THE OHIO STATE UNIVERSITY
COLLEGE OF
EDUCATION AND HUMAN ECOLOGY

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.℠

Diet Patterns, Nutrient Intake, and Depression in Adolescents with Mood Disorders

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Global Burden of Mood Disorders- Adolescents

- About 3 million teens ages 12 to 17 had at least one major depressive episode in 2014[1]
- By age 18, 11% of US adolescents have a depressive disorder[2]
- Suicide is the second leading cause of death for ages 15-39[3]
- Of those who commit suicide, 90% have a pre-existing mental health condition.

***Mood disorders are the leading mental health condition associated with suicide.**

[1] Department of Health and Human Services; [2]National institute of Mental Health, [3]Center for Disease Control;

Current Treatment Options

- Psychopharmacological Treatment options
  - Antidepressants
  - Mood Stabilizers
  - Antipsychotics

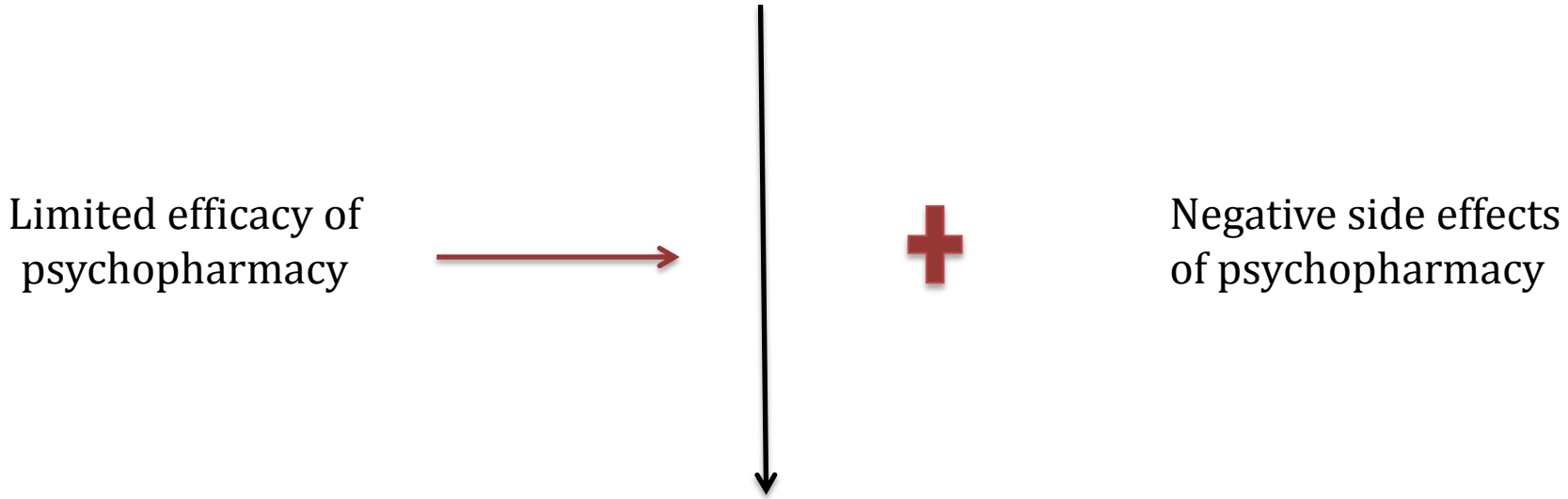
- Psychotherapy Treatment Options
  - Cognitive Behavioral Therapy (CBT)
  - Interpersonal-Therapy (IPT)
  - Family-based therapy

Psychopharmacology Concerns

- In many, no clinically significant improvement in symptoms within the first year of diagnosis after attempting multiple treatment plans
- High rate of relapse
- Side effects: metabolic and cardiovascular
  - tardive dyskinesia
  - increased prolactin levels
  - fatty liver
  - increased T2 diabetes risk
  - significant weight gain
  - sexual dysfunction
- Long-term treatment side effects still unknown

