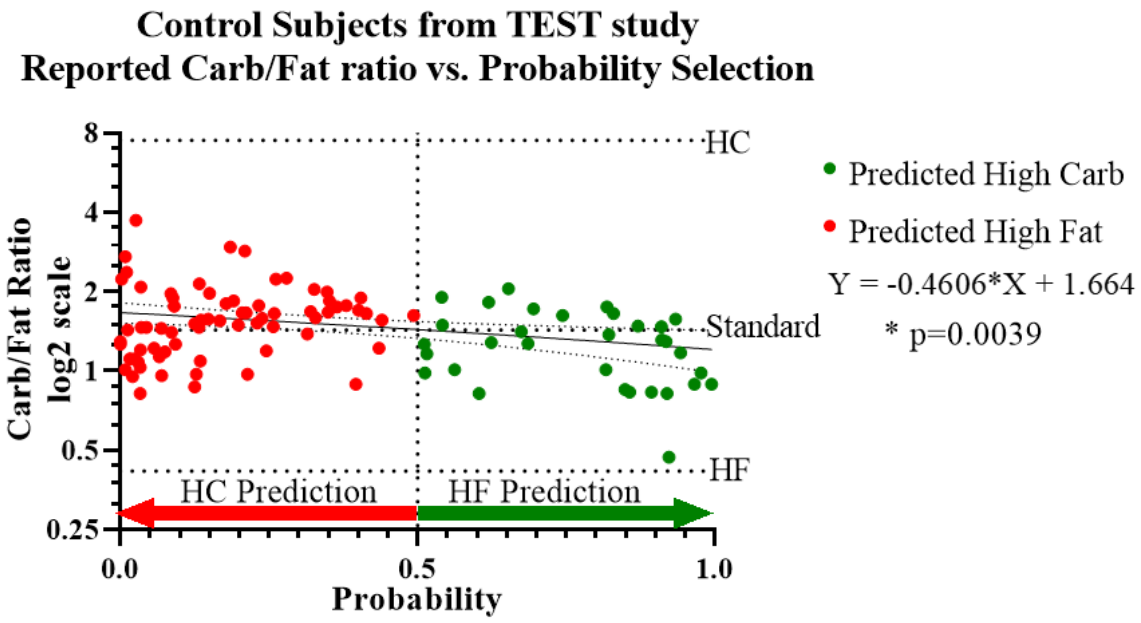
Figure S2.2 Study design for the MEAL Study



Day	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Blood	X			X		X					X							X							X
DNA	X																								
DXA	X																								
FFQ	X																								
Dietary Recall	X			X	1x, random							1x, random							1x, random						
Food Pick-Up	X	X		X		X			X		X		X			X		X		X			X		X
Weigh-In	X	X		X		X			X		X		X			X		X		X			X		X

The MEAL study followed a parallel-randomized block study design blocked by sex. It involved a cohort of 23 subjects (11♀, 12♂). The first 3 days subjects were given a standard diet (15% Protein/35% Fat/50% Carbohydrate) which was followed by 21 days of either a high carbohydrate (15% Protein/10% Fat/75% Carbohydrate) or high fat diet (15% Protein/60% Fat/25% Carbohydrate). Blood was drawn for plasma on days -3 (B), 0 (STD), 2, 7, 14, & 21. 24HR recalls were given on days -3, 0, and once per week during the experimental diet. On the first day, written and oral consent, DNA, height & weight, and an FFQ was also collected. Subjects picked up food and weighed in every 2-4 days throughout the study.

Figure 2.5. Predicted carbohydrate/fat ratios from TEST study subjects using the "Sentinel Lipids"

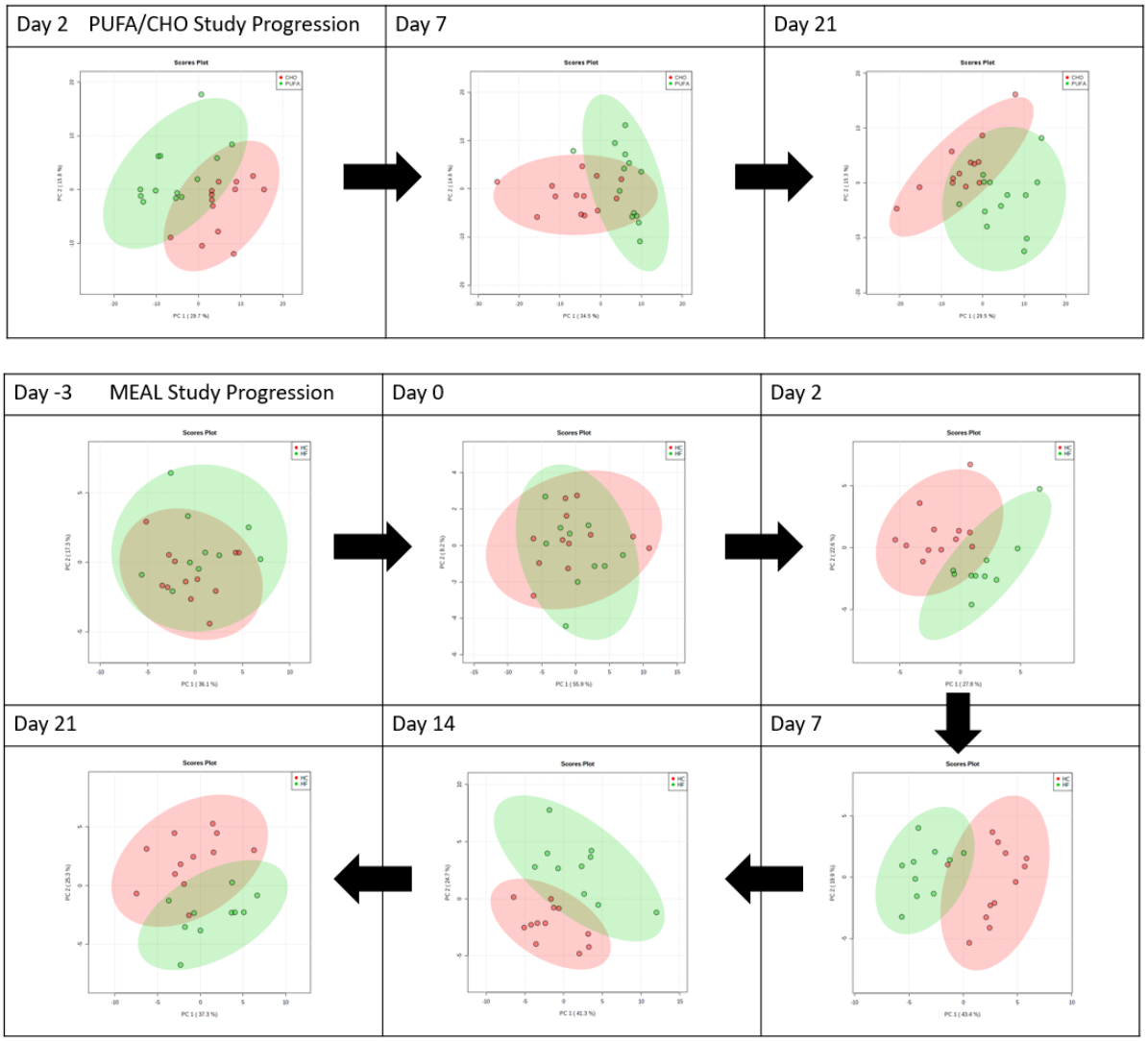


Subject predicted class (either HC or HF) using SVM based on 12 highest selected important features from the Sentinel lipids to predict plasma samples as either high carb (red) or high fat (green). A score of 0.0 to 0.5 is indicative of a high carbohydrate prediction and a score of 0.5 to 1.0 is indicative of high fat. Values closer to 0.5 are less confident than those that are closer to 0.0 and 1.0. The Y-axis indicates the average carbohydrate percentage to fat percentage ratio reported by these subjects in seven dietary journals on consecutive days. The dashed lines labeled HC, Standard, and HF are there to reference the carbohydrate/fat ratios in the MEAL study HC = 7.5, Standard = 1.43, and HF = 0.42. The linear regression line formula is indicated on the right and the p value is significant for deviance from a slope of zero indicating that there is a significant relationship between lower Carb/Fat ratio and higher probability scores ($p<0.05$).

Table 2.1A. Subject characteristics for A) PUFA/CHO, B) MEAL, and C) Community studies				
	A) PUFA/CHO Study	B) MEAL Study		C) TEST Study
n=	12	HF n=10	HC n=13	102 (59 BP, 46 controls)
Sex distribution	6 ♀, 6 ♂	5 ♂,6 ♀	7 ♂,6 ♀	41 ♂,61 ♀
Age in yrs. (SD)	28.2(5.8)	23.9 (2.6)	24.9 (4.0)	*44.1(14.1)
Weight Change (Δkg)	-0.8 (1.2)	0.30 (0.9)	-0.05 (1.0)	N/A
Caloric Intake (kCal/day)	2687 (676.8)	2740 (502.2)	2825 (521.4)	2024.4 (638.5)
BMI kg/m2	24.5(4.2)	23.2 (3.1)	23.1(2.8)	26.3(4.7)
All subject characteristic represented as average (SD). Caloric intake for PUFA/CHO studies were amount of kCal food provided and Community study was average kCal/day reported via food journals. * = $p<0.05$ for significance between studies using ANOVA with Tukey's post hoc analysis.				

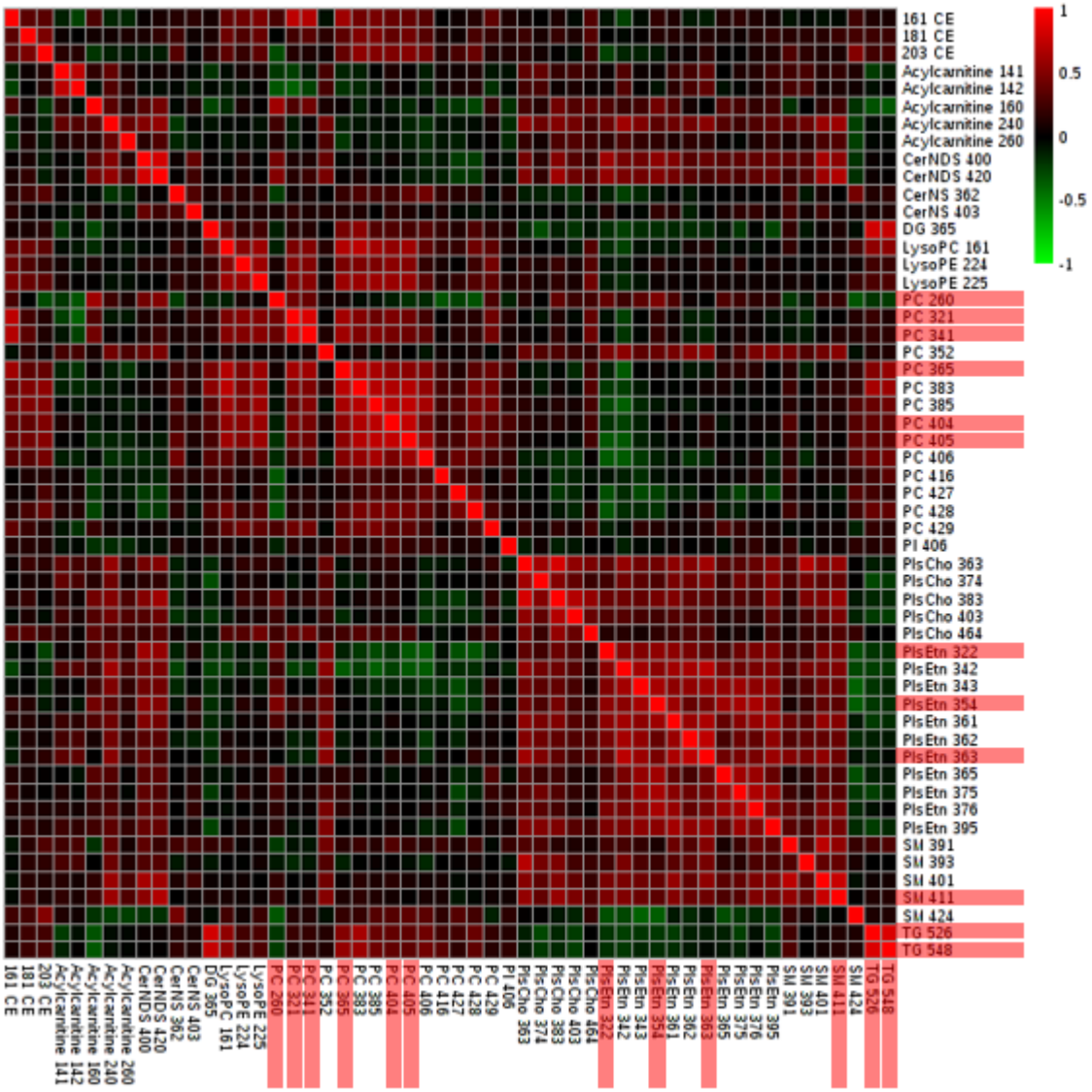
Table 2.1B. Community study mean reported macronutrient intake		
Dietary Data	Reported intake from 7 consecutive food journals as % of total energy, mean (SD)	
	Total Protein	15.5(3.2)
	Total Carb	48.6(8.6)
	Total Fat	33.6(6.4)
	Total Calories	2024.4 (638.5)
Data represented as average percent data reported in 7 consecutive food journals (SD).		

Figure S2.3. PCA plots showing discrimination of Sentinel lipids by day in PUFA/CHO and MEAL studies.



PCA analysis of all 54 sentinel lipids during the time course of PUFA/CHO (top) and MEAL (bottom) studies. In these graphs green circles represent PUFA/HF and red represent CHO/HC with 95% confidence intervals represented by the large green and red ovals. This graphs primary component 1 (PC1) vs primary component 2 (PC2). Discrimination is nearly immediate and persistent in PUFA/CHO while discrimination occurs after the beginning of the experimental diet in MEAL.

Figure S2.4. Correlation heat map of 54 Sentinel Lipids.



Correlation heat map of 54 Sentinel Lipids with the range of correlation running from Red = 1.0 to Green -1.0. Important Selected Features are highlighted in light red. This shows that many of these lipids are very highly correlated with clusters appearing in the Plasmalogens and PCs.

Table S2.1. Annotated lipids in PUFA/CHO, MEAL, and TEST studies.

Lipid Species		PUFA/CHO Study		MEAL Study		TEST Study	
Class Name	Abbreviation	Species, n=	Range of Species	Species, n=	Range of Species	Species, n=	Range of Species
Cholesteryl Ester	CE	12	[16:0] to [22:6]	12	[16:0] to [22:6]	15	[16:0] to [22:6]
Acylcarnitine	ACAR	12	[10:0] to [26:0]	13	[10:0] to [26:0]	13	[10:0] to [24:0]
Ceramide [AS]	Cer [AS]	1	[34:1]	2	[34:1] to [42:2]	1	[34:1]
Ceramide [ADS]	Cer [ADS]	0	--	0	--	1	[38:0]
Ceramide [EODS]	Cer [EODS]	1	[58:0]	3	[57:2] to [60:0]	4	[57:1] to [59:2]
Ceramide [NDS]	Cer [NDS]	6	[34:0] to [42:1]	10	[34:0] to [43:0]	7	[34:0] to [42:1]
Ceramide [NP]	Cer [NP]	3	[34:0] to [42:1]	6	[34:0] to [42:1]	2	[34:0] to [42:0]
Ceramide [NS]	Cer [NS]	21	[32:1] to [43:2]	28	[32:1] to [46:5]	23	[32:1] to [45:1]
Diacylglycerol	DG	27	[30:0] to [40:7]	28	[30:0] to [40:7]	36	[30:0] to [42:0]
Free Fatty Acids	FFA	16	[16:0] to [24:3]	16	[16:0] to [24:3]	16	[16:0] to [24:3]
Glucoceramide [NS]	GluCer[AS]	6	[34:1] to [42:2]	6	[34:1] to [42:2]	5	[34:1] to [42:1]
Lysophosphatidylcholine	LPC	26	[14:0] to [26:1]	26	[14:0] to [26:1]	26	[14:0] to [24:1]
Lysophosphatidylethanolamine	LPE	10	[16:0] to [22:6]	15	[16:0] to [24:0]	11	[16:0] to [22:6]
Phosphatidic Acid	PA	1	[34:2]	7	[34:1] to [38:6]	0	--
Phostphatidylecholine	PC	73	[26:0] to [44:4]	86	[24:0] to [46:4]	79	[26:0] to [44:4]
Phosphatidylethanolamine	PE	29	[32:1] to [40:8]	34	[30:0] to [42:10]	23	[30:0] to [40:7]
Phophatidylglycerol	PG	5	[33:0] to [36:3]	7	[33:0] to [38:4]	2	[33:0] to [36:0]
Phostphatidylinositol	PI	9	[34:2] to [40:6]	12	[25:0] to [40:6]	9	[32:1] to [38:6]
Plasmenyl-phosphatidylcholine	PlsCho	47	[24:0] to [46:4]	52	[24:0] to [46:4]	51	[24:0] to [46:4]
Plasmenyl-phosphatidylethanolamine	PlsEtn	39	[32:1] to [44:6]	47	[32:0] to [44:6]	34	[32:1] to [42:6]
Phosphatidylserine	PS	0	--	2	[36:1] to [38:4]	5	[34:0] to [40:6]
Sphingomyelin	SM	51	[30:0] to [44:6]	52	[30:1] to [45:7]	64	[28:1] to [46:7]
Triacylglycerol	TG	85	[38:0] to [60:12]	107	[36:0] to [62:12]	100	[36:0] to [64:17]
Total	--	480	--	571	--	527	--

This table represents all lipids annotated in each study. Data represented as number of lipids and the range of lipid species from shortest chain length to longest.

Table S2.2A: PUFA/CHO study significant differences for within and between diet comparisons for all lipids (16:0 Cholesterol ester to Ceramide [NS] 42:1)

	Mean Log2 AUC Values For Each Lipid Species						
		PUFA Diet			CHO Diet		
Lipid/Day	Baseline	P2	P7	P21	C2	C7	C21
16:0 CE	15.4341	15.5099	15.7852	15.5495	15.4463	15.2095	15.3436
16:1 CE	13.4622	13.1963	13.4501	13.2436	13.5638	13.2153	14.1224
18:0 CE	14.4033	14.1994	14.5798	14.2584	14.3243	14.3748	14.2262
18:1 CE	18.1682	18.0362	18.2756	18.0411	18.2224	18.1644	18.2224
18:2 CE	21.0659	21.0790	21.1136	21.1332	21.0205	21.0942	21.0999
18:3 CE	18.3468	18.0519	18.2255	18.2713	18.3171	18.2798	18.1504
20:3 CE	18.0490	17.9988	17.8033	17.8057	18.0321	17.9513	18.0754
20:4 CE	20.1003	20.5156	20.0205	20.1046	20.2032	20.0714	19.9252
20:5 CE	16.8851	17.0804	16.3761	16.2744	16.5337	16.8252	16.1858
22:4 CE	14.1059	14.4420	14.0699	13.9857	14.2339	13.9640	14.1167
22:5 CE	15.1060	15.4812	15.0179	14.8508	15.1790	15.1154	15.0836
22:6 CE	18.3000	18.6137	18.2404	18.2098	18.3862	18.3475	18.1653
ACAR 10:0	13.3492	13.0555	12.6641	13.1027	13.0142	13.1392	13.3443
ACAR 10:1	12.4621	12.3978	12.3553	12.8495	12.3441	12.2360	12.5165
ACAR 12:0	13.4597	12.8835	13.2838	13.5791	13.2436	13.0980	13.3251
ACAR 14:0	13.6567	13.0695	13.1503	13.7341	13.2551	13.2594	13.5408
ACAR 14:1	14.5802	14.0114	14.3027	14.7991	14.2620	14.2828	14.7164
ACAR 14:2	13.7877	13.1589	13.6134	14.4539	13.5136	13.6268	14.0939
ACAR 16:0	15.9190	15.3644	15.6543	15.6912	15.4559	15.4752	15.8242
ACAR 18:0	14.4009	13.9119	14.2122	14.3708	14.1983	14.3267	14.0926
ACAR 18:1	16.4888	16.2522	16.3722	16.5541	16.1309	16.1114	16.6379
ACAR 18:2	16.2886	16.1841	16.2509	16.7773	16.0873	16.1903	16.3747
ACAR 24:0	12.9768	11.9392	12.8535	12.9467	12.6737	12.6354	12.7412
ACAR 26:0	12.5097	12.0304	12.1837	12.9665	12.2561	12.2207	12.4377
Cer[AS] 34:1	12.1429	12.3923	12.1703	12.2578	12.2568	12.4043	12.4281
Cer[EODS] 58:0	12.5432	12.4759	12.6235	12.2838	12.4834	12.3352	12.2244
Cer[NDS] 34:0	16.2186	16.2164	16.5037	16.2213	16.1882	16.1463	16.2273
Cer[NDS] 36:0	14.5785	14.9324	14.6831	13.5209	14.4791	14.3054	14.6443
Cer[NDS] 38:0	11.3980	10.9287	11.4542	10.9172	11.0821	10.9589	11.1524
Cer[NDS] 40:0	17.6723	17.0808	17.8786	17.1533	17.3668	17.2410	17.3893
Cer[NDS] 42:0	15.2266	14.7051	15.2587	14.9780	15.2252	14.9395	15.1202
Cer[NDS] 42:1	18.2605	17.7557	18.0587	18.0145	18.1130	18.0648	17.8975
Cer[NP] 34:0	12.7327	12.4515	12.9196	12.5704	12.3443	12.3841	12.1476
Cer[NP] 42:0	16.4170	15.7440	16.2909	16.1486	15.9742	15.9874	15.8973
Cer[NP] 42:1	15.8596	15.4965	16.0642	16.0975	15.8205	15.9111	15.8471
Cer[NS] 32:1	14.1568	13.6005	14.0239	13.5816	13.6823	13.9373	13.8792
Cer[NS] 33:1	15.1139	15.2099	15.3278	14.8350	14.9446	14.9790	15.0989
Cer[NS] 34:1	19.9253	19.9588	20.0006	20.0158	19.9226	19.8812	19.8991
Cer[NS] 34:2	14.4849	14.8935	14.4792	14.2698	14.1238	14.4146	14.3633
Cer[NS] 35:1	19.0252	19.0338	19.0905	19.0441	18.9710	19.0130	19.0533
Cer[NS] 36:1	16.7724	17.0696	16.6459	16.0937	16.5397	16.5156	16.6933
Cer[NS] 36:2	14.5995	15.2348	14.4772	14.0735	14.3792	14.4870	14.6963
Cer[NS] 37:1	15.4510	15.6329	15.3921	15.2814	15.3239	15.3442	15.4162
Cer[NS] 38:1	17.3338	17.0820	17.2101	16.8981	16.8598	16.7736	16.9323
Cer[NS] 38:2	14.7598	15.0067	14.5444	14.5557	14.5133	14.1064	14.6715
Cer[NS] 39:1	12.8768	12.6230	12.5998	12.7851	12.5197	12.7840	12.7912
Cer[NS] 40:1	16.6642	16.2094	16.4567	16.2758	16.3647	16.3525	16.2915
Cer[NS] 40:2	17.7241	17.3830	17.4973	17.4168	17.2645	17.2322	17.3459
Cer[NS] 40:3	13.6829	13.7548	13.5651	13.1585	13.6332	13.2209	13.6915
Cer[NS] 41:1	16.6771	16.1908	16.4428	16.3584	16.4581	16.4699	16.3503
Cer[NS] 41:2	18.1577	17.9501	17.9342	18.0924	17.9250	17.8002	17.9057
Cer[NS] 42:1	21.4834	20.9353	21.2748	21.2221	21.1871	21.0899	20.9374

Table S2.2B: PUFA/CHO study significant differences for within and between diet comparisons for all lipids (Ceramide [NS] 42:2 to Lysophosphatidylcholine 14:0)

	Mean Log2 AUC Values For Each Lipid Species						
		PUFA Diet			CHO Diet		
Lipid/Day	Baseline	P2	P7	P21	C2	C7	C21
Cer[NS] 42:2	17.3154	17.0444	17.1320	17.2326	17.1447	17.1647	17.2347
Cer[NS] 42:3	17.7285	17.7316	17.6075	17.7539	17.5323	17.3418	17.6770
Cer[NS] 43:1	18.9684	18.4032	18.7926	18.6924	18.7962	18.5572	18.3718
Cer[NS] 43:2	14.0785	13.7449	13.9592	13.9781	14.1602	13.7685	13.8595
DG 30:0	13.1456	12.6078	12.9096	12.7223	12.8453	12.9258	13.0172
DG 30:1	10.8027	9.8727	10.4568	10.5719	10.5194	10.4818	10.8858
DG 32:0	18.3548	18.3724	18.5016	18.4859	18.3525	18.3911	18.4662
DG 32:1	14.1418	13.0987	14.0251	13.5095	13.9429	13.7858	14.3001
DG 32:2	12.0332	11.7884	12.5106	11.6961	12.4983	12.0835	12.7990
DG 33:0	15.1634	15.1705	15.2236	15.2010	15.0911	15.1002	15.2224
DG 33:1	11.3827	10.6504	11.4196	11.1917	11.3222	11.3499	11.6308
DG 34:0	22.2416	22.0726	22.3208	22.3286	22.2157	22.2316	22.2377
DG 34:2	16.3911	16.3795	16.8596	16.4687	16.3158	15.9959	16.8878
DG 34:3	13.8543	13.7983	14.4027	13.7902	14.4188	13.9167	14.7210
DG 35:1	12.8067	12.4886	12.9097	12.1992	12.5293	12.7357	12.7513
DG 35:2	12.2221	11.5728	12.2875	11.7880	12.0023	12.1202	12.4838
DG 35:3	11.4645	11.1808	11.7142	10.9676	11.7710	11.5519	11.9856
DG 36:0	23.0698	22.7611	23.1701	23.2853	23.1233	23.0483	23.0481
DG 36:1	18.8686	18.7707	18.9332	18.9222	18.8580	18.8998	18.9221
DG 36:2	17.9225	17.6665	18.4194	17.8835	18.0510	17.9078	18.2765
DG 36:3	17.2988	17.2384	17.9473	17.5157	17.5399	17.2942	17.8374
DG 36:4	16.9750	17.0897	17.9237	17.5874	17.3750	17.1599	17.7618
DG 36:5	13.0643	13.0843	13.7410	13.4910	14.2018	13.8688	14.1233
DG 38:1	12.6731	12.4634	12.6901	12.5945	12.8263	12.6718	12.5583
DG 38:2	12.6710	12.3570	12.9418	12.1363	12.4954	12.6141	13.0524
DG 38:3	13.1480	12.9627	13.4374	13.4275	13.2561	13.0235	13.6431
DG 38:4	14.1693	13.8757	14.1547	14.0972	14.2772	13.6336	14.4653
DG 38:5	14.6116	14.6843	14.9398	14.6979	14.9319	14.3921	14.8455
DG 38:6	14.1889	14.2391	14.3746	14.1689	14.5744	14.2157	14.5162
DG 40:6	12.5704	12.1826	12.2839	11.9832	12.8109	12.3384	12.7313
DG 40:7	13.0335	13.0729	13.2232	13.1113	13.4019	13.3619	13.5097
FFA(16:0)	24.8597	24.8942	24.8068	24.7943	24.6327	24.6328	24.8653
FFA(18:0)	24.5469	24.4764	24.5286	24.5878	24.5271	24.4481	24.4301
FFA(18:1)	24.9922	25.0033	24.8083	24.6831	24.3854	24.5146	24.9970
FFA(18:2)	24.2924	24.5494	24.3168	24.2575	23.7622	24.0686	24.5303
FFA(20:0)	19.3237	19.2070	19.4400	19.4493	19.3125	19.2182	19.2533
FFA(20:1)	19.1763	19.1143	18.8347	18.9061	18.5502	18.6696	19.1888
FFA(20:2)	18.7766	18.9668	18.4873	18.6193	18.2770	18.3969	18.9922
FFA(20:4)	20.7488	20.6123	20.4927	20.2678	20.1834	20.1504	20.5579
FFA(22:0)	17.6006	17.3910	17.7405	17.7012	17.4381	17.4670	17.5666
FFA(22:1)	16.3341	16.0329	16.1076	16.4935	16.0711	16.0966	16.1950
FFA(22:2)	14.7002	14.5073	14.4822	14.4645	14.2886	14.2722	14.5835
FFA(22:3)	15.2519	15.1771	14.9000	15.1094	14.6603	14.6865	15.3224
FFA(24:0)	17.5507	17.4720	17.5282	17.5491	17.3030	17.5041	17.2704
FFA(24:1)	17.1782	17.0917	17.3669	17.3874	16.8594	16.9402	17.2385
FFA(24:2)	15.4807	15.5602	15.5667	15.4303	15.0658	14.9688	15.5665
FFA(24:3)	13.0845	12.8322	12.8585	12.8112	12.4936	12.5305	12.8754
GlcCer[NS] 34:1	13.5381	13.7684	13.5973	13.3584	13.4819	13.3557	13.3402
GlcCer[NS] 34:2	10.6009	10.1950	10.8994	10.3261	10.2931	9.6427	10.5623
GlcCer[NS] 40:1	15.1024	15.0604	14.9514	15.2016	14.9572	14.7028	14.9905
GlcCer[NS] 41:1	14.5057	14.4874	14.1976	14.5003	14.3217	14.0783	14.4258
GlcCer[NS] 42:1	15.8246	15.6915	15.6597	15.8918	15.7555	15.5046	15.8034
GlcCer[NS] 42:2	15.2015	15.3042	15.2647	15.4513	15.3470	15.0803	15.2966
LysoPC 14:0	15.8345	14.9216	15.3896	15.4095	15.4857	15.4669	15.5729

Table S2.2C: PUFA/CHO study significant differences for within and between diet comparisons for all lipids (Lysophosphatidylcholine 15:0 to Phosphatidylcholine 34:5)

	Mean Log2 AUC Values For Each Lipid Species						
		PUFA Diet			CHO Diet		
Lipid/Day	Baseline	P2	P7	P21	C2	C7	C21
LysoPC 15:0	15.0506	14.6372	14.8903	15.2056	14.8637	14.8746	14.9943
LysoPC 15:1	15.3941	14.8060	15.4779	15.6740	15.0656	15.2370	15.4833
LysoPC 16:0	23.0260	22.6593	22.9745	23.0214	22.8921	22.7842	22.8949
LysoPC 16:1	17.4435	17.1130	17.5135	17.4135	17.3535	17.1982	17.6015
LysoPC 17:1	14.7376	14.3064	14.5348	14.5070	14.5007	14.4821	14.4968
LysoPC 18:0	22.0595	21.6663	22.1760	21.8505	21.7786	21.9451	21.7397
LysoPC 18:1	21.0995	20.7233	21.0445	21.0684	20.7578	20.7699	20.9397
LysoPC 18:2	21.9356	21.6363	21.8753	22.3194	21.6843	21.6817	21.8082
LysoPC 18:3	15.6827	15.1170	15.5090	15.5652	15.2514	15.3640	15.2284
LysoPC 19:0	14.7073	14.4121	14.8335	14.9294	14.5083	14.7562	14.7015
LysoPC 19:1	13.2802	12.9154	13.3304	13.2941	13.1274	13.0348	13.1071
LysoPC 20:0	14.3592	14.0115	14.5397	14.7782	14.2197	14.3874	14.2986
LysoPC 20:1	15.0866	14.6170	14.9334	15.2999	14.7512	14.8198	14.9685
LysoPC 20:2	15.5473	15.3746	15.5405	15.9865	15.4579	15.4968	15.6958
LysoPC 20:3	17.8987	17.4568	17.5729	17.9071	17.6264	17.4838	17.8624
LysoPC 20:4	18.5209	18.5129	18.3673	18.3757	18.2447	18.0237	18.0673
LysoPC 20:5	17.9945	17.7431	17.9837	18.4394	17.8052	17.8491	17.9448
LysoPC 22:0	12.7826	12.4128	12.6859	12.9595	12.6675	12.6528	12.6630
LysoPC 22:4	14.3349	13.9226	14.2878	14.1062	14.0424	13.8090	14.2882
LysoPC 22:5	15.9951	15.6532	15.8161	15.5861	15.5742	15.3031	15.6536
LysoPC 22:6	16.3507	16.3686	16.2273	16.2538	16.0604	15.8354	16.0770
LysoPC 23:0	10.9046	9.9134	10.8292	11.1495	10.6135	10.6176	10.5149
LysoPC 24:0	13.5165	13.1270	13.5396	13.9560	13.4425	13.6393	13.5068
LysoPC 24:1	12.0328	11.7441	12.2243	12.5759	12.1204	12.0846	12.2088
LysoPC 26:1	10.6134	10.0702	10.4728	10.6588	10.1006	10.2573	10.6154
LysoPE 16:0	14.7211	14.0794	14.6704	15.1141	14.7502	14.5093	15.0607
LysoPE 18:0	15.8126	15.2495	15.7798	15.8341	15.6524	15.5417	15.8482
LysoPE 18:1	16.4085	15.3152	16.3772	16.4073	15.7963	15.7489	16.0832
LysoPE 18:2	16.2814	15.7798	16.4856	16.7435	15.9580	16.0539	16.4141
LysoPE 20:3	13.4341	12.9975	12.8344	13.3748	13.0866	12.9874	13.5229
LysoPE 20:4	15.9447	15.6073	15.7868	15.8173	15.7360	15.5352	15.8265
LysoPE 20:5	11.6560	10.7188	11.2660	11.2566	11.4140	11.4983	11.5579
LysoPE 22:4	12.2595	11.5866	12.4051	11.7633	12.1340	11.6074	12.3251
LysoPE 22:5	13.7978	13.2361	13.4298	13.3016	13.3377	12.9650	13.9577
LysoPE 22:6	15.6269	15.5593	15.4808	15.4034	15.4832	15.2097	15.6630
PA 34:2	12.0610	12.2918	11.9612	11.9994	11.8965	11.8006	12.1680
PC 26:0	10.5024	8.5085	9.7334	9.8268	10.1339	10.1198	10.0781
PC 29:0	12.5867	10.9910	11.6652	12.1988	12.2547	12.1129	12.4329
PC 30:0	15.6312	14.6621	15.0617	15.1234	15.3514	14.9963	15.5991
PC 30:2	12.3302	10.6301	11.5946	11.9749	12.0516	11.8130	12.3830
PC 31:0	14.9039	14.0130	14.4565	14.5836	14.6303	14.4911	14.7155
PC 31:1	14.1107	13.3514	14.0839	14.1421	14.0862	13.7063	14.7292
PC 32:0	19.7533	19.2790	19.6533	19.9112	19.6652	19.4520	19.9411
PC 32:1	17.1928	16.1292	16.9125	17.1049	17.0950	16.8218	17.5353
PC 32:2	18.8191	18.0022	18.5008	18.8258	18.6286	18.4622	19.0029
PC 32:3	13.8330	13.0658	13.1912	13.5594	13.4920	13.3232	13.7461
PC 33:0	15.4463	14.7905	15.0092	15.2315	15.2194	15.0406	15.3506
PC 33:1	17.6358	16.8037	17.3182	17.4134	17.5555	17.4547	17.5887
PC 33:2	18.4074	17.6703	18.1781	18.5573	18.3877	18.1851	18.4911
PC 33:3	13.7404	13.0422	13.5630	13.6915	13.6772	13.6425	13.7529
PC 34:1	23.5746	23.1121	23.4520	23.5693	23.4570	23.2610	23.6502
PC 34:2	21.8777	21.4117	21.8280	22.1305	21.7982	21.6324	21.9559
PC 34:3	18.2038	17.8446	18.2797	18.4646	18.2470	17.9626	18.5851
PC 34:4	15.8827	15.1432	15.5074	15.5864	15.6679	15.4238	15.7439
PC 34:5	13.0868	12.9839	12.9319	13.1254	12.7553	13.1521	13.2528

Table S2.2D: PUFA/CHO study significant differences for within and between diet comparisons for all lipids (Phosphatidylcholine 35:0 to Phosphatidylethanolamine 32:1)

	Mean Log2 AUC Values For Each Lipid Species						
		PUFA Diet			CHO Diet		
Lipid/Day	Baseline	P2	P7	P21	C2	C7	C21
PC 35:0	13.8225	13.1468	13.6672	13.6973	13.3307	13.4745	13.7801
PC 35:1	15.8061	15.3849	15.6337	15.7501	15.7456	15.6857	15.8593
PC 35:2	19.5321	18.9191	19.5135	19.6912	19.3704	19.4141	19.5555
PC 35:3	15.1829	14.8200	15.4411	15.6878	14.8966	15.1348	15.5110
PC 35:4	16.5822	16.2072	16.3501	16.4967	16.6432	16.4945	16.5641
PC 35:5	13.3563	12.6924	12.6329	12.8931	13.2542	13.2651	13.0200
PC 36:0	14.8159	14.6687	14.8316	14.7918	14.5061	14.7429	14.7572
PC 36:1	20.5871	19.9745	20.5953	20.2551	20.2845	20.3973	20.4266
PC 36:2	24.0233	23.6832	24.1303	24.0914	23.8693	23.9374	24.0109
PC 36:3	20.5912	20.1694	20.5994	20.7300	20.5059	20.3427	20.6462
PC 36:4	20.4393	20.1711	20.2922	20.2196	20.3101	20.1344	20.3903
PC 36:5	19.7572	19.5940	19.5779	19.5078	19.7715	19.7910	19.7430
PC 36:6	15.7492	15.2265	15.3487	15.5650	15.7279	15.4783	15.8101
PC 37:1	14.4093	13.8810	14.3265	14.3398	14.3808	14.2633	14.2384
PC 37:2	16.1915	15.5961	16.2386	16.4942	16.0892	16.0877	16.2228
PC 37:3	17.1669	16.7328	17.0340	17.1869	17.1005	17.0697	17.2646
PC 37:4	18.3405	18.1681	18.1751	18.1207	18.2429	18.1947	18.1410
PC 37:5	16.4725	16.3220	16.5988	16.2630	16.3931	16.3083	16.3979
PC 37:6	14.7070	14.6595	14.8542	14.7459	14.7495	14.6306	14.7643
PC 37:7	14.7449	14.5856	14.6528	15.3073	15.0114	14.4228	15.3416
PC 38:1	15.0832	14.6662	15.1361	15.0797	15.0325	14.9923	15.0423
PC 38:2	18.4923	18.0053	18.7111	18.7024	18.4567	18.5360	18.6756
PC 38:3	21.1857	20.7304	21.1707	20.8713	21.1093	21.1171	21.2629
PC 38:4	22.7591	22.9346	22.7700	22.2400	22.7506	22.6665	22.5301
PC 38:5	21.9527	21.9141	22.0171	21.5290	21.8349	21.6649	21.7885
PC 38:6	22.4078	22.4610	22.5695	22.3644	22.5292	22.2405	22.4881
PC 38:7	17.7460	17.5242	17.7975	17.6092	17.7124	17.7088	17.8044
PC 39:3	13.9703	13.4469	14.1172	14.0785	14.0505	13.8506	14.1877
PC 39:4	15.2959	15.0817	15.2207	15.2922	15.1889	15.1327	15.2412
PC 39:5	15.9200	15.6625	15.8120	15.5846	15.8627	15.7563	15.6701
PC 39:6	16.4966	16.4813	16.3777	16.2638	16.4639	16.4502	16.3330
PC 39:7	13.7020	13.5941	13.9302	13.8324	13.8460	13.6722	13.6520
PC 40:1	12.9468	12.4919	12.5152	12.8675	12.7946	12.6484	12.6992
PC 40:2	13.9821	13.6273	14.1099	14.4502	13.9767	13.9127	14.2811
PC 40:3	15.1674	14.8103	15.1089	15.4023	15.0679	15.0484	15.3431
PC 40:4	16.2596	15.9992	16.5176	16.0105	16.1709	16.0297	16.2021
PC 40:5	17.0769	16.9775	17.3135	16.6473	17.0500	16.8875	17.0985
PC 40:6	19.9883	20.1464	20.2869	19.5269	20.0913	19.9973	20.0215
PC 40:7	18.3406	18.4175	18.5075	18.2939	18.3576	18.2053	18.4070
PC 40:8	15.2061	15.3767	15.3108	15.6218	15.1168	15.2845	15.5232
PC 40:9	12.4534	11.2977	12.2230	12.0502	12.1696	12.4806	11.9897
PC 41:6	11.6554	12.3812	12.2355	11.8255	12.2743	12.5147	12.0673
PC 41:7	10.1650	11.3106	11.3777	11.2244	11.1748	11.4201	10.9379
PC 42:1	12.2569	11.5320	11.7310	12.3688	11.9031	11.8150	12.4475
PC 42:10	14.5122	14.1728	14.4904	14.4629	14.4105	14.4037	14.2768
PC 42:2	12.9854	11.9651	13.2876	13.2933	12.7587	12.6590	13.1814
PC 42:3	12.7637	12.7116	13.0694	13.5647	12.8688	12.8929	13.3144
PC 42:4	13.5223	12.7988	13.3488	13.7932	13.2036	13.1101	13.8750
PC 42:5	14.5252	13.6418	14.5407	14.3435	14.4582	14.1146	14.6688
PC 42:6	14.1239	13.9570	14.3435	13.7569	14.1797	13.9055	14.4197
PC 42:7	14.1382	13.9435	14.1211	14.4162	14.1496	13.7687	14.3247
PC 42:8	14.1140	13.9644	14.2283	14.5286	14.0121	14.0454	14.3806
PC 42:9	14.0807	13.4963	13.9146	13.7341	13.7241	13.7130	13.7679
PC 44:4	12.6018	11.7300	12.8295	12.7864	12.7445	12.5122	12.7469
PE 32:1	12.7744	11.7523	12.5625	12.7270	12.8045	12.2779	13.3919

Table S2.2E: PUFA/CHO study significant differences for within and between diet comparisons for all lipids (Phosphatidylethanolamine 32:2 to Plasmenyl-phosphatidylcholine 36:2)

	Mean Log2 AUC Values For Each Lipid Species						
		PUFA Diet			CHO Diet		
Lipid/Day	Baseline	P2	P7	P21	C2	C7	C21
PE 32:2	10.8398	10.3072	10.3227	10.6473	10.7812	10.6655	11.2484
PE 33:0	11.1837	11.4161	11.5629	11.8669	11.2610	11.4911	11.4783
PE 33:1	10.7058	10.2169	9.9078	11.0513	11.1295	10.9160	11.2951
PE 33:2	12.2536	11.1758	11.6560	12.9319	11.6219	11.8848	13.0170
PE 34:0	18.6807	18.5979	18.7295	18.7619	18.6391	18.6306	18.8398
PE 34:1	14.1667	13.3864	14.1083	14.1763	14.0679	13.6738	14.7009
PE 34:2	16.2009	15.7024	16.2308	17.0404	16.1780	15.7236	17.0150
PE 34:3	14.5077	13.6978	14.4372	14.9236	14.6565	14.4440	15.1570
PE 35:1	12.0500	11.8808	12.5096	12.6848	12.3498	12.2266	12.8539
PE 35:2	13.2966	12.4871	13.2584	13.8660	13.6422	12.9921	13.9489
PE 35:4	12.1931	11.8119	11.9014	12.5777	12.2500	11.9958	12.6848
PE 36:0	14.1722	14.0775	14.1932	14.3078	14.0525	14.1683	14.1969
PE 36:1	15.4442	15.0139	15.5936	15.3960	15.0732	15.2593	15.6997
PE 36:2	16.9031	16.3213	17.1364	17.4026	16.8447	16.7219	17.4502
PE 36:3	17.5742	16.7283	17.8735	18.6795	17.5463	17.2203	18.2451
PE 36:4	17.4308	16.8135	17.8103	18.5451	17.5292	17.0577	18.0334
PE 36:5	14.4340	13.6647	13.9454	14.6638	14.7029	14.3617	14.8203
PE 37:4	13.8993	13.3056	13.4834	14.0169	13.7440	13.3892	14.1248
PE 38:3	16.2157	15.9145	16.2604	16.5139	16.1517	15.8069	16.7005
PE 38:4	19.0604	18.9268	18.9758	19.2196	19.0497	18.6685	19.2469
PE 38:5	16.5626	16.2480	16.4864	16.9148	16.4735	16.0970	17.0794
PE 38:6	18.7076	18.5742	18.2734	19.3071	18.9921	18.1975	19.4603
PE 38:7	13.3707	13.0755	12.9838	13.5922	13.2760	12.8280	13.6043
PE 40:4	14.4294	13.4170	14.3971	14.1322	14.2704	13.6147	14.5411
PE 40:5	15.8583	15.6772	15.8470	15.8092	15.8368	15.5354	16.1064
PE 40:6	17.4233	17.6117	17.4031	17.4261	17.6006	16.9984	17.8487
PE 40:7	15.4588	15.2942	15.3873	16.0047	15.6588	14.7349	16.1210
PE 40:8	12.9873	12.4892	12.7850	13.4454	13.2164	12.6088	13.5135
PG 33:0	13.3135	13.5331	12.8362	12.6606	12.9543	12.9606	13.1116
PG 34:2	10.9755	10.7386	10.6666	10.8269	11.0090	10.9844	11.4843
PG 36:0	14.5892	14.6343	14.8676	14.8048	14.3413	14.9466	14.5516
PG 36:2	14.3803	13.8687	14.5287	14.4931	14.0964	14.0577	14.4499
PG 36:3	11.9232	11.3894	11.9983	11.7926	11.8956	11.7077	11.8414
PI 34:2	13.9076	13.2592	14.4324	13.7322	14.1889	14.2223	14.1939
PI 36:1	13.6703	12.8066	13.4245	13.1456	13.0289	13.4491	12.9364
PI 36:2	16.2933	15.9370	16.7696	16.4002	16.3665	16.4866	16.4937
PI 36:4	14.1448	13.1857	14.3311	14.1416	14.3362	14.1884	14.2186
PI 38:3	16.5387	16.3245	16.6265	16.1685	16.3293	16.4035	16.5780
PI 38:4	18.0354	17.8465	18.1267	17.6990	17.9750	18.0775	17.9667
PI 38:5	14.1903	13.7616	14.4494	13.6285	14.3479	14.4474	14.1124
PI 38:6	11.7690	11.3217	12.1479	11.5485	12.0632	12.1808	11.9877
PI 40:6	13.1300	13.2039	13.2130	13.0270	13.4493	13.4521	13.0399
PlsCho 24:0	12.0666	11.7540	12.2381	12.5878	12.1016	12.0534	12.1822
PlsCho 32:0	16.4487	16.6831	16.3627	16.3337	16.2229	16.5648	16.0613
PlsCho 32:1	13.8642	13.6128	13.7962	13.9399	13.8892	14.0162	13.5472
PlsCho 33:0	12.4738	12.0374	12.1296	11.8894	11.9404	12.1182	12.4112
PlsCho 34:0	18.1060	17.7092	17.8023	18.3219	17.8431	17.6957	18.0899
PlsCho 34:1	18.4815	17.9769	18.4490	18.8229	18.2400	18.3266	18.5745
PlsCho 34:2	19.1738	18.6438	18.9259	19.7451	19.1347	19.0185	19.3184
PlsCho 34:3	14.9020	14.5169	14.4094	14.7487	14.5821	14.6429	14.4630
PlsCho 35:1	12.5706	12.0630	12.7079	12.1886	12.5602	12.2495	12.3995
PlsCho 35:2	14.9639	14.4113	14.9347	15.1617	14.9797	14.7301	15.1039
PlsCho 35:3	14.5569	14.0105	13.7197	13.8089	14.1293	14.1525	13.8906
PlsCho 36:0	16.6471	16.2286	16.2919	16.4486	16.4226	16.3593	16.4258
PlsCho 36:2	17.0771	16.5518	16.4639	17.3355	16.7539	16.6369	16.9814

Table S2.2F: PUFA/CHO study significant differences for within and between diet comparisons for all lipids (Plasmenyl-phosphatidylcholine 36:3 to Plasmenyl-phosphatidylethanolamine 37:5)

	Mean Log2 AUC Values For Each Lipid Species						
		PUFA Diet			CHO Diet		
Lipid/Day	Baseline	P2	P7	P21	C2	C7	C21
PlsCho 36:3	20.2453	19.7406	20.0767	20.1130	19.9130	19.7907	20.0048
PlsCho 36:4	19.5773	18.9890	19.4649	19.5626	19.3946	19.2970	19.3406
PlsCho 36:5	15.5974	15.0886	15.7359	15.5570	15.1480	15.6385	15.2004
PlsCho 36:6	13.6808	13.1595	13.4268	13.4427	13.6136	13.3565	13.5197
PlsCho 37:1	13.1938	12.7648	13.2506	12.6342	13.0606	13.0474	13.0539
PlsCho 37:3	13.1608	12.8984	13.1095	13.0217	13.1072	12.8191	13.0770
PlsCho 37:4	15.8494	15.3344	15.6252	15.6549	15.5603	15.4312	15.6136
PlsCho 37:6	16.0650	15.4429	15.8811	15.6679	15.7478	15.9157	15.7136
PlsCho 38:1	16.8456	15.7698	16.6851	16.7810	17.1158	17.0451	17.0240
PlsCho 38:3	19.0183	18.5950	18.6628	18.6833	18.6926	18.4382	18.7937
PlsCho 38:4	19.7708	19.5584	19.6557	19.7523	19.5485	19.4022	19.6903
PlsCho 38:5	18.7283	18.3614	18.6145	18.5776	18.4831	18.4613	18.5397
PlsCho 38:6	17.2212	16.9251	17.0826	17.2121	17.0808	17.1354	16.8406
PlsCho 39:3	17.9364	17.3284	17.9877	17.6734	18.0081	17.4323	18.3912
PlsCho 39:4	16.2464	16.1425	16.2302	15.9396	16.1675	16.0376	16.1739
PlsCho 39:5	16.1977	16.0579	16.3632	16.1288	16.3317	16.0984	16.2263
PlsCho 39:6	13.6140	13.3718	13.2382	13.3281	13.4440	13.4878	13.1922
PlsCho 40:1	15.2388	15.2467	15.0778	15.4230	15.2362	15.0616	15.3115
PlsCho 40:3	17.3781	17.1230	17.0740	17.0019	17.1508	16.9293	17.2408
PlsCho 40:4	17.6534	17.5872	17.5187	17.4183	17.4090	17.1823	17.6579
PlsCho 40:5	17.1854	16.7036	17.2613	17.1207	16.7593	16.7346	17.0939
PlsCho 40:6	15.6519	15.3487	15.3220	15.5187	15.4635	15.3243	15.3486
PlsCho 42:0	11.9878	11.4197	11.7576	11.9948	11.7769	11.7230	11.8621
PlsCho 42:1	14.3341	13.9316	14.0684	14.0980	13.8206	13.8148	14.3255
PlsCho 42:2	15.3402	15.1221	15.1814	15.6898	15.1469	14.9932	15.7174
PlsCho 42:3	15.9316	15.5640	15.8030	16.2813	15.7007	15.4842	16.0324
PlsCho 42:4	16.9337	16.8455	16.6396	16.8338	16.5855	16.2264	17.0823
PlsCho 42:5	16.4319	16.7297	16.4670	16.8589	16.4845	16.3177	16.8131
PlsCho 42:6	15.3379	15.4166	15.1900	15.2969	15.0091	14.9246	15.6197
PlsCho 44:3	15.0916	14.7861	14.6494	15.1561	14.6842	14.6138	15.4849
PlsCho 44:4	17.2295	16.9592	16.9202	17.3994	16.9314	16.5278	17.6169
PlsCho 44:5	16.5547	16.8942	16.7010	17.2216	16.7361	16.4554	17.3611
PlsCho 44:6	15.3078	15.5688	15.1739	15.6946	15.3183	15.1268	15.6096
PlsCho 46:4	14.0412	13.6771	13.7053	14.2964	13.6748	13.4551	14.4824
PlsEth 32:1	13.1766	12.7113	13.1408	12.6920	12.9933	12.9504	12.9126
PlsEth 32:2	11.5391	11.2461	11.4324	11.4435	11.1139	11.2643	11.3170
PlsEth 33:2	11.0422	9.5308	10.6512	10.8091	10.3739	10.8782	10.6121
PlsEth 34:0	14.8482	14.7825	14.6896	14.7254	14.6811	14.5230	14.6938
PlsEth 34:1	16.5972	16.0940	16.8055	16.4272	16.4336	16.2942	16.4697
PlsEth 34:2	15.8393	14.8727	15.8288	15.9019	15.5304	15.7731	15.6190
PlsEth 34:3	13.1197	11.9910	12.8190	12.6893	12.6379	12.9921	12.0840
PlsEth 34:4	12.5721	11.5223	12.2298	11.9401	11.4208	12.1683	12.0591
PlsEth 35:1	12.9272	12.2471	12.9493	12.8424	12.6491	12.6234	12.8891
PlsEth 35:2	14.6399	13.4892	14.3632	14.3347	13.9670	14.4070	13.9306
PlsEth 35:4	13.2204	11.6327	12.9932	12.6534	12.6990	12.5350	12.2173
PlsEth 36:1	16.7399	15.6038	16.2538	15.9743	16.0702	16.1593	16.1898
PlsEth 36:2	16.7944	15.8905	16.6713	16.6967	16.3813	16.6284	16.3911
PlsEth 36:3	18.7162	17.9725	18.8506	18.8223	18.3160	18.6349	18.4689
PlsEth 36:4	17.5677	16.8956	17.8471	17.4149	17.2695	17.5590	17.1770
PlsEth 36:5	16.2122	14.9447	16.1766	15.3007	15.3557	15.8901	15.4151
PlsEth 36:6	11.8885	11.4956	11.6856	11.6313	11.7749	11.7927	11.7901
PlsEth 37:1	13.5265	12.6576	13.7665	14.1641	13.2965	13.3584	14.1144
PlsEth 37:2	12.6468	12.2144	13.1334	13.7537	12.5888	12.4256	13.4140
PlsEth 37:4	14.0456	13.0911	13.7696	13.4978	13.5072	13.7110	13.3994
PlsEth 37:5	14.2763	13.4684	13.7109	13.1294	13.4443	13.8067	13.4117

Table S2.2FG: PUFA/CHO study significant differences for within and between diet comparisons for all lipids (Plasmenyl-phosphatidylethanolamine 37:6 to Sphingomyelin 42:1)

	Mean Log2 AUC Values For Each Lipid Species						
		PUFA Diet			CHO Diet		
Lipid/Day	Baseline	P2	P7	P21	C2	C7	C21
PlsEth 37:6	13.1881	12.1807	13.1534	12.7880	12.9597	13.1243	12.7014
PlsEth 38:1	14.0967	13.2178	14.2878	13.7179	13.8287	13.7299	13.9064
PlsEth 38:2	15.5743	15.1773	15.7746	15.5307	15.4134	15.4277	15.4479
PlsEth 38:3	17.7422	16.7313	17.4204	17.3180	17.0359	17.2730	17.2356
PlsEth 38:4	17.7781	17.0074	17.6313	17.4630	17.4991	17.6013	17.2082
PlsEth 38:5	17.8328	17.3381	17.7850	17.6486	17.4723	17.6476	17.3798
PlsEth 38:6	19.1827	18.5392	19.0856	19.0735	18.9183	18.9596	18.7195
PlsEth 39:4	14.0723	13.1818	14.0724	13.6624	13.7829	13.6791	13.6038
PlsEth 39:5	14.5032	14.1661	14.4418	14.2659	14.2318	14.3745	14.1006
PlsEth 39:6	15.3597	14.9053	15.1371	14.8086	14.9051	15.0589	14.8710
PlsEth 40:2	14.1009	13.8954	14.6024	13.9010	13.8277	14.0056	14.1125
PlsEth 40:4	14.9277	14.4970	15.1201	14.7338	14.4603	14.7565	14.7530
PlsEth 40:5	17.6031	16.8756	17.2113	16.9761	17.0203	17.1285	16.8149
PlsEth 40:6	16.0911	15.4491	15.8867	15.6680	15.7266	15.8811	15.6787
PlsEth 42:4	15.1971	15.1078	15.5684	14.7354	14.7188	15.0996	14.9478
PlsEth 42:5	14.9426	14.7483	15.3316	14.7980	14.7072	14.7872	14.8554
PlsEth 42:6	15.0700	14.6947	15.5484	14.5162	14.6981	14.7429	14.8624
PlsEth 44:6	11.7030	11.8243	12.4832	11.9515	11.8704	12.0116	11.7090
SM 30:0	11.0131	9.9937	10.7141	9.5203	10.4744	10.1075	10.6125
SM 30:1	14.8914	14.0543	14.3571	14.1689	14.5078	14.4753	14.6195
SM 30:2	11.5081	11.2261	10.8863	11.3239	11.4988	11.3246	11.4523
SM 31:1	14.7240	13.9380	14.3707	14.2615	14.5664	14.5051	14.4706
SM 32:0	15.1041	14.5626	15.1483	14.9033	14.8653	15.0289	14.9619
SM 32:1	18.9678	18.2867	18.8468	18.6794	18.7307	18.6855	18.7009
SM 32:2	16.0826	15.7948	15.7747	15.4883	15.8134	15.7766	15.9955
SM 33:1	18.0823	17.6460	17.9322	17.8489	17.9765	17.8468	17.8326
SM 33:2	14.0265	13.7211	14.0795	13.9925	14.0275	13.8170	14.0191
SM 34:0	17.5612	17.2737	17.2759	17.2289	17.3019	17.3378	17.4507
SM 34:1	20.7700	20.6682	20.7351	20.7052	20.7938	20.7081	20.6980
SM 34:2	19.5272	19.3837	19.4669	19.2914	19.3638	19.2558	19.3760
SM 34:3	14.0225	14.0356	14.1806	13.4667	14.1089	13.9517	14.0553
SM 35:2	14.7368	14.6551	14.4481	14.1050	14.5171	14.5571	14.2783
SM 36:1	18.0794	18.3635	17.8514	17.6163	18.1088	17.9135	17.9291
SM 36:2	17.7240	18.1395	17.6057	17.2388	17.4984	17.4940	17.4954
SM 36:3	16.6273	16.9353	16.6286	16.3777	16.6160	16.4961	16.7328
SM 36:4	13.9274	14.0785	14.1344	14.0743	14.1062	13.9273	13.9782
SM 37:1	14.8950	14.9730	14.4332	14.7045	14.7762	14.5557	14.6689
SM 37:2	15.2173	15.3517	14.9353	15.3256	15.1563	14.9118	15.2332
SM 38:0	11.2788	11.1924	11.4441	11.3856	11.1176	11.1512	11.4483
SM 38:1	18.3329	18.1650	18.1603	18.2157	18.3979	18.2026	18.1439
SM 38:2	16.0684	16.4716	15.9909	16.0255	16.1661	15.9838	16.1718
SM 38:3	14.7749	15.1508	14.6558	14.5270	14.8167	14.6922	15.0877
SM 38:4	13.1438	13.1942	12.9087	13.2008	13.2910	13.0770	13.3515
SM 39:1	17.9034	17.4011	17.6213	17.4608	17.8117	17.6807	17.5603
SM 39:2	15.5877	15.6780	15.3200	15.4001	15.5577	15.4155	15.5656
SM 39:3	15.0865	14.6493	14.9469	15.0801	14.8322	14.5876	14.8424
SM 40:1	20.0581	19.7345	19.9304	19.7374	19.9437	19.8388	19.7426
SM 40:2	20.1827	19.9827	20.0044	20.0313	20.1120	20.0067	20.0823
SM 40:3	17.0189	17.2343	17.0649	16.9916	17.1461	17.0228	17.3466
SM 40:5	12.9681	12.3566	12.7753	12.6320	13.0082	12.4609	13.1547
SM 41:1	19.7889	19.4738	19.6103	19.5814	19.8328	19.7630	19.5850
SM 41:2	18.8977	18.8268	18.6672	18.8580	18.9203	18.7594	18.7518
SM 41:4	14.7505	14.5550	14.7707	14.9135	14.6968	14.4985	14.8169
SM 41:6	13.0777	12.8916	13.0255	12.8362	12.9416	12.6324	13.0044
SM 42:1	20.5494	20.2232	20.3869	20.4661	20.5494	20.5914	20.3439

Table S2.2H: PUFA/CHO study significant differences for within and between diet comparisons for all lipids (Sphingomyelin 42:2 to Triacylglycerol 52:2)

	Mean Log2 AUC Values For Each Lipid Species						
		PUFA Diet			CHO Diet		
Lipid/Day	Baseline	P2	P7	P21	C2	C7	C21
SM 42:2	21.2841	21.2420	21.2948	21.3989	21.3860	21.3683	21.4066
SM 42:3	20.5116	20.6102	20.5286	20.6842	20.6487	20.5481	20.8150
SM 42:4	17.1705	17.6487	17.0830	17.2804	17.3732	17.2533	17.6501
SM 42:5	14.5143	14.5511	14.5690	14.4532	14.9004	14.4631	15.1043
SM 42:6	13.8966	13.8295	13.9746	13.4948	14.0374	13.7640	14.3384
SM 43:1	16.5805	16.1524	16.3285	16.2056	16.5970	16.3524	16.2063
SM 43:2	16.9347	16.7924	16.9070	16.9117	17.1293	16.7950	16.8761
SM 43:3	15.4008	15.4307	15.3972	15.2804	15.4116	15.2852	15.4946
SM 43:6	12.6412	12.7272	12.6566	12.7804	12.5766	12.7499	12.9763
SM 44:1	13.4704	13.1900	13.3197	13.2960	13.4926	13.5106	13.2698
SM 44:2	14.8758	14.7738	14.8415	14.8012	15.0175	14.7369	14.7617
SM 44:3	14.3227	14.6079	14.5527	14.6572	14.4767	14.5108	14.8251
SM 44:4	13.8337	13.8811	13.2945	14.6799	14.0184	13.9697	14.2220
SM 44:6	12.1872	11.6393	11.4725	12.7004	12.0153	12.1561	12.4723
TG 38:0	15.5609	15.0369	15.3126	15.2460	15.3613	15.3801	15.4013
TG 39:0	15.2288	14.9942	15.1395	15.1993	15.1644	15.1255	15.2778
TG 40:0	14.2387	13.6842	13.9105	13.9672	14.0716	14.1003	14.1021
TG 41:0	13.3587	12.8422	12.9934	12.9449	13.1087	13.3217	13.1333
TG 42:0	14.6572	13.4796	14.0103	13.9571	14.2340	14.3375	14.3954
TG 42:1	14.3256	12.8889	13.6709	13.5661	13.8681	13.9635	14.0894
TG 43:1	12.9152	11.6642	12.2611	12.1585	12.6511	12.7354	12.6813
TG 44:2	15.7173	14.2691	15.0987	14.8190	15.2362	15.3448	15.5043
TG 45:0	13.6183	12.6973	12.9721	12.9392	13.2009	13.3229	13.1939
TG 45:1	13.9146	12.6952	13.4486	13.1083	13.5757	13.6608	13.7088
TG 45:2	13.6250	12.3889	12.9041	12.6824	13.3544	13.4116	13.3712
TG 46:0	16.1034	14.6814	15.5996	15.3704	15.8235	15.8626	16.0007
TG 46:1	17.6364	15.9666	16.8637	16.7101	17.1955	17.1658	17.4521
TG 46:3	16.3579	15.2656	16.1049	15.5506	16.0165	16.0576	16.3837
TG 47:0	13.6285	12.3395	12.9578	12.9203	13.3732	13.4082	13.3610
TG 47:1	14.7674	13.3247	13.9900	13.4920	14.4192	14.5106	14.4143
TG 47:2	14.9318	13.4107	14.2429	13.8818	14.6425	14.6422	14.7402
TG 48:0	16.7938	15.5232	16.3043	16.1441	16.6452	16.6830	16.7923
TG 48:1	19.4511	18.0246	18.9195	18.5066	19.1077	19.0244	19.3750
TG 48:3	18.8112	17.6240	18.6335	18.1176	18.6675	18.4860	19.0039
TG 48:4	17.4644	16.7535	17.6307	17.0399	17.3709	17.3278	17.7102
TG 48:5	15.1455	14.6457	15.4684	14.9445	15.0977	15.1448	15.4752
TG 49:0	13.7878	12.6736	13.3478	12.9536	13.6911	13.7124	13.7479
TG 49:1	16.1831	14.7074	15.4293	15.0876	15.9089	15.8786	15.9370
TG 49:2	16.5328	15.3107	16.0696	15.6031	16.4069	16.2856	16.4895
TG 49:3	15.7347	14.8666	15.6442	15.1211	15.8318	15.6573	15.9039
TG 50:0	17.0064	15.7024	16.7298	15.9966	16.9228	16.9375	17.1827
TG 50:1	20.3004	19.3130	20.1418	19.7440	20.2939	20.1571	20.5827
TG 50:2	21.2000	20.4757	21.2249	20.7485	21.3030	21.1154	21.5790
TG 50:3	21.0190	20.2355	21.1518	20.6154	21.1187	20.9099	21.4036
TG 50:4	20.0251	19.5473	20.4611	20.0206	20.2100	20.0147	20.4817
TG 50:5	17.8423	17.5492	18.4983	17.8681	18.2543	18.0893	18.3668
TG 50:6	15.6908	15.4371	16.3046	15.6185	15.9053	15.7989	16.0100
TG 51:1	15.8792	14.7614	15.6448	14.9203	15.8568	15.9038	15.8988
TG 51:2	17.9370	17.0533	17.8029	17.1705	17.9506	17.8229	17.9535
TG 51:3	17.9646	17.3715	18.0784	17.7435	18.1904	18.0017	18.1256
TG 51:4	17.1157	16.6778	17.4708	17.2308	17.3678	17.2733	17.2757
TG 51:5	15.5675	15.3061	16.0139	15.6352	15.9133	15.8826	15.5671
TG 52:0	16.8263	16.0775	16.8877	16.5115	16.7605	16.9460	16.8268
TG 52:1	19.6156	18.6205	19.4146	18.6585	19.5177	19.6736	19.6450
TG 52:2	21.9087	21.3302	22.0444	21.5598	22.0403	21.9131	22.0477

Table S2.2I: PUFA/CHO study significant differences for within and between diet comparisons for all lipids (Triacylglycerol 52:3 to Triacylglycerol 60:12)

