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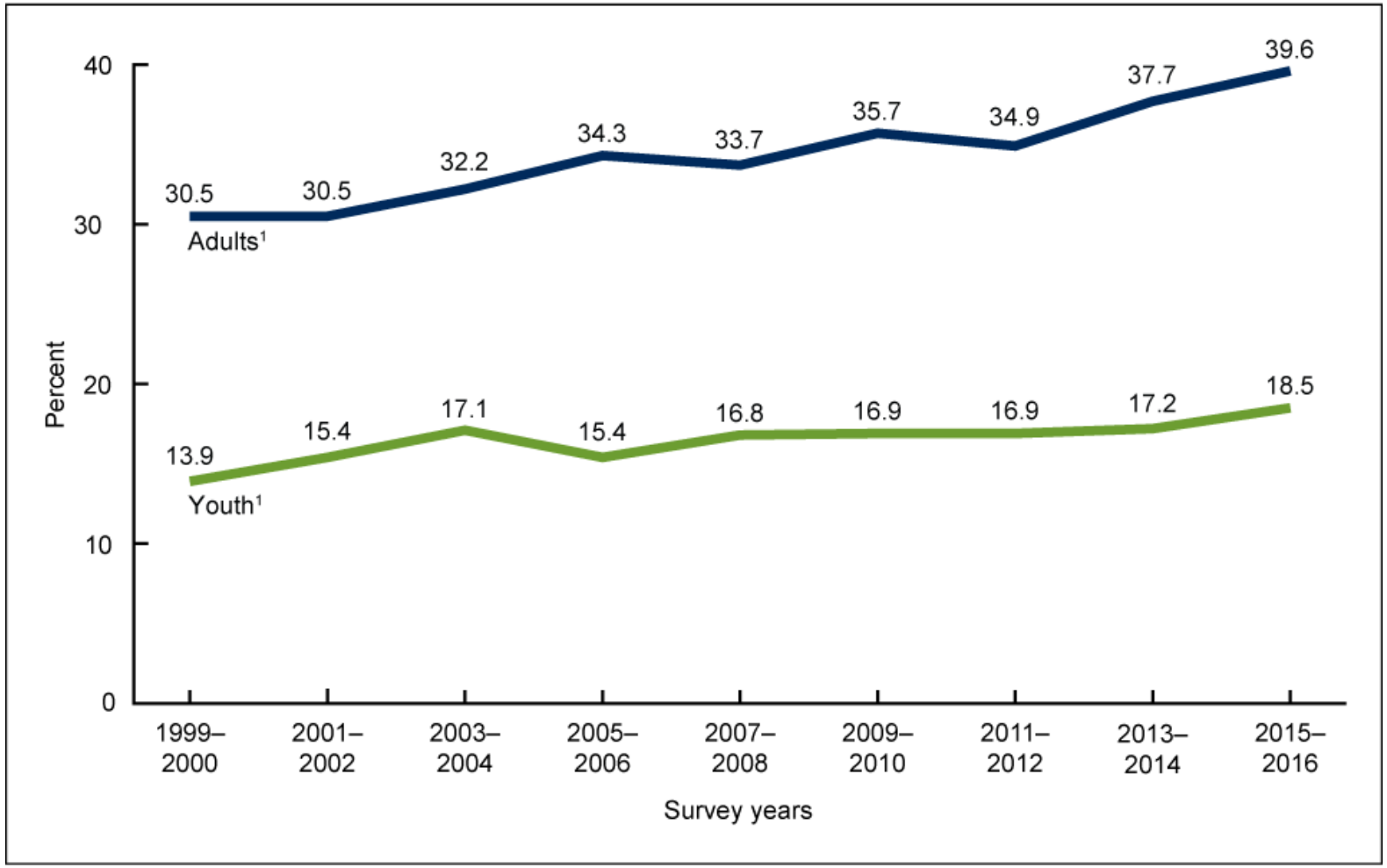
MICROBIOME LABS

METABOLIC RECONDITIONING

MICROBIOME TARGETED WEIGHT LOSS

KIRAN KRISHNAN

Figure 5. Trends in obesity prevalence among adults aged 20 and over (age adjusted) and youth aged 2–19 years: United States, 1999–2000 through 2015–2016