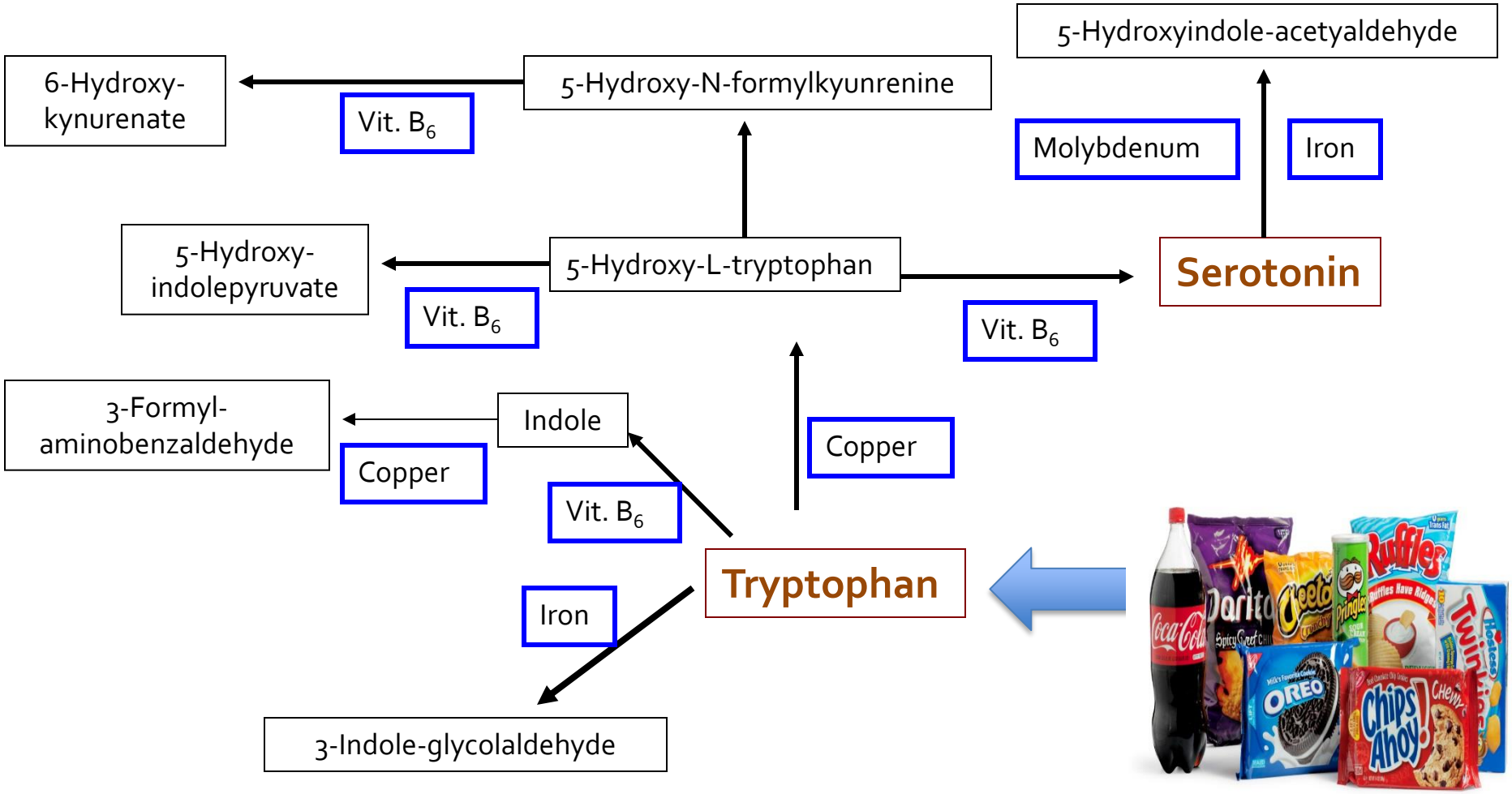
THE CLINICAL CHALLENGE

Increasing rates of Mood Disorders



**** Many of the biochemical and neural functions regulating mood involve the metabolic activity of micronutrients.**

One small portion of serotonin pathway



Diet is associated with mood disorders

Selected diet studies in mental health

- Cross-sectional
- Longitudinal
- Prospective cohorts
- Meta-analyses
- RCTs
  - Major centers: Australia, Spain, the Netherlands, Canada, and the UK

Longitudinal diet studies in youth

- **Perth Longitudinal Cohort Study**
  - **14 y/o youth with Western diet patterns had more internalizing (withdrawn/depressed) and externalizing (delinquent/aggressive) behaviors**
    - **Especially for sweets, take-out food, and red meat**
    - **Related to more TV time, parental smoking, lower incomes**
  - **The 11% of youth who ate 3 food groups at breakfast had more favorable CBCL scores**
  - Youth with better diets more likely to: be female, have greater maternal education, lower television exposure, better family functioning, and a two-parent household

Oddy et al 2009; Ambrosini et al 2009; O'Sullivan et al 2009; Larsen et al 2007

Fruits and vegetables lower risk for mood and anxiety disorders in adults and teens

