

**ESSENTIAL FATTY ACID ABNORMALITIES  
AND LOW LINOLEIC ACID INTAKE IS  
COMMON IN THE SECOND YEAR OF LIFE  
IN CHILDREN WITH CYSTIC FIBROSIS**

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2015-2016

# OUTLINE

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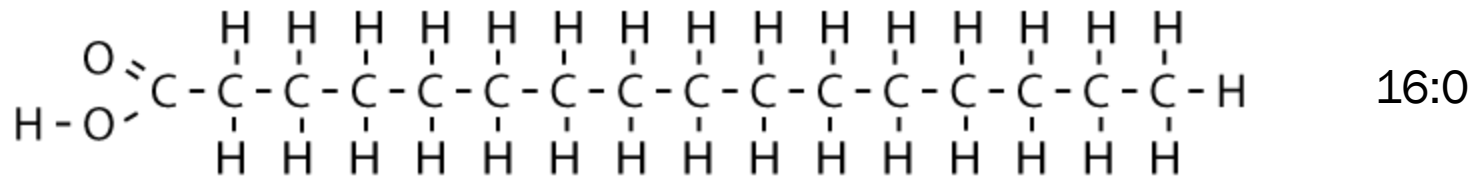
- ▶ Background
- ▶ FIRST Study
  - ▶ Feeding Infants **R**ight... from the **S**Tart
- ▶ Preliminary Results
- ▶ Summary



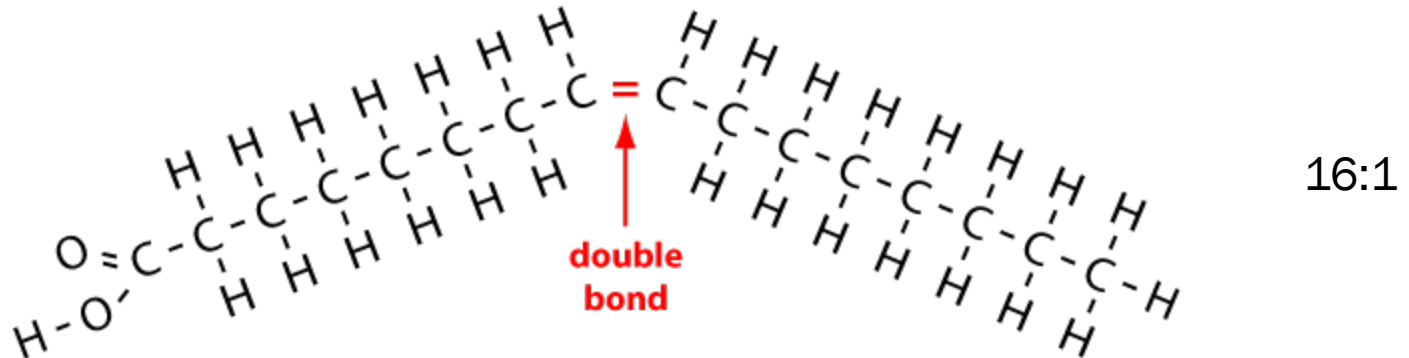
# BACKGROUND

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## saturated fatty acid



## unsaturated fatty acid



# BACKGROUND

- ▶ Essential fatty acids cannot be synthesized by the body
  - ▶ n-6 (Omega-6)
  - ▶ n-3 (Omega-3)
- ▶ Sources of EFA
  - ▶ **Omega-6:** Safflower, Soybean, Grapeseed, Sunflower oils
  - ▶ **Omega-3:** Flaxseed oil, Salmon, Walnuts

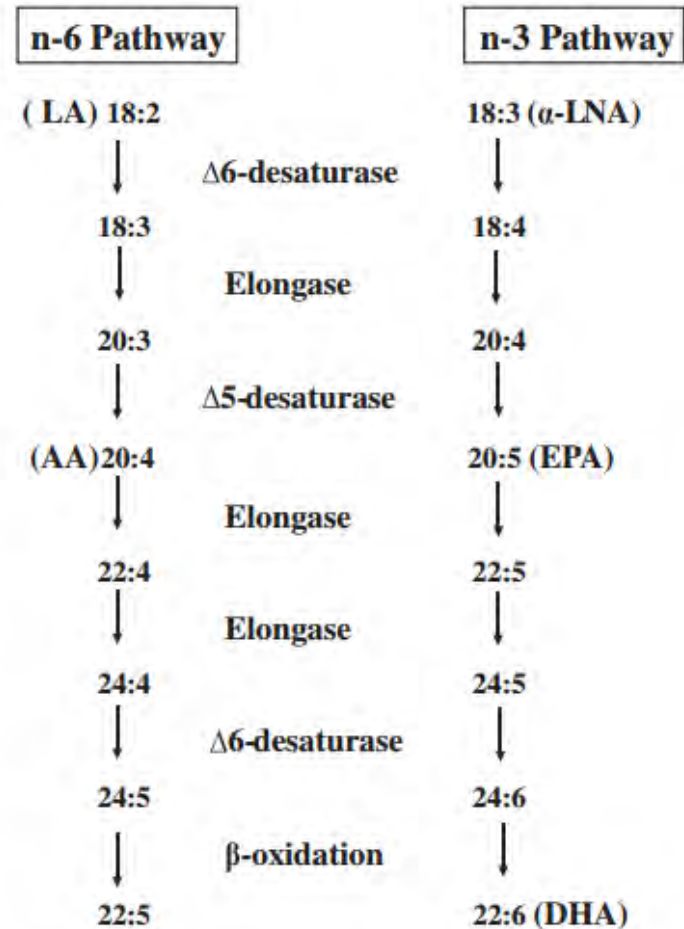
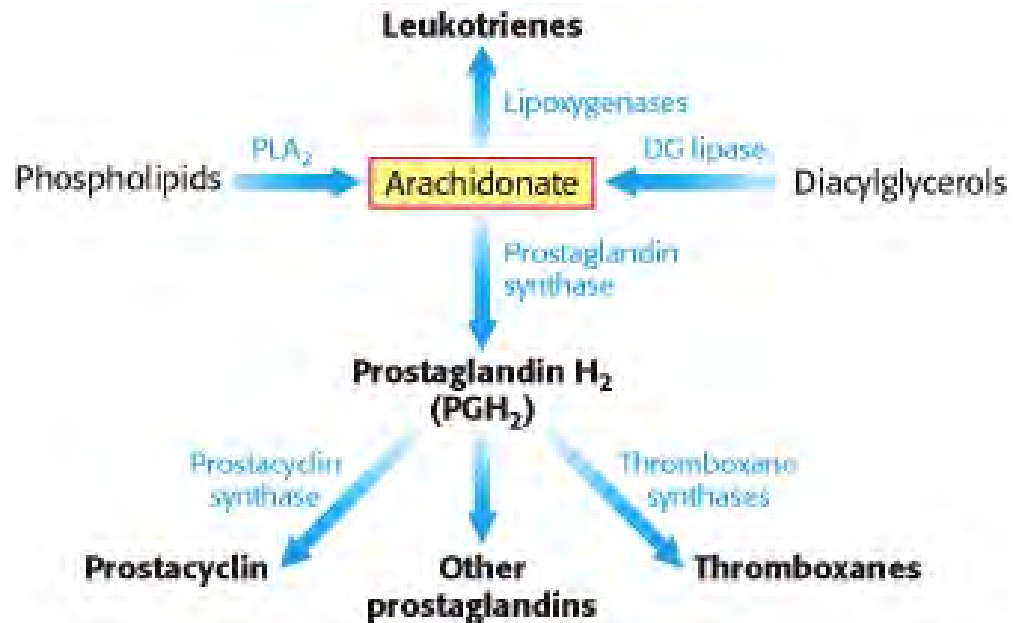


Fig. 1. Metabolic pathways of n-3 and n-6 fatty acids.