	Mean Log2 AUC Values For Each Lipid Species						
		PUFA Diet			CHO Diet		
Lipid/Day	Baseline	P2	P7	P21	C2	C7	C21
TG 52:3	22.7645	22.6627	23.0786	22.8410	23.0803	22.9409	23.0877
TG 52:4	22.4518	22.4419	22.9904	22.8340	22.8793	22.6923	22.8984
TG 52:5	17.4742	17.4432	17.5991	17.5236	17.7531	17.5291	17.6518
TG 52:6	18.6709	18.7444	19.3183	19.1001	19.2491	19.0131	19.1958
TG 52:7	16.0607	16.1877	16.6628	16.2649	16.6747	16.4863	16.4706
TG 53:0	13.2553	12.6732	13.3400	13.1567	13.1946	13.3108	13.2502
TG 53:1	14.5533	13.7783	13.8366	13.8446	14.5392	14.7025	14.6934
TG 53:2	15.9839	16.0649	16.5204	15.9704	16.5587	16.6895	16.6671
TG 53:3	17.8560	17.5413	18.1111	17.8048	18.1233	18.0782	17.9821
TG 53:4	17.3970	17.3411	17.8264	17.7375	17.7265	17.7234	17.6238
TG 53:5	16.3326	16.2360	16.7778	16.6680	16.7040	16.6849	16.4381
TG 54:0	16.7251	16.1905	16.8869	16.8927	16.7732	16.8480	16.7125
TG 54:1	17.0780	15.9120	16.9468	16.2524	16.8939	17.2195	16.8893
TG 54:2	19.3927	18.7099	19.6604	18.8664	19.4684	19.7132	19.3820
TG 54:3	20.2470	20.0231	20.8475	20.4337	20.5034	20.6334	20.4635
TG 54:4	21.3399	21.3486	22.0504	21.8645	21.6601	21.8118	21.6802
TG 54:5	21.3495	21.5192	22.1814	22.0959	21.7620	21.8849	21.7521
TG 54:6	20.9255	21.2727	21.8545	21.8530	21.4188	21.4814	21.3273
TG 54:7	19.1309	19.4139	19.8840	19.7360	19.6760	19.7531	19.4835
TG 54:8	16.7989	17.0186	17.2857	17.1121	17.4210	17.3440	16.9255
TG 55:0	11.8260	11.5373	11.6711	11.6741	11.8114	12.0514	11.8631
TG 55:3	13.5836	13.1035	13.9515	13.7482	13.8527	13.8174	13.4256
TG 55:4	14.5066	13.9814	14.4810	14.5506	13.5991	14.7356	14.4892
TG 55:5	14.6868	14.3120	14.6339	14.5908	14.8159	14.8880	14.5650
TG 56:0	12.6427	11.9887	12.7529	12.5447	12.5720	12.6424	12.5567
TG 56:1	14.3772	13.0854	14.1235	13.6911	13.9831	14.4146	14.1344
TG 56:2	15.7728	14.8201	15.9060	15.1931	15.5660	16.0173	15.6794
TG 56:3	16.3864	15.8438	16.6962	16.4088	16.4494	16.7769	16.6697
TG 56:4	16.6111	16.5511	16.9880	16.8696	16.7971	16.9507	16.9398
TG 56:5	18.3591	18.3373	18.4916	18.6603	18.5635	18.5514	18.6569
TG 56:6	19.0250	19.1710	19.1553	19.3305	19.3353	19.2649	19.2122
TG 56:7	19.2233	19.4176	19.3555	19.4218	19.5686	19.4532	19.2834
TG 56:8	18.7281	19.2148	19.0344	19.2304	19.3004	19.2149	18.9522
TG 56:9	16.8880	17.5006	17.2100	17.4152	17.6482	17.6034	17.1442
TG 58:10	16.5686	17.2266	16.7296	17.2168	17.1768	17.3286	16.7688
TG 58:11	14.5134	15.4601	14.8423	15.1703	15.3565	15.5953	14.9073
TG 58:2	14.2199	13.2070	14.2259	13.8306	13.9397	14.3833	14.2568
TG 58:3	14.2984	13.6036	14.6781	14.1261	14.1488	14.5895	14.4163
TG 58:6	15.2622	15.1692	15.3118	15.3556	15.4510	15.4131	15.5142
TG 58:7	16.3364	16.2954	16.1942	16.3583	16.5411	16.5224	16.3785
TG 58:8	16.8233	17.0023	16.8818	17.0961	17.1653	17.2411	16.9617
TG 58:9	16.8179	17.3137	17.0137	17.3853	17.3563	17.4598	16.9500
TG 60:11	14.2457	14.6512	13.9795	14.4610	14.7273	14.6618	14.3432
TG 60:12	13.7449	14.5381	13.7080	14.2002	14.3926	14.6349	14.0260

Table S2.3A: PUFA/CHO study significant differences for within diet comparisons for all lipids (16:0 Cholesterol ester to Ceramide [NP] 42:0)

	Within Diet Comparisons FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
16:0 CE	0.9012	0.9883	0.9288	0.07667	0.5484	0.9008	0.4199	0.9532	0.8643
16:1 CE	0.8499	0.8841	0.7603	0.0043	0.4059	0.9324	0.0160	0.0010	0.1248
18:0 CE	0.9896	0.9106	0.8832	0.2365	0.7257	0.8314	0.1690	0.2871	0.8504
18:1 CE	0.8325	0.5580	0.8832	0.2129	0.3169	0.5971	0.2233	0.0930	0.9327
18:2 CE	0.0425	0.6154	0.9287	0.6709	0.9283	0.5971	0.7100	0.0224	0.1262
18:3 CE	0.9598	0.3847	0.9291	0.1350	0.4059	0.7053	0.0318	0.1237	0.8093
20:3 CE	0.2041	0.3847	0.1982	0.3518	0.3323	0.8886	0.0140	0.0010	0.6487
20:4 CE	0.0227	0.8122	0.7954	0.0302	0.9109	0.9405	0.4524	0.0884	0.5093
20:5 CE	0.8081	0.6632	0.7057	0.9628	0.3323	0.9910	0.0324	0.0185	0.9392
22:4 CE	0.4889	0.9883	0.4055	0.8045	0.7450	0.9008	0.4521	0.3754	0.9022
22:5 CE	0.0729	0.8122	0.7603	0.5149	0.5954	0.9790	0.5834	0.7348	0.9512
22:6 CE	0.1937	0.9106	0.9287	0.0749	0.8884	0.8440	0.7200	0.6975	0.9468
ACAR 10:0	0.9012	0.9883	0.7977	0.9771	0.8467	0.8371	0.4012	0.4087	0.1250
ACAR 10:1	0.0350	0.9961	0.8159	0.0348	0.4750	0.7179	0.1575	0.0010	0.0274
ACAR 12:0	0.9375	0.9961	0.9291	0.4789	0.9976	0.8825	0.4472	0.8050	0.3745
ACAR 14:0	0.6625	0.9106	0.8171	0.6890	0.7560	0.8886	0.2507	0.9124	0.4093
ACAR 14:1	0.6693	0.9883	0.8261	0.6560	0.8348	0.8886	0.5945	0.4847	0.3930
ACAR 14:2	0.3028	0.9909	0.8102	0.2222	0.8406	0.8371	0.7200	0.0246	0.1248
ACAR 16:0	0.1067	0.9338	0.9523	0.1416	0.7631	0.9253	0.0275	0.1608	0.6487
ACAR 18:0	0.7139	0.9883	0.9848	0.9077	0.8066	0.9910	0.4170	0.7653	0.8018
ACAR 18:1	0.7709	0.9612	0.9832	0.9845	0.8467	0.8371	0.6320	0.9124	0.8504
ACAR 18:2	0.5181	0.9941	0.9887	0.2129	0.7433	0.8371	0.3730	0.0251	0.3601
ACAR 24:0	0.8747	0.9106	0.9832	0.0369	0.9346	0.8371	0.8990	0.0053	0.0469
ACAR 26:0	0.8355	0.9707	0.9523	0.3156	0.7560	0.9276	0.8407	0.5439	0.5724
Cer[AS] 34:1	0.9979	0.9541	0.9832	0.7870	0.9342	0.9795	0.5925	0.9006	0.6487
Cer[EODS] 58:0	0.6984	0.7039	0.8171	0.6381	0.8467	0.7579	0.9111	0.1924	0.3930
Cer[NDS] 34:0	0.9990	0.9612	0.9848	0.5186	0.8884	0.7736	0.6488	0.8050	0.5954
Cer[NDS] 36:0	0.7402	0.9883	0.9832	0.9292	0.6687	0.7579	0.4170	0.0701	0.4650
Cer[NDS] 38:0	0.5374	0.9106	0.8102	0.9077	0.4775	0.9169	0.1151	0.2095	0.9327
Cer[NDS] 40:0	0.8674	0.9106	0.9788	0.2660	0.7560	0.9276	0.4369	0.4655	0.3067
Cer[NDS] 42:0	0.9484	0.8841	0.9709	0.8030	0.9346	0.8371	0.3804	0.5023	0.2835
Cer[NDS] 42:1	0.8586	0.8660	0.7665	0.3411	0.9342	0.7991	0.0282	0.6909	0.1250
Cer[NP] 34:0	0.7942	0.9883	0.9957	0.4116	0.5954	0.8661	0.7200	0.7148	0.5299
Cer[NP] 42:0	0.8355	0.6632	0.9709	0.3074	0.5907	0.7991	0.0717	0.4898	0.1250

Table S2.3B: PUFA/CHO study significant differences for within diet comparisons for all lipids (Ceramide [NP] 42:1 to Diacylglycerol 35:3)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
Cer[NP] 42:1	0.1846	0.7970	0.9957	0.1753	0.5954	0.9389	0.8784	0.9903	0.9512
Cer[NS] 32:1	0.9793	0.8122	0.9848	0.5236	0.3479	0.7736	0.1973	0.8034	0.4650
Cer[NS] 33:1	0.9271	0.6632	0.7977	0.8587	0.9548	0.7736	0.9070	0.4898	0.6487
Cer[NS] 34:1	0.6506	0.9298	0.9832	0.8070	0.8712	0.9910	0.7388	0.9021	0.6487
Cer[NS] 34:2	0.8112	0.9106	0.9709	0.8856	0.7910	0.9253	0.4369	0.4350	0.9163
Cer[NS] 35:1	0.9979	0.9961	0.9832	0.9077	0.8335	0.7579	0.8297	0.5095	0.8522
Cer[NS] 36:1	0.7402	0.9106	0.9523	0.6709	0.4750	0.9910	0.1151	0.0292	0.6524
Cer[NS] 36:2	0.9054	0.8846	0.9523	0.9479	0.5954	0.8886	0.6805	0.1215	0.5023
Cer[NS] 37:1	0.9859	0.9298	0.9957	0.9115	0.7139	0.9795	0.5925	0.3315	0.8643
Cer[NS] 38:1	0.8355	0.7395	0.9832	0.7649	0.5954	0.9925	0.0717	0.2304	0.5724
Cer[NS] 38:2	0.9012	0.9298	0.8102	0.9979	0.5954	0.9577	0.0945	0.0297	0.9139
Cer[NS] 39:1	0.6984	0.9883	0.9832	0.7179	0.4775	0.6005	0.4174	0.8492	0.5425
Cer[NS] 40:1	0.6984	0.9106	0.8102	0.3072	0.8467	0.5971	0.0160	0.6285	0.0350
Cer[NS] 40:2	0.9012	0.6154	0.9832	0.8917	0.5560	0.7824	0.0160	0.0712	0.3601
Cer[NS] 40:3	0.7733	0.9916	0.9533	0.3671	0.9098	0.8371	0.2044	0.0224	0.6487
Cer[NS] 41:1	0.7521	0.9106	0.7603	0.1933	0.8971	0.7991	0.0216	0.2587	0.1876
Cer[NS] 41:2	0.9598	0.7393	0.9709	0.9292	0.5030	0.8371	0.0436	0.0585	0.6487
Cer[NS] 42:1	0.9587	0.5039	0.9957	0.7574	0.6687	0.8830	0.0324	0.7363	0.1794
Cer[NS] 42:2	0.9012	0.9106	0.7954	0.1795	0.8275	0.6676	0.0436	0.4063	0.3210
Cer[NS] 42:3	0.9847	0.8122	0.9957	0.6829	0.6687	0.9601	0.0715	0.0081	0.6524
Cer[NS] 43:1	0.8747	0.6632	0.9832	0.7140	0.4750	0.9405	0.0324	0.1215	0.5954
Cer[NS] 43:2	0.8112	0.9483	0.7603	0.0402	0.8642	0.9925	0.0717	0.0240	0.9139
DG 30:0	0.0227	0.9027	0.7603	0.0899	0.5100	0.8371	0.0555	0.1146	0.9477
DG 30:1	0.1260	0.7464	0.9832	0.6437	0.4465	0.9778	0.2137	0.1350	0.8093
DG 32:0	0.8844	0.9298	0.8171	0.4882	0.8275	0.7736	0.4813	0.9486	0.6375
DG 32:1	0.0095	0.3847	0.8832	0.0043	0.7310	0.8452	0.0284	0.0167	0.7314
DG 32:2	0.5258	0.7393	0.9523	0.0318	0.8467	0.8886	0.6195	0.0716	0.5165
DG 33:0	0.8747	0.9883	0.9832	0.1509	0.8467	0.8371	0.4236	0.1827	0.7516
DG 33:1	0.0658	0.5742	0.9291	0.1757	0.7560	0.9925	0.4630	0.0183	0.3930
DG 34:0	0.9859	0.9298	0.8102	0.1795	0.6945	0.6769	0.6208	0.4702	0.4093
DG 34:2	0.6733	0.9883	0.9523	0.1598	0.9152	0.9086	0.7633	0.2557	0.5724
DG 34:3	0.9012	0.9106	0.9709	0.0437	0.8712	0.8371	0.7712	0.0854	0.3770
DG 35:1	0.0615	0.6182	0.9533	0.0143	0.9026	0.8886	0.0845	0.0297	0.8093
DG 35:2	0.0410	0.6632	0.9832	0.1507	0.5954	0.8371	0.3133	0.0397	0.5724
DG 35:3	0.9012	0.9883	0.9523	0.0937	0.8884	0.7991	0.4552	0.3133	0.8504

Table S2.3C: PUFA/CHO study significant differences for within diet comparisons for all lipids (Diacylglycerol 36:0 to Glucoceramide [NS] 41:1)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
DG 36:0	0.9033	0.7395	0.7977	0.6287	0.8467	0.7728	0.9706	0.3554	0.5165
DG 36:1	0.9979	0.9883	0.7603	0.0152	0.9159	0.7824	0.1192	0.2977	0.9731
DG 36:2	0.2692	0.8122	0.9832	0.0120	0.9342	0.9178	0.5517	0.0137	0.3783
DG 36:3	0.9012	0.9338	0.9523	0.3651	0.9283	0.8886	0.6347	0.6904	0.5054
DG 36:4	0.2599	0.9186	0.9788	0.9875	0.8327	0.7991	0.2151	0.2557	0.9243
DG 36:5	0.5181	0.8660	0.9287	0.6074	0.8763	0.7736	0.4170	0.8188	0.4093
DG 38:1	0.9054	0.9048	0.9832	0.9147	0.4569	0.9581	0.4326	0.1455	0.6547
DG 38:2	0.7457	0.9359	0.9607	0.0482	0.8348	0.8371	0.1692	0.0505	0.7314
DG 38:3	0.8112	0.9961	0.9832	0.1005	0.9568	0.9324	0.7661	0.2444	0.5964
DG 38:4	0.1778	0.9883	0.9533	0.0044	0.9494	0.9405	0.1718	0.0265	0.4650
DG 38:5	0.6656	0.9298	0.9832	0.0097	0.8969	0.8371	0.4199	0.0444	0.4093
DG 38:6	0.9012	0.9541	0.9957	0.1717	0.9342	0.8371	0.9643	0.8492	0.9022
DG 40:6	0.2831	0.9883	0.9887	0.0352	0.9109	0.9423	0.1595	0.0400	0.6387
DG 40:7	0.9896	0.9106	0.9832	0.0116	0.8434	0.9405	0.5871	0.0854	0.4946
FFA(16:0)	0.9676	0.9298	0.9788	0.3988	0.6687	0.9778	0.8037	0.9533	0.8504
FFA(18:0)	0.9012	0.9298	0.9533	0.4709	0.6345	0.8371	0.9785	0.8390	0.9022
FFA(18:1)	0.8355	0.9961	0.9832	0.5784	0.9494	0.8886	0.4206	0.9124	0.5538
FFA(18:2)	0.6625	0.9883	0.9957	0.0749	0.9342	0.9910	0.4206	0.1305	0.5054
FFA(20:0)	0.9246	0.9883	0.9523	0.4092	0.6687	0.7991	0.5655	0.4350	0.9327
FFA(20:1)	0.8355	0.9939	0.9788	0.8991	0.9875	0.9276	0.3703	0.9851	0.5638
FFA(20:2)	0.9990	0.9961	0.9832	0.4347	0.9346	0.8886	0.7799	0.7887	0.6487
FFA(20:4)	0.4942	0.9395	0.9788	0.0951	0.4775	0.8371	0.1192	0.9174	0.3828
FFA(22:0)	0.9990	0.9883	0.9709	0.2129	0.6239	0.8886	0.6624	0.5545	0.9022
FFA(22:1)	0.9182	0.8846	0.9533	0.2842	0.8577	0.8886	0.8407	0.8492	0.8093
FFA(22:2)	0.8009	0.9883	0.9709	0.9133	0.9342	0.9925	0.1973	0.9872	0.3745
FFA(22:3)	0.8112	0.8660	0.9832	0.9077	0.7433	0.8371	0.1151	0.1007	0.9512
FFA(24:0)	0.9771	0.9883	0.9287	0.0152	0.9014	0.9276	0.4921	0.0068	0.1794
FFA(24:1)	0.5662	0.7659	0.7977	0.0277	0.7560	0.8371	0.3282	0.1507	0.9139
FFA(24:2)	0.9896	0.9106	0.8171	0.4530	0.9568	0.9276	0.7764	0.4791	0.7516
FFA(24:3)	0.8206	0.9298	0.9291	0.4532	0.9283	0.9324	0.5120	0.6615	0.4093
GlcCer[NS] 34:1	0.9054	0.8122	0.8102	0.4237	0.7310	0.8886	0.8651	0.7795	0.7286
GlcCer[NS] 34:2	0.8747	0.9106	0.9523	0.8856	0.9342	0.8371	0.3727	0.4464	0.7998
GlcCer[NS] 40:1	0.6984	0.8846	0.9832	0.7870	0.6945	0.7600	0.8033	0.0373	0.0274
GlcCer[NS] 41:1	0.8947	0.8122	0.8289	0.9565	0.9109	0.9405	0.2731	0.9355	0.3783

Table S2.3D: PUFA/CHO study significant differences for within diet comparisons for all lipids (Glucoceramide [NS] 42:1 to Lysophosphatidylcholine 20:4)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
GlcCer[NS] 42:1	0.8324	0.9106	0.8832	0.9469	0.8577	0.7579	0.4170	0.6426	0.2546
GlcCer[NS] 42:2	0.7525	0.9298	0.9832	0.9292	0.8563	0.9090	0.6805	0.9807	0.7998
LysoPC 14:0	0.0121	0.9298	0.9832	0.0299	0.5560	0.8470	0.0160	0.0394	0.8038
LysoPC 15:0	0.1937	0.9338	0.7812	0.6656	0.9026	0.9276	0.8861	0.6909	0.8504
LysoPC 15:1	0.4367	0.9106	0.9832	0.9292	0.8092	0.6426	0.8480	0.5181	0.5299
LysoPC 16:0	0.1762	0.9916	0.9709	0.1795	0.7433	0.7826	0.1328	0.4156	0.7516
LysoPC 16:1	0.1919	0.9883	0.9832	0.0056	0.8288	0.7579	0.0811	0.0701	0.8938
LysoPC 17:1	0.0727	0.9612	0.9832	0.0161	0.8719	0.7991	0.0160	0.0280	0.7121
LysoPC 18:0	0.3883	0.9707	0.9709	0.9638	0.8092	0.6769	0.4326	0.5436	0.3424
LysoPC 18:1	0.4022	0.9481	0.9788	0.8886	0.8642	0.7736	0.4206	0.8492	0.4274
LysoPC 18:2	0.7942	0.9883	0.9848	0.5981	0.8712	0.7991	0.8528	0.1014	0.2546
LysoPC 18:3	0.0209	0.9298	0.9832	0.0306	0.9875	0.7991	0.0403	0.3413	0.7314
LysoPC 19:0	0.9761	0.9883	0.9832	0.7179	0.6687	0.5971	0.6856	0.8652	0.6487
LysoPC 19:1	0.6500	0.9481	0.9788	0.9628	0.4059	0.5971	0.4170	0.8390	0.3831
LysoPC 20:0	0.3493	0.9106	0.8289	0.2871	0.6687	0.7053	0.1695	0.0074	0.1262
LysoPC 20:1	0.8324	0.8259	0.7977	0.8991	0.9109	0.6769	0.8014	0.1215	0.1248
LysoPC 20:2	0.6904	0.9106	0.8761	0.9245	0.5954	0.7811	0.3145	0.0208	0.3745
LysoPC 20:3	0.2599	0.9106	0.8832	0.0306	0.5954	0.8371	0.0207	0.0373	0.9888
LysoPC 20:4	0.7942	0.7393	0.9287	0.7342	0.4775	0.8371	0.2866	0.7138	0.7308
LysoPC 20:5	0.5773	0.9106	0.9832	0.6074	0.9892	0.7991	0.8407	0.1961	0.4274
LysoPC 22:0	0.9054	0.9106	0.8247	0.2790	0.9391	0.5971	0.5914	0.0081	0.0813
LysoPC 22:4	0.2692	0.9883	0.9887	0.1713	0.4775	0.9276	0.0501	0.0378	0.9327
LysoPC 22:5	0.2279	0.9106	0.8102	0.2409	0.3598	0.9276	0.0140	0.0224	0.8093
LysoPC 22:6	0.9012	0.8122	0.9832	0.9979	0.6239	0.8886	0.2328	0.4839	0.8504
LysoPC 23:0	0.6984	0.8942	0.9832	0.2046	0.7560	0.8886	0.8424	0.3516	0.3745
LysoPC 24:0	0.5544	0.9298	0.9832	0.9133	0.7560	0.5971	0.6665	0.0270	0.2221
LysoPC 24:1	0.6904	0.9106	0.9887	0.7342	0.9875	0.7991	0.8431	0.8732	0.9856
LysoPC 26:1	0.7942	0.9106	0.9832	0.8383	0.6657	0.5971	0.5693	0.7653	0.4533
LysoPE 16:0	0.2984	0.9607	0.9832	0.0605	0.6687	0.8371	0.2119	0.0374	0.5724
LysoPE 18:0	0.2094	0.9298	0.9523	0.1828	0.8046	0.7728	0.0664	0.3202	0.6487
LysoPE 18:1	0.1100	0.9106	0.9832	0.9845	0.7560	0.6769	0.2295	0.4350	0.1248
LysoPE 18:2	0.8324	0.9883	0.9533	0.7574	0.9922	0.6769	0.8209	0.2820	0.3601
LysoPE 20:3	0.1364	0.9961	0.9957	0.1753	0.8188	0.8582	0.1002	0.1992	0.9337
LysoPE 20:4	0.1398	0.9883	0.8442	0.0302	0.7546	0.8661	0.0238	0.0839	0.7308

Table S2.3E: PUFA/CHO study significant differences for within diet comparisons for all lipids (Lysophosphatidylcholine 20:5 to Phosphatidylcholine 36:4)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
LysoPE 20:5	0.0838	0.9546	0.9832	0.0386	0.6687	0.7991	0.0574	0.1118	0.9453
LysoPE 22:4	0.6625	0.9298	0.9523	0.0614	0.9391	0.9405	0.0956	0.0402	0.9327
LysoPE 22:5	0.1577	0.9298	0.7057	0.0389	0.4059	0.9778	0.0140	0.0029	0.8093
LysoPE 22:6	0.6984	0.9106	0.8261	0.0248	0.6757	0.8886	0.0223	0.0224	0.9328
PA 34:2	0.0705	0.4849	0.9887	0.2654	0.3341	0.8886	0.6805	0.6768	0.4653
PC 26:0	0.0778	0.6154	0.9788	0.9746	0.3323	0.9276	0.2106	0.1635	0.8989
PC 29:0	0.0227	0.9106	0.7977	0.0278	0.5696	0.9324	0.0207	0.0246	0.9477
PC 30:0	0.0095	0.8122	0.7977	0.0411	0.4775	0.8886	0.0160	0.0020	0.6487
PC 30:2	0.1022	0.9707	0.9832	0.2992	0.8467	0.8214	0.0973	0.1801	0.9022
PC 31:0	0.0095	0.7311	0.7603	0.0217	0.4298	0.9008	0.0160	0.0027	0.7516
PC 31:1	0.1778	0.7311	0.8171	0.0278	0.8884	0.9276	0.1973	0.0385	0.6487
PC 32:0	0.5623	0.9883	0.7603	0.0535	0.5954	0.7991	0.0562	0.0374	0.9328
PC 32:1	0.0778	0.9298	0.7954	0.0120	0.6687	0.9276	0.0294	0.0063	0.4567
PC 32:2	0.5010	0.9961	0.9709	0.2337	0.9687	0.8470	0.1864	0.6187	0.6487
PC 32:3	0.0218	0.8841	0.8107	0.0043	0.9342	0.8371	0.0216	0.0137	0.9453
PC 33:0	0.0778	0.9338	0.7057	0.0265	0.5306	0.9090	0.0140	0.0021	0.8599
PC 33:1	0.0095	0.8855	0.7603	0.0021	0.5701	0.8470	0.0140	0.0010	0.5093
PC 33:2	0.8747	0.9961	0.9523	0.6675	0.8884	0.8886	0.4206	0.8876	0.4943
PC 33:3	0.0548	0.8846	0.9533	0.0348	0.9873	0.9276	0.0612	0.0338	0.8093
PC 34:1	0.0778	0.9106	0.7603	0.0001	0.8602	0.7991	0.0140	0.0010	0.6487
PC 34:2	0.6984	0.7393	0.9523	0.5473	0.9159	0.8371	0.9639	0.2578	0.3745
PC 34:3	0.9814	0.9106	0.9291	0.4702	0.9875	0.7991	0.9471	0.9826	0.9817
PC 34:4	0.0567	0.9298	0.9523	0.6074	0.6687	0.8470	0.0948	0.4360	0.8093
PC 34:5	0.9012	0.9298	0.9872	0.2849	0.6345	0.7736	0.6665	0.3621	0.9702
PC 35:0	0.6904	0.3847	0.9533	0.3890	0.9875	0.6769	0.0753	0.0297	0.6691
PC 35:1	0.4942	0.9909	0.7603	0.0358	0.3751	0.8886	0.0664	0.0035	0.6194
PC 35:2	0.9967	0.9883	0.8102	0.6194	0.9152	0.6676	0.4115	0.4413	0.1518
PC 35:3	0.6984	0.9106	0.9709	0.4247	0.9705	0.8249	0.5900	0.7863	0.8813
PC 35:4	0.8054	0.9415	0.8102	0.0555	0.7325	0.8371	0.0811	0.0390	0.9969
PC 35:5	0.0778	0.7427	0.9533	0.0240	0.9593	0.9405	0.0324	0.0185	0.7418
PC 36:0	0.5087	0.9298	0.9287	0.9166	0.8467	0.5971	0.6856	0.4789	0.3783
PC 36:1	0.0591	0.9106	0.9533	0.0075	0.4775	0.7736	0.0159	0.0068	0.9139
PC 36:2	0.9484	0.9861	0.9287	0.9771	0.9976	0.5971	0.7200	0.1608	0.1262
PC 36:3	0.9392	0.8122	0.9287	0.9316	0.6687	0.7736	0.5945	0.9650	0.6487
PC 36:4	0.6984	0.5910	0.9848	0.4702	0.6345	0.9910	0.0690	0.0318	0.7120

Table S2.3F: PUFA/CHO study significant differences for within diet comparisons for all lipids (Phosphatidylcholine 36:5 to Phosphatidylcholine 42:2)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
PC 36:5	0.2929	0.9106	0.7603	0.0033	0.6757	0.7811	0.0166	0.0020	0.5538
PC 36:6	0.2410	0.9883	0.9523	0.0152	0.8348	0.7826	0.0574	0.0738	0.9184
PC 37:1	0.3652	0.9106	0.7603	0.3015	0.3728	0.7826	0.0466	0.0224	0.8938
PC 37:2	0.9990	0.9707	0.9709	0.9077	0.9043	0.7991	0.6309	0.9282	0.6118
PC 37:3	0.7942	0.9106	0.7603	0.0751	0.3341	0.5971	0.0445	0.0222	0.9731
PC 37:4	0.6984	0.8346	0.7603	0.0229	0.6687	0.6769	0.0140	0.0229	0.5819
PC 37:5	0.6984	0.9338	0.9287	0.0701	0.7560	0.7991	0.0980	0.0712	0.9512
PC 37:6	0.6625	0.8846	0.7603	0.6074	0.6050	0.9336	0.2254	0.0394	0.6487
PC 37:7	0.9484	0.9298	0.8895	0.4530	0.9312	0.8520	0.7894	0.5859	0.8504
PC 38:1	0.9896	0.8122	0.9533	0.9945	0.8467	0.7991	0.6828	0.7363	0.6487
PC 38:2	0.9896	0.9883	0.9523	0.1638	0.9494	0.7053	0.5727	0.9486	0.7516
PC 38:3	0.6304	0.5910	0.8102	0.0222	0.4059	0.7579	0.0166	0.0205	0.9243
PC 38:4	0.7525	0.9883	0.7954	0.1118	0.9152	0.8371	0.0680	0.1801	0.7314
PC 38:5	0.6911	0.8122	0.7603	0.0060	0.4750	0.6769	0.0140	0.0053	0.7314
PC 38:6	0.8184	0.9298	0.7603	0.1057	0.8467	0.8371	0.2631	0.0882	0.8599
PC 38:7	0.8355	0.8802	0.9848	0.9077	0.8884	0.9276	0.7632	0.7564	0.6387
PC 39:3	0.9182	0.9883	0.7954	0.4709	0.4356	0.7736	0.3387	0.2016	0.9139
PC 39:4	0.8324	0.9106	0.7977	0.0437	0.3323	0.7991	0.0219	0.0297	0.9327
PC 39:5	0.5376	0.9481	0.7603	0.1428	0.4059	0.8371	0.0207	0.0059	0.9849
PC 39:6	0.6984	0.9106	0.6986	0.0116	0.4775	0.8452	0.0140	0.0068	0.8649
PC 39:7	0.8355	0.9607	0.8895	0.3840	0.9875	0.9276	0.5945	0.3175	0.7516
PC 40:1	0.9598	0.5580	0.7603	0.0639	0.9210	0.8371	0.7854	0.0854	0.2861
PC 40:2	0.8009	0.9961	0.9832	0.6709	0.9342	0.7943	0.5824	0.1573	0.6487
PC 40:3	0.9823	0.9338	0.9709	0.4268	0.5954	0.5971	0.4421	0.9761	0.5724
PC 40:4	0.7942	0.9370	0.8482	0.2049	0.4812	0.9324	0.0680	0.0046	0.4274
PC 40:5	0.9896	0.7393	0.7603	0.3015	0.3341	0.9795	0.0466	0.0020	0.4093
PC 40:6	0.9859	0.9359	0.7057	0.0043	0.8066	0.8371	0.0294	0.0053	0.5724
PC 40:7	0.6625	0.8259	0.9709	0.1713	0.9108	0.7579	0.6707	0.8781	0.6487
PC 40:8	0.5181	0.8122	0.9832	0.7870	0.8763	0.7991	0.7764	0.4230	0.4946
PC 40:9	0.3211	0.9298	0.9708	0.1920	0.9098	0.7991	0.0836	0.9187	0.5832
PC 41:6	0.2823	0.9106	0.9832	0.1553	0.6945	0.8886	0.4676	0.8544	0.7516
PC 41:7	0.1565	0.8122	0.9832	0.4220	0.8719	0.7579	0.2631	0.7777	0.5083
PC 42:1	0.9905	0.9298	0.7603	0.3163	0.8884	0.8314	0.1604	0.9540	0.3601
PC 42:10	0.6984	0.9883	0.7603	0.0599	0.9262	0.7600	0.0723	0.2095	0.4647
PC 42:2	0.6984	0.9106	0.9832	0.9342	0.8719	0.7579	0.9471	0.2304	0.3067

Table S2.3G: PUFA/CHO study significant differences for within diet comparisons for all lipids (Phosphatidylcholine 42:3 to Phosphatidylethanolamine 40:6)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
PC 42:3	0.0492	0.9106	0.9859	0.9057	0.4750	0.9276	0.1575	0.2449	0.8504
PC 42:4	0.8747	0.9961	0.9957	0.9133	0.9152	0.8371	0.6805	0.8845	0.8623
PC 42:5	0.8324	0.9883	0.7977	0.4709	0.7325	0.8886	0.1156	0.3859	0.7516
PC 42:6	0.9031	0.9106	0.9287	0.3618	0.4059	0.8371	0.2842	0.1761	0.8813
PC 42:7	0.9012	0.9883	0.9887	0.9565	0.7658	0.9081	0.8990	0.4096	0.6487
PC 42:8	0.6984	0.9883	0.9957	0.9479	0.9342	0.5971	0.6135	0.1528	0.5054
PC 42:9	0.2599	0.9883	0.9848	0.9343	0.3341	0.5971	0.0477	0.9540	0.1250
PC 44:4	0.9012	0.9607	0.7603	0.3489	0.8642	0.6426	0.5763	0.4898	0.3745
PE 32:1	0.0336	0.3847	0.7977	0.0358	0.7631	0.8886	0.1192	0.0373	0.6070
PE 32:2	0.9868	0.9106	0.8102	0.1529	0.8046	0.7991	0.1702	0.0977	0.8093
PE 33:0	0.7112	0.9883	0.9832	0.4268	0.9109	0.8661	0.4779	0.2711	0.9337
PE 33:1	0.9012	0.9883	0.9788	0.6329	0.7560	0.9276	0.7200	0.4105	0.8093
PE 33:2	0.8355	0.9883	0.9523	0.2654	0.8467	0.8886	0.3313	0.3202	0.9337
PE 34:0	0.9182	0.9961	0.9523	0.8988	0.9109	0.7914	0.7396	0.6509	0.9327
PE 34:1	0.1229	0.7393	0.9287	0.0265	0.8951	0.9276	0.1575	0.0441	0.7047
PE 34:2	0.7942	0.9106	0.9523	0.1434	0.9312	0.8886	0.6665	0.4663	0.8093
PE 34:3	0.6739	0.8122	0.7603	0.0791	0.8719	0.9910	0.2197	0.0375	0.4093
PE 35:1	0.9896	0.9106	0.9291	0.1123	0.9124	0.8825	0.9480	0.3175	0.6547
PE 35:2	0.7879	0.9106	0.9709	0.3840	0.8348	0.8371	0.6805	0.3955	0.8038
PE 35:4	0.9182	0.9707	0.8102	0.1847	0.9494	0.9276	0.4676	0.2820	0.8638
PE 36:0	0.7942	0.9106	0.9832	0.9565	0.8763	0.8886	0.8674	0.9826	0.9328
PE 36:1	0.4277	0.9298	0.9523	0.3840	0.9705	0.7600	0.8033	0.7863	0.6691
PE 36:2	0.9868	0.9583	0.9895	0.8201	0.9875	0.7728	0.8162	0.4898	0.6959
PE 36:3	0.9271	0.9941	0.9788	0.9565	0.9875	0.7826	0.5771	0.3724	0.7843
PE 36:4	0.9990	0.9298	0.9957	0.9565	0.8719	0.8661	0.6537	0.9282	0.8504
PE 36:5	0.7733	0.7393	0.7603	0.0239	0.8467	0.9276	0.0574	0.0161	0.4093
PE 37:4	0.4535	0.9961	0.9523	0.3890	0.6345	0.8371	0.2515	0.1589	0.8599
PE 38:3	0.9054	0.9338	0.9848	0.7256	0.7560	0.9531	0.5921	0.2095	0.5744
PE 38:4	0.9033	0.9106	0.9887	0.7256	0.6732	0.8371	0.4851	0.3554	0.8504
PE 38:5	0.8009	0.9883	0.9832	0.2842	0.9312	0.8371	0.5945	0.4704	0.9109
PE 38:6	0.9831	0.9883	0.9709	0.5214	0.8467	0.9381	0.6347	0.2557	0.6487
PE 38:7	0.9012	0.9298	0.9832	0.6074	0.7910	0.8371	0.5693	0.5604	0.9801
PE 40:4	0.0834	0.8122	0.9709	0.3895	0.6687	0.7991	0.1973	0.4789	0.8813
PE 40:5	0.8747	0.9298	0.8895	0.4220	0.5100	0.8371	0.1973	0.0441	0.5908
PE 40:6	0.9990	0.9106	0.9832	0.5236	0.8467	0.8886	0.5925	0.2977	0.6691

Table S2.3H: PUFA/CHO study significant differences for within diet comparisons for all lipids (Phosphatidylethanolamine 40:7 to Plasmenyl-phosphatidylcholine 37:3)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
PE 40:7	0.8324	0.9106	0.9832	0.9628	0.9875	0.8371	0.8509	0.6509	0.8504
PE 40:8	0.9012	0.9106	0.9709	0.9226	0.9109	0.8660	0.8810	0.6168	0.8504
PG 33:0	0.9033	0.9106	0.9335	0.4805	0.6139	0.8371	0.5437	0.9006	0.6375
PG 34:2	0.9054	0.8122	0.8102	0.7701	0.6687	0.8099	0.6105	0.5915	0.9953
PG 36:0	0.9012	0.9106	0.9832	0.4358	0.8467	0.7179	0.2726	0.0854	0.5538
PG 36:2	0.7002	0.8511	0.7603	0.6559	0.6565	0.7991	0.2647	0.2444	0.9856
PG 36:3	0.9979	0.9106	0.9832	0.7045	0.8712	0.9778	0.6488	0.8210	0.8497
PI 34:2	0.9648	0.9883	0.9832	0.2871	0.6945	0.8371	0.8861	0.4087	0.5908
PI 36:1	0.2041	0.9883	0.9523	0.6031	0.9159	0.8886	0.0829	0.4180	0.2861
PI 36:2	0.4022	0.9883	0.9788	0.3747	0.5954	0.8886	0.1575	0.0224	0.6487
PI 36:4	0.5269	0.9883	0.9523	0.1416	0.9873	0.9925	0.3372	0.1089	0.5724
PI 38:3	0.8947	0.9883	0.9533	0.9077	0.9210	0.8886	0.4464	0.2139	0.9832
PI 38:4	0.9182	0.9918	0.9533	0.7256	0.8467	0.8314	0.5871	0.4096	0.9453
PI 38:5	0.7942	0.9298	0.9848	0.2491	0.6687	0.8565	0.6488	0.4422	0.8043
PI 38:6	0.9776	0.9883	0.8560	0.2337	0.9346	0.9405	0.5900	0.2711	0.6487
PI 40:6	0.9033	0.9883	0.9887	0.6329	0.9494	0.7811	0.9609	0.0375	0.1250
PlsCho 24:0	0.7525	0.9106	0.9887	0.6437	0.9705	0.7738	0.9653	0.8555	0.9327
PlsCho 32:0	0.9472	0.9078	0.9291	0.7140	0.9109	0.7991	0.9950	0.9998	0.9961
PlsCho 32:1	0.7237	0.9106	0.7057	0.2773	0.5954	0.8314	0.4095	0.9282	0.3067
PlsCho 33:0	0.6625	0.9825	0.9832	0.6233	0.9159	0.8371	0.4421	0.9979	0.5908
PlsCho 34:0	0.9012	0.9338	0.9832	0.9226	0.9494	0.7991	0.4245	0.5023	0.2546
PlsCho 34:1	0.1953	0.9825	0.9832	0.0555	0.8642	0.6676	0.3387	0.0029	0.0274
PlsCho 34:2	0.7942	0.9883	0.9832	0.7342	0.8884	0.7991	0.8417	0.1438	0.3783
PlsCho 34:3	0.8445	0.9883	0.7603	0.4431	0.6687	0.9008	0.1250	0.8492	0.2546
PlsCho 35:1	0.9979	0.7311	0.9333	0.5473	0.6345	0.8470	0.5900	0.5450	0.9512
PlsCho 35:2	0.9012	0.9106	0.9848	0.9332	0.9391	0.7991	0.8674	0.3859	0.5819
PlsCho 35:3	0.1778	0.9883	0.9788	0.5625	0.9875	0.9276	0.1690	0.6909	0.1794
PlsCho 36:0	0.9884	0.8122	0.8159	0.6048	0.9109	0.8314	0.0403	0.1853	0.0274
PlsCho 36:2	0.8324	0.9298	0.9832	0.8729	0.9875	0.9405	0.4236	0.8050	0.4274
PlsCho 36:3	0.9054	0.9106	0.7603	0.4347	0.4059	0.6769	0.0664	0.4789	0.0274
PlsCho 36:4	0.9979	0.9883	0.7603	0.6381	0.8467	0.7991	0.1973	0.4180	0.1250
PlsCho 36:5	0.8355	0.9106	0.8107	0.4709	0.4059	0.6676	0.4977	0.6909	0.5724
PlsCho 36:6	0.4942	0.9298	0.9523	0.9979	0.9465	0.7991	0.2497	0.4435	0.8590
PlsCho 37:1	0.9859	0.9961	0.7977	0.1173	0.5152	0.9276	0.3387	0.3859	0.1258
PlsCho 37:3	0.7942	0.9883	0.9832	0.7574	0.4569	0.7991	0.4813	0.8595	0.6487

Table S2.3I: PUFA/CHO study significant differences for within diet comparisons for all lipids (Plasmenyl-phosphatidylcholine 37:3 to Plasmenyl-phosphatidylethanolamine 34:3)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
PlsCho 37:4	0.9761	0.9883	0.7603	0.7574	0.8719	0.9778	0.1186	0.9190	0.2288
PlsCho 37:6	0.9012	0.9106	0.9832	0.0617	0.5954	0.7736	0.2633	0.1215	0.0469
PlsCho 38:1	0.9182	0.9106	0.7603	0.4688	0.9159	0.8371	0.4151	0.3136	0.8693
PlsCho 38:3	0.6984	0.8122	0.7603	0.9565	0.5152	0.7991	0.0140	0.8032	0.0274
PlsCho 38:4	0.7942	0.9106	0.9709	0.3784	0.7631	0.6769	0.6083	0.1215	0.0469
PlsCho 38:5	0.9012	0.9298	0.7603	0.3586	0.6250	0.6769	0.2119	0.1904	0.0469
PlsCho 38:6	0.9182	0.9481	0.9297	0.4530	0.8719	0.8371	0.4813	0.3859	0.2546
PlsCho 39:3	0.8355	0.9106	0.9287	0.6437	0.8101	0.5971	0.6856	0.5859	0.5054
PlsCho 39:4	0.7237	0.9961	0.7603	0.2129	0.4059	0.5971	0.0466	0.1086	0.6487
PlsCho 39:5	0.7116	0.9392	0.6175	0.1205	0.4750	0.5971	0.1192	0.2738	0.5969
PlsCho 39:6	0.8720	0.9106	0.9291	0.7140	0.9683	0.9405	0.4716	0.8555	0.5014
PlsCho 40:1	0.8586	0.9106	0.9709	0.1378	0.8348	0.9405	0.6105	0.2747	0.7512
PlsCho 40:3	0.8206	0.7311	0.9957	0.0736	0.7257	0.9090	0.4170	0.2292	0.1262
PlsCho 40:4	0.9054	0.9481	0.7603	0.7870	0.7631	0.8371	0.1740	0.8150	0.1250
PlsCho 40:5	0.9012	0.9106	0.9709	0.7574	0.8642	0.7991	0.2382	0.8555	0.3745
PlsCho 40:6	0.9831	0.9106	0.7977	0.5236	0.7560	0.9910	0.1192	0.9285	0.1542
PlsCho 42:0	0.9495	0.6987	0.9709	0.6074	0.9312	0.9499	0.3865	0.7067	0.5087
PlsCho 42:1	0.9012	0.8122	0.7603	0.4823	0.9468	0.9910	0.1449	0.6103	0.4943
PlsCho 42:2	0.6625	0.9106	0.9832	0.8201	0.8467	0.9324	0.9480	0.4096	0.5740
PlsCho 42:3	0.6625	0.8841	0.9291	0.9511	0.6687	0.8371	0.6624	0.7863	0.5957
PlsCho 42:4	0.9896	0.9106	0.8152	0.9565	0.6687	0.9910	0.1121	0.4898	0.5028
PlsCho 42:5	0.8355	0.9961	0.9788	0.6709	0.9548	0.7179	0.4199	0.5023	0.9139
PlsCho 42:6	0.9598	0.9106	0.9914	0.8587	0.9262	0.8371	0.5548	0.9254	0.6466
PlsCho 44:3	0.8747	0.7427	0.7977	0.1988	0.9548	0.9324	0.1517	0.3175	0.7121
PlsCho 44:4	0.9366	0.9106	0.8171	0.6559	0.8719	0.8886	0.1655	0.2709	0.8504
PlsCho 44:5	0.6984	0.9481	0.7603	0.8150	0.7433	0.7579	0.0834	0.4898	0.4946
PlsCho 44:6	0.8112	0.9939	0.9709	0.9077	0.5701	0.7736	0.9885	0.8613	0.8813
PlsCho 46:4	0.9012	0.9883	0.9533	0.7574	0.9875	0.7943	0.4104	0.3175	0.9512
PlsEth 32:1	0.1827	0.9541	0.9287	0.9292	0.4750	0.7579	0.2802	0.6237	0.7102
PlsEth 32:2	0.8997	0.6154	0.9709	0.3015	0.8467	0.9675	0.6990	0.5238	0.4567
PlsEth 33:2	0.8355	0.9106	0.9887	0.5124	0.6154	0.8825	0.4407	0.8634	0.5635
PlsEth 34:0	0.9979	0.9338	0.9923	0.3266	0.9109	0.9276	0.6537	0.4941	0.3858
PlsEth 34:1	0.9979	0.8660	0.9334	0.6048	0.9705	0.9910	0.6320	0.5575	0.4785
PlsEth 34:2	0.6984	0.9298	0.9832	0.0565	0.9875	0.7991	0.8990	0.0224	0.0933
PlsEth 34:3	0.9922	0.6506	0.9788	0.1267	0.4290	0.5971	0.2356	0.1007	0.1023

Table S2.3J: PUFA/CHO study significant differences for within diet comparisons for all lipids (Plasmenyl-phosphatidylethanolamine 34:4 to Sphingomyelin 30:2)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
PlsEth 34:4	0.6984	0.8122	0.9533	0.9077	0.9705	0.9276	0.1575	0.8163	0.2546
PlsEth 35:1	0.6984	0.9106	0.9523	0.8186	0.4356	0.8886	0.4450	0.7067	0.8523
PlsEth 35:2	0.7942	0.5580	0.9832	0.0535	0.4750	0.7179	0.4326	0.0839	0.0545
PlsEth 35:4	0.2599	0.8122	0.9533	0.7140	0.5954	0.8314	0.0344	0.3935	0.3360
PlsEth 36:1	0.6625	0.5039	0.9709	0.2694	0.4750	0.9276	0.0324	0.9540	0.1357
PlsEth 36:2	0.9472	0.9298	0.9832	0.0120	0.6139	0.7579	0.7854	0.0161	0.0350
PlsEth 36:3	0.6693	0.8846	0.9523	0.0073	0.5987	0.8371	0.6097	0.0315	0.2546
PlsEth 36:4	0.7942	0.9106	0.9523	0.0598	0.5954	0.8371	0.8407	0.2556	0.3828
PlsEth 36:5	0.9054	0.7039	0.7977	0.9077	0.3323	0.7736	0.0680	0.7824	0.3601
PlsEth 36:6	0.9484	0.9106	0.9832	0.5236	0.8101	0.9577	0.7200	0.8781	0.7314
PlsEth 37:1	0.9012	0.9027	0.9832	0.9022	0.9152	0.7811	0.7422	0.3737	0.6407
PlsEth 37:2	0.9367	0.9106	0.9832	0.8238	0.6687	0.7579	0.2446	0.0971	0.6487
PlsEth 37:4	0.6984	0.9106	0.9334	0.2337	0.4059	0.8371	0.0612	0.9826	0.2860
PlsEth 37:5	0.6904	0.6182	0.7977	0.6010	0.7910	0.9698	0.0160	0.2304	0.3071
PlsEth 37:6	0.8747	0.6154	0.7603	0.7870	0.4356	0.7736	0.1973	0.3988	0.6387
PlsEth 38:1	0.8947	0.8122	0.9523	0.9327	0.9342	0.9265	0.2731	0.5736	0.6524
PlsEth 38:2	0.7733	0.9106	0.9887	0.1655	0.6687	0.8371	0.9609	0.2578	0.5054
PlsEth 38:3	0.7701	0.7393	0.9709	0.2654	0.3598	0.9048	0.0282	0.6122	0.3783
PlsEth 38:4	0.8747	0.8885	0.8399	0.6010	0.5306	0.7991	0.0993	0.9533	0.1542
PlsEth 38:5	0.9979	0.9298	0.7977	0.2670	0.4465	0.6769	0.1953	0.2977	0.1023
PlsEth 38:6	0.6861	0.7393	0.9832	0.2222	0.8467	0.8371	0.7209	0.1924	0.1794
PlsEth 39:4	0.9067	0.8846	0.7977	0.6675	0.8406	0.8886	0.1994	0.8050	0.3721
PlsEth 39:5	0.9305	0.6154	0.9832	0.1416	0.3323	0.8886	0.1718	0.9190	0.4946
PlsEth 39:6	0.8417	0.5580	0.9709	0.3618	0.6687	0.7826	0.0387	0.3692	0.1276
PlsEth 40:2	0.7161	0.9546	0.9523	0.1998	0.5954	0.8565	0.9827	0.5345	0.7057
PlsEth 40:4	0.8324	0.7393	0.9851	0.2660	0.6565	0.9276	0.5655	0.8032	0.5740
PlsEth 40:5	0.9012	0.7311	0.9523	0.2735	0.4775	0.7991	0.0436	0.6509	0.1023
PlsEth 40:6	0.7942	0.9142	0.9709	0.1432	0.6757	0.7736	0.1379	0.1215	0.0274
PlsEth 42:4	0.9979	0.9106	0.9848	0.7574	0.9548	0.9157	0.6595	0.9646	0.8182
PlsEth 42:5	0.6711	0.9106	0.9523	0.5473	0.5560	0.8371	0.6537	0.8576	0.6487
PlsEth 42:6	0.6693	0.9106	0.9832	0.3747	0.9705	0.9531	0.6856	0.4108	0.3858
PlsEth 44:6	0.6984	0.9961	0.9523	0.7477	0.9342	0.9324	0.8121	0.4789	0.5724
SM 30:0	0.2907	0.9961	0.7603	0.6709	0.6687	0.7579	0.0235	0.0297	0.7335
SM 30:1	0.5667	0.9106	0.6175	0.2435	0.4059	0.9276	0.0140	0.0429	0.3783
SM 30:2	0.9896	0.8122	0.9923	0.7870	0.6345	0.8886	0.6805	0.6644	0.9034

Table S2.3K: PUFA/CHO study significant differences for within diet comparisons for all lipids (Sphingomyelin 31:1 to Sphingomyelin 42:2)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
SM 31:1	0.6984	0.9106	0.7603	0.6381	0.3323	0.9405	0.0160	0.0324	0.6487
SM 32:0	0.7219	0.9923	0.9533	0.2402	0.4750	0.9276	0.6805	0.9282	0.7516
SM 32:1	0.9012	0.8122	0.9832	0.6564	0.4775	0.8661	0.0680	0.4898	0.4093
SM 32:2	0.7525	0.9106	0.6175	0.0800	0.4775	0.9531	0.0147	0.0102	0.5908
SM 33:1	0.9990	0.8122	0.9957	0.6424	0.6687	0.9086	0.1250	0.8599	0.4093
SM 33:2	0.8325	0.9106	0.8391	0.5825	0.9705	0.8371	0.2941	0.9028	0.4274
SM 34:0	0.5623	0.9298	0.9333	0.5097	0.7560	0.7235	0.1745	0.2738	0.9328
SM 34:1	0.5544	0.5580	0.9523	0.4092	0.6565	0.9796	0.7200	0.9799	0.8504
SM 34:2	0.9495	0.7393	0.9635	0.3749	0.5954	0.9778	0.2303	0.8492	0.4946
SM 34:3	0.9472	0.9883	0.8102	0.8469	0.8467	0.9276	0.6885	0.9540	0.8504
SM 35:2	0.8355	0.9106	0.9709	0.9077	0.6687	0.8886	0.1250	0.8131	0.3858
SM 36:1	0.9012	0.7039	0.9709	0.6437	0.8348	0.9276	0.5655	0.8919	0.8504
SM 36:2	0.6984	0.6154	0.9957	0.7171	0.5907	0.9086	0.3282	0.6509	0.8182
SM 36:3	0.5667	0.9298	0.9832	0.6424	0.8406	0.7991	0.6314	0.1215	0.4122
SM 36:4	0.1240	0.9707	0.8071	0.9469	0.4059	0.7728	0.3366	0.0251	0.3093
SM 37:1	0.9468	0.9883	0.9523	0.4702	0.9079	0.8371	0.5243	0.3202	0.3210
SM 37:2	0.6495	0.9106	0.7603	0.2344	0.8348	0.7991	0.1433	0.5103	0.6020
SM 38:0	0.9054	0.9298	0.9957	0.9417	0.6345	0.8371	0.8674	0.9190	0.9849
SM 38:1	0.6984	0.7393	0.9523	0.2491	0.7631	0.7728	0.9921	0.0457	0.2546
SM 38:2	0.0468	0.7658	0.9832	0.3793	0.7910	0.8371	0.4676	0.3621	0.8038
SM 38:3	0.6693	0.9298	0.9832	0.9327	0.7560	0.9910	0.7200	0.6509	0.8813
SM 38:4	0.9054	0.9883	0.9523	0.4347	0.9582	0.6769	0.3638	0.0292	0.3783
SM 39:1	0.9761	0.9106	0.9788	0.2854	0.7560	0.7991	0.2905	0.2095	0.1250
SM 39:2	0.7579	0.9186	0.6175	0.5124	0.8642	0.5971	0.1127	0.8652	0.1794
SM 39:3	0.7525	0.9106	0.7977	0.8201	0.8712	0.7736	0.2690	0.4441	0.1023
SM 40:1	0.8324	0.5580	0.9533	0.1927	0.7560	0.7579	0.3638	0.0240	0.0403
SM 40:2	0.9033	0.9395	0.4083	0.6424	0.9079	0.5971	0.0831	0.0315	0.0274
SM 40:3	0.7942	0.9298	0.7954	0.1598	0.7433	0.9276	0.9509	0.8188	0.8639
SM 40:5	0.9990	0.9106	0.9832	0.9226	0.9346	0.7991	0.4703	0.6798	0.8813
SM 41:1	0.7942	0.9106	0.7603	0.7574	0.9829	0.8371	0.1953	0.2825	0.1248
SM 41:2	0.6500	0.7311	0.9533	0.7574	0.6687	0.8371	0.2119	0.8781	0.5623
SM 41:4	0.5667	0.8784	0.9832	0.9628	0.9548	0.5971	0.9605	0.1065	0.2391
SM 41:6	0.9587	0.9298	0.9291	0.9022	0.6345	0.7736	0.6707	0.8492	0.6487
SM 42:1	0.6898	0.9106	0.7603	0.6010	0.9342	0.6769	0.3202	0.0297	0.0274
SM 42:2	0.8355	0.9392	0.9832	0.8991	0.9312	0.9276	0.3703	0.4364	0.9781

Table S2.3L: PUFA/CHO study significant differences for within diet comparisons for all lipids (Sphingomyelin 42:3 to Triacylglycerol 48:5)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
SM 42:3	0.5667	0.9338	0.8107	0.5784	0.9283	0.8371	0.5921	0.8599	0.6466
SM 42:4	0.9012	0.9106	0.8171	0.1280	0.9109	0.9276	0.9757	0.1608	0.2546
SM 42:5	0.9472	0.9106	0.9287	0.8617	0.9342	0.9276	0.9640	0.5607	0.6487
SM 42:6	0.8325	0.9883	0.8171	0.7534	0.8348	0.8470	0.7200	0.8050	0.9731
SM 43:1	0.9054	0.9707	0.7603	0.8045	0.9079	0.8886	0.0690	0.9399	0.2411
SM 43:2	0.8324	0.9106	0.7954	0.7045	0.9109	0.9795	0.3032	0.5181	0.9158
SM 43:3	0.9979	0.9961	0.9287	0.7574	0.8467	0.9910	0.5605	0.4898	0.9139
SM 43:6	0.8324	0.9961	0.9832	0.6437	0.9892	0.7991	0.7209	0.9190	0.7516
SM 44:1	0.6861	0.9298	0.9555	0.8965	0.8884	0.8655	0.3202	0.9650	0.6487
SM 44:2	0.9896	0.9941	0.9788	0.9416	0.9548	0.8886	0.7200	0.7765	0.6111
SM 44:3	0.4210	0.9106	0.8102	0.7179	0.8763	0.8371	0.1575	0.3568	0.6487
SM 44:4	0.9012	0.9106	0.9533	0.7202	0.7257	0.7991	0.5763	0.5009	0.8813
SM 44:6	0.9979	0.9883	0.9709	0.5171	0.8467	0.8459	0.6037	0.9827	0.7255
TG 38:0	0.0373	0.8660	0.7603	0.7123	0.9875	0.7600	0.2541	0.4087	0.1794
TG 39:0	0.7521	0.9883	0.8102	0.0419	0.6687	0.7736	0.0948	0.0301	0.8759
TG 40:0	0.0227	0.7311	0.0000	0.0749	0.0018	0.0630	0.6856	0.1656	0.3581
TG 41:0	0.0470	0.8122	0.8102	0.6010	0.6687	0.5971	0.3387	0.4145	0.3018
TG 42:0	0.0110	0.4063	0.7603	0.0856	0.4059	0.6769	0.0160	0.6168	0.2646
TG 42:1	0.0138	0.5039	0.0455	0.1178	0.4059	0.7579	0.0207	0.5598	0.4093
TG 43:1	0.0195	0.5064	0.9832	0.0386	0.5999	0.7991	0.0378	0.2095	0.6487
TG 44:2	0.0095	0.3847	0.9832	0.0044	0.5611	0.7811	0.0153	0.1475	0.6278
TG 45:0	0.0122	0.7464	0.6986	0.8988	0.3323	0.8886	0.0324	0.0292	0.8093
TG 45:1	0.0195	0.5580	0.9523	0.1065	0.3968	0.8886	0.0649	0.0313	0.9817
TG 45:2	0.0102	0.3847	0.8102	0.0075	0.5100	0.8822	0.0189	0.0094	0.9512
TG 46:0	0.0110	0.3847	0.7977	0.0043	0.4059	0.8371	0.0141	0.0251	0.9856
TG 46:1	0.0095	0.3847	0.9533	0.0080	0.4059	0.8371	0.0160	0.0163	0.9953
TG 46:3	0.0095	0.3847	0.9533	0.0097	0.6345	0.7991	0.0318	0.0426	0.9832
TG 47:0	0.0218	0.6154	0.9957	0.3175	0.4059	0.9920	0.0304	0.0324	0.9512
TG 47:1	0.0095	0.3847	0.7977	0.0302	0.3341	0.8886	0.0180	0.0068	0.8813
TG 47:2	0.0095	0.4849	0.9291	0.0047	0.6345	0.8371	0.0235	0.0139	0.9512
TG 48:0	0.0128	0.3847	0.7603	0.0043	0.5954	0.8371	0.0160	0.0149	0.9022
TG 48:1	0.0095	0.3847	0.8540	0.0043	0.4775	0.8371	0.0141	0.0034	0.8018
TG 48:3	0.0111	0.5847	0.9333	0.0060	0.6687	0.8134	0.0294	0.0149	0.8093
TG 48:4	0.1768	0.9298	0.9848	0.0240	0.7910	0.7736	0.1151	0.1475	0.9327
TG 48:5	0.3211	0.9298	0.9887	0.0902	0.6945	0.8371	0.3202	0.0974	0.6487

Table S2.3M: PUFA/CHO study significant differences for within diet comparisons for all lipids (Triacylglycerol 49:0 to Triacylglycerol 54:4)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
TG 49:0	0.0347	0.5580	0.7977	0.0097	0.4775	0.8886	0.0301	0.0086	0.8504
TG 49:1	0.0095	0.3847	0.8102	0.0120	0.3762	0.8886	0.0160	0.0037	0.7998
TG 49:2	0.0095	0.4849	0.7977	0.0075	0.4356	0.8520	0.0207	0.0029	0.6487
TG 49:3	0.0218	0.7393	0.8474	0.0045	0.6687	0.8655	0.0420	0.0035	0.4650
TG 50:0	0.0138	0.3847	0.7603	0.0110	0.6139	0.8371	0.0284	0.0149	0.7121
TG 50:1	0.0122	0.3863	0.7603	0.0043	0.6757	0.8371	0.0284	0.0048	0.4946
TG 50:2	0.0314	0.8122	0.8159	0.0045	0.6687	0.8371	0.0436	0.0029	0.3067
TG 50:3	0.0780	0.9298	0.9523	0.0060	0.8712	0.8371	0.0704	0.0076	0.4650
TG 50:4	0.8355	0.9612	0.9887	0.0535	0.9312	0.7991	0.4332	0.1966	0.6524
TG 50:5	0.9182	0.9961	0.9709	0.0358	0.9109	0.7991	0.5997	0.1215	0.4274
TG 50:6	0.9776	0.9338	0.9533	0.0402	0.8719	0.7736	0.4332	0.3692	0.8038
TG 51:1	0.0095	0.3847	0.7977	0.0060	0.5987	0.8371	0.0324	0.0053	0.5740
TG 51:2	0.0095	0.7311	0.9287	0.0043	0.6687	0.8371	0.0284	0.0020	0.4653
TG 51:3	0.1937	0.9298	0.9709	0.0120	0.9079	0.8371	0.1575	0.0086	0.4174
TG 51:4	0.9896	0.9707	0.9832	0.0957	0.9109	0.7991	0.6734	0.4341	0.8093
TG 51:5	0.9012	0.9298	0.9523	0.0749	0.9391	0.7736	0.5764	0.3621	0.8093
TG 52:0	0.1057	0.6154	0.8560	0.0146	0.9109	0.7991	0.0973	0.2738	0.9454
TG 52:1	0.0095	0.4849	0.7977	0.0043	0.6657	0.7736	0.0207	0.0053	0.6487
TG 52:2	0.0208	0.8841	0.9533	0.0043	0.9159	0.7826	0.0496	0.0037	0.3071
TG 52:3	0.9979	0.9607	0.7977	0.0096	0.9548	0.6769	0.4813	0.0712	0.3831
TG 52:4	0.5202	0.9298	0.9832	0.2795	0.9548	0.7053	0.6512	0.9021	0.5832
TG 52:5	0.9761	0.9338	0.9523	0.0043	0.9210	0.7991	0.4003	0.0377	0.3745
TG 52:6	0.2961	0.8841	0.9832	0.1456	0.8467	0.7728	0.6068	0.9540	0.6387
TG 52:7	0.2811	0.8122	0.9957	0.0461	0.9109	0.8314	0.8407	0.3841	0.3783
TG 53:0	0.4461	0.9106	0.9832	0.1758	0.9875	0.8886	0.4236	0.4663	0.9856
TG 53:1	0.0978	0.7393	0.9709	0.0190	0.6565	0.8459	0.0948	0.0029	0.4274
TG 53:2	0.9012	0.8122	0.8171	0.0060	0.6945	0.7579	0.7824	0.0053	0.4943
TG 53:3	0.7077	0.9883	0.9832	0.0138	0.8712	0.7738	0.4851	0.0657	0.5635
TG 53:4	0.1953	0.9298	0.9709	0.3440	0.7257	0.5971	0.5618	0.4111	0.8504
TG 53:5	0.3566	0.9106	0.9832	0.1828	0.8712	0.8371	0.8528	0.6909	0.5832
TG 54:0	0.8325	0.9106	0.9832	0.5645	0.7560	0.8886	0.8861	0.6552	0.8599
TG 54:1	0.0095	0.3847	0.8560	0.0543	0.6687	0.7736	0.1099	0.0851	0.9670
TG 54:2	0.0350	0.7039	0.9790	0.0348	0.7557	0.7179	0.3037	0.0338	0.6387
TG 54:3	0.9979	0.9106	0.9832	0.2486	0.8884	0.5971	0.5655	0.7611	0.8093
TG 54:4	0.0717	0.9909	0.9832	0.9416	0.6345	0.5971	0.0973	0.0669	0.9953

Table S2.3N: PUFA/CHO study significant differences for within diet comparisons for all lipids (Triacylglycerol 54:5 to Triacylglycerol 60:12)

	Within Diet Comparisons								
	FDR <0.1 = pink								
Lipid/Day	B to P2	P2 to P7	P7 to P21	P21 to C2	C2 to C7	C7 to C21	B to P21	P21 to C21	B to C21
TG 54:5	0.0121	0.9106	0.9872	0.7477	0.5100	0.5971	0.0703	0.0224	0.7516
TG 54:6	0.0095	0.8122	0.9832	0.7574	0.5274	0.6769	0.0948	0.0222	0.5449
TG 54:7	0.0851	0.8846	0.9832	0.4530	0.6687	0.7736	0.2507	0.3621	0.8599
TG 54:8	0.6711	0.8336	0.9887	0.0152	0.8467	0.7738	0.9885	0.4789	0.6278
TG 55:0	0.1229	0.5580	0.9291	0.2153	0.8406	0.9276	0.2866	0.0074	0.2835
TG 55:3	0.8324	0.8122	0.9709	0.0565	0.9108	0.8371	0.4676	0.2488	0.6466
TG 55:4	0.9979	0.8335	0.9709	0.4805	0.9346	0.6676	0.5834	0.8492	0.5740
TG 55:5	0.4309	0.8122	0.9709	0.1290	0.8719	0.7728	0.4692	0.5859	0.8813
TG 56:0	0.6625	0.9298	0.9887	0.1795	0.8658	0.7736	0.3727	0.8695	0.4567
TG 56:1	0.0113	0.4849	0.9832	0.0290	0.8348	0.7579	0.0324	0.2774	0.5954
TG 56:2	0.0314	0.7393	0.9291	0.0985	0.6687	0.7579	0.2608	0.3621	0.9512
TG 56:3	0.5258	0.8846	0.9832	0.1927	0.8467	0.7053	0.8407	0.5436	0.8234
TG 56:4	0.5834	0.9106	0.9957	0.2096	0.9875	0.7579	0.7854	0.8492	0.6691
TG 56:5	0.6464	0.9106	0.9848	0.2747	0.8951	0.7736	0.8407	0.7653	0.6466
TG 56:6	0.1229	0.8846	0.9709	0.2634	0.6945	0.7914	0.6195	0.9540	0.7125
TG 56:7	0.3512	0.8378	0.8832	0.0551	0.7631	0.8371	0.9706	0.5023	0.6524
TG 56:8	0.0218	0.7393	0.9287	0.2046	0.4812	0.8371	0.2850	0.4382	0.8093
TG 56:9	0.0324	0.6632	0.9832	0.0348	0.5954	0.7991	0.3684	0.9124	0.4943
TG 58:10	0.0314	0.8660	0.9832	0.6709	0.6687	0.8371	0.1685	0.2557	0.8504
TG 58:11	0.1229	0.8122	0.9832	0.1298	0.8046	0.8371	0.2850	0.5103	0.3093
TG 58:2	0.0567	0.7037	0.8102	0.3323	0.8642	0.6676	0.5834	0.6114	0.4650
TG 58:3	0.6331	0.8660	0.9832	0.4882	0.9079	0.7991	0.8674	0.4829	0.6466
TG 58:6	0.9012	0.9106	0.9957	0.1428	0.9875	0.8371	0.7633	0.3621	0.6487
TG 58:7	0.8355	0.9106	0.8102	0.0302	0.8971	0.8371	0.2850	0.2319	0.9243
TG 58:8	0.2806	0.9106	0.7977	0.0937	0.7560	0.8371	0.9785	0.6995	0.8093
TG 58:9	0.0249	0.8841	0.7603	0.1632	0.5152	0.8491	0.4343	0.7079	0.8504
TG 60:11	0.6904	0.9106	0.7603	0.0348	0.9391	0.8371	0.5834	0.0556	0.6194
TG 60:12	0.0914	0.7393	0.8102	0.0358	0.5907	0.9672	0.7947	0.4791	0.5946

Table S2.4A: PUFA/CHO study significant differences for between diet comparisons for all lipids (16:0 Cholesterol ester to Ceramide [NS] 43:1)