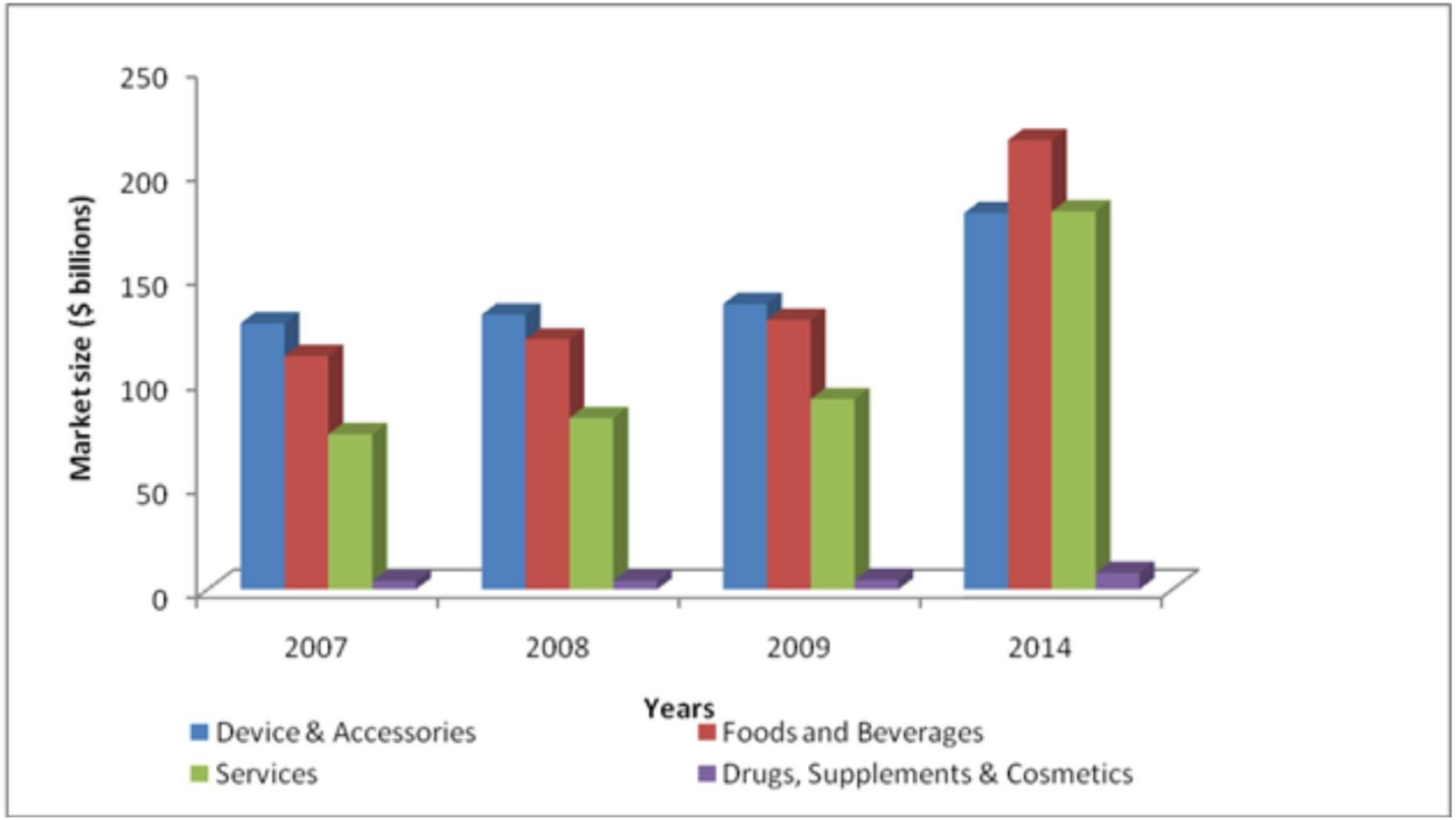
[1]Significant increasing linear trend from 1999–2000 through 2015–2016.
NOTES: All estimates for adults are age adjusted by the direct method to the 2000 U.S. census population using the age groups 20–39, 40–59, and 60 and over.
Access data table for Figure 5 at: https://www.cdc.gov/nchs/data/databriefs/db288_table.pdf#5.
SOURCE: NCHS, National Health and Nutrition Examination Survey, 1999–2016.

OBESITY IN THE UNITED STATES

2/3 OF THE U.S. POPULATION IS OVERWEIGHT OR OBESE

Source: U.S. Census Data, CDC Data, IBIS World, MarketData Enterprises

GLOBAL WEIGHT MANAGEMENT MARKET BY PRODUCT THROUGH 2014 ($ Billions)



Source: MarketsandMarkets

GLOBAL SPENDING ON WEIGHT LOSS

$700B+ MARKET

U.S. Weight Loss Market is Estimated to be a $65B per Year Industry

Total Market – $65B

Served Market – $18B

Source: U.S. Census Data, CDC Data, IBIS World, MarketData Enterprises

MISSING LINK??

ROLE OF THE MICROBIOME IN WEIGHT MANAGEMENT

MICROBIOME OBESITY AND METABOLIC DISEASE

COMMENSAL BACTERIA THAT PROTECT AGAINST OBESITY

***Akkermansia Muciniphila*:**

- Mucin degrading commensal anaerobe
- Presence is inversely correlated with body weight in rodents and humans
- Increase in growth of A. *muciniphila* improved weight and metabolic response in Type 2 and obese mice
- Demonstrated to reverse high-fat diet induced fat-mass gain, adipose tissue inflammation and insulin resistance.
- Effects require live, viable bacteria as heat-killed strains did not provide any effect

***Lactobacillus* Species**:

- Shown to reduce fat mass in mice by producing endogenous Conjugated Linoleic Acids (CLA). CLAs have been shown to induce fat burn and fat loss in animals and humans. Humans have low CLA production and are dependent on dietary sources. Commensal *lactobacillus* provide substantial amount of CLA from metabolism of linoleic acids.
- Dietary CLAs are mainly absorbed in the small bowel, thus most large intestine CLA must be generated by the colonic microbiota. Viable *lactobacillus* is a major producer of colonic CLA. This reduces inflammation and permeability that is associated with obesity