# BACKGROUND

- ▶ Decreased levels of linoleic acid
- ▶ Decreased levels of DHA
- ▶ Alterations involving arachidonic acid



Al-Turkmani MR, Freedman SD, Laposata M. Fatty acid alterations and n-3 fatty acid supplementation in cystic fibrosis. *Prostaglandins, Leukotrienes and Essential Fatty Acids*. 2007;77(5-6):309-318.

Berg JM, Tymoczko JL, Stryer L. Biochemistry. 5th edition. New York: W H Freeman; 2002. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK21154/>



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**Does the prevalence of essential fatty acid abnormalities differ among feeding types in infants?**



# OBJECTIVES

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1. To determine if similar fatty acid abnormality is present in the first 2 years of life
2. To evaluate feeding type and phenotype at baseline and explore relationships with fatty acid pattern observed
  - ▶ Feeding types: exB, exF, mixed (B+F)
  - ▶ Phenotypes: MI, PS, PI
3. To assess total dietary fat intake and its association with fatty acid pattern observed in the 2<sup>nd</sup> year of life



# Feeding Infants Right... from the Start (FIRST) Study

a prospective multicenter longitudinal study launched in 2012

to investigate the potential benefits & risks of  
exclusive breastfeeding in CF

**Salt Lake City** ★

**Milwaukee**

**Madison**

**Indianapolis**

**Boston**

**Madison Coordinating Center**

**PI: Lai**  
Shoff  
Laxova  
Zhang  
Schuchardt  
Busche  
Huebner  
Chin, Ronne

**Multi-Site Advisor Farrell**

**Neonatologist Consultant Greer**



# FIRST Study Design

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- ▶ Enroll **160 infants** from 5 CF centers in the US from 2012-2016
- ▶ Systematically collect data on complete feeding history
- ▶ Phase 1: **0-2 years**
  - ▶ Diagnosed through newborn screening
- ▶ Phase II: **2-6 years**



# FIRST Study Design

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- ▶ Primary outcomes
  - ▶ Weight gain
  - ▶ Incidence of Pseudomonas infection at 2 years of age
- ▶ Secondary outcomes
  - ▶ Nutritional – Growth measurements, EFA status, fat-soluble vitamin status
  - ▶ Pulmonary – Inflammatory markers, other respiratory pathogens, respiratory symptoms, CXR scores



# FIRST Study Design

Visit number	1	A <sup>§</sup>	B <sup>§</sup>	C <sup>§</sup>	2	3	4	5	6	7	8	9	10	11	12	13
Age*	Dx*	2 wk	4 wk	6 wk	2 mo	3 mo	4 mo	5 mo	6 mo	8 mo	10 mo	1 y	1y 3mo	1y 6mo	1y 9mo	2 y
<b>Routine care components:</b>																
CF diagnosis	Diagnosis by age 8 wks															
Physical exam	R				R	R	R	R	R	R	R	R	R	R	R	R
Interval history (nutritional/GI)	R				R	R	R	R	R	R	R	R	R	R	R	R
Interval history (pulmonary)	R				R	R	R	R	R	R	R	R	R	R	R	R
Growth (weight, length, HC)	R				R	R	R	R	R	R	R	R	R	R	R	R
Chest radiograph							R <sup>¶</sup>					R				R
Respiratory culture	R				R	R	R	R	R	R	R	R	R	R	R	R
Blood draw							R <sup>¶</sup>					R		S		R
Fecal specimen	R				S <sup>‡</sup>		S <sup>‡</sup>		S <sup>‡</sup>	S <sup>‡</sup>		S <sup>‡</sup>		S <sup>‡</sup>		S <sup>‡</sup>
<b>FIRST Study Specific Components:</b>																
Enroll infant, sign consent/HIPAA	Enroll by age 10 wks															
Parental Questionnaires					S				S			S				S
Daily Feeding Calendar					S	S	S	S	SS	SS	SS	S				
3-day Feeding record					S	S	S	S	S	S	S	S		S		S
Reminder phone calls					SS	SS	SS	SS	SS	SS	SS	SS		S		S

\*Dx=Diagnosis, ideally by age 2-4 wks (J Pediatr 2008). Enter data collected at the diagnosis visit in this column after enrollment.

§Visits A, B and C are extra visits/columns to enter data if infant is diagnosed early and has clinic visits between diagnosis and age 2 mo.

¶Window periods for visit number 2-6: ±1 wk, for visit number 7-9: ±2 wks, and for visit number 10-13: ±1 mo.

¶First (baseline) chest radiograph and blood sample collected at age 4 mo.

‡Fecal elastase-1 should be measured at these visits until PI is demonstrated by 2 consecutive values of < 100 µg/g.

R=Routine clinic visit activity

S=study-only activity; these study-only activities are conducted during routine clinic visit by usual medical personnel.

SS=activity will be done two times between visits

# Data Collection

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- ▶ Nutrition
  - ▶ Feeding, supplements, GI symptoms
- ▶ Pulmonary
  - ▶ Acute infections, respiratory symptoms, medication
- ▶ Specimens
  - ▶ Feces, blood, sputum



# Biomarkers

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- ▶ Fatty acid composition from erythrocytes
  - ▶ Concentrations were quantitated by capillary gas liquid chromatography
- ▶ Elevated Pathologic Triene (mead acid)
  - ▶  $> 0.1\%$  of total fatty acid concentration
- ▶ EFA Insufficiency
  - ▶ Triene:Tetraene ratio  $> 0.01$
- ▶ EFA Deficiency
  - ▶ Triene:Tetraene ratio  $> 0.02$

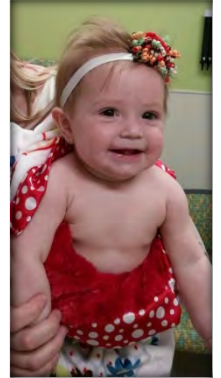




# **Preliminary Results**

# Characteristics of Study Population

- ▶ 62 infants born during 02/2012 to 05/2014
- ▶ Diagnosed through newborn screening
- ▶ Enrolled at age  $1.4 \pm 0.1$  months
  
- ▶ Blood specimen collected at 4, 12, 18, and 24 months
  - ▶ Baseline, n=52 ( $3.5 \pm 0.2$  months)
  - ▶ 12 months, n=29
  - ▶ 18-24 months, n=28