	Between Diet Comparisons FDR <0.1		
Lipid/Day	Day 2	Day 7	Day 21
16:0 CE	0.4467	0.7765	0.9357
16:1 CE	0.1855	0.0060	0.0009
18:0 CE	0.7137	0.4118	0.2082
18:1 CE	0.3514	0.0041	0.1098
18:2 CE	0.0203	0.0997	0.0282
18:3 CE	0.4007	0.0013	0.0144
20:3 CE	0.0011	0.0567	0.0009
20:4 CE	0.0002	0.0091	0.0329
20:5 CE	0.0011	0.1789	0.0023
22:4 CE	0.0270	0.0856	0.2803
22:5 CE	0.0013	0.3461	0.5882
22:6 CE	0.0048	0.0403	0.5826
ACAR 10:0	0.0733	0.0521	0.2274
ACAR 10:1	0.0127	0.0001	0.0023
ACAR 12:0	0.1156	0.1215	0.7328
ACAR 14:0	0.4779	0.2385	0.8534
ACAR 14:1	0.0152	0.0210	0.3039
ACAR 14:2	0.0286	0.0022	0.0214
ACAR 16:0	0.2467	0.0955	0.0922
ACAR 18:0	0.8331	0.5884	0.7113
ACAR 18:1	0.7969	0.4393	0.8534
ACAR 18:2	0.1600	0.0040	0.0178
ACAR 24:0	0.0246	0.0161	0.0126
ACAR 26:0	0.0087	0.1695	0.4286
Cer[AS] 34:1	0.5986	0.8036	0.7943
Cer[EODS] 58:0	0.4221	0.4317	0.1888
Cer[NDS] 34:0	0.7750	0.8252	0.7165
Cer[NDS] 36:0	0.6730	0.2570	0.0123
Cer[NDS] 38:0	0.4862	0.9597	0.1098
Cer[NDS] 40:0	0.1802	0.9488	0.0356
Cer[NDS] 42:0	0.0403	0.5592	0.2975
Cer[NDS] 42:1	0.2711	0.9080	0.3788
Cer[NP] 34:0	0.3579	0.8876	0.7158
Cer[NP] 42:0	0.1134	0.6820	0.2471
Cer[NP] 42:1	0.0233	0.8876	0.9807
Cer[NS] 32:1	0.0709	0.3276	0.7323
Cer[NS] 33:1	0.5660	0.3887	0.3003
Cer[NS] 34:1	0.6299	0.7835	0.8422
Cer[NS] 34:2	0.2823	0.8694	0.1033
Cer[NS] 35:1	0.9508	0.3248	0.3714
Cer[NS] 36:1	0.6692	0.0425	0.0071
Cer[NS] 36:2	0.7137	0.0142	0.0354
Cer[NS] 37:1	0.6482	0.5235	0.2182
Cer[NS] 38:1	0.1574	0.2986	0.0094
Cer[NS] 38:2	0.3969	0.1938	0.0110
Cer[NS] 39:1	0.7969	0.1338	0.7328
Cer[NS] 40:1	0.3670	0.5862	0.2864
Cer[NS] 40:2	0.1544	0.0603	0.0023
Cer[NS] 40:3	0.6731	0.4090	0.0106
Cer[NS] 41:1	0.4173	0.4417	0.0301
Cer[NS] 41:2	0.0767	0.2997	0.0108
Cer[NS] 42:1	0.0875	0.5399	0.4691
Cer[NS] 42:2	0.5410	0.1375	0.2187
Cer[NS] 42:3	0.6625	0.0599	0.0023
Cer[NS] 43:1	0.1156	0.1978	0.0070

Table S2.4B: PUFA/CHO study significant differences for between diet comparisons for all lipids (Ceramide [NS] 43:2 to Lysophosphatidylcholine 16:1)

	Between Diet Comparisons		
	FDR <0.1		
Lipid/Day	Day 2	Day 7	Day 21
Cer[NS] 43:2	0.8359	0.3335	0.0009
DG 30:0	0.0283	0.0060	0.1131
DG 30:1	0.1815	0.0246	0.1356
DG 32:0	0.0586	0.0184	0.9046
DG 32:1	0.0013	0.0041	0.0150
DG 32:2	0.0029	0.0060	0.0350
DG 33:0	0.3127	0.1204	0.1129
DG 33:1	0.0203	0.0070	0.0090
DG 34:0	0.3889	0.8254	0.4021
DG 34:2	0.0066	0.0164	0.0088
DG 34:3	0.0030	0.0010	0.0143
DG 35:1	0.0122	0.0543	0.0150
DG 35:2	0.0063	0.0048	0.0292
DG 35:3	0.0673	0.0821	0.2079
DG 36:0	0.4161	0.1933	0.2533
DG 36:1	0.3051	0.1663	0.2270
DG 36:2	0.0004	0.0015	0.0006
DG 36:3	0.0048	0.0251	0.2132
DG 36:4	0.7450	0.8496	0.0294
DG 36:5	0.3051	0.0190	0.3767
DG 38:1	0.2921	0.1565	0.1196
DG 38:2	0.1464	0.0041	0.0085
DG 38:3	0.0018	0.0195	0.0129
DG 38:4	0.0018	0.0018	0.0040
DG 38:5	0.0118	0.0063	0.0109
DG 38:6	0.2290	0.2257	0.6988
DG 40:6	0.0206	0.0017	0.0126
DG 40:7	0.0031	0.0206	0.0184
FFA(16:0)	0.3386	0.7474	0.9316
FFA(18:0)	0.4910	0.5313	0.8160
FFA(18:1)	0.3386	0.3400	0.8452
FFA(18:2)	0.0979	0.0599	0.0515
FFA(20:0)	0.7155	0.6038	0.4393
FFA(20:1)	0.3902	0.4854	0.9744
FFA(20:2)	0.2543	0.2392	0.6064
FFA(20:4)	0.1549	0.9859	0.8534
FFA(22:0)	0.4116	0.8442	0.5522
FFA(22:1)	0.1475	0.9488	0.7489
FFA(22:2)	0.6720	0.7191	0.9807
FFA(22:3)	0.6000	0.2324	0.0524
FFA(24:0)	0.0865	0.0787	0.0063
FFA(24:1)	0.0665	0.9087	0.1261
FFA(24:2)	0.5975	0.8471	0.2428
FFA(24:3)	0.6692	0.9488	0.4362
GlcCer[NS] 34:1	0.3898	0.2847	0.6048
GlcCer[NS] 34:2	0.3902	0.6464	0.2411
GlcCer[NS] 40:1	0.1172	0.0580	0.0227
GlcCer[NS] 41:1	0.1156	0.2570	0.9046
GlcCer[NS] 42:1	0.0895	0.6450	0.5403
GlcCer[NS] 42:2	0.6068	0.5546	0.9556
LysoPC 14:0	0.0142	0.0009	0.0224
LysoPC 15:0	0.5336	0.3021	0.5933
LysoPC 15:1	0.1549	0.3461	0.2638
LysoPC 16:0	0.1464	0.0040	0.2055
LysoPC 16:1	0.0233	0.0012	0.0239

Table S2.4C: PUFA/CHO study significant differences for between diet comparisons for all lipids (Lysophosphatidylcholine 17:1 to Phosphatidylcholine 35:3)

	Between Diet Comparisons		
	FDR <0.1		
Lipid/Day	Day 2	Day 7	Day 21
LysoPC 17:1	0.1404	0.0060	0.0148
LysoPC 18:0	0.7919	0.0158	0.1828
LysoPC 18:1	0.6900	0.0578	0.6603
LysoPC 18:2	0.1566	0.0578	0.0068
LysoPC 18:3	0.0145	0.0029	0.1201
LysoPC 19:0	0.8866	0.0543	0.7158
LysoPC 19:1	0.9688	0.0153	0.7442
LysoPC 20:0	0.2921	0.0063	0.0009
LysoPC 20:1	0.9688	0.3274	0.0566
LysoPC 20:2	0.9508	0.6358	0.0130
LysoPC 20:3	0.2497	0.0027	0.0045
LysoPC 20:4	0.3144	0.0473	0.3742
LysoPC 20:5	0.0803	0.1695	0.0222
LysoPC 22:0	0.2939	0.0801	0.0066
LysoPC 22:4	0.2239	0.0060	0.0259
LysoPC 22:5	0.4381	0.0185	0.0068
LysoPC 22:6	0.2069	0.1983	0.2552
LysoPC 23:0	0.3889	0.2967	0.2675
LysoPC 24:0	0.4520	0.0974	0.0023
LysoPC 24:1	0.8866	0.6450	0.7158
LysoPC 26:1	0.9107	0.1179	0.7422
LysoPE 16:0	0.0221	0.0123	0.0181
LysoPE 18:0	0.1739	0.0869	0.1647
LysoPE 18:1	0.4161	0.5142	0.1632
LysoPE 18:2	0.7012	0.8876	0.0763
LysoPE 20:3	0.2280	0.0169	0.1418
LysoPE 20:4	0.2377	0.1701	0.1033
LysoPE 20:5	0.0407	0.0195	0.1212
LysoPE 22:4	0.1544	0.1725	0.0599
LysoPE 22:5	0.4910	0.1376	0.0044
LysoPE 22:6	0.7750	0.2091	0.0086
PA 34:2	0.3902	0.8885	0.6064
PC 26:0	0.1472	0.0084	0.1247
PC 29:0	0.0100	0.0012	0.0114
PC 30:0	0.0172	0.0012	0.0030
PC 30:2	0.2341	0.9625	0.1385
PC 31:0	0.0036	0.0030	0.0026
PC 31:1	0.0011	0.0123	0.0122
PC 32:0	0.0645	0.0041	0.0009
PC 32:1	0.0183	0.0017	0.0058
PC 32:2	0.0719	0.1338	0.3646
PC 32:3	0.0029	0.0011	0.0225
PC 33:0	0.2210	0.0016	0.0032
PC 33:1	0.0005	0.0012	0.0015
PC 33:2	0.9209	0.5295	0.6849
PC 33:3	0.0048	0.2140	0.0153
PC 34:1	0.0029	0.0012	0.0004
PC 34:2	0.0980	0.9625	0.0040
PC 34:3	0.2901	0.0556	0.9641
PC 34:4	0.1903	0.0041	0.2132
PC 34:5	0.4161	0.1338	0.2522
PC 35:0	0.8255	0.0079	0.0169
PC 35:1	0.2939	0.0012	0.0009
PC 35:2	0.5778	0.2799	0.0928
PC 35:3	0.2333	0.6160	0.7362

Table S2.4D: PUFA/CHO study significant differences for between diet comparisons for all lipids (Phosphatidylcholine 35:4 to Phosphatidylethanolamine 33:2)

	Between Diet Comparisons		
	FDR <0.1		
Lipid/Day	Day 2	Day 7	Day 21
PC 35:4	0.4313	0.0298	0.0045
PC 35:5	0.0729	0.0091	0.0181
PC 36:0	0.6731	0.0182	0.4076
PC 36:1	0.0572	0.0041	0.0023
PC 36:2	0.4577	0.2201	0.0637
PC 36:3	0.6625	0.0361	0.8469
PC 36:4	0.7750	0.0071	0.0172
PC 36:5	0.0087	0.0041	0.0043
PC 36:6	0.0094	0.0182	0.0159
PC 37:1	0.8331	0.0387	0.0099
PC 37:2	0.5761	0.8496	0.8534
PC 37:3	0.8056	0.0005	0.0023
PC 37:4	0.6731	0.0033	0.0023
PC 37:5	0.3857	0.0729	0.0230
PC 37:6	0.2290	0.2748	0.0047
PC 37:7	0.3945	0.6371	0.2009
PC 38:1	0.4161	0.3644	0.6804
PC 38:2	0.1131	0.1067	0.8556
PC 38:3	0.3144	0.0015	0.0043
PC 38:4	0.3776	0.1636	0.0437
PC 38:5	0.6967	0.0030	0.0002
PC 38:6	0.6629	0.4418	0.0220
PC 38:7	0.4989	0.8314	0.6969
PC 39:3	0.9703	0.1646	0.0644
PC 39:4	0.9688	0.0176	0.0080
PC 39:5	0.9688	0.0172	0.0043
PC 39:6	0.7825	0.0165	0.0023
PC 39:7	0.9325	0.8885	0.2822
PC 40:1	0.0673	0.8072	0.0599
PC 40:2	0.6247	0.4583	0.1033
PC 40:3	0.7990	0.0250	0.9341
PC 40:4	0.8340	0.0097	0.0026
PC 40:5	0.1884	0.0043	0.0015
PC 40:6	0.0719	0.0365	0.0004
PC 40:7	0.9250	0.4565	0.8534
PC 40:8	0.3537	0.8314	0.2471
PC 40:9	0.2519	0.0773	0.8535
PC 41:6	0.0759	0.9080	0.8481
PC 41:7	0.5916	0.3502	0.6308
PC 42:1	0.8056	0.7474	0.9192
PC 42:10	0.3548	0.4331	0.1041
PC 42:2	0.3079	0.3852	0.0727
PC 42:3	0.4015	0.0070	0.1975
PC 42:4	0.8837	0.7462	0.8361
PC 42:5	0.4251	0.2601	0.0698
PC 42:6	0.2921	0.2056	0.1033
PC 42:7	0.7529	0.5294	0.0682
PC 42:8	0.7634	0.9332	0.0233
PC 42:9	0.7590	0.0041	0.9313
PC 44:4	0.9722	0.5399	0.2829
PE 32:1	0.0096	0.0060	0.0150
PE 32:2	0.7390	0.8885	0.0364
PE 33:0	0.4779	0.7091	0.1792
PE 33:1	0.3893	0.4331	0.3646
PE 33:2	0.2901	0.8036	0.1056

Table S2.4E: PUFA/CHO study significant differences for between diet comparisons for all lipids (Phosphatidylethanolamine 34:0 to Plasmenyl-phosphatidylcholine 36:6)

	Between Diet Comparisons		
	FDR <0.1		
Lipid/Day	Day 2	Day 7	Day 21
PE 34:0	0.0497	0.2601	0.5912
PE 34:1	0.0011	0.0091	0.0122
PE 34:2	0.0040	0.1745	0.0071
PE 34:3	0.0220	0.0153	0.0101
PE 35:1	0.0673	0.0586	0.2533
PE 35:2	0.1990	0.0161	0.2357
PE 35:4	0.2319	0.1420	0.1417
PE 36:0	0.5112	0.6988	0.9587
PE 36:1	0.0206	0.0597	0.5942
PE 36:2	0.3902	0.6820	0.0730
PE 36:3	0.6251	0.7725	0.0122
PE 36:4	0.6244	0.6820	0.7869
PE 36:5	0.0731	0.0040	0.0118
PE 37:4	0.3291	0.0125	0.0627
PE 38:3	0.8613	0.0564	0.0171
PE 38:4	0.9529	0.0070	0.0219
PE 38:5	0.0473	0.0012	0.0219
PE 38:6	0.5467	0.0091	0.0009
PE 38:7	0.6237	0.8252	0.1975
PE 40:4	0.1217	0.0599	0.2169
PE 40:5	0.9289	0.0012	0.0033
PE 40:6	0.6629	0.0091	0.0291
PE 40:7	0.7450	0.4967	0.2278
PE 40:8	0.9518	0.7555	0.4533
PG 33:0	0.4387	0.2766	0.8509
PG 34:2	0.9728	0.8294	0.5826
PG 36:0	0.7783	0.8314	0.1261
PG 36:2	0.8248	0.3373	0.2132
PG 36:3	0.8340	0.8844	0.7731
PI 34:2	0.3967	0.8876	0.3215
PI 36:1	0.7595	0.9057	0.3651
PI 36:2	0.3293	0.1563	0.0032
PI 36:4	0.0614	0.0191	0.0555
PI 38:3	0.9688	0.9488	0.2237
PI 38:4	0.9508	0.6820	0.2533
PI 38:5	0.3334	0.7555	0.2925
PI 38:6	0.3902	0.9242	0.1913
PI 40:6	0.4488	0.8380	0.0575
PlsCho 24:0	0.9980	0.6032	0.6894
PlsCho 32:0	0.5778	0.8496	0.9998
PlsCho 32:1	0.5467	0.1123	0.9108
PlsCho 33:0	0.6692	0.7877	0.9955
PlsCho 34:0	0.1842	0.4974	0.0950
PlsCho 34:1	0.0137	0.0060	0.0009
PlsCho 34:2	0.0733	0.0955	0.0075
PlsCho 34:3	0.1054	0.2681	0.8187
PlsCho 35:1	0.1652	0.3476	0.4429
PlsCho 35:2	0.3969	0.8866	0.1986
PlsCho 35:3	0.7450	0.7791	0.6929
PlsCho 36:0	0.0536	0.1864	0.0928
PlsCho 36:2	0.3144	0.5399	0.5777
PlsCho 36:3	0.0034	0.1663	0.2533
PlsCho 36:4	0.0080	0.1016	0.2079
PlsCho 36:5	0.1966	0.1380	0.6572
PlsCho 36:6	0.9376	0.6186	0.3999

Table S2.4F: PUFA/CHO study significant differences for between diet comparisons for all lipids (Plasmenyl-phosphatidylcholine 37:1 to Plasmenyl-phosphatidylethanolamine 38:3)

	Between Diet Comparisons		
	FDR <0.1		
Lipid/Day	Day 2	Day 7	Day 21
PlsCho 37:1	0.5315	0.3274	0.4286
PlsCho 37:3	0.6629	0.5989	0.8176
PlsCho 37:4	0.0403	0.2101	0.8835
PlsCho 37:6	0.0187	0.3549	0.1201
PlsCho 38:1	0.8631	0.4417	0.2889
PlsCho 38:3	0.0086	0.6507	0.6070
PlsCho 38:4	0.0214	0.2223	0.0575
PlsCho 38:5	0.0029	0.0720	0.1301
PlsCho 38:6	0.0198	0.1279	0.1791
PlsCho 39:3	0.6702	0.6698	0.1041
PlsCho 39:4	0.8695	0.1440	0.1032
PlsCho 39:5	0.1600	0.4583	0.1879
PlsCho 39:6	0.0384	0.1338	0.7574
PlsCho 40:1	0.1662	0.2385	0.2767
PlsCho 40:3	0.0011	0.2901	0.2298
PlsCho 40:4	0.0100	0.0184	0.6953
PlsCho 40:5	0.3579	0.7555	0.7682
PlsCho 40:6	0.0092	0.1074	0.8534
PlsCho 42:0	0.5977	0.8285	0.6048
PlsCho 42:1	0.1156	0.3569	0.3974
PlsCho 42:2	0.2031	0.1111	0.1208
PlsCho 42:3	0.1399	0.0091	0.6969
PlsCho 42:4	0.0048	0.6820	0.1815
PlsCho 42:5	0.2889	0.2733	0.3559
PlsCho 42:6	0.6900	0.6649	0.8847
PlsCho 44:3	0.2820	0.7462	0.1360
PlsCho 44:4	0.0080	0.7083	0.0293
PlsCho 44:5	0.2733	0.0567	0.0126
PlsCho 44:6	0.7434	0.2333	0.7158
PlsCho 46:4	0.7453	0.8306	0.0299
PlsEth 32:1	0.6566	0.0365	0.5851
PlsEth 32:2	0.0240	0.7462	0.5299
PlsEth 33:2	0.1156	0.8609	0.8201
PlsEth 34:0	0.0895	0.6985	0.4463
PlsEth 34:1	0.3924	0.9859	0.3695
PlsEth 34:2	0.0043	0.0176	0.0023
PlsEth 34:3	0.0390	0.7555	0.0873
PlsEth 34:4	0.1966	0.6318	0.4286
PlsEth 35:1	0.8518	0.7299	0.6804
PlsEth 35:2	0.0034	0.3032	0.0386
PlsEth 35:4	0.4932	0.1097	0.0873
PlsEth 36:1	0.0228	0.6032	0.9108
PlsEth 36:2	0.0005	0.0146	0.0065
PlsEth 36:3	0.0059	0.3476	0.0053
PlsEth 36:4	0.0010	0.0669	0.0729
PlsEth 36:5	0.0151	0.3650	0.4362
PlsEth 36:6	0.2204	0.9646	0.8534
PlsEth 37:1	0.3276	0.8252	0.0575
PlsEth 37:2	0.1208	0.8036	0.0287
PlsEth 37:4	0.0499	0.9625	0.9744
PlsEth 37:5	0.1880	0.7568	0.0752
PlsEth 37:6	0.0203	0.7025	0.2796
PlsEth 38:1	0.0198	0.8314	0.5217
PlsEth 38:2	0.0250	0.4672	0.0752
PlsEth 38:3	0.0203	0.6324	0.3651

Table S2.4G: PUFA/CHO study significant differences for between diet comparisons for all lipids (Phosphatidylethanolamine 38:4 to Sphingomyelin 42:5)

	Between Diet Comparisons		
	FDR <0.1		
Lipid/Day	Day 2	Day 7	Day 21
PlsEth 38:4	0.0053	0.7690	0.9192
PlsEth 38:5	0.0077	0.2733	0.1828
PlsEth 38:6	0.0207	0.5735	0.0099
PlsEth 39:4	0.0521	0.2766	0.7158
PlsEth 39:5	0.0138	0.8314	0.8828
PlsEth 39:6	0.0105	0.7725	0.3444
PlsEth 40:2	0.0245	0.4756	0.3003
PlsEth 40:4	0.0175	0.9778	0.7143
PlsEth 40:5	0.0175	0.7835	0.3088
PlsEth 40:6	0.0233	0.2970	0.1217
PlsEth 42:4	0.3460	0.8668	0.9530
PlsEth 42:5	0.0230	0.8668	0.7158
PlsEth 42:6	0.0087	0.3650	0.2132
PlsEth 44:6	0.7750	0.9859	0.3113
SM 30:0	0.1852	0.8046	0.0301
SM 30:1	0.1544	0.2066	0.0022
SM 30:2	0.1100	0.3042	0.6253
SM 31:1	0.0340	0.1535	0.0023
SM 32:0	0.7662	0.6160	0.8954
SM 32:1	0.1573	0.2901	0.0928
SM 32:2	0.2559	0.0875	0.0006
SM 33:1	0.1447	0.7474	0.6913
SM 33:2	0.3902	0.8036	0.8847
SM 34:0	0.3969	0.5870	0.1769
SM 34:1	0.1123	0.5603	0.9587
SM 34:2	0.1447	0.5546	0.7089
SM 34:3	0.4673	0.1620	0.9357
SM 35:2	0.1705	0.8559	0.5562
SM 36:1	0.1870	0.7117	0.7071
SM 36:2	0.0719	0.4014	0.3183
SM 36:3	0.0787	0.0856	0.0763
SM 36:4	0.3073	0.0310	0.0268
SM 37:1	0.3036	0.4057	0.2265
SM 37:2	0.1472	0.9488	0.4286
SM 38:0	0.4932	0.5546	0.8954
SM 38:1	0.0704	0.8285	0.0063
SM 38:2	0.0657	0.5583	0.0729
SM 38:3	0.4989	0.3723	0.4286
SM 38:4	0.7969	0.8685	0.0288
SM 39:1	0.1156	0.4331	0.0437
SM 39:2	0.0206	0.4577	0.6988
SM 39:3	0.0196	0.1434	0.3461
SM 40:1	0.0353	0.6820	0.0085
SM 40:2	0.0094	0.0060	0.0356
SM 40:3	0.3514	0.6649	0.5888
SM 40:5	0.3181	0.8876	0.4327
SM 41:1	0.0048	0.0141	0.2009
SM 41:2	0.1125	0.8876	0.7134
SM 41:4	0.2467	0.9778	0.1212
SM 41:6	0.2187	0.0486	0.7328
SM 42:1	0.0138	0.0023	0.0222
SM 42:2	0.9751	0.5235	0.3252
SM 42:3	0.8528	0.9778	0.7096
SM 42:4	0.0586	0.3335	0.0117
SM 42:5	0.9270	0.6071	0.2246

Table S2.4H: PUFA/CHO study significant differences for between diet comparisons for all lipids (Sphingomyelin 42:6 to Triacylglycerol 52:6)

	Between Diet Comparisons		
	FDR <0.1		
Lipid/Day	Day 2	Day 7	Day 21
SM 42:6	0.3386	0.0875	0.6378
SM 43:1	0.0829	0.0597	0.9316
SM 43:2	0.1023	0.6032	0.4060
SM 43:3	0.8294	0.7453	0.2925
SM 43:6	0.4673	0.6301	0.9046
SM 44:1	0.8331	0.9254	0.9575
SM 44:2	0.8331	0.7698	0.7377
SM 44:3	0.8866	0.6988	0.2221
SM 44:4	0.0207	0.4014	0.1647
SM 44:6	0.7969	0.9859	0.9742
TG 38:0	0.0343	0.0597	0.3654
TG 39:0	0.3386	0.8046	0.0034
TG 40:0	0.0338	0.0001	0.1761
TG 41:0	0.0383	0.0571	0.3461
TG 42:0	0.0207	0.0026	0.5888
TG 42:1	0.0245	0.0021	0.5139
TG 43:1	0.0206	0.0184	0.1986
TG 44:2	0.0100	0.0052	0.1033
TG 45:0	0.0746	0.0056	0.0729
TG 45:1	0.0319	0.0066	0.0438
TG 45:2	0.0123	0.0057	0.0150
TG 46:0	0.0135	0.0046	0.0291
TG 46:1	0.0105	0.0021	0.0202
TG 46:3	0.0042	0.0015	0.0262
TG 47:0	0.0572	0.0124	0.0233
TG 47:1	0.0105	0.0019	0.0179
TG 47:2	0.0037	0.0014	0.0121
TG 48:0	0.0100	0.0015	0.0138
TG 48:1	0.0018	0.0008	0.0059
TG 48:3	0.0012	0.0008	0.0063
TG 48:4	0.0110	0.0012	0.0259
TG 48:5	0.0204	0.0176	0.0282
TG 49:0	0.0206	0.0065	0.0219
TG 49:1	0.0040	0.0012	0.0094
TG 49:2	0.0006	0.0014	0.0043
TG 49:3	0.0006	0.0012	0.0043
TG 50:0	0.0070	0.0041	0.0068
TG 50:1	0.0019	0.0016	0.0043
TG 50:2	0.0004	0.0009	0.0026
TG 50:3	0.0005	0.0009	0.0023
TG 50:4	0.0101	0.0084	0.0152
TG 50:5	0.0105	0.0043	0.0068
TG 50:6	0.1320	0.0182	0.0468
TG 51:1	0.0009	0.0017	0.0063
TG 51:2	0.0001	0.0010	0.0023
TG 51:3	0.0005	0.0012	0.0023
TG 51:4	0.0036	0.0573	0.0641
TG 51:5	0.1544	0.0590	0.0253
TG 52:0	0.0145	0.0327	0.1136
TG 52:1	0.0002	0.0013	0.0044
TG 52:2	0.0001	0.0009	0.0013
TG 52:3	0.0101	0.0285	0.0099
TG 52:4	0.1652	0.1689	0.8399
TG 52:5	0.0080	0.0170	0.0044
TG 52:6	0.0979	0.0590	0.8835

Table S2.4I: PUFA/CHO study significant differences for between diet comparisons for all lipids (Triacylglycerol 52:7 to Triacylglycerol 60:12)

	Between Diet Comparisons		
	FDR <0.1		
Lipid/Day	Day 2	Day 7	Day 21
TG 52:7	0.1174	0.0216	0.0391
TG 53:0	0.1399	0.1695	0.2738
TG 53:1	0.0239	0.0034	0.0033
TG 53:2	0.0004	0.0015	0.0043
TG 53:3	0.0001	0.0031	0.0063
TG 53:4	0.7750	0.9950	0.2992
TG 53:5	0.2703	0.4727	0.6205
TG 54:0	0.3494	0.7758	0.5932
TG 54:1	0.0016	0.0015	0.0152
TG 54:2	0.0000	0.0003	0.0033
TG 54:3	0.0011	0.0603	0.5983
TG 54:4	0.9911	0.2570	0.0396
TG 54:5	0.0829	0.0702	0.0184
TG 54:6	0.0102	0.0702	0.0126
TG 54:7	0.6900	0.8252	0.1208
TG 54:8	0.0286	0.0383	0.0350
TG 55:0	0.0466	0.2797	0.0134
TG 55:3	0.0080	0.0043	0.1582
TG 55:4	0.3902	0.0200	0.8176
TG 55:5	0.0730	0.1779	0.3999
TG 56:0	0.2226	0.3903	0.7808
TG 56:1	0.0052	0.0043	0.0923
TG 56:2	0.0019	0.0021	0.0368
TG 56:3	0.0044	0.0048	0.1971
TG 56:4	0.1174	0.0829	0.6988
TG 56:5	0.2152	0.2697	0.5888
TG 56:6	0.9688	0.9136	0.9518
TG 56:7	0.4007	0.2901	0.4691
TG 56:8	0.6438	0.3021	0.3654
TG 56:9	0.4042	0.3644	0.7921
TG 58:10	0.4649	0.4194	0.1869
TG 58:11	0.4013	0.2896	0.1457
TG 58:2	0.0105	0.0114	0.3935
TG 58:3	0.0403	0.6036	0.2274
TG 58:6	0.0496	0.1146	0.1129
TG 58:7	0.2709	0.2896	0.1791
TG 58:8	0.7634	0.8668	0.6849
TG 58:9	0.6904	0.1737	0.6925
TG 60:11	0.3514	0.2303	0.0108
TG 60:12	0.6053	0.9165	0.3295

Table S2.5A: MEAL Study Mean Log2 Area under the Curve for Lipids (16:0 Cholesterol ester to Ceramide [NS] 35:1)

	Mean Log2 AUC Values For Each Lipid Species												
	High Fat Diet							High Carbohydrate Diet					
Lipid/Day	B	S	2	7	14	21		B	S	2	7	14	21
16:0 CE	14.11	14.00	14.15	14.23	13.99	14.20		14.18	14.37	14.19	14.20	14.29	14.01
16:1 CE	12.74	12.75	12.86	12.31	12.11	12.40		12.92	12.50	13.29	13.33	13.49	13.31
18:0 CE	12.13	11.86	12.52	12.39	12.17	12.46		12.88	12.81	12.64	12.76	12.68	12.45
18:1 CE	17.15	17.17	16.94	17.09	16.89	17.00		17.29	17.54	17.33	17.35	17.34	17.26
18:2 CE	19.59	19.81	19.84	19.81	19.77	19.71		19.92	20.04	19.88	19.67	19.64	19.54
18:3 CE	15.32	15.37	15.28	15.31	15.28	15.08		15.46	15.65	15.45	15.66	15.64	15.48
20:3 CE	15.40	15.77	15.72	15.30	15.24	15.20		15.94	16.05	15.86	16.07	15.99	15.96
20:4 CE	17.01	17.38	17.54	17.54	17.31	17.35		17.80	17.87	17.65	17.65	17.64	17.52
20:5 CE	13.68	13.92	13.91	13.86	14.02	13.92		14.61	14.46	13.99	14.48	14.32	14.28
22:4 CE	10.88	11.14	11.18	11.32	10.70	11.01		10.61	11.60	11.39	11.57	11.21	11.15
22:5 CE	12.41	12.79	12.46	12.47	12.62	12.48		13.09	13.12	13.07	13.06	13.16	13.01
22:6 CE	14.92	15.14	15.03	15.24	15.02	15.12		15.31	15.49	15.19	15.36	15.60	15.56
ACAR 10:0	12.62	13.26	13.70	13.36	13.01	13.47		13.26	13.43	12.77	12.87	12.98	13.17
ACAR 10:1	11.82	12.10	12.47	12.02	11.76	12.06		11.87	11.98	11.91	11.51	11.89	11.83
ACAR 12:0	12.87	13.38	13.78	13.62	13.32	13.79		13.17	13.25	12.59	13.01	13.15	13.35
ACAR 14:0	13.70	14.00	14.09	14.30	14.02	14.11		13.88	14.09	13.87	13.64	13.87	13.80
ACAR 14:1	13.74	14.33	14.51	14.07	13.99	14.29		14.16	14.39	13.59	13.97	14.13	14.15
ACAR 14:2	12.62	13.15	13.54	12.79	12.65	12.95		12.74	13.47	12.54	12.70	12.71	12.89
ACAR 16:0	15.95	16.18	16.04	16.45	16.16	16.29		16.03	16.08	15.86	15.84	16.09	15.97
ACAR 18:0	15.23	15.26	15.40	15.46	15.40	15.45		15.28	15.23	14.95	14.93	14.98	14.86
ACAR 18:1	16.32	16.36	16.31	16.43	16.13	16.27		16.44	16.32	16.12	16.18	16.40	16.29
ACAR 18:2	15.77	16.05	15.88	15.94	15.64	15.73		15.82	15.96	15.69	15.69	15.78	15.73
ACAR 20:0	13.16	12.96	13.14	12.78	12.64	12.96		13.06	12.97	12.47	12.51	12.62	12.44
ACAR 24:0	14.09	14.33	14.23	14.17	14.09	14.35		14.31	14.14	13.66	13.42	13.50	13.46
ACAR 26:0	12.83	13.33	13.25	12.89	13.36	13.12		12.71	13.00	12.44	11.88	12.07	11.76
Cer[AS] 34:1	11.95	11.85	12.02	12.06	11.74	12.39		12.41	12.14	12.23	11.96	12.15	12.07
Cer[AS] 42:2	14.27	14.14	14.40	13.76	13.91	13.48		14.10	14.21	14.01	13.99	13.98	13.60
Cer[EODS] 57:2	12.20	12.45	12.43	12.54	12.25	12.63		12.52	12.06	12.22	11.93	11.97	11.97
Cer[EODS] 58:0	12.13	11.97	12.16	11.81	11.77	11.78		11.56	11.54	11.80	11.32	11.01	11.40
Cer[EODS] 60:0	11.80	11.82	11.52	11.34	11.38	11.79		12.04	11.49	11.17	11.23	11.05	10.98
Cer[NDS] 34:0	15.34	15.30	15.52	15.61	15.47	15.58		15.45	15.36	15.21	15.12	15.27	15.18
Cer[NDS] 36:0	13.24	13.09	13.84	13.48	13.37	13.41		12.92	12.70	12.53	12.64	12.99	13.17
Cer[NDS] 38:0	13.47	13.83	14.13	13.77	13.43	14.00		13.57	13.62	13.36	13.15	13.56	13.18
Cer[NDS] 39:0	12.88	13.17	13.28	13.32	13.12	13.13		12.53	12.46	12.32	12.30	12.55	12.27
Cer[NDS] 40:0	15.74	15.83	16.00	15.93	15.41	15.73		15.76	15.51	15.14	14.99	15.03	15.04
Cer[NDS] 41:0	15.39	15.36	15.76	15.72	15.50	15.42		15.12	15.12	14.75	14.71	14.78	14.76
Cer[NDS] 42:0	17.17	17.27	17.51	17.37	17.05	17.28		16.97	16.90	16.66	16.55	16.65	16.53
Cer[NDS] 42:1	19.62	19.70	19.73	19.59	19.39	19.54		19.54	19.43	19.32	19.14	19.16	19.00
Cer[NDS] 42:2	15.52	15.53	15.50	15.28	15.37	15.28		15.53	15.45	15.56	15.49	15.59	15.46
Cer[NDS] 43:0	14.31	14.59	15.08	14.95	14.55	15.07		14.33	14.49	14.22	14.16	14.08	14.04
Cer[NP] 34:0	11.75	12.31	12.12	12.65	12.44	12.02		12.51	12.39	12.00	12.01	11.88	11.73
Cer[NP] 40:0	14.64	14.81	14.75	14.70	14.48	14.73		14.52	14.69	13.86	13.76	14.00	13.74
Cer[NP] 41:0	15.55	15.50	15.62	15.63	15.41	15.64		15.70	15.85	15.36	15.36	15.39	15.13
Cer[NP] 41:1	13.99	14.10	14.15	13.72	13.66	13.80		13.81	14.02	13.70	13.47	13.88	13.52
Cer[NP] 42:0	16.13	16.18	16.00	16.06	15.76	16.05		16.31	16.34	15.97	15.82	15.71	15.76
Cer[NP] 42:1	14.74	14.91	15.06	14.43	14.65	14.52		14.64	14.59	14.26	14.29	14.30	14.03
Cer[NS] 32:1	14.42	14.62	14.60	14.50	14.26	14.65		14.94	14.79	14.62	14.64	14.72	14.44
Cer[NS] 33:1	14.61	14.30	14.52	14.49	14.28	14.41		14.69	14.76	14.59	14.49	14.84	14.56
Cer[NS] 33:4	11.70	11.27	10.91	11.15	10.83	10.72		10.82	10.99	10.40	10.48	9.99	11.00
Cer[NS] 34:1	18.25	18.12	18.13	18.17	17.91	18.06		18.38	18.24	18.31	18.22	18.37	18.25
Cer[NS] 34:2	14.00	14.08	14.16	13.98	13.90	13.84		14.17	14.45	13.85	13.94	14.31	14.05
Cer[NS] 35:1	23.13	23.00	23.08	22.99	22.78	22.97		23.24	23.15	23.21	23.14	23.18	23.12

Table S2.5B: MEAL Study Mean Log2 Area under the Curve for Lipids (Ceramide [NS] 36:1 to Free Fatty Acid 18:1)

	Mean Log2 AUC Values For Each Lipid Species												
	High Fat Diet							High Carbohydrate Diet					
Lipid/Day	B	S	2	7	14	21		B	S	2	7	14	21
Cer[NS] 36:1	16.17	16.36	16.51	16.45	16.15	16.56		16.45	16.46	16.48	16.35	16.50	16.43
Cer[NS] 36:2	13.25	13.42	13.78	13.40	12.98	13.49		13.67	13.70	13.64	13.65	13.92	13.82
Cer[NS] 37:1	13.87	13.79	13.98	13.83	13.66	13.78		13.44	13.47	13.50	13.33	13.56	13.34
Cer[NS] 38:1	16.94	17.03	17.06	16.88	16.75	17.10		17.27	17.32	17.25	16.88	17.08	16.88
Cer[NS] 38:2	14.17	14.28	14.33	14.02	13.85	14.03		14.46	14.54	14.47	14.20	14.30	14.33
Cer[NS] 39:1	14.75	14.71	14.91	14.79	14.73	15.06		14.89	14.98	14.72	14.42	14.59	14.27
Cer[NS] 40:1	19.57	19.54	19.56	19.36	19.32	19.52		19.80	19.70	19.49	19.31	19.33	19.19
Cer[NS] 40:2	17.24	17.21	17.19	16.90	16.83	17.03		17.51	17.44	17.48	17.12	17.33	17.15
Cer[NS] 40:3	11.65	11.72	12.15	12.09	11.84	12.03		11.48	11.45	11.34	11.60	11.44	11.86
Cer[NS] 41:1	19.32	19.22	19.38	19.30	19.19	19.35		19.49	19.54	19.38	19.20	19.21	19.08
Cer[NS] 41:2	17.43	17.34	17.39	17.27	17.02	17.29		17.71	17.63	17.73	17.50	17.61	17.45
Cer[NS] 41:4	12.99	12.54	12.88	12.82	12.96	13.01		13.18	13.01	13.22	13.52	13.10	13.31
Cer[NS] 42:1	21.28	21.20	21.16	20.94	20.90	21.03		21.37	21.36	21.24	20.92	20.98	20.85
Cer[NS] 42:2	19.78	19.76	19.75	19.47	19.37	19.48		19.96	19.93	19.96	19.80	19.98	19.82
Cer[NS] 42:3	15.46	15.62	15.47	15.41	15.18	15.36		15.55	15.65	15.53	15.60	15.81	15.68
Cer[NS] 43:1	18.57	18.87	19.10	18.95	18.87	19.09		18.95	19.19	18.91	18.67	18.77	18.65
Cer[NS] 43:2	14.90	15.11	15.26	15.00	14.78	14.94		14.98	15.02	14.87	14.72	14.90	14.86
Cer[NS] 44:1	15.01	15.06	15.38	15.29	15.05	15.39		14.95	15.05	14.73	14.78	14.85	14.83
Cer[NS] 44:2	13.80	14.06	14.15	13.97	13.76	14.00		13.83	13.66	13.57	13.76	13.95	14.03
Cer[NS] 44:4	19.21	19.38	19.27	19.33	19.20	19.31		19.40	19.38	19.20	19.17	19.09	18.97
Cer[NS] 45:1	11.83	12.31	12.59	12.53	12.04	12.57		12.25	12.50	11.88	11.84	12.13	11.93
Cer[NS] 46:5	13.50	13.74	13.76	13.69	13.52	13.68		13.62	13.72	13.55	13.78	13.87	13.86
DG 30:0	10.50	9.87	10.35	10.80	9.87	10.63		9.89	10.21	10.14	10.88	10.95	10.67
DG 30:1	10.17	9.90	10.24	9.86	10.26	10.41		10.19	10.13	10.85	10.22	9.98	10.32
DG 32:0	11.94	11.78	11.45	11.74	12.02	11.68		11.28	11.20	11.89	11.83	11.57	11.92
DG 32:1	12.54	12.49	11.87	12.63	12.43	12.12		11.92	12.01	13.29	12.72	13.05	13.00
DG 32:2	12.27	11.59	11.77	11.73	12.11	11.57		11.47	11.67	12.42	12.28	11.56	11.82
DG 33:0	10.15	9.94	9.43	9.64	10.02	9.09		9.16	9.51	10.04	9.75	9.97	9.73
DG 33:1	9.88	9.56	9.59	9.76	9.93	9.62		9.55	9.39	10.29	9.75	9.75	10.30
DG 34:0	12.23	11.73	11.59	11.90	11.95	11.85		11.64	11.44	12.10	11.99	11.93	12.00
DG 34:2	15.03	14.87	14.76	14.89	14.79	14.58		14.54	14.75	15.33	15.17	15.35	15.30
DG 34:3	13.48	13.37	12.91	13.15	13.07	12.61		13.06	13.41	14.03	13.88	13.79	13.89
DG 35:1	10.78	10.42	10.30	10.89	10.61	10.78		10.64	10.18	10.66	10.61	10.80	10.91
DG 35:2	10.06	10.13	10.41	10.66	10.16	10.20		10.38	10.10	11.03	10.18	10.66	10.47
DG 35:3	10.43	10.06	10.12	10.46	10.12	9.86		9.95	9.57	10.57	10.17	10.53	10.50
DG 36:0	11.97	11.65	12.10	11.80	11.84	11.88		11.57	11.51	12.05	11.64	11.72	11.64
DG 36:1	13.19	12.74	12.64	12.84	13.06	12.94		12.77	12.45	13.14	13.05	13.00	13.06
DG 36:2	16.06	15.85	15.35	15.54	15.38	15.42		15.82	15.56	16.19	16.03	16.04	16.10
DG 36:3	15.91	15.91	15.68	15.71	15.54	15.38		15.97	15.94	16.20	16.09	16.10	16.26
DG 36:4	15.59	15.96	15.82	15.68	15.65	15.40		15.45	15.79	15.79	15.52	15.62	15.59
DG 36:5	12.67	12.81	12.84	12.57	12.95	12.10		12.55	12.82	13.28	13.04	12.88	13.19
DG 38:1	11.94	11.83	11.97	12.33	12.50	12.36		11.82	11.13	11.54	10.99	11.25	11.29
DG 38:2	11.29	11.06	11.31	10.86	11.03	10.84		11.02	10.54	11.12	10.91	10.88	10.89
DG 38:3	11.65	11.81	11.75	11.54	11.67	11.72		11.81	11.72	12.02	11.90	12.10	11.77
DG 38:4	12.27	12.26	11.88	12.40	11.95	12.14		12.34	12.15	12.58	12.53	12.58	12.34
DG 38:5	13.65	13.48	13.30	13.36	13.36	12.84		13.50	13.39	13.79	13.83	13.74	13.76
DG 38:6	13.47	13.64	13.42	13.50	13.62	13.22		13.54	13.71	13.78	13.84	13.99	13.95
DG 38:7	10.67	10.88	11.21	10.82	10.84	10.27		10.41	10.77	11.29	11.04	11.35	11.06
DG 40:6	11.39	11.03	11.10	10.76	10.91	10.45		11.09	11.12	11.77	11.21	11.60	11.47
DG 40:7	11.65	12.09	12.34	12.04	11.90	11.40		11.69	11.60	12.02	12.31	11.92	11.98
FFA 16:0	25.40	25.40	25.47	25.35	25.24	25.23		25.44	25.43	25.30	25.37	25.44	25.37
FFA 18:0	25.85	25.76	25.75	25.69	25.62	25.62		25.86	25.74	25.67	25.77	25.75	25.73
FFA 18:1	24.52	24.80	24.79	24.57	24.41	24.40		24.61	24.97	24.71	24.65	25.04	24.67

Table S2.5C: MEAL Study Mean Log2 Area Under the Curve for Lipids (Ceramide [NS] 36:1 to Free Fatty Acid 18:2 to Lysophosphatidylethanolamine 20:2)

	Mean Log2 AUC Values For Each Lipid Species												
	High Fat Diet							High Carbohydrate Diet					
Lipid/Day	B	S	2	7	14	21		B	S	2	7	14	21
FFA 18:2	23.63	24.10	24.24	23.86	23.75	23.75		23.71	24.24	23.82	23.78	24.19	23.79
FFA 20:0	20.77	20.55	20.51	20.54	20.33	20.38		20.67	20.44	20.35	20.52	20.45	20.43
FFA 20:1	19.03	19.07	18.98	18.77	18.55	18.61		18.99	19.19	18.95	18.90	19.21	18.84
FFA 20:2	18.55	18.73	18.55	18.27	18.07	18.11		18.64	18.93	18.70	18.72	19.01	18.64
FFA 20:4	20.06	20.43	20.29	20.01	19.81	20.04		20.42	20.61	20.46	20.51	20.65	20.40
FFA 22:0	19.88	19.68	19.45	19.69	19.44	19.53		19.73	19.48	19.40	19.64	19.46	19.44
FFA 22:1	16.81	16.56	16.94	16.61	16.26	16.39		16.76	16.60	16.34	16.59	16.88	16.47
FFA 22:2	15.10	14.91	14.79	14.72	14.52	14.38		15.05	15.05	14.80	14.82	14.86	14.69
FFA 22:3	15.21	15.13	14.87	14.88	14.80	14.74		15.23	15.30	15.38	15.02	15.27	15.01
FFA 24:0	18.34	18.36	18.35	18.17	18.16	18.47		18.45	18.40	18.43	18.30	18.18	18.26
FFA 24:1	17.73	17.63	17.54	17.48	17.37	17.20		17.63	17.63	17.40	17.35	17.56	17.42
FFA 24:2	15.77	15.68	15.76	15.49	15.27	15.46		15.82	15.90	15.64	15.57	15.66	15.63
FFA 24:3	13.16	12.85	13.10	12.96	12.56	12.68		13.14	12.91	13.11	12.59	12.75	12.59
GlcCer[NS] 34:1	18.03	18.29	18.20	18.06	18.03	18.03		18.27	18.41	18.13	17.89	18.24	17.98
GlcCer[NS] 34:2	12.03	12.41	12.70	12.38	12.46	12.23		11.88	12.21	11.91	11.56	11.67	11.85
GlcCer[NS] 40:1	17.61	17.69	17.68	17.53	17.54	17.68		18.00	18.15	17.92	17.46	17.48	17.32
GlcCer[NS] 41:1	12.45	12.69	12.61	12.67	12.62	12.58		12.42	12.45	12.65	12.28	12.24	12.22
GlcCer[NS] 42:1	17.53	17.66	17.63	17.54	17.52	17.54		18.08	18.12	17.93	17.54	17.76	17.50
GlcCer[NS] 42:2	17.41	17.55	17.49	17.33	17.20	17.34		17.79	17.95	17.85	17.70	17.91	17.83
LysoPC 14:0	15.94	16.00	15.86	15.99	16.13	15.76		15.77	15.92	16.08	15.81	15.92	15.74
LysoPC 15:0	15.71	15.98	15.99	15.96	15.96	15.82		15.77	15.94	15.87	15.68	15.74	15.64
LysoPC 15:1	16.29	15.99	15.91	15.77	15.97	15.91		15.88	15.67	15.75	15.54	15.91	15.67
LysoPC 16:0	21.93	21.96	21.77	21.60	21.57	21.58		21.90	22.05	22.01	21.89	22.03	21.90
LysoPC 16:1	17.44	17.28	16.78	16.85	16.77	16.74		17.17	17.15	17.54	17.40	17.58	17.45
LysoPC 17:1	14.69	14.66	14.43	14.61	14.66	14.56		14.61	14.64	14.85	14.79	14.83	14.68
LysoPC 18:0	21.91	22.09	21.82	21.73	21.88	21.72		22.05	22.11	22.00	21.77	21.93	21.83
LysoPC 18:1	21.23	21.09	20.87	20.73	20.77	20.70		21.08	20.95	20.95	20.94	21.04	20.99
LysoPC 18:2	22.21	22.31	22.21	22.20	22.21	22.14		22.00	22.10	21.72	21.75	21.77	21.77
LysoPC 18:3	16.03	15.78	15.55	15.62	15.70	15.34		15.66	15.55	15.61	15.64	15.66	15.65
LysoPC 19:0	15.09	15.05	15.04	14.96	14.93	14.93		15.13	15.25	15.18	15.05	15.09	15.09
LysoPC 19:1	13.65	13.67	13.61	13.67	13.51	13.61		13.47	13.64	13.52	13.63	13.60	13.53
LysoPC 20:0	15.16	15.06	14.81	14.68	14.86	14.87		15.14	15.03	15.01	14.68	14.79	14.60
LysoPC 20:1	15.57	15.50	15.04	14.93	14.97	15.02		15.53	15.44	15.44	15.23	15.49	15.33
LysoPC 20:2	15.64	15.72	15.27	15.16	15.27	15.21		15.55	15.67	15.53	15.52	15.57	15.51
LysoPC 20:3	18.14	18.30	17.86	17.80	17.69	17.79		18.14	18.13	18.18	18.24	18.22	18.20
LysoPC 20:4	19.55	19.74	19.50	19.51	19.42	19.44		19.61	19.68	19.63	19.64	19.75	19.62
LysoPC 20:5	20.35	20.34	20.15	20.32	20.38	20.32		20.25	19.81	20.00	20.13	20.03	20.03
LysoPC 22:0	13.31	13.22	13.19	12.83	12.81	12.75		13.42	13.29	13.06	12.70	12.66	12.66
LysoPC 22:4	14.56	14.60	14.37	14.19	14.27	14.43		14.58	14.61	14.70	14.85	14.88	14.72
LysoPC 22:5	16.02	16.11	15.71	15.81	15.63	15.71		16.01	16.05	16.07	16.24	16.30	16.23
LysoPC 22:6	17.40	17.62	17.28	17.23	17.29	17.25		17.53	17.50	17.52	17.53	18.00	17.92
LysoPC 23:0	11.74	11.78	11.91	11.83	11.59	11.42		11.41	11.87	12.02	11.56	11.69	11.25
LysoPC 24:0	14.12	14.15	13.85	13.68	13.54	13.66		14.22	14.13	14.02	13.73	13.89	13.69
LysoPC 24:1	12.55	12.53	12.30	12.12	12.14	11.89		12.61	12.24	12.60	12.36	12.58	12.46
LysoPC 26:1	11.95	11.67	11.32	10.63	10.97	10.89		11.71	11.78	11.79	11.59	12.25	11.73
LysoPE 16:0	17.86	17.91	17.62	17.42	17.49	17.47		17.71	17.98	18.11	17.94	18.24	18.00
LysoPE 16:1	11.46	11.15	10.53	11.13	11.18	10.45		10.71	11.10	11.57	11.64	11.78	11.34
LysoPE 17:0	13.50	13.20	13.51	13.24	13.13	13.19		13.69	13.55	13.58	13.67	13.90	13.75
LysoPE 18:0	18.11	18.16	18.01	17.74	17.87	17.98		18.29	18.44	18.29	18.09	18.31	18.07
LysoPE 18:1	18.45	18.20	17.93	17.70	17.86	17.93		18.10	17.99	17.91	17.78	18.01	17.79
LysoPE 18:2	19.28	19.32	19.41	19.08	19.27	19.16		18.81	19.07	18.62	18.52	18.80	18.55
LysoPE 18:3	12.63	12.25	12.23	12.39	12.60	12.23		12.33	12.12	12.10	12.46	12.48	12.33
LysoPE 20:2	13.04	13.07	12.71	12.37	12.67	12.64		12.93	12.98	12.89	12.72	12.95	12.69

Table S2.5D: MEAL Study Mean Log2 Area under the Curve for Lipids (Lysophosphatidylethanolamine 20:3 to Phosphatidylcholine 37:3)

	Mean Log2 AUC Values For Each Lipid Species												
	High Fat Diet							High Carbohydrate Diet					
Lipid/Day	B	S	2	7	14	21		B	S	2	7	14	21
LysoPE 20:3	16.32	16.26	15.97	15.55	15.64	15.55		15.95	16.27	16.31	16.28	16.39	16.16
LysoPE 20:4	18.68	18.78	18.70	18.48	18.44	18.56		18.65	18.81	18.59	18.56	18.79	18.49
LysoPE 20:5	13.08	12.68	12.93	12.54	12.27	11.95		12.96	12.45	12.64	12.84	13.00	12.79
LysoPE 22:4	14.20	14.00	13.75	13.60	13.49	13.49		13.84	14.07	14.18	14.40	14.39	14.24
LysoPE 22:5	16.47	16.47	16.25	15.95	15.98	15.86		16.34	16.60	16.65	16.55	16.81	16.60
LysoPE 22:6	18.07	18.13	17.99	17.71	17.82	17.80		17.87	18.08	17.86	17.92	18.31	17.98
LysoPE 24:0	12.97	12.85	13.14	12.82	12.54	12.45		13.01	13.29	13.12	12.64	13.09	12.67
PA 34:1	14.98	14.74	14.35	14.47	14.42	14.49		14.56	14.51	14.79	14.77	14.75	14.96
PA 34:2	16.62	16.51	16.48	16.45	16.45	16.36		16.20	16.24	16.15	16.13	16.05	16.11
PA 36:1	15.18	14.65	14.99	14.37	14.49	14.87		14.57	15.05	14.53	14.80	14.61	14.75
PA 36:2	16.83	16.82	16.65	16.46	16.86	16.56		16.55	16.77	16.70	16.53	16.50	16.71
PA 36:3	17.44	17.33	17.37	17.38	17.36	17.36		17.10	17.11	16.88	16.87	16.87	16.96
PA 36:4	16.28	16.23	16.03	16.11	15.84	16.17		16.25	16.03	15.95	15.86	15.86	15.94
PA 38:6	15.17	15.28	15.16	15.21	14.83	15.28		15.39	15.32	15.22	15.41	15.36	15.52
PC 24:0	11.47	11.49	12.54	11.95	12.56	11.22		11.32	11.08	11.62	11.08	11.73	11.41
PC 26:0	12.56	12.31	13.79	13.45	14.00	12.80		12.48	12.61	12.76	12.57	12.68	12.26
PC 27:0	10.67	10.38	11.14	10.78	10.73	10.75		10.11	10.39	10.61	10.15	10.30	10.12
PC 28:2	9.33	9.12	9.05	9.04	8.51	8.96		8.52	9.14	8.91	8.31	9.13	8.40
PC 29:0	13.55	13.93	14.48	14.48	14.56	14.22		13.63	14.00	14.08	13.90	13.90	13.87
PC 30:0	18.80	18.96	19.16	19.07	19.26	18.88		18.69	18.85	19.21	18.97	19.15	19.03
PC 30:2	13.10	12.94	13.52	13.28	13.84	12.57		12.61	12.88	13.24	12.38	12.92	12.44
PC 31:0	15.71	15.93	16.26	16.34	16.42	16.38		15.86	16.03	16.04	15.96	16.03	16.02
PC 31:1	14.66	14.90	14.85	14.54	14.60	14.76		14.48	14.74	15.21	14.91	15.11	14.93
PC 32:0	20.77	20.86	20.84	20.79	20.77	20.71		20.66	20.70	20.73	20.60	20.81	20.67
PC 32:1	20.61	20.47	20.21	20.13	20.23	20.02		20.33	20.22	21.01	20.82	20.93	20.81
PC 32:2	19.95	20.16	19.99	19.93	20.03	19.57		19.76	19.96	19.87	19.57	19.64	19.47
PC 32:3	14.91	14.55	14.51	14.55	14.46	13.96		14.34	14.27	14.74	14.07	14.61	14.37
PC 33:0	12.43	12.39	12.26	12.71	12.36	12.28		12.34	12.39	12.37	12.31	12.47	12.49
PC 33:1	15.97	16.05	16.01	16.24	15.98	15.94		15.95	15.89	16.30	16.19	16.27	16.09
PC 33:2	19.17	19.55	19.74	19.72	19.60	19.61		19.25	19.49	19.21	19.05	19.07	19.01
PC 33:3	14.89	14.86	14.97	15.00	14.74	14.68		14.84	14.89	14.81	14.67	14.52	14.74
PC 34:1	24.55	24.45	24.23	24.15	24.26	24.19		24.48	24.33	24.61	24.52	24.65	24.58
PC 34:2	25.50	25.53	25.51	25.55	25.57	25.51		25.56	25.57	25.45	25.47	25.45	25.40
PC 34:3	18.58	18.45	18.18	18.17	18.11	18.04		18.36	18.30	18.50	18.34	18.46	18.28
PC 34:4	18.14	18.29	18.13	18.02	18.10	17.75		18.24	18.24	18.38	18.16	18.27	18.05
PC 34:5	11.17	12.66	12.18	11.43	12.23	11.19		12.57	12.20	11.87	11.90	11.71	11.96
PC 35:0	14.02	14.44	14.38	14.59	14.30	14.24		13.58	14.27	13.76	13.79	13.99	13.97
PC 35:1	15.87	15.82	15.76	15.90	15.93	16.05		16.15	15.97	16.29	16.33	16.31	16.05
PC 35:2	17.26	17.33	17.35	17.21	17.41	17.52		17.34	17.42	16.91	16.98	16.89	16.90
PC 35:3	15.94	16.09	15.79	15.78	15.73	15.67		15.51	15.67	15.33	15.49	15.30	15.66
PC 35:4	17.37	17.62	17.75	17.75	17.55	17.72		17.60	17.74	17.75	17.64	17.71	17.54
PC 35:5	17.22	17.03	17.12	16.96	17.04	17.06		17.09	17.06	17.30	17.09	17.23	17.01
PC 35:6	16.16	15.89	16.18	16.10	15.93	16.30		16.13	16.00	16.50	16.43	16.51	16.46
PC 36:0	15.46	15.43	15.33	15.32	15.22	15.39		15.63	15.36	15.34	15.28	15.34	15.30
PC 36:1	22.12	21.99	21.87	21.68	21.95	21.83		21.96	21.63	21.71	21.74	21.78	21.77
PC 36:2	21.43	21.47	21.44	21.21	21.33	21.25		21.53	21.54	21.27	21.10	21.17	21.07
PC 36:3	24.41	24.42	24.19	24.11	24.03	23.97		24.29	24.27	24.24	24.16	24.21	24.15
PC 36:4	20.79	21.05	20.86	20.71	20.55	20.71		20.87	21.07	20.99	20.92	21.09	20.85
PC 36:5	20.92	20.66	20.52	20.46	20.37	20.21		20.92	20.51	20.82	20.90	20.99	20.91
PC 36:6	17.44	17.30	16.78	17.05	16.89	16.94		16.89	16.90	17.03	16.88	16.75	16.71
PC 37:1	14.96	14.96	14.53	14.92	14.32	14.78		14.78	14.44	14.66	14.62	14.82	14.75
PC 37:2	17.37	17.48	17.53	17.48	17.46	17.42		17.64	17.52	17.42	17.34	17.34	17.32
PC 37:3	14.95	15.15	15.12	15.22	14.89	15.07		15.12	15.30	15.26	15.37	15.07	15.12

Table S2.5E: MEAL Study Mean Log2 Area under the Curve for Lipids (Phosphatidylcholine 37:4 to Phosphatidylethanolamine 33:1)

	Mean Log2 AUC Values For Each Lipid Species												
	High Fat Diet							High Carbohydrate Diet					
Lipid/Day	B	S	2	7	14	21		B	S	2	7	14	21
PC 37:4	15.74	16.08	16.06	15.87	15.90	15.93		16.15	16.10	16.14	16.18	16.21	15.95
PC 37:5	16.63	16.59	16.61	16.58	16.42	16.48		16.80	16.62	16.87	16.81	16.87	16.89
PC 37:6	16.05	16.18	16.21	16.34	15.91	16.26		16.14	16.28	16.25	16.16	16.38	16.32
PC 37:7	14.73	14.67	14.67	14.52	14.37	14.42		14.77	14.36	14.61	14.37	14.75	14.43
PC 38:1	15.85	15.71	15.46	15.23	15.35	15.49		15.78	15.58	15.56	15.52	15.65	15.60
PC 38:2	16.87	16.86	16.69	16.30	16.41	16.53		16.88	16.83	16.60	16.52	16.65	16.55
PC 38:3	22.03	22.08	21.77	21.46	21.55	21.39		22.33	22.22	22.40	22.24	22.37	22.26
PC 38:4	23.05	23.19	23.14	23.15	23.02	23.06		23.34	23.35	23.43	23.38	23.45	23.37
PC 38:5	22.23	22.15	22.01	22.00	21.92	21.92		22.36	22.27	22.42	22.38	22.54	22.35
PC 38:6	23.02	23.14	22.96	22.98	22.94	22.89		23.18	23.14	23.31	23.28	23.49	23.36
PC 38:7	17.97	17.79	17.60	17.57	17.50	17.43		17.92	17.69	17.94	17.86	17.99	17.91
PC 39:3	14.48	14.69	14.45	14.52	14.58	14.58		14.90	14.84	14.70	14.81	14.73	14.77
PC 39:4	16.09	16.06	16.10	16.29	16.09	15.99		16.39	16.37	16.40	16.34	16.39	16.26
PC 39:6	16.77	16.82	16.83	16.87	16.94	16.97		17.05	17.03	17.22	17.12	17.28	17.26
PC 39:7	13.64	13.52	13.65	13.33	13.51	13.52		13.67	13.49	14.13	14.05	14.10	13.73
PC 39:8	13.58	13.45	13.59	13.59	13.53	13.57		13.47	13.50	13.62	13.73	13.70	13.49
PC 40:0	11.55	11.52	11.05	11.17	10.81	11.35		12.00	11.79	11.63	11.67	11.45	11.41
PC 40:1	13.22	13.10	12.95	12.87	12.57	12.98		13.07	13.07	12.95	12.94	12.85	12.91
PC 40:2	14.44	14.16	13.75	13.91	13.81	13.82		14.06	13.90	13.84	13.68	13.87	13.67
PC 40:4	16.12	16.05	16.00	15.84	15.62	15.85		16.26	16.18	16.24	16.25	16.40	16.25
PC 40:5	16.70	16.70	16.49	16.44	16.22	16.35		16.91	16.85	17.06	16.95	17.19	17.29
PC 40:6	20.42	20.55	20.44	20.39	20.41	20.35		20.62	20.58	20.89	20.74	21.03	20.98
PC 40:7	15.88	15.90	15.74	15.48	15.47	15.53		16.12	15.87	16.16	15.83	16.04	15.96
PC 40:8	17.28	17.42	17.82	17.19	16.63	17.03		17.99	17.78	18.49	17.62	17.69	17.59
PC 41:3	13.16	13.25	13.16	13.28	13.26	13.02		13.19	13.04	13.29	13.23	13.03	13.01
PC 41:4	13.48	13.10	13.33	13.33	13.27	13.27		13.10	13.20	13.17	13.25	13.34	12.97
PC 41:5	13.16	13.33	13.49	13.51	13.54	13.32		13.51	13.57	13.65	13.53	13.79	13.66
PC 41:6	13.22	13.26	13.14	13.42	13.52	13.54		13.27	13.71	13.92	13.85	14.02	13.93
PC 41:7	11.96	11.69	12.03	11.82	11.91	11.99		12.38	11.90	12.13	12.16	12.00	12.33
PC 42:1	13.10	13.01	12.66	12.38	12.25	12.40		13.25	13.05	13.14	12.69	12.94	12.97
PC 42:10	15.39	15.21	15.26	15.00	15.01	15.13		15.25	15.15	15.38	15.20	15.49	15.38
PC 42:2	14.01	13.86	13.47	13.33	13.21	13.12		13.85	13.65	13.60	13.41	13.40	13.30
PC 42:3	13.30	13.51	12.87	13.08	13.04	12.63		13.28	13.10	13.26	13.23	13.26	13.06
PC 42:4	14.03	13.61	13.57	13.44	13.53	13.47		13.82	13.91	13.82	13.95	13.97	13.77
PC 42:5	14.98	14.58	14.59	14.68	14.30	14.39		14.97	14.93	14.85	14.97	14.97	14.93
PC 42:6	14.90	14.89	14.85	14.45	14.13	14.34		15.25	14.82	15.25	15.26	15.28	15.29
PC 42:7	14.79	14.64	14.28	14.54	14.02	14.53		14.76	14.86	15.01	14.63	14.87	14.78
PC 42:8	14.30	14.24	14.09	13.86	13.84	13.69		14.40	14.40	14.56	14.55	14.65	14.43
PC 42:9	14.93	14.84	14.74	14.65	14.62	14.76		15.17	14.71	15.33	15.17	15.29	15.40
PC 44:12	12.15	11.79	11.85	11.65	12.06	11.83		12.46	11.90	12.27	12.05	12.34	12.19
PC 44:2	12.72	12.88	12.17	12.03	12.10	12.12		12.50	11.99	12.26	12.19	12.57	12.35
PC 44:3	11.89	11.71	11.53	11.55	11.22	10.86		11.68	11.97	12.07	11.67	11.64	11.98
PC 44:4	13.05	12.69	12.68	12.35	12.52	12.51		12.98	12.97	13.14	12.90	12.82	12.84
PC 44:5	12.45	12.40	11.92	12.25	12.02	11.99		12.45	12.29	12.76	12.35	12.65	12.72
PC 44:6	12.16	12.02	11.62	11.87	11.70	11.43		12.14	11.90	11.75	11.97	11.77	11.60
PC 44:8	11.69	12.04	11.98	11.82	12.00	12.18		11.53	11.65	11.74	11.29	11.91	11.36
PC 46:4	11.96	11.91	11.62	10.84	11.36	11.10		12.26	11.40	12.10	12.10	12.04	11.69
PE 30:0	12.29	12.39	13.03	12.49	13.20	12.15		12.01	11.99	12.31	12.03	12.46	12.23
PE 32:0	15.18	15.27	15.46	15.51	15.34	15.22		14.86	14.98	15.45	15.15	15.31	15.13
PE 32:1	15.33	14.79	14.68	14.86	14.59	14.79		14.76	14.70	15.65	15.41	15.58	15.29
PE 32:2	12.66	13.12	12.25	12.94	13.50	12.98		12.67	12.06	12.44	12.15	12.32	12.44
PE 33:0	13.35	13.43	13.61	13.66	13.34	13.44		13.56	13.46	13.61	13.63	13.59	13.52
PE 33:1	13.32	13.16	12.93	13.13	13.40	12.81		13.76	13.28	13.82	13.30	13.57	13.83

Table S2.5F: MEAL Study Mean Log2 Area under the Curve for Lipids (Phosphatidylethanolamine 33:2 to Plasmenyl-phosphatidylcholine 34:0)