- Canadian cohort including adolescents
  - across all 5 waves, ~ 2 years apart, greater fruit and vegetable intake associated with lower odds of MDE in the previous 12 months (OR 0.72; 95% CI 0.71-0.75);
  - previous mood or anxiety disorder diagnosis also related to lower fruit and vegetable intake (pp<0.05)
- Perth cohort
  - Youth with more green leafy vegetable and fresh fruit intakes had better behavioral scores
  - Family meals during adolescence predicted higher quality diet at young adulthood
    - greater intake of fruit, vegetables, especially dark-green and orange vegetables, and lower intakes of soft drinks

McMartin et al 2013; Larson et al 2007

MH and diet patterns in women: The Geelong Osteoporosis Study

In over 1,000 women ages 20-93:

- A Western diet of processed or fried foods, refined grains, sugary products and beer
  - associated with a higher score on the 12-item General Health Questionnaire (GHQ-12)
- A traditional diet of vegetables, fruit, meat, fish, and whole grains
  - associated with lower odds for major depression, dysthymia, and anxiety disorders, via SCID (Structured Clinical Interview for DSM-IV-TR).

There were no confounds by age, SES, education, or other health behaviors on the GHQ-12 results.

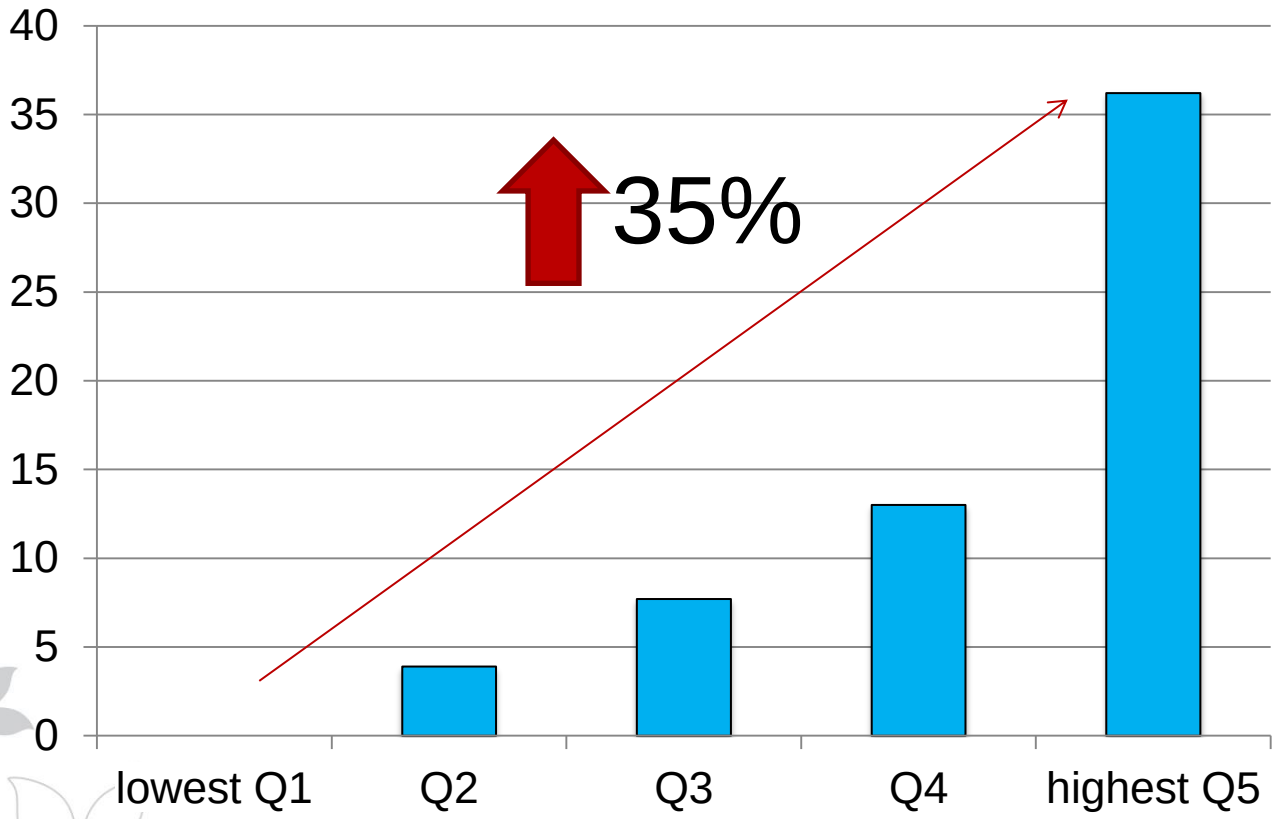
Jacka et al 2010 Am J Psychiatry

Diet patterns and women with bipolar disorder

- In population-based adult women (also the Geelong study, using the Cancer Council Victoria FFQ and the SCID-I/NP):
  - women with BP disorder had higher scores for a Western diet ($p<0.03$) vs. those without psychopathology
    - trended toward higher glycemic loads;
  - Adjusted odds (for energy intake) for BP disorder increased for each standard deviation increase in:
    - **unfavorable 'western' diet- OR 1.88** (95% CI1.33-2-65)
    - '**modern' diet- OR 1.72**, (95% CI 1.14-2.39)
    - glycemic load- **OR 1.56**, (95% CI 1.13-2.14)
  - Jacka et al 2011, J Affect Disord