MICROBIOME OBESITY AND METABOLIC DISEASE

COMMENSAL BACTERIA THAT PROTECT AGAINST OBESITY

Bifidobacterium Species:

- Presence is inversely correlated with body weight in humans and animals – especially *B. animalis*
- In mice fed a high-fat diet, viable *bifidobacterium* administration was shown to reduce liver triglycerides, total cholesterol, total lipid deposition and body weight gain.
- Efficient producers of CLA
- Increases the production of SCFAs and GLP-1

MICROBIOME OBESITY AND METABOLIC DISEASE

POST-BIOTICS THAT PROTECT AGAINST OBESITY

SHORT-CHAIN FATTY ACIDS (BUTYRATE, ACETATE and PROPRIONATE):

- Increased production of butyrate and acetate are associated with leaner body mass
- SCFAs act as signaling molecules that interact with the G-protein-coupled receptors,Gpr41 and Gpr43, expressed on adipocytes and intestinal epithelium – Gpr41 activation by SCFAs stimulates leptin production which reduces appetite.
- Adipocytes sense intestinal SCFA production and release adiponectin in response. Adiponectin is associated with an up-regulation of AMPK, which is an enzyme that monitors cellular energy status and stimulates fatty acid oxidation in peripheral tissues.
- In obesity, low SCFAs are produced, thereby less adiponectin is generated and AMPK which dramatically decreases fatty acid oxidation and an increased influx of free fatty acids into the liver – NAFLD is associated with obesity.

MICROBIOME OBESITY AND METABOLIC DISEASE

INTESTINAL DYSFUNCTIONS THAT PLAY A CAUSAL ROLE IN OBESITY

METABOLIC ENDOTOXEMIA:

- Characterized by a sharp increase in serum LPS levels post-prandial
- Post-prandial endotoxemia is followed by TLR4-CD14 immune activation and chronic, low grade inflammation.
- Metabolic endotoxemia is associated with a dysbiotic microbiota and is caused by a dysfunctional intestinal barrier.
- Metabolic endotoxemia induces obesity and diabetes
- Increased circulating LPS causes insulin resistance via hypothalamic JNK expression (inflammation) irrespective of body weight
- LPS causes morphological changes and swelling of adipocytes
- LPS disrupts the function of the enteric nervous system and causes leptin resistance by disrupting metabolic signals from the gut to the brain

MICROBIOME OBESITY AND METABOLIC DISEASE

American Diabetes Association. diabetes.

Obesity Studies

Metabolic Endotoxemia Initiates Obesity and Insulin Resistance

Patrice D. Cani[12], Jacques Amar[3], Miguel Angel Iglesias[1], Marjorie Poggi[4], Claude Knauf[1], Delphine Bastelica[4], Audrey M. Neyrinck[2], Francesca Fava[5], Kieran M. Tuohy[5], Chantal Chabo[1], Aurélie Waget[1], Evelyne Delmée[2], Béatrice Cousin[6], Thierry Sulpice[7], Bernard Chamontin[3], Jean Ferrières[3], Jean-François Tanti[8], Glenn R. Gibson[5], Louis Casteilla[6], Nathalie M. Delzenne[2], Marie Christine Alessi[4] **and** Rémy Burcelin[1]

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Diabetes 2007 Jul; 56(7): 1761-1772.
https://doi.org/10.2337/db06-1491

MICROBIOME OBESITY AND METABOLIC DISEASE

OBESITY IS ASSOCIATED WITH:

- LOW LEVELS OF *BIFIDOBACTERIA SP*.
- LOW LEVELS OF *A. MUCINIPHILA*
- LOW LEVELS OF CERTAIN POST-BIOTICS – SCFAs, CLAs, etc.
- HIGH LEVELS OF METABOLIC ENDOTOXEMIA

MICROBIOME TARGETED WEIGHT LOSS

- INCREASING ENDOGENOUS LEVELS OF *BIFIDOBACTERIA SP*.
- INCREASING ENDOGENOUS LEVELS OF *A. MUCINIPHILA*
- INCREASING SCFA PRODUCTION
- REDUCING OR ALEVIATING METABOLIC ENDOTOXEMIA

AIDP AND MICROBIOME LABS HAVE COLLABORATED TO DEVELOP A MICROBIOME FOCUSED WEIGHT MANAGEMENT SOLUTION BY UTILIZING THE POWER OF SYNBIOTICS