	Mean Log2 AUC Values For Each Lipid Species												
	High Fat Diet							High Carb Diet					
Lipid/Day	B	S	2.00	7.00	14.00	21.00		B	S	2.00	7.00	14.00	21.00
PE 33:2	14.69	14.77	15.15	14.83	14.92	14.77		14.39	14.54	14.69	14.54	14.49	14.19
PE 34:0	19.98	19.87	19.91	20.00	19.91	19.92		20.01	19.88	20.02	19.95	19.95	19.96
PE 34:1	18.75	18.46	18.30	18.08	18.09	18.27		18.40	18.29	18.78	18.54	18.76	18.63
PE 34:2	19.60	19.61	19.53	19.63	19.65	19.60		19.41	19.57	19.73	19.55	19.63	19.48
PE 34:3	17.79	17.41	17.45	17.42	17.38	17.20		17.23	17.27	17.68	17.47	17.61	17.50
PE 34:4	13.55	13.44	13.11	13.14	12.85	13.39		13.17	13.45	13.63	12.79	13.46	13.51
PE 35:0	13.79	13.37	13.44	13.49	13.56	13.57		13.87	13.61	13.66	13.60	13.67	13.40
PE 35:1	14.61	14.72	14.60	14.40	14.51	14.67		14.68	14.54	14.84	14.58	14.56	14.33
PE 35:2	15.85	15.79	15.80	15.66	15.84	15.91		15.67	15.60	15.84	15.76	15.76	15.70
PE 35:4	15.05	15.34	15.10	15.31	15.43	15.42		15.13	15.35	15.23	15.26	15.23	15.00
PE 36:0	16.68	16.44	16.62	16.58	16.26	16.50		16.75	16.64	16.68	16.60	16.69	16.64
PE 36:1	18.65	18.26	18.15	18.01	18.12	18.18		18.33	18.11	18.24	18.17	18.31	18.27
PE 36:2	20.85	20.69	20.64	20.52	20.64	20.57		20.59	20.54	20.56	20.32	20.45	20.34
PE 36:3	20.01	19.84	19.79	19.75	19.78	19.73		19.61	19.57	19.55	19.45	19.51	19.35
PE 36:4	19.91	19.87	19.83	19.84	19.80	19.89		20.07	20.11	20.41	20.26	20.43	20.22
PE 36:5	17.76	17.39	17.49	17.31	17.52	17.26		17.59	17.32	17.87	17.86	17.99	17.79
PE 37:4	16.34	16.46	16.44	16.26	16.49	16.53		16.62	16.48	16.67	16.53	16.58	16.50
PE 38:3	18.63	18.50	18.69	18.53	18.14	18.47		18.85	18.67	18.77	18.57	18.75	18.54
PE 38:4	21.50	21.59	21.53	21.29	21.38	21.57		21.73	21.77	21.83	21.59	21.81	21.61
PE 38:5	20.28	20.34	20.25	20.00	20.02	20.17		20.35	20.36	20.53	20.29	20.50	20.25
PE 38:6	20.64	20.61	20.59	20.42	20.41	20.57		20.45	20.54	20.66	20.60	20.90	20.67
PE 38:7	15.06	15.09	14.89	14.88	14.74	14.88		15.07	15.21	15.22	15.07	15.13	15.05
PE 40:4	17.32	17.40	17.31	17.22	17.10	17.34		17.55	17.54	17.60	17.37	17.55	17.44
PE 40:5	18.08	18.12	18.05	17.84	17.79	17.98		18.16	18.16	18.36	18.25	18.50	18.15
PE 40:6	19.12	19.24	19.17	19.02	18.99	19.10		19.07	19.05	19.40	19.22	19.54	19.38
PE 40:7	17.44	17.41	17.24	17.06	17.17	17.35		17.52	17.46	17.58	17.29	17.55	17.46
PE 40:8	16.27	16.25	16.05	15.83	16.20	16.29		16.25	16.24	16.26	16.04	16.32	16.08
PE 42:10	13.70	13.78	13.73	12.98	13.81	13.83		13.56	13.55	13.71	13.40	13.78	13.70
PG 33:0	15.05	15.51	15.62	15.11	14.87	15.05		15.50	15.48	15.43	15.24	15.28	15.38
PG 34:0	18.97	19.19	19.48	18.77	19.11	19.17		19.11	18.91	19.18	18.65	19.15	18.95
PG 34:2	13.10	13.19	13.29	12.30	12.49	12.76		13.13	13.58	13.58	13.28	13.67	13.22
PG 36:0	16.53	16.40	16.60	16.32	16.07	16.35		16.59	16.58	16.53	16.32	16.30	16.36
PG 36:2	16.20	16.39	16.30	15.56	15.86	15.81		16.15	16.36	16.71	16.24	16.31	16.20
PG 36:3	14.26	14.49	14.43	13.94	13.67	13.96		14.37	14.49	14.57	14.22	14.56	14.21
PG 38:4	13.60	14.06	13.75	13.36	13.62	13.82		13.77	14.09	14.04	13.73	13.93	13.71
PI 25:0	13.85	13.95	14.40	13.74	13.43	13.97		14.41	14.06	14.64	13.86	13.96	13.90
PI 34:1	15.72	15.85	16.11	14.92	15.49	15.51		16.04	15.98	16.45	15.49	15.75	15.54
PI 34:2	15.87	16.22	16.35	15.56	15.55	15.52		16.22	16.34	16.70	15.62	16.00	15.71
PI 36:1	16.15	16.04	16.61	15.46	15.83	16.07		16.46	16.14	16.20	15.58	15.72	15.71
PI 36:2	18.73	18.84	19.11	18.14	18.42	18.42		18.81	18.72	18.94	17.99	18.37	18.17
PI 36:4	16.00	16.40	16.55	15.50	15.74	15.86		16.72	16.70	17.25	16.24	16.60	16.18
PI 38:3	18.79	19.07	19.34	18.53	18.35	18.65		19.47	19.37	19.93	18.96	19.24	19.06
PI 38:4	20.44	20.70	20.93	20.03	20.27	20.43		20.81	20.77	21.15	20.19	20.61	20.39
PI 38:5	16.00	16.08	16.33	15.46	15.64	15.77		16.46	16.47	17.02	15.96	16.30	15.93
PI 38:6	13.43	13.16	13.87	12.77	12.70	12.93		13.87	13.67	14.43	13.33	13.75	13.39
PI 40:5	16.07	16.14	16.41	15.42	15.66	15.82		16.26	16.27	16.78	15.79	16.36	16.20
PI 40:6	15.24	15.47	15.81	14.74	15.03	15.13		15.49	15.48	15.94	15.21	15.87	15.53
PlsCho 24:0	12.55	12.53	12.30	12.12	12.14	11.89		12.61	12.24	12.60	12.36	12.58	12.46
PlsCho 28:0	9.88	10.91	10.85	10.89	11.13	10.85		10.90	10.45	10.47	10.55	10.61	10.43
PlsCho 32:0	16.46	16.79	16.58	16.67	15.81	16.47		16.35	16.10	16.38	16.41	15.64	16.02
PlsCho 32:1	13.55	13.36	13.78	13.70	14.08	13.76		13.55	13.21	13.27	13.57	13.19	12.99
PlsCho 33:0	13.23	13.86	14.10	14.35	14.13	14.20		14.35	14.15	13.94	14.05	14.17	13.96
PlsCho 34:0	19.39	19.35	19.31	19.20	19.13	19.11		19.46	19.40	19.31	19.10	19.26	19.12

Table S2.5G: MEAL Study Mean Log2 Area under the Curve for Lipids (Plasmenyl-phosphatidylcholine 34:1 to Plasmenyl-phosphatidylethanolamine 34:1)

	Mean Log2 AUC Values For Each Lipid Species											
	High Fat Diet						High Carb Diet					
Lipid/Day	B	S	2.00	7.00	14.00	21.00	B	S	2.00	7.00	14.00	21.00
PlsCho 34:1	18.42	18.39	18.35	18.32	18.26	18.23	18.59	18.48	18.40	18.27	18.39	18.25
PlsCho 34:2	20.07	20.08	20.09	20.04	20.15	20.17	20.24	20.09	19.93	19.84	19.86	19.68
PlsCho 34:3	15.20	14.68	15.11	15.10	15.26	15.30	15.35	14.72	14.98	15.02	14.82	14.80
PlsCho 35:0	14.53	14.66	14.86	15.06	14.65	14.84	13.95	13.78	13.83	14.34	14.51	13.71
PlsCho 35:1	17.14	16.81	16.63	17.22	16.80	16.99	16.56	16.47	16.38	16.82	16.38	16.50
PlsCho 35:2	13.32	13.11	13.19	13.34	13.36	13.49	13.42	13.43	13.23	13.26	13.09	13.21
PlsCho 35:3	14.33	13.98	14.15	14.05	14.33	14.89	14.60	13.87	14.17	14.33	14.08	14.20
PlsCho 35:4	14.77	14.64	15.32	14.66	14.97	15.23	15.00	14.58	14.97	14.32	14.97	14.76
PlsCho 36:0	15.82	15.84	15.48	15.31	16.00	15.72	15.85	15.79	15.66	15.18	15.52	15.34
PlsCho 36:2	18.34	18.10	18.34	18.29	18.30	18.36	18.61	18.55	18.31	18.25	18.28	18.24
PlsCho 36:3	20.85	20.96	20.99	21.02	20.96	21.05	20.96	20.97	20.76	20.75	20.81	20.63
PlsCho 36:4	20.17	20.22	20.21	20.21	20.22	20.33	20.55	20.41	20.31	20.26	20.30	20.09
PlsCho 36:5	15.97	15.65	15.99	15.92	15.94	16.13	16.34	15.78	15.80	15.90	16.00	15.87
PlsCho 36:6	13.81	13.78	14.20	14.19	14.21	14.21	14.22	14.09	13.91	13.77	14.12	14.19
PlsCho 37:1	12.45	12.38	12.08	12.58	11.98	12.02	12.32	11.92	12.12	11.96	12.05	12.20
PlsCho 37:2	12.85	12.85	13.06	12.65	12.79	12.81	12.59	12.81	12.45	12.85	12.38	12.54
PlsCho 37:3	16.35	16.26	16.39	16.59	16.66	16.80	16.64	16.50	16.53	16.46	16.55	16.27
PlsCho 37:4	16.06	15.95	16.17	16.48	16.53	16.75	16.78	16.32	16.28	16.37	16.57	16.01
PlsCho 37:6	17.24	17.37	17.66	17.61	17.45	17.62	17.84	17.59	17.47	17.33	17.51	17.33
PlsCho 38:0	13.54	13.71	13.87	13.55	13.60	13.72	13.59	13.66	13.77	13.25	13.77	13.62
PlsCho 38:1	15.01	15.16	14.79	15.06	15.06	15.06	15.11	14.81	14.99	14.76	14.83	14.78
PlsCho 38:3	20.02	20.13	20.14	20.21	20.29	20.27	20.22	20.19	20.10	19.95	20.00	19.83
PlsCho 38:4	20.31	20.26	19.90	20.24	20.10	20.26	20.32	20.20	20.15	20.01	20.05	19.76
PlsCho 38:5	19.19	19.13	19.21	19.20	19.12	19.31	19.32	19.20	19.06	19.12	19.19	19.04
PlsCho 38:6	17.53	17.50	17.47	17.60	17.59	17.68	17.76	17.63	17.44	17.58	17.67	17.45
PlsCho 39:3	17.20	16.81	16.92	17.14	16.98	17.07	16.98	16.73	16.80	16.63	16.59	16.87
PlsCho 39:4	16.14	15.98	15.83	16.17	15.95	16.00	15.92	15.79	15.71	16.06	16.06	15.71
PlsCho 39:5	16.62	16.37	16.22	16.72	16.49	16.50	16.09	16.01	15.92	16.32	15.92	16.07
PlsCho 39:6	13.24	13.22	13.49	13.89	13.65	13.96	14.27	13.63	13.84	13.55	13.99	13.72
PlsCho 40:0	14.37	14.51	14.34	14.25	13.97	14.09	14.46	14.59	14.47	14.42	14.40	14.14
PlsCho 40:1	15.01	15.03	14.99	14.89	14.62	14.68	14.99	14.97	14.97	14.50	14.77	14.62
PlsCho 40:3	17.52	17.62	17.61	17.63	17.74	17.78	17.55	17.60	17.55	17.26	17.36	17.31
PlsCho 40:4	18.42	18.47	18.40	18.37	18.28	18.28	18.33	18.26	18.28	18.20	18.28	18.17
PlsCho 40:5	17.67	17.59	17.82	17.99	17.87	17.95	17.89	17.81	17.75	17.57	17.62	17.72
PlsCho 40:6	17.35	17.34	17.41	17.34	17.18	17.24	17.40	17.31	17.14	17.18	17.40	17.23
PlsCho 42:1	15.38	15.31	15.40	15.19	15.17	14.99	15.63	15.57	15.50	15.17	15.41	15.25
PlsCho 42:2	15.92	16.14	16.03	15.90	15.72	15.67	15.94	16.02	15.90	15.71	15.75	15.66
PlsCho 42:3	16.72	16.98	16.79	16.65	16.74	16.64	16.69	16.70	16.78	16.17	16.56	16.44
PlsCho 42:4	17.39	17.47	17.40	17.32	17.11	17.14	17.41	17.33	17.46	17.24	17.36	17.37
PlsCho 42:5	16.76	16.82	16.80	16.93	16.34	16.59	16.48	16.69	16.54	16.41	16.59	16.51
PlsCho 42:6	15.54	16.05	15.78	15.78	15.26	15.40	15.76	15.69	15.64	15.44	15.75	15.50
PlsCho 44:3	15.53	15.59	15.52	15.72	15.51	15.30	15.90	15.90	16.03	15.97	15.96	15.79
PlsCho 44:4	17.79	17.93	17.82	17.78	17.49	17.40	17.81	17.89	17.75	17.67	17.90	17.76
PlsCho 44:5	16.94	16.90	16.70	16.90	16.09	16.54	17.21	17.19	16.97	16.69	17.28	17.12
PlsCho 44:6	15.84	15.67	15.62	15.43	15.50	15.19	15.48	15.63	15.63	15.47	15.67	15.63
PlsCho 46:4	15.05	15.11	14.98	15.04	14.66	14.41	15.18	15.18	15.26	15.15	15.38	15.21
PlsEth 32:0	14.30	14.38	14.40	14.22	13.90	14.24	14.27	14.45	14.30	14.20	14.20	14.09
PlsEth 32:1	14.36	14.49	14.63	14.62	14.67	14.46	14.57	14.61	14.21	14.31	14.35	14.14
PlsEth 32:2	13.91	14.48	15.09	15.10	14.95	14.99	14.18	14.69	13.56	13.37	13.09	12.92
PlsEth 33:1	13.29	13.03	13.96	13.99	13.93	13.91	13.71	13.72	13.29	12.84	12.86	12.96
PlsEth 33:2	13.32	13.90	14.28	14.46	14.32	14.24	13.79	14.10	12.87	12.98	12.87	12.75
PlsEth 34:0	16.56	16.32	16.29	16.19	15.91	16.01	16.41	16.24	15.95	15.99	15.98	15.89
PlsEth 34:1	18.55	18.66	18.68	18.45	18.25	18.43	18.54	18.57	18.23	18.11	18.23	18.11

Table S2.5H: MEAL Study Mean Log2 Area under the Curve for Lipids (Plasmenyl-phosphatidylethanolamine 34:2 to Sphingomyelin 35:2)

	Mean Log2 AUC Values For Each Lipid Species												
	High Fat Diet							High Carb Diet					
Lipid/Day	B	S	2.00	7.00	14.00	21.00		B	S	2.00	7.00	14.00	21.00
PlsEth 34:2	19.72	19.97	20.01	19.87	19.81	19.80		19.83	19.94	19.51	19.32	19.35	19.31
PlsEth 34:3	15.16	15.37	15.63	15.55	15.58	15.59		15.41	15.38	14.80	14.89	14.91	14.88
PlsEth 34:4	15.18	15.45	16.04	15.99	16.05	16.30		15.93	15.83	15.05	15.07	14.99	15.08
PlsEth 35:1	14.73	14.76	15.03	14.77	15.05	14.88		14.95	14.87	14.65	14.59	14.61	14.43
PlsEth 35:2	12.87	12.51	13.26	13.51	13.41	13.45		13.46	13.16	12.28	12.49	12.53	12.54
PlsEth 35:4	15.13	15.33	15.93	16.04	16.00	16.24		15.87	15.64	15.03	15.13	15.11	15.13
PlsEth 36:0	15.70	15.54	15.64	15.45	15.28	15.34		15.61	15.51	15.59	15.56	15.31	15.35
PlsEth 36:1	18.74	18.68	18.83	18.63	18.62	18.71		18.81	18.79	18.27	18.14	18.21	18.09
PlsEth 36:2	20.24	20.35	20.50	20.33	20.36	20.36		20.33	20.34	19.73	19.63	19.56	19.53
PlsEth 36:3	20.53	20.70	20.77	20.60	20.43	20.62		20.63	20.70	20.31	20.27	20.34	20.22
PlsEth 36:4	21.91	22.26	22.10	21.95	21.85	22.06		22.14	22.29	22.03	21.86	22.14	21.98
PlsEth 36:5	17.97	18.11	18.35	18.30	18.16	18.28		18.22	18.16	17.51	17.73	17.85	17.96
PlsEth 36:6	14.49	14.69	15.08	15.13	15.06	15.17		15.00	14.96	14.50	14.71	14.63	14.48
PlsEth 37:1	15.66	15.29	15.45	15.60	15.02	15.37		15.13	14.85	15.01	15.08	14.74	14.63
PlsEth 37:2	14.40	14.33	14.38	14.12	14.41	14.50		14.61	14.72	14.14	13.98	14.22	13.88
PlsEth 37:3	15.73	15.71	16.00	16.01	15.87	16.12		16.28	15.92	15.73	15.93	15.80	15.81
PlsEth 37:4	18.21	18.36	18.58	18.51	18.62	18.88		18.98	18.77	18.44	18.50	18.62	18.43
PlsEth 37:5	15.75	15.74	16.25	16.34	16.31	16.32		16.33	16.05	15.75	15.92	15.90	15.82
PlsEth 37:6	15.51	15.62	16.09	16.12	16.13	16.24		15.77	15.79	15.34	15.32	15.22	15.23
PlsEth 38:1	15.64	15.70	15.77	15.51	15.39	15.51		15.77	15.97	15.37	15.25	15.47	15.26
PlsEth 38:2	17.67	17.85	17.90	17.63	17.55	17.56		17.88	17.93	17.53	17.44	17.40	17.38
PlsEth 38:3	19.75	19.96	20.09	20.05	19.75	20.00		20.20	20.14	19.78	19.84	19.75	19.69
PlsEth 38:4	22.16	22.37	22.37	22.27	22.27	22.46		22.63	22.56	22.32	22.24	22.35	22.15
PlsEth 38:5	22.14	22.29	22.30	22.14	22.08	22.30		22.35	22.35	22.08	22.03	22.19	22.05
PlsEth 38:6	21.18	21.35	21.39	21.30	21.16	21.32		21.44	21.45	21.18	21.09	21.26	21.16
PlsEth 39:2	14.94	14.42	14.54	14.83	14.10	14.42		14.23	14.24	14.20	14.08	14.19	14.32
PlsEth 39:4	16.42	16.43	16.55	16.42	16.63	16.75		16.90	16.86	16.57	16.57	16.70	16.43
PlsEth 39:5	16.67	16.68	17.04	16.90	16.88	17.06		16.98	16.88	16.61	16.70	16.66	16.64
PlsEth 39:6	17.08	16.93	17.10	17.13	17.12	17.32		17.41	17.11	17.08	17.03	17.14	17.12
PlsEth 40:1	12.89	13.21	12.97	12.78	12.64	12.73		13.60	13.55	13.38	13.07	13.09	12.90
PlsEth 40:2	15.56	15.67	15.58	15.60	15.08	15.24		15.74	15.92	15.49	15.12	15.41	15.20
PlsEth 40:4	20.00	20.24	20.22	20.08	19.97	20.34		20.37	20.47	20.19	20.04	20.29	20.04
PlsEth 40:5	19.85	20.05	20.05	19.99	19.85	20.11		20.11	20.09	19.87	19.67	19.84	19.73
PlsEth 40:6	20.19	20.31	20.36	20.40	20.34	20.50		20.66	20.58	20.41	20.21	20.29	20.27
PlsEth 41:4	13.89	13.81	13.93	13.88	13.81	14.14		14.38	14.23	14.27	14.10	14.34	13.97
PlsEth 41:6	14.65	14.37	14.57	14.36	14.55	14.42		14.74	14.71	14.43	14.71	14.63	14.40
PlsEth 42:4	16.94	16.92	17.12	16.56	16.72	16.76		17.37	17.38	16.94	16.90	17.26	16.72
PlsEth 42:5	17.39	17.48	17.56	17.41	17.10	17.50		17.63	17.67	17.51	17.36	17.69	17.41
PlsEth 42:6	12.68	13.23	13.03	12.95	13.14	13.30		13.15	13.12	13.15	13.25	13.42	12.97
PlsEth 44:6	15.32	15.19	15.56	14.84	14.66	14.86		15.70	15.31	15.00	15.16	15.44	15.47
PS 36:1	16.33	16.12	16.57	16.00	15.80	16.14		16.25	15.96	16.10	15.82	15.94	15.94
PS 38:4	15.97	15.96	16.33	15.50	15.68	16.43		15.90	15.81	16.08	15.45	15.67	15.44
SM 30:1	14.65	14.65	14.88	14.73	14.77	14.76		14.85	14.98	14.79	14.53	14.68	14.37
SM 30:2	12.13	12.07	12.38	12.53	12.37	12.30		12.13	12.09	11.88	11.72	12.10	11.54
SM 32:0	14.72	14.84	14.96	15.12	15.00	14.99		15.19	15.08	15.03	14.68	14.86	14.59
SM 32:1	18.89	19.05	19.08	19.03	19.07	19.12		19.18	19.26	19.14	18.98	19.04	18.88
SM 32:2	16.50	16.59	16.55	16.63	16.52	16.48		16.75	16.70	16.76	16.58	16.62	16.46
SM 33:1	17.84	18.02	18.04	17.93	17.99	18.12		18.16	18.27	18.14	17.96	18.05	17.86
SM 34:0	17.32	17.53	17.44	17.57	17.03	17.38		17.62	17.50	17.45	17.43	17.37	17.28
SM 34:1	23.37	23.52	23.55	23.46	23.48	23.46		23.51	23.49	23.53	23.32	23.46	23.34
SM 34:2	20.78	20.94	20.87	20.81	20.78	20.70		20.96	20.98	20.93	20.70	20.87	20.71
SM 34:3	14.84	14.40	14.82	14.83	14.51	14.61		14.69	14.81	14.58	14.55	14.74	14.64
SM 35:2	15.32	15.61	15.43	15.40	15.32	15.46		15.38	15.33	15.29	15.04	15.52	15.21

Table S2.5I: MEAL Study Mean Log2 Area under the Curve for Lipids (Sphingomyelin 36:1 to Triacylglycerol 43:1)

	Mean Log2 AUC Values For Each Lipid Species												
	High Fat Diet							High Carb Diet					
Lipid/Day	B	S	2.00	7.00	14.00	21.00		B	S	2.00	7.00	14.00	21.00
SM 36:1	20.90	21.07	21.19	21.25	21.22	21.22		21.08	21.13	21.11	20.95	21.17	21.05
SM 36:2	20.44	20.69	20.80	20.71	20.69	20.75		20.49	20.49	20.55	20.35	20.62	20.49
SM 36:3	15.12	15.29	15.41	15.15	15.27	15.32		15.24	15.25	15.12	14.88	15.13	14.82
SM 36:4	15.46	15.42	15.36	15.51	15.33	15.44		15.53	15.53	15.38	15.52	15.34	15.20
SM 37:1	16.77	16.94	17.13	17.41	17.31	17.39		16.95	17.07	16.99	16.93	17.04	16.93
SM 37:2	15.31	15.27	15.63	15.71	15.53	15.64		15.14	15.47	15.48	15.37	15.39	15.36
SM 38:0	12.47	12.44	11.38	11.96	12.23	11.90		11.46	11.97	12.33	11.58	12.12	12.17
SM 38:1	20.60	20.62	20.69	20.65	20.65	20.66		21.00	20.98	20.87	20.61	20.76	20.57
SM 38:2	15.89	15.98	15.90	15.83	15.74	15.85		16.04	16.20	16.01	15.93	16.03	15.86
SM 38:3	14.97	15.13	15.10	15.19	15.03	15.15		15.22	15.09	15.24	15.18	15.18	15.05
SM 38:4	14.31	14.58	14.31	14.60	14.29	14.27		14.02	13.97	13.79	13.86	14.07	13.88
SM 39:0	15.27	15.21	15.37	15.59	15.49	15.45		15.26	15.28	15.07	15.09	15.04	14.73
SM 39:1	17.48	17.55	17.65	17.63	17.50	17.61		17.66	17.67	17.50	17.32	17.34	17.11
SM 39:2	16.43	16.45	16.43	16.59	16.54	16.62		16.63	16.50	16.50	16.33	16.43	16.27
SM 39:3	15.39	15.37	15.38	15.86	15.51	15.76		15.31	15.15	15.01	15.18	14.94	14.81
SM 40:1	20.50	20.59	20.57	20.57	20.54	20.55		20.65	20.66	20.53	20.24	20.26	20.07
SM 40:2	21.28	21.38	21.27	21.24	21.26	21.22		21.35	21.31	21.27	21.10	21.22	21.02
SM 40:3	17.24	17.43	17.50	17.52	17.43	17.48		17.36	17.37	17.39	17.38	17.59	17.42
SM 40:5	13.59	13.20	13.37	13.44	13.02	13.40		13.33	13.17	13.42	13.19	13.48	13.23
SM 41:1	19.59	19.74	19.79	19.92	19.88	19.86		19.82	19.87	19.74	19.50	19.58	19.42
SM 41:2	18.14	18.18	18.23	18.15	17.94	18.10		18.17	18.37	18.24	18.10	18.23	18.02
SM 41:3	16.79	16.81	16.90	17.02	16.71	16.98		16.93	16.92	16.96	17.02	17.11	16.94
SM 41:4	15.18	15.31	15.13	15.54	15.17	15.12		14.91	15.00	14.81	14.71	14.75	14.63
SM 41:6	10.71	11.32	10.72	9.95	10.88	10.43		10.20	10.22	10.54	9.75	10.73	9.57
SM 42:1	20.56	20.67	20.60	20.62	20.51	20.49		20.72	20.73	20.64	20.36	20.41	20.21
SM 42:2	21.26	21.39	21.33	21.28	21.09	21.12		21.30	21.30	21.29	21.19	21.44	21.30
SM 42:3	21.37	21.52	21.38	21.36	21.31	21.21		21.35	21.28	21.39	21.35	21.55	21.41
SM 42:4	17.60	17.70	17.72	17.69	17.43	17.53		17.74	17.80	17.90	17.90	18.10	17.99
SM 42:5	14.93	15.13	15.28	15.11	15.00	15.00		15.06	15.22	15.08	15.13	15.47	15.35
SM 42:6	14.01	14.51	14.21	14.28	14.35	14.35		14.17	14.34	14.16	14.19	14.48	14.05
SM 43:1	15.35	15.78	15.83	15.90	15.79	15.83		15.91	16.05	15.76	15.44	15.71	15.43
SM 43:2	16.87	17.07	17.19	17.30	17.25	17.17		17.03	17.14	17.07	16.99	17.17	17.04
SM 43:3	15.07	15.22	15.34	15.40	15.35	15.25		15.14	15.20	15.05	15.17	15.39	15.19
SM 43:6	13.01	12.47	13.07	13.33	13.44	13.05		12.94	12.95	12.68	12.94	12.85	12.67
SM 43:8	14.20	14.24	14.28	13.37	14.04	13.78		14.22	13.76	14.06	13.99	14.51	14.30
SM 44:1	13.69	13.95	13.94	13.95	13.96	13.98		13.95	14.02	13.92	13.76	13.96	13.67
SM 44:2	14.79	14.87	14.81	14.96	14.66	14.76		14.89	14.96	14.82	14.81	14.92	14.94
SM 44:3	14.44	14.96	14.26	14.63	14.38	14.50		14.15	14.51	14.17	14.44	14.46	14.51
SM 44:5	13.51	13.83	12.94	13.46	13.35	12.92		13.70	13.35	13.64	13.70	14.24	13.17
SM 44:6	12.12	12.30	12.21	12.19	11.58	12.06		12.55	12.34	12.72	12.30	12.51	12.40
SM 45:7	11.98	11.56	11.55	11.70	11.36	11.66		11.27	11.20	11.77	10.98	11.18	11.72
TG 36:0	13.24	12.67	13.43	13.55	14.05	13.33		12.42	12.44	12.77	12.59	12.88	12.67
TG 38:0	13.57	13.08	14.12	14.14	14.82	13.75		12.64	12.69	12.99	13.09	13.26	12.95
TG 39:0	12.31	11.61	12.27	12.15	12.32	12.14		11.88	11.65	11.72	11.81	11.94	11.53
TG 40:0	13.76	13.49	14.80	14.78	15.53	14.33		13.00	12.90	13.80	13.60	13.66	13.38
TG 40:1	13.55	12.86	13.53	13.90	14.56	13.64		12.03	12.20	12.81	13.06	12.93	12.79
TG 41:0	11.88	11.34	12.32	12.53	12.93	12.02		11.05	11.02	11.41	11.69	11.60	11.39
TG 42:0	14.71	14.26	15.40	15.64	16.23	15.29		13.54	13.81	14.64	14.69	14.53	14.30
TG 42:1	14.87	14.33	15.22	15.09	15.91	14.92		13.65	13.59	14.75	14.58	14.35	14.19
TG 42:2	13.97	13.98	14.59	14.69	15.53	14.26		12.85	13.12	13.55	13.70	13.53	13.42
TG 42:3	12.75	12.36	12.64	12.34	13.33	12.28		11.34	11.84	11.79	12.32	11.96	11.73
TG 43:0	12.18	12.07	12.89	13.24	13.59	12.94		11.68	11.91	12.22	12.24	12.02	12.11
TG 43:1	12.62	12.18	12.86	12.92	13.38	12.97		11.87	11.77	12.58	12.53	12.50	12.28

Table S2.5J: MEAL Study Mean Log2 Area under the Curve for Lipids (Triacylglycerol 43:2 to Triacylglycerol 53:5)

	Mean Log2 AUC Values For Each Lipid Species											
	High Fat Diet							High Carb Diet				
Lipid/Day	B	S	2.00	7.00	14.00	21.00		B	S	2.00	7.00	14.00	21.00
TG 43:2	12.24	11.68	12.10	11.61	12.71	11.88		11.03	11.55	12.21	11.50	11.68	11.46
TG 44:0	15.05	14.65	15.66	15.93	16.64	15.63		14.34	14.35	15.18	15.18	15.15	14.95
TG 44:1	16.21	15.69	16.32	16.48	17.13	16.39		15.23	15.30	16.38	16.29	16.14	15.98
TG 44:2	15.77	15.55	16.06	16.15	16.77	15.86		14.69	15.10	15.55	15.57	15.50	15.29
TG 44:3	14.40	14.10	14.51	14.46	15.13	14.23		13.28	13.57	13.87	14.03	13.87	13.71
TG 45:0	12.59	12.20	13.08	13.45	14.02	13.59		12.35	12.30	12.85	13.05	12.87	12.80
TG 45:1	13.50	12.91	13.63	13.99	14.39	13.89		13.07	12.71	13.54	13.54	13.49	13.49
TG 45:2	13.33	13.05	13.46	13.49	14.09	13.45		12.59	12.85	13.34	13.20	13.26	13.11
TG 46:0	16.32	15.60	16.34	16.55	16.91	16.56		15.11	15.26	16.36	16.44	16.20	16.20
TG 46:1	17.49	16.95	17.37	17.58	18.22	17.32		16.72	16.69	17.83	17.64	17.58	17.43
TG 46:2	17.45	17.24	17.54	17.57	18.28	17.38		16.67	16.90	17.87	17.56	17.59	17.38
TG 46:3	16.26	16.07	16.21	16.27	16.87	16.01		15.41	15.72	16.32	16.08	16.21	16.01
TG 47:0	13.66	13.05	13.74	14.07	14.14	13.98		12.84	13.08	13.48	13.63	13.61	13.58
TG 47:1	14.47	14.09	14.58	14.85	15.14	14.78		14.16	14.13	14.99	14.80	14.85	14.82
TG 47:2	14.46	14.57	14.74	15.07	15.24	14.86		14.15	14.43	15.05	14.90	14.78	14.77
TG 47:3	13.91	13.79	13.97	14.08	14.47	13.80		13.24	13.63	13.98	13.77	13.89	13.78
TG 48:0	17.43	16.89	17.23	17.56	17.76	17.60		16.56	16.71	17.40	17.44	17.30	17.20
TG 48:1	19.17	18.69	18.79	19.05	19.32	18.92		18.43	18.58	19.49	19.30	19.26	19.23
TG 48:2	19.33	19.17	19.10	19.29	19.60	19.09		18.78	18.94	19.74	19.49	19.48	19.46
TG 48:3	18.58	18.55	18.26	18.39	18.85	18.10		18.03	18.26	18.99	18.61	18.68	18.61
TG 48:4	17.19	17.18	17.11	16.92	17.63	16.60		16.69	16.89	17.45	17.20	17.25	16.98
TG 48:5	15.48	15.49	15.55	15.50	15.71	15.05		15.23	15.25	15.72	15.53	15.53	15.42
TG 49:0	14.29	13.86	14.31	14.96	14.92	14.92		13.84	13.90	14.43	14.38	14.32	14.52
TG 49:1	16.02	15.97	16.32	16.60	16.66	16.55		15.80	15.98	16.55	16.42	16.46	16.39
TG 49:2	16.35	16.34	16.58	16.78	16.78	16.61		16.15	16.36	16.77	16.61	16.67	16.70
TG 49:3	15.67	15.67	15.65	15.99	16.04	15.67		15.47	15.71	16.19	15.84	15.86	15.96
TG 50:0	17.96	17.50	17.78	18.04	18.13	18.00		17.18	17.20	17.71	18.01	17.95	17.83
TG 50:1	20.42	20.21	20.29	20.42	20.52	20.45		19.94	19.97	20.60	20.57	20.56	20.49
TG 50:2	20.98	20.84	20.70	20.83	20.92	20.76		20.62	20.73	21.38	21.15	21.22	21.12
TG 50:3	20.59	20.58	20.23	20.36	20.47	20.18		20.28	20.48	20.96	20.63	20.75	20.73
TG 50:4	19.52	19.65	19.25	19.25	19.45	18.99		19.08	19.46	19.74	19.41	19.51	19.49
TG 50:5	17.59	17.59	17.23	17.17	17.47	16.85		17.11	17.39	17.81	17.46	17.55	17.49
TG 50:6	15.46	15.33	15.34	15.08	15.56	14.75		14.98	15.16	15.55	15.28	15.44	15.23
TG 51:0	19.36	19.56	19.55	19.47	19.14	19.29		19.48	19.63	19.57	19.40	19.53	19.52
TG 51:1	16.49	16.29	16.60	16.87	16.95	16.94		16.37	16.28	16.92	16.83	16.79	16.77
TG 51:2	17.60	17.66	17.70	17.82	17.93	17.91		17.60	17.62	18.12	17.91	18.04	17.97
TG 51:3	17.62	17.88	17.76	17.97	17.96	17.77		17.62	17.86	18.01	17.77	17.85	17.83
TG 51:4	17.06	17.33	17.18	17.48	17.41	16.89		16.65	17.29	17.07	16.84	16.80	17.11
TG 51:5	16.44	17.24	17.51	16.57	16.76	17.08		16.78	16.79	16.58	16.30	16.92	16.91
TG 52:0	16.91	16.54	16.63	17.03	17.15	17.26		16.43	16.17	16.59	16.82	16.69	16.70
TG 52:1	20.06	19.76	19.66	19.90	20.01	20.00		19.75	19.63	20.09	20.10	20.00	19.94
TG 52:2	22.12	22.13	21.88	21.98	21.96	21.95		22.19	22.12	22.47	22.33	22.40	22.28
TG 52:3	22.45	22.70	22.47	22.48	22.44	22.33		22.48	22.61	22.70	22.51	22.58	22.54
TG 52:4	21.83	22.11	22.06	21.93	21.90	21.72		21.78	22.01	21.96	21.77	21.84	21.85
TG 52:5	20.25	20.39	20.13	20.02	20.02	19.70		20.02	20.30	20.38	20.17	20.26	20.24
TG 52:6	18.16	18.12	17.71	17.57	17.75	17.21		17.80	18.02	18.32	18.09	18.17	18.16
TG 52:7	15.77	15.64	15.39	15.20	15.43	14.95		15.38	15.46	15.84	15.69	15.78	15.72
TG 53:0	14.15	14.29	14.11	14.45	14.55	14.12		14.25	14.13	14.13	14.15	14.12	14.19
TG 53:1	15.39	15.13	15.23	15.54	15.79	15.81		15.12	15.04	15.41	15.52	15.25	15.31
TG 53:2	17.16	17.19	17.12	17.26	17.30	17.33		17.30	17.02	17.50	17.35	17.41	17.40
TG 53:3	17.36	17.56	17.56	17.54	17.61	17.57		17.55	17.56	17.72	17.50	17.55	17.57
TG 53:4	17.02	17.36	17.39	17.30	17.26	17.14		17.09	17.21	17.21	17.08	16.96	17.14
TG 53:5	16.09	16.42	16.32	16.01	16.20	15.81		16.11	16.15	16.18	15.99	16.06	15.95

Table S2.5K: MEAL Study Mean Log2 Area under the Curve for Lipids (Triacylglycerol 54:0 to Triacylglycerol 62:12)

	Mean Log2 AUC Values For Each Lipid Species											
	High Fat Diet						High Carb Diet					
Lipid/Day	B	S	2.00	7.00	14.00	21.00	B	S	2.00	7.00	14.00	21.00
TG 54:0	14.68	14.55	14.52	14.92	15.32	14.84	13.66	13.96	14.20	14.39	14.26	14.02
TG 54:1	17.73	17.21	17.14	17.48	17.72	17.80	17.23	16.86	17.10	17.21	16.96	17.14
TG 54:2	19.77	19.46	19.13	19.26	19.48	19.47	19.57	19.18	19.41	19.45	19.37	19.37
TG 54:3	20.83	20.74	20.28	20.36	20.43	20.42	20.76	20.46	20.58	20.52	20.54	20.48
TG 54:4	21.00	21.10	20.62	20.62	20.73	20.52	20.92	20.82	20.82	20.73	20.72	20.73
TG 54:5	20.85	20.93	20.57	20.49	20.52	20.29	20.68	20.73	20.66	20.57	20.61	20.59
TG 54:6	20.15	20.27	20.05	19.82	19.89	19.62	19.92	20.08	19.95	19.90	19.93	19.91
TG 54:7	18.79	18.76	18.54	18.16	18.36	17.88	18.39	18.58	18.50	18.47	18.54	18.54
TG 54:8	16.45	16.44	16.11	15.85	16.12	15.46	16.14	16.22	16.42	16.29	16.34	16.33
TG 55:0	10.31	10.71	10.91	10.39	11.18	10.81	10.25	8.85	9.76	10.78	10.51	10.35
TG 55:2	14.21	14.03	14.20	13.69	14.18	14.33	14.07	13.79	13.92	14.03	13.73	13.93
TG 55:3	14.75	15.01	14.83	14.67	14.86	14.89	14.58	14.65	14.76	14.50	14.60	14.41
TG 55:4	14.67	15.08	14.99	14.88	14.73	14.82	14.53	14.65	14.62	14.61	14.73	14.60
TG 55:5	14.55	14.62	15.02	15.18	14.79	14.88	14.72	14.63	14.89	14.76	14.84	14.79
TG 56:0	11.85	10.98	11.27	11.79	12.08	11.93	11.08	10.97	10.63	11.07	10.92	10.91
TG 56:1	14.44	14.23	13.99	14.10	14.73	14.94	13.95	13.71	13.82	13.79	13.52	13.73
TG 56:10	14.10	13.97	14.09	13.55	13.74	13.16	13.87	13.77	14.00	14.00	13.94	13.90
TG 56:2	16.14	15.82	15.54	15.68	15.80	16.06	15.62	15.24	15.39	15.55	15.39	15.45
TG 56:3	16.72	16.75	16.11	16.18	16.32	16.29	16.39	16.20	16.33	16.42	16.34	16.34
TG 56:4	17.28	17.41	17.00	16.92	16.95	16.86	17.14	17.09	17.20	17.20	17.17	17.19
TG 56:5	18.18	18.46	18.18	18.05	18.07	18.01	18.34	18.27	18.33	18.33	18.36	18.32
TG 56:6	18.84	19.01	18.83	18.72	18.65	18.59	18.93	18.90	18.91	18.93	18.95	18.89
TG 56:7	18.93	19.05	19.04	18.87	18.82	18.68	18.93	18.92	18.92	18.95	19.02	18.96
TG 56:8	18.27	18.38	18.50	18.19	18.22	18.10	18.15	18.22	18.14	18.20	18.22	18.19
TG 56:9	16.59	16.54	16.54	16.19	16.28	15.94	16.37	16.41	16.40	16.41	16.51	16.42
TG 57:2	15.00	15.04	14.72	14.80	14.82	14.75	14.99	14.98	15.31	15.14	14.98	15.06
TG 57:4	14.65	15.10	14.72	14.85	14.63	14.35	14.64	15.07	14.68	14.57	14.97	14.77
TG 58:1	12.78	12.69	12.19	12.30	12.54	12.79	12.31	11.51	11.82	12.29	11.45	12.07
TG 58:10	16.09	16.13	16.26	15.95	16.04	15.83	15.92	15.98	15.82	15.96	15.99	15.90
TG 58:11	14.44	14.38	14.61	14.11	14.39	13.96	14.25	14.11	14.11	14.22	14.40	14.22
TG 58:2	14.12	13.87	13.54	12.97	13.79	13.54	13.56	12.62	13.29	13.51	13.57	13.17
TG 58:3	14.26	14.31	13.40	13.64	13.80	13.62	13.53	13.13	12.91	13.61	13.52	13.54
TG 58:4	14.07	14.40	13.88	13.76	13.71	13.73	13.71	13.34	13.62	13.93	13.98	13.83
TG 58:5	14.96	14.96	14.72	14.44	14.58	14.49	14.66	14.71	14.78	14.79	14.99	14.74
TG 58:6	15.72	15.79	15.69	15.53	15.49	15.48	15.73	15.76	15.72	15.74	15.87	15.81
TG 58:7	16.43	16.39	16.29	16.12	16.21	16.13	16.44	16.29	16.38	16.43	16.45	16.35
TG 58:8	16.64	16.75	16.74	16.49	16.49	16.40	16.70	16.59	16.60	16.75	16.76	16.72
TG 58:9	16.56	16.70	16.73	16.44	16.50	16.35	16.60	16.50	16.39	16.52	16.62	16.43
TG 60:10	14.06	14.12	14.39	13.98	13.92	14.03	14.14	13.95	14.17	14.31	14.32	14.16
TG 60:11	14.01	14.10	14.40	14.11	14.23	14.05	14.03	13.91	13.84	14.15	14.23	14.00
TG 60:12	13.57	13.44	13.89	13.39	13.71	13.57	13.34	13.30	13.19	13.42	13.60	13.52
TG 62:12	11.19	11.44	11.67	11.36	11.13	11.53	11.43	10.94	11.50	11.39	11.49	11.39

Table S2.6A: Significant difference within diet comparisons for all lipids (16:0 Cholesterol ester to Ceramide [NS] 36:1)

	Within Diet Comparisons (FDR <0.1)															
	High Fat Diet								High Carbohydrate Diet							
Lipid/Day	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21
16:0 CE	1.00	0.99	1.00	0.99	1.00	0.90	0.99	0.75	1.00	0.75	1.00	1.00	1.00	0.78	0.94	0.53
16:1 CE	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.80	1.00	0.80	1.00	1.00	1.00	0.57	0.35	0.34
18:0 CE	1.00	0.99	1.00	0.99	1.00	0.80	0.85	0.55	1.00	0.55	1.00	1.00	1.00	0.96	0.95	0.65
18:1 CE	1.00	0.99	1.00	0.99	1.00	0.94	0.73	0.81	1.00	0.81	1.00	1.00	1.00	0.75	0.81	0.61
18:2 CE	1.00	0.99	1.00	0.99	1.00	0.99	0.96	0.90	1.00	0.90	1.00	1.00	1.00	0.57	0.55	0.30
18:3 CE	1.00	0.99	1.00	0.99	1.00	0.95	0.87	0.67	1.00	0.67	1.00	1.00	1.00	0.99	0.98	0.78
20:3 CE	1.00	0.99	1.00	0.99	1.00	0.80	0.67	0.49	1.00	0.49	1.00	1.00	1.00	0.98	0.96	0.89
20:4 CE	1.00	0.99	1.00	0.99	1.00	0.91	0.93	0.98	1.00	0.98	1.00	1.00	1.00	0.74	0.82	0.61
20:5 CE	1.00	0.99	1.00	0.99	1.00	0.97	0.87	1.00	1.00	1.00	1.00	1.00	1.00	0.98	0.95	0.86
22:4 CE	1.00	0.99	1.00	0.99	1.00	0.93	0.74	0.92	1.00	0.92	1.00	1.00	1.00	0.99	0.89	0.77
22:5 CE	1.00	0.99	1.00	0.99	1.00	0.90	0.83	0.70	1.00	0.70	1.00	1.00	1.00	0.94	0.96	0.89
22:6 CE	1.00	0.99	1.00	0.99	1.00	0.94	0.90	0.99	1.00	0.99	1.00	1.00	1.00	0.89	0.95	0.95
ACAR 10:0	1.00	0.99	1.00	0.99	1.00	0.94	0.79	0.86	1.00	0.86	1.00	1.00	1.00	0.62	0.64	0.64
ACAR 10:1	1.00	0.99	1.00	0.99	1.00	0.95	0.73	0.98	1.00	0.98	1.00	1.00	1.00	0.64	0.96	0.85
ACAR 12:0	1.00	0.99	1.00	0.99	1.00	0.91	0.96	0.65	1.00	0.65	1.00	1.00	1.00	0.81	0.93	0.86
ACAR 14:0	1.00	0.99	1.00	0.99	1.00	0.90	0.99	0.91	1.00	0.91	1.00	1.00	1.00	0.57	0.83	0.61
ACAR 14:1	1.00	0.99	1.00	0.99	1.00	0.91	0.74	0.98	1.00	0.98	1.00	1.00	1.00	0.64	0.83	0.73
ACAR 14:2	1.00	0.99	1.00	0.99	1.00	0.89	0.68	0.88	1.00	0.88	1.00	1.00	1.00	0.56	0.55	0.33
ACAR 16:0	1.00	0.99	1.00	0.99	1.00	0.81	0.98	0.89	1.00	0.89	1.00	1.00	1.00	0.62	0.99	0.80
ACAR 18:0	1.00	0.99	1.00	0.99	1.00	0.85	0.79	0.73	1.00	0.73	1.00	1.00	1.00	0.69	0.81	0.55
ACAR 18:1	1.00	0.99	1.00	0.99	1.00	0.94	0.75	0.91	1.00	0.91	1.00	1.00	1.00	0.80	0.94	0.95
ACAR 18:2	1.00	0.99	1.00	0.99	1.00	0.91	0.67	0.49	1.00	0.49	1.00	1.00	1.00	0.64	0.83	0.61
ACAR 20:0	1.00	0.99	1.00	0.99	1.00	0.91	0.76	1.00	1.00	1.00	1.00	1.00	1.00	0.65	0.82	0.55
ACAR 24:0	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.98	1.00	0.98	1.00	1.00	1.00	0.34	0.43	0.17
ACAR 26:0	1.00	0.99	1.00	0.99	1.00	0.90	0.99	0.90	1.00	0.90	1.00	1.00	1.00	0.34	0.56	0.17
Cer[AS] 34:1	1.00	0.99	1.00	0.99	1.00	0.94	0.96	0.78	1.00	0.78	1.00	1.00	1.00	0.89	0.99	0.95
Cer[AS] 42:2	1.00	0.99	1.00	0.99	1.00	0.91	0.87	0.67	1.00	0.67	1.00	1.00	1.00	0.78	0.90	0.55
Cer[EODS] 57:2	1.00	0.99	1.00	0.99	1.00	0.96	0.84	0.90	1.00	0.90	1.00	1.00	1.00	0.89	0.96	0.92
Cer[EODS] 58:0	1.00	0.99	1.00	0.99	1.00	0.94	0.85	0.90	1.00	0.90	1.00	1.00	1.00	0.87	0.83	0.94
Cer[EODS] 60:0	1.00	0.99	1.00	0.99	1.00	0.90	0.74	0.99	1.00	0.99	1.00	1.00	1.00	0.85	0.81	0.61
Cer[NDS] 34:0	1.00	0.99	1.00	0.99	1.00	0.81	0.74	0.61	1.00	0.61	1.00	1.00	1.00	0.64	0.90	0.74
Cer[NDS] 36:0	1.00	0.99	1.00	0.99	1.00	0.89	0.77	0.70	1.00	0.70	1.00	1.00	1.00	0.96	0.87	0.61
Cer[NDS] 38:0	1.00	0.99	1.00	0.99	1.00	0.98	0.75	0.88	1.00	0.88	1.00	1.00	1.00	0.58	0.96	0.55
Cer[NDS] 39:0	1.00	0.99	1.00	0.99	1.00	0.94	0.98	0.98	1.00	0.98	1.00	1.00	1.00	0.89	0.96	0.86
Cer[NDS] 40:0	1.00	0.99	1.00	0.99	1.00	0.94	0.74	0.90	1.00	0.90	1.00	1.00	1.00	0.62	0.64	0.55
Cer[NDS] 41:0	1.00	0.99	1.00	0.99	1.00	0.90	0.90	0.97	1.00	0.97	1.00	1.00	1.00	0.57	0.71	0.61
Cer[NDS] 42:0	1.00	0.99	1.00	0.99	1.00	0.94	0.83	0.99	1.00	0.99	1.00	1.00	1.00	0.66	0.82	0.64
Cer[NDS] 42:1	1.00	0.99	1.00	0.99	1.00	0.94	0.76	0.89	1.00	0.89	1.00	1.00	1.00	0.71	0.81	0.55
Cer[NDS] 42:2	1.00	0.99	1.00	0.99	1.00	0.90	0.83	0.70	1.00	0.70	1.00	1.00	1.00	0.95	0.83	0.98
Cer[NDS] 43:0	1.00	0.99	1.00	0.99	1.00	0.82	0.98	0.43	1.00	0.43	1.00	1.00	1.00	0.64	0.71	0.54
Cer[NP] 34:0	1.00	0.99	1.00	0.99	1.00	0.90	0.90	0.84	1.00	0.84	1.00	1.00	1.00	0.76	0.71	0.55
Cer[NP] 40:0	1.00	0.99	1.00	0.99	1.00	0.94	0.76	0.94	1.00	0.94	1.00	1.00	1.00	0.29	0.35	0.07
Cer[NP] 41:0	1.00	0.99	1.00	0.99	1.00	0.94	0.96	0.90	1.00	0.90	1.00	1.00	1.00	0.57	0.57	0.17
Cer[NP] 41:1	1.00	0.99	1.00	0.99	1.00	0.90	0.81	0.76	1.00	0.76	1.00	1.00	1.00	0.48	0.89	0.56
Cer[NP] 42:0	1.00	0.99	1.00	0.99	1.00	0.94	0.74	0.90	1.00	0.90	1.00	1.00	1.00	0.57	0.42	0.28
Cer[NP] 42:1	1.00	0.99	1.00	0.99	1.00	0.86	0.82	0.70	1.00	0.70	1.00	1.00	1.00	0.76	0.83	0.61
Cer[NS] 32:1	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.98	1.00	0.98	1.00	1.00	1.00	0.85	0.95	0.55
Cer[NS] 33:1	1.00	0.99	1.00	0.99	1.00	0.91	0.98	0.90	1.00	0.90	1.00	1.00	1.00	0.62	0.93	0.65
Cer[NS] 33:4	1.00	0.99	1.00	0.99	1.00	0.94	0.74	0.59	1.00	0.59	1.00	1.00	1.00	0.69	0.55	0.99
Cer[NS] 34:1	1.00	0.99	1.00	0.99	1.00	0.91	0.68	0.90	1.00	0.90	1.00	1.00	1.00	0.95	0.81	0.95
Cer[NS] 34:2	1.00	0.99	1.00	0.99	1.00	0.92	0.78	0.70	1.00	0.70	1.00	1.00	1.00	0.48	0.89	0.55
Cer[NS] 35:1	1.00	0.99	1.00	0.99	1.00	0.98	0.73	0.92	1.00	0.92	1.00	1.00	1.00	0.97	0.96	0.92
Cer[NS] 36:1	1.00	0.99	1.00	0.99	1.00	0.93	0.77	0.70	1.00	0.70	1.00	1.00	1.00	0.87	0.96	0.95

Table S2.6B: MEAL Study significant difference within diet comparisons for all lipids (Ceramide [NS] 36:2 to Free Fatty Acid 20:0)

	Within Diet Comparisons (FDR <0.1)															
	High Fat Diet								High Carbohydrate Diet							
Lipid/Day	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21
Cer[NS] 36:2	1.00	0.99	1.00	0.99	1.00	0.99	0.68	0.96	1.00	0.96	1.00	1.00	1.00	0.95	0.81	0.86
Cer[NS] 37:1	1.00	0.99	1.00	0.99	1.00	0.98	0.90	0.99	1.00	0.99	1.00	1.00	1.00	0.85	0.95	0.90
Cer[NS] 38:1	1.00	0.99	1.00	0.99	1.00	0.91	0.79	0.92	1.00	0.92	1.00	1.00	1.00	0.56	0.81	0.53
Cer[NS] 38:2	1.00	0.99	1.00	0.99	1.00	0.90	0.68	0.78	1.00	0.78	1.00	1.00	1.00	0.65	0.77	0.74
Cer[NS] 39:1	1.00	0.99	1.00	0.99	1.00	0.97	0.99	0.70	1.00	0.70	1.00	1.00	1.00	0.54	0.64	0.25
Cer[NS] 40:1	1.00	0.99	1.00	0.99	1.00	0.91	0.83	0.99	1.00	0.99	1.00	1.00	1.00	0.57	0.56	0.34
Cer[NS] 40:2	1.00	0.99	1.00	0.99	1.00	0.90	0.74	0.88	1.00	0.88	1.00	1.00	1.00	0.65	0.89	0.63
Cer[NS] 40:3	1.00	0.99	1.00	0.99	1.00	0.82	0.85	0.70	1.00	0.70	1.00	1.00	1.00	0.85	0.99	0.55
Cer[NS] 41:1	1.00	0.99	1.00	0.99	1.00	0.96	0.98	0.90	1.00	0.90	1.00	1.00	1.00	0.65	0.66	0.43
Cer[NS] 41:2	1.00	0.99	1.00	0.99	1.00	0.96	0.76	0.98	1.00	0.98	1.00	1.00	1.00	0.86	0.98	0.77
Cer[NS] 41:4	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.67	1.00	0.67	1.00	1.00	1.00	0.57	0.96	0.73
Cer[NS] 42:1	1.00	0.99	1.00	0.99	1.00	0.90	0.76	0.85	1.00	0.85	1.00	1.00	1.00	0.56	0.55	0.30
Cer[NS] 42:2	1.00	0.99	1.00	0.99	1.00	0.90	0.74	0.75	1.00	0.75	1.00	1.00	1.00	0.85	0.96	0.86
Cer[NS] 42:3	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.78	1.00	0.78	1.00	1.00	1.00	0.95	0.87	0.97
Cer[NS] 43:1	1.00	0.99	1.00	0.99	1.00	0.95	1.00	0.75	1.00	0.75	1.00	1.00	1.00	0.45	0.55	0.33
Cer[NS] 43:2	1.00	0.99	1.00	0.99	1.00	0.94	0.81	0.90	1.00	0.90	1.00	1.00	1.00	0.76	0.95	0.88
Cer[NS] 44:1	1.00	0.99	1.00	0.99	1.00	0.90	0.99	0.67	1.00	0.67	1.00	1.00	1.00	0.73	0.83	0.77
Cer[NS] 44:2	1.00	0.99	1.00	0.99	1.00	0.94	0.76	0.96	1.00	0.96	1.00	1.00	1.00	0.90	0.81	0.61
Cer[NS] 44:4	1.00	0.99	1.00	0.99	1.00	0.97	0.80	0.91	1.00	0.91	1.00	1.00	1.00	0.72	0.64	0.34
Cer[NS] 45:1	1.00	0.99	1.00	0.99	1.00	0.91	0.83	0.86	1.00	0.86	1.00	1.00	1.00	0.57	0.64	0.61
Cer[NS] 46:5	1.00	0.99	1.00	0.99	1.00	0.97	0.76	0.95	1.00	0.95	1.00	1.00	1.00	0.94	0.90	0.86
DG 30:0	1.00	0.99	1.00	0.99	1.00	0.81	1.00	0.70	1.00	0.70	1.00	1.00	1.00	0.62	0.55	0.77
DG 30:1	1.00	0.99	1.00	0.99	1.00	0.99	0.82	0.70	1.00	0.70	1.00	1.00	1.00	0.97	0.96	0.89
DG 32:0	1.00	0.99	1.00	0.99	1.00	0.99	0.83	0.94	1.00	0.94	1.00	1.00	1.00	0.65	0.86	0.55
DG 32:1	1.00	0.99	1.00	0.99	1.00	0.95	0.98	0.85	1.00	0.85	1.00	1.00	1.00	0.71	0.56	0.55
DG 32:2	1.00	0.99	1.00	0.99	1.00	0.96	0.76	0.99	1.00	0.99	1.00	1.00	1.00	0.73	0.96	0.95
DG 33:0	1.00	0.99	1.00	0.99	1.00	0.91	0.96	0.53	1.00	0.53	1.00	1.00	1.00	0.87	0.81	0.89
DG 33:1	1.00	0.99	1.00	0.99	1.00	0.94	0.83	0.98	1.00	0.98	1.00	1.00	1.00	0.81	0.88	0.54
DG 34:0	1.00	0.99	1.00	0.99	1.00	0.94	0.83	0.91	1.00	0.91	1.00	1.00	1.00	0.58	0.64	0.61
DG 34:2	1.00	0.99	1.00	0.99	1.00	0.99	0.96	0.84	1.00	0.84	1.00	1.00	1.00	0.65	0.55	0.55
DG 34:3	1.00	0.99	1.00	0.99	1.00	0.91	0.82	0.65	1.00	0.65	1.00	1.00	1.00	0.65	0.81	0.64
DG 35:1	1.00	0.99	1.00	0.99	1.00	0.90	0.85	0.70	1.00	0.70	1.00	1.00	1.00	0.73	0.56	0.53
DG 35:2	1.00	0.99	1.00	0.99	1.00	0.90	0.99	0.98	1.00	0.98	1.00	1.00	1.00	0.97	0.71	0.82
DG 35:3	1.00	0.99	1.00	0.99	1.00	0.91	0.98	0.91	1.00	0.91	1.00	1.00	1.00	0.73	0.55	0.55
DG 36:0	1.00	0.99	1.00	0.99	1.00	0.94	0.87	0.89	1.00	0.89	1.00	1.00	1.00	0.89	0.85	0.91
DG 36:1	1.00	0.99	1.00	0.99	1.00	0.97	0.80	0.90	1.00	0.90	1.00	1.00	1.00	0.57	0.64	0.61
DG 36:2	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.70	1.00	0.70	1.00	1.00	1.00	0.57	0.64	0.48
DG 36:3	1.00	0.99	1.00	0.99	1.00	0.92	0.76	0.67	1.00	0.67	1.00	1.00	1.00	0.86	0.90	0.68
DG 36:4	1.00	0.99	1.00	0.99	1.00	0.91	0.78	0.61	1.00	0.61	1.00	1.00	1.00	0.73	0.90	0.80
DG 36:5	1.00	0.99	1.00	0.99	1.00	0.91	0.90	0.49	1.00	0.49	1.00	1.00	1.00	0.83	0.96	0.61
DG 38:1	1.00	0.99	1.00	0.99	1.00	0.90	0.68	0.70	1.00	0.70	1.00	1.00	1.00	0.89	0.95	0.88
DG 38:2	1.00	0.99	1.00	0.99	1.00	0.94	0.99	0.91	1.00	0.91	1.00	1.00	1.00	0.72	0.83	0.71
DG 38:3	1.00	0.99	1.00	0.99	1.00	0.91	0.87	0.92	1.00	0.92	1.00	1.00	1.00	0.88	0.81	0.95
DG 38:4	1.00	0.99	1.00	0.99	1.00	0.94	0.76	0.91	1.00	0.91	1.00	1.00	1.00	0.71	0.71	0.86
DG 38:5	1.00	0.99	1.00	1.00	1.00	0.94	0.90	0.59	1.00	0.59	1.00	1.00	1.00	0.64	0.81	0.65
DG 38:6	1.00	0.99	1.00	0.99	1.00	0.94	0.99	0.75	1.00	0.75	1.00	1.00	1.00	0.89	0.83	0.77
DG 38:7	1.00	0.99	1.00	1.00	1.00	0.98	0.99	0.67	1.00	0.67	1.00	1.00	1.00	0.85	0.77	0.85
DG 40:6	1.00	0.99	1.00	0.99	1.00	0.91	0.93	0.72	1.00	0.72	1.00	1.00	1.00	0.95	0.81	0.82
DG 40:7	1.00	0.99	1.00	0.99	1.00	0.98	0.88	0.67	1.00	0.67	1.00	1.00	1.00	0.62	0.89	0.80
FFA 16:0	1.00	0.99	1.00	0.99	1.00	0.94	0.77	0.70	1.00	0.70	1.00	1.00	1.00	0.88	0.98	0.86
FFA 18:0	1.00	0.99	1.00	0.99	1.00	0.91	0.74	0.70	1.00	0.70	1.00	1.00	1.00	0.89	0.96	0.99
FFA 18:1	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.70	1.00	0.70	1.00	1.00	1.00	0.71	0.96	0.70
FFA 18:2	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.70	1.00	0.70	1.00	1.00	1.00	0.62	0.96	0.55
FFA 20:0	1.00	0.99	1.00	0.99	1.00	0.99	0.73	0.77	1.00	0.77	1.00	1.00	1.00	0.88	0.99	0.97

Table S2.6C: MEAL Study significant difference within diet comparisons for all lipids (Free Fatty Acid 20:1 to Lysophosphatidylethanolamine 20:5)

	Within Diet Comparisons (FDR <0.1)															
	High Fat Diet								High Carbohydrate Diet							
Lipid/Day	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21
FFA 20:1	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.70	1.00	0.70	1.00	1.00	1.00	0.75	0.99	0.68
FFA 20:2	1.00	0.99	1.00	0.99	1.00	0.89	0.73	0.65	1.00	0.65	1.00	1.00	1.00	0.81	0.96	0.74
FFA 20:4	1.00	0.99	1.00	0.99	1.00	0.86	0.68	0.70	1.00	0.70	1.00	1.00	1.00	0.89	0.96	0.75
FFA 22:0	1.00	0.99	1.00	0.99	1.00	0.99	0.73	0.81	1.00	0.81	1.00	1.00	1.00	0.75	0.98	0.95
FFA 22:1	1.00	0.99	1.00	0.99	1.00	0.98	0.76	0.88	1.00	0.88	1.00	1.00	1.00	0.99	0.83	0.88
FFA 22:2	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.49	1.00	0.49	1.00	1.00	1.00	0.72	0.83	0.53
FFA 22:3	1.00	0.99	1.00	0.99	1.00	0.90	0.74	0.59	1.00	0.59	1.00	1.00	1.00	0.73	0.98	0.74
FFA 24:0	1.00	1.00	1.00	0.99	1.00	0.91	0.80	0.91	1.00	0.91	1.00	1.00	1.00	0.89	0.77	0.77
FFA 24:1	1.00	0.99	1.00	0.99	1.00	0.91	0.75	0.50	1.00	0.50	1.00	1.00	1.00	0.69	0.96	0.74
FFA 24:2	1.00	0.99	1.00	0.99	1.00	0.91	0.74	0.81	1.00	0.81	1.00	1.00	1.00	0.62	0.81	0.68
FFA 24:3	1.00	0.99	1.00	0.99	1.00	0.94	0.76	0.88	1.00	0.88	1.00	1.00	1.00	0.76	0.93	0.77
GlcCer[NS] 34:1	1.00	0.99	1.00	0.99	1.00	0.90	0.78	0.70	1.00	0.70	1.00	1.00	1.00	0.48	0.87	0.35
GlcCer[NS] 34:2	1.00	0.99	1.00	0.99	1.00	0.99	0.97	0.90	1.00	0.90	1.00	1.00	1.00	0.57	0.56	0.61
GlcCer[NS] 40:1	1.00	0.99	1.00	1.00	1.00	0.91	0.87	0.99	1.00	0.99	1.00	1.00	1.00	0.36	0.43	0.08
GlcCer[NS] 41:1	1.00	0.99	1.00	0.99	1.00	0.99	0.92	0.86	1.00	0.86	1.00	1.00	1.00	0.85	0.84	0.77
GlcCer[NS] 42:1	1.00	0.99	1.00	0.99	1.00	0.92	0.87	0.90	1.00	0.90	1.00	1.00	1.00	0.57	0.77	0.33
GlcCer[NS] 42:2	1.00	0.99	1.00	0.99	1.00	0.91	0.74	0.81	1.00	0.81	1.00	1.00	1.00	0.75	0.96	0.86
LysoPC 14:0	1.00	0.99	1.00	0.99	1.00	0.99	0.88	0.70	1.00	0.70	1.00	1.00	1.00	0.89	1.00	0.82
LysoPC 15:0	1.00	0.99	1.00	1.00	1.00	0.99	0.98	0.73	1.00	0.73	1.00	1.00	1.00	0.71	0.83	0.61
LysoPC 15:1	1.00	0.99	1.00	0.99	1.00	0.91	0.98	0.91	1.00	0.91	1.00	1.00	1.00	0.89	0.90	1.00
LysoPC 16:0	1.00	0.99	1.00	0.99	1.00	0.80	0.68	0.41	1.00	0.41	1.00	1.00	1.00	0.83	0.99	0.77
LysoPC 16:1	1.00	0.86	1.00	0.99	1.00	0.80	0.64	0.13	1.00	0.13	1.00	1.00	1.00	0.81	0.77	0.74
LysoPC 17:1	1.00	0.99	1.00	0.99	1.00	0.97	1.00	0.90	1.00	0.90	1.00	1.00	1.00	0.88	0.90	0.95
LysoPC 18:0	1.00	0.99	1.00	0.99	1.00	0.83	0.79	0.53	1.00	0.53	1.00	1.00	1.00	0.74	0.93	0.77
LysoPC 18:1	1.00	0.99	1.00	0.99	1.00	0.81	0.73	0.49	1.00	0.49	1.00	1.00	1.00	0.99	0.96	0.96
LysoPC 18:2	1.00	0.99	1.00	0.99	1.00	0.94	0.87	0.81	1.00	0.81	1.00	1.00	1.00	0.76	0.83	0.77
LysoPC 18:3	1.00	0.99	1.00	0.99	1.00	0.91	0.90	0.49	1.00	0.49	1.00	1.00	1.00	0.95	0.96	0.94
LysoPC 19:0	1.00	0.99	1.00	0.99	1.00	0.94	0.87	0.88	1.00	0.88	1.00	1.00	1.00	0.83	0.89	0.83
LysoPC 19:1	1.00	0.99	1.00	0.99	1.00	0.99	0.81	0.91	1.00	0.91	1.00	1.00	1.00	0.99	0.98	0.92
LysoPC 20:0	1.00	0.99	1.00	0.99	1.00	0.82	0.81	0.76	1.00	0.76	1.00	1.00	1.00	0.69	0.83	0.55
LysoPC 20:1	1.00	0.99	1.00	0.99	1.00	0.70	0.67	0.49	1.00	0.49	1.00	1.00	1.00	0.84	0.96	0.90
LysoPC 20:2	1.00	0.99	1.00	0.99	1.00	0.43	0.53	0.19	1.00	0.19	1.00	1.00	1.00	0.89	0.96	0.86
LysoPC 20:3	1.00	0.99	1.00	0.99	1.00	0.59	0.45	0.16	1.00	0.16	1.00	1.00	1.00	0.94	0.96	0.95
LysoPC 20:4	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.50	1.00	0.50	1.00	1.00	1.00	0.97	0.96	0.95
LysoPC 20:5	1.00	0.99	1.00	0.99	1.00	0.98	0.93	0.98	1.00	0.98	1.00	1.00	1.00	0.88	0.96	0.92
LysoPC 22:0	1.00	0.99	1.00	0.99	1.00	0.82	0.73	0.50	1.00	0.50	1.00	1.00	1.00	0.48	0.55	0.33
LysoPC 22:4	1.00	0.99	1.00	0.99	1.00	0.80	0.73	0.78	1.00	0.78	1.00	1.00	1.00	0.85	0.89	0.92
LysoPC 22:5	1.00	0.99	1.00	0.99	1.00	0.83	0.67	0.53	1.00	0.53	1.00	1.00	1.00	0.88	0.90	0.86
LysoPC 22:6	1.00	0.99	1.00	0.99	1.00	0.81	0.73	0.67	1.00	0.67	1.00	1.00	1.00	0.98	0.77	0.70
LysoPC 23:0	1.00	0.99	1.00	0.99	1.00	0.99	0.85	0.83	1.00	0.83	1.00	1.00	1.00	0.76	0.93	0.55
LysoPC 24:0	1.00	0.99	1.00	0.99	1.00	0.81	0.67	0.49	1.00	0.49	1.00	1.00	1.00	0.66	0.83	0.57
LysoPC 24:1	1.00	0.99	1.00	0.99	1.00	0.80	0.73	0.39	1.00	0.39	1.00	1.00	1.00	0.89	0.81	0.80
LysoPC 26:1	1.00	0.99	1.00	0.99	1.00	0.53	0.73	0.42	1.00	0.42	1.00	1.00	1.00	0.87	0.73	0.96
LysoPE 16:0	1.00	0.99	1.00	0.99	1.00	0.80	0.73	0.49	1.00	0.49	1.00	1.00	1.00	0.95	0.83	0.99
LysoPE 16:1	1.00	0.99	1.00	0.99	1.00	0.99	0.98	0.56	1.00	0.56	1.00	1.00	1.00	0.65	0.71	0.82
LysoPE 17:0	1.00	0.99	1.00	0.99	1.00	0.99	0.96	1.00	1.00	1.00	1.00	1.00	1.00	0.89	0.81	0.83
LysoPE 18:0	1.00	0.99	1.00	0.99	1.00	0.81	0.76	0.81	1.00	0.81	1.00	1.00	1.00	0.65	0.94	0.55
LysoPE 18:1	1.00	0.99	1.00	0.99	1.00	0.81	0.74	0.70	1.00	0.70	1.00	1.00	1.00	0.86	0.99	0.86
LysoPE 18:2	1.00	0.99	1.00	0.99	1.00	0.91	0.98	0.89	1.00	0.89	1.00	1.00	1.00	0.66	0.90	0.61
LysoPE 18:3	1.00	0.99	1.00	0.99	1.00	0.94	0.73	0.99	1.00	0.99	1.00	1.00	1.00	0.71	0.81	0.85
LysoPE 20:2	1.00	0.99	1.00	0.99	1.00	0.80	0.74	0.67	1.00	0.67	1.00	1.00	1.00	0.85	0.99	0.80
LysoPE 20:3	1.00	0.99	1.00	0.99	1.00	0.67	0.67	0.39	1.00	0.39	1.00	1.00	1.00	0.99	0.96	0.91
LysoPE 20:4	1.00	0.99	1.00	0.99	1.00	0.90	0.74	0.75	1.00	0.75	1.00	1.00	1.00	0.85	0.99	0.74
LysoPE 20:5	1.00	0.99	1.00	0.99	1.00	0.94	0.74	0.65	1.00	0.65	1.00	1.00	1.00	0.85	0.83	0.85