Risk of depression within 6.2 years in ~9,000 people

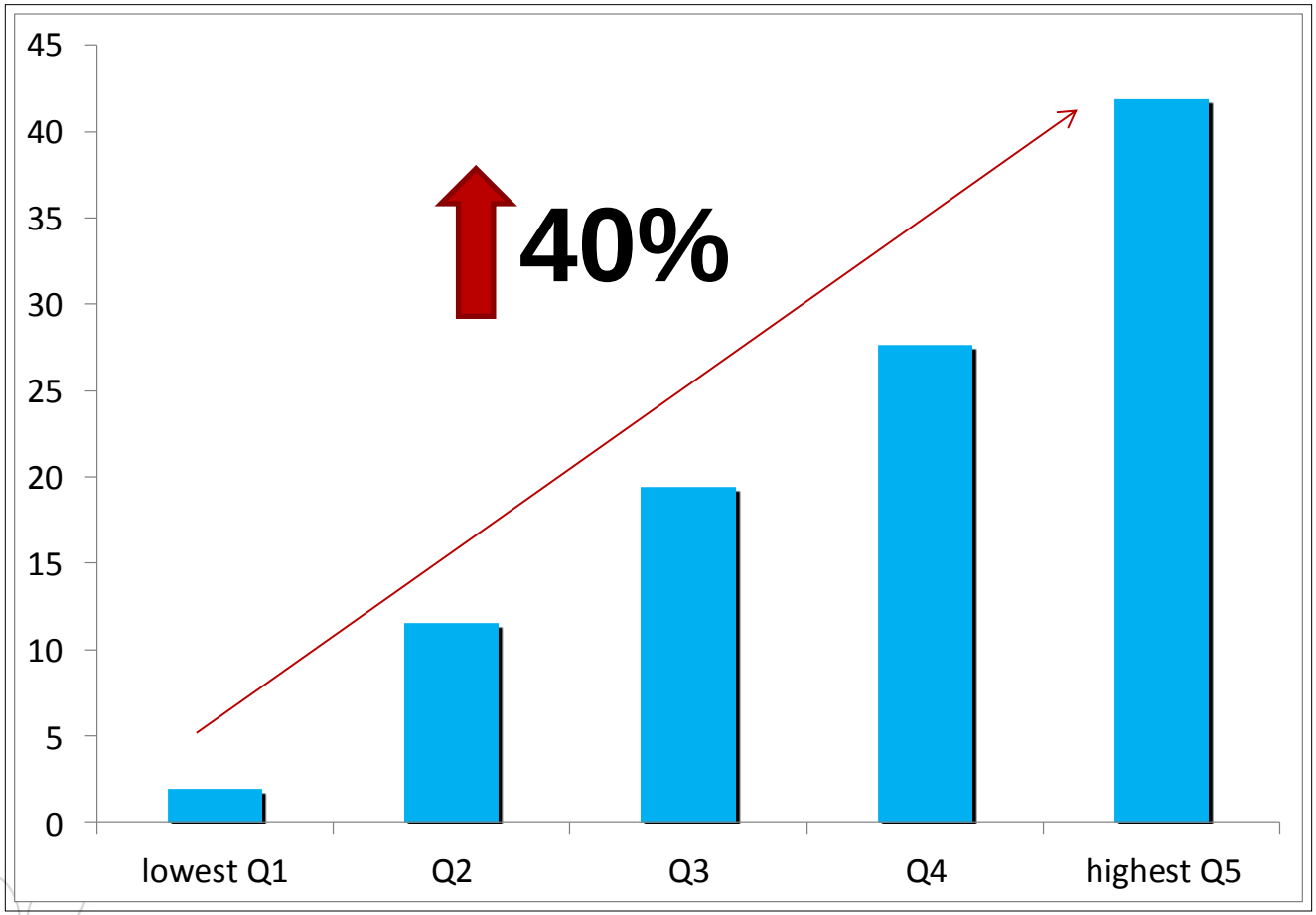
Based on processed pastries (muffins, doughnuts)