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MICROBIOME LABS

MICROBIOME TARGETED WEIGHT LOSS

PRETICX (XYLOOLIGOSACCHARIED) + SPORE-BASED PROBIOTICS

PreticX

Optimize Your Flora

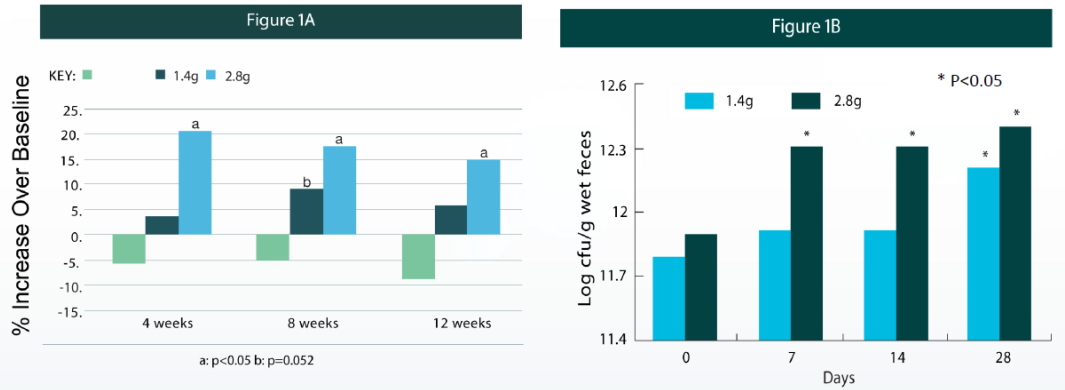
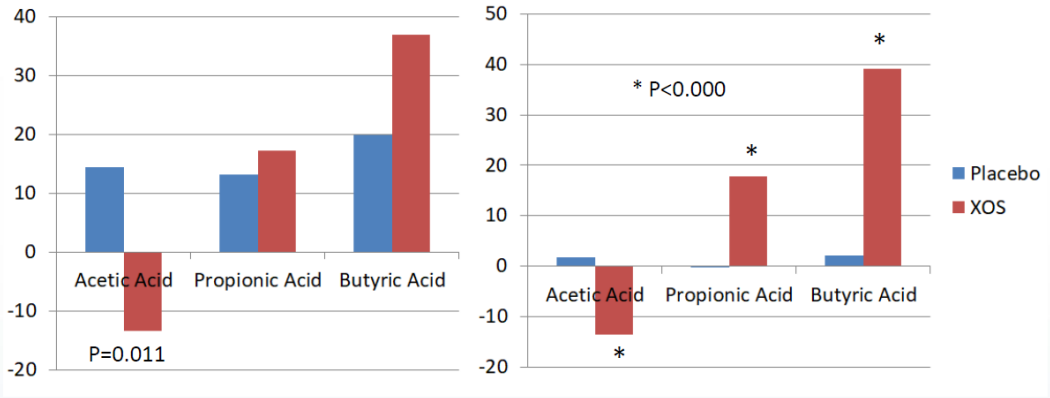


Figure1: PreticX increases Bifidobacterial as low as 1.4g/day

A: UCLA study (Dr. Li and Dr. Heber, et al Food Funct., 2014, 5, 436)

5g XOS supplementation leads to a switch of Acetate to Propionate and Butyric production in Human



Percentage change of Concentration

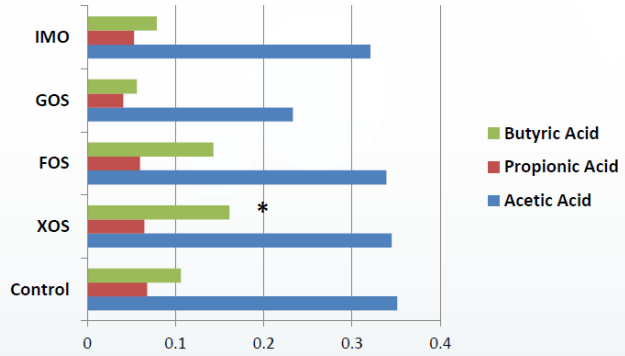
Percentage change of Profile (% of Total SCFA)

J. Lecerf, et.al. British Journal of Nutrition (2012), 108, 1847–1858

Optimize Your Flora

SCFA production profile of Different Prebiotics in Animal Model of Constipation

KunMing Mice: 14 days of Supplementation at 2.0g/kg BW



Preticx

Optimize Your Flora

World Journal of Gastrointestinal Pathophysiology

Submit a Manuscript: http://www.f6publishing.com

World J Gastrointest Pathophysiol 2017 August 15; 8(3): 117-126

DOI: 10.4291/wjgp.v8.i3.117

ISSN 2150-5330 (online)

ORIGINAL ARTICLE

Prospective Study

Oral spore-based probiotic supplementation was associated with reduced incidence of post-prandial dietary endotoxin, triglycerides, and disease risk biomarkers

Brian K McFarlin, Andrea L Henning, Erin M Bowman, Melody M Gary, Kimberly M Carbajal

Brian K McFarlin, Andrea L Henning, Erin M Bowman, Melody M Gary, Applied Physiology Laboratory, University of North Texas, Denton, TX 76203, United States

Brian K McFarlin, Andrea L Henning, Kimberly M Carbajal, Department of Biological Sciences, University of North Texas, Denton, TX 76203, United States

Author contributions: McFarlin BK designed the study, collected data, interrupted findings, and prepared manuscript; Henning AL, Bowman EM, Gary MM and Carbajal KM collected data, interrupted findings, and prepared manuscript.