# OBJECTIVES 1 + 2

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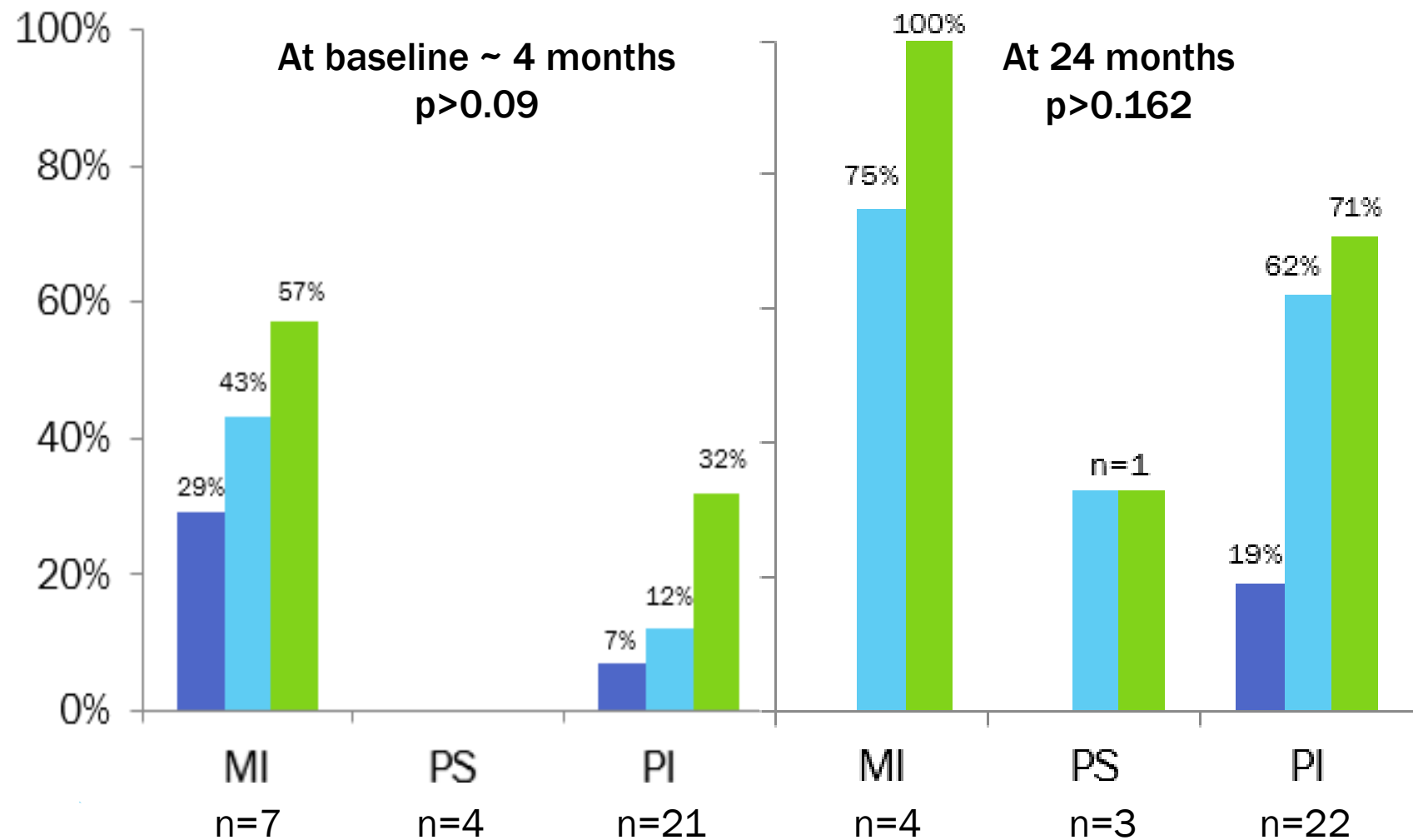
- ▶ To determine if similar fatty acid abnormality is present in the first 2 years of life
- ▶ To evaluate phenotype at baseline and explore relationships with fatty acid pattern observed
  - ▶ Phenotypes: MI, PS, PI





# EFA abnormalities tended to be highest in MI, followed by PI, lowest in PS, but these differences were not significant

■ EFAD ■ EFAI ■ Elevated Triene



# No significant age trend in EFAD prevalence

## Significant age trend in EFAI and elevated triene

- ▶ Prevalence of EFAI and elevated triene is higher at 24 months compared to baseline

	4 months (n=38)	12 months (n=19)	24 months (n=21)	p
No EFAD	35 (92%)	19 (100%)	17 (81%)	0.107
EFAD	3 (8%)	0	4 (19%)	

No EFAI	34 (90%)	18 (95%)	8 (38%)	<0.0001
EFAI	4 (11%)	1 (5%)	13 (62%)	

Triene < 0.1%	26 (68%)	18 (95%)	6 (29%)	<0.0001
Triene > 0.1%	12 (32%)	1 (5%)	15 (71%)	