Table S2.6D: MEAL Study significant difference within diet comparisons for all lipids (Lysophosphatidylethanolamine 22:4 to Phosphatidylcholine 37:7)

	Within Diet Comparisons (FDR <0.1)															
	High Fat Diet								High Carbohydrate Diet							
Lipid/Day	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21
LysoPE 22:4	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.49	1.00	0.49	1.00	1.00	1.00	0.82	0.90	0.89
LysoPE 22:5	1.00	0.99	1.00	0.99	1.00	0.80	0.71	0.41	1.00	0.41	1.00	1.00	1.00	0.95	0.90	0.99
LysoPE 22:6	1.00	0.99	1.00	0.99	1.00	0.81	0.74	0.67	1.00	0.67	1.00	1.00	1.00	0.89	0.89	0.93
LysoPE 24:0	1.00	0.99	1.00	0.99	1.00	0.99	0.85	0.78	1.00	0.78	1.00	1.00	1.00	0.57	0.92	0.54
PA 34:1	1.00	0.99	1.00	0.99	1.00	0.81	0.67	0.69	1.00	0.69	1.00	1.00	1.00	0.72	0.77	0.33
PA 34:2	1.00	0.99	1.00	0.99	1.00	0.91	0.81	0.70	1.00	0.70	1.00	1.00	1.00	0.86	0.83	0.86
PA 36:1	1.00	0.99	1.00	0.99	1.00	0.91	0.93	0.90	1.00	0.90	1.00	1.00	1.00	0.73	0.71	0.66
PA 36:2	1.00	0.99	1.00	0.81	1.00	0.43	0.91	0.50	1.00	0.50	1.00	1.00	1.00	0.65	0.77	0.91
PA 36:3	1.00	0.99	1.00	0.99	1.00	0.93	0.95	0.98	1.00	0.98	1.00	1.00	1.00	0.72	0.77	0.82
PA 36:4	1.00	0.99	1.00	0.99	1.00	0.91	0.68	0.91	1.00	0.91	1.00	1.00	1.00	0.83	0.89	0.89
PA 38:6	1.00	0.99	1.00	0.99	1.00	0.94	0.67	1.00	1.00	1.00	1.00	1.00	1.00	0.89	0.97	0.77
PC 24:0	1.00	0.36	1.00	0.99	0.59	0.87	0.45	0.70	1.00	0.70	1.00	1.00	1.00	1.00	0.71	0.77
PC 26:0	1.00	0.10	1.00	0.99	1.00	0.43	0.42	0.54	1.00	0.54	1.00	1.00	1.00	0.97	0.96	0.71
PC 27:0	1.00	0.99	1.00	0.99	1.00	0.93	0.83	0.75	1.00	0.75	1.00	1.00	1.00	0.86	0.96	0.82
PC 28:2	1.00	0.99	1.00	0.99	1.00	0.98	0.76	0.91	1.00	0.91	1.00	1.00	1.00	0.62	0.99	0.62
PC 29:0	1.00	0.99	1.00	0.99	1.00	0.81	0.73	0.80	1.00	0.80	1.00	1.00	1.00	0.91	0.96	0.90
PC 30:0	1.00	0.99	1.00	0.99	1.00	0.92	0.73	0.90	1.00	0.90	1.00	1.00	1.00	0.85	0.71	0.77
PC 30:2	1.00	0.99	1.00	0.99	1.00	0.87	0.45	0.72	1.00	0.72	0.79	1.00	1.00	0.65	0.98	0.64
PC 31:0	1.00	0.99	1.00	0.99	1.00	0.53	0.45	0.41	1.00	0.41	1.00	1.00	1.00	0.86	1.00	0.99
PC 31:1	1.00	0.99	1.00	0.99	1.00	0.89	0.77	0.90	1.00	0.90	1.00	1.00	1.00	0.86	0.77	0.80
PC 32:0	1.00	0.99	1.00	0.99	1.00	0.91	0.84	0.69	1.00	0.69	1.00	1.00	1.00	0.85	0.88	0.95
PC 32:1	1.00	0.99	1.00	0.99	1.00	0.80	0.75	0.41	1.00	0.41	1.00	1.00	1.00	0.48	0.35	0.37
PC 32:2	1.00	0.99	1.00	0.99	1.00	0.91	0.90	0.50	1.00	0.50	1.00	1.00	1.00	0.64	0.81	0.51
PC 32:3	1.00	0.99	1.00	0.99	1.00	0.99	0.95	0.65	1.00	0.65	0.79	1.00	1.00	0.85	0.77	0.91
PC 33:0	1.00	0.99	1.00	0.99	1.00	0.67	0.96	0.75	1.00	0.75	1.00	1.00	1.00	0.89	0.96	0.90
PC 33:1	1.00	0.99	1.00	0.99	1.00	0.91	0.90	0.88	1.00	0.88	1.00	1.00	1.00	0.69	0.64	0.77
PC 33:2	1.00	0.99	1.00	0.99	1.00	0.89	0.90	0.90	1.00	0.90	1.00	1.00	1.00	0.12	0.20	0.07
PC 33:3	1.00	0.99	1.00	0.99	1.00	0.91	0.85	0.72	1.00	0.72	1.00	1.00	1.00	0.73	0.66	0.80
PC 34:1	1.00	0.99	1.00	0.99	1.00	0.71	0.74	0.53	1.00	0.53	1.00	1.00	1.00	0.73	0.55	0.59
PC 34:2	1.00	0.99	1.00	0.99	1.00	0.97	0.90	0.98	1.00	0.98	1.00	1.00	1.00	0.73	0.73	0.55
PC 34:3	1.00	0.99	1.00	0.99	1.00	0.84	0.73	0.49	1.00	0.49	1.00	1.00	1.00	0.95	0.83	0.95
PC 34:4	1.00	0.99	1.00	0.99	1.00	0.91	0.86	0.64	1.00	0.64	1.00	1.00	1.00	0.94	0.98	0.82
PC 34:5	1.00	0.99	1.00	0.99	1.00	0.53	0.73	0.59	1.00	0.59	1.00	1.00	1.00	0.88	0.84	0.88
PC 35:0	1.00	0.99	1.00	0.99	1.00	0.91	0.85	0.81	1.00	0.81	1.00	1.00	1.00	0.45	0.71	0.59
PC 35:1	1.00	0.99	1.00	0.99	1.00	0.94	0.85	0.70	1.00	0.70	1.00	1.00	1.00	0.48	0.56	0.86
PC 35:2	1.00	0.99	1.00	0.99	1.00	0.91	0.90	0.67	1.00	0.67	1.00	1.00	1.00	0.48	0.31	0.13
PC 35:3	1.00	0.99	1.00	0.99	1.00	0.83	0.73	0.49	1.00	0.49	1.00	1.00	1.00	0.85	0.77	0.99
PC 35:4	1.00	0.99	1.00	0.99	1.00	0.91	0.91	0.91	1.00	0.91	1.00	1.00	1.00	0.86	0.96	0.61
PC 35:5	1.00	0.99	1.00	0.99	1.00	0.94	0.99	0.98	1.00	0.98	1.00	1.00	1.00	0.95	0.83	0.94
PC 35:6	1.00	0.99	1.00	0.99	1.00	0.91	0.98	0.70	1.00	0.70	1.00	1.00	1.00	0.65	0.69	0.55
PC 36:0	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.93	1.00	0.93	1.00	1.00	1.00	0.89	0.96	0.91
PC 36:1	1.00	0.99	1.00	0.99	1.00	0.80	0.95	0.72	1.00	0.72	1.00	1.00	1.00	0.89	0.92	0.86
PC 36:2	1.00	0.99	1.00	0.99	1.00	0.82	0.83	0.70	1.00	0.70	1.00	1.00	1.00	0.45	0.55	0.17
PC 36:3	1.00	0.99	1.00	0.99	1.00	0.80	0.67	0.39	1.00	0.39	1.00	1.00	1.00	0.85	0.95	0.80
PC 36:4	1.00	0.99	1.00	0.99	1.00	0.87	0.68	0.70	1.00	0.70	1.00	1.00	1.00	0.85	0.99	0.74
PC 36:5	1.00	0.99	1.00	0.99	1.00	0.91	0.74	0.49	1.00	0.49	1.00	1.00	1.00	0.65	0.64	0.55
PC 36:6	1.00	0.99	1.00	0.99	1.00	0.80	0.68	0.49	1.00	0.49	1.00	1.00	1.00	0.99	0.90	0.82
PC 37:1	1.00	0.99	1.00	0.99	1.00	0.98	0.73	0.88	1.00	0.88	1.00	1.00	1.00	0.85	0.77	0.74
PC 37:2	1.00	0.99	1.00	0.99	1.00	0.99	0.98	0.91	1.00	0.91	1.00	1.00	1.00	0.78	0.83	0.77
PC 37:3	1.00	0.99	1.00	0.99	1.00	0.94	0.74	0.90	1.00	0.90	1.00	1.00	1.00	0.89	0.81	0.74
PC 37:4	1.00	0.99	1.00	0.99	1.00	0.91	0.83	0.89	1.00	0.89	1.00	1.00	1.00	0.89	0.93	0.77
PC 37:5	1.00	0.99	1.00	0.99	1.00	0.99	0.74	0.89	1.00	0.89	1.00	1.00	1.00	0.73	0.77	0.55
PC 37:6	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.92	1.00	0.92	1.00	1.00	1.00	0.85	0.90	0.95
PC 37:7	1.00	1.00	1.00	0.99	1.00	0.93	0.75	0.84	1.00	0.84	1.00	1.00	1.00	0.99	0.71	0.94

Table S2.6E: MEAL Study significant difference within diet comparisons for all lipids (Phosphatidylcholine 38:1 to Phosphatidylethanolamine 34:3)

	Within Diet Comparisons (FDR <0.1)															
	High Fat Diet								High Carbohydrate Diet							
Lipid/Day	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21
PC 38:1	1.00	0.99	1.00	0.99	1.00	0.71	0.73	0.70	1.00	0.70	1.00	1.00	1.00	0.93	0.95	0.97
PC 38:2	1.00	0.99	1.00	0.99	1.00	0.45	0.68	0.64	1.00	0.64	1.00	1.00	1.00	0.62	0.81	0.54
PC 38:3	1.00	0.99	1.00	0.99	1.00	0.79	0.73	0.49	1.00	0.49	1.00	1.00	1.00	0.98	0.92	0.95
PC 38:4	1.00	0.99	1.00	0.99	1.00	0.94	0.76	0.78	1.00	0.78	1.00	1.00	1.00	0.95	0.92	0.97
PC 38:5	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.53	1.00	0.53	1.00	1.00	1.00	0.84	0.64	0.85
PC 38:6	1.00	0.99	1.00	0.99	1.00	0.91	0.80	0.76	1.00	0.76	1.00	1.00	1.00	0.85	0.66	0.74
PC 38:7	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.70	1.00	0.70	1.00	1.00	1.00	0.85	0.77	0.75
PC 39:3	1.00	0.99	1.00	0.99	1.00	0.91	0.88	0.90	1.00	0.90	1.00	1.00	1.00	0.95	0.94	0.92
PC 39:4	1.00	0.99	1.00	0.99	1.00	0.83	0.98	0.91	1.00	0.91	1.00	1.00	1.00	0.95	0.98	0.82
PC 39:6	1.00	0.99	1.00	0.99	1.00	0.96	0.83	0.83	1.00	0.83	1.00	1.00	1.00	0.88	0.77	0.74
PC 39:7	1.00	0.99	1.00	0.99	1.00	0.93	0.99	1.00	1.00	1.00	1.00	1.00	1.00	0.48	0.32	0.74
PC 39:8	1.00	0.99	1.00	0.99	1.00	0.91	0.93	0.90	1.00	0.90	1.00	1.00	1.00	0.65	0.77	0.98
PC 40:0	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.91	1.00	0.91	1.00	1.00	1.00	0.92	0.83	0.77
PC 40:1	1.00	0.99	1.00	0.99	1.00	0.91	0.67	0.90	1.00	0.90	1.00	1.00	1.00	0.89	0.86	0.86
PC 40:2	1.00	0.99	1.00	0.99	1.00	0.90	0.74	0.67	1.00	0.67	1.00	1.00	1.00	0.76	0.98	0.74
PC 40:4	1.00	0.99	1.00	0.99	1.00	0.90	0.68	0.75	1.00	0.75	1.00	1.00	1.00	0.89	0.77	0.89
PC 40:5	1.00	0.99	1.00	0.99	1.00	0.85	0.67	0.64	1.00	0.64	1.00	1.00	1.00	0.85	0.66	0.33
PC 40:6	1.00	0.99	1.00	0.99	1.00	0.91	0.84	0.80	1.00	0.80	1.00	1.00	1.00	0.81	0.55	0.53
PC 40:7	1.00	0.99	1.00	0.99	1.00	0.81	0.68	0.65	1.00	0.65	1.00	1.00	1.00	0.95	0.83	0.86
PC 40:8	1.00	0.99	1.00	0.99	1.00	0.91	0.67	0.84	1.00	0.84	1.00	1.00	1.00	0.89	0.96	0.86
PC 41:3	1.00	0.99	1.00	0.99	1.00	0.98	0.99	0.67	1.00	0.67	1.00	1.00	1.00	0.76	0.99	0.95
PC 41:4	1.00	0.99	1.00	0.99	1.00	0.90	0.81	0.86	1.00	0.86	1.00	1.00	1.00	0.95	0.93	0.86
PC 41:5	1.00	0.99	1.00	0.99	1.00	0.91	0.80	0.99	1.00	0.99	1.00	1.00	1.00	0.95	0.83	0.89
PC 41:6	1.00	0.99	1.00	0.99	1.00	0.92	0.76	0.78	1.00	0.78	1.00	1.00	1.00	0.86	0.69	0.68
PC 41:7	1.00	0.99	1.00	0.99	1.00	0.94	0.83	0.86	1.00	0.86	1.00	1.00	1.00	0.81	0.96	0.68
PC 42:1	1.00	0.99	1.00	0.99	1.00	0.81	0.73	0.65	1.00	0.65	1.00	1.00	1.00	0.73	0.95	0.95
PC 42:10	1.00	0.99	1.00	1.00	1.00	0.91	0.80	0.92	1.00	0.92	1.00	1.00	1.00	0.95	0.77	0.77
PC 42:2	1.00	0.99	1.00	0.99	1.00	0.81	0.68	0.49	1.00	0.49	1.00	1.00	1.00	0.78	0.83	0.62
PC 42:3	1.00	0.99	1.00	0.99	1.00	0.81	0.71	0.13	1.00	0.13	1.00	1.00	1.00	0.89	0.90	0.96
PC 42:4	1.00	0.99	1.00	0.99	1.00	0.91	0.93	0.90	1.00	0.90	1.00	1.00	1.00	0.95	0.96	0.86
PC 42:5	1.00	0.99	1.00	0.99	1.00	0.94	0.81	0.90	1.00	0.90	1.00	1.00	1.00	0.95	0.96	1.00
PC 42:6	1.00	0.99	1.00	0.99	1.00	0.81	0.45	0.49	1.00	0.49	1.00	1.00	1.00	0.62	0.64	0.37
PC 42:7	1.00	0.99	1.00	0.99	1.00	0.94	0.67	0.91	1.00	0.91	1.00	1.00	1.00	0.81	0.99	0.91
PC 42:8	1.00	0.99	1.00	0.99	1.00	0.88	0.73	0.49	1.00	0.49	1.00	1.00	1.00	0.83	0.81	0.96
PC 42:9	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.90	1.00	0.90	1.00	1.00	1.00	0.74	0.77	0.55
PC 44:12	1.00	0.99	1.00	0.99	1.00	0.94	0.74	0.98	1.00	0.98	1.00	1.00	1.00	0.89	0.75	0.77
PC 44:2	1.00	0.99	1.00	0.99	1.00	0.45	0.67	0.41	1.00	0.41	1.00	1.00	1.00	0.90	0.82	0.85
PC 44:3	1.00	0.99	1.00	0.99	1.00	0.94	0.81	0.70	1.00	0.70	1.00	1.00	1.00	0.87	0.90	0.99
PC 44:4	1.00	0.99	1.00	0.99	1.00	0.90	0.87	0.90	1.00	0.90	1.00	1.00	1.00	0.95	0.94	0.89
PC 44:5	1.00	0.99	1.00	0.99	1.00	0.92	0.73	0.54	1.00	0.54	0.92	1.00	1.00	0.94	0.71	0.55
PC 44:6	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.41	1.00	0.41	1.00	1.00	1.00	0.92	0.93	0.65
PC 44:8	1.00	0.99	1.00	0.99	1.00	0.91	0.96	0.89	1.00	0.89	1.00	1.00	1.00	0.78	0.88	0.82
PC 46:4	1.00	0.99	1.00	0.99	1.00	0.64	0.73	0.49	1.00	0.49	1.00	1.00	1.00	0.66	0.81	0.86
PE 30:0	1.00	0.99	1.00	0.99	1.00	0.95	0.67	0.86	1.00	0.86	1.00	1.00	1.00	0.96	0.82	0.82
PE 32:0	1.00	0.99	1.00	0.99	1.00	0.90	0.95	0.96	1.00	0.96	1.00	1.00	1.00	0.85	0.77	0.86
PE 32:1	1.00	0.99	1.00	0.99	1.00	0.97	0.85	1.00	1.00	1.00	1.00	1.00	1.00	0.61	0.55	0.62
PE 32:2	1.00	0.99	1.00	0.99	1.00	0.93	0.74	0.91	1.00	0.91	1.00	1.00	1.00	0.95	0.94	0.83
PE 33:0	1.00	0.99	1.00	0.99	1.00	0.89	0.90	0.99	1.00	0.99	1.00	1.00	1.00	0.85	0.90	0.92
PE 33:1	1.00	0.99	1.00	0.99	1.00	0.99	0.76	0.90	1.00	0.90	1.00	1.00	1.00	0.98	0.83	0.54
PE 33:2	1.00	0.99	1.00	0.99	1.00	0.98	0.83	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.96	0.64
PE 34:0	1.00	0.99	1.00	0.99	1.00	0.85	0.94	0.90	1.00	0.90	1.00	1.00	1.00	0.81	0.85	0.80
PE 34:1	1.00	0.99	1.00	1.00	1.00	0.82	0.73	0.84	1.00	0.84	1.00	1.00	1.00	0.76	0.63	0.62
PE 34:2	1.00	0.99	1.00	0.99	1.00	0.99	0.98	0.99	1.00	0.99	1.00	1.00	1.00	0.98	0.96	0.91
PE 34:3	1.00	0.99	1.00	0.99	1.00	0.99	0.98	0.85	1.00	0.85	1.00	1.00	1.00	0.86	0.82	0.83

Table S2.6F: MEAL Study significant difference within diet comparisons for all lipids (Phosphatidylethanolamine 34:4 to Plasmenyl-phosphatidylcholine 35:3)

	Within Diet Comparisons (FDR <0.1)															
	High Fat Diet								High Carbohydrate Diet							
Lipid/Day	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21
PE 34:4	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.98	1.00	0.98	1.00	1.00	1.00	0.66	1.00	0.95
PE 35:0	1.00	0.99	1.00	0.99	1.00	0.93	0.83	0.89	1.00	0.89	1.00	1.00	1.00	0.99	0.96	0.77
PE 35:1	1.00	0.99	1.00	0.99	1.00	0.90	0.80	0.98	1.00	0.98	1.00	1.00	1.00	0.95	0.99	0.84
PE 35:2	1.00	0.99	1.00	0.99	1.00	0.91	0.96	0.90	1.00	0.90	1.00	1.00	1.00	0.85	0.87	0.88
PE 35:4	1.00	0.99	1.00	0.99	1.00	0.99	0.93	0.92	1.00	0.92	1.00	1.00	1.00	0.89	0.94	0.57
PE 36:0	1.00	0.99	1.00	0.99	1.00	0.90	0.79	0.91	1.00	0.91	1.00	1.00	1.00	0.89	0.94	0.98
PE 36:1	1.00	0.99	1.00	0.99	1.00	0.90	0.87	0.91	1.00	0.91	1.00	1.00	1.00	0.94	0.83	0.82
PE 36:2	1.00	0.99	1.00	0.99	1.00	0.91	0.96	0.89	1.00	0.89	1.00	1.00	1.00	0.72	0.93	0.70
PE 36:3	1.00	0.99	1.00	0.99	1.00	0.94	0.96	0.90	1.00	0.90	1.00	1.00	1.00	0.88	0.96	0.74
PE 36:4	1.00	0.99	1.00	0.99	1.00	0.99	0.96	0.99	1.00	0.99	1.00	1.00	1.00	0.88	0.81	0.89
PE 36:5	1.00	0.99	1.00	0.99	1.00	0.97	0.90	0.91	1.00	0.91	1.00	1.00	1.00	0.65	0.64	0.64
PE 37:4	1.00	0.99	1.00	0.99	1.00	0.90	0.97	0.91	1.00	0.91	1.00	1.00	1.00	0.94	0.93	0.97
PE 38:3	1.00	0.99	1.00	0.99	1.00	0.98	0.73	0.97	1.00	0.97	1.00	1.00	1.00	0.88	0.95	0.86
PE 38:4	1.00	0.99	1.00	0.99	1.00	0.80	0.77	0.99	1.00	0.99	1.00	1.00	1.00	0.74	0.96	0.71
PE 38:5	1.00	0.99	1.00	0.99	1.00	0.85	0.73	0.86	1.00	0.86	1.00	1.00	1.00	0.92	0.93	0.86
PE 38:6	1.00	0.99	1.00	1.00	1.00	0.91	0.85	0.99	1.00	0.99	1.00	1.00	1.00	0.95	0.81	0.90
PE 38:7	1.00	0.99	1.00	0.99	1.00	0.91	0.74	0.89	1.00	0.89	1.00	1.00	1.00	0.89	0.96	0.86
PE 40:4	1.00	0.99	1.00	0.99	1.00	0.91	0.74	0.94	1.00	0.94	1.00	1.00	1.00	0.76	0.99	0.86
PE 40:5	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.90	1.00	0.90	1.00	1.00	1.00	0.90	0.71	0.99
PE 40:6	1.00	0.99	1.00	0.99	1.00	0.91	0.83	0.91	1.00	0.91	1.00	1.00	1.00	0.88	0.66	0.71
PE 40:7	1.00	0.99	1.00	0.99	1.00	0.90	0.83	0.98	1.00	0.98	1.00	1.00	1.00	0.85	0.96	0.99
PE 40:8	1.00	0.99	1.00	0.99	1.00	0.81	0.96	0.98	1.00	0.98	1.00	1.00	1.00	0.77	0.95	0.78
PE 42:10	1.00	0.99	1.00	0.99	1.00	0.59	0.98	0.98	1.00	0.98	1.00	1.00	1.00	0.89	0.81	0.85
PG 33:0	1.00	0.99	1.00	0.99	1.00	0.80	0.42	0.49	1.00	0.49	1.00	1.00	1.00	0.73	0.83	0.89
PG 34:0	1.00	0.99	1.00	0.99	1.00	0.49	0.85	0.98	1.00	0.98	0.79	1.00	1.00	0.65	0.77	0.95
PG 34:2	1.00	0.99	1.00	0.99	1.00	0.43	0.68	0.67	1.00	0.67	1.00	1.00	1.00	0.81	0.96	0.70
PG 36:0	1.00	0.99	1.00	0.99	1.00	0.94	0.73	0.94	1.00	0.94	1.00	1.00	1.00	0.65	0.64	0.68
PG 36:2	1.00	0.99	1.00	0.99	1.00	0.44	0.67	0.49	1.00	0.49	0.79	1.00	1.00	0.88	0.96	0.84
PG 36:3	1.00	0.99	1.00	0.99	1.00	0.80	0.67	0.67	1.00	0.67	1.00	1.00	1.00	0.85	0.96	0.79
PG 38:4	1.00	0.99	1.00	0.99	1.00	0.53	0.67	0.81	1.00	0.81	1.00	1.00	1.00	0.73	0.87	0.58
PI 25:0	1.00	0.99	1.00	0.99	1.00	0.90	0.68	0.99	1.00	0.99	1.00	1.00	1.00	0.86	0.96	0.89
PI 34:1	1.00	0.99	1.00	0.99	1.00	0.76	0.76	0.88	1.00	0.88	1.00	1.00	1.00	0.69	0.90	0.74
PI 34:2	1.00	0.99	1.00	1.00	1.00	0.79	0.67	0.67	1.00	0.67	0.79	1.00	1.00	0.57	0.81	0.55
PI 36:1	1.00	0.99	1.00	0.99	1.00	0.81	0.81	0.99	1.00	0.99	1.00	1.00	1.00	0.44	0.64	0.54
PI 36:2	1.00	0.99	1.00	0.99	1.00	0.59	0.68	0.70	1.00	0.70	0.44	1.00	1.00	0.34	0.70	0.53
PI 36:4	1.00	0.99	1.00	0.99	1.00	0.70	0.67	0.70	1.00	0.70	1.00	1.00	1.00	0.73	0.96	0.70
PI 38:3	1.00	0.99	1.00	0.99	1.00	0.80	0.63	0.78	1.00	0.78	0.79	1.00	1.00	0.70	0.95	0.77
PI 38:4	1.00	0.99	1.00	0.99	1.00	0.45	0.67	0.78	1.00	0.78	0.44	1.00	1.00	0.48	0.87	0.61
PI 38:5	1.00	0.99	1.00	0.99	1.00	0.81	0.74	0.88	1.00	0.88	0.79	1.00	1.00	0.69	0.93	0.63
PI 38:6	1.00	0.99	1.00	0.99	1.00	0.91	0.82	0.91	1.00	0.91	0.79	1.00	1.00	0.85	0.96	0.86
PI 40:5	1.00	0.99	1.00	0.99	1.00	0.64	0.67	0.75	1.00	0.75	0.51	1.00	1.00	0.62	0.95	0.95
PI 40:6	1.00	0.99	1.00	0.99	1.00	0.80	0.73	0.84	1.00	0.84	1.00	1.00	1.00	0.81	0.74	0.97
PlsCho 24:0	1.00	0.99	1.00	0.99	1.00	0.80	0.73	0.39	1.00	0.39	1.00	1.00	1.00	0.89	0.81	0.80
PlsCho 28:0	1.00	0.99	1.00	0.99	1.00	0.99	0.87	0.98	1.00	0.98	1.00	1.00	1.00	0.95	0.95	0.99
PlsCho 32:0	1.00	0.99	1.00	0.99	1.00	0.94	0.42	0.79	1.00	0.79	1.00	1.00	1.00	0.83	0.81	0.95
PlsCho 32:1	1.00	0.99	1.00	0.99	1.00	0.90	0.50	0.67	1.00	0.67	1.00	1.00	1.00	0.71	0.99	0.82
PlsCho 33:0	1.00	0.99	1.00	0.99	1.00	0.78	0.78	0.65	1.00	0.65	1.00	1.00	1.00	0.91	0.98	0.82
PlsCho 34:0	1.00	0.99	1.00	0.99	1.00	0.91	0.79	0.73	1.00	0.73	1.00	1.00	1.00	0.62	0.89	0.57
PlsCho 34:1	1.00	0.99	1.00	0.99	1.00	0.94	0.85	0.86	1.00	0.86	1.00	1.00	1.00	0.76	0.95	0.74
PlsCho 34:2	1.00	0.99	1.00	0.99	1.00	0.94	0.87	0.90	1.00	0.90	1.00	1.00	1.00	0.73	0.83	0.55
PlsCho 34:3	1.00	0.99	1.00	0.99	1.00	0.43	0.45	0.08	1.00	0.08	1.00	1.00	1.00	0.80	0.95	0.93
PlsCho 35:0	1.00	0.99	1.00	0.99	1.00	0.94	1.00	0.98	1.00	0.98	1.00	1.00	1.00	0.75	0.77	0.97
PlsCho 35:1	1.00	0.99	1.00	0.99	1.00	0.81	0.99	0.90	1.00	0.90	1.00	1.00	1.00	0.73	0.96	0.97
PlsCho 35:2	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.64	1.00	0.64	1.00	1.00	1.00	0.86	0.81	0.77
PlsCho 35:3	1.00	0.99	1.00	0.99	1.00	0.95	0.73	0.12	1.00	0.12	1.00	1.00	1.00	0.61	0.88	0.61

Table S2.6G: MEAL Study significant difference within diet comparisons for all lipids (Plasmenyl-phosphatidylcholine 35:4 to Plasmenyl-phosphatidylethanolamine 36:2)

	Within Diet Comparisons (FDR <0.1)															
	High Fat Diet								High Carbohydrate Diet							
Lipid/Day	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21
PlsCho 35:4	1.00	0.99	1.00	0.99	1.00	0.99	0.80	0.67	1.00	0.67	1.00	1.00	1.00	0.83	0.66	0.80
PlsCho 36:0	1.00	0.99	1.00	0.99	1.00	0.82	0.86	0.86	1.00	0.86	0.79	1.00	1.00	0.48	0.87	0.55
PlsCho 36:2	1.00	0.99	1.00	1.00	1.00	0.91	0.81	0.78	1.00	0.78	1.00	1.00	1.00	0.71	0.77	0.61
PlsCho 36:3	1.00	0.99	1.00	0.99	1.00	0.92	0.99	0.78	1.00	0.78	1.00	1.00	1.00	0.72	0.87	0.54
PlsCho 36:4	1.00	0.99	1.00	0.99	1.00	0.99	0.99	0.70	1.00	0.70	1.00	1.00	1.00	0.85	0.95	0.61
PlsCho 36:5	1.00	0.99	1.00	0.99	1.00	0.81	0.73	0.49	1.00	0.49	1.00	1.00	1.00	0.89	0.83	0.92
PlsCho 36:6	1.00	0.99	1.00	0.99	1.00	0.43	0.42	0.49	1.00	0.49	1.00	1.00	1.00	0.71	0.98	0.89
PlsCho 37:1	1.00	0.99	1.00	0.99	1.00	0.91	0.74	0.68	1.00	0.68	1.00	1.00	1.00	0.96	0.94	0.68
PlsCho 37:2	1.00	0.99	1.00	0.99	1.00	0.91	0.97	0.98	1.00	0.98	1.00	1.00	1.00	0.95	0.66	0.73
PlsCho 37:3	1.00	0.99	1.00	0.99	1.00	0.26	0.45	0.00	1.00	0.00	1.00	1.00	1.00	0.96	0.96	0.74
PlsCho 37:4	1.00	0.99	1.00	0.99	1.00	0.43	0.42	0.02	1.00	0.02	1.00	1.00	1.00	0.95	0.81	0.71
PlsCho 37:6	1.00	0.99	1.00	0.99	1.00	0.90	0.92	0.70	1.00	0.70	1.00	1.00	1.00	0.80	0.96	0.79
PlsCho 38:0	1.00	0.99	1.00	0.99	1.00	0.91	0.85	0.99	1.00	0.99	0.79	1.00	1.00	0.64	0.95	0.96
PlsCho 38:1	1.00	0.99	1.00	1.00	1.00	0.92	0.90	0.90	1.00	0.90	1.00	1.00	1.00	0.96	0.99	0.97
PlsCho 38:3	1.00	0.99	1.00	0.99	1.00	0.93	0.80	0.81	1.00	0.81	1.00	1.00	1.00	0.73	0.83	0.55
PlsCho 38:4	1.00	0.99	1.00	0.99	1.00	0.98	0.80	0.99	1.00	0.99	1.00	1.00	1.00	0.72	0.86	0.53
PlsCho 38:5	1.00	0.99	1.00	0.99	1.00	0.93	0.98	0.65	1.00	0.65	1.00	1.00	1.00	0.89	0.99	0.77
PlsCho 38:6	1.00	0.99	1.00	0.99	1.00	0.91	0.81	0.67	1.00	0.67	1.00	1.00	1.00	0.95	0.96	0.81
PlsCho 39:3	1.00	0.99	1.00	0.99	1.00	0.81	0.82	0.75	1.00	0.75	1.00	1.00	1.00	0.93	0.96	0.86
PlsCho 39:4	1.00	0.99	1.00	0.99	1.00	0.92	0.99	0.99	1.00	0.99	1.00	1.00	1.00	0.76	0.83	0.95
PlsCho 39:5	1.00	0.99	1.00	0.99	1.00	0.90	0.91	0.92	1.00	0.92	1.00	1.00	1.00	0.71	0.96	0.95
PlsCho 39:6	1.00	0.99	1.00	0.99	1.00	0.59	0.67	0.15	1.00	0.15	1.00	1.00	1.00	0.94	0.71	0.89
PlsCho 40:0	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.70	1.00	0.70	1.00	1.00	1.00	0.87	0.92	0.77
PlsCho 40:1	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.65	1.00	0.65	1.00	1.00	1.00	0.64	0.90	0.70
PlsCho 40:3	1.00	0.99	1.00	0.99	1.00	0.99	0.80	0.72	1.00	0.72	1.00	1.00	1.00	0.64	0.83	0.63
PlsCho 40:4	1.00	0.99	1.00	0.99	1.00	0.91	0.74	0.68	1.00	0.68	1.00	1.00	1.00	0.94	0.98	0.89
PlsCho 40:5	1.00	0.99	1.00	0.99	1.00	0.80	0.74	0.53	1.00	0.53	1.00	1.00	1.00	0.73	0.83	0.89
PlsCho 40:6	1.00	0.99	1.00	0.99	1.00	1.00	0.79	0.88	1.00	0.88	1.00	1.00	1.00	0.82	0.93	0.86
PlsCho 42:1	1.00	0.99	1.00	0.99	1.00	0.94	0.91	0.80	1.00	0.80	1.00	1.00	1.00	0.65	0.93	0.70
PlsCho 42:2	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.54	1.00	0.54	1.00	1.00	1.00	0.73	0.83	0.64
PlsCho 42:3	1.00	0.99	1.00	0.99	1.00	0.79	0.73	0.49	1.00	0.49	0.79	1.00	1.00	0.57	0.94	0.75
PlsCho 42:4	1.00	0.99	1.00	0.99	1.00	0.91	0.68	0.49	1.00	0.49	1.00	1.00	1.00	0.89	0.98	0.95
PlsCho 42:5	1.00	0.99	1.00	0.99	1.00	0.91	0.67	0.69	1.00	0.69	1.00	1.00	1.00	0.73	0.95	0.80
PlsCho 42:6	1.00	0.99	1.00	0.99	1.00	0.80	0.45	0.13	1.00	0.13	1.00	1.00	1.00	0.76	0.96	0.80
PlsCho 44:3	1.00	0.99	1.00	0.99	1.00	0.94	0.96	0.86	1.00	0.86	1.00	1.00	1.00	0.95	0.96	0.91
PlsCho 44:4	1.00	0.99	1.00	0.99	1.00	0.91	0.71	0.42	1.00	0.42	1.00	1.00	1.00	0.85	0.99	0.89
PlsCho 44:5	1.00	0.99	1.00	0.99	1.00	0.99	0.68	0.70	1.00	0.70	1.00	1.00	1.00	0.64	0.95	0.93
PlsCho 44:6	1.00	0.99	1.00	0.99	1.00	0.90	0.78	0.46	1.00	0.46	1.00	1.00	1.00	0.77	0.96	1.00
PlsCho 46:4	1.00	0.99	1.00	0.99	1.00	0.96	0.74	0.49	1.00	0.49	1.00	1.00	1.00	0.98	0.93	0.97
PlsEth 32:0	1.00	0.99	1.00	0.99	1.00	0.91	0.71	0.88	1.00	0.88	1.00	1.00	1.00	0.76	0.83	0.61
PlsEth 32:1	1.00	0.99	1.00	0.99	1.00	0.91	0.81	0.98	1.00	0.98	1.00	1.00	1.00	0.65	0.81	0.38
PlsEth 32:2	1.00	0.99	1.00	0.99	1.00	0.59	0.68	0.49	1.00	0.49	1.00	1.00	1.00	0.10	0.05	0.07
PlsEth 33:1	1.00	0.78	1.00	0.99	1.00	0.35	0.45	0.18	1.00	0.18	1.00	1.00	1.00	0.44	0.32	0.17
PlsEth 33:2	1.00	0.99	1.00	0.99	1.00	0.64	0.72	0.70	1.00	0.70	1.00	1.00	1.00	0.29	0.10	0.07
PlsEth 34:0	1.00	0.99	1.00	0.99	1.00	0.91	0.68	0.63	1.00	0.63	1.00	1.00	1.00	0.62	0.71	0.51
PlsEth 34:1	1.00	0.99	1.00	0.99	1.00	0.90	0.67	0.65	1.00	0.65	1.00	1.00	1.00	0.44	0.64	0.24
PlsEth 34:2	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.73	1.00	0.73	1.00	1.00	1.00	0.40	0.35	0.17
PlsEth 34:3	1.00	0.99	1.00	0.99	1.00	0.90	0.74	0.70	1.00	0.70	1.00	1.00	1.00	0.62	0.64	0.53
PlsEth 34:4	1.00	0.99	1.00	0.99	1.00	0.59	0.50	0.13	1.00	0.13	1.00	1.00	1.00	0.39	0.20	0.12
PlsEth 35:1	1.00	0.99	1.00	0.99	1.00	0.99	0.71	0.86	1.00	0.86	1.00	1.00	1.00	0.72	0.77	0.53
PlsEth 35:2	1.00	0.99	1.00	0.99	1.00	0.43	0.45	0.39	1.00	0.39	1.00	1.00	1.00	0.62	0.71	0.55
PlsEth 35:4	1.00	0.78	1.00	0.99	1.00	0.26	0.42	0.07	1.00	0.07	1.00	1.00	1.00	0.58	0.55	0.33
PlsEth 36:0	1.00	0.99	1.00	0.99	1.00	0.92	0.73	0.67	1.00	0.67	1.00	1.00	1.00	0.92	0.81	0.70
PlsEth 36:1	1.00	0.99	1.00	1.00	1.00	0.94	0.93	0.98	1.00	0.98	1.00	1.00	1.00	0.34	0.35	0.08
PlsEth 36:2	1.00	0.99	1.00	0.99	1.00	0.98	0.99	0.99	1.00	0.99	1.00	1.00	1.00	0.34	0.20	0.07

Table S2.6H: MEAL Study significant difference within diet comparisons for all lipids (Plasmenyl-phosphatidylethanolamine 36:3 to Sphingomyelin 38:4)

	Within Diet Comparisons (FDR <0.1)															
	High Fat Diet								High Carbohydrate Diet							
Lipid/Day	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21
PlsEth 36:3	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.90	1.00	0.90	1.00	1.00	1.00	0.48	0.56	0.22
PlsEth 36:4	1.00	0.99	1.00	0.99	1.00	0.70	0.67	0.65	1.00	0.65	1.00	1.00	1.00	0.45	0.83	0.55
PlsEth 36:5	1.00	0.99	1.00	0.99	1.00	0.90	0.92	0.86	1.00	0.86	1.00	1.00	1.00	0.66	0.83	0.86
PlsEth 36:6	1.00	0.99	1.00	0.99	1.00	0.79	0.73	0.49	1.00	0.49	1.00	1.00	1.00	0.85	0.81	0.61
PlsEth 37:1	1.00	0.99	1.00	0.99	1.00	0.90	0.76	0.91	1.00	0.91	1.00	1.00	1.00	0.81	0.95	0.85
PlsEth 37:2	1.00	0.99	1.00	0.99	1.00	0.92	0.95	0.88	1.00	0.88	1.00	1.00	1.00	0.62	0.55	0.17
PlsEth 37:3	1.00	0.99	1.00	0.99	1.00	0.81	0.78	0.49	1.00	0.49	1.00	1.00	1.00	0.99	0.93	0.86
PlsEth 37:4	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.18	1.00	0.18	1.00	1.00	1.00	0.73	0.91	0.55
PlsEth 37:5	1.00	0.51	1.00	0.99	1.00	0.18	0.42	0.18	1.00	0.18	1.00	1.00	1.00	0.89	0.93	0.80
PlsEth 37:6	1.00	0.86	1.00	0.99	1.00	0.45	0.50	0.15	1.00	0.15	1.00	1.00	1.00	0.58	0.55	0.34
PlsEth 38:1	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.86	1.00	0.86	1.00	1.00	1.00	0.34	0.57	0.13
PlsEth 38:2	1.00	0.99	1.00	0.99	1.00	0.90	0.74	0.65	1.00	0.65	1.00	1.00	1.00	0.57	0.55	0.34
PlsEth 38:3	1.00	0.99	1.00	0.99	1.00	0.94	0.76	0.97	1.00	0.97	1.00	1.00	1.00	0.62	0.55	0.17
PlsEth 38:4	1.00	0.99	1.00	1.00	1.00	0.91	0.88	0.90	1.00	0.90	1.00	1.00	1.00	0.62	0.81	0.33
PlsEth 38:5	1.00	0.99	1.00	0.99	1.00	0.90	0.74	0.99	1.00	0.99	1.00	1.00	1.00	0.62	0.83	0.54
PlsEth 38:6	1.00	0.99	1.00	0.99	1.00	0.96	0.78	0.98	1.00	0.98	1.00	1.00	1.00	0.62	0.83	0.61
PlsEth 39:2	1.00	0.99	1.00	0.99	1.00	0.71	0.73	0.99	1.00	0.99	1.00	1.00	1.00	0.89	0.97	0.95
PlsEth 39:4	1.00	0.99	1.00	0.99	1.00	0.99	0.77	0.61	1.00	0.61	1.00	1.00	1.00	0.72	0.89	0.55
PlsEth 39:5	1.00	0.99	1.00	0.99	1.00	0.81	0.74	0.41	1.00	0.41	1.00	1.00	1.00	0.80	0.81	0.61
PlsEth 39:6	1.00	0.99	1.00	0.99	1.00	0.90	0.78	0.49	1.00	0.49	1.00	1.00	1.00	0.91	0.98	0.99
PlsEth 40:1	1.00	0.99	1.00	0.99	1.00	0.90	0.74	0.81	1.00	0.81	1.00	1.00	1.00	0.74	0.81	0.55
PlsEth 40:2	1.00	0.99	1.00	0.99	1.00	0.95	0.68	0.65	1.00	0.65	1.00	1.00	1.00	0.44	0.66	0.34
PlsEth 40:4	1.00	0.99	1.00	0.99	1.00	0.91	0.78	0.91	1.00	0.91	1.00	1.00	1.00	0.45	0.83	0.28
PlsEth 40:5	1.00	0.99	1.00	0.99	1.00	0.94	0.78	0.91	1.00	0.91	1.00	1.00	1.00	0.44	0.71	0.33
PlsEth 40:6	1.00	0.99	1.00	0.99	1.00	0.94	0.98	0.80	1.00	0.80	1.00	1.00	1.00	0.65	0.81	0.70
PlsEth 41:4	1.00	0.99	1.00	0.99	1.00	0.98	1.00	0.84	1.00	0.84	1.00	1.00	1.00	0.89	0.96	0.82
PlsEth 41:6	1.00	0.99	1.00	0.99	1.00	0.99	0.83	0.98	1.00	0.98	1.00	1.00	1.00	1.00	0.96	0.73
PlsEth 42:4	1.00	0.99	1.00	0.99	1.00	0.90	0.83	0.89	1.00	0.89	1.00	1.00	1.00	0.57	0.93	0.46
PlsEth 42:5	1.00	0.99	1.00	0.99	1.00	0.94	0.74	0.99	1.00	0.99	1.00	1.00	1.00	0.57	0.98	0.55
PlsEth 42:6	1.00	0.99	1.00	0.99	1.00	0.90	0.93	0.97	1.00	0.97	1.00	1.00	1.00	0.92	0.89	0.92
PlsEth 44:6	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.86	1.00	0.86	1.00	1.00	1.00	0.89	0.95	0.85
PS 36:1	1.00	0.99	1.00	0.99	1.00	0.94	0.74	0.99	1.00	0.99	1.00	1.00	1.00	0.87	0.98	0.98
PS 38:4	1.00	0.99	1.00	0.99	1.00	0.79	0.74	0.54	1.00	0.54	1.00	1.00	1.00	0.75	0.95	0.74
SM 30:1	1.00	0.99	1.00	0.99	1.00	0.94	0.90	0.91	1.00	0.91	1.00	1.00	1.00	0.45	0.65	0.13
SM 30:2	1.00	0.99	1.00	0.99	1.00	0.81	0.76	0.84	1.00	0.84	1.00	1.00	1.00	0.65	0.99	0.13
SM 32:0	1.00	0.99	1.00	0.99	1.00	0.90	0.87	0.90	1.00	0.90	1.00	1.00	1.00	0.65	0.88	0.55
SM 32:1	1.00	0.99	1.00	0.99	1.00	0.99	0.99	0.92	1.00	0.92	1.00	1.00	1.00	0.64	0.77	0.40
SM 32:2	1.00	0.99	1.00	0.99	1.00	0.98	0.95	0.91	1.00	0.91	1.00	1.00	1.00	0.88	0.96	0.74
SM 33:1	1.00	0.99	1.00	0.99	1.00	0.91	0.98	0.88	1.00	0.88	1.00	1.00	1.00	0.62	0.76	0.30
SM 34:0	1.00	0.99	1.00	0.99	1.00	0.97	0.67	0.90	1.00	0.90	1.00	1.00	1.00	0.89	0.93	0.77
SM 34:1	1.00	0.99	1.00	0.99	1.00	0.91	0.93	0.89	1.00	0.89	1.00	1.00	1.00	0.75	0.96	0.77
SM 34:2	1.00	0.99	1.00	0.99	1.00	0.91	0.85	0.75	1.00	0.75	1.00	1.00	1.00	0.72	0.95	0.70
SM 34:3	1.00	0.99	1.00	0.99	1.00	0.81	0.93	0.85	1.00	0.85	1.00	1.00	1.00	0.73	0.95	0.77
SM 35:2	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.83	1.00	0.83	1.00	1.00	1.00	0.73	0.90	0.89
SM 36:1	1.00	0.99	1.00	0.99	1.00	0.89	0.78	0.78	1.00	0.78	1.00	1.00	1.00	0.75	0.96	0.89
SM 36:2	1.00	0.99	1.00	0.99	1.00	0.99	1.00	0.91	1.00	0.91	1.00	1.00	1.00	0.85	0.92	0.99
SM 36:3	1.00	0.99	1.00	0.99	1.00	0.91	0.98	0.98	1.00	0.98	1.00	1.00	1.00	0.57	0.91	0.35
SM 36:4	1.00	0.99	1.00	0.99	1.00	0.91	0.81	0.98	1.00	0.98	1.00	1.00	1.00	0.97	0.81	0.34
SM 37:1	1.00	0.99	1.00	0.99	1.00	0.18	0.45	0.12	1.00	0.12	1.00	1.00	1.00	0.75	0.96	0.74
SM 37:2	1.00	0.99	1.00	0.99	1.00	0.80	0.74	0.59	1.00	0.59	1.00	1.00	1.00	0.89	0.96	0.86
SM 38:0	1.00	0.99	1.00	0.99	1.00	0.81	0.86	0.67	1.00	0.67	1.00	1.00	1.00	0.86	0.93	0.82
SM 38:1	1.00	0.99	1.00	1.00	1.00	0.99	0.99	0.98	1.00	0.98	1.00	1.00	1.00	0.64	0.81	0.53
SM 38:2	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.90	1.00	0.90	1.00	1.00	1.00	0.64	0.81	0.52
SM 38:3	1.00	0.99	1.00	0.99	1.00	0.94	0.85	0.99	1.00	0.99	1.00	1.00	1.00	0.88	0.93	0.95
SM 38:4	1.00	0.99	1.00	0.99	1.00	0.99	0.74	0.73	1.00	0.73	1.00	1.00	1.00	0.89	0.95	0.92

Table S2.6I: MEAL Study significant difference within diet comparisons for all lipids (Sphingomyelin 39:0 to Triacylglycerol 47:0)

	Within Diet Comparisons (FDR <0.1)																
	High Fat Diet									High Carbohydrate Diet							
Lipid/Day	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21		B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21
SM 39:0	1.00	0.99	1.00	0.99	1.00	0.80	0.74	0.70		1.00	0.70	1.00	1.00	1.00	0.80	0.82	0.34
SM 39:1	1.00	0.99	1.00	0.99	1.00	0.92	0.95	0.91		1.00	0.91	1.00	1.00	1.00	0.44	0.35	0.07
SM 39:2	1.00	0.99	1.00	0.99	1.00	0.91	0.87	0.71		1.00	0.71	1.00	1.00	1.00	0.81	0.96	0.70
SM 39:3	1.00	0.99	1.00	0.99	1.00	0.80	0.87	0.67		1.00	0.67	1.00	1.00	1.00	0.97	0.90	0.71
SM 40:1	1.00	0.99	1.00	0.99	1.00	0.99	0.95	0.93		1.00	0.93	0.79	1.00	1.00	0.44	0.43	0.08
SM 40:2	1.00	0.99	1.00	0.99	1.00	0.90	0.83	0.75		1.00	0.75	1.00	1.00	1.00	0.71	0.92	0.55
SM 40:3	1.00	0.99	1.00	0.99	1.00	0.91	1.00	0.92		1.00	0.92	1.00	1.00	1.00	0.97	0.77	0.91
SM 40:5	1.00	0.99	1.00	0.99	1.00	0.90	0.86	0.88		1.00	0.88	1.00	1.00	1.00	0.97	0.83	0.95
SM 41:1	1.00	0.99	1.00	0.99	1.00	0.90	0.83	0.88		1.00	0.88	1.00	1.00	1.00	0.58	0.75	0.34
SM 41:2	1.00	0.99	1.00	0.99	1.00	0.98	0.74	0.90		1.00	0.90	1.00	1.00	1.00	0.60	0.83	0.33
SM 41:3	1.00	0.99	1.00	0.99	1.00	0.90	0.91	0.83		1.00	0.83	1.00	1.00	1.00	0.86	0.82	0.97
SM 41:4	1.00	0.99	1.00	0.99	1.00	0.91	0.85	0.84		1.00	0.84	1.00	1.00	1.00	0.75	0.83	0.69
SM 41:6	1.00	0.99	1.00	0.99	1.00	0.79	0.82	0.66		1.00	0.66	1.00	1.00	1.00	0.85	0.83	0.80
SM 42:1	1.00	0.99	1.00	0.99	1.00	0.95	0.83	0.78		1.00	0.78	1.00	1.00	1.00	0.62	0.77	0.34
SM 42:2	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.65		1.00	0.65	1.00	1.00	1.00	0.86	0.90	1.00
SM 42:3	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.50		1.00	0.50	1.00	1.00	1.00	0.90	0.81	0.85
SM 42:4	1.00	0.99	1.00	0.99	1.00	0.99	0.73	0.75		1.00	0.75	1.00	1.00	1.00	0.85	0.56	0.61
SM 42:5	1.00	0.99	1.00	0.99	1.00	0.99	0.88	0.90		1.00	0.90	1.00	1.00	1.00	0.89	0.81	0.86
SM 42:6	1.00	0.99	1.00	0.99	1.00	0.91	0.86	0.90		1.00	0.90	1.00	1.00	1.00	0.89	0.93	0.75
SM 43:1	1.00	0.99	1.00	0.99	1.00	0.93	0.99	0.95		1.00	0.95	1.00	1.00	1.00	0.10	0.64	0.07
SM 43:2	1.00	0.99	1.00	0.99	1.00	0.90	0.80	0.90		1.00	0.90	1.00	1.00	1.00	0.85	0.98	0.89
SM 43:3	1.00	0.99	1.00	0.99	1.00	0.90	0.84	0.98		1.00	0.98	1.00	1.00	1.00	0.97	0.89	0.99
SM 43:6	1.00	0.99	1.00	0.99	1.00	0.43	0.45	0.65		1.00	0.65	1.00	1.00	1.00	0.99	0.95	0.77
SM 43:8	1.00	0.99	1.00	0.99	1.00	0.35	0.81	0.65		1.00	0.65	1.00	1.00	1.00	0.85	0.36	0.53
SM 44:1	1.00	0.99	1.00	0.99	1.00	0.99	1.00	0.99		1.00	0.99	1.00	1.00	1.00	0.78	0.96	0.71
SM 44:2	1.00	0.99	1.00	0.99	1.00	0.94	0.76	0.89		1.00	0.89	1.00	1.00	1.00	0.85	0.96	0.97
SM 44:3	1.00	0.78	1.00	0.99	1.00	0.90	0.67	0.70		1.00	0.70	1.00	1.00	1.00	0.95	0.96	1.00
SM 44:5	1.00	0.99	1.00	0.99	1.00	0.81	0.67	0.42		1.00	0.42	1.00	1.00	1.00	0.85	0.66	0.92
SM 44:6	1.00	0.99	1.00	0.99	1.00	0.95	0.73	0.89		1.00	0.89	1.00	1.00	1.00	0.95	0.94	0.95
SM 45:7	1.00	0.99	1.00	0.99	1.00	0.96	0.90	0.98		1.00	0.98	1.00	1.00	1.00	0.88	0.99	0.55
TG 36:0	1.00	0.99	1.00	0.99	1.00	0.71	0.45	0.59		1.00	0.59	1.00	1.00	1.00	0.85	0.77	0.80
TG 38:0	1.00	0.99	1.00	0.99	1.00	0.79	0.45	0.70		1.00	0.70	1.00	1.00	1.00	0.72	0.77	0.85
TG 39:0	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.78		1.00	0.78	1.00	1.00	1.00	0.89	0.92	0.95
TG 40:0	1.00	0.99	1.00	0.99	1.00	0.80	0.49	0.70		1.00	0.70	1.00	1.00	1.00	0.66	0.81	0.79
TG 40:1	1.00	0.99	1.00	0.99	1.00	0.83	0.67	0.75		1.00	0.75	1.00	1.00	1.00	0.65	0.81	0.79
TG 41:0	1.00	0.99	1.00	0.99	1.00	0.80	0.67	0.75		1.00	0.75	1.00	1.00	1.00	0.69	0.82	0.83
TG 42:0	1.00	0.99	1.00	0.99	1.00	0.79	0.53	0.67		1.00	0.67	1.00	1.00	1.00	0.62	0.82	0.80
TG 42:1	1.00	0.99	1.00	0.99	1.00	0.90	0.67	0.78		1.00	0.78	1.00	1.00	1.00	0.62	0.82	0.78
TG 42:2	1.00	0.99	1.00	0.99	1.00	0.90	0.67	0.91		1.00	0.91	1.00	1.00	1.00	0.79	0.92	0.89
TG 42:3	1.00	0.99	1.00	0.99	1.00	0.99	0.73	0.98		1.00	0.98	1.00	1.00	1.00	0.71	0.96	0.95
TG 43:0	1.00	0.99	1.00	0.99	1.00	0.78	0.53	0.64		1.00	0.64	1.00	1.00	1.00	0.85	0.96	0.89
TG 43:1	1.00	0.99	1.00	0.99	1.00	0.90	0.68	0.67		1.00	0.67	1.00	1.00	1.00	0.64	0.77	0.78
TG 43:2	1.00	0.99	1.00	0.99	1.00	0.99	0.72	0.91		1.00	0.91	1.00	1.00	1.00	0.97	0.96	0.95
TG 44:0	1.00	0.99	1.00	0.99	1.00	0.79	0.45	0.65		1.00	0.65	1.00	1.00	1.00	0.64	0.81	0.75
TG 44:1	1.00	0.99	1.00	0.99	1.00	0.87	0.67	0.70		1.00	0.70	1.00	1.00	1.00	0.57	0.77	0.73
TG 44:2	1.00	0.99	1.00	0.99	1.00	0.90	0.71	0.90		1.00	0.90	1.00	1.00	1.00	0.79	0.89	0.92
TG 44:3	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.96		1.00	0.96	1.00	1.00	1.00	0.76	0.90	0.95
TG 45:0	1.00	0.99	1.00	0.99	1.00	0.79	0.42	0.43		1.00	0.43	1.00	1.00	1.00	0.57	0.81	0.75
TG 45:1	1.00	0.99	1.00	0.99	1.00	0.71	0.45	0.49		1.00	0.49	1.00	1.00	1.00	0.65	0.77	0.68
TG 45:2	1.00	0.99	1.00	0.99	1.00	0.91	0.68	0.85		1.00	0.85	1.00	1.00	1.00	0.82	0.83	0.86
TG 46:0	1.00	0.99	1.00	0.99	1.00	0.81	0.67	0.64		1.00	0.64	1.00	1.00	1.00	0.48	0.71	0.55
TG 46:1	1.00	0.99	1.00	0.99	1.00	0.85	0.62	0.82		1.00	0.82	1.00	1.00	1.00	0.57	0.71	0.62
TG 46:2	1.00	0.99	1.00	0.99	1.00	0.91	0.68	0.93		1.00	0.93	1.00	1.00	1.00	0.65	0.77	0.75
TG 46:3	1.00	0.99	1.00	0.99	1.00	0.94	0.73	0.98		1.00	0.98	1.00	1.00	1.00	0.83	0.81	0.84
TG 47:0	1.00	0.99	1.00	0.99	1.00	0.80	0.68	0.49		1.00	0.49	1.00	1.00	1.00	0.71	0.81	0.74

Table S2.6J: MEAL Study significant difference within diet comparisons for all lipids (Triacylglycerol 47:1 to Triacylglycerol 56:0)

	Within Diet Comparisons (FDR <0.1)																	
	High Fat Diet									High Carbohydrate Diet								
Lipid/Day	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21		B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21
TG 47:1	1.00	0.99	1.00	0.99	1.00	0.81	0.67	0.65		1.00	0.65	1.00	1.00	1.00	0.64	0.71	0.60
TG 47:2	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.86		1.00	0.86	1.00	1.00	1.00	0.71	0.83	0.79
TG 47:3	1.00	0.99	1.00	0.99	1.00	0.91	0.73	1.00		1.00	1.00	1.00	1.00	1.00	0.89	0.83	0.89
TG 48:0	1.00	0.99	1.00	0.99	1.00	0.81	0.68	0.65		1.00	0.65	1.00	1.00	1.00	0.62	0.77	0.70
TG 48:1	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.88		1.00	0.88	1.00	1.00	1.00	0.62	0.71	0.61
TG 48:2	1.00	0.99	1.00	0.99	1.00	0.94	0.74	0.96		1.00	0.96	1.00	1.00	1.00	0.65	0.77	0.64
TG 48:3	1.00	0.99	1.00	0.99	1.00	0.94	0.82	0.67		1.00	0.67	1.00	1.00	1.00	0.78	0.81	0.77
TG 48:4	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.64		1.00	0.64	1.00	1.00	1.00	0.80	0.81	0.94
TG 48:5	1.00	0.99	1.00	0.99	1.00	0.99	0.87	0.67		1.00	0.67	1.00	1.00	1.00	0.72	0.81	0.86
TG 49:0	1.00	0.99	1.00	0.99	1.00	0.70	0.67	0.49		1.00	0.49	1.00	1.00	1.00	0.73	0.83	0.61
TG 49:1	1.00	0.99	1.00	0.99	1.00	0.82	0.71	0.65		1.00	0.65	1.00	1.00	1.00	0.71	0.77	0.74
TG 49:2	1.00	0.99	1.00	1.00	1.00	0.90	0.74	0.84		1.00	0.84	1.00	1.00	1.00	0.85	0.81	0.74
TG 49:3	1.00	0.99	1.00	0.99	1.00	0.91	0.76	1.00		1.00	1.00	1.00	1.00	1.00	0.89	0.93	0.79
TG 50:0	1.00	0.99	1.00	0.99	1.00	0.82	0.71	0.70		1.00	0.70	1.00	1.00	1.00	0.45	0.55	0.55
TG 50:1	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.84		1.00	0.84	1.00	1.00	1.00	0.57	0.55	0.55
TG 50:2	1.00	0.99	1.00	0.99	1.00	0.99	0.95	0.92		1.00	0.92	1.00	1.00	1.00	0.65	0.56	0.61
TG 50:3	1.00	0.99	1.00	0.99	1.00	0.91	0.90	0.65		1.00	0.65	1.00	1.00	1.00	0.87	0.81	0.74
TG 50:4	1.00	0.99	1.00	0.99	1.00	0.89	0.85	0.49		1.00	0.49	1.00	1.00	1.00	0.96	0.96	0.97
TG 50:5	1.00	0.99	1.00	0.99	1.00	0.90	0.93	0.43		1.00	0.43	1.00	1.00	1.00	0.95	0.93	0.93
TG 50:6	1.00	0.99	1.00	0.99	1.00	0.91	0.85	0.61		1.00	0.61	1.00	1.00	1.00	0.91	0.82	0.95
TG 51:0	1.00	0.99	1.00	0.99	1.00	0.93	0.68	0.70		1.00	0.70	1.00	1.00	1.00	0.79	0.95	0.89
TG 51:1	1.00	0.99	1.00	0.99	1.00	0.81	0.68	0.64		1.00	0.64	1.00	1.00	1.00	0.62	0.66	0.61
TG 51:2	1.00	0.99	1.00	0.99	1.00	0.91	0.78	0.78		1.00	0.78	1.00	1.00	1.00	0.75	0.64	0.62
TG 51:3	1.00	0.99	1.00	1.00	1.00	0.94	0.92	0.90		1.00	0.90	1.00	1.00	1.00	0.89	0.99	0.95
TG 51:4	1.00	0.99	1.00	0.99	1.00	0.91	0.92	0.49		1.00	0.49	1.00	1.00	1.00	0.62	0.55	0.77
TG 51:5	1.00	0.99	1.00	0.99	1.00	0.80	0.74	0.88		1.00	0.88	1.00	1.00	1.00	0.71	0.95	0.90
TG 52:0	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.65		1.00	0.65	1.00	1.00	1.00	0.57	0.75	0.61
TG 52:1	1.00	0.99	1.00	0.99	1.00	0.93	0.81	0.83		1.00	0.83	1.00	1.00	1.00	0.61	0.71	0.74
TG 52:2	1.00	0.99	1.00	0.99	1.00	0.91	0.83	0.86		1.00	0.86	1.00	1.00	1.00	0.73	0.58	0.77
TG 52:3	1.00	0.99	1.00	0.99	1.00	0.90	0.76	0.64		1.00	0.64	1.00	1.00	1.00	0.86	0.96	0.89
TG 52:4	1.00	0.99	1.00	0.99	1.00	0.91	0.81	0.55		1.00	0.55	1.00	1.00	1.00	0.71	0.87	0.77
TG 52:5	1.00	0.99	1.00	1.00	1.00	0.81	0.73	0.18		1.00	0.18	1.00	1.00	1.00	0.86	0.96	0.94
TG 52:6	1.00	0.99	1.00	0.99	1.00	0.80	0.74	0.15		1.00	0.15	1.00	1.00	1.00	0.94	0.93	0.86
TG 52:7	1.00	0.99	1.00	0.99	1.00	0.85	0.85	0.49		1.00	0.49	1.00	1.00	1.00	0.85	0.82	0.79
TG 53:0	1.00	0.99	1.00	0.99	1.00	0.93	0.81	0.91		1.00	0.91	1.00	1.00	1.00	0.98	0.99	0.95
TG 53:1	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.64		1.00	0.64	1.00	1.00	1.00	0.62	0.87	0.78
TG 53:2	1.00	0.99	1.00	0.99	1.00	0.96	0.90	0.90		1.00	0.90	1.00	1.00	1.00	0.68	0.64	0.55
TG 53:3	1.00	0.99	1.00	0.99	1.00	0.99	0.96	0.99		1.00	0.99	1.00	1.00	1.00	0.91	0.98	0.99
TG 53:4	1.00	0.99	1.00	0.99	1.00	0.96	0.88	0.70		1.00	0.70	1.00	1.00	1.00	0.85	0.81	0.90
TG 53:5	1.00	0.99	1.00	0.99	1.00	0.85	0.84	0.49		1.00	0.49	1.00	1.00	1.00	0.88	0.95	0.80
TG 54:0	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.92		1.00	0.92	1.00	1.00	1.00	0.62	0.83	0.95
TG 54:1	1.00	0.99	1.00	0.99	1.00	0.91	0.74	0.67		1.00	0.67	1.00	1.00	1.00	0.69	0.96	0.77
TG 54:2	1.00	0.99	1.00	0.99	1.00	0.91	0.99	0.99		1.00	0.99	1.00	1.00	1.00	0.65	0.81	0.77
TG 54:3	1.00	0.99	1.00	0.99	1.00	0.82	0.74	0.70		1.00	0.70	1.00	1.00	1.00	0.89	0.93	0.95
TG 54:4	1.00	0.99	1.00	0.99	1.00	0.80	0.73	0.49		1.00	0.49	1.00	1.00	1.00	0.88	0.93	0.86
TG 54:5	1.00	0.99	1.00	0.99	1.00	0.80	0.73	0.30		1.00	0.30	1.00	1.00	1.00	0.81	0.92	0.78
TG 54:6	1.00	0.99	1.00	0.99	1.00	0.80	0.73	0.24		1.00	0.24	1.00	1.00	1.00	0.81	0.89	0.77
TG 54:7	1.00	0.99	1.00	0.99	1.00	0.79	0.73	0.12		1.00	0.12	1.00	1.00	1.00	0.89	0.96	0.95
TG 54:8	1.00	0.99	1.00	0.99	1.00	0.80	0.76	0.13		1.00	0.13	1.00	1.00	1.00	0.95	0.95	0.90
TG 55:0	1.00	0.99	1.00	0.99	1.00	0.93	0.78	0.98		1.00	0.98	1.00	1.00	1.00	0.10	0.35	0.33
TG 55:2	1.00	0.99	1.00	0.99	1.00	0.91	0.92	0.80		1.00	0.80	1.00	1.00	1.00	0.78	0.96	0.86
TG 55:3	1.00	0.99	1.00	0.99	1.00	0.90	0.88	0.90		1.00	0.90	1.00	1.00	1.00	0.88	0.96	0.74
TG 55:4	1.00	0.99	1.00	0.99	1.00	0.91	0.73	0.75		1.00	0.75	1.00	1.00	1.00	0.95	0.95	0.95
TG 55:5	1.00	0.99	1.00	0.99	1.00	0.79	0.84	0.80		1.00	0.80	1.00	1.00	1.00	0.85	0.81	0.77
TG 56:0	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.76		1.00	0.76	1.00	1.00	1.00	0.97	0.98	0.97

Table S2.6K: MEAL Study significant difference within diet comparisons for all lipids (Triacylglycerol 56:1 to Triacylglycerol 62:12)