Institutional review board statement: The study was reviewed

Manuscript source: Invited manuscript

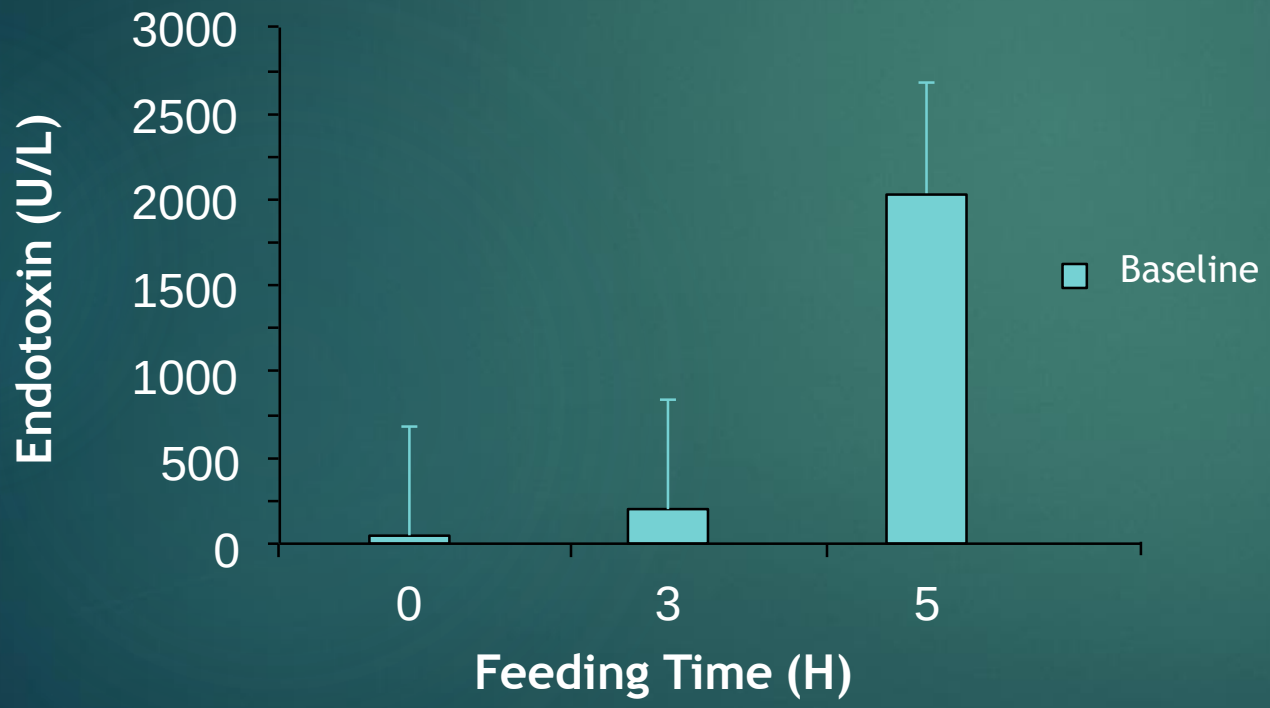
Correspondence to: Brian K McFarlin, PhD, FACSM, FTOS, Associate Professor, Applied Physiology Laboratory, University of North Texas, 1921 West Chestnut Street, PEB Room 209, Denton, TX 76203, United States. brian.mcfarlin@unt.edu
Telephone: +1-940-5653165
Fax: +1-940-5654904

Received: January 26, 2017
Peer-review started: February 8, 2017
First decision: April 17, 2017

METABOLIC ENDOTOXEMIA

The effect of 30-days of probiotic supplementation on post-prandial responses to a high-fat meal: Pilot Study

Principal Investigator: Brian K. McFarlin, PhD, FACSM, FTOS
University of North Texas