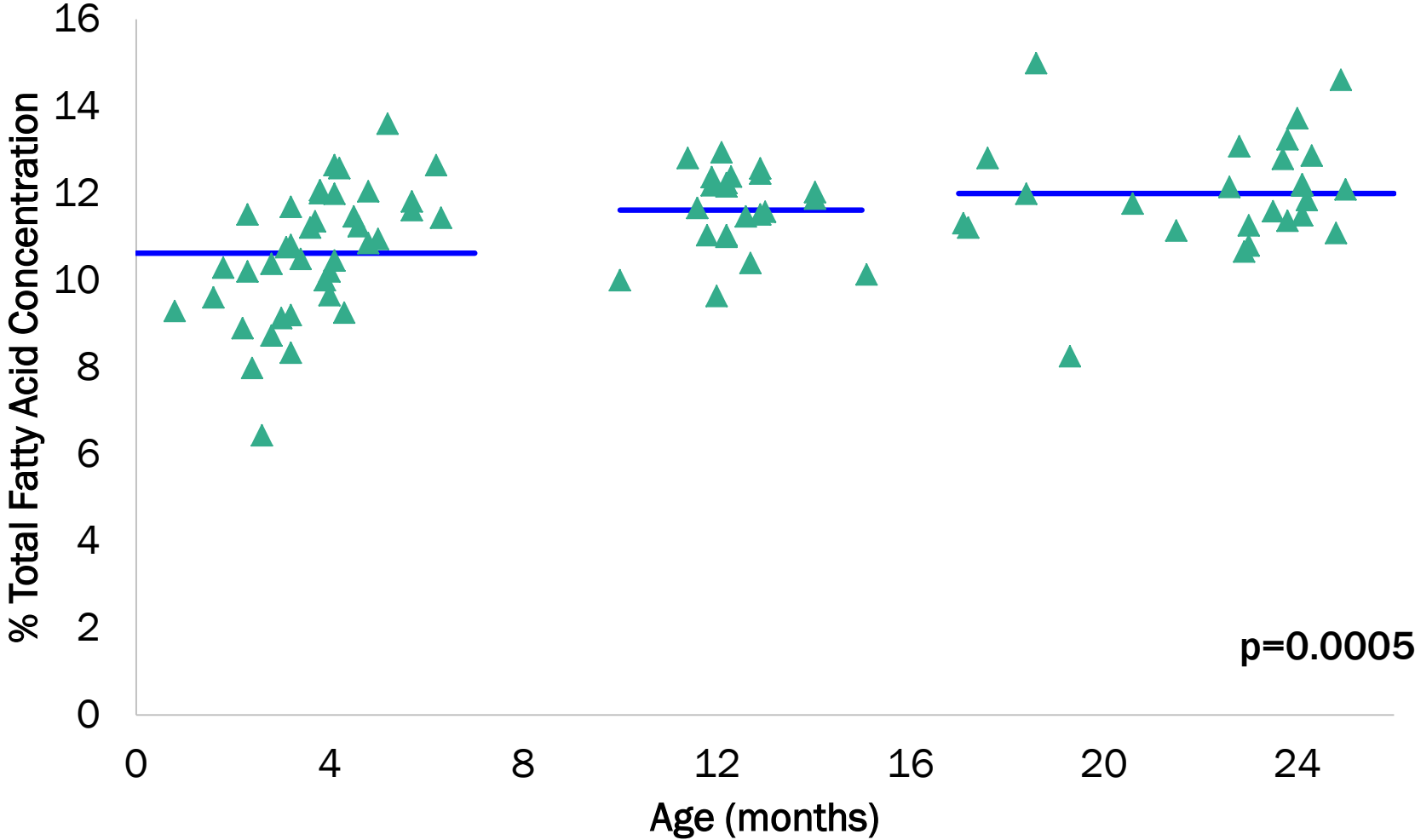


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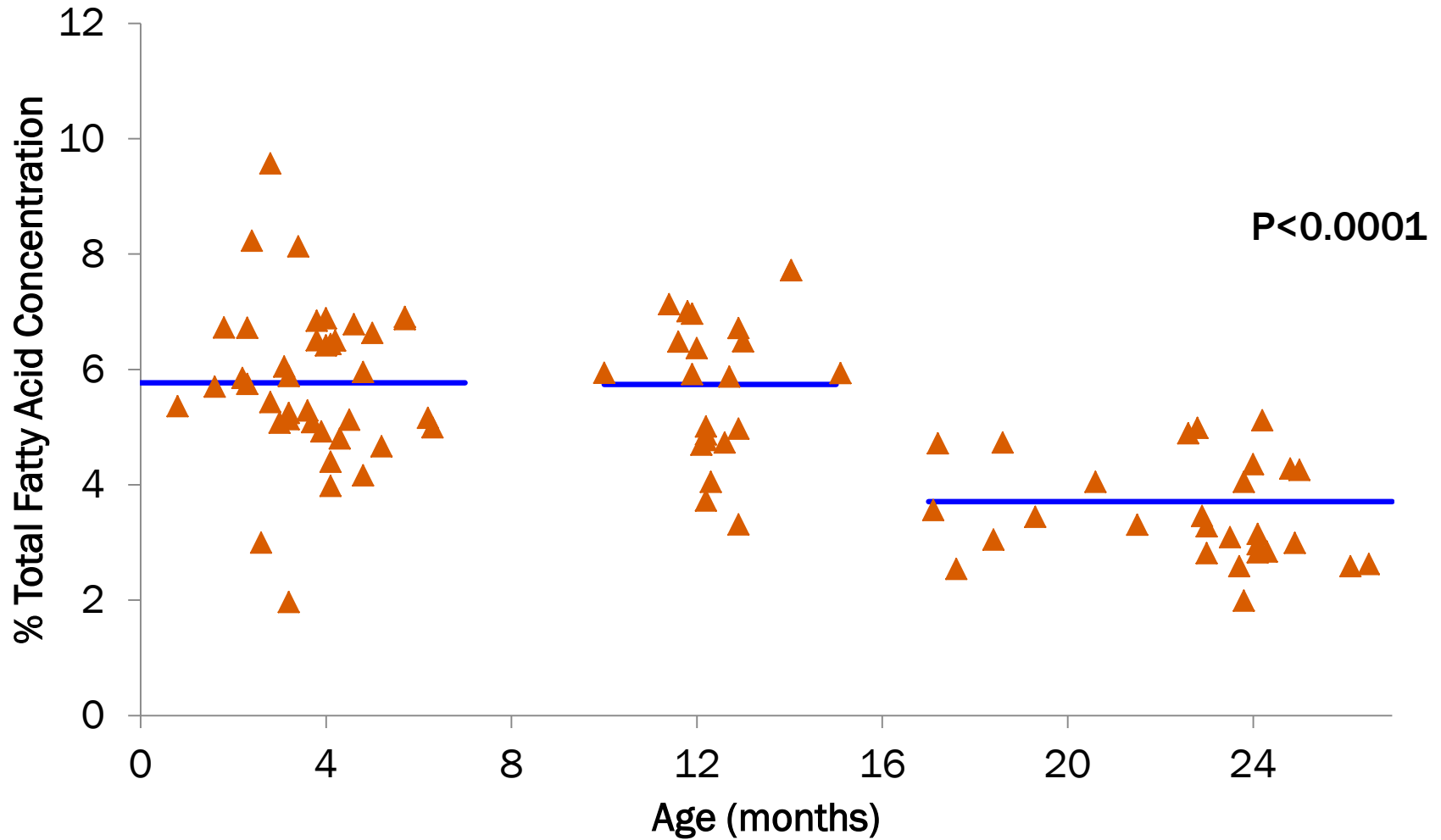
**What about linoleic acid, DHA, and arachidonic acid concentrations?**