	Within Diet Comparisons (FDR <0.1)															
	High Fat Diet								High Carbohydrate Diet							
Lipid/Day	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21	B to S	S to 2	2 to 7	7 to 14	14 to 21	S to 7	S to 14	S to 21
TG 56:1	1.00	0.99	1.00	0.99	1.00	0.97	0.79	0.70	1.00	0.70	1.00	1.00	1.00	0.94	0.93	0.99
TG 56:10	1.00	0.99	1.00	0.99	1.00	0.82	0.79	0.18	1.00	0.18	1.00	1.00	1.00	0.86	0.94	0.89
TG 56:2	1.00	0.99	1.00	0.99	1.00	0.94	0.99	0.90	1.00	0.90	1.00	1.00	1.00	0.71	0.93	0.82
TG 56:3	1.00	0.99	1.00	0.99	1.00	0.81	0.73	0.67	1.00	0.67	1.00	1.00	1.00	0.71	0.90	0.83
TG 56:4	1.00	0.99	1.00	0.99	1.00	0.80	0.71	0.49	1.00	0.49	1.00	1.00	1.00	0.87	0.96	0.86
TG 56:5	1.00	0.99	1.00	0.99	1.00	0.80	0.68	0.49	1.00	0.49	1.00	1.00	1.00	0.91	0.94	0.92
TG 56:6	1.00	0.99	1.00	0.99	1.00	0.81	0.73	0.49	1.00	0.49	1.00	1.00	1.00	0.97	0.96	0.98
TG 56:7	1.00	0.99	1.00	0.99	1.00	0.91	0.76	0.64	1.00	0.64	1.00	1.00	1.00	0.97	0.94	0.95
TG 56:8	1.00	0.99	1.00	0.99	1.00	0.91	0.84	0.70	1.00	0.70	1.00	1.00	1.00	0.98	0.99	0.96
TG 56:9	1.00	0.99	1.00	0.99	1.00	0.86	0.76	0.41	1.00	0.41	1.00	1.00	1.00	1.00	0.95	0.99
TG 57:2	1.00	0.99	1.00	0.99	1.00	0.90	0.73	0.61	1.00	0.61	1.00	1.00	1.00	0.73	1.00	0.87
TG 57:4	1.00	0.99	1.00	0.99	1.00	0.90	0.72	0.39	1.00	0.39	1.00	1.00	1.00	0.48	0.95	0.68
TG 58:1	1.00	0.99	1.00	0.99	1.00	0.91	0.95	0.98	1.00	0.98	1.00	1.00	1.00	0.45	0.99	0.62
TG 58:10	1.00	0.99	1.00	0.99	1.00	0.91	0.90	0.67	1.00	0.67	1.00	1.00	1.00	0.99	0.99	0.94
TG 58:11	1.00	0.99	1.00	0.99	1.00	0.90	0.99	0.63	1.00	0.63	1.00	1.00	1.00	0.94	0.87	0.92
TG 58:2	1.00	0.99	1.00	0.99	1.00	0.86	0.98	0.90	1.00	0.90	1.00	1.00	1.00	0.65	0.71	0.77
TG 58:3	1.00	0.99	1.00	0.99	1.00	0.90	0.79	0.70	1.00	0.70	1.00	1.00	1.00	0.71	0.83	0.73
TG 58:4	1.00	0.99	1.00	0.99	1.00	0.81	0.73	0.65	1.00	0.65	1.00	1.00	1.00	0.62	0.64	0.61
TG 58:5	1.00	0.99	1.00	0.99	1.00	0.79	0.73	0.53	1.00	0.53	1.00	1.00	1.00	0.92	0.81	0.97
TG 58:6	1.00	0.99	1.00	0.99	1.00	0.90	0.76	0.70	1.00	0.70	1.00	1.00	1.00	0.99	0.93	0.95
TG 58:7	1.00	0.99	1.00	0.99	1.00	0.90	0.81	0.75	1.00	0.75	1.00	1.00	1.00	0.85	0.89	0.93
TG 58:8	1.00	0.99	1.00	1.00	1.00	0.90	0.76	0.67	1.00	0.67	1.00	1.00	1.00	0.85	0.90	0.85
TG 58:9	1.00	0.99	1.00	0.99	1.00	0.90	0.78	0.65	1.00	0.65	1.00	1.00	1.00	0.98	0.95	0.94
TG 60:10	1.00	0.99	1.00	0.99	1.00	0.92	0.80	0.91	1.00	0.91	1.00	1.00	1.00	0.73	0.81	0.82
TG 60:11	1.00	0.99	1.00	0.99	1.00	0.99	0.86	0.98	1.00	0.98	1.00	1.00	1.00	0.85	0.83	0.93
TG 60:12	1.00	0.99	1.00	0.99	1.00	0.98	0.80	0.91	1.00	0.91	1.00	1.00	1.00	0.94	0.90	0.86
TG 62:12	1.00	0.99	1.00	0.99	1.00	0.98	0.85	0.98	1.00	0.98	1.00	1.00	1.00	0.85	0.83	0.77

Table S2.7A: MEAL Study significant differences for between diet comparisons for all lipids (16:0 Cholesterol ester to Ceramide [NS] 36:2)

	Between Diet Comparisons FDR <0.1					
Lipid/Day	B v B	S v S	2v2	7v7	14v14	21v21
16:0 CE	0.961	0.994	0.941	0.957	0.365	0.570
16:1 CE	0.923	0.994	0.538	0.308	0.031	0.073
18:0 CE	0.781	0.994	0.872	0.732	0.673	0.983
18:1 CE	0.899	0.994	0.224	0.644	0.078	0.426
18:2 CE	0.781	0.994	0.881	0.797	0.694	0.596
18:3 CE	0.909	0.994	0.766	0.496	0.222	0.243
20:3 CE	0.781	0.994	0.829	0.127	0.043	0.039
20:4 CE	0.781	0.994	0.868	0.855	0.375	0.702
20:5 CE	0.781	0.994	0.884	0.440	0.622	0.434
22:4 CE	0.956	0.994	0.872	0.847	0.564	0.874
22:5 CE	0.781	0.994	0.297	0.406	0.211	0.175
22:6 CE	0.818	0.994	0.870	0.918	0.258	0.282
ACAR 10:0	0.781	0.994	0.235	0.661	0.962	0.527
ACAR 10:1	0.981	0.994	0.566	0.642	0.886	0.733
ACAR 12:0	0.899	0.994	0.224	0.459	0.731	0.187
ACAR 14:0	0.909	0.994	0.722	0.218	0.796	0.418
ACAR 14:1	0.800	0.994	0.071	0.934	0.880	0.753
ACAR 14:2	0.937	0.994	0.064	0.939	0.942	0.906
ACAR 16:0	0.917	0.994	0.691	0.005	0.883	0.108
ACAR 18:0	0.967	0.994	0.277	0.203	0.258	0.084
ACAR 18:1	0.909	0.994	0.740	0.644	0.563	0.961
ACAR 18:2	0.963	0.994	0.620	0.644	0.821	0.986
ACAR 20:0	0.950	0.994	0.214	0.769	0.989	0.243
ACAR 24:0	0.804	0.994	0.110	0.127	0.245	0.009
ACAR 26:0	0.951	0.994	0.410	0.362	0.211	0.094
Cer[AS] 34:1	0.781	0.994	0.878	0.948	0.643	0.701
Cer[AS] 42:2	0.909	0.994	0.654	0.871	0.954	0.912
Cer[EODS] 57:2	0.899	0.994	0.741	0.526	0.795	0.213
Cer[EODS] 58:0	0.781	0.994	0.566	0.642	0.471	0.669
Cer[EODS] 60:0	0.910	0.994	0.842	0.939	0.699	0.099
Cer[NDS] 34:0	0.909	0.994	0.397	0.320	0.457	0.201
Cer[NDS] 36:0	0.818	0.994	0.140	0.398	0.583	0.588
Cer[NDS] 38:0	0.956	0.994	0.055	0.459	0.883	0.059
Cer[NDS] 39:0	0.891	0.994	0.314	0.306	0.375	0.175
Cer[NDS] 40:0	0.987	0.994	0.038	0.235	0.586	0.109
Cer[NDS] 41:0	0.899	0.994	0.038	0.127	0.258	0.175
Cer[NDS] 42:0	0.909	0.994	0.051	0.218	0.480	0.072
Cer[NDS] 42:1	0.961	0.994	0.277	0.588	0.698	0.295
Cer[NDS] 42:2	0.987	0.994	0.880	0.756	0.585	0.646
Cer[NDS] 43:0	0.989	0.994	0.055	0.141	0.457	0.009
Cer[NP] 34:0	0.781	0.994	0.884	0.418	0.268	0.682
Cer[NP] 40:0	0.944	0.994	0.055	0.238	0.354	0.010
Cer[NP] 41:0	0.909	0.994	0.736	0.795	0.981	0.248
Cer[NP] 41:1	0.923	0.994	0.271	0.847	0.883	0.669
Cer[NP] 42:0	0.909	0.994	0.953	0.847	0.951	0.527
Cer[NP] 42:1	0.961	0.994	0.172	0.892	0.628	0.527
Cer[NS] 32:1	0.781	0.994	0.947	0.852	0.314	0.588
Cer[NS] 33:1	0.909	0.994	0.881	0.994	0.142	0.642
Cer[NS] 33:4	0.804	0.994	0.566	0.541	0.338	0.740
Cer[NS] 34:1	0.818	0.994	0.102	0.852	0.078	0.371
Cer[NS] 34:2	0.899	0.994	0.466	0.957	0.330	0.667
Cer[NS] 35:1	0.834	0.994	0.581	0.666	0.211	0.511
Cer[NS] 36:1	0.800	0.994	0.957	0.891	0.454	0.753
Cer[NS] 36:2	0.800	0.994	0.867	0.769	0.029	0.548

Table S2.7B: MEAL Study significant differences for between diet comparisons for all lipids (Ceramide [NS] 37:1 to Free Fatty Acid 20:1)

	Between Diet Comparisons					
	FDR <0.1					
Lipid/Day	B v B	S v S	2v2	7v7	14v14	21v21
Cer[NS] 37:1	0.781	0.994	0.171	0.398	0.883	0.527
Cer[NS] 38:1	0.799	0.994	0.725	0.992	0.620	0.640
Cer[NS] 38:2	0.818	0.994	0.842	0.847	0.295	0.578
Cer[NS] 39:1	0.909	0.994	0.741	0.756	0.883	0.109
Cer[NS] 40:1	0.818	0.994	0.884	0.958	0.996	0.491
Cer[NS] 40:2	0.818	0.994	0.566	0.847	0.338	0.843
Cer[NS] 40:3	0.923	0.994	0.073	0.387	0.400	0.680
Cer[NS] 41:1	0.899	0.994	0.988	0.930	0.977	0.585
Cer[NS] 41:2	0.818	0.994	0.495	0.839	0.280	0.770
Cer[NS] 41:4	0.899	0.994	0.738	0.298	0.883	0.642
Cer[NS] 42:1	0.910	0.994	0.881	0.979	0.907	0.667
Cer[NS] 42:2	0.899	0.994	0.706	0.706	0.258	0.505
Cer[NS] 42:3	0.961	0.994	0.907	0.847	0.136	0.527
Cer[NS] 43:1	0.781	0.994	0.738	0.756	0.891	0.294
Cer[NS] 43:2	0.961	0.994	0.501	0.813	0.898	0.926
Cer[NS] 44:1	0.961	0.994	0.184	0.459	0.810	0.213
Cer[NS] 44:2	0.987	0.994	0.135	0.847	0.796	0.961
Cer[NS] 44:4	0.781	0.998	0.842	0.812	0.788	0.213
Cer[NS] 45:1	0.818	0.994	0.055	0.524	0.899	0.449
Cer[NS] 46:5	0.909	0.994	0.566	0.890	0.353	0.616
DG 30:0	0.899	0.994	0.908	0.957	0.381	0.982
DG 30:1	0.991	0.994	0.657	0.906	0.891	0.940
DG 32:0	0.818	0.994	0.725	0.957	0.696	0.819
DG 32:1	0.852	0.994	0.198	0.959	0.583	0.456
DG 32:2	0.800	0.994	0.654	0.847	0.754	0.873
DG 33:0	0.781	0.994	0.606	0.939	0.962	0.566
DG 33:1	0.909	0.994	0.561	0.992	0.894	0.527
DG 34:0	0.818	0.994	0.566	0.955	0.989	0.874
DG 34:2	0.818	0.994	0.448	0.847	0.442	0.398
DG 34:3	0.818	0.994	0.109	0.459	0.375	0.179
DG 35:1	0.961	0.994	0.761	0.852	0.858	0.885
DG 35:2	0.909	0.994	0.583	0.847	0.701	0.823
DG 35:3	0.899	0.994	0.799	0.866	0.699	0.471
DG 36:0	0.818	0.994	0.941	0.918	0.890	0.771
DG 36:1	0.907	0.994	0.566	0.891	0.951	0.912
DG 36:2	0.909	0.994	0.198	0.644	0.338	0.349
DG 36:3	0.981	0.994	0.434	0.756	0.408	0.198
DG 36:4	0.944	0.994	0.978	0.883	0.975	0.761
DG 36:5	0.961	0.994	0.691	0.691	0.937	0.050
DG 38:1	0.956	0.994	0.590	0.140	0.031	0.119
DG 38:2	0.909	0.994	0.867	0.971	0.891	0.968
DG 38:3	0.937	0.994	0.706	0.797	0.530	0.952
DG 38:4	0.975	0.994	0.237	0.923	0.286	0.804
DG 38:5	0.951	0.994	0.566	0.706	0.641	0.185
DG 38:6	0.981	0.994	0.706	0.830	0.671	0.248
DG 38:7	0.934	0.994	0.941	0.855	0.636	0.393
DG 40:6	0.907	0.994	0.417	0.758	0.454	0.393
DG 40:7	0.987	0.994	0.763	0.847	0.986	0.612
FFA 16:0	0.909	0.994	0.566	0.957	0.509	0.540
FFA 18:0	0.981	0.994	0.782	0.830	0.530	0.616
FFA 18:1	0.956	0.994	0.909	0.936	0.338	0.646
FFA 18:2	0.963	0.994	0.566	0.940	0.505	0.952
FFA 20:0	0.899	0.994	0.691	0.964	0.699	0.901
FFA 20:1	0.981	0.994	0.978	0.892	0.375	0.718

Table S2.7C: MEAL Study significant differences for between diet comparisons for all lipids (Fatty Acid 20:2 to Lysophosphatidylethanolamine 22:4)

	Between Diet Comparisons					
	FDR <0.1					
Lipid/Day	B v B	S v S	2v2	7v7	14v14	21v21
FFA 20:2	0.961	0.994	0.870	0.630	0.211	0.455
FFA 20:4	0.781	0.994	0.820	0.444	0.226	0.451
FFA 22:0	0.865	0.994	0.875	0.923	0.951	0.819
FFA 22:1	0.975	0.994	0.109	0.983	0.391	0.897
FFA 22:2	0.967	0.994	0.988	0.892	0.539	0.527
FFA 22:3	0.987	0.994	0.208	0.871	0.469	0.642
FFA 24:0	0.909	0.994	0.871	0.852	0.959	0.566
FFA 24:1	0.909	0.994	0.784	0.852	0.731	0.534
FFA 24:2	0.975	0.994	0.871	0.892	0.498	0.646
FFA 24:3	0.987	0.994	0.988	0.746	0.813	0.901
GlcCer[NS] 34:1	0.818	0.994	0.881	0.811	0.721	0.874
GlcCer[NS] 34:2	0.931	0.994	0.313	0.322	0.154	0.526
GlcCer[NS] 40:1	0.781	0.994	0.706	0.934	0.938	0.371
GlcCer[NS] 41:1	0.981	0.994	0.941	0.418	0.371	0.213
GlcCer[NS] 42:1	0.781	0.994	0.563	0.992	0.698	0.952
GlcCer[NS] 42:2	0.800	0.994	0.561	0.589	0.233	0.172
LysoPC 14:0	0.909	0.994	0.761	0.847	0.788	0.964
LysoPC 15:0	0.951	0.994	0.842	0.648	0.671	0.527
LysoPC 15:1	0.818	0.994	0.867	0.844	0.938	0.592
LysoPC 16:0	0.981	0.994	0.606	0.692	0.290	0.212
LysoPC 16:1	0.818	0.994	0.071	0.460	0.163	0.041
LysoPC 17:1	0.956	0.994	0.389	0.847	0.798	0.785
LysoPC 18:0	0.909	0.994	0.784	0.957	0.938	0.701
LysoPC 18:1	0.909	0.994	0.884	0.847	0.652	0.431
LysoPC 18:2	0.907	0.994	0.492	0.621	0.408	0.425
LysoPC 18:3	0.818	0.994	0.943	0.982	0.962	0.560
LysoPC 19:0	0.967	0.994	0.754	0.892	0.746	0.591
LysoPC 19:1	0.909	0.994	0.884	0.958	0.890	0.871
LysoPC 20:0	0.989	0.994	0.672	0.998	0.915	0.359
LysoPC 20:1	0.981	0.994	0.276	0.706	0.338	0.425
LysoPC 20:2	0.951	0.994	0.644	0.644	0.529	0.451
LysoPC 20:3	0.992	0.994	0.593	0.617	0.375	0.278
LysoPC 20:4	0.961	0.994	0.875	0.891	0.598	0.596
LysoPC 20:5	0.917	0.994	0.820	0.812	0.338	0.349
LysoPC 22:0	0.925	0.994	0.875	0.852	0.823	0.789
LysoPC 22:4	0.989	0.998	0.657	0.325	0.314	0.526
LysoPC 22:5	0.996	0.994	0.606	0.643	0.326	0.282
LysoPC 22:6	0.917	0.994	0.784	0.784	0.245	0.200
LysoPC 23:0	0.899	0.994	0.881	0.847	0.891	0.874
LysoPC 24:0	0.950	0.994	0.784	0.954	0.480	0.930
LysoPC 24:1	0.961	0.994	0.566	0.715	0.457	0.109
LysoPC 26:1	0.899	0.994	0.496	0.322	0.163	0.110
LysoPE 16:0	0.902	0.994	0.419	0.588	0.245	0.213
LysoPE 16:1	0.781	0.994	0.169	0.617	0.454	0.231
LysoPE 17:0	0.899	0.994	0.909	0.715	0.190	0.418
LysoPE 18:0	0.899	0.994	0.673	0.706	0.526	0.871
LysoPE 18:1	0.834	0.994	0.988	0.944	0.883	0.791
LysoPE 18:2	0.818	0.994	0.357	0.644	0.529	0.243
LysoPE 18:3	0.818	0.994	0.893	0.936	0.880	0.899
LysoPE 20:2	0.961	0.994	0.831	0.769	0.747	0.940
LysoPE 20:3	0.818	0.994	0.654	0.396	0.338	0.248
LysoPE 20:4	0.981	0.994	0.884	0.947	0.651	0.874
LysoPE 20:5	0.951	0.994	0.843	0.847	0.466	0.425
LysoPE 22:4	0.818	0.994	0.620	0.415	0.338	0.088

Table S2.7D: MEAL Study significant differences for between diet comparisons for all lipids (Lysophosphatidylethanolamine 22:5 to Phosphatidylcholine 38:1)

	Between Diet Comparisons					
	FDR <0.1					
Lipid/Day	B v B	S v S	2 v 2	7 v 7	14 v 14	21 v 21
LysoPE 22:5	0.909	0.994	0.566	0.412	0.239	0.089
LysoPE 22:6	0.899	0.994	0.875	0.847	0.457	0.739
LysoPE 24:0	0.981	0.994	0.987	0.854	0.583	0.734
PA 34:1	0.781	0.994	0.263	0.644	0.258	0.152
PA 34:2	0.781	0.994	0.456	0.325	0.277	0.527
PA 36:1	0.781	0.994	0.240	0.459	0.891	0.776
PA 36:2	0.781	0.994	0.881	0.847	0.277	0.548
PA 36:3	0.781	0.994	0.128	0.235	0.078	0.248
PA 36:4	0.975	0.994	0.876	0.661	0.975	0.503
PA 38:6	0.899	0.994	0.881	0.661	0.245	0.425
PC 24:0	0.937	0.994	0.038	0.398	0.314	0.725
PC 26:0	0.975	0.994	0.095	0.351	0.211	0.285
PC 27:0	0.818	0.994	0.656	0.847	0.731	0.321
PC 28:2	0.818	0.994	0.916	0.614	0.671	0.581
PC 29:0	0.977	0.994	0.566	0.453	0.363	0.585
PC 30:0	0.929	0.994	0.941	0.871	0.880	0.739
PC 30:2	0.818	0.994	0.768	0.238	0.268	0.871
PC 31:0	0.909	0.994	0.593	0.235	0.273	0.255
PC 31:1	0.917	0.994	0.566	0.706	0.457	0.753
PC 32:0	0.818	0.994	0.768	0.469	0.898	0.891
PC 32:1	0.818	0.994	0.062	0.298	0.226	0.093
PC 32:2	0.909	0.994	0.867	0.644	0.535	0.871
PC 32:3	0.799	0.994	0.796	0.588	0.843	0.527
PC 33:0	0.909	0.994	0.844	0.398	0.843	0.566
PC 33:1	0.981	0.994	0.566	0.940	0.339	0.636
PC 33:2	0.907	0.994	0.020	0.008	0.044	0.007
PC 33:3	0.967	0.994	0.784	0.541	0.669	0.872
PC 34:1	0.909	0.994	0.098	0.322	0.226	0.136
PC 34:2	0.909	0.994	0.855	0.814	0.496	0.581
PC 34:3	0.818	0.994	0.277	0.814	0.413	0.501
PC 34:4	0.961	0.994	0.763	0.892	0.858	0.616
PC 34:5	0.818	0.994	0.875	0.847	0.690	0.646
PC 35:0	0.904	0.994	0.208	0.127	0.462	0.541
PC 35:1	0.818	0.994	0.315	0.406	0.344	0.986
PC 35:2	0.909	0.994	0.098	0.692	0.226	0.010
PC 35:3	0.781	0.994	0.341	0.644	0.340	0.986
PC 35:4	0.818	0.994	0.988	0.852	0.713	0.616
PC 35:5	0.909	0.994	0.784	0.854	0.714	0.929
PC 35:6	0.987	0.994	0.691	0.744	0.286	0.739
PC 36:0	0.818	0.994	0.988	0.942	0.701	0.776
PC 36:1	0.899	0.994	0.774	0.935	0.723	0.884
PC 36:2	0.909	0.994	0.583	0.847	0.723	0.511
PC 36:3	0.859	0.994	0.878	0.923	0.592	0.526
PC 36:4	0.961	0.994	0.855	0.813	0.340	0.753
PC 36:5	0.996	0.994	0.553	0.617	0.245	0.078
PC 36:6	0.478	0.994	0.782	0.847	0.830	0.615
PC 37:1	0.899	0.994	0.864	0.715	0.564	0.968
PC 37:2	0.781	0.994	0.741	0.847	0.813	0.789
PC 37:3	0.899	0.994	0.838	0.847	0.788	0.901
PC 37:4	0.781	0.994	0.875	0.643	0.556	0.968
PC 37:5	0.899	0.994	0.436	0.691	0.226	0.221
PC 37:6	0.945	0.994	0.941	0.847	0.277	0.874
PC 37:7	0.981	0.994	0.941	0.852	0.344	0.986
PC 38:1	0.961	0.994	0.829	0.654	0.415	0.680

Table S2.7E: MEAL Study significant differences for between diet comparisons for all lipids (Phosphatidylcholine 38:2 to Phosphatidylethanolamine 34:4)

	Between Diet Comparisons					
	FDR <0.1					
Lipid/Day	B v B	S v S	2 v 2	7 v 7	14 v 14	21 v 21
PC 38:2	0.984	0.994	0.774	0.758	0.622	0.952
PC 38:3	0.800	0.994	0.064	0.263	0.174	0.046
PC 38:4	0.781	0.994	0.467	0.592	0.258	0.213
PC 38:5	0.825	0.994	0.172	0.263	0.043	0.046
PC 38:6	0.899	0.998	0.331	0.644	0.205	0.235
PC 38:7	0.967	0.994	0.357	0.706	0.277	0.221
PC 39:3	0.781	0.994	0.761	0.617	0.820	0.652
PC 39:4	0.781	0.994	0.467	0.934	0.526	0.431
PC 39:6	0.818	0.994	0.320	0.666	0.338	0.448
PC 39:7	0.981	0.994	0.389	0.459	0.245	0.669
PC 39:8	0.910	0.994	0.941	0.847	0.775	0.874
PC 40:0	0.902	0.994	0.466	0.644	0.526	0.952
PC 40:1	0.909	0.994	0.996	0.934	0.526	0.885
PC 40:2	0.781	0.994	0.867	0.756	0.907	0.642
PC 40:4	0.899	0.994	0.566	0.415	0.084	0.212
PC 40:5	0.818	0.994	0.055	0.140	0.040	0.009
PC 40:6	0.899	0.994	0.171	0.478	0.120	0.092
PC 40:7	0.818	0.994	0.389	0.644	0.210	0.243
PC 40:8	0.781	0.994	0.581	0.644	0.120	0.566
PC 41:3	0.981	0.994	0.725	0.934	0.496	0.982
PC 41:4	0.818	0.994	0.838	0.930	0.891	0.702
PC 41:5	0.818	0.994	0.761	0.964	0.599	0.272
PC 41:6	0.981	0.994	0.071	0.617	0.154	0.330
PC 41:7	0.836	0.994	0.916	0.813	0.928	0.680
PC 42:1	0.917	0.994	0.466	0.812	0.391	0.319
PC 42:10	0.903	0.994	0.868	0.847	0.268	0.589
PC 42:2	0.909	0.994	0.875	0.934	0.816	0.701
PC 42:3	0.981	0.994	0.397	0.847	0.626	0.131
PC 42:4	0.899	0.994	0.754	0.459	0.353	0.573
PC 42:5	0.992	0.994	0.595	0.541	0.258	0.174
PC 42:6	0.781	0.994	0.271	0.235	0.027	0.015
PC 42:7	0.981	0.994	0.268	0.934	0.070	0.667
PC 42:8	0.909	0.994	0.309	0.298	0.108	0.064
PC 42:9	0.818	0.994	0.055	0.398	0.070	0.029
PC 44:12	0.834	0.994	0.620	0.756	0.525	0.592
PC 44:2	0.894	0.994	0.941	0.852	0.496	0.669
PC 44:3	0.956	0.994	0.586	0.944	0.796	0.291
PC 44:4	0.961	0.994	0.394	0.322	0.574	0.451
PC 44:5	0.996	0.994	0.020	0.918	0.226	0.066
PC 44:6	0.981	0.994	0.867	0.892	0.891	0.669
PC 44:8	0.951	0.994	0.864	0.532	0.886	0.125
PC 46:4	0.818	0.994	0.389	0.235	0.403	0.411
PE 30:0	0.909	0.994	0.512	0.642	0.462	0.928
PE 32:0	0.844	0.994	0.988	0.617	0.962	0.869
PE 32:1	0.818	0.994	0.111	0.645	0.237	0.559
PE 32:2	0.996	0.994	0.884	0.450	0.226	0.566
PE 33:0	0.899	0.994	0.997	0.974	0.586	0.871
PE 33:1	0.818	0.994	0.271	0.906	0.858	0.425
PE 33:2	0.874	0.994	0.405	0.814	0.404	0.179
PE 34:0	0.917	0.994	0.665	0.854	0.886	0.874
PE 34:1	0.828	0.994	0.373	0.617	0.245	0.512
PE 34:2	0.909	0.994	0.784	0.938	0.962	0.819
PE 34:3	0.818	0.994	0.829	0.958	0.783	0.645
PE 34:4	0.818	0.994	0.566	0.847	0.432	0.843

Table S2.7F: MEAL Study significant differences for between diet comparisons for all lipids (Phosphatidylethanolamine 35:0 to Plasmenyl-phosphatidylcholine 35:3)

	Between Diet Comparisons					
	FDR <0.1					
Lipid/Day	B v B	S v S	2 v 2	7 v 7	14 v 14	21 v 21
PE 35:0	0.961	0.994	0.606	0.871	0.886	0.776
PE 35:1	0.975	0.994	0.750	0.847	0.943	0.636
PE 35:2	0.909	0.994	0.941	0.919	0.891	0.646
PE 35:4	0.961	0.994	0.871	0.957	0.795	0.372
PE 36:0	0.909	0.994	0.817	0.958	0.239	0.611
PE 36:1	0.896	0.994	0.881	0.849	0.788	0.871
PE 36:2	0.884	0.994	0.878	0.811	0.707	0.527
PE 36:3	0.818	0.994	0.716	0.706	0.591	0.252
PE 36:4	0.924	0.994	0.277	0.644	0.287	0.527
PE 36:5	0.950	0.994	0.606	0.661	0.526	0.443
PE 37:4	0.818	0.994	0.691	0.706	0.883	0.945
PE 38:3	0.899	0.994	0.878	0.957	0.245	0.884
PE 38:4	0.818	0.994	0.412	0.614	0.344	0.926
PE 38:5	0.961	0.994	0.566	0.706	0.353	0.867
PE 38:6	0.922	0.994	0.941	0.871	0.457	0.901
PE 38:7	0.996	0.994	0.699	0.847	0.589	0.799
PE 40:4	0.818	0.994	0.538	0.847	0.375	0.834
PE 40:5	0.951	0.994	0.561	0.643	0.211	0.760
PE 40:6	0.981	0.994	0.820	0.852	0.375	0.669
PE 40:7	0.961	0.994	0.561	0.847	0.526	0.871
PE 40:8	0.981	0.994	0.686	0.841	0.873	0.635
PE 42:10	0.937	0.994	0.988	0.715	0.945	0.871
PG 33:0	0.478	0.994	0.784	0.852	0.315	0.426
PG 34:0	0.907	0.994	0.639	0.847	0.921	0.255
PG 34:2	0.983	0.994	0.761	0.322	0.136	0.526
PG 36:0	0.951	0.994	0.884	0.992	0.452	0.982
PG 36:2	0.975	0.994	0.496	0.325	0.375	0.526
PG 36:3	0.951	0.998	0.855	0.811	0.142	0.666
PG 38:4	0.909	0.994	0.741	0.753	0.375	0.874
PI 25:0	0.781	0.994	0.868	0.847	0.314	0.940
PI 34:1	0.899	0.994	0.844	0.661	0.731	0.982
PI 34:2	0.818	0.994	0.829	0.957	0.457	0.874
PI 36:1	0.899	0.994	0.737	0.918	0.883	0.610
PI 36:2	0.961	0.994	0.875	0.852	0.919	0.739
PI 36:4	0.781	0.994	0.566	0.588	0.163	0.761
PI 38:3	0.781	0.994	0.621	0.648	0.094	0.642
PI 38:4	0.800	0.994	0.839	0.847	0.330	0.956
PI 38:5	0.818	0.994	0.566	0.706	0.297	0.885
PI 38:6	0.818	0.994	0.691	0.692	0.338	0.703
PI 40:5	0.899	0.994	0.741	0.706	0.136	0.630
PI 40:6	0.899	0.994	0.900	0.692	0.070	0.668
PlsCho 24:0	0.961	0.994	0.566	0.715	0.457	0.109
PlsCho 28:0	0.781	0.994	0.763	0.760	0.454	0.635
PlsCho 32:0	0.951	0.994	0.868	0.852	0.883	0.592
PlsCho 32:1	0.996	0.994	0.419	0.921	0.136	0.165
PlsCho 33:0	0.781	0.994	0.784	0.644	0.943	0.404
PlsCho 34:0	0.909	0.994	0.998	0.847	0.807	0.952
PlsCho 34:1	0.818	0.994	0.884	0.930	0.818	0.952
PlsCho 34:2	0.818	0.998	0.706	0.652	0.375	0.109
PlsCho 34:3	0.909	0.994	0.803	0.934	0.338	0.175
PlsCho 35:0	0.899	0.994	0.535	0.769	0.928	0.393
PlsCho 35:1	0.781	0.994	0.620	0.644	0.492	0.425
PlsCho 35:2	0.937	0.994	0.947	0.930	0.564	0.529
PlsCho 35:3	0.825	0.994	0.957	0.756	0.699	0.073

Table S2.7G: MEAL Study significant differences for between diet comparisons for all lipids (Plasmenyl-phosphatidylcholine 35:4 to Plasmenyl-phosphatidylethanolamine 36:1)

	Between Diet Comparisons					
	FDR <0.1					
Lipid/Day	B v B	S v S	2 v 2	7 v 7	14 v 14	21 v 21
PlsCho 35:4	0.899	0.994	0.691	0.847	0.996	0.201
PlsCho 36:0	0.981	0.994	0.878	0.921	0.526	0.237
PlsCho 36:2	0.818	0.994	0.947	0.957	0.975	0.791
PlsCho 36:3	0.909	0.994	0.563	0.398	0.699	0.012
PlsCho 36:4	0.781	0.994	0.844	0.934	0.890	0.296
PlsCho 36:5	0.818	0.994	0.784	0.974	0.907	0.611
PlsCho 36:6	0.781	0.994	0.561	0.398	0.832	0.982
PlsCho 37:1	0.910	0.994	0.953	0.342	0.920	0.667
PlsCho 37:2	0.895	0.994	0.140	0.821	0.457	0.573
PlsCho 37:3	0.818	0.994	0.761	0.814	0.831	0.009
PlsCho 37:4	0.478	0.994	0.845	0.871	0.891	0.030
PlsCho 37:6	0.781	0.994	0.741	0.715	0.928	0.559
PlsCho 38:0	0.961	0.994	0.880	0.617	0.713	0.871
PlsCho 38:1	0.917	0.994	0.836	0.459	0.629	0.291
PlsCho 38:3	0.818	0.994	0.941	0.546	0.466	0.034
PlsCho 38:4	0.987	0.994	0.761	0.422	0.907	0.185
PlsCho 38:5	0.899	0.994	0.706	0.847	0.858	0.136
PlsCho 38:6	0.834	0.994	0.948	0.958	0.858	0.512
PlsCho 39:3	0.899	0.994	0.855	0.644	0.699	0.666
PlsCho 39:4	0.909	0.994	0.881	0.930	0.899	0.716
PlsCho 39:5	0.799	0.994	0.689	0.644	0.338	0.534
PlsCho 39:6	0.781	0.994	0.606	0.756	0.480	0.581
PlsCho 40:0	0.956	0.994	0.784	0.852	0.530	0.961
PlsCho 40:1	0.987	0.994	0.978	0.592	0.880	0.888
PlsCho 40:3	0.981	0.994	0.908	0.398	0.338	0.066
PlsCho 40:4	0.910	0.994	0.774	0.746	0.996	0.635
PlsCho 40:5	0.874	0.994	0.884	0.459	0.598	0.527
PlsCho 40:6	0.961	0.994	0.475	0.715	0.526	0.952
PlsCho 42:1	0.874	0.994	0.872	0.971	0.775	0.602
PlsCho 42:2	0.984	0.994	0.820	0.812	0.956	0.986
PlsCho 42:3	0.975	0.994	0.993	0.238	0.722	0.490
PlsCho 42:4	0.981	0.994	0.881	0.892	0.598	0.243
PlsCho 42:5	0.781	0.994	0.741	0.298	0.570	0.725
PlsCho 42:6	0.818	0.994	0.818	0.440	0.338	0.791
PlsCho 44:3	0.818	0.994	0.208	0.847	0.567	0.425
PlsCho 44:4	0.981	0.994	0.884	0.890	0.442	0.213
PlsCho 44:5	0.818	0.994	0.741	0.847	0.136	0.248
PlsCho 44:6	0.781	0.994	0.988	0.957	0.593	0.213
PlsCho 46:4	0.917	0.994	0.654	0.891	0.295	0.099
PlsEth 32:0	0.981	0.994	0.849	0.971	0.615	0.691
PlsEth 32:1	0.899	0.994	0.277	0.552	0.375	0.434
PlsEth 32:2	0.907	0.994	0.001	0.003	0.007	0.002
PlsEth 33:1	0.818	0.994	0.140	0.127	0.043	0.010
PlsEth 33:2	0.818	0.994	0.055	0.029	0.019	0.021
PlsEth 34:0	0.909	0.994	0.190	0.706	0.891	0.703
PlsEth 34:1	0.989	0.994	0.140	0.459	0.981	0.189
PlsEth 34:2	0.917	0.994	0.178	0.238	0.222	0.099
PlsEth 34:3	0.909	0.994	0.038	0.308	0.116	0.072
PlsEth 34:4	0.781	0.994	0.038	0.127	0.019	0.002
PlsEth 35:1	0.874	0.994	0.277	0.847	0.222	0.248
PlsEth 35:2	0.818	0.994	0.132	0.218	0.188	0.105
PlsEth 35:4	0.781	0.994	0.020	0.127	0.031	0.002
PlsEth 36:0	0.909	0.994	0.881	0.847	0.938	0.983
PlsEth 36:1	0.961	0.994	0.051	0.308	0.330	0.014

Table S2.7H: MEAL Study significant differences for between diet comparisons for all lipids (Plasmenyl-phosphatidylethanolamine 36:2 to Sphingomyelin 38:2)

	Between Diet Comparisons					
	FDR <0.1					
Lipid/Day	B v B	S v S	2 v 2	7 v 7	14 v 14	21 v 21
PlsEth 36:2	0.950	0.994	0.038	0.141	0.031	0.007
PlsEth 36:3	0.929	0.994	0.095	0.459	0.843	0.084
PlsEth 36:4	0.818	0.994	0.872	0.847	0.375	0.761
PlsEth 36:5	0.909	0.994	0.055	0.398	0.592	0.612
PlsEth 36:6	0.818	0.994	0.135	0.706	0.425	0.174
PlsEth 37:1	0.818	0.994	0.492	0.459	0.526	0.131
PlsEth 37:2	0.899	0.994	0.706	0.939	0.788	0.243
PlsEth 37:3	0.781	0.994	0.566	0.918	0.891	0.418
PlsEth 37:4	0.781	0.994	0.761	0.982	0.996	0.109
PlsEth 37:5	0.781	0.994	0.055	0.642	0.349	0.295
PlsEth 37:6	0.852	0.994	0.020	0.127	0.040	0.009
PlsEth 38:1	0.909	0.994	0.311	0.706	0.913	0.566
PlsEth 38:2	0.874	0.994	0.237	0.812	0.843	0.667
PlsEth 38:3	0.781	0.994	0.297	0.706	0.995	0.213
PlsEth 38:4	0.781	0.994	0.881	0.957	0.891	0.243
PlsEth 38:5	0.818	0.994	0.396	0.847	0.821	0.242
PlsEth 38:6	0.818	0.994	0.563	0.706	0.858	0.612
PlsEth 39:2	0.781	0.994	0.592	0.398	0.905	0.901
PlsEth 39:4	0.781	0.994	0.978	0.847	0.906	0.380
PlsEth 39:5	0.800	0.994	0.095	0.732	0.526	0.059
PlsEth 39:6	0.781	0.994	0.960	0.866	0.962	0.529
PlsEth 40:1	0.818	0.994	0.701	0.847	0.652	0.874
PlsEth 40:2	0.909	0.994	0.881	0.617	0.671	0.961
PlsEth 40:4	0.818	0.994	0.941	0.934	0.583	0.426
PlsEth 40:5	0.818	0.994	0.566	0.398	0.981	0.107
PlsEth 40:6	0.781	0.994	0.934	0.814	0.928	0.573
PlsEth 41:4	0.799	0.994	0.644	0.847	0.526	0.823
PlsEth 41:6	0.951	0.994	0.866	0.502	0.898	0.982
PlsEth 42:4	0.781	0.994	0.836	0.706	0.349	0.952
PlsEth 42:5	0.818	0.994	0.881	0.920	0.314	0.753
PlsEth 42:6	0.818	0.994	0.900	0.617	0.583	0.553
PlsEth 44:6	0.818	0.994	0.271	0.847	0.396	0.310
PS 36:1	0.950	0.994	0.563	0.847	0.823	0.704
PS 38:4	0.968	0.994	0.820	0.957	0.994	0.064
SM 30:1	0.909	0.994	0.829	0.789	0.891	0.425
SM 30:2	0.996	0.994	0.218	0.238	0.639	0.024
SM 32:0	0.781	0.994	0.882	0.614	0.883	0.471
SM 32:1	0.781	0.994	0.878	0.934	0.944	0.491
SM 32:2	0.825	0.994	0.566	0.934	0.858	0.982
SM 33:1	0.781	0.994	0.796	0.957	0.905	0.283
SM 34:0	0.818	0.994	0.988	0.847	0.481	0.874
SM 34:1	0.799	0.994	0.941	0.617	0.938	0.527
SM 34:2	0.818	0.994	0.881	0.847	0.883	0.982
SM 34:3	0.909	0.994	0.566	0.692	0.698	0.945
SM 35:2	0.967	0.994	0.868	0.553	0.699	0.534
SM 36:1	0.818	0.994	0.855	0.271	0.886	0.527
SM 36:2	0.967	0.994	0.706	0.416	0.880	0.435
SM 36:3	0.909	0.994	0.566	0.644	0.821	0.107
SM 36:4	0.917	0.994	0.951	0.969	0.981	0.172
SM 37:1	0.818	0.994	0.656	0.082	0.363	0.032
SM 37:2	0.899	0.994	0.820	0.617	0.788	0.311
SM 38:0	0.781	0.994	0.319	0.854	0.910	0.749
SM 38:1	0.781	0.994	0.706	0.959	0.882	0.871
SM 38:2	0.899	0.994	0.833	0.847	0.425	0.982

Table S2.7I: MEAL Study significant differences for between diet comparisons for all lipids (Sphingomyelin 38:3 to Triacylglycerol 46:1)

	Between Diet Comparisons					
	FDR <0.1					
Lipid/Day	B v B	S v S	2 v 2	7 v 7	14 v 14	21 v 21
SM 38:3	0.818	0.994	0.784	0.981	0.702	0.791
SM 38:4	0.818	0.994	0.315	0.308	0.723	0.534
SM 39:0	0.987	0.994	0.561	0.238	0.312	0.046
SM 39:1	0.818	0.994	0.761	0.418	0.678	0.089
SM 39:2	0.781	0.994	0.875	0.493	0.788	0.100
SM 39:3	0.967	0.994	0.410	0.325	0.375	0.059
SM 40:1	0.800	0.994	0.881	0.263	0.365	0.021
SM 40:2	0.907	0.994	0.988	0.680	0.891	0.359
SM 40:3	0.874	0.994	0.845	0.672	0.622	0.843
SM 40:5	0.818	0.994	0.941	0.706	0.545	0.786
SM 41:1	0.781	0.994	0.881	0.203	0.373	0.050
SM 41:2	0.981	0.994	0.988	0.892	0.391	0.760
SM 41:3	0.899	0.994	0.892	0.992	0.363	0.885
SM 41:4	0.899	0.994	0.592	0.243	0.457	0.411
SM 41:6	0.818	0.994	0.881	0.934	0.906	0.591
SM 42:1	0.818	0.994	0.916	0.546	0.880	0.285
SM 42:2	0.967	0.994	0.916	0.844	0.314	0.425
SM 42:3	0.981	0.994	0.988	0.974	0.375	0.426
SM 42:4	0.899	0.994	0.620	0.589	0.019	0.029
SM 42:5	0.909	0.994	0.820	0.982	0.375	0.434
SM 42:6	0.912	0.994	0.957	0.937	0.880	0.610
SM 43:1	0.781	0.994	0.880	0.398	0.891	0.175
SM 43:2	0.899	0.994	0.829	0.406	0.883	0.667
SM 43:3	0.955	0.994	0.574	0.459	0.935	0.873
SM 43:6	0.967	0.994	0.592	0.706	0.365	0.635
SM 43:8	0.987	0.994	0.900	0.398	0.363	0.358
SM 44:1	0.818	0.994	0.987	0.812	0.996	0.527
SM 44:2	0.909	0.994	0.988	0.769	0.526	0.544
SM 44:3	0.818	0.994	0.867	0.852	0.891	0.986
SM 44:5	0.884	0.994	0.566	0.773	0.070	0.776
SM 44:6	0.781	0.994	0.561	0.921	0.375	0.636
SM 45:7	0.781	0.994	0.871	0.614	0.927	0.926
TG 36:0	0.781	0.994	0.348	0.238	0.239	0.385
TG 38:0	0.799	0.994	0.239	0.398	0.239	0.471
TG 39:0	0.850	0.994	0.740	0.852	0.843	0.680
TG 40:0	0.839	0.994	0.496	0.459	0.256	0.503
TG 40:1	0.781	0.994	0.763	0.706	0.338	0.619
TG 41:0	0.818	0.994	0.533	0.666	0.363	0.636
TG 42:0	0.818	0.994	0.706	0.642	0.338	0.526
TG 42:1	0.818	0.994	0.820	0.847	0.375	0.642
TG 42:2	0.818	0.994	0.596	0.617	0.238	0.573
TG 42:3	0.781	0.994	0.621	0.989	0.338	0.701
TG 43:0	0.909	0.994	0.691	0.580	0.268	0.491
TG 43:1	0.818	0.994	0.872	0.847	0.529	0.619
TG 43:2	0.802	0.994	0.941	0.958	0.408	0.776
TG 44:0	0.899	0.994	0.829	0.706	0.363	0.635
TG 44:1	0.818	0.994	0.978	0.934	0.540	0.776
TG 44:2	0.818	0.994	0.812	0.789	0.375	0.667
TG 44:3	0.799	0.994	0.706	0.839	0.338	0.680
TG 45:0	0.956	0.994	0.881	0.847	0.349	0.527
TG 45:1	0.909	0.994	0.951	0.823	0.480	0.740
TG 45:2	0.818	0.994	0.934	0.871	0.496	0.782
TG 46:0	0.818	0.994	0.988	0.957	0.670	0.776
TG 46:1	0.818	0.994	0.784	0.971	0.674	0.945

Table S2.7J: MEAL Study significant differences for between diet comparisons for all lipids (Triacylglycerol 46:2 to Triacylglycerol 55:2)

	Between Diet Comparisons					
	FDR <0.1					
Lipid/Day	B v B	S v S	2 v 2	7 v 7	14 v 14	21 v 21
TG 46:2	0.818	0.994	0.849	0.992	0.585	0.997
TG 46:3	0.818	0.994	0.941	0.930	0.570	0.998
TG 47:0	0.818	0.994	0.867	0.847	0.722	0.725
TG 47:1	0.919	0.994	0.782	0.976	0.858	0.982
TG 47:2	0.910	0.994	0.833	0.930	0.692	0.940
TG 47:3	0.818	0.994	0.988	0.847	0.506	0.986
TG 48:0	0.818	0.994	0.884	0.938	0.710	0.701
TG 48:1	0.818	0.994	0.561	0.870	0.962	0.753
TG 48:2	0.818	0.994	0.561	0.892	0.912	0.669
TG 48:3	0.818	0.994	0.496	0.876	0.891	0.560
TG 48:4	0.818	0.994	0.784	0.847	0.711	0.635
TG 48:5	0.909	0.994	0.870	0.971	0.883	0.581
TG 49:0	0.899	0.994	0.941	0.706	0.586	0.690
TG 49:1	0.937	0.994	0.844	0.918	0.880	0.874
TG 49:2	0.923	0.994	0.867	0.899	0.907	0.924
TG 49:3	0.917	0.994	0.535	0.927	0.871	0.680
TG 50:0	0.818	0.994	0.948	0.981	0.883	0.874
TG 50:1	0.818	0.994	0.741	0.892	0.959	0.961
TG 50:2	0.818	0.994	0.198	0.784	0.661	0.566
TG 50:3	0.836	0.994	0.140	0.838	0.682	0.313
TG 50:4	0.818	0.994	0.563	0.892	0.944	0.425
TG 50:5	0.818	0.994	0.563	0.847	0.931	0.321
TG 50:6	0.818	0.994	0.855	0.871	0.891	0.527
TG 51:0	0.956	0.994	0.981	0.934	0.462	0.699
TG 51:1	0.967	0.994	0.770	0.971	0.886	0.871
TG 51:2	0.996	0.994	0.563	0.940	0.891	0.929
TG 51:3	0.996	0.994	0.691	0.847	0.880	0.923
TG 51:4	0.818	0.994	0.878	0.418	0.230	0.572
TG 51:5	0.899	0.994	0.184	0.852	0.891	0.791
TG 52:0	0.899	0.994	0.980	0.882	0.633	0.570
TG 52:1	0.899	0.994	0.586	0.852	0.994	0.945
TG 52:2	0.961	0.994	0.135	0.661	0.344	0.540
TG 52:3	0.981	0.994	0.566	0.958	0.795	0.616
TG 52:4	0.967	0.994	0.869	0.847	0.931	0.739
TG 52:5	0.899	0.994	0.691	0.852	0.723	0.177
TG 52:6	0.818	0.994	0.315	0.617	0.532	0.059
TG 52:7	0.818	0.994	0.592	0.644	0.652	0.175
TG 53:0	0.975	0.994	0.988	0.814	0.583	0.952
TG 53:1	0.925	0.994	0.871	0.985	0.526	0.559
TG 53:2	0.961	0.994	0.566	0.934	0.890	0.928
TG 53:3	0.911	0.998	0.820	0.957	0.907	0.986
TG 53:4	0.975	0.994	0.741	0.789	0.530	0.986
TG 53:5	0.987	0.994	0.878	0.982	0.883	0.810
TG 54:0	0.825	0.994	0.833	0.706	0.258	0.632
TG 54:1	0.899	0.994	0.978	0.847	0.371	0.391
TG 54:2	0.925	0.994	0.725	0.847	0.890	0.874
TG 54:3	0.975	0.994	0.566	0.847	0.873	0.891
TG 54:4	0.967	0.994	0.725	0.871	0.996	0.595
TG 54:5	0.909	0.994	0.878	0.930	0.891	0.385
TG 54:6	0.899	0.994	0.878	0.930	0.951	0.426
TG 54:7	0.818	0.994	0.957	0.769	0.831	0.091
TG 54:8	0.899	0.994	0.737	0.706	0.795	0.069
TG 55:0	0.987	0.994	0.401	0.847	0.564	0.739
TG 55:2	0.961	0.994	0.761	0.852	0.633	0.534

Table S2.7K: MEAL Study significant differences for between diet comparisons for all lipids (Triacylglycerol 55:3 to Triacylglycerol 62:12)

	Between Diet Comparisons					
	FDR <0.1					
Lipid/Day	B v B	S v S	2 v 2	7 v 7	14 v 14	21 v 21
TG 55:3	0.956	0.994	0.916	0.892	0.699	0.385
TG 55:4	0.950	0.994	0.397	0.756	0.996	0.652
TG 55:5	0.909	0.994	0.829	0.614	0.937	0.874
TG 56:0	0.818	0.998	0.761	0.811	0.230	0.534
TG 56:1	0.899	0.994	0.909	0.852	0.226	0.179
TG 56:10	0.909	0.994	0.882	0.706	0.816	0.099
TG 56:2	0.818	0.994	0.875	0.911	0.603	0.391
TG 56:3	0.899	0.994	0.774	0.821	0.981	0.952
TG 56:4	0.917	0.994	0.761	0.715	0.731	0.488
TG 56:5	0.909	0.994	0.784	0.692	0.564	0.421
TG 56:6	0.923	0.994	0.875	0.784	0.563	0.371
TG 56:7	0.996	0.994	0.829	0.934	0.723	0.527
TG 56:8	0.923	0.994	0.496	0.982	0.996	0.871
TG 56:9	0.899	0.994	0.864	0.847	0.739	0.278
TG 57:2	0.992	0.994	0.071	0.630	0.643	0.425
TG 57:4	0.987	0.994	0.941	0.662	0.526	0.418
TG 58:1	0.899	0.994	0.833	0.992	0.639	0.566
TG 58:10	0.909	0.994	0.410	0.983	0.948	0.896
TG 58:11	0.923	0.994	0.401	0.934	0.994	0.630
TG 58:2	0.895	0.994	0.868	0.746	0.880	0.770
TG 58:3	0.818	0.994	0.829	0.982	0.832	0.940
TG 58:4	0.899	0.994	0.819	0.891	0.788	0.912
TG 58:5	0.865	0.994	0.941	0.720	0.535	0.662
TG 58:6	0.992	0.994	0.943	0.828	0.526	0.534
TG 58:7	0.992	0.994	0.876	0.706	0.690	0.669
TG 58:8	0.967	0.994	0.829	0.797	0.674	0.527
TG 58:9	0.981	0.994	0.566	0.934	0.890	0.874
TG 60:10	0.967	0.994	0.741	0.789	0.526	0.843
TG 60:11	0.987	0.994	0.271	0.969	0.996	0.952
TG 60:12	0.917	0.994	0.271	0.982	0.910	0.952
TG 62:12	0.945	0.994	0.876	0.989	0.788	0.884

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Chapter 3: A Comparison of Actual and Reported Energy and Macronutrient Intake in a Well-Controlled Human Feeding Study

Abstract

Objectives: Dietary guidelines are largely based on epidemiological studies that rely on memory-based dietary assessments (MBDA) such as 24-hour recalls (24HR). Well-controlled feeding studies are often used to help confirm these larger epidemiological studies findings and help draw associations between diet and disease (1). Few studies have compared actual and reported dietary intake in well-controlled feeding studies. This study sought to directly compare discrepancies between dietary intake from experimental diets and reported 24HR intake in free-living participants.

Methods: Eucaloric diets were provided to 24 participants (50% female, mean age 24.4(3.4); mean BMI 23.1(SD 2.9) for 24 days. Participants were provided a standard diet (15% protein (PRO): 35% fat: 50% carbohydrate (CHO)) for 3 days and then randomly assigned to either a 21-day high fat (60% fat, HF) or a high CHO (75% CHO, HC). PRO% was held constant at 15%. Percent difference from provided food was calculated as (g reported/g actual)*100. Dietitians prepared diets with macronutrient compositions adjusted to achieve targeted percentages, either overtly (added sugary drinks) or covertly (added coconut oil). Total provided energy intake (EI)

was adjusted to maintain weight (±1 kg) over the course of the study. Trained staff at the Michigan Nutrition Obesity Research Center administered four 24HR; one after completing the 3-day standard diet, then once a week during the 21-day experimental diets. Participants were instructed to return uneaten food and beverages for accurate calculation of dietary intake. Actual and reported energy intake (EI) and macronutrient intakes were estimated using the Nutrition Data System for Research software (NDSR) and compared within group via paired Student's t-tests (α=0.05).

Results:

No difference was observed between actual EI and reported EI during the standard or experimental diet for HF or HC groups. PRO intake was over-reported by all participants during the standard diet by 27.4% (11.3) and during the HC by 15.6% (7.2) and HF by 16.1% (5.6). Differences in protein intake between actual and reported was due to over-reporting of animal protein in foods. During the experimental diet, HC participants over-reported CHO by 66.4% (11.4) and under-reported fat by 6.3% (4.7) while HF participants under-reported CHO by 10.8% (6.5) and over-reported fat by 19.8% (6.7). ($p<0.05$).

Conclusion:

In this well-controlled feeding study in free-living participants, EI was accurately reported. Participants over-reported animal protein intake. When given extreme diets, participants tended to underreport the experimental macronutrient (HF or HC). These results suggest that while EI can be estimated from feeding studies, estimates of macronutrients should be determined directly from food consumed in the test diets.

Introduction

Measuring food and nutrient intake is challenging for nutrition researchers and health practitioners. To do this, most researchers rely on MBDA such as food frequency questionnaires (FFQ) and 24-hour recalls (24HR) (2, 3). Despite their widespread use, under-reporting of EI is a well-known problem with MBDAs (4-10) and established methods to adjust for known over and under-reporting are widely used (11-14). Examples of errors include respondent systematic over-reporting or under-reporting of a certain foods consumed as well as respondent random memory lapses resulting in unintentionally omitting or adding foods during the recall (15). Misrepresentation or misreporting of portion size is also an important factor associated with misreporting of EI and macronutrient intake (15). Influences on this misreporting include a social desirability trait (6, 16-18) which has been associated with bias in dietary recall and/or changing dietary intake as a reaction to the act of completing the MBDA (reactivity) (19). For example, it has been reported that in feeding studies women will eat less perceived unhealthy foods when they know that they are being overtly observed but not when covertly observed (20, 21).

Accurate quantification of dietary intake has important implications for determining individual and population-wide trends relating food intake with disease (22-28). Recommendations about energy and macronutrient intake are based on large cross-sectional studies, such as What We Eat in America (WWEIA), which is based on the National Health and Nutrition Examination Survey (NHANES) (29). These surveys rely on memory-based dietary assessments (MBDA) such as food frequency questionnaires (FFQs) and 24-hour dietary recalls (24HR) (2, 3). For health practitioners and researchers to make effective recommendations,

accurate caloric and macronutrient intake must be known. (24, 28). One major problem associated with the under-reporting of macronutrients is that this leads to misrepresentation of the health effects from reliance on self-reported macronutrients (22-26). Equations have been developed which attempt to adjust for known over- and underreporting of energy intake (11-14). Additionally, recovery biomarkers exist for EI (doubly labeled water) and for protein intake (24 hour urinary nitrogen). However, these biomarkers are expensive, difficult to use in large populations, and are not yet available for carbohydrate and fat intake (2, 9). For these reasons, it is necessary to further classify the accuracy of MBDAs on actual energy intake and macronutrient intake, potentially elucidating types of foods contributing to over- and under-reporting.

Despite the challenges with self-report methods of diet assessment, 24HR are still considered the least biased of MBDAs to estimate EI (9) and remain the most important source of information on dietary intake of large populations in surveys such as NHANES (29, 30). The limitations of 24HR are well known and can be controlled for statistically in large studies (11-14). However, do the limitations of 24HR carry over into feeding studies? Well-controlled feeding studies are often used to help confirm these larger epidemiological studies findings and help draw associations between diet and disease (1). But the use of 24HR in controlled feeding studies is not well understood, with only a few studies comparing actual intake to reported intake with 24HR with some balanced and some under-reporting of fats and carbohydrates (21, 26, 31, 32).

The aim of this analysis is to analyze discrepancies in EI and macronutrient intake between actual dietary intake from experimental diets and reported 24HR intake in free-living participants. To conduct this aim, we will use a well-controlled feeding trial and will provide

participants with all their meals as previous studies report strong adherence to meals provided (33). Our hypothesis is that energy and macronutrient intake in our controlled feeding study will be under-reported by 24HR compared to actual intake, but to a lesser extent than that reported in the literature (6, 10, 17, 19, 22-24, 34).

Materials/Subjects and Methods

Subjects:

Our study design is shown in **Figure 1.** 12 men and 12 women participated in this study. Inclusion criteria were age between 19-45 years, no history of metabolic disorders, body mass index (BMI) between 18.5 and 27, not currently taking metabolism altering drugs and weight stable +/- 2kg for the last 6 months. Prospective participants were recruited through umclinicalresearch.org and asked to visit the Michigan Clinical Research Unit at the University of Michigan.

Recruitment and Ethics:

All procedures involved in this study were approved by the University of Michigan Institutional Review Board, HUM#000110543. Written and signed informed consent forms were obtained from all participants before beginning any portion of the study.

Study design summary and randomization scheme:

Participants completed baseline assessments, consumed a ‘standard’ diet for 3 days, and were then randomly assigned to one of two experimental diet groups for the following 21 days (figure 1). Randomization was based upon date of consent and sex was balanced between groups. Participants returned to the study location every 2-4 days for repeated assessments and to pick-up food.

Body composition and anthropometry:

Height using a wall-mounted stadiometer (Easy-Glide Bearing Stadiometer, Perspective Enterprises, Portage, MI) was measured in duplicate to the nearest 0.5 cm. Baseline fasted weight was measured in light clothing using a calibrated scale (Scale-Tronix Model 6002, White Plains, NY) to the nearest 0.1 kg. Body composition was measured by trained technicians using dual x-ray absorptiometry (Lunar DPX DEXA Scanner, Madison, WI, USA). Weight was measured during the study during picked-up. If body weight fluctuated more than 1kg, the total kJ provided were adjusted to maintain baseline body weight.

Blood collection:

Fasted blood samples were collected in EDTA treated vacutainers on days -3, 0, 2, 7, 14 and 21. Samples were immediately inverted 7x and placed on ice. Plasma was frozen at -80^0C for later LC/MS analysis.

Diets:

Subjects' target kJ for eucaloric diets was determined using the Institutes of Medicine (IOM) formulas based upon height, weight, age, and reported physical activity levels (35). For men ages 19 years and older, estimated energy requirement (EER) = 4.184*(662 – (9.53 x age [yrs.]) + Physical activity (PA) x (15.91 x weight [kg] + 539.2 x height [m])) where PA was assumed to be 1.25 for active men (35). For women ages 19 years and older, EER = 4.184*(354 – (9.91 x age) + PA x (9.36 x weight + 726 x height)) where PA was assumed to be 1.27 for active women (35). Diets were designed by registered dietitians and prepared by the Michigan Nutrition and Obesity Research Center metabolic kitchen staff. All foodstuffs except commercially available prepackaged foods (i.e. granola bars, cans of soda) were weighed to the gram. All diets comprised "every day" foods which were designed to be palatable for a wide

variety of individuals (Table 3.3). For three days, participants were provided a eucaloric diet meant to match the average macronutrient intake reported in NHANES (Standard) and to provide a brief habitual diet 'wash-out' period for all participants (36, 37). All participants consumed the same foods during this period, with quantities determined by estimated caloric requirements. Standard diet macronutrient proportions approximated usual intake among adults in the United States at 15% protein, 35% fat (50% saturated/50% unsaturated), and 50% carbohydrate (28). During the experimental diet phase (21 days total), participants were provided with HC (15% protein/10% fat (50% saturated/50% unsaturated)/75% carbohydrate) diets or HF (15% protein/60% fat (50% saturated/50% unsaturated)/25% carbohydrate) diets. Subjects were instructed to eat and drink everything provided and return uneaten food to the metabolic kitchen on their subsequent visit to be weighed and recorded. Subjects were permitted as many non-caloric beverages as they wished. If subjects requested cream or sugar to add to their coffee or tea this was provided by the metabolic kitchen and accounted for in the foods provided.

24-hour dietary calls (24HR) and food frequency questionnaires (FFQ):

24-hour recalls were collected using standard protocols (2) during the standard diet (1 recall) and during the 3-week experimental diet (3 recalls; 1 per week). Recalls were unannounced, conducted during times when the participant stated they were usually available and occurred on any day of the week. All recalls were administered by trained bionutrition staff from the University of Michigan Nutrition and Obesity Research Core (MNORC) staff at the MCRU. Most recalls were conducted via phone unless this was unfeasible, then they were administered in person by study dietitians during a food pick up. The Nutrition Data System for Research (NDSR) software, version 2016, developed by the Nutrition Coordinating Center (NCC), University of Minnesota, Minneapolis, MN (38), was utilized to administer the recall and

determine the energy, macronutrient and micronutrient content of the diet (Reported). Each subject's actual diet (Actual) was also entered into NDSR to determine EI and macronutrient content. NDSR provided amounts and sources of kilojoules, macronutrients, and micronutrients. These amounts included sources and amounts of vegetable animal proteins. Uneaten foodstuffs was weighed and subtracted from provided. For each subject this produced 4 time points for comparison: during the 3-day standard diet and then during week 1, week 2, and week 3 of the experimental diet. In order to assess usual intake, subjects also completed the Harvard University2007 validated FFQ during the baseline visit. (https://regepi.bwh.harvard.edu/health/FFQ/files/2007%20BOOKLET%20FFQ.pdf) (39, 40).

Statistical Analysis:

NDSR summary data for each subject's individual diets from individual days were used to estimate EI and macronutrient intake. The EI and % macronutrients provided in the Actual diet was determined using NDSR and was compared for all participants to identify differences in EI and macronutrients between and within diet groups. These comparisons were conducted at the standard diet and for each week of the experimental diet. Mean EI and % macronutrients were also compared between and within the HF and HC groups during the experimental diet. Descriptive statistics (age, weight, caloric intake, BMI and DEXA measurements) were found to be normally distributed using Shapiro-Wilks tests ($p>0.5$) and computed and compared between groups (HC vs. HF) using Student's T-tests ($p<0.05$) to confirm randomization was successful. Week 1 through 3 values for EI and macronutrients for each individual were compared with one-way repeated measures ANOVA with random intercept ($\alpha=0.05$) and were not found to be significantly different for EI, %FAT, %PRO, and %CHO. Bland-Altman plots comparing the difference in actual and reported intake with the average between these two measures were used

to evaluate the agreement between the two methods of dietary assessment; 24HR and actual intake. Over/under-reporting was calculated using the following formula (reported nutrient/actual nutrient * 100) with a score of 100% representing perfect agreement between recall and actual intake (Figure 3.1A). All statistical analysis was done using SAS software version 9.4 TS Level 1M3 of the SAS System for Windows (SAS Institute Inc., Cary, NC; copyright 2002-2012). FFQ data measuring usual intake for EI, %PRO, %FAT, and %CHO was compared to baseline 24HR using Student's T-tests. Pearson's correlations between FFQ data and baseline 24HR were also compared for kJ, %PRO, %FAT, and %CHO.

Results

Baseline anthropometric data did not differ significantly between HC and HF groups (Table 3.1). Furthermore, subject weight change over the course of the experiment did not differ significantly between HC and HF groups (p=0.38).

Actual vs Reported intake

The estimates of EI in kJ/day did not significantly differ between actual intake and 24HR during the standard diet (102.5((25.1)), in the HC diet (101.7 (40.5)), nor in the HF diet (103.7 (25.0)) (Figure 3.1). However, protein was over reported during all diet conditions (Standard diet 127.4 (42.3), HC diet 115.6 (42.4), and HF 116.1 (31.4). Fat was over-reported (166 (67.7)) and carbohydrate was under-reported (89.2 (36.3)) in the HC diet. Conversely in the HF diet, fat was under-reported (93.7 (25.9)) and carbohydrate was over-reported (119.8 (37.5)), (Figure 3.1)

Next, we compared actual diet and reported diet when macronutrients are taken as a percentage of total kilojoules reported or consumed (3.1). Percent protein reporting was significantly higher in all diets with standard diet at 14.4% actual vs 17.8% reported ($p<0.0001$), participants on the

HC diet at 14.8% actual vs. 17.1% reported (p=0.0006), and in HF participants at 15.0% in actual vs 17.1% reported (p=0.027). Percent fat did not differ between participants during the standard diet; 35.8% actual vs 33.5% reported (p=0.0678), but HC participants reported 17.2% fat vs. 10.4% actual fat (p<0.0001) and HF participants reported 53.7% fat vs. 60.1% actual (p=0.0002). Similarly, percent carbohydrates did not differ during the standard diet; 49.8% actual vs. 48.8% reported (p=0.5828), but HC participants reported 65.8% carbohydrates vs. 74.8% actual intake (p<0.0001) and HF participants reported 29.2% carbs vs. 24.8% actual intake (p=0.015) (Figure 1).

The relationship between Reported diet and Actual diet was also plotted as Bland-Altman diagrams for EI, %PRO, %FAT, and %CHO for the experimental diets (figure 3.2) and for the standard diet (figure 3.4). In the Standard diet (figure 3.4), it can be seen that reported means (dark blue line) are very similar to actual means (light grey line). There does appear to be a slight proportional bias shown in a slight positive slope of all data, which is indicative of an increase in error with higher caloric intake (41). For the experimental diets, EI and %PRO show similar proportional bias as the standard diet (figure 3.2). EI shows similar reporting between recall and actual diet regardless of study group (figure 3.1). Protein is over-reported by both groups with proportional bias shown as a positive slope in Bland-Altman plots (figure 3). This is indicative of an increase in recall error with an increase in EI Figures 3.1 and 3.2 show %FAT is over-reported by HC and underreported by HF while %CHO is over-reported by HF and underreported by HC. Animal protein was over-reported compared to vegetable protein by all participants at each time point while vegetable protein was well reported (Table 3.2 & Figure 3.3). During the standard diet, subjects reported 84.2g (34.4) animal protein compared to 62.1g (14.3) of actual intake (p<0.02) in contrast to 36.5g (9.2) reported vegetable protein vs. 32.7g

(5.9) actual intake, a difference that was not statistically significant. The tendency to in over-report animal protein but not vegetable protein was also seen in the HC diet and the HF diets (table 3.2 & figure 3.2).