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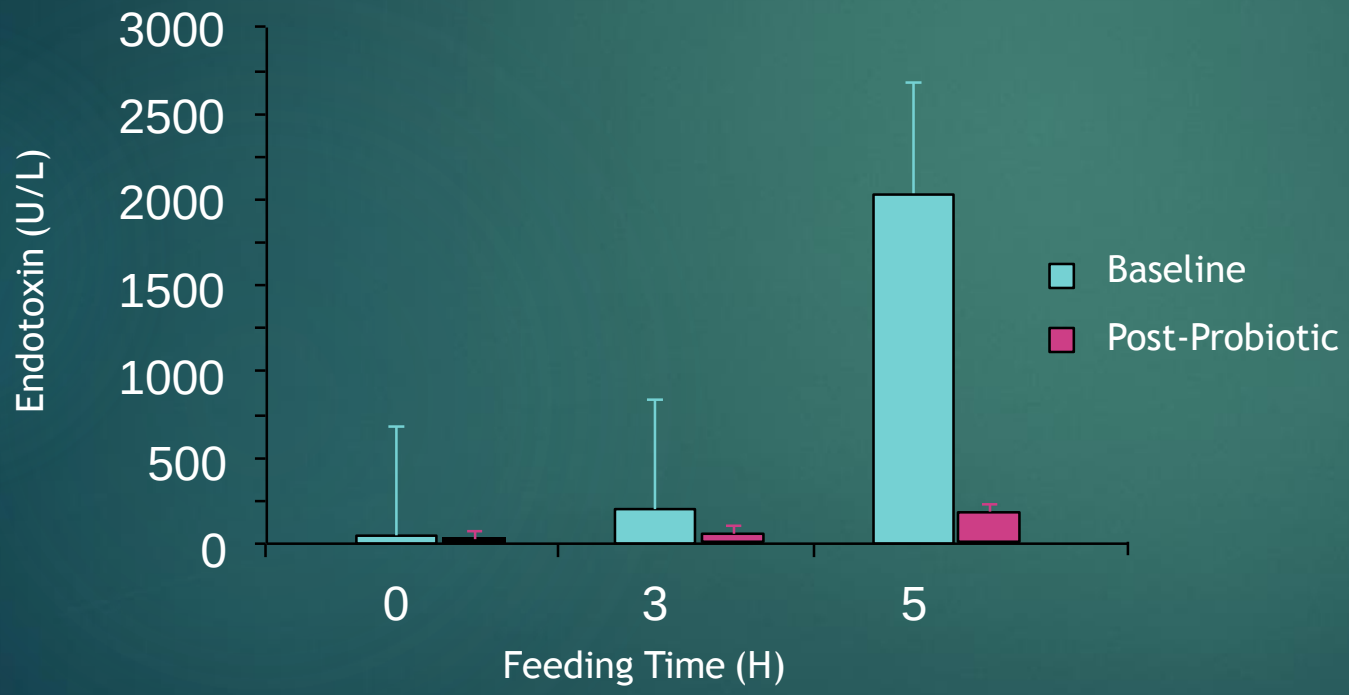

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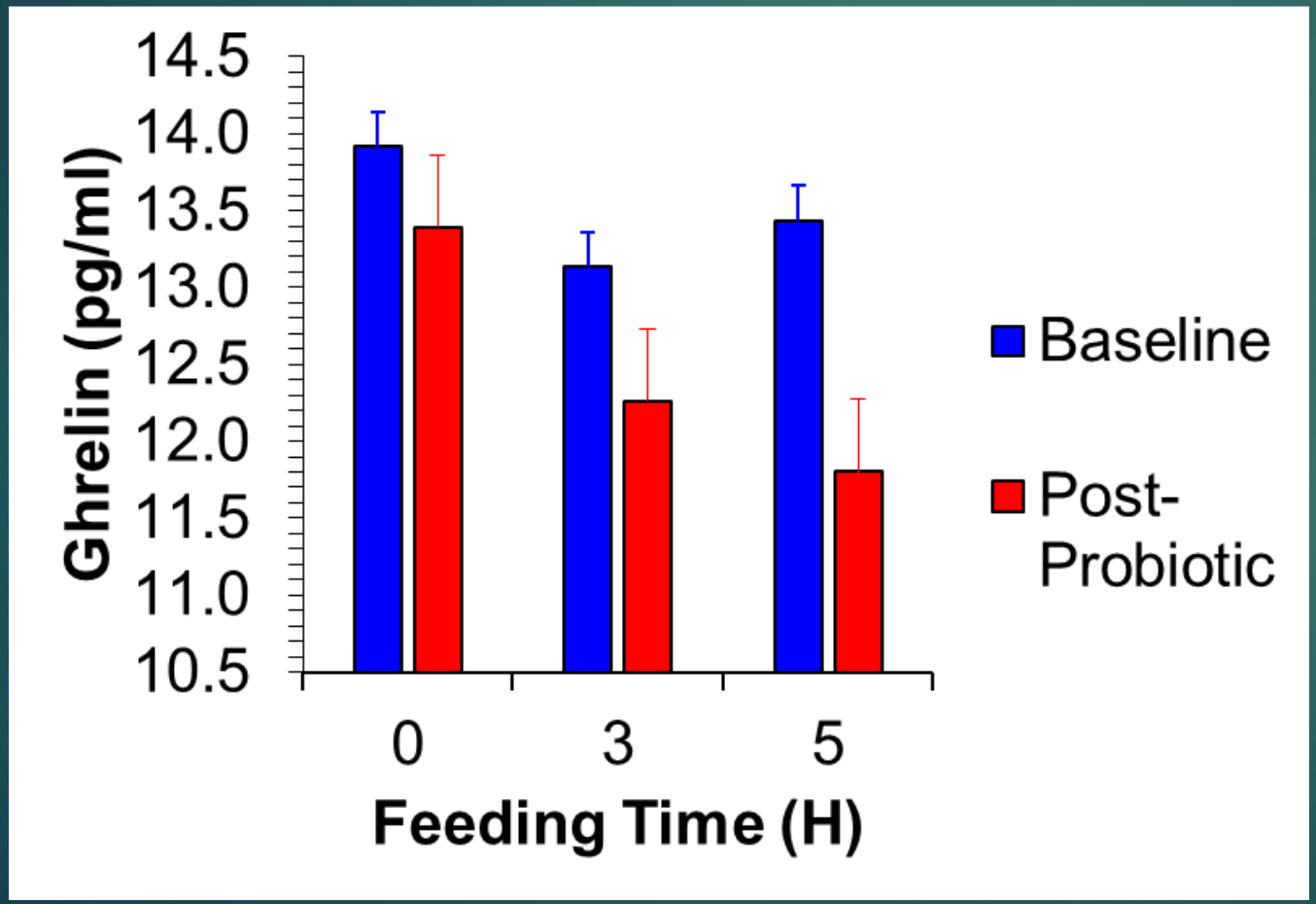
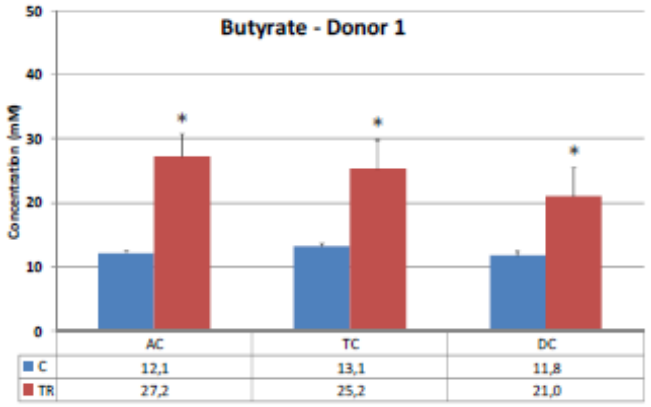
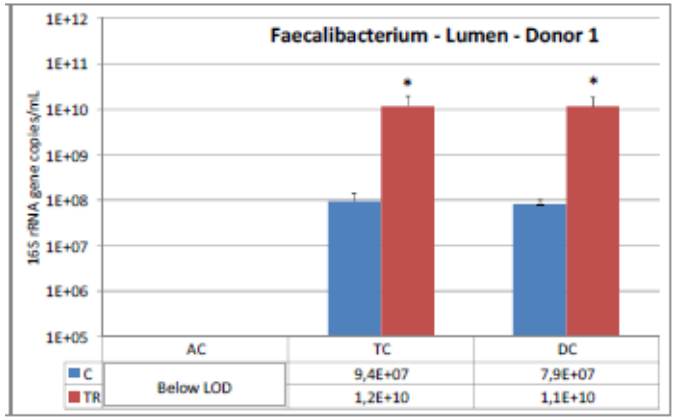