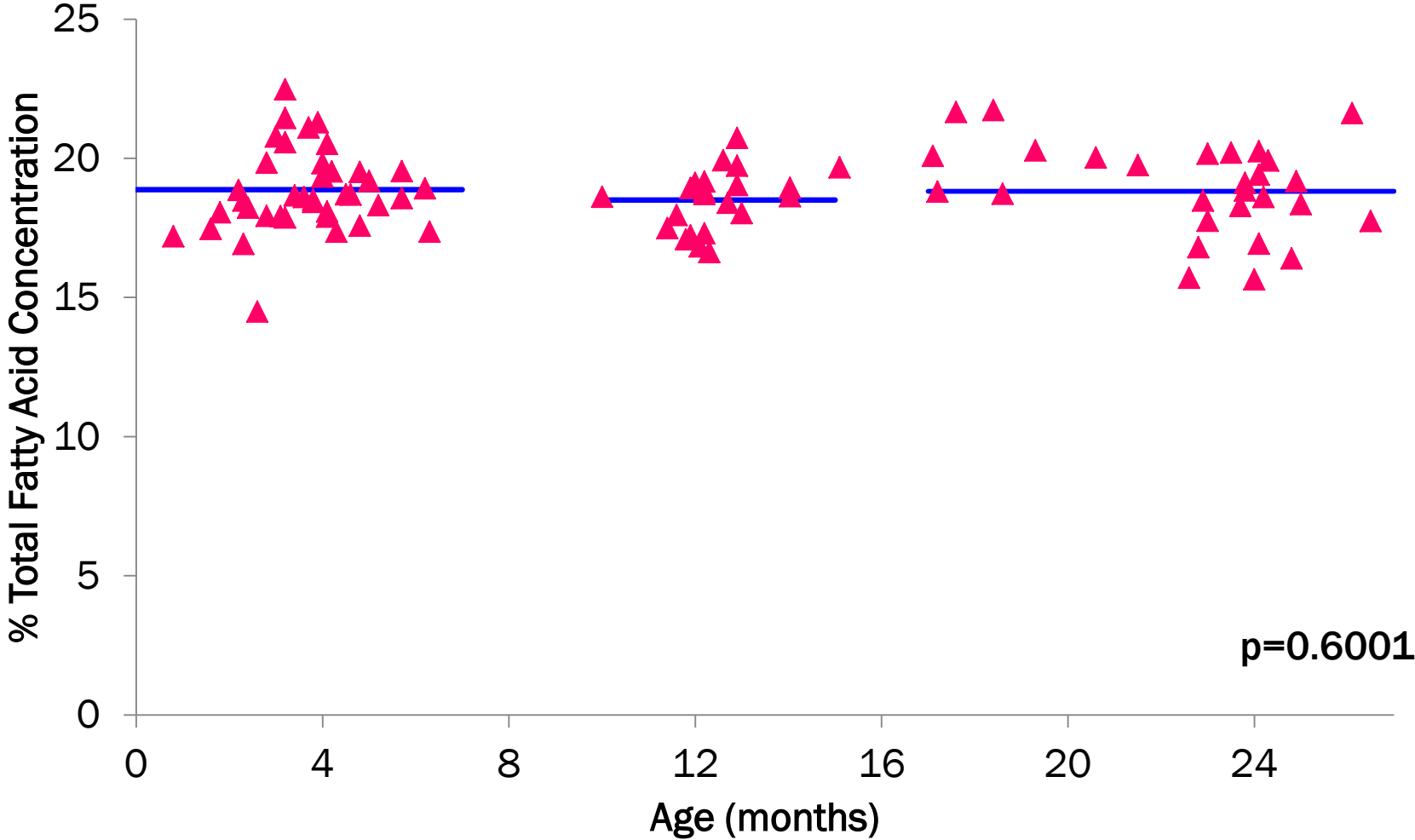
# LA concentration significantly lower at baseline compared to 12 months and at 24 months



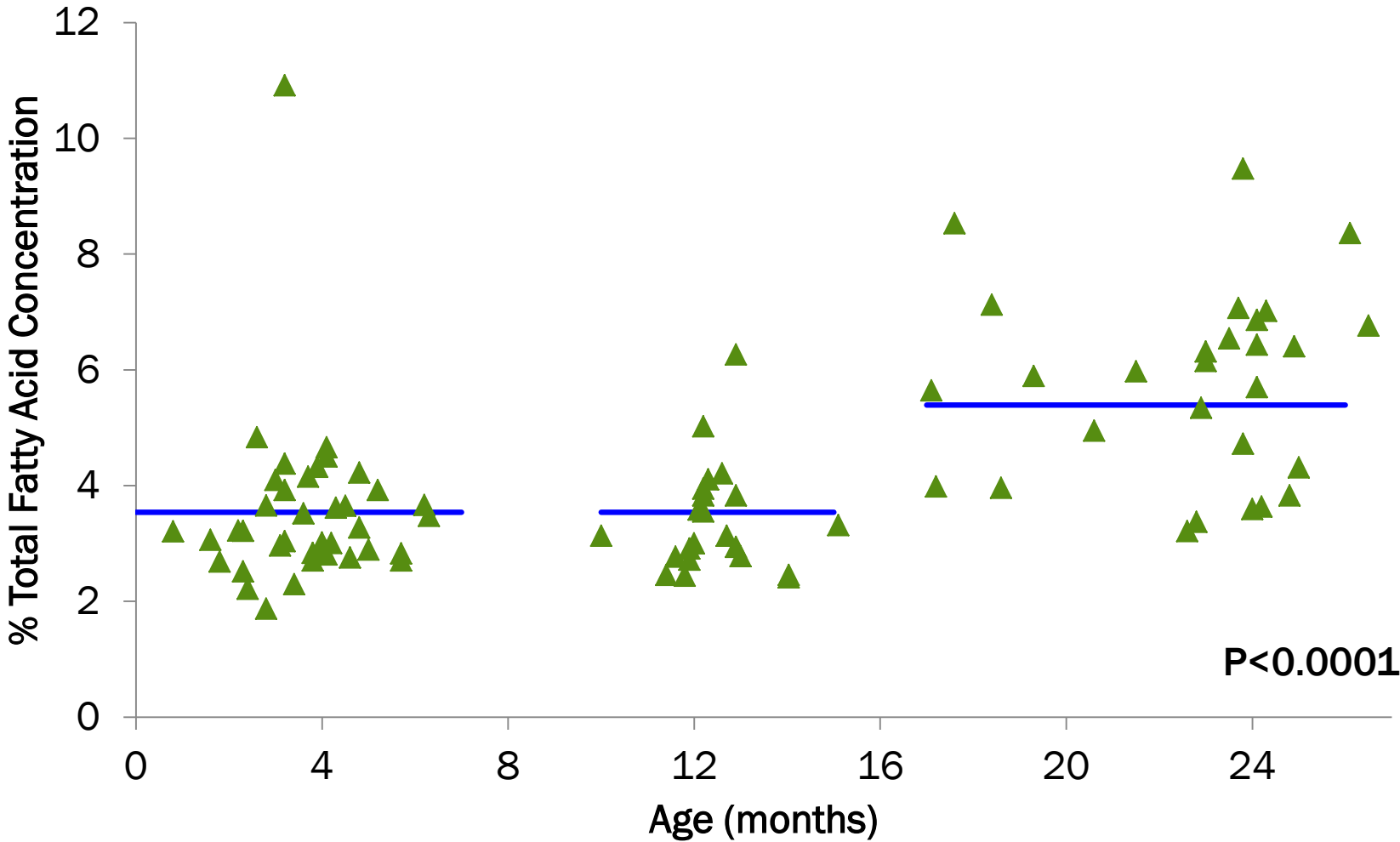
# DHA concentration was significantly lower at 24 months compared to baseline and at 12 months