Sanchez-Villegas et al., *Public Health and Nutrition*, 2012

Risk of depression within 6.2 years in ~9000 people

Based on fast food (hamburgers, pizza)



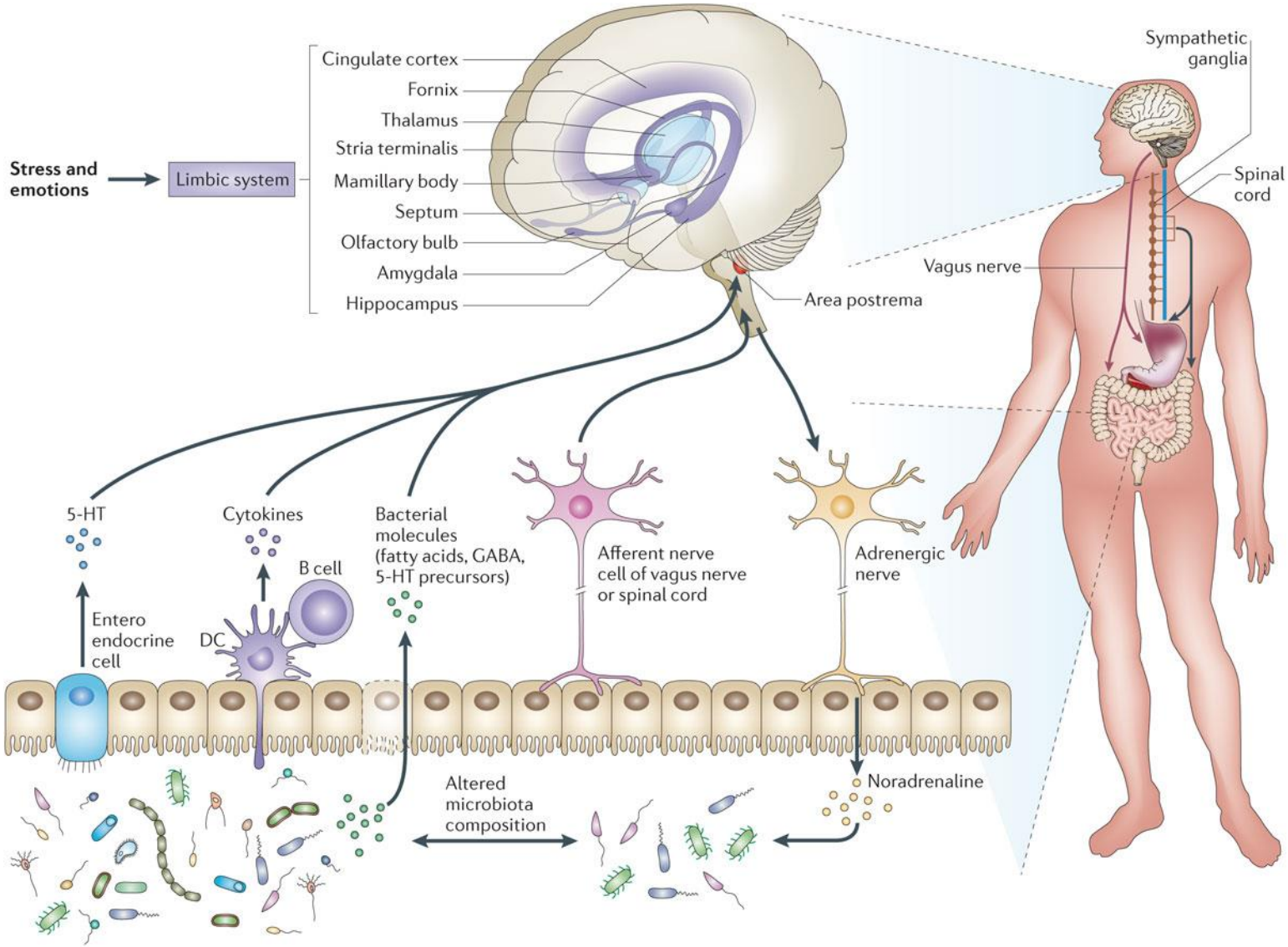
Meta-analyses: Mediterranean Diet and CNS health

- Lai et al. Am J Clin Nutrition; 2014
  - 13 observational studies pooled for meta-analysis
  - The healthy diet pattern was associated with reduced odds of depression (OR: 0.84; 95% CI: 0.76, 0.92; P < 0.001).
  - high intakes of fruit, vegetables, fish, and whole grains may be associated with reduced risk for depression

- Psaltopoulou et al. Ann Neurol. 2013:580-91.
  - 22 studies pooled for meta-analysis
    (11 stroke, 9 depression, and 8 cognitive impairment)
  - High adherence to Mediterranean diet reduced risk for:
    - stroke (RR = 0.71, 95% [CI] = 0.57-0.89)
    - depression (RR = 0.68, 95% CI = 0.54-0.86)
    - cognitive impairment (RR = 0.60, 95% CI = 0.43-0.83)

Can the associations between diet and mood be linked to known mechanisms for mood disorders?