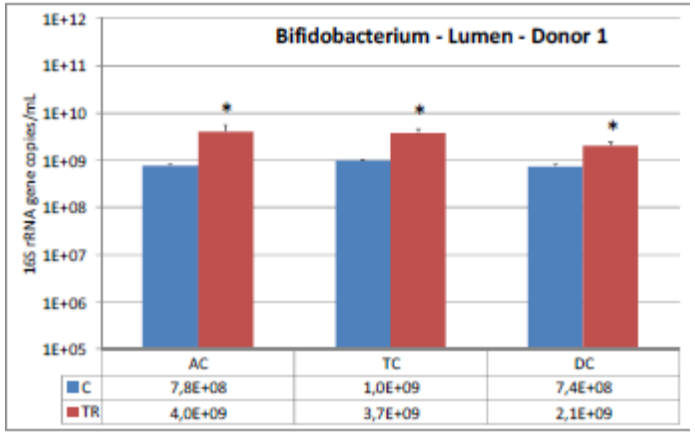
ProDigest

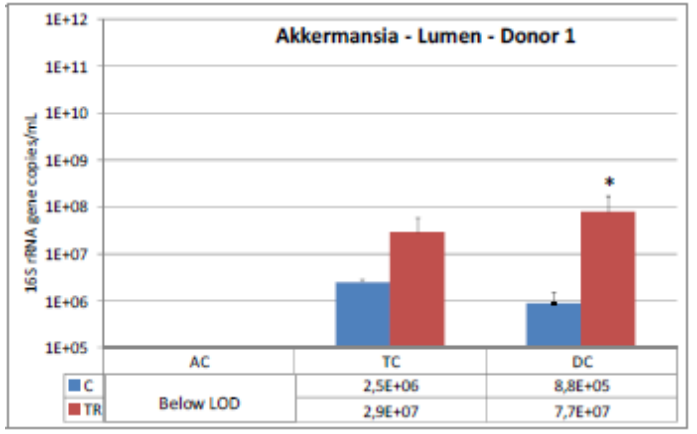
Gastrointestinal Expertise

PRELIMINARY TRIAL ON THE XOS + BACILLUS ENDOSPORE SYNBIOTIC


Butyrate - Donor 1
Concentration (mM)
50
40
30
20
10
0
*
*
*
AC TC DC
C 12,1 13,1 11,8
TR 27,2 25,2 21,0


Faecalibacterium - Lumen - Donor 1
16S rRNA gene copies/mL
1E+12
1E+11
1E+10
1E+09
1E+08
1E+07
1E+06
1E+05
*
*
AC TC DC
C Below LOD 9,4E+07 7,9E+07
TR 1,2E+10 1,1E+10