# No significant age trend in arachidonic acid concentration



# AA/DHA significantly higher at 24 months compared to baseline and at 12 months



## OBJECTIVE 2

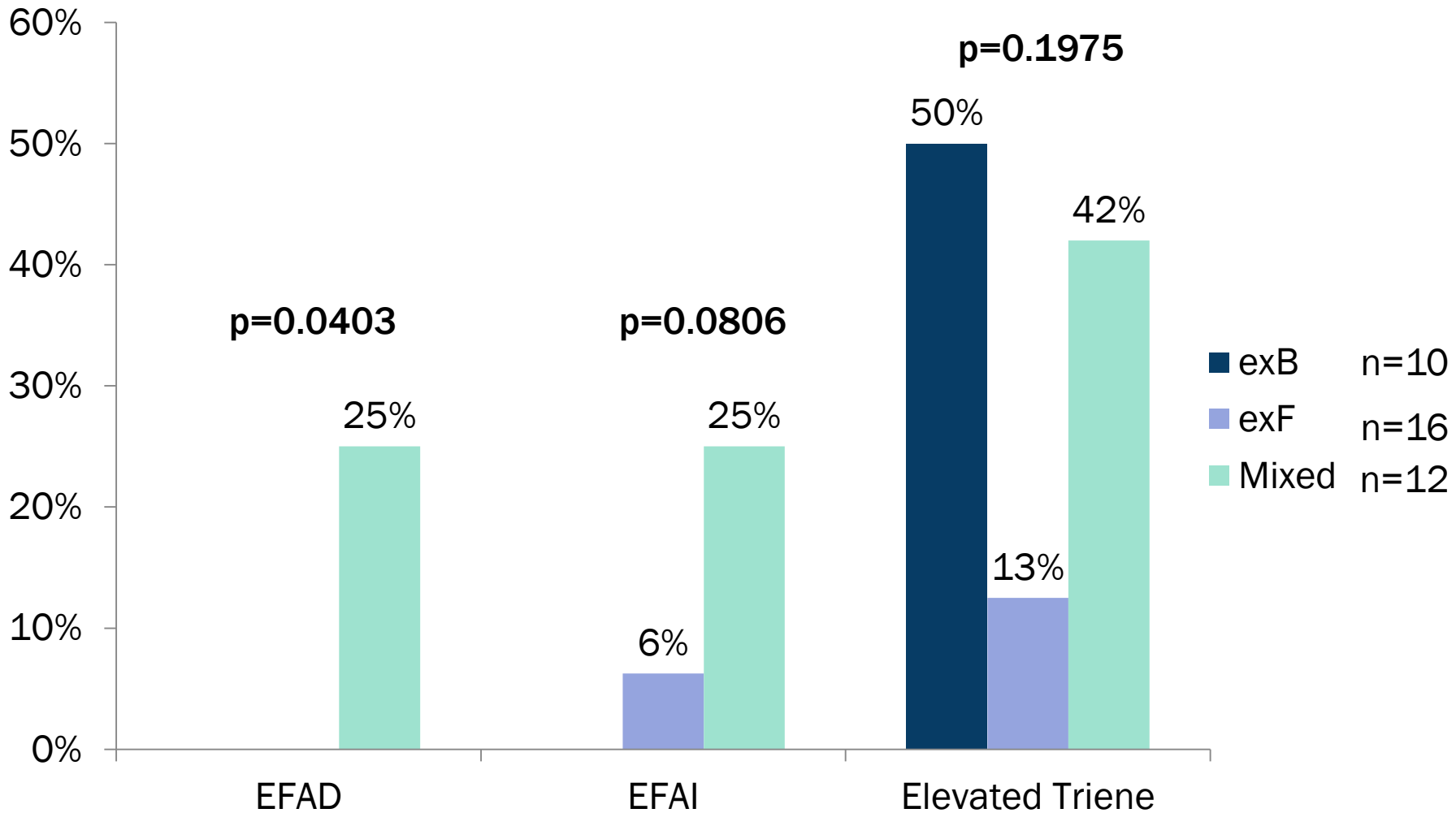
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- ▶ To evaluate feeding type at baseline and explore relationships with fatty acid pattern observed
  - ▶ Feeding types: exB, exF, mixed (B+F)