The bidirectional microbiota–gut–brain axis.
The interplay between the intestinal microbiota and the brain



Collins SM et al 2012:10, 735-742

Mechanisms for microbiota regulation of neuroimmune signalling

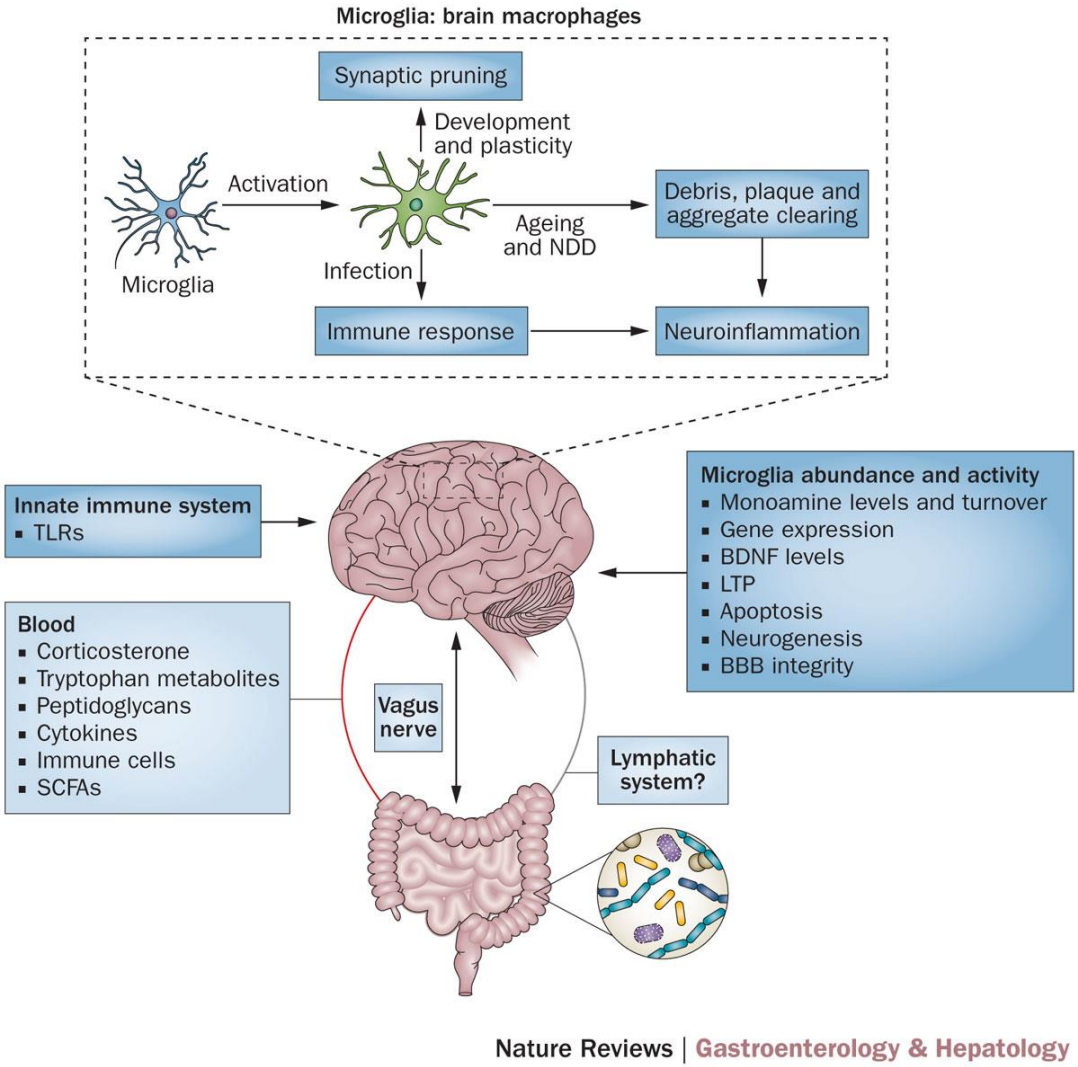


Figure developed by Dr R. Stilling, APC Microbiome Institute, University College Cork

Cryan, J. F. & Dinan, T. G. (2015) Microbiota and neuroimmune signalling—Metchnikoff to microglia
Nat. Rev. Gastroenterol. Hepatol. doi:10.1038/ nrgastro.2015.127

Is there any level "A" evidence documenting positive effects of diet change on mood symptoms?