FFQ estimates of usual intake of EI, %PRO, %FAT, and %CHO of subjects was compared to baseline 24HR recalls and were not found to be significantly different between groups with FFQ's reporting 9769.2 kJ (4748.8), 16.4%PRO, 34.1%FAT, and 48.2%CHO while baseline 24HR showed 9683.4 kJ (3474.4), 16.7%PRO, 32.1%FAT, and 48.4%CHO. Pearson's correlation between EI and macronutrients was also good with r for kJ = 0.44, %PRO = 0.32, %FAT =0.52, %CHO = 0.82.

Discussion

In this study, our objective was to compare 24HR estimated nutrient intake vs. actual intake in the standard and experimental diets, as we hypothesized that, consistent with literature, there would be significant under-reporting of energy, CHO, and fats. However, in this study, we found no difference in actual EI vs reported in any of the diet conditions. We provided all foodstuffs for this study for participants which was consumed during the study period and used 24HR recalls to establish dietary intake. We found that, in the feeding study setting, our participants reported EI accurately. For macronutrient intake, we found that animal protein was over reported in both the standard diet and during the experimental diet. During the standardized diet, fat and carbohydrate were accurately reported by study participants, but during the experimental diet, participants on the high fat diet under-reported fat and over-reported carbohydrate intake while participants on the high carbohydrate diet under-reported carbohydrate and over-reported fat intake.

The use of dietary recall in feeding studies is sparse, with just a few studies identified (21, 31, 32, 42). Unlike our study, each of these studies provided food *ad libitum* and determined actual food intake using a covert design using video recordings of subject food choices (20, 21, 31) or were cross-sectional (42). Our study, in contrast, was a eucaloric feeding study in which participants were free-living and took prepared food home. Because well-controlled feeding studies are used to confirm the science of larger epidemiological studies (1), we believe it is important to understand how 24HR perform in these types of studies and what proportion of macronutrients are being consumed. Furthermore, the systematic under-reporting of EI or any one macronutrient could diminish the accuracy of associations between disease and diet (22).

Overall, the participants in this study were very consistent reporters. The agreement between their FFQ and the baseline 24HR recall was very good with no statistically significant difference between kJ, %PRO, %FAT, or %CHO. While one 24HR recall is not a good measure of habitual intake, the baseline 24HR recall did compare favorably with the FFQ.

The under-reporting of EI by MBDA such as the 24HR is well documented (4, 6-9, 43, 44). Under-reporting of EI is especially associated with women, obese status, and the desire to lose weight. Furthermore, other studies find under-reporting when comparing laboratory settings with dietary recalls (21, 31, 32). In contrast to the literature, we found accurate EI reporting by 24HR between actual and reported intake, similar to one study which looked at 24HR vs actual at one day (42). Our study population was small (n=24), and largely comprised of conscientious graduate students who were weight stable and not overweight. Our reports are also not in accordance the findings of Hebert et al. (45) who demonstrated that women who are highly educated report more downward desirability bias (under-reporting) in 24HR than women who are less educated. Most of our subjects were graduate students and, regardless of sex, under-

reported carbohydrates on the high carbohydrate diet and under-reported fat on the high fat diet. Higher education level has been found to be associated with less bias in the 24HR recall, which could explain the accurate recall of our population which was highly educated (4). Perhaps the accuracy and reliability of response for our subjects was increased due to their level of education, conscientious natures, and investment in science as graduate students. Secondly, our diets were provided on a cycle of 4 possible meals for breakfast, lunch, and dinner, so it is possible that our participants were able to recall their meals better.

While our participants were not aware of when they would receive recalls, they did know that they were coming and perhaps were better at recalling than true free-living individuals. This is similar to an observational cross-sectional study that found that when comparing actual observed diet to the USDA five-step multi-pass method for dietary recall that men (ages 21-65) reported EI, protein, fat, and carbohydrate very well (42). One possibility is that the mere act of subjects knowing they are being observed increased the accuracy of their response as in this study and the Stubbs studies (20, 21, 42).

Although carbohydrates and fats are underreported in the literature, we found that if participants were given a high carbohydrate diet which was necessarily low fat, they tended to under-report carbohydrates and over-report fats. Consistent with the literature, we found that macronutrients are differentially misreported (46). Specifically, participants on a high fat diet tended to under-report fat and over-report carbohydrates. In other feeding studies, energy intake was under-reported by both men and women at all levels of intake (17, 20, 21, 31, 47). This seems to be associated with under-reporting of high carbohydrate and high fat foods (17, 48). While the participants in our study were not told the diet to which they were randomized, it was impossible to hide the true nature of the food they were eating from them. Perhaps, in this case,

participants were under-reporting the macronutrients in the very high fat or very high carbohydrate diets because of social desirability, but this seems unlikely. More likely, subjects are under-reporting fats or carbohydrates because these diets are so very high in these macronutrients.

The nature of the eucaloric, targeted macronutrient diet may have contributed to this pattern we observed, with subjects on HC diets under-reporting carbohydrates and subjects on the HF diet under-reporting fat. Diets were prepared from real food to reach particular macronutrient percentages. Often, excess fats and excess carbohydrates were "hidden" in foods by adding foods such as butter and coconut oil for fat and soda or candy for high carbohydrates. Because participants did not prepare their own foods, they did not necessarily know how much of these balancing foods were added to their foods. Although, one might assume that if "hidden" foods were under-reported, EI would be under-reported as well, but rather EI was not differentially reported from actual intake.

We found that protein was over-reported by all participants during the standard diet as well as in HC and HF diets. In the literature, misreporting of protein is not consistent, with some studies reporting no misreporting (6), some under reporting (24), and some over-reporting (22, 23, 34, 49). This finding is in accordance with research which compares observed intake with 24HR which shows that protein is often well reported (20). This was also found in a large epidemiological study which showed high correlation between urinary nitrogen, a biomarker of protein intake, and dietary recall (50).

While our participants reported EI equal to their intake but over-reporting of protein, both (or either) carbohydrates and fats must be under-reported to conserve caloric balance. Our results suggest that the over-reporting of protein is due to over-reporting of animal proteins. This is

perhaps due to the sources of meat in these particular diets as many animal protein sources were in the form of ground beef in foods such as lasagna and meat loaf. While this is a small study, it is important to understand that animal protein may be over estimated by 24HR as animal protein intake has been associated with obesity (51).

Strengths/Limitations

The strengths of this study include the experimental design and the direct comparison between 24HR and provided diet. This study was well-controlled in that our subjects were provided with all food that they consumed. The generalizability to a "real world" setting of this study, given the free-living subjects is better than studies with participants kept in a hospital setting during the study. Limitations of this study are the heterogeneity of the population and small population size (n=23). The subjects in this study were, for the most part, undergraduate student and graduate students at the University of Michigan, which could diminish the generalizability of this study to a larger population. This population was also composed of young, metabolically healthy and non-overweight individuals, which is not reflective of the general population of the United States. Finally, we used weight change as a metric for compliance to the diet. It may be naïve to assume that the participants in this study were 100% compliant to the diet for the entire study.

Conclusion

This study is unique in that it shows that, in a well-controlled feeding study amongst free-living healthy individuals, 24HR recall may adequately estimate EI. As these studies are used to confirm large epidemiological studies, it is important to know that the over-reporting seen in MBDAs may not co-vary with these sorts of studies. Energy intake, while highly variable between participants, does seem to be accurate in the laboratory feeding study setting. This leads

to our conclusion that 24HR accurately estimate EI in controlled feeding studies. However, in studies such as this one, which looked at very high macronutrient intakes, tested macronutrients may be under/over-reported when assessed by 24HR. In this study, participants on very high fat diets under reported fat and over reported carbohydrates and participants on very high carbohydrate diets under-reported carbohydrates and over-reported fat. We would further conclude that in studies which use over-feeding/under-feeding of carbohydrates and fats, 24HR does not accurately assess macronutrient intake as seen in our studies. Finally, from this study, it appears that the 24HR may overestimate animal protein in the context of an experimental feeding trial.

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Tables and Figures:

Table 3.1 *Baseline participant data of the HC and HF study groups.*

		HC (n=13 - 7♂,6♀)	HF (n=11 - 5♂,6♀)
	Age (yrs.)	24.85 (4.04)	23.91 (2.63)
	Weight Change (Δkg)	-0.05 (1.02)	0.3 (0.85)
	Caloric Intake (kJ)	11819.8 (2181.6)	11466.0 (2101.4)
	BMI kg/m^2	23.1(2.8)	23.2(3.1)
DEXA Measurements	Total Mass (kg)	70.52 (7.8)	68.08 (7.64)
	Tissue (kg)	67.67 (7.45)	65.48 (7.31)
	Fat (kg)	15.32 (5.49)	16.88 (7.36)
	Lean (kg)	52.36 (10.31)	48.6 (8.34)
	BMC (kg)	2.86 (0.46)	2.69 (0.58)
	FFM (kg)	53.65 (13.88)	51.29 (8.85)
	Android %FAT	21.98 (10.96)	23.22 (11.1)
	Gynoid %FAT	25.62 (10.78)	29.42 (13.03)
	A/G Ratio	0.85 (0.21)	0.8 (0.19)
	BF%	23.06 (8.97)	25.54 (10.44)
	BMD	1.28 (0.12)	1.24 (0.14)
	BMR (J)	6279.2 (884.0)	5983.9 (706.2)

Data presented as mean (SD). No data reached the threshold for significance (α=0.05) within these data when compared using Student's paired t-tests. FFM = fat free mass, BMC = bone mineral content, BMD = bone mineral density, BMR = basal metabolic rate.

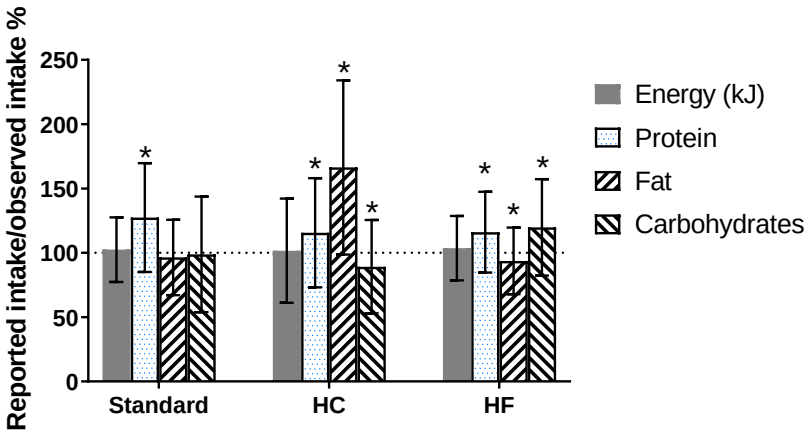
Table 3.2: *A comparison of reported and actual animal and vegetable protein during the Standard diet and during the HC and HF experimental diets*

Diet	Standard Diet (n=23)			High Carbohydrate Diet (n=13)			High Fat Diet (n=10)		
	Actual	Reported	p-value	Actual	Reported	p-value	Actual	Reported	p-value
Animal Protein	62.1 (14.3)	84.2 (34.4)	0.02*	65.0 (13.7)	80.9 (34.9)	0.04*	77.0 (15.1)	88.8 (26.5)	0.04*
Vegetable Protein	32.7 (5.9)	36.5 (9.2)	0.10	38.5 (6.4)	37.9 (10.7)	0.80	23.2 (4.2)	27.2 (8.2)	0.08

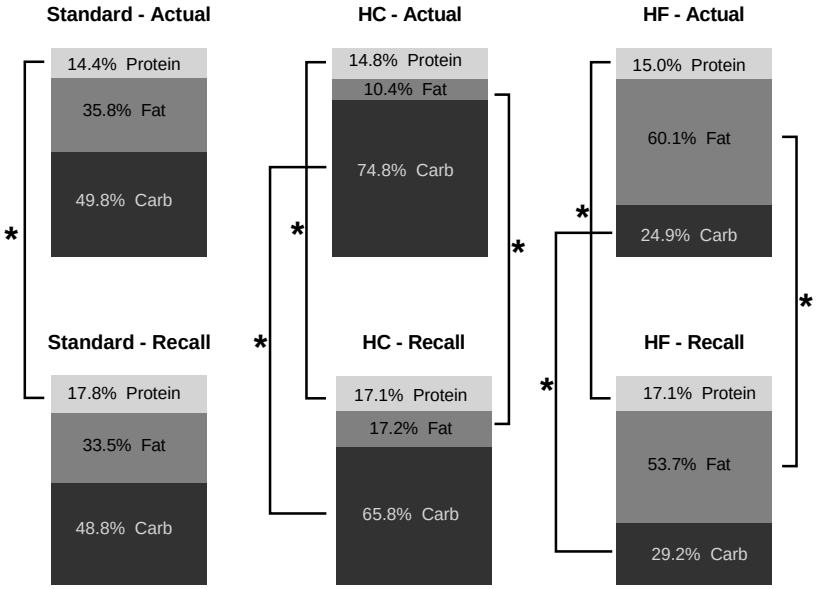
*Data represent grams of reported or actual protein (SD). * represents a p-value <0.05 for paired Student's t-tests*

Figure 3.1 Comparisons between actual and reported macronutrient intake.

A



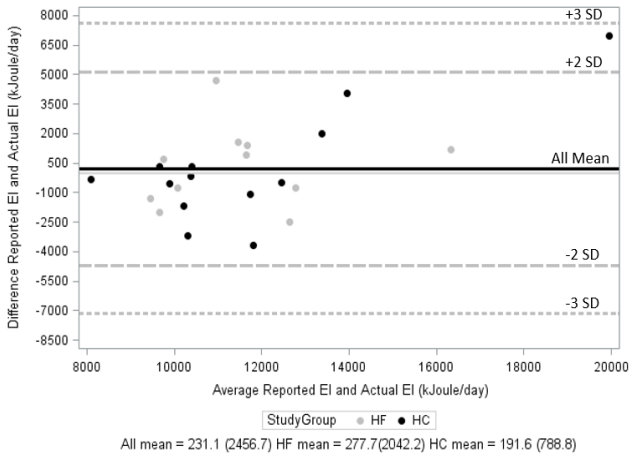
B



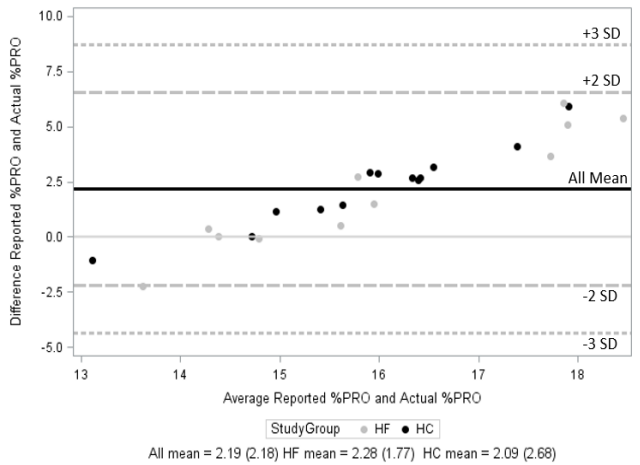
(A) The proportion of over and under-reported energy in kJ and macronutrients with 24-hour recall compared to actually consumed during the standard diet (both groups combined) and the average intake of weeks 1 through 3 for HC and HF experimental diet eaters expressed as a ratio (reported nutrient/actual nutrient). Above 100 represent over-reporting of energy/nutrients while values below 100 represent under-reporting. (B) Comparison of the percentage of actual provided macronutrients with the percentage of reported macronutrients for HC and HF diets during experimental weeks. * = $p<0.5$ for paired Student's T-tests comparing Actual intake with Reported intake. Error bars represent SD.

Figure 3.2. *Bland-Altman plots of differences in Experimental diets for (A) EI, (B) %PRO, (C) %FAT, and (D) %CHO (mean reported nutrient – mean actual nutrient) against the mean of the two measures for 23 participants.*

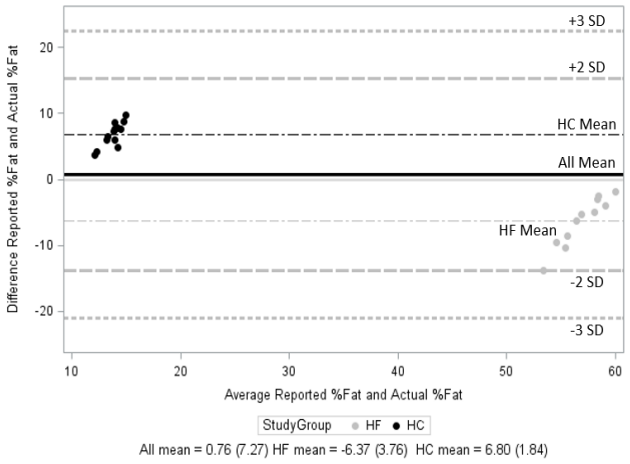
A)



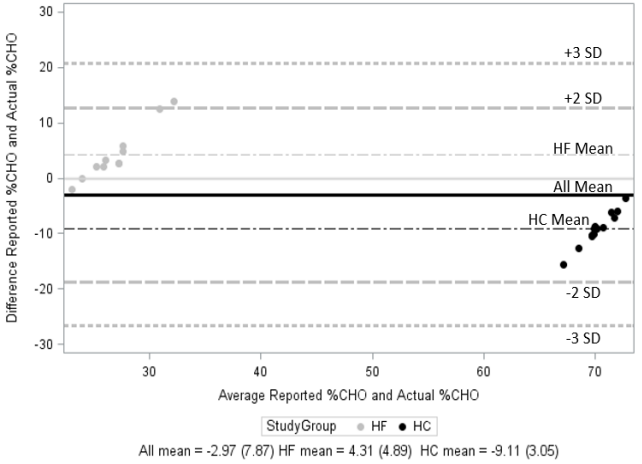
B)



C)

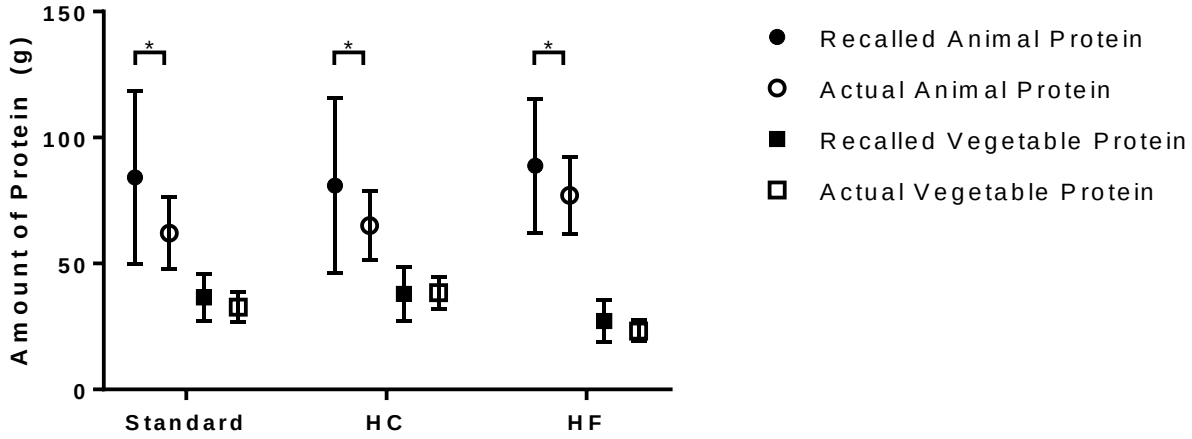


D)



Means for all participants and study groups are at the bottom of the plots and are presented as mean (SD). The black solid line is the mean difference for all participants, grey line represents a mean difference of 0. For C and D, gray dot-dashed lines represent mean difference for HF and black dot-dashed line represents mean difference for HC. These lines are absent from A &B because they are not significantly different

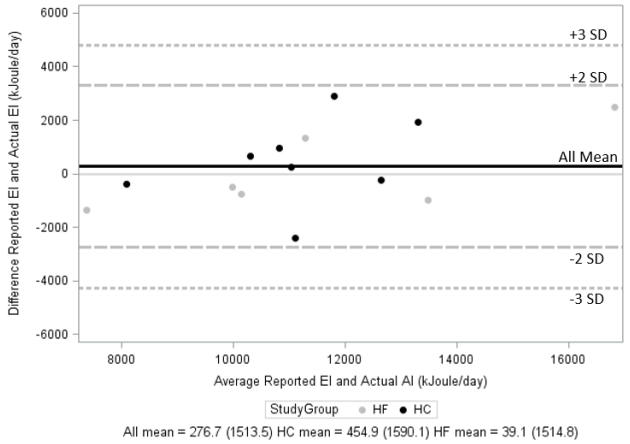
Figure 3.3. *Comparison of sources of protein (animal or plant) during the Standard diet and during the experimental diet (HC and HF).*



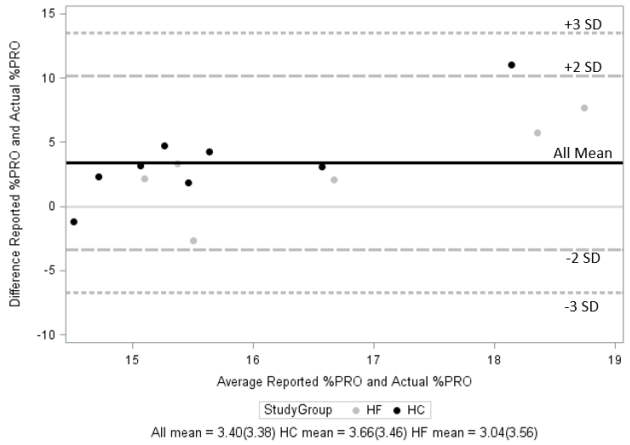
Data represented as grams (SD) of protein reported compared to grams of actual protein.

Figure 3.4. *Bland-Altman plots of differences in Standard diets for (A) EI, (B) %PRO, (C) %FAT, and (D) %CHO (mean reported nutrient – mean actual nutrient) against the mean of the two measures for 23 participants.*

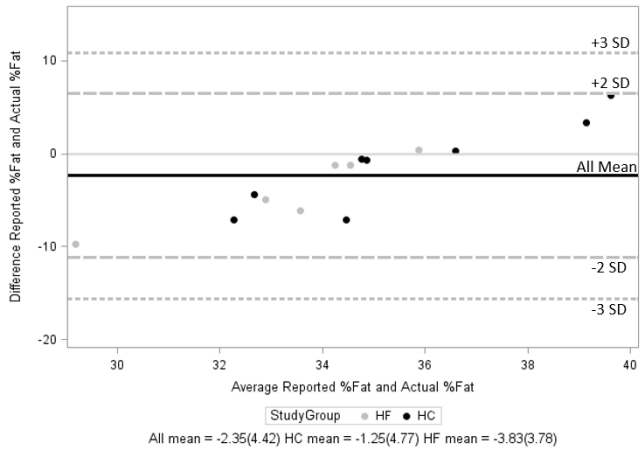
A)



B)



C)



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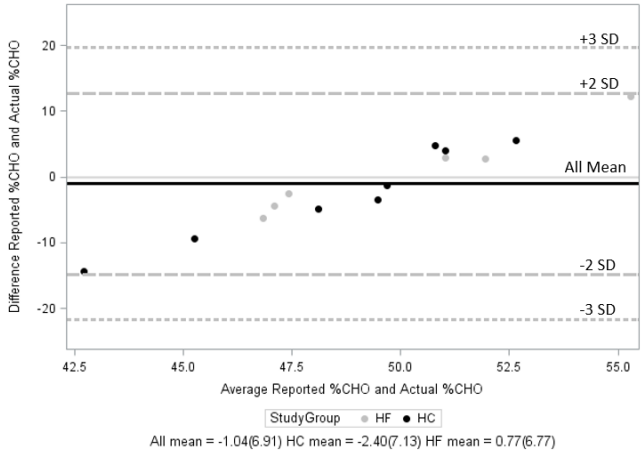

Means for all participants and study groups are at the bottom of the plots and are represented as mean (SD). The black line is the mean difference for all participants; the grey line represents a mean difference of 0.

Table 3.3 Sample menus based on a 2000 kcal diet for the standard diet (A-C), high carbohydrate diet (D-G), and high fat diet (H-K). Summary data includes actual calculated grams and kcal of macronutrients as well as target grams and kcal of macronutrients in diets.

A) Sample Standard Diet #1

FOOD	AMT	kcal	PRO (g)	FAT (g)	SAT FAT (g)	CARB (g)
Breakfast						
Rice Chex	1 bowl	70	1	0	0	16
2% milk	240 ml	113	7.6	4.4	2.7	11
Strawberry yogurt	6 oz. carton	160	5	1.5	0	33
Banana	medium	111	1.2	0.6	0	28
Lunch						
Pepperoni pizza-convenience	1 unit	381	19.1	14.1	7.5	42
Applesauce	1 container	51	0.2	0.1	0	13
Trail mix	1 package	290	8	18	4.5	27
Dinner						
Chicken Primavera	325 g	346	29.4	8.5	3.3	38
Butter in Primavera	10 g	72	0	8	5.2	0
Cream of broccoli soup	168 g	137	4.8	7.3	2.3	14
Butter in soup	10 g	72	0	8	5.2	0
Chocolate chip cookie	1 (36 g)	160	2	8	4	23
Summary						
Actual		1963	78.3 g	78.5 g	34.7 g	245 g
Percent of kCal			16.0%	36.0%	15.9%	49.9%
Goal		2000	76 g	78 g	39 g	250 g
Percent of kCal			15%	35%	17.5%	50%
PARTICIPANT MAY DRINK NON-CALORIC BEVERAGES						

B) Sample Standard Diet #2

FOOD	AMT	kcal	PRO (g)	FAT (g)	SATFAT (g)	CARB (g)
Breakfast						
Breakfast Sandwich	1	251	19.6	7.9	4.5	25
Orange juice	2	122	0	0	0	28
Clementine	1	50	0.7	0.2		13
Raisins	30 g	94	0.8	0	0	25
Lunch						
Sliced turkey	40 g	48	12	0	0	0
Mayonnaise-light	2 packets	50	0	5	0	0
Tomato slice	3 slices	12	0.5	0.2	0	3
Potato chips	1 bag	160	2	11	3	15
String cheese	2 sticks	160	12	12	7	0
White bread	1 slice	83	2.5	0.5		16
lemonheads	2 boxes	180	0	0	0	44
Dinner						
Butter split between macaroni and cheese and vegetables	5 g	36	0	4	2.6	0
Garden medley vegetables	112 g	42	1.7	0	0	8
Macaroni and cheese	120 g	231	10	13.8	7.75	16
BBQ chicken breast	60 g	75	10	2.1	0.2	4
Donut chocolate	1 unit	365	3.3	20.7	8.4	42
Summary						
Actual		2042	77.6	77.9	33.45	255
Percent of kCal			15.2%	34.3%	14.7%	50.0%
Goal		2000	76 g	78 g	39 g	250 g
Percent of kCal			15%	35%	17.5%	50%
PARTICIPANT MAY DRINK NON-CALORIC BEVERAGES						

C) Sample Standard Diet #3

FOOD	AMT	kcal	PRO (g)	FAT (g)	SATFAT (g)	CARB (g)
Breakfast						
Pancakes	2	126	2.8	1.1	0.4	26
Pancake syrup	1 packet	120	0	0	0	30
Putter for pancakes	10 g	72	0	8	5.2	0
Orange juice	1	61				14
Omelet (with cheese)	1 package	288	20.2	21	7.3	6
Lunch						
Garden burger	1 patty	180	5.1	9.5	1	21
White bun	1 whole	110	3	2	0	21
Mayonnaise-light	2 packets	50	0	5	0	0
Cheddar Cheese	23 g	84	5.3	7.3	4.6	0
Potato chips	1 bag	160	2	11	3	15
Banana	medium	111	1.2	0.6	0	28
Dinner						
Chicken parmesan	157 g	233	27.6	7.7	1.9	13
Penne	98 g	159	5.3	0.8	0	32
Marinara sauce	56 g	24	1	0.4	0	4
White roll	28 g	80	2.5	1	0.5	15
Butter for roll	5 g	36		4	2.6	0
Raspberry sherbet	1 carton	120	0	1.5	1	27
Summary						
Actual		2014	76	80.9	27.5	252
Percent of kCal			15.1%	36.2%	12.3%	50.0%
Goal		2000	76 g	78 g	39 g	250 g
Percent of kCal			15%	35%	17.5%	50%
PARTICIPANT MAY DRINK NON-CALORIC BEVERAGES						

D) Sample High Carbohydrate Diet #1

FOOD	AMT	kcal	PRO (g)	FAT (g)	SAT-FAT (g)	CARB (g)
Breakfast						
Frosted Flakes	"Bowl"	110	1	0	0	26
Skim milk	236 g carton	79	7.7	0.4	0.3	11
Fat free strawberry yogurt	170 g carton	90	6	0	0	17
Apple Juice	4 oz. carton	61	0	0	0	15
Coffee	1 cup	4	0.4	0	0	0
Lunch						
Chicken noodle canned	206 g	50	3	0	0.5	8
Fresh cut vegetables	96 g	21	0.7	0.3	0	5
Ranch dressing	30 g	44	0.8	3.4	1	2.8
Grilled chicken breast	67 g	85	15.5	2.4	0.2	0
Lettuce leaf	15 g	4	0	0	0	0.4
Wheat bun	1	145	7	1	0	28
Butter on bun	5 g	36	0	4	2.6	0
Vernor's ginger ale	8 oz. can	96	0	0	0	26
Banana	small 6-6.8"	90	1.1	0.3	0.1	23
Dinner						
Lasagna half serving	78 g	118	9	5.4	3	7
Grape juice	2 cartons	122	0	0	0	30
Tossed greens	116 g	16	1.2	0.2	0	3
Raisins in salad	32 g	90	0.9	0.1	0	24
Fat free Italian dressing	22 g	10	0	0	0	2
Garden vegetable medley	113 g	42	1.7	0	0	8
Lemon ice	23 g carton	80	0	0	0	20
Sliced peaches	140 g	66	0	0	0	14.9
Snacks						
Banana, honey, coconut, juice, protein, yogurt Smoothie	240 g	243	9.6	5.1	3.6	43
US crackers	2 package	50	2	0	0	10
Grape jelly	3 packets	105	0	0	0	27
Skim milk to mix with:	236 g carton	79	7.7	0.4	0.3	11
Vanilla CIB no sugar	20 g packet	70	5	0	0	12
Summary						
TOTALS		2006	80.3	23	11.6	374.1
Percent of Kcal			16.1%	11%	5.2%	75%
GOALS		2000	77	22	11	375
Percent of Kcal			15	10	5	75
PARTICIPANT MAY DRINK NON-CALORIC BEVERAGES						

E) Sample High Carbohydrate Diet #2

FOOD	AMT	kcal	PRO	FAT	SAT-FAT	CARB
Breakfast						
Orange juice	1 carton g	61	0	0	0	14
Oatmeal	142 g	92	2.7	1.8	0	17
Raisins	35 g	110	1	0.2	0	27
Brown sugar	18 g	68	0	0	0	17.7
Skim milk	8 oz. carton	79	7.7	0.4	0.3	11
Coffee	1 cup	4	0.3	0	0	1
Lunch						
Tuna salad	68 g	88	13	3.5	0.4	1.7
Wheat bread	2 Slices	146	8	0.6	0	28
Pretzels	28 g package	110	2	1	0	23
Clementine	one (~ 113 g)	50	0.7	0.2	0	13
Lemon ice	carton	80	0	0	0	20
Soft drink	8 oz. can	90	0	0	0	24
Dinner						
Chili	160 g	137	8.5	3.8	1.5	16
Baked potato	250 g	247	5.2	0.2	0.1	57
Butter on potato	4 g	29	0	3.3	2.1	0
Sour cream	1/3 packet	20	0.3	1.7	1	0.7
Rasp sherbet	carton	120	0	1.5	1	27
Skim milk	236 g carton	79	7.7	0.4	0.3	11
Snacks						
Banana, honey, coconut, juice, protein, yogurt Smoothie	~ 240 g	243	9.6	5.1	3.6	43
Skim milk	236 g carton	79	7.7	0.4	0.3	11
Vanilla CIB no sugar	20 g packet	70	5	0	0	12
Summary						
TOTALS		2002	79.4	24.1	10.6	375.1
Percent of Kcal			15.9%	10.8 %	4.8%	74.9%
GOALS		2000	77	22	11	375
Percent of Kcal			15%	10%	5%	75%
PARTICIPANT MAY DRINK NON-CALORIC BEVERAGES						

F) Sample High Carbohydrate Diet #3

FOOD	AMT	kcal	PRO (g)	FAT (g)	SAT-FAT (g)	CARB (g)
Breakfast						
Raisin Bran	1 bowl	126	3	1	0	27
Extra raisins in cereal	32 g	90	0.9	0.1	0	24
Honey	2 packets	60	0	0	0	16
Skim milk	236 g carton	79	7.7	0.4	0.3	11
Clementine	one (~ 113 g)	50	0.7	0.2	0	13
Coffee	1 cup	4	0.4	0	0	0
Grape juice	carton	61	0	0	0	15
Lunch						
White bread bun	one	114	3	2	0	21
Sliced ham	57 g	50	9	1.5	0.5	1
Sliced turkey	33 g	40	9.7	0	0	0
Leaf lettuce	15 g	4	0	0	0	0.4
American cheese	17 g	51	2.6	4.3	2.6	0.9
Hellman's light mayonnaise	6 g	13	0	1.4	0	0.2
Pretzels	28 g package	110	2	1	0	23
Fresh grapes	120 g	83	0.9	0.2	0	21
Raspberry sherbet	1 carton	120	0	1.5	1	27
Skim milk	236 g carton	79	7.7	0.4	0.3	11
Dinner						
Penne pasta	99 g	160	5.3	0.8	0	32
Marinara sauce	113 g	48	2	0.8	0	8
Parmesan cheese	1 packet	15	1.3	1	0.6	0
Green beans	90 g	25	1.4	0.2	0	6
Tossed greens	116 g	16	1.2	0.2	0	3
Fat free Italian dressing	22 g	10	0	0	0	2
Orange jello	1 carton	73	1.5	0	0	17
Soft drink	1 can	95	0	0	0	24
Banana and coconut	small 6-6.8"	90	1.1	0.3	0.1	23
Unsweetened coconut	5 g	33	0.3	3.2	2.9	1.2
Snacks						
Skim milk	236 g carton	79	7.7	0.4	0.3	11
Vanilla CIB no sugar	20 g packet	70	5	0	0	12
Chocolate pudding	1 carton	128	3	2	1.5	24
Summary						
TOTALS		1976	77.4	22.9	10.1	374.7
Percent of Kcal			15.7%	10.4%	4.6%	75.9%
GOALS		2000	77	22	11	375
			15%	10%	5%	75%
PARTICIPANT MAY DRINK NON-CALORIC BEVERAGES						

G) Sample High Carbohydrate Diet #4

FOOD	AMT	kcal	PRO (g)	FAT (g)	SAT-FAT (g)	CARB (g)
Breakfast						
Omelet half serving	120 g	50	4.4	3.4	1.1	0.4
Pancakes reduced sugar	1 serving (2)	126	2.8	1.1	0.4	26
Pancake syrup	1 package	120	0	0	0	30
Skim milk	236 g carton	79	7.7	0.4	0.3	11
Coffee	1 cup	4	0.4	0	0	0
Orange juice carton	1 carton	60	0	0	0	14
Lunch						
Cream of tomato soup	170 g bowl	113	4.6	3	1.8	17
White bread	1 slice	83	2.5	0.5	0	16
Sliced ham	22 g	19	3.5	0.6	0.2	0.4
Swiss cheese	15 g	56	3.6	4.6	3.1	0
Pretzels	28 g package	110	2	1	0	23
Apple juice	two 4-oz carton	122	0	0	0	30
Yogurt Greek strawberry	140 g	121	11	0	0	20.5
Unsweetened coconut	5 g	33	0.3	3.2	2.9	1.2
Dinner						
BBQ sauce packet	2 packets	30	0	0	0	8
Grilled chicken breast	85 g	108	19.6	3	0.3	0
Wild rice half	50 g	48	1.1	0.8	0.1	9
White rice	55 g	63	1.3	0.2	0	18.5
Garden vegetable medley	113 g	40	1.7	0	0	8
Strawberry jello	116 g	71	1	0	0	17
Vernor's ginger ale	8 oz. can	100	0	0	0	26
Raisins	20 g	60	0.6	0	0	15
Snacks						
Skim milk	236 g carton	79	7.7	0.4	0.3	11
Rice Chex	1 bowl	70	1	0	0	16
Sugar for cereal	2 packets	22	0	0	0	6
Banana	small 6-6.8"	90	1.1	0.3	0.1	23
Unsalted crackers	2 package	50	2	0	0	10
Fruit Jelly	2 package	70	0	0	0	18
Summary						
TOTALS		1997	79.9	22.5	10.6	375
Percent of kCal			16.0%	10.1%	4.8%	75.1%
GOALS		2000	77	22	11	375
Percent of kCal			15%	10%	5%	75%
PARTICIPANT MAY DRINK NON-CALORIC BEVERAGES						

H) Sample High Fat Diet #1

FOOD	AMT	kcal	PRO (g)	FAT (g)	SAT-FAT (g)	CARB (g)
Breakfast						
Egg omelet with cheese	99 g	180	10	13	5	4
Sausage link	2 each	146	6	13.2	5.3	1
Wheat bread for toast	1 slice	73	4	0.3	0	14
Butter for bread	10 g	72	0	8	5.1	0
Coffee provided by participant	1 cup	4	0.4	0	0	0
Half and half	2 tubs (30 g)	39	0.9	3.5	2.2	1.3
Lunch						
Grilled ham and cheese	138 g (less than one)	344	20.6	17.8	10	28
Potato chips	1 package 28-29 g	160	2	11	3	15
Dinner						
Meatloaf	125 g	213	15.8	11.2	4.3	12.3
Macaroni and cheese	95 g	180	7.8	10.8	6	12.5
Green beans	91 g	25	1.4	0.2	0	6
Butter on beans/macaroni and cheese	30 g	216	0.2	24.4	15.4	0
Snacks						
Cheesecake	97 g slice	291	4.7	19.7	12.5	26
Summary						
TOTALS		1943	73.8	133.1	68.8	120.1
Percent of Kcal			15.2%	61.7%	31.9%	24.7%
GOALS		2000	76	133	66.5	125
			15%	60%	30%	25%
PARTICIPANT MAY DRINK NON-CALORIC BEVERAGES						

I) Sample High Fat Diet #2

FOOD	AMT	kcal	PRO (g)	FAT (g)	SAT-FAT (g)	CARB (g)
Breakfast						
Coffee participant provides						
Half and half	2 tubs (30 g)	39	0.9	3.5	2.2	1.3
Oatmeal	195 g	123	3.6	2.4	0	23
Coconut oil in oatmeal	11 g	95	0	11	9.5	0
Butter in oatmeal	10 g	72	0	8.1	5.1	0
no calorie sweetener	1 packet	0	0	0	0	0
Vanilla Greek yogurt	125 g	91	10.8	0	0	12.5
Lunch						
Caesar salad	one 100 g	49	5.1	2.9	1.8	2
Caesar dressing	one packet	233	1	25	4	1
Grilled chicken breast	75 g	95	17.2	2.6	0.3	0
Corn	45 g	36	1.2	0.2	0.05	8.5
Butter in corn and on chicken	10 g	72	0	8	5.2	0
Dinner						
Potato crusted cod	85 g	151	15.8	6	2.3	7.5
Tartar sauce	12 g packet	40	0	4	0	2
Baked potato (half)	112 g	113	2.3	0.1	0	26.1
Sour cream	1 packet	60	1	5	3	2
Broccoli	85 g	21	2.3	0.1	0	4
Shredded cheddar on vegetables	29 g	113	7.1	9.1	5.1	1
Butter on broccoli	10 g	72	0	8.1	5.1	0
Butter in potato	14 g	100	0.1	11.4	7.2	0
Almond joy	45 g	220	2	13	8	26
String cheese	28-29 g stick	80	6	6	3.5	0
Potato chips	28-29 g bag	160	2	11	3	15
Summary						
TOTALS		2035	78.4	137.5	65.35	131.9
Percent of kCals			15.4%	60.8%	28.9%	25.9%
GOALS		2000	76	133	66.5	125
			15%	60%	30%	25%
PARTICIPANT MAY DRINK NON-CALORIC BEVERAGES						

J) Sample High Fat Diet #3

FOOD	AMT	kcal	PRO (g)	FAT (g)	SAT-FAT (g)	CARB (g)
Breakfast						
Breakfast Wrap	one (~ 125 g)	328	16.6	16	6	29
Coffee provided by participant	1 cup	4	0.4	0	0	0
Half and half	2 tubs (30 g)	39	0.9	3.5	2.2	1.3
Lunch						
Grilled cheese	1 sandwich	343	16.3	19.2	11.1	28
potato chips	1 bag	160	2	11	3	15
Dinner						
Grilled chicken breast	72 g	91	16.7	2.6	0.3	0
Broccoli	82 g	23	2.5	0.1	0	4
Butter on broccoli	15 g (1 T)	108	0.1	12.2	7.7	0
Garden vegetable medley	57 g	21	0.9	0	0	4
Butter in macaroni and cheese	15 g (1 T)	108	0.1	12.2	7.7	0
Macaroni & cheese	196 g	375	16.2	22.4	12.6	26
Butter in vegetable	15 g (1 T)	108	0.1	12.2	7.7	0
Salt and pepper						
Vegetable oil in macaroni and cheese	10 g	91	0	10	0	0
Snacks						
Cheesecake	68 g	195	3.1	13.2	8.4	17
Summary						
TOTALS		1994	75.9	134.6	66.7	124.3
Percent of Kcal			15.2%	60.8%	30.1%	24.9%
GOALS		2000	76	133	66.5	125
			15%	60%	30%	25%
PARTICIPANT MAY DRINK NON-CALORIC BEVERAGES						

K) Sample High Fat Diet #4

FOOD	AMT	kcal	PRO (g)	FAT (g)	SAT-FAT (g)	CARB (g)
Breakfast						
Egg omelet with cheese	99 g	180	10	13	5	4
Sausage link	2 links	146	6	13.2	5.3	1
Coffee participant to provide	1 cup	4	0.3	0	0	1
Half and half	2 tubs (30 g)	39	0.9	3.5	2.2	1.3
Lunch						
Cheesy potato bisque	1 serving (170 g)	180	6.5	10.4	6.5	15
Butter in soup	10 g	72	0	8	5.1	0
Beef brisket sandwich made of:						
Roast beef	81 g	110	10.3	4.9	1.9	4.5
Cheddar cheese	23 g	84	5.3	7.3	4.6	0
Wheat roll	1 (35 g)	81	3.1	0.8	0	15
Butter on roll	10 g	72	0	8	5.1	0
Mustard packet	one	3	0.2	0.2	0	0.3
Dinner						
Meat sauce	113.5 g	113	7.7	5.3	0	9
Penne plain	99 g	159	5.3	0.8		32
Butter in penne	20 g	144	0	16	10.2	0
Broccoli	82 g	23	2.5	0.1	0	0
Cheddar cheese on broccoli	23 g	84	5.5	7.3	4.6	0
Butter in broccoli	7 g	50	0	5.6	3.6	0
Snacks						
Chocolate cake	78 g	285	3	17.7	6.9	31
Summary						
TOTALS		2009	76.6	135.1	66	118.1
Percent of Kcal			15.3%	60.5%	29.6%	23.5%
GOALS		2000	76	133	66.5	125
			15%	60%	30%	25%
PARTICIPANT MAY DRINK NON-CALORIC BEVERAGES						

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Chapter 4: Dynamic Response of the Metabolome During the Hyperinsulinemic-Euglycemic Clamp in Healthy Obese Individuals

Abstract

Although the vast majority of obese adults are insulin resistant (IR), some obese individuals remain relatively insulin sensitive (IS), though the underlying mechanisms for this difference are unclear. The hyperinsulinemic-euglycemic clamp (HEIC) is the gold standard test for insulin sensitivity. However, it is not clear if the differences in insulin-mediated changes in glucose metabolism between IS and IR obese individuals extend to other key metabolites.

In this study, we monitored the dynamics of 62 metabolites in obese-IR, obese-IS, and lean controls during a HEIC. From an original screening of 28 obese adults, twelve non-diabetic subjects, matched for age, sex, BMI, fat mass and fat-free mass were divided into the 6 most IS and 6 most IR women based on glucose infusion rate during a HEIC. 6 lean controls were also measured as a negative control. After initial groups as obese-IR, obese,-IS, and lean it was apparent that the lean controls clustered with the obese subjects by glucose infusion rate (GIR) rather than by obesity. All subjects were then recharacterized as either low GIR or high GIR with 9 subjects (6 obese and 3 lean) falling into both groups.

Fasting insulin was 16.4(7.9) and 9.4(2.0) between low GIR and high GIR groups respectively ($p<0.05$). Serum metabolite levels were measured at 8 time points during the clamp using liquid chromatography-mass spectrometry (LC-MS): 2 samples at baseline, immediately prior to insulin infusion, every 20 minutes during the insulin infusion (4 samples), and 2 samples at steady state (SS) glucose levels (after ~2h of insulin infusion). We quantitated metabolite levels by peak area, with stable-isotope internal standards used to allow absolute quantitation of select metabolites. Statistical differences between IS and IR groups were assessed using paired Student's t-tests and ANOVA with Tukey's post-hoc analysis.

Regardless of adiposity, branched chain amino acids (BCAA) and free fatty acids (FFA) were higher in the low GIR group throughout the clamp ($p<0.05$). Acylcarnitines (ACAR) were significantly higher ($p<0.05$) in low GIR subjects from ACAR 2:0 through ACAR 14:1 and again at ACAR 18:1. However, this pattern was not evident in the longer chain ACAR except for 18:0 and 18:1. The suppression of lipolysis is seen in all FFA and in most acylcarnitines. However, while FFA is reduced to near zero, their longer chain cognate acylcarnitines do not see a similar and expected reduction.

These findings indicate that obese adults, who are seemingly "protected" against a decline in insulin-mediated glucose uptake, also demonstrate improved response of insulin to lower BCAA and other amino acids, as well as short and medium-chain acylcarnitines which have been associated with an increased risk of development of type 2 diabetes. These results suggest that insulin resistance and not obesity per se drive changes in the plasma level of metabolites associated with risk of type 2 diabetes. Furthermore, the differential suppression of acylcarnitines with short and medium chain acylcarnitines are reduced but long chain

acylcarnitines not suggests that acylcarnitines are either differentially metabolized or exhibit differential clearance.

Introduction

Obesity is a growing global public health problem (1) and is associated with metabolic disorders such as insulin resistance and type 2 diabetes mellitus (T2DM) which lead to an increased risk for cardiovascular disease (2-4). While the connection between obesity and insulin resistance is well established (5), not all obese individuals become insulin resistant (6-8). These metabolically healthy obese people exhibit excess adiposity yet have favorable lipid, cytokine, and inflammatory profiles not seen in their metabolically unhealthy obese counterparts (6, 7, 9-11). Metabolically healthy, obese individuals have been found to have less risk for cancer mortality (12), T2DM (13, 14), coronary heart disease, and other cardiovascular diseases when compared to their metabolically unhealthy counter parts (13, 15). Metabolically healthy subjects also have a similar response in insulin sensitivity and adaptation to caloric challenge (high caloric meal) as metabolically, lean individuals when compared to unhealthy subjects (16).

Recently, the use of high-throughput profiling of metabolic status or metabolomics has shown the ability to elucidate differences between insulin resistant and insulin sensitive individuals including differences in levels of amino acids, TCA cycle intermediates, and fatty acids (17, 18). Using metabolomics, circulating branched chain amino acids (BCAA) are shown to be negatively correlated with insulin sensitivity and obesity induced T2DM (19). Elevated plasma BCAAs and aromatic amino acids appear to be potential predictors of future diabetes in healthy individuals identified using metabolomics (20-22). This finding highlights the use of

emerging technologies of metabolomics to enhance our knowledge and understanding of metabolic disorders like insulin resistance and T2DM and their causes (9, 18, 23, 24).

Currently, the HIEC is considered the gold standard for assessing *in vivo* insulin sensitivity (25, 26). Studies using metabolomic profiling have shown blunted responses in key metabolites related to proteolysis (19, 27), lipolysis (27-29), and glycolysis (30). Researchers have conducted metabolomic studies using glucose challenges such as oral glucose tests (20, 27-30) but not using the HIEC.

In this study, we sought to compare the metabolic response in metabolically healthy obese individuals with lean healthy controls during the HEIC.

Research Design and Methods

Study Sample

We recruited a cohort of 28 metabolically healthy obese individuals for an initial study of fat cell metabolism (31). From this group we chose to further assess the plasma metabolomics profiles on the 6 most sensitive (Obese-IS) and 6 least sensitive (Obese-IR) individuals as determined by HIEC as well as 6 lean individuals (Lean) which were chosen as a negative control group (Table 4.1). Written, informed consent was obtained from all subjects before beginning any testing. The University of Michigan Institutional Review Board approved all study procedures. All obese subjects were female, but LEAN was comprised of 2 males and 4 females. When grouped with LEAN and with Low GIR/High GIR the men did not significantly differ in metabolites from their female counterparts ($p > 0.05$) so were retained in the study.

Exclusion criteria included coronary heart disease, T2DM, hypertension, clinically significant hypertriacylglycerolemia, or taking regular medications known to affect metabolic

processes. Inclusion criteria included BMI > 30 for obese subjects BMI <27 for lean subjects, ages between 21-45, and no history of metabolic disorder for either group. All subjects were nonsmokers, weight stable (±2 kg) for the past 6 months, and no participation in regular exercise for the prior 6 months.

Clinical Assessment

Subjects arrived and were admitted to the Michigan Clinical Research Unit (MCRU) following an overnight fast on the morning of the study. The clamp was preceded by 2 hours with subcutaneous adipose tissue collection and ^{13}C-palmitate infusion to measure resting fatty acid rate of appearance in the plasma. The clamp was performed using a primed 2 hour insulin infusion at a rate of 100μM/m^2/min. This rate was selected to inhibit hepatic glucose production, even in insulin resistant subjects (32). Glucose was infused at a variable rate to maintain plasma concentrations. Insulin sensitivity was determined using samples collected in the final 20 minutes of the HIEC. Blood samples were taken at 9 time points during the clamp and immediately processed to extract plasma (figure 4.1). Samples were taken before beginning of the HEIC to establish a background measurement, twice for baseline values before insulin and glucose infusion, 5 times every 20 minutes during the infusion until a SS glucose level was reached, and twice during SS 5 minutes apart (figure 4.1). Average plasma glucose concentrations during the final 20 minutes of the clamp was 98 ± 5% of baseline fasting glucose concentration values. Insulin sensitivity level is defined as the GIR during the last 20 minutes of the HIEC/fat-free mass. The entire procedures are further described in a prior paper by this study group (31). Plasma samples were frozen in liquid nitrogen as soon as possible after extraction and stored at -80^{0}C until it was needed for LC/MS.

Metabolic profiling

Metabolites were extracted and analyzed by LC-MS-based metabolomics using methods similar to those previously described elsewhere (33). Briefly, extraction solvent was prepared by adding stable-isotope labeled internal standards at the concentration specified in Table 1 to a 1:1:1 mixture of methanol:acetonitrile:acetone. Plasma samples were thawed at 4°C and a 50 µL aliquot was extracted by addition of 200 µL of extraction solvent followed by vortexing. After incubating on ice 5 minutes, samples were centrifuged at 15,000 x g for 10 minutes. The supernatant was transferred to autosampler vials for analysis. Polar metabolites (Amino acids, TCA cycle metabolites, etc.) were analyzed by hydrophilic interaction chromatography-electrospray time-of-flight mass spectrometry (HILIC-ESI-TOF-MS) (34) on an Agilent 6220 TOF-MS. The column used was a Phenomenex Luna NH_2, 3µ particle diameter, 150 mm x 1 mm i.d. Mobile phase A was 5 mM ammonium acetate in water, adjusted to pH 9.9 with ammonium hydroxide; mobile phase B was acetonitrile. The gradient consisted of a 10 minute linear ramp from 80% to 0% B, a 5 minute hold at 0%B, and a 12 minute re-equilibration at 80%B. The injection volume was 10 µL and the flow rate was 0.07 mL/min. MS parameters were as follows: drying gas temp 350°C, drying gas flow rate 10 L/min, nebulizer 20 psig, capillary voltage 3500 V, negative ion mode. ACAR were analyzed using reversed phase liquid chromatography-electrospray ionization-tandem quadrupole mass spectrometry (RPLC-ESI-QQQ-MS) (35, 36) on an Agilent 6410 LC-MS. The column used was a Waters HSS T3, 1.8µ particle diameter, 100 mm x 2.1 mm i.d. Mobile phase A was 0.1% formic acid in water; mobile phase B was 0.1% formic acid in acetonitrile. The gradient consisted of a 7 minute linear ramp from 0 to 99% B, a 3 minute hold at 99%B, and a 5 minute re-equilibration at 0%B. The injection volume was 5 µL

and the flow rate was 0.20 mL/min. MS parameters were as follows: drying gas temp 320°C, drying gas flow rate 10 L/min, nebulizer 40 psig, capillary voltage 4000 V, positive ion mode. MRM transitions for acylcarnitines (ACAR) were the same as those specified previously (33). Targeted metabolites were identified based on retention time and accurate mass (for HILIC-TOF data) or MRM transition (for RPLC-QQQ data) determined by previous analysis of authentic standards (table 4.2). We performed relative quantitation by measuring peak area using Agilent Masshunter Quantitative Analysis Software version B.07.00 (Santa Clara, CA).

Subject Grouping

Initially, we performed metabolomic profiling on 28 obese subjects recruited to the study. They were then separated into the 6 most glucose sensitive (Obese-IS) and 6 most glucose resistant (Obese-IR). These 6 were compared to the metabolomic profiles of 6 LEAN subjects that also went through the screening and HEIC. This grouping into three groups was called Obese-IR/Obese-IS/Lean and will be called grouping by adiposity from this point forward.

When it was noted that the metabolic profile of the LEAN group tended to fall in between the Obese-IR and Obese-IS instead of grouping with the Obese-IS group as expected, subjects were regrouped into two groups based upon their glucose infusion rate (GIR) (High GIR vs Low GIR). This grouping is referred to as grouping by GIR from this point forward.

Statistical analysis

Baseline data grouped by adiposity was compared using One-Way Analysis of Variance (ANOVA) with a Fisher's Least Significant Difference (LSD) post-hoc test with a cutoff of $p<0.05$ using Prism 7.04 (www.graphpad.com) (table 4.2). Grouping by GIR was compared using Students T-tests with a cutoff of $p<0.05$ using Excel 2016 (table 4.2). Metabolite peak areas were corrected for minor instrument peak area drift. This correction was performed using

locally estimated scatterplot smoothing (LOESS) performed in MetaboDrift software operating in Microsoft Excel 2016 (37). Metabolite data was normalized using Metaboanalyst using drift corrected peak intensity data files. Missing values were replaced with small values by default. Data was filtered using the interquartile range (IQR) and data was normalized by log transformation and autoscaling (mean/SD). Metabolite areas under the curve (AUC) and internal standard ratios were compared using either ANOVA with a Fisher's LSD post-hoc test or Student's t-tests using Metaboanalyst with $p<0.05$ with a false discovery rate (FDR) cutoff of 0.1. (www.metaboanalyst.ca) (38, 39). Fold-change was calculated using Microsoft Excel 2016 using a negative ratio of baseline value to clamp value for a decrease over the clamp and a positive ratio of baseline value to clamp value for an increase over the clamp.

Results

Subject characteristics

There were no differences in age between adiposity or GIR groupings. As expected, the lean subjects had a significantly lower body mass, BMI, and body fat percentage when compared with obese groups (Table 4.1). Subjects were well matched for BMI and body composition between obese-IR and obese-IS differing only in fat mass and BMI between both obese groups and lean (Table 4.2). When stratified into GIR groups, there were no differences in physical characteristics between subjects (Table 4.2). Groups only differed in mass and BMI between obese groups and lean groups. GIR expressed in mg/kg FFM/min was significantly different between Obese-IR and Obese-IS, between Obese-IS and lean, but not between Obese-IR and lean ($p<0.05$). GIR was also significantly higher in Obese-IR and Obese-IS when sorted by GIR ($p<0.05$) (Table 4.2 & Fig. 4.2). Assayed glucose was not different between any groups whether sorted by adiposity or GIR at neither the beginning of the clamp nor SS (Table 4.2).

Differences between groups when comparing grouping by adiposity

Subjects were initially divided into Obese-IR, Obese-IS, and LEAN. Only glutamate was found to be different at any time point (20 minutes and at Clamp) (Figure 4). In general, it was found that the LEAN subjects average metabolite values mediated Obese-IR and Obese-IS, falling in between Obese-IR and Obese-IS. A representative sample of these values are found in Figure 4.5. While abundance of lipids was not significantly different between groups, the rate of decrease for fatty acids, specifically oleic, palmitic, stearic, and linoleic acids, was greater in Obese-IR than in Obese-IS and LEAN during the clamp (figure 4.5). This was not found in phospholipid species (figure 4.7b). Fold change was also computed for metabolite levels and only ACAR 16:0 showed a statistical difference between groups with the Obese-IS group reporting a larger fold change decrease compared to the lean group and no difference between Obese-IR and lean (figure 4.4 & figure 4.8c). LEAN subjects followed a mediating pattern between the Obese-IR and Obese-IS groups (figures 4.5 – 4.10). This led us to choose to separate subjects by a measure of insulin resistance, glucose infusion rate (GIR).

Difference between groups when sorted by grouping by GIR

The differences in metabolite changes were more profound when sorted into relatively Low GIR and High GIR than when these differences were mediated by the LEAN subjects being separated out. For all metabolites, no groups differed at baseline (figures 4.5 – 4.10). However, for amino acids, the branched chained amino acids (BCAAs) were higher for Low GIR subjects throughout the time course for isoleucine/leucine and at the end of the time course (time 80 min and clamp) for valine (figures 4.4 - 4.6). Similarly, glutamate was higher throughout the time course for Low GIR, but was only significant at time 20 and at the clamp (figures 4.4 – 4.6).

Lipid patterns were similar, if even more profound, when grouped as High GIR vs Low GIR (figure 4.5). Low GIR subjects had higher abundance of fatty acids during all time points of the clamp for oleic, stearic, and palmitic acid and linoleic acid followed the same pattern but did not reach significance at 60 or 80 minutes. Like the earlier grouping, the less insulin sensitive group had a steeper slope than the more insulin sensitive group early in the clamp (figure 4.5). As with the earlier grouping, fatty acids were the only type of lipids that reached significance during the clamp. Fold change did not differ between groups for any lipid species.

Short and mid-chain acylcarnitines were significantly higher in Low GIR subjects than in High GIR subjects toward the end of the clamp, 80 minutes and at SS (figures 4.4 & 4.5). This pattern was found in ACAR 2:0 through ACAR 14:1 carnitines and again in ACAR 18:1 carnitine (figures 4.8a – 4.8c). This pattern was evident in other acylcarnitines, but did not reach the threshold for significance. The slope of acylcarnitines were not significantly different between groups except for in ACAR 6:0, ACAR 8:0, and ACAR 10:0 all seeing the Obese-IS group having a steeper slope between the 20 minute and 40 minute of the clamp. Finally, when comparing the fold change in acylcarnitines the IS group showed greater fold change decrease in many of the acylcarnitine species. Specifically ACAR 6:0, ACAR 8:0, ACAR 10:0, ACAR 12:1, ACAR 12:0, ACAR 16:1, ACAR 14:1, ACAR 16:0, and ACAR 18:0 (figure 4.4). Fold changes were also computed for other metabolites but they were not found to be statistically different between Low GIR and High GIR groups (figure 4.4).

Discussion

General Summary

Using a simple, yet systematic approach, we have demonstrated differences between obese, yet metabolically healthy individuals based on insulin sensitivity expressed at GIR and

established during the HIEC. Further, we have shown that these differences appear to be primarily due to insulin resistance rather than excess adiposity. Before grouping by GIR, it was expected that LEAN subjects would cluster nicely with the "healthier" Obese-IS group. Instead, most LEAN metabolites tended to mediate between Obese-IR and Obese-IS subjects. Lastly, we have identified differences in metabolite responses in lean, Obese-IR, and Obese-IS subjects during the HIEC which may be used to indicate metabolic phenotypes for future studies.

To the best of our knowledge, this is the first study to describe physiological changes in metabolites during the HIEC. Specifically, in healthy, yet obese individuals and their lean counterparts. Several studies have reported changes during caloric challenges (16) and oral glucose tolerance tests (OGTT) (20, 28-30, 40), but few have been done during the HIEC. In an HIEC, subjects are given insulin appropriate to their body volume while glucose is infused to maintain blood glucose levels (26, 31), while in an OGTT, a glucose bolus is ingested and insulin response is measured (41). Due to these differences in assessment method, we have shown metabolite differences due to insulin action as opposed to response to glucose. While subtle, this may be important for drawing physiological conclusions.

Amino Acids

All amino acids, except for alanine, dropped significantly from their baseline levels independent of grouping figure 4.6. This drastic drop in amino acid levels is a clear indication of a downregulation of proteolysis, probably due to an increase in insulin (42). However, it was only when grouped by GIR that we see significant differences between groups. Leucine/Isoleucine (20, 40, 60, 80, SS), Valine (80, SS), and Glutamate (20, SS) were higher in the Low GIR group compared to the High GIR group. At the time points indicated in parenthesis. There is ample evidence that insulin resistance and obesity have an effect on branched chain

amino acid differences between obese, insulin resistant subjects and lean subjects (30, 43-45). However, in this instance, the lean subjects did not differ from either obese-IR or obese-IS subjects, but rather these differences were revealed when taking insulin resistance (GIR) into account. In this population, this is evidence that insulin resistance, rather than obesity alone is the cause of these differences in amino acid differences. Our results suggest that disordered BCAA short chain acylcarnitine metabolism could be due to decreased insulin sensitivity (45, 46) independent of obesity.

Lipids

All fatty acids, both saturated (stearic acid – 18:0, palmitic acid – 16:0) and unsaturated (oleic acid – 18:1, linoleic acid – 18:2) showed a significant and drastic suppression of lipid abundance during the clamp (figures 4.5 & 4.7). The levels of circulating free fatty acids (FFA) are dependent upon the rates of lipolysis within adipose tissues (47). The decrease seen in our study is likely due to the effects of both insulin and glucose inhibiting lipolysis (47-49). However, there was a slight yet significant dampening of this decrease in lipolysis in all of these fatty acids with the abundance levels of all four being higher in low GIR subjects compared to high GIR subjects throughout the clamp and at baseline (figures 4.5 & 4.7). Impaired fatty acid oxidation may be indicative of increased insulin resistance (50), and may be implicated in the differences we see in Low GIR and High GIR subjects. Increased accumulations of fatty acids could also lead to alterations in the insulin signaling pathway which we may be seeing in a decrease insulin sensitivity in Low GIR subjects here (51).

Acylcarnitines

Like amino acids and fatty acids, there were no significant differences throughout the course of the clamp. However, when subjects were sorted by GIR, a very interesting result

emerged. There were few differences between GIR groups at the beginning of the clamp, but the short and medium chain acylcarnitines (C2:0 – C14:1, but not C8:1) were significantly lower in High GIR subjects than Low GIR subjects at SS (C2:0 –C14:1, but not C8:1) and also at 80 minutes (C5:6, C6:0, C10:0, C12:0, C12:1, and C16:1) (figures 4.4 & 4.5). This leads to two important insights.

First, GIR differences rather than obesity are playing a part in these differences as we do not see these differences between groups when sorted by obesity (figure 4.5). While none of these subjects have diabetes, some are able to infuse glucose better to other due to the action of insulin and are thus slightly more insulin sensitive (High GIR) than the others (Low GIR). These differences must be due to these slight differences in insulin resistance, and not due to obesity. Acylcarnitines have been established as being associated with insulin resistance in many studies (28, 52-55). In particular, C10:0 and C12:0 are suppressed less in insulin resistant individuals (28), this is mirrored in our data. Short chain acylcarnitines have also been associated in insulin resistance, as in our data (56). Incomplete fatty acid oxidation may be implicated in this phenomenon and could be associated with insulin resistance (52-54).

Secondly, acylcarnitines are indicative of fatty acid metabolism and as such would be expected to decrease in concert with fatty acids This should be especially true of the longer chain acylcarnitines which are direct metabolites of their fatty acid cognates (i.e. Oleic acid – 18:1 → C18:1). Levels of oleate (18:1) and palmitate (16:0) are significantly decreased during the course of the HEIC while their cognate acylcarnitines, C18:1 and C16:0 respectively, are not (figures 4.4 & 4.5).

One potential reason for this is that acylcarnitines are cleared from the blood by the kidneys (57). Kalim et al. found that carnitines are preferentially cleared from the blood

according to carbon chain length (58). Our data support this by showing that short and medium chain acylcarnitines are decreasing significantly through the clamp while longer chain acylcarnitines are not. This pattern is also found in other studies (28, 59, 60). This leads us to wonder if other studies that find major clearance of medium but not longer chain acylcarnitines could potentially be due to a lack of clearance rather than just action of the medium chain acylcarnitines. Our lab is currently analyzing urine acylcarnitine levels during HEIC which should provide evidence to help determine differential renal clearance of acylcarnitines.

Another potential reason for this discrepancy in the clearance of acylcarnitine by carbon chain length could be due to the action of glucose on the acylcarnitine enzymes. Carnitine palmitoyltransferase I (CPT1) is a mitochondrial enzyme that acts to produce long chain acylcarnitines from long chain fatty acyl-CoA through the replacement of a carnitine for a CoA (57). Malonyl-CoA inhibits the action of CPT1 that produced in the presence of excess glucose such as during the HEIC (57). This promotes glycolysis and lipogenesis while inhibiting lipolysis in the presence of excess glucose (57). However, medium chain acylcarnitines are produced by a proxosomal enzyme called peroxisomal carnitine O-octanolytransferace (CrOT) which is not inhibited by malonyl-CoA (61). It is possible that medium chain acylcarnitines are produced and undergo lipolytic metabolism under the presence of excess glucose while stalling this process for longer chain acylcarnitines.

Strengths/Limitations

This particular study uses metabolically healthy individuals that could potentially provide insight into the etiology of diseases such as T2DM. The use of healthy obese participants as well as lean negative controls leads to strong conclusions concerning the role of GIR in metabolomic difference instead of adiposity. The inclusion of lean negative controls with obese-IR and obese-

IS highlights the control of metabolomic difference is from GIR rather than adiposity. Further, the use internal standards and targeted metabolomics lends confidence to our results. The use of the HEIC is particular useful in illuminating dynamic changes in metabolomic profiles due to acute glucose and insulin infusions.

This particular study was small (n=18) with 6 obese-IR, 6 obese-IS, and 6 lean subjects and a further study involving a larger population is warranted to validate these results. This is also a cross-sectional study so obesity histories are unknown for these subjects. As such, it is difficult to understand long-term repercussions of obesity to the metabolomic profiles of these participants. As such, a longitudinal study involving obese-healthy and lean subjects could be used to follow-up this study.

Conclusion

While this was a small, cross-sectional study, it does raise important findings concerning the metabolomic dynamics during the HEIC. First, differences in suppression of levels of fatty acids, amino acids, and short to medium-chain acylcarnitines appear to be due to differences in innate insulin sensitivity of participants rather than due to adiposity. However, this is a small study and is cross-sectional so warrants a larger, longitudinal study using more metabolically healthy lean and obese participants. Secondly, we saw clearance of short and medium chain acylcarnitines but not long chain acylcarnitines. Concurrently, reciprocal long chain fatty acids that should mirror these unchanging long chain acylcarnitines are highly suppressed. This discrepancy is perhaps due to a differential clearance of acylcarnitines, which decreases with increasing carbon length (58). Further metabolomic analysis of differential clearance of urine acylcarnitines will help elucidate whether the differences we see in clearance is due to metabolic processes or renal clearance differences. Alternatively, medium chain acylcarnitine production is

not inhibited by high glucose induced production of malonyl-CoA at peroxisomal CrOT while long chain acylcarnitine production is inhibited at CPT1.