# Feeding type was significant for EFAD prevalence but not EFAI or elevated triene



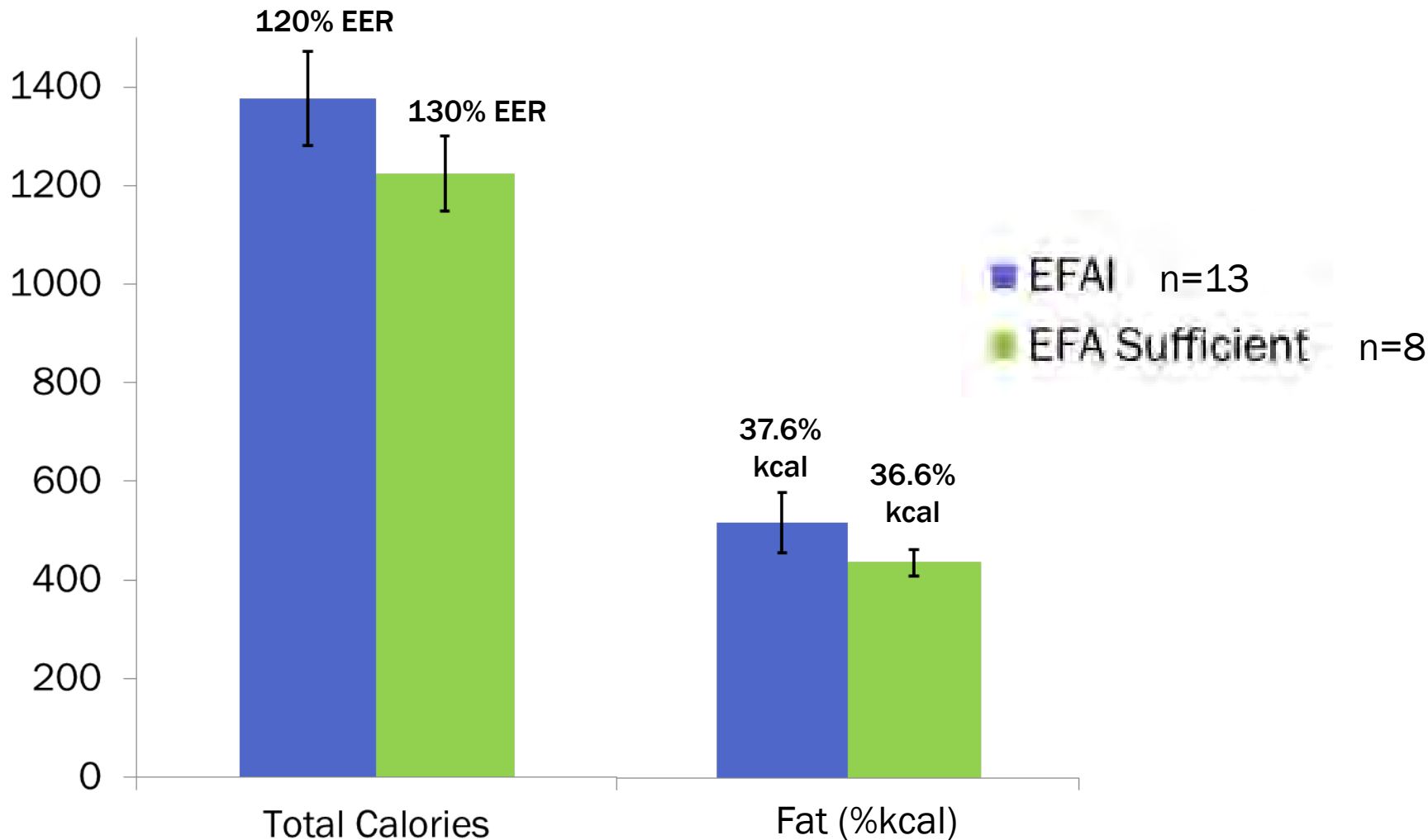
## Objective 3

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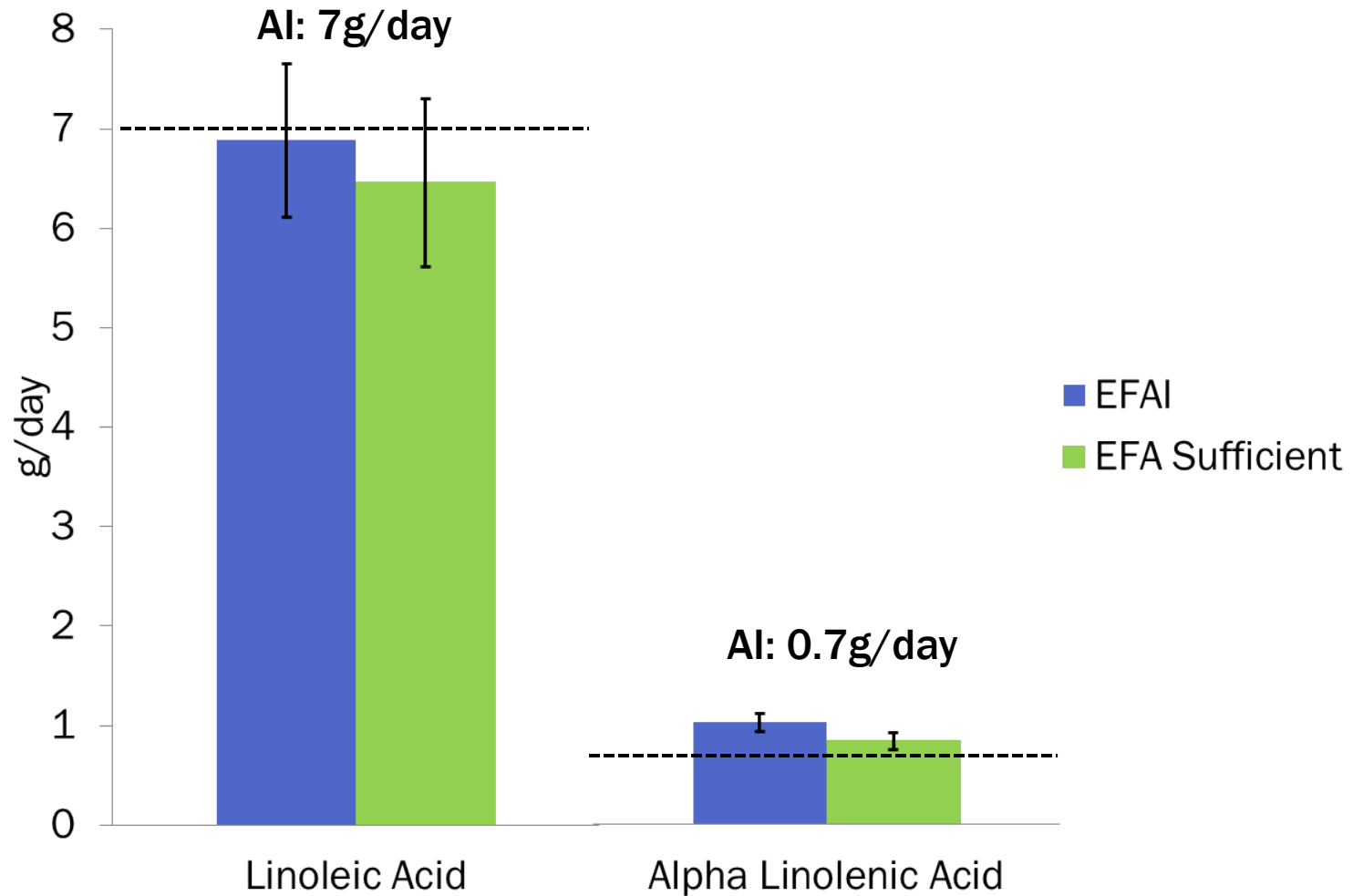
- ▶ To assess total dietary fat intake and its association with fatty acid pattern observed in the 2<sup>nd</sup> year of life



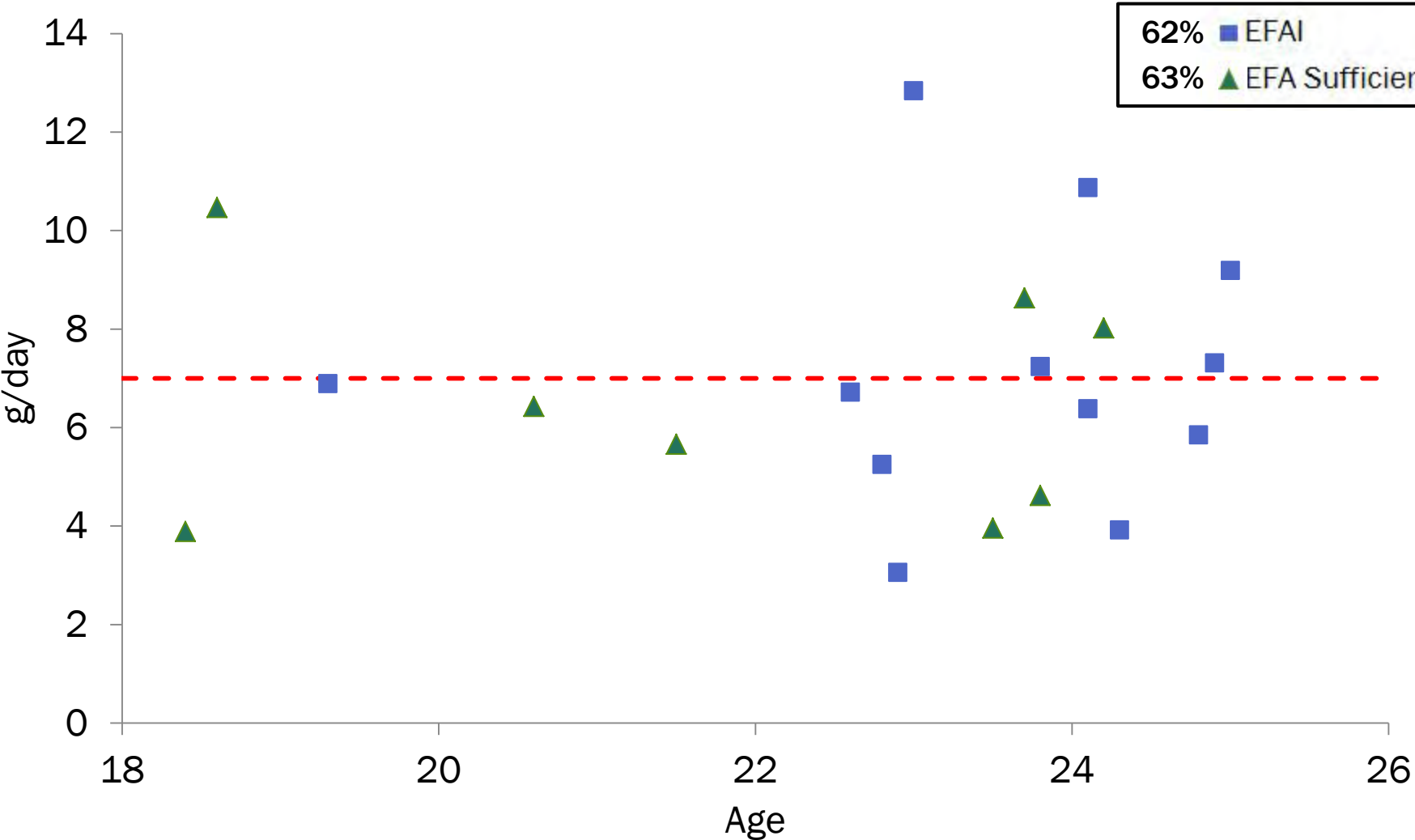
# No significant differences in total caloric intake & dietary fat intake (18-24 months)