Fruit and vegetable intervention for inflammation: proof of concept

Do different vegetable and fruit intakes modulate immunologic markers?

- In an RCT of nonsmoking men:
  - consumed x 4 wks ≤ 2 servings veggies and fruit/day
  - randomly assigned to 1 of 3 groups, 2 vs. 5 or 8 servings /day x 4 weeks, of carotenoid-rich vegetables and fruit
  - plasma vitamins C and E and carotenoids, N and activity of natural killer cells, cytokines, lymphocyte proliferation, and plasma CRP concentrations measured
- CRP was lower at wk 8 in those eating 8 servings/day of vegetables and fruit vs. those eating 2 servings/day.

Watzl et al.
Am J Clin Nutr 2005

The SMILES TRIAL= 1st RCT of diet as adjunct tx

- Inclusion criteria:
  - Adults with MADRAS score > 18
    - Poor diet quality
    - Antidepressant dose stable x 2 weeks
- Randomized to social vs. dietary support
  - 7-60 minute sessions across 12 weeks
  - Focus on “Modern Mediterranean Diet”
- Results: 67 randomized; 56 completed
  - Outcome: MADRAS <10: 32% for diet vs. 8% controls
  - NNT 4.4; top 25% adherence associated w/ improvement
  - Legumes, fish, vegetable soup cost-effective
  - Gut health, BDNF, inflammatory biomarkers pending
  - Jacka F, oral presentation July 2016, ISNPR; under review

Currently underway:

- The MooDFOOD prevention trial
  - 1000 adults 18 to 75 years at risk for MDD due to overweight/class I obesity and depressive symptoms
  - 2x2 factorial design, 4 European sites, randomized to:
    - Daily multi-nutrient supplements (O3FA, calcium, selenium, B11(folic acid) and D3) vs. placebo;
    - Food-related Behavioral Activation vs. control
  - 12-month intervention with outcome measures quarterly
  - Mediterranean diet-based
  - €11.4 million cost

http://www.exeter.ac.uk/mooddisorders/research/currentprojects/moodfood/

Roca et al. BMC Psychiatry 2016;16:192

Micronutrient Research

Single Nutrient Trials

- Observational Studies:
  - Deficiencies seen in B vitamins
  - Amino acids tryptophan and tyrosine
  - Omega 3 fatty acids
- Single Nutrient Clinical Trials:
  - L-methyl folate as adjunctive treatment for depression
  - Omega 3 fatty acids as monotherapeutic or adjunctive treatment for severe depression and bipolar disorder
  - Vitamin D as adjunctive treatment (lowers severity of manic episodes,)

Multinutrient Trials

- Utilizes the synergism of nutrients
- Most success in clinical trials for symptom alleviation
- EMPowerplus (EMP+) and Daily Essential Nutrients (DEN)

Missing in the field?

- Little to no research for the following:
  - Dietary patterns and nutrient intake of youth with mood disorders
  - Relationships between nutrition and mood disorder symptom severity
  - Relationship between nutrition and response to treatment

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Leanna Perez, PhD
OSU Interdisciplinary Nutrition Science Program

OSU “Partners in Nutritional Health”

- Dissertation funding provided by:
  - OSU Department of Nutrition
  - OSU Center for Integrative Health and Wellness
  - OSU Center for Advanced Functional Foods and Entrepreneurship
  - NCH Center for Innovation in Pediatric Practice-Jeffrey Research Fellowship

Goal of Dissertation Study Series

- ✓ Descriptive and Biologic Data
- ✓ Hypothesis Generating
- ✓ Better Tailor Nutrition Interventions

Primary Methods:

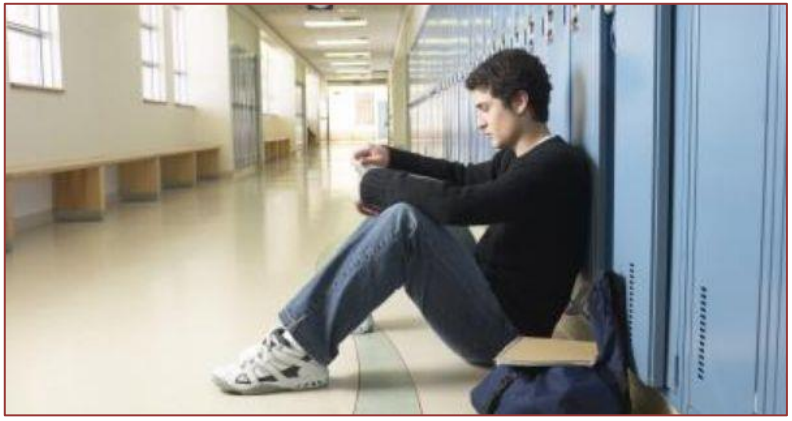
- *Interview-assisted qualitative research*
- *Importance of subgroup identification*