Bifidobacterium - Lumen - Donor 1
16S rRNA gene copies/mL
1E+12
1E+11
1E+10
1E+09
1E+08
1E+07
1E+06
1E+05
*
*
*
AC TC DC
C 7,8E+08 1,0E+09 7,4E+08
TR 4,0E+09 3,7E+09 2,1E+09


Akkermansia - Lumen - Donor 1
16S rRNA gene copies/mL
1E+12
1E+11
1E+10
1E+09
1E+08
1E+07
1E+06
1E+05
*
AC TC DC
C Below LOD 2,5E+06 8,8E+05
TR 2,9E+07 7,7E+07

The Effect of 90-days of Fiber/Probiotic Supplementation on Body Composition and Weight Management in Overweight Individuals

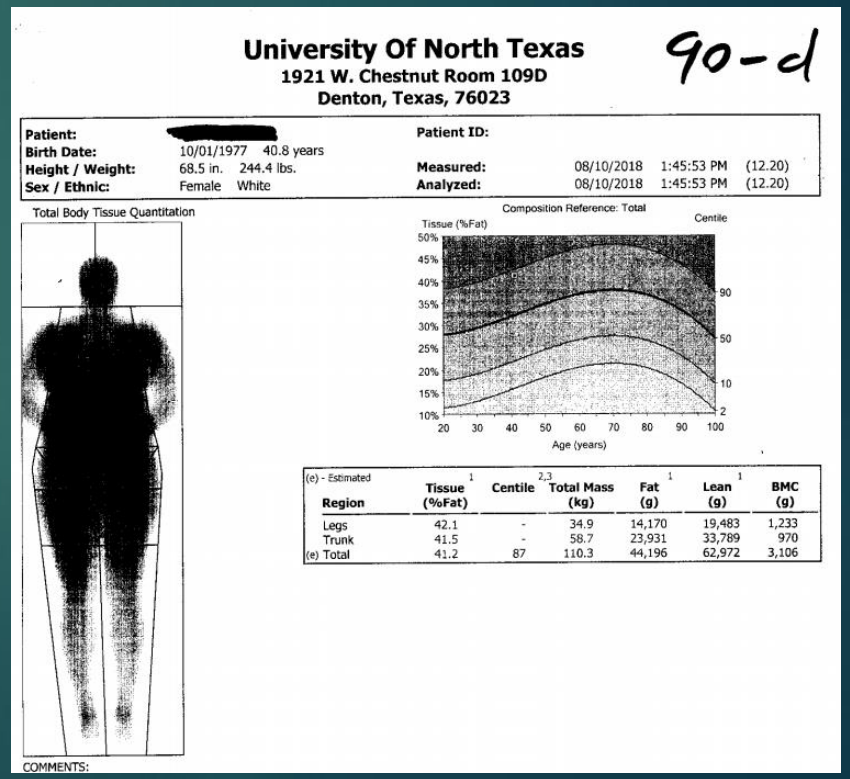
Principal Investigator:
Brian K. McFarlin, PhD, FACSM, FTOS
Associate Professor
Department of Kinesiology, Health Promotion and

SAMPLE RESULTS

After 90-d:

- 4 kg increase in lean mass
- ~1.5 kg drop in fat mass
- % Fat dropped from 43% to 41%.

NO DIET CHANGES, EXERCISE OR ANY LIFESTYLE MODIFICATION.



University Of North Texas
1921 W. Chestnut Room 109D
Denton, Texas, 76023

90-d

Patient: [redacted]
Birth Date: 10/01/1977 40.8 years
Height / Weight: 68.5 in. 244.4 lbs.
Sex / Ethnic: Female White

Patient ID:
Measured: 08/10/2018 1:45:53 PM (12.20)
Analyzed: 08/10/2018 1:45:53 PM (12.20)

Total Body Tissue Quantitation

Composition Reference: Total

Tissue (%Fat) / Centile

Age (years)

Region	Tissue (%Fat)	Centile	Total Mass (kg)	Fat (g)	Lean (g)	BMC (g)
Legs	42.1	-	34.9	14,170	19,483	1,233
Trunk	41.5	-	58.7	23,931	33,789	970
(e) Total	41.2	87	110.3	44,196	62,972	3,106

(e) - Estimated

COMMENTS:

MICROBIOME TARGETED WEIGHT LOSS WITH A SYNBIOTIC (XOS AND SPORES)

THIS UNIQUE SYNBIOTIC:

- INCREASES ENDOGENOUS LEVELS OF *BIFIDOBACTERIA SP.*
- INCREASES ENDOGENOUS LEVELS OF *A. MUCINIPHILA*
- INCREASES SCFA PRODUCTION
- REDUCES METABOLIC ENDOTOXEMIA
- ALLOWS FOR STEADY FAT LOSS AND INCREASE IN LEAN MUSCLE MASS EVEN WITHOUT DIET OR EXERCISE
- AS PART OF A HEALTHY WEIGHT MANAGEMENT PROGRAM, THIS SYNBIOTIC COULD DRAMATICALLY IMPROVE RESULTS

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