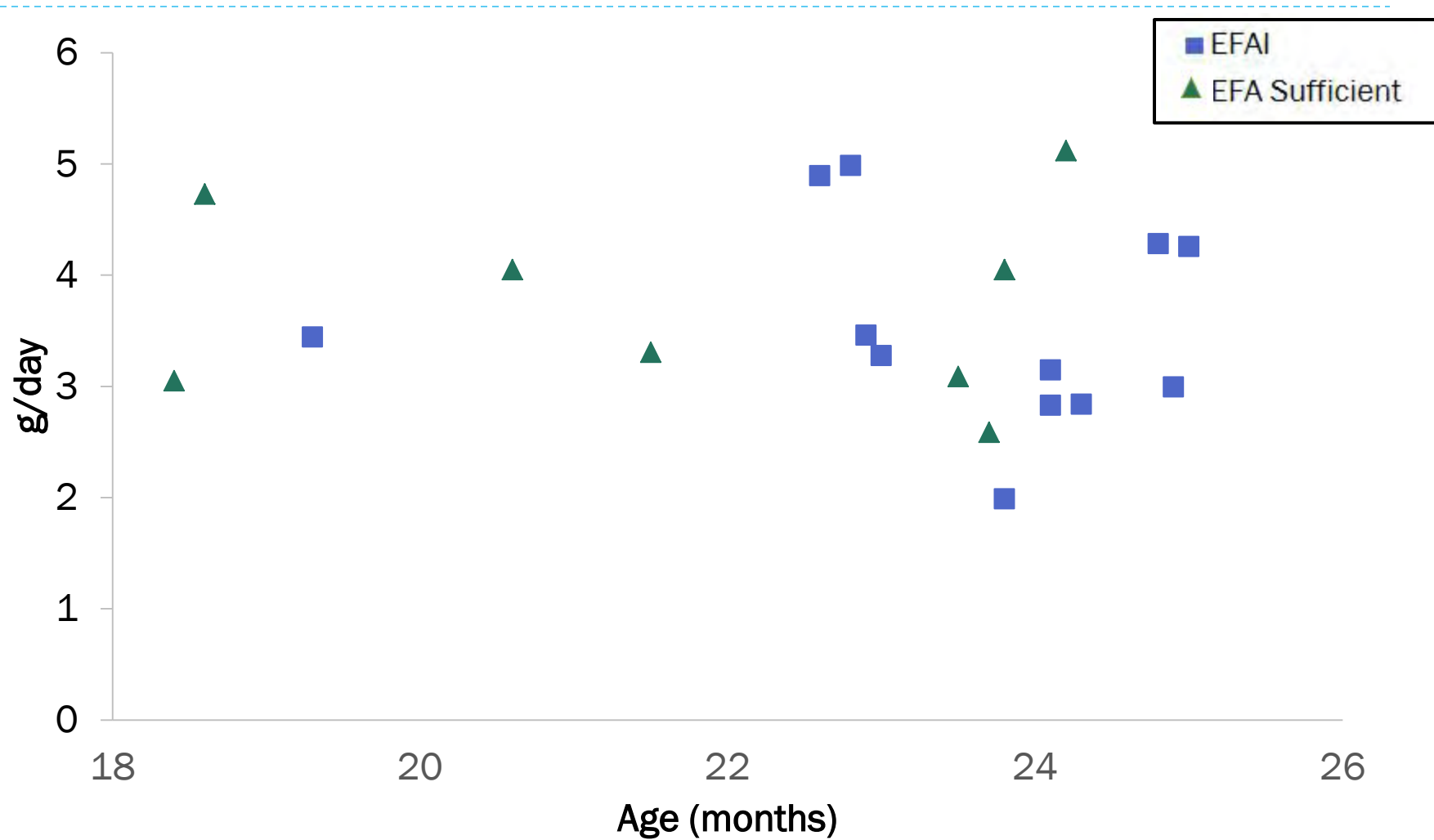
# No significant differences in LA & ALA intake at 24 months



# Low dietary LA intake is common at 24 months



# DHA Intake at 24 months



# CONCLUSIONS

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- ▶ EFA abnormalities are common in children with CF
  - ▶ More than 60% of PI subjects had EFAI and/or elevated triene
- ▶ Linoleic acid intake is low in the second year of life
  - ▶ More than 60% are below the AI
  - ▶ Enrich diet to meet AI



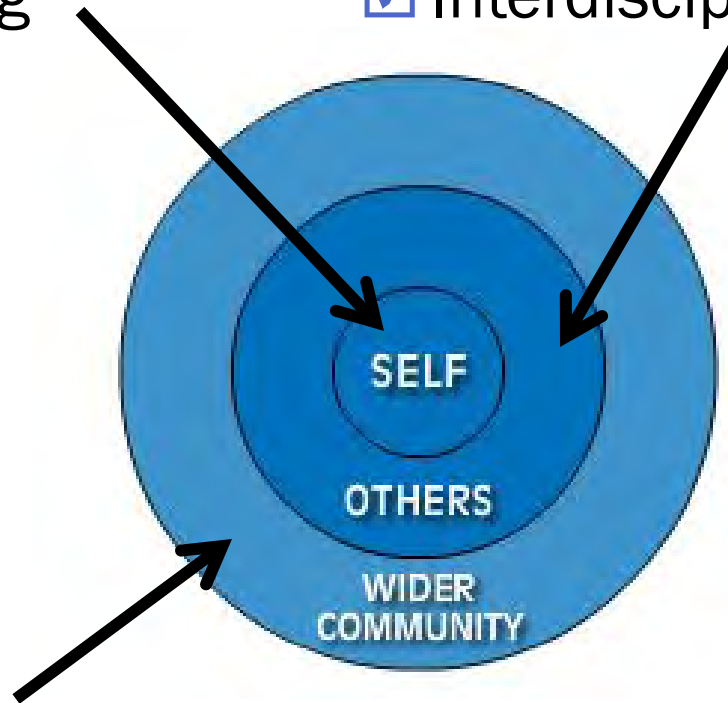


# **MCH LEADERSHIP COMPETENCIES**



- ✓ MCH Knowledge Base
- ✓ Self-Reflection
- ✓ Ethics & Professionalism
- ✓ Critical Thinking

- ✓ Communication
- ✓ Cultural Competency
- ✓ Family-Centered Care
- ✓ Interdisciplinary Team Building



- ✓ Working with Communities and Systems
- ✓ Policy and Advocacy

# Acknowledgements

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## ▶ PPC

- ▶ Mary Marcus
- ▶ Leslie Lord
- ▶ Erin Seffrood
- ▶ Darci Pfeil
- ▶ Mary Schroth

## ▶ Lai Lab

- ▶ HuiChuan Lai
- ▶ Lisa Davis

## ▶ Ntambi Lab

- ▶ Sabrina Dumas



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Questions?

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