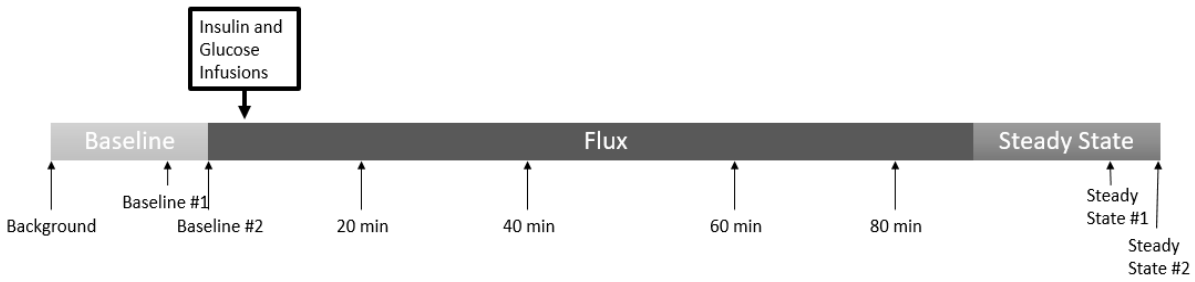
Tables and Figures

Table 4.1: Hyperinsulinemic-euglycemic Clamp Subject characteristics

	Grouped by Obese-IR, Obese-IS, & Lean (A)			**Grouped by GIR (B)**	
	Obese-IR[(a)]	**Obese-IS[(b)]**	**Lean[(c)]**	**LOW GIR**	**High GIR**
Sex (m/f)	(0/6)	(0/6)	(2/4)	(1/8)	(1/8)
Age (years)	32.8(7.0)	33.3(10.1)	28.8(9.2)	30.2(7.9)	33.1(9.9)
Mass (kg)	101.7(11.9)	94.3(8.1)	70.8(6.3) *	92(17.3)	85.9(13.9)
BMI (kg/m^2)	37.7(3.8)	35.4(3.2)	23.2(1.2) *	33.1(7.3)	31.1(6.6)
Body Fat (%)	47.6(11.6)	52.0(3.1)	29.5(8.0) *	41.6(12.2)	44.5(12.4)
Fat Mass (kg)	48.8(11.6)	49.2(6.3)	20.5(4.4) *	39.5(17.5)	39.5(15.7)
Fat Free Mass (kg)	52.9(6.9)	45.1(3.4)	50.4(10.1)	52.5(8.9)	46.5(6.6)
Assayed Glucose (Baseline) (mg/dL)†	83.7(3.6)	83.6(16.4)	80.7(6.4)	82.2(5.0)	83.8(15.0)
Assayed Glucose (SS) (mg/dL)†	81.0(2.7)	83.6(14.5)	80.3(5.6)	80.2(3.6)	83.9(13.3)
Fasting Glucose	4.8(0.8)	4.7(0.5)	4.7(0.2)	4.8(0.7)	4.7(0.4)
Fasting insulin [µU/mL]	19.7(6.6)*	10.9(4.0)	8.2(3.0)	16.4(7.9)*	9.4(2.0)
HOMA-IR [(FG*FI)/22.5]	4.4(1.8)	2.3(1.0)	1.7(0.7)*	3.6(2.0)	2.0(0.9)
FA Ra/kg (umol/kgFM/min)	17.5(4.2)	7.6(2.5)*	n/a	n/a	n/a
M3 (mg/kgFFM/min)	7.4(1.0)	15.6(2.1)*	n/a	n/a	n/a
TG (mg/dL)	77.2(42.1)	47.4(19.5)	95.3(29.8)*	83.5(44.0)	63.1(29.8)
Total cholesterol	157.5(12.1)	166.7(40.3)	141.8(29.0)	7.6(1.2)	14.9(2.1)

Data are presented as Mean (SD) unless otherwise noted. * = $p < 0.05$ using ANOVA with Tukey's post-hoc test for the grouping by adiposity and $p < 0.05$ using student's t-test for grouping by GIR. Lean measurements for fasting insulin, fatty acid rate of appearance (FA RA), M3, triglyceride, and cholesterol were not available do they are not included in the analysis. †Two lean subject glucose assays were unavailable, so for glucose assay n=16.

Figure 4.1: Time line for the HIEC.

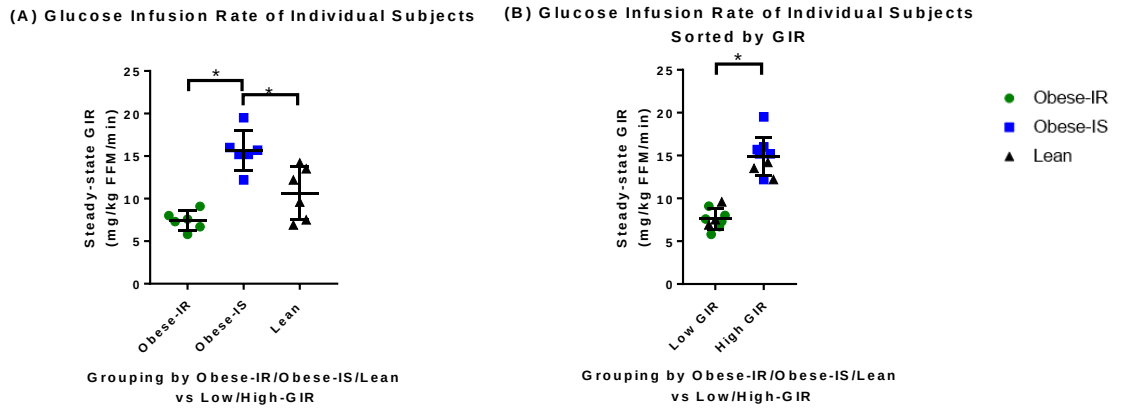


Small samples (3 ml) were taken throughout the clamp to monitor glucose levels throughout the HIEC. Large vials (10 ml) were taken at the time points indicated above. Baseline measurements were taken as an average of Baseline #1 and Baseline #2 and Steady State (SS) measurements were taken as an average of the two SS measurements.

Table 4.2: Authentic C-13 labeled internal standards added to LC/MS plasma samples for comparison/identification of targeted metabolites.

Amino Acids	**Acylcarnitines**		
Leucine/Isoleucine	L-carnitine	ACAR 8:0	ACAR 16:2
Phenylalanine	ACAR 3:0	ACAR 10:1	ACAR 14:0
Valine	ACAR 2:0	ACAR 10:0	ACAR 16:1
Methionine	ACAR 4:0	ACAR 12:1	ACAR 18:2
Alanine	ACAR 5:0	ACAR 14:2	ACAR 16:0
Tyrosine	ACAR 6:0	ACAR 12:0	ACAR 18:1
Threonine	ACAR 8:1	ACAR 14:1	ACAR 18:0
Histidine	**Lipids**	**Glucose Metabolites**	
Serine	Oleic acid	Hexose	Succinate
Aspartate	Palmitic acid	Lactate	Malate
Glutamate		Citrate/isocitrate	

Figure 4.2: GIR Infusion rates of individual subjects grouped as either Obese-IR/Obese-IS/Lean (A) or High-GIR/Low-GIR (B)

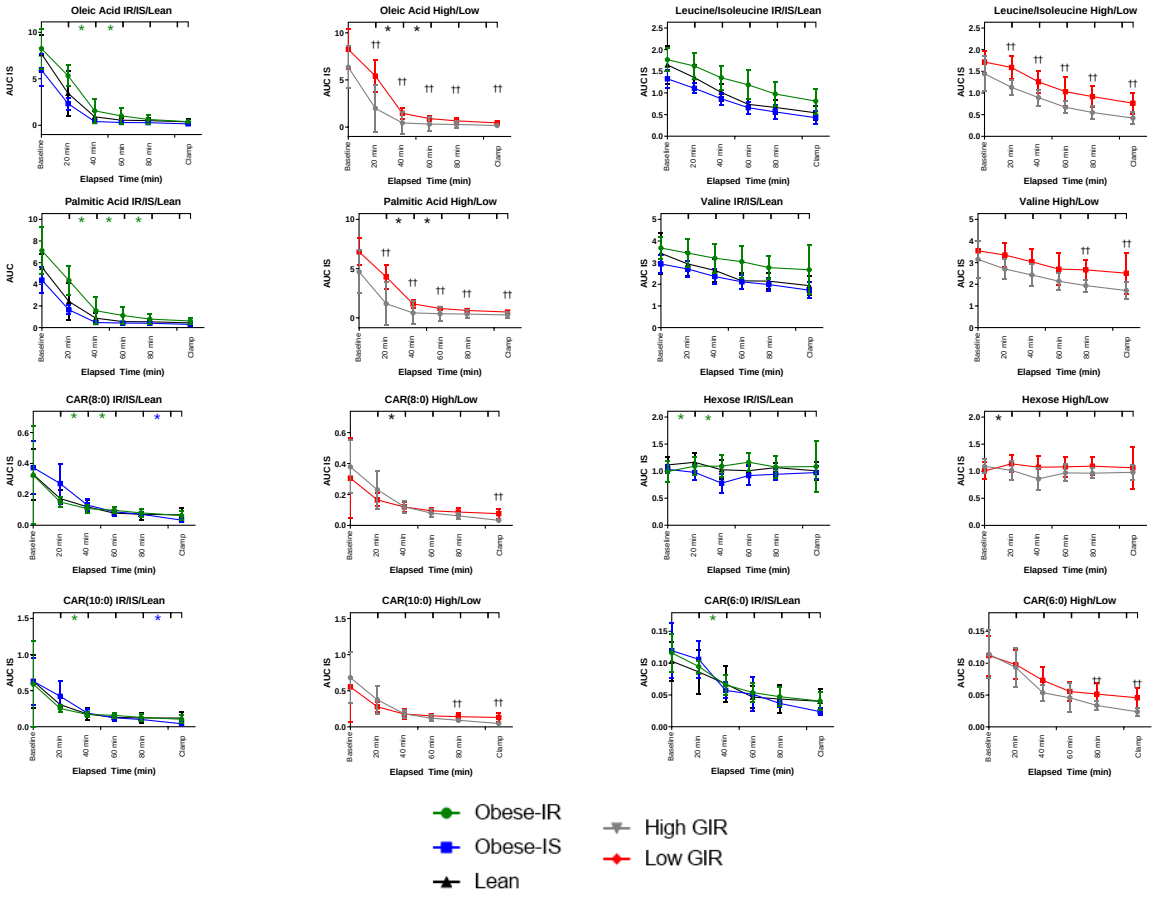


One-way ANOVA with Tukey's post-hoc test was run for data in A with * representing $p<0.05$ showing GIR was statistically higher than both Obese-IR and Lean. Students T-tests were run to compare GIR between Low GIR and High GIR with * signifying $p<0.05$. Subject symbols and colors remain constant from grouping A to grouping B to show where lean subjects fall into the GIR spectrum.

Figure 4.4: Heat map representing z-scored changes abundance in 62 targeted metabolites between High GIR and Low GIR subjects.

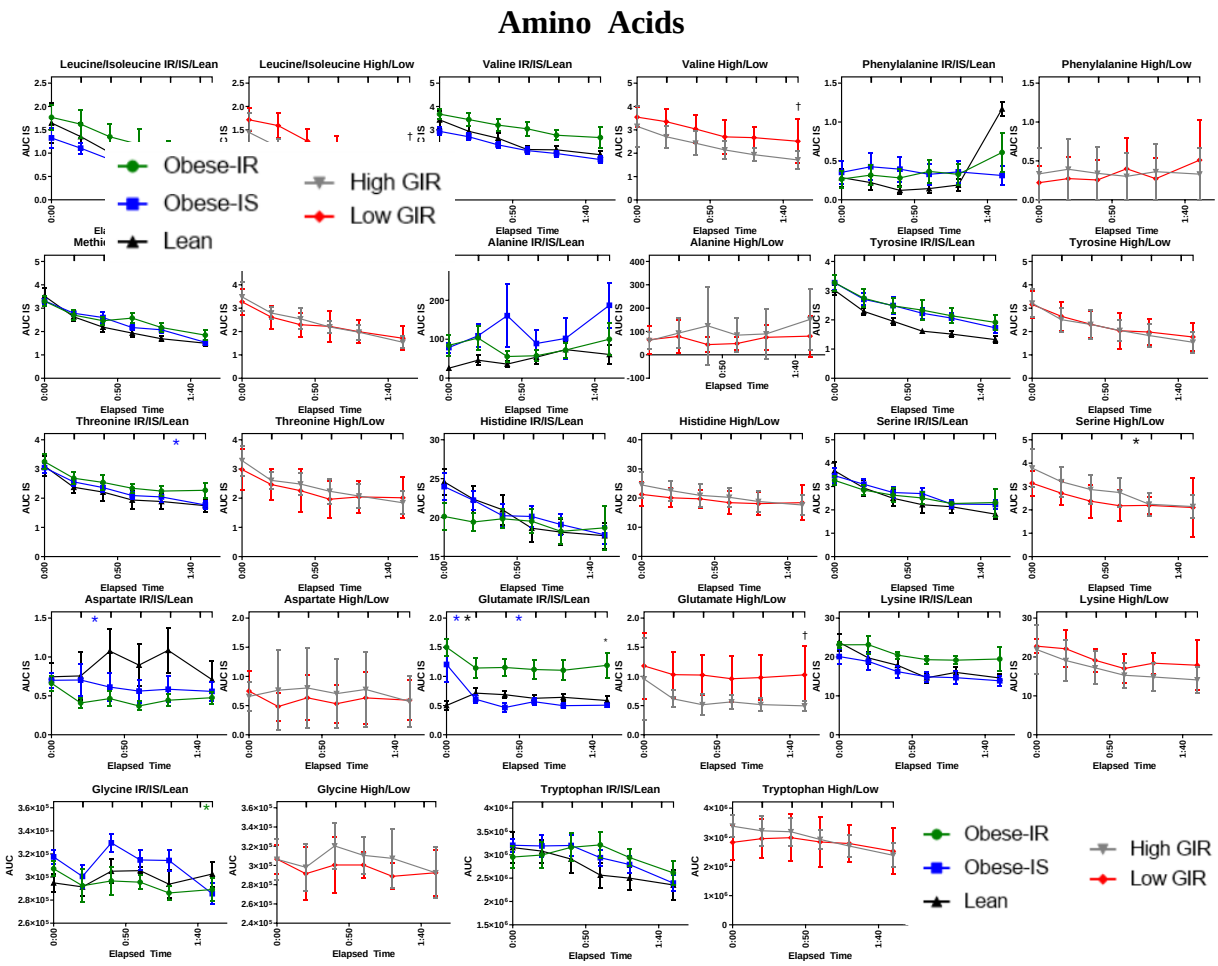
* = FDR < 0.1 comparing Students T-tests between groups at each time point. Time points are at Baseline, 20 minutes, 40 minutes, 60 minutes, 80 minutes, and at the average of two clamp (C) time points. The range goes from Bright Red (0.98 STD above the mean) to Bright Green (0.97 STD below the mean).

Figure 4.5: Changes in representative significantly different metabolite abundance over the course of the clamp.



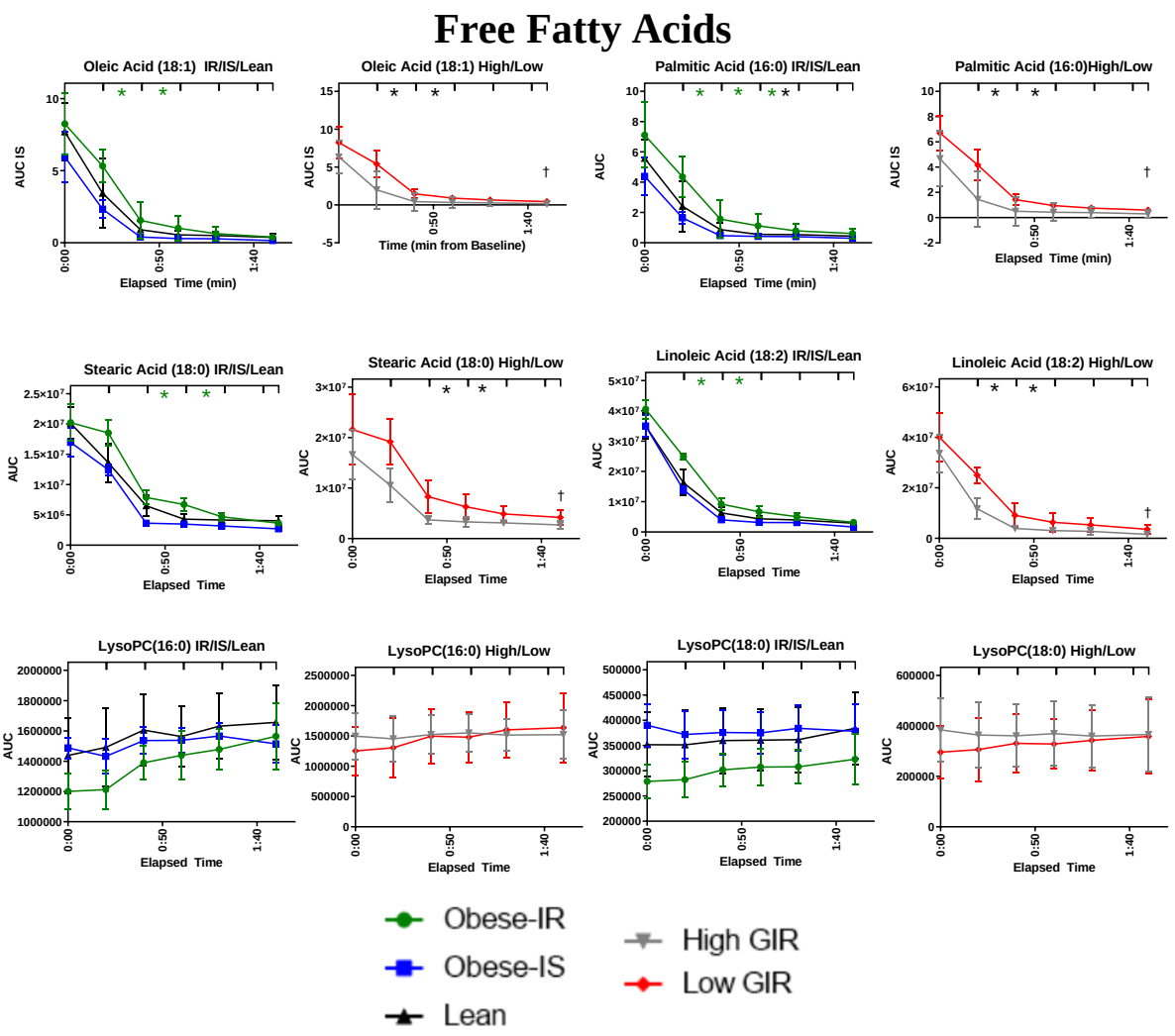
Data is presented as a ratio of AUC/AUC of authentic internal standard +/- SD (AUC IS) or area under the curve (AUC). Slope differences are represented as * = $p<0.05$ ANOVA with Tukey's post hoc for Obese-IR/Obese-IS/LEAN or Student's T-test for High GIR vs Low GIR. The color of the * represents the group identified as different using Tukey's post hoc. †† = FDR <0.1 using Student's T-test for abundance between High GIR vs Low GIR.

Figure 4.6: Changes in amino acid abundance over the course of the clamp.



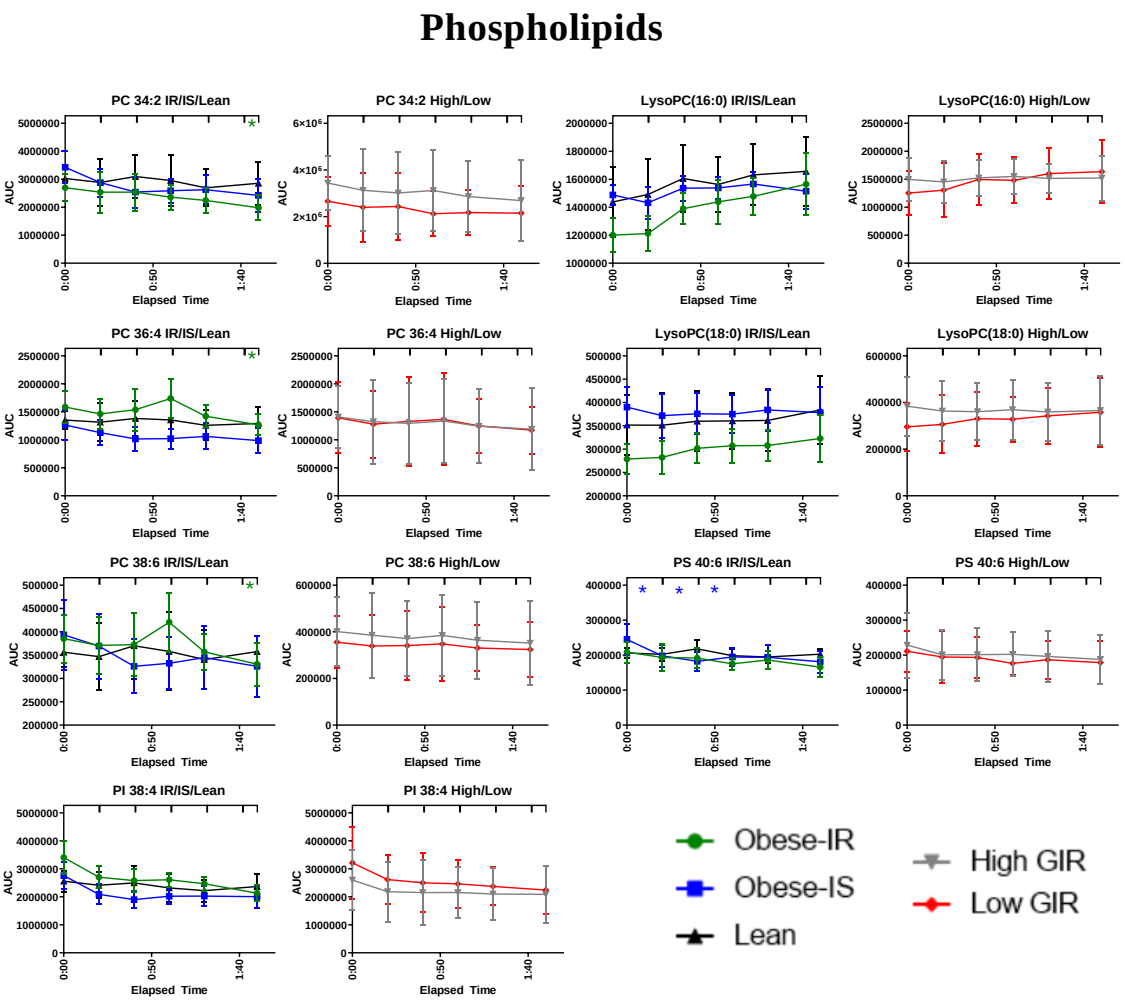
Data are presented as a ratio of AUC/AUC of authentic internal standard +/- SD (AUC IS) or area under the curve (AUC). Slope differences are represented as * = $p<0.05$ ANOVA with Tukey's post hoc for Obese-IR/Obese-IS/LEAN or Student's T-test for High GIR vs Low GIR. The color of the * represents the group identified as different using Tukey's post hoc. †† = FDR <0.1 using Student's T-test for abundance between High GIR vs Low GIR.

Figure 4.7a: Changes in free fatty acid abundance over the course of the clamp.



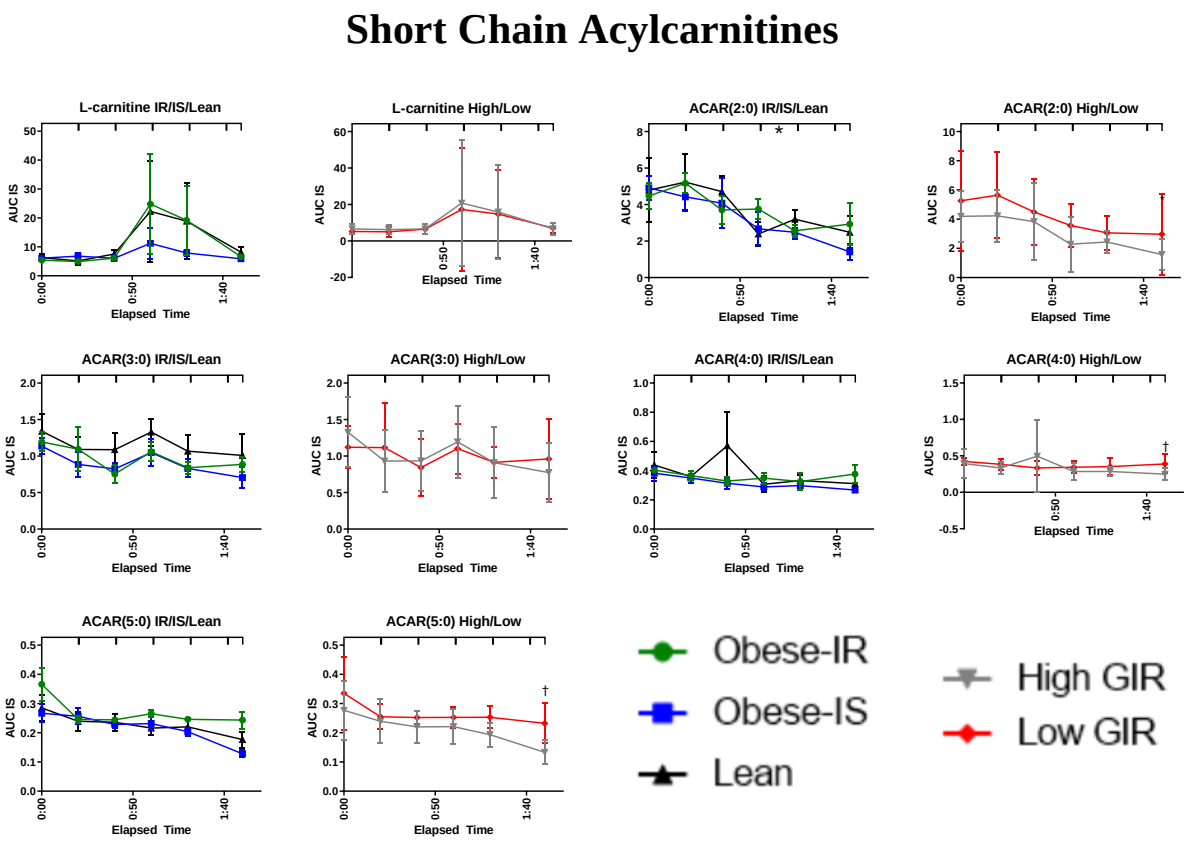
Data are presented as a ratio of AUC/AUC of authentic internal standard +/- SD (AUC IS) or area under the curve (AUC). Slope differences are represented as * = $p<0.05$ ANOVA with Tukey's post hoc for Obese-IR/Obese-IS/LEAN or Student's T-test for High GIR vs Low GIR. The color of the * represents the group identified as different using Tukey's post hoc. †† = FDR <0.1 using Student's T-test for abundance between High GIR vs Low GIR.

Figure 4.7b: Changes in phospholipid abundance over the course of the clamp.



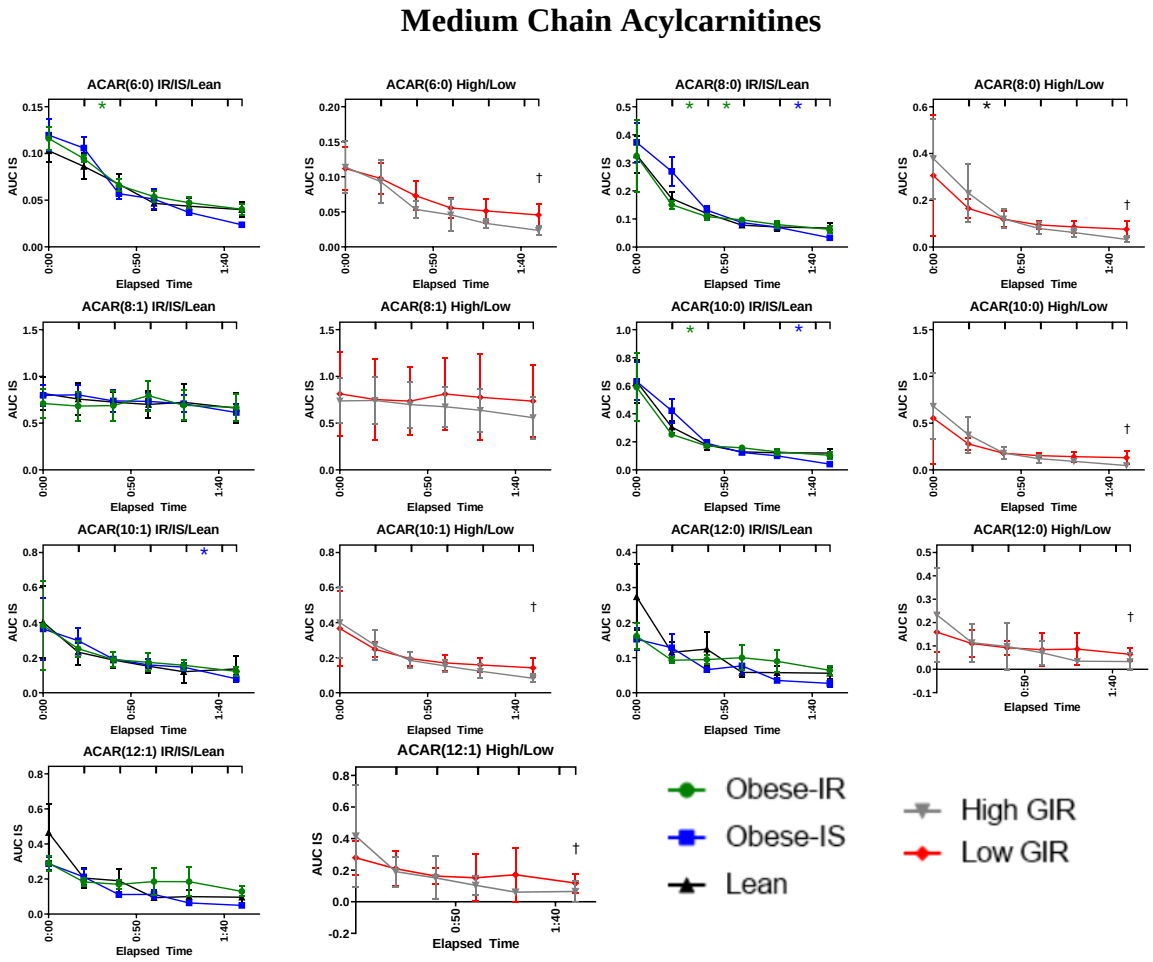
Data are presented as a ratio of AUC/AUC of authentic internal standard +/- SD (AUC IS) or area under the curve (AUC). Slope differences are represented as * = $p<0.05$ ANOVA with Tukey's post hoc for Obese-IR/Obese-IS/LEAN or Student's T-test for High GIR vs Low GIR. The color of the * represents the group identified as different using Tukey's post hoc. †† = FDR <0.1 using Student's T-test for abundance between High GIR vs Low GIR.

Figure 4.8a: Changes in short chain acylcarnitine (L-carnitine to ACAR 5:0) abundance over the course of the clamp.



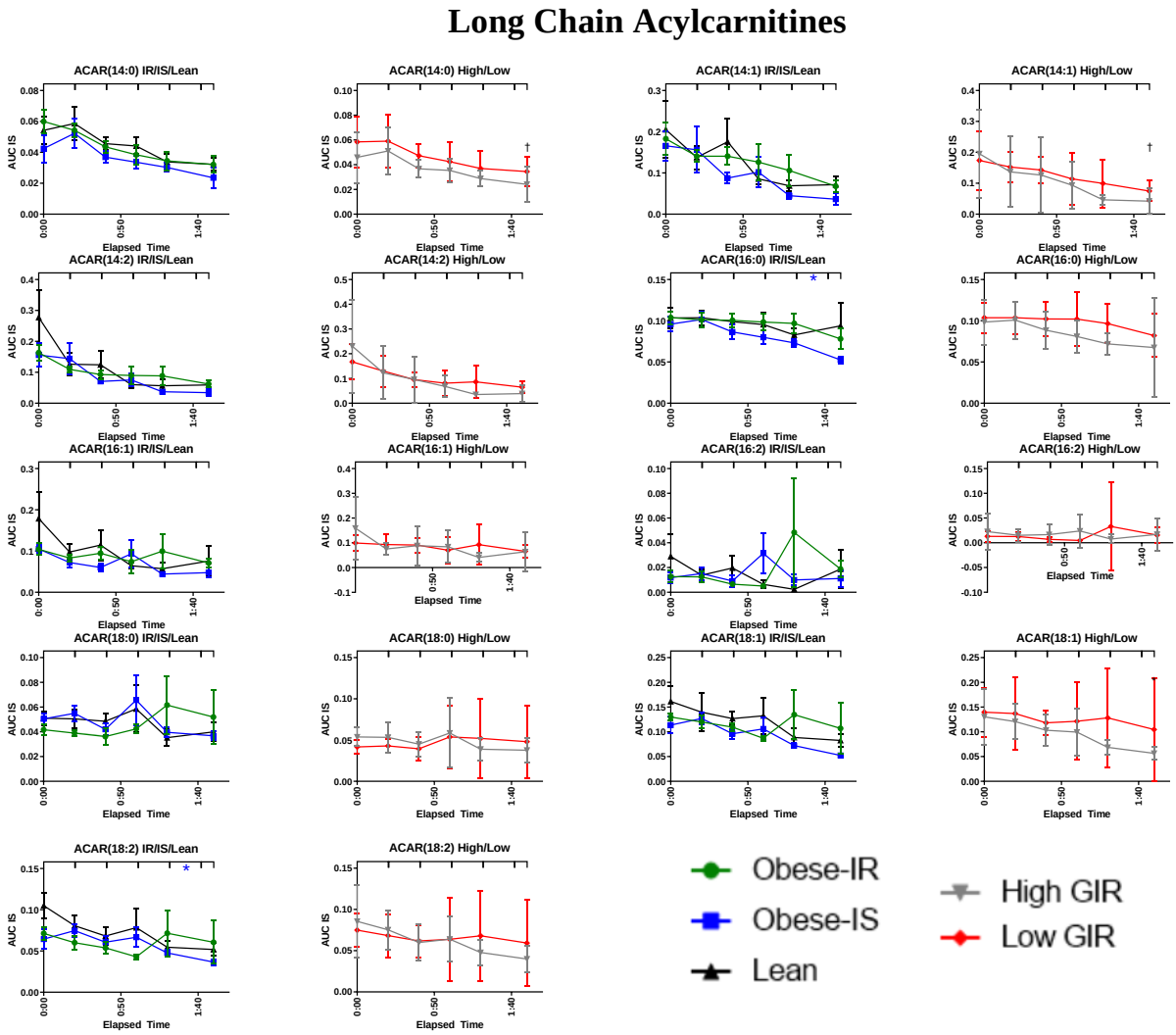
Data are presented as a ratio of AUC/AUC of authentic internal standard +/- SD (AUC IS) or area under the curve (AUC). Slope differences are represented as * = $p<0.05$ ANOVA with Tukey's post hoc for Obese-IR/Obese-IS/LEAN or Student's T-test for High GIR vs Low GIR. The color of the * represents the group identified as different using Tukey's post hoc. †† = FDR <0.1 using Student's T-test for abundance between High GIR vs Low GIR.

Figure 4.8b: Changes in medium chain acylcarnitine (ACAR 8:0 to ACAR 12:1) abundance over the course of the clamp.



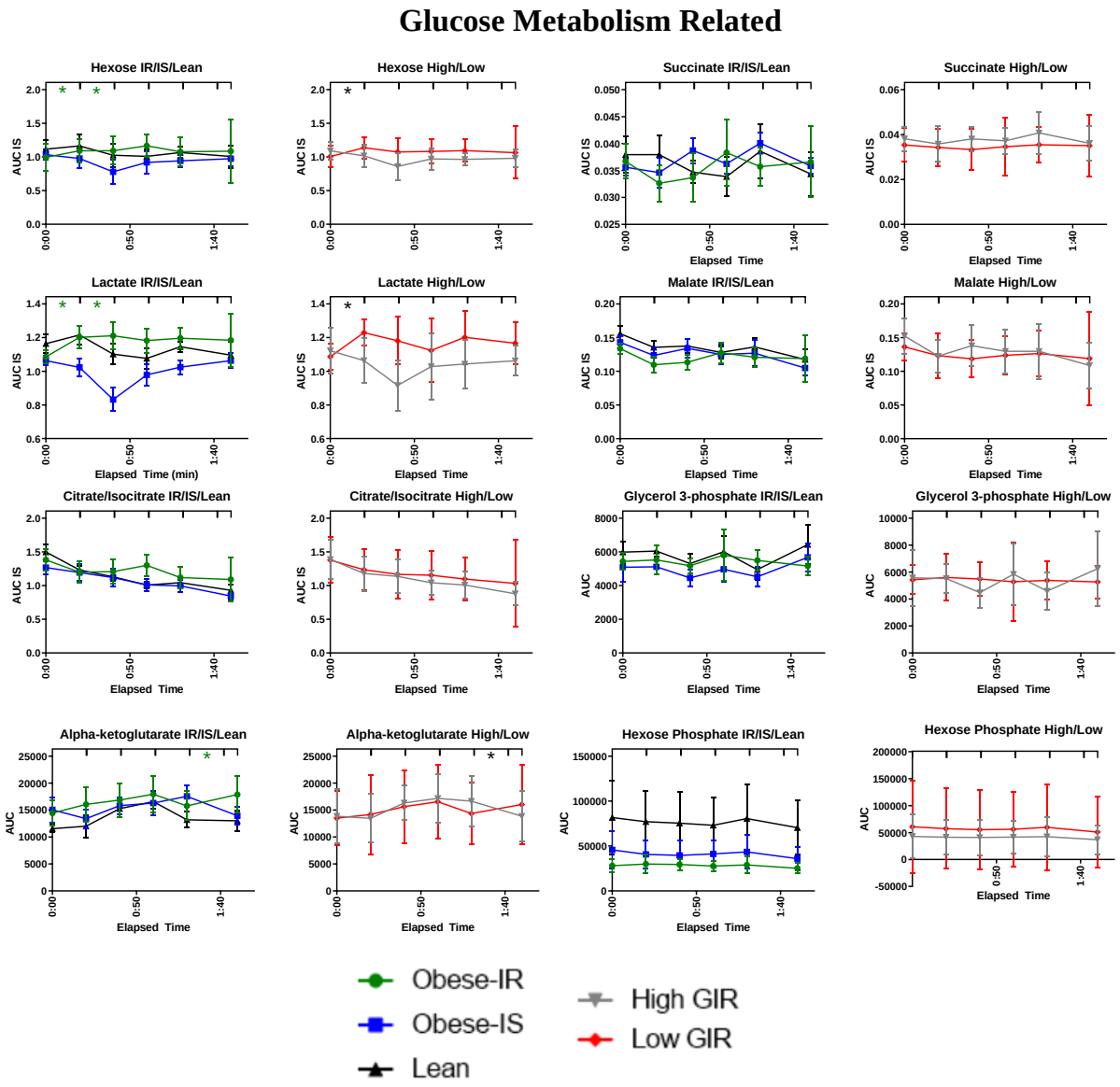
Data are presented as a ratio of AUC/AUC of authentic internal standard +/- SD (AUC IS) or area under the curve (AUC). Slope differences are represented as * = $p<0.05$ ANOVA with Tukey's post hoc for Obese-IR/Obese-IS/LEAN or Student's T-test for High GIR vs Low GIR. The color of the * represents the group identified as different using Tukey's post hoc. †† = FDR <0.1 using Student's T-test for abundance between High GIR vs Low GIR.

Figure 4.8c: Changes in long chain acylcarnitine (ACAR 14:0 – ACAR 18:2) abundance over the course of the clamp.



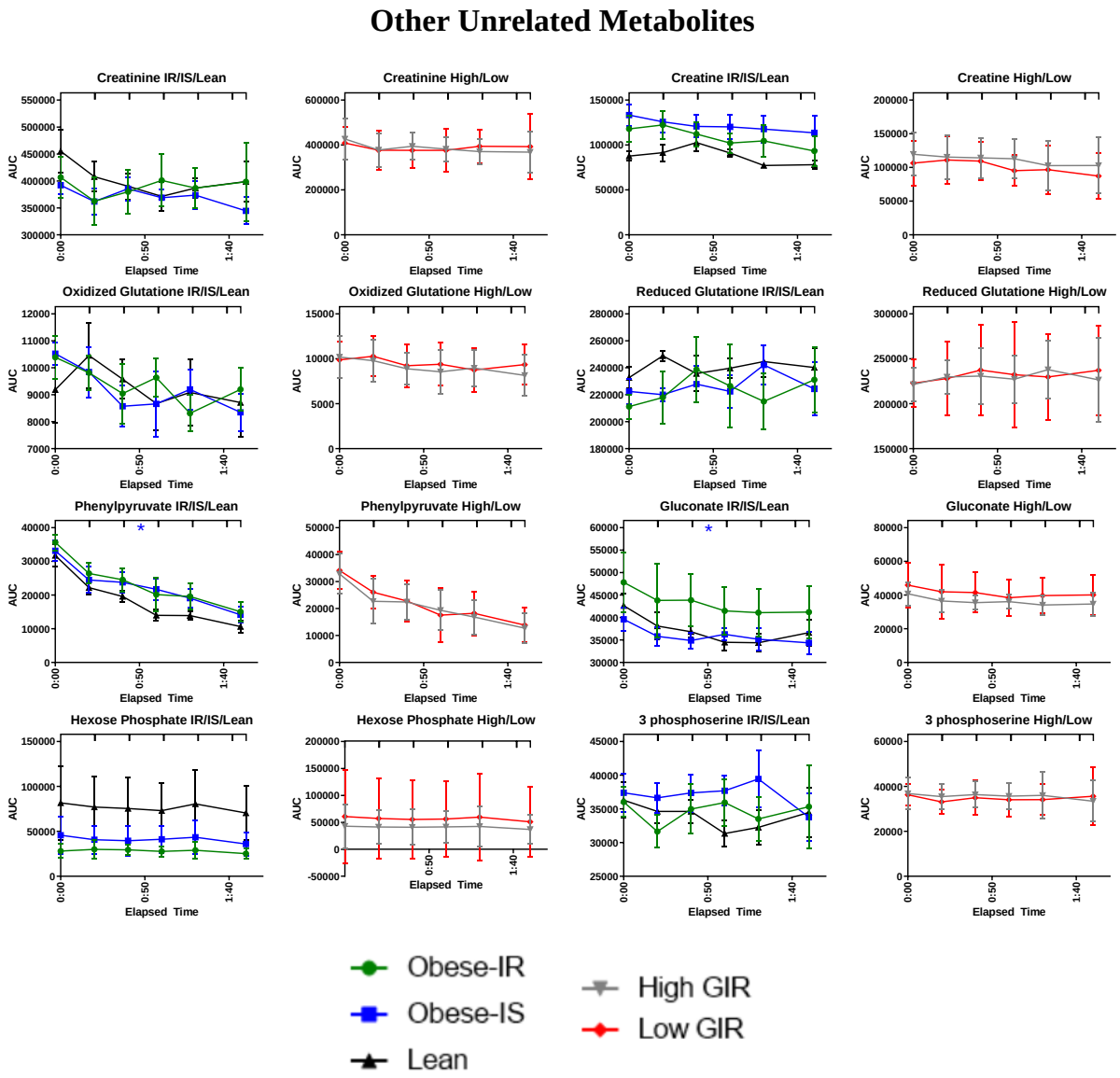
Data are presented as a ratio of AUC/AUC of authentic internal standard +/- SD (AUC IS) or area under the curve (AUC). Slope differences are represented as * = $p<0.05$ ANOVA with Tukey's post hoc for Obese-IR/Obese-IS/LEAN or Student's T-test for High GIR vs Low GIR. The color of the * represents the group identified as different using Tukey's post hoc. †† = FDR <0.1 using Student's T-test for abundance between High GIR vs Low GIR.

Figure 4.9: Changes in glucose metabolism related metabolite abundance over the course of the clamp.



Data are presented as a ratio of AUC/AUC of authentic internal standard +/- SD (AUC IS) or area under the curve (AUC). Slope differences are represented as * = $p<0.05$ ANOVA with Tukey's post hoc for Obese-IR/Obese-IS/LEAN or Student's T-test for High GIR vs Low GIR. The color of the * represents the group identified as different using Tukey's post hoc. †† = FDR <0.1 using Student's T-test for abundance between High GIR vs Low GIR.

Figure 4.10: Changes in other unrelated metabolite abundance over the course of the clamp. Data are presented as a ratio of AUC/AUC of authentic internal standard +/- SD (AUC IS) or area under the curve (AUC).



Slope differences are represented as * = $p<0.05$ ANOVA with Tukey's post hoc for Obese-IR/Obese-IS/LEAN or Student's T-test for High GIR vs Low GIR. The color of the * represents the group identified as different using Tukey's post hoc. †† = FDR <0.1 using Student's T-test for abundance between High GIR vs Low GIR.

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Chapter 5: Discussion

Significance of Research Findings

The importance of nutrition to health

Nutrition science is one of the most important and impactful areas of biomedical research because the energy content and composition of the diet has important and profound effects on disease risk (1). Diets that score highly using indexes of quality such as the Healthy Eating Index, the Alternative Healthy Eating Index, and the Dietary Approaches to Stop Hypertension are associated with significant reductions in diseases such as cancer, type 2 diabetes, cardiometabolic diseases, and overall mortality (2, 3). Macronutrient overconsumption is an important and very controllable factor for controlling these causes of death (4). Specifically, overconsumption of calories has been associated with cardiovascular diseases and type 2 diabetes mellitus (5, 6), though total nutrient intake seems to be more important when considering the causative association between obesity and diabetes.

Current methods for knowing dietary intake

In order to make recommendations concerning dietary intake, policy makers must first understand the consumption patterns of populations and individuals. Current information about

macronutrient intake depend on large epidemiological studies such as the report from the National Health and Examination Survey (NHANES) entitled 'What We Eat in America' (WWEIA) which is composed of data that is produced using memory-based dietary assessment method (MBDA) (7-10). Consumption data from these studies are the basis for dietary guidelines such as the Dietary Guidelines for Americans (DGA), which outlines American federal nutrition policy and recommendations (11). Health researchers and practitioners draw associations between nutritional intake and disease based on data produced from MBDAs (12, 13). However, data obtained from MBDA is questionable due to misreporting of energy and macronutrient intake (14-22). The inaccuracies of MBDA are due to errors in subject recall, subject reactivity, or misrepresentation of diet due to social desirability (16, 23-26). The use of misreported dietary information could potentially lead to misrepresentation of the effects of diet on health (27-31). Despite their limitations, MBDAs remain the most highly used and least biased tools for researchers to know dietary intake (9, 10, 19). However, given these limitations, developing an objective tool to assess dietary intake would provide a significant improvement to nutrition research and the ability to make health recommendations concerning nutritional intake (32)

Metabolomics as an objective measure of dietary intake

Metabolomics is a technology that uses high throughput methods to study small molecules present in biological samples paired with advanced statistical to derive insights into biological processes (33, 34). These small molecules are collectively referred to as the "metabolome" and reflect the downstream precursors and products of metabolism (33-35). Given the need to find a more objective measure of dietary intake than the more subjective MBDA (36-41), it has been proposed that metabolomics could answer to this problem (36, 37, 39, 41). The use of metabolomics as a form of dietary analysis in humans is relatively new and focuses on

three areas: understanding diet using large epidemiological studies (42), identifying specific metabolomic patterns related to dietary intake (43), and to identifying compounds specific to the consumption of specific foods (44-46(47, 48). Recently, metabolomics been employed to analyze dynamic changes in the metabolome due to diet. Frahnow and associates used metabolomics, specifically lipidomics, to identify patterns of changes in lipid classes after 1 and 6 weeks of a high fat diet in a controlled feeding study (47). Similar to our study, they found that the lipidome is rapidly altered by diet and should be controlled in clinical association studies (47). They were further able to classify specific classes of lipids into patterns of change such as monotonous reactions, time dependent increase or decrease, and counter regulation (47).

A study by Pellis, et al., identified acute changes in the metabolome during the 6 hours following consumption of a standardized dairy shake containing 59% lipids, 30% carbohydrates, and 12% protein (49). Finally, Wellington, et al., identified trajectories of change in metabolites following a two-week prescribed "Western" rich in trans fats, red meats, sweetened beverages, and processed foods or "Prudent" diet pattern which included a greater intake of fruits, vegetables, lean meats, and whole grains (43).

The main goal of this dissertation was to examine, identify, and provide insight into dynamic changes in the metabolome due to changes in macronutrient intake, both long term and acute. Furthermore, this study strives to provide the first steps toward an objective identification of macronutrient intake using the tools of metabolomics.

Summary of Research Findings

The goals of this dissertation can be divided into three distinct aims: 1a) determine dynamic changes in the lipidome due to high carbohydrate and high fat diets, 1b) using the results from aim 1a develop lipidomic biomarkers which differentiate between high fat and high

carbohydrate diets, 2) compare the recalled macronutrient intake with actual macronutrient intake of participants in a controlled feeding study, and 3) compare the metabolomic profile of obese yet metabolically healthy and lean individuals during a hyperinsulinemic-euglycemic clamp. In order to address aim 1a and 1b, these studies used two distinct research populations to investigate dynamic changes in the metabolome using high throughput metabolomics. We used two feeding studies with extreme macronutrient diets to illuminate these changes. The first feeding study (PUFA/CHO) involve feeding participants (n=12) a eucaloric high PUFA diet for 21 days followed by a eucaloric high CHO diet for 21 days. The second study was a high fat/high carbohydrate-controlled feeding study called the Metabolomic Analysis of Diet Study (MEAL). Participants in this study (n=23) were provided prepared diets which were consumed throughout the experiment Participants consumed a standard diet for 3 days, and then randomized to either a very high fat diet or a very high carbohydrate diet for the following 21 days.

Aim 1a sought to identify the dynamic response of the lipidome on very high fat enriched in polyunsaturated fatty acids followed by a very high carbohydrate diet. Aim 1b used discriminating lipids from Aim 1a to identify diets from the plasma samples from the MEAL and PUFA/CHO studies as well as samples from a control study. A set of 12 discriminating lipids which we named “Sentinel Lipids” were found to be effective at discriminating between high fat and high carbohydrate diets after 2 days through 21 days of diet. To demonstrate the effectiveness of the sentinel lipids, a population of community members provided cross-sectional plasma samples as well as diets well characterized by 7 consecutive days of dietary journals were successfully identified as consumers of either high fat or high carbohydrate diets.

Aim 2 for this dissertation sought to investigate the differences between actual (provided) diets with reported diet using the 24H$ during the MEAL study. We collected 24HR during the MEAL study after the standard diet and at random times during each of the 3 weeks of the experimental diets. Proportions of macronutrients (proteins, fats, and carbohydrates) as well as energy intake (EI) of provided foods were compared to these same measures reported via 24HR.

Aim 3 sought to compare the dynamic changes in the metabolome and metabolomic profiles in **obese** yet metabolically healthy individuals as well as lean controls. We collected plasma samples as these participants underwent an acute intravenous glucose and insulin infusion during a hyperinsulinemic-euglycemic clamp. The obese participants differed based on their status as either more insulin resistant or insulin sensitive.

Summary of Dynamic Changes in the Metabolome Due to Diet

Chapter 2 focused on the lipidomic analysis of the dietary feeding study also used in Chapter 3. Participants ate a standard diet for 3 days followed by either a very high fat diet or a very high carbohydrate diet for 21 days. We collected plasma from all participants before the study began (baseline), after 3 days of a standard diet (standard), and again at days 2, 7, 14, and 21 of the experimental diets. We also included a more extreme feeding study which was conducted in our lab several years ago. In this study, participants ate a high polyunsaturated fatty acid diet for 21 days followed immediately by a high carbohydrate diet for another 21 days. While this diet was more extreme in the unsaturated fatty acid profile of foods consumed, it was comparable to our study and provided more samples in order to identify differences between high fat and high carbohydrate eaters. We had three specific aims to this paper: 1) identify how the lipidome reacts to 3 days of a standard diet, 2) identify specific dynamic changes and differences in the lipidome due to high fat or high carbohydrate diet, and 3) identify “sentinel

lipids" which can be used to discriminate between high fat and high carbohydrate eaters. To further aim 3 we also tested the plasma of free-living individuals with known diets against our sentinel lipids to evaluate the real-world efficacy of our test.

Aim's 1a and 1b presented in Chapter 2 were similar in scope and used overlapping populations. For aim 1a we successfully showed that the variability between free-living baseline lipidome signatures was less after eating 3 days of a standard diet. Furthermore, the variability was less after participants then went on the experimental diets. This indicates that the lipidome is dynamic and changes in a very short period. Furthermore, it suggests that researchers conducting nutrition-based metabolomics studies should strongly consider 3 days of a standard diet in order to produce a homogenous lipidome in their participants before introducing experimental diets.

The dynamic change shown in the lipidome was the focus of aim 1a and it used plasma samples from the MEAL study and the PUFA study to identify differences between the plasma lipidome of high fat and high carbohydrate diets and to describe the dynamic changes seen in lipid patterns. We showed that PUFA diet was more than the MEAL diet showing more changes and larger differences in lipids at all experimental time points. In particular, both diets resulted in differences in the levels of TG, CER, DG, PE, and PC. We were able to show that the lipidome change was quite rapid, with more than half of the lipids species changing within 2 days of starting either a high fat or high carbohydrate diet. However, LPCs, LPEs, PlsChos, and PlsEths slowly changed. There was also a pattern present in the phosphatidylethanolamine plasmalogens, which is present in both diets, but most pronounced in the MEAL study (Figures 2.1 & 2.2). We identified in both diets what appears to be an adaptive response, e.g. more and more pronounced differences in lipid species were observed after 2 days of diet but many of

these returned to near baseline after 21 days of diet. This was especially apparent in longer chained polyunsaturated TGs.

Aim 1b was to identify and use "sentinel lipids" as a diagnostic test to discriminate high carbohydrate and high fat diets. We identified 54 sentinel lipids that were significantly different at any experimental time point between high fat and high carbohydrate diets in the MEAL study and were identified in both the MEAL and PUFA study. These sentinel lipids were used in an online R package called Metaboanalyst (www.metaboanalyst.ca) using the multivariate biomarker analysis feature. From these sentinel lipids we identified 12 discriminating features. Receiver operator curves (ROC) were generated using Monte-Carlo cross validation using 2/3 of the participants to evaluate features of importance and the other 1/3 to test. This was iterated 100 times to characterize the ROC, which indicated a very high discrimination between high fat and high carbohydrate diets using the sentinel lipids.

To test our sentinel lipids on a free-living sample and inform generalizability from the laboratory, we used plasma sampled from free-living participants from the community (Community). The participants (n=102) provided a cross-sectional sample of blood after 7 days of food diaries. A carbohydrate/fat ratio was produced to indicate the macronutrient pattern consumed by these participants. Using a supervised machine learning method (SVM) in the online R Metaboanalyst package (www.metaboanalyst.ca) these unknown samples were given a probability score to indicate their identity as high carbohydrate (0.0 – most confidence to 0.5 – least confidence) or high fat (0.5 – least confidence to 1.0 – most confidence). When probability scores were graphed versus carbohydrate: fat ratio from participants' food journals, there was a non-statistically significant pattern with a lower ratio (more carbohydrate) being identified as high carbohydrate and higher ratio (more fat) as high fat.

Aim 1 has many strengths that set it apart from traditional nutritional science studies (Table 5.1). First, the use of state of the art untargeted shotgun lipidomic and targeted metabolomic profiling to determine and describe dynamic changes due to diet. Because all of these results of these studies conducted on free-living human populations are potentially translatable to the larger human population. Secondly, Aim 1 used three human study populations (PUFA/CHO, MEAL, and Community) which enhances generalizability of these findings. The PUFA/CHO and MEAL studies used well characterized diets designed by trained clinical dietitians in the metabolic kitchen. The use of the Community population to test the ability of the sentinel lipids in Aim 1b to identify high fat and high carbohydrate diets is a particular strength of this dissertation. The diets of the Community population were well known and characterized using 7 consecutive days of food journals which diminishes day to day variation inherent in the use of single day food journals and 24HR (9, 10).

While Aim 1 had several strengths, there were several limitations as well (Table 5.1). When determining lipid differences between high fat and high carbohydrate diets in Aim 1a, we correctly chose to use an FDR correction for multiple comparisons. However, the lipids compared were very highly correlated (Figure S2.4). The use of the highly stringent FDR correction may be obfuscating true statistical differences and a less stringent nominal p-value from a Student's T-test may be more appropriate. As with many human studies, in order to have good generalizability, this study suffers from a limited population due to financial, time and ethical reasons. This reduces the strength of our findings and indicates that a larger study should be conducted to reduce variability and other issues associated with small populations. Secondly, the diets used in both of these feeding studies used extreme macronutrient proportions that are rarely consumed by the population at large. Finally, all of these studies were conducted in

healthy, young adult volunteer participants who were primarily undergraduate and graduate students at the University of Michigan. The demographics of our populations do not reflect the population of the United States as a whole and this reduces the generalizability of our results

Summary of Dietary Analysis Study

Chapter 3 was focused on the discrepancies in controlled feeding studies between reported dietary intake and actual dietary intake. The literature suggests that 24HR often under-report energy intake as well as macronutrient intake (14-20), but this is poorly in the laboratory setting. Unlike the literature, during the standard diet we found that energy, carbohydrate, and fat intake were well reported by our participants by the 24HR. During the experimental diet, participants tended to over-report whichever macronutrient was provided in excess of the standard diet and under-report that which was provided at a lower level than the standard diet. In other words, if participants were on a high fat diet, they under-reported fat and over-reported carbohydrate. We also found that protein intake over-reported by participants regardless of diet, furthermore, during the standard diet, high carbohydrate, and fat diet all participants reported eating more animal protein than they were provided. One possible reason for this misreporting of macronutrients could be due to the motivation and education level of our participants. Our participants were, for the most part, graduate students at the University of Michigan and their performance is consistent with previous findings that higher education is associated with less bias in the 24HR (14). Furthermore, while the 24HR were unannounced, the participants were aware of pending interviews. Perhaps the knowledge that their 24HR were observed and recorded by the research team might have decreased recall bias in our participants. This is consistent with the findings of several studies showing decreased misreporting when participants

are aware their diets are observed (50-52). Finally, the food for our studies was provided on a cycle of 4 possible meals for breakfast, lunch, and dinner and may have increased the recall accuracy of our study.

Regardless of the reasons for the accuracy of our participants 24HR, we did find that subjects misreported macronutrient intake on the high fat and high carbohydrate diets and under-reported animal protein. Participants provided very high fat diets under-reported fat intake and participants provided very high carbohydrate diet under-reported carbohydrate intake. The results of our study suggest that, while 24HR may have its limitations in epidemiological studies and large population-based studies, perhaps energy recall can be trusted in controlled feeding studies. However, in studies in which fat and carbohydrate intake are extreme, subjects may under report macronutrients that are provided in proportions that are very high compared to habitual intake. Conversely, participants may over report macronutrients that are provided in proportions that are very low compared to habitual intake. Misreporting of protein, due to under reporting of animal protein, must be considered when planning and analyzing feeding studies.

Summary of Hyperinsulinemic-euglycemic Clamp Study

Chapter 4 in this dissertation focused on metabolomic differences between obese healthy individuals who were either more insulin resistant, more insulin sensitive, and lean controls. We found that metabolomic differences were primarily due to innate insulin resistance measured with glucose infusion rate rather than obesity. These differences were in metabolites associated with lipolysis (fatty acids), amino acids (BCAAs and glutamate), and short and medium chain acylcarnitines. BCAAs and glutamate were significantly lower in participants who were more insulin resistant than those who were more insulin sensitive regardless of obesity. Also, lipolysis

shown in levels of fatty acids was impaired in those who were more insulin resistant. Interestingly, long change acylcarnitines did not show a clearance while we saw a suppression of long chain fatty acids. We concluded that this discrepancy is perhaps due to a differential clearance of acylcarnitines by carbon chain length.

Strengths of this study start with the use of state of the art targeted metabolomic profiling. These subjects were compared based on glucose infusion rate but were metabolically healthy. This provides some insight into the etiology and development of insulin resistance and the role of innate glucose infusion rate rather than obesity in this development. We chose to include lean controls as a negative control comparison with the obese subjects of varied insulin resistance. The use of these lean controls highlighted the role of glucose infusion rate and diminished the role of obesity in the metabolomic changes and differences seen during the clamp in branched chain amino acids and fatty acids. Finally, the use of plasma samples collected throughout the time course of the clamp allowed for identification of dynamic changes in the metabolome not previously found in the literature. This was a cross sectional study and was small study (n=18) but the results are important and warrant a further look. Further work should follow obese participants using both insulin resistance and metabolomics to see how these factors change over time. More participants should be included in further studies to increase the power of results.

Future Directions and Applications

The results of this dissertation, especially in the development of an objective measure to identify high fat and high carbohydrate diet, were very promising. However, these results also lead to several questions that lead to future directions and possible studies.

The fat and carbohydrate percentages chosen for our HC and HF diets in the MEAL

Study were extreme, with both approaching 3 standard deviations above and below that reported by the American public (53). While our sentinel lipids performed very well on these extreme diets and seemed to do a reasonable job at identification of high carbohydrate and high fat consumption in our control population, they do not represent diets consumed by the "average" consumer (53). Future controlled feeding studies with incrementally decreasing/increasing carbohydrate and fat concentrations to further refine our model are called for. Our participants were all healthy individuals and within a limited range of BMI and ages. Further studies with a broader range of participants should be conducted as well including increasing the range of ethnicities, ages, BMIs, and health conditions.

The development of objective biomarkers of macronutrient intake is promising and leads us to ponder a future study in which participants habitual diet is determined using food journals or 24HR. Plasma samples could be collected at baseline and analyzed to determine the baseline lipidome. Participants would then be provided 3 days of diet with macronutrient proportions matching the reported habitual intake identified at baseline. Lipidomics before and after this macronutrient feeding could be compared for agreement. This study would further establish our understanding of the strength of using lipidomics as an objective measure of dietary intake in coordination with memory based dietary assessments.

Our diets (PUFA/CHO and MEAL) manipulated fat and carbohydrate concentrations but kept protein concentrations constant at 15%. However, we know that while protein intake is consistent within individuals, there is variations (9,10,53). We would like to continue the work done in Aim 1 while manipulating the protein content and holding either fat or carbohydrate constant.

One of the limitations of these human feeding studies was that they were conducted in healthy, young populations of mostly graduate students. This does not reflect the population of the United States as a whole. We would like to expand these studies to include a range of ages, body compositions regional locations, races, and ethnicities to reflect and enhance generalizability to the larger US population.

We identified 55 sentinel lipids, which discriminated very high fat and very high carbohydrate consumers. There was a very high level of intercorrelation between the sentinel lipids and we suspect that a smaller subset of sentinel lipids may produce a more refined model for identification of macronutrient intake.

For the HEIC study, this was a very small population (n=18) and was cross-sectional. We were not aware of the prior obesity status of these individuals nor was there follow-up on these participants to identify their metabolic status to determine risk. While the results are interesting and provide novel identification of differential acylcarnitine clearance, these results warrant a much larger study, which includes a larger range of participants. Also, a longitudinal study which follows participants over several years would provide more insight into the metabolomic differences we see between insulin resistant and insulin sensitive individuals independent of obesity status.

Tables and Figures

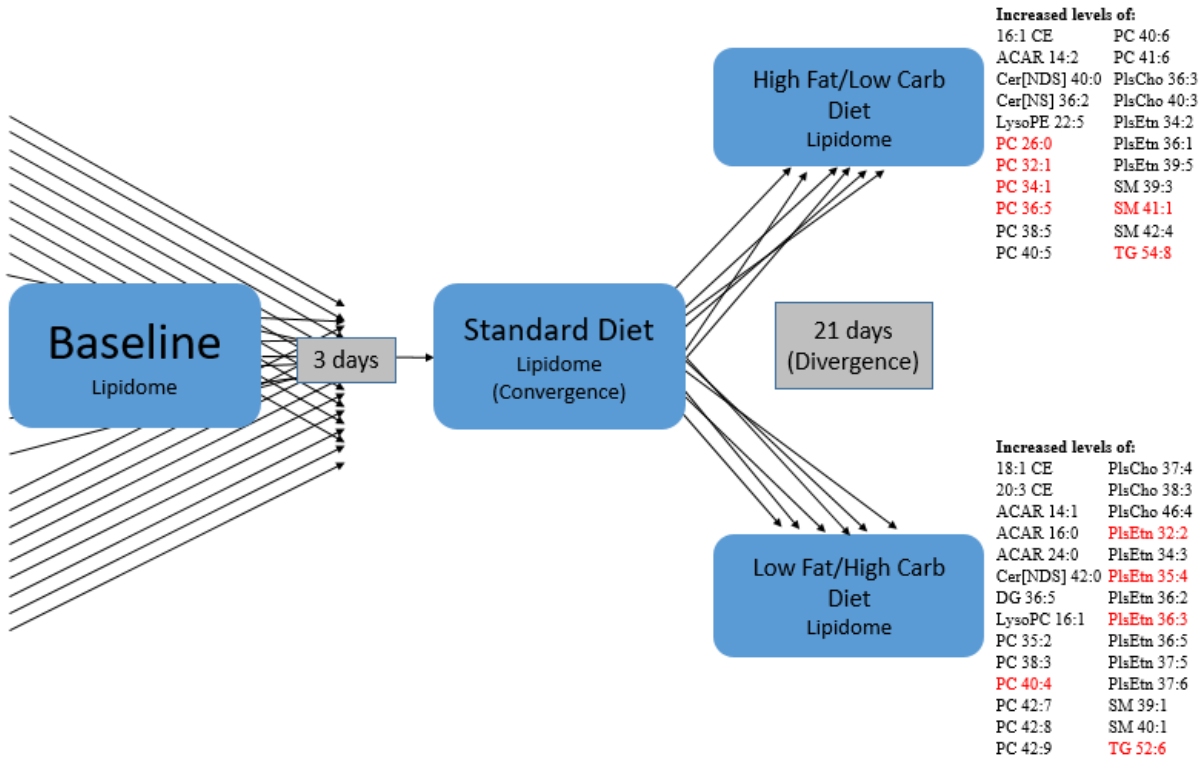
Table 5.1: Dissertation Strengths and Limitations for all Aims

	Strengths	Limitations

Aims 1a/1b/2
 	
PUFA/CHO & MEAL studies
	• PUFA/CHO and MEAL were well-controlled longitudinal feeding studies
	• The MEAL study included a standard diet that demonstrates lipidomic convergence after only 3 days
	• Aims 1a & 1b used state of the art untargeted shotgun lipidomic methodologies
	• Unsupervised machine learning provides unbiased prediction of dietary intake
	• The Community study has well-characterized diets and provides insight into the efficacy of the use of sentinel lipids to identify macronutrient intake
	• Aim 2 compared actual diet with reported diet giving insight into true sources of misreporting
		• Fairly small sample sizes
		  o PUFA/CHO (n=12)
		  o MEAL (n=23)
		• Diets were extreme with no natural progression to approximate "real-world" diets
		• Lipids have a very high level of intercorrelation and the use of the FDR may be too stringent hiding true associations
		• Conducted in healthy, young, well-educated populations which may not reflect the population of the country as a whole

Aim 3	• State of the art targeted metabolomics • Subjects were metabolically healthy which could provide insight into the development of insulin resistance • Lean subjects provide a negative control group with respect to obesity • Time course study within the hyperinsulinemic-euglycemic clamp helps elucidate dynamic changes in metabolites in response to an acute glucose feed	• Cross-sectional study design does not provide insight into the progression of insulin resistance or prior health status of these subjects • Small sample size (n=18) • Targeted metabolomics identified only specific metabolites while unexpected metabolomic difference may go unnoticed

Figure 5.1 Summary of Aim 1 PUFA/CHO and MEAL Study Findings



Schematic of the findings of Aim 1 from the PUFA/CHO and MEAL studies. The Lipidome converged after 3 days of a standard diet then diverged to high fat/low carbohydrate and low fat/high carbohydrate phenotypes. The 54 sentinel lipids are listed on the right with 12 final sentinel lipids in red.

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