Study: Dietary Patterns in Youth with Depressive Disorders

Objectives

Characterize common trends in dietary and lifestyle patterns of youth with a diagnosed depressive disorder

> Cross sectional study design



Inclusion and Exclusion Criteria

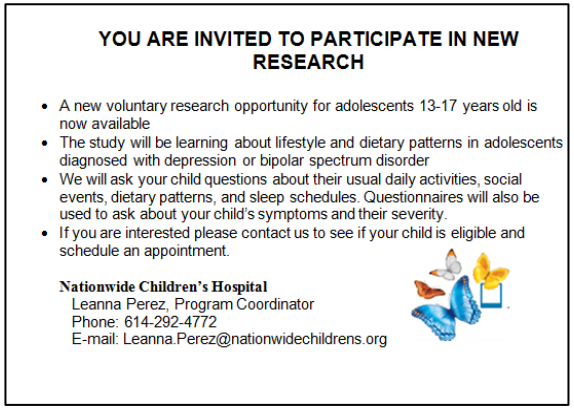
- Inclusion criteria:
  - ✓ Youth aged 13-18 years
  - ✓ Diagnosed with a mood disorder by a licensed psychologist, social worker, or psychiatrist,
  - ✓ Enrolled in outpatient psychiatric treatment

- Exclusion criteria:
  - x Pregnant, within 6 months postpartum, or breastfeeding
  - x Experiencing protracted nausea for any reason including an adverse effect associated with a medication
  - x Presence of significant eating disorder pathology as determined by the clinical care team or study staff

Recruitment Methods

- Electronic and on-site advertisements:
  - Email advertisement to hospital employees
  - Letters/postcards
  - Flyers on-site, with a section for the family to provide contact information if interested.

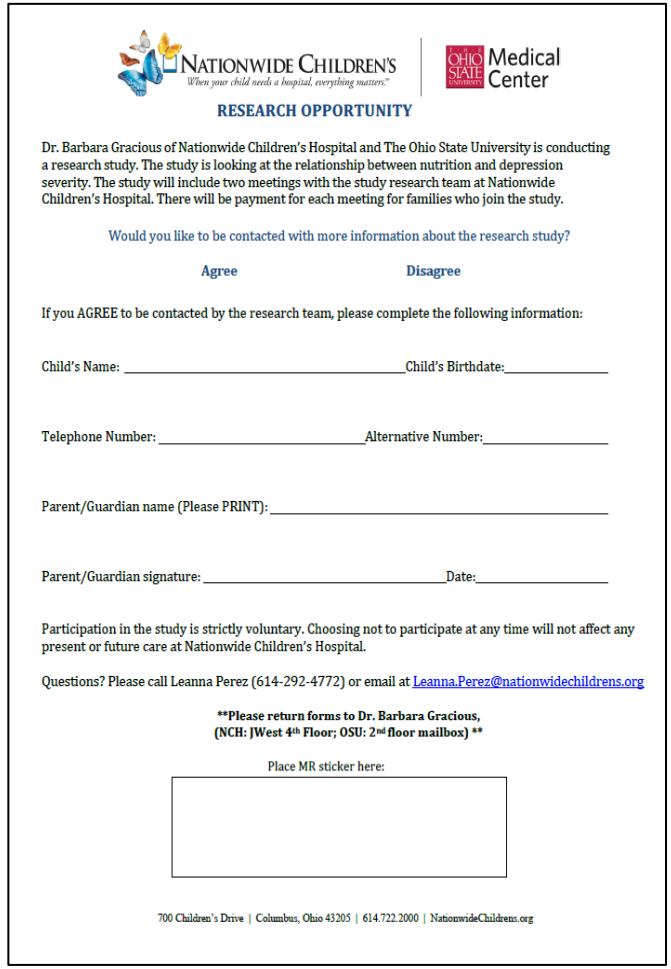
- Electronic medical record screening
  - Assessed for eligibility by telephone or an online survey



YOU ARE INVITED TO PARTICIPATE IN NEW RESEARCH

- A new voluntary research opportunity for adolescents 13-17 years old is now available
- The study will be learning about lifestyle and dietary patterns in adolescents diagnosed with depression or bipolar spectrum disorder
- We will ask your child questions about their usual daily activities, social events, dietary patterns, and sleep schedules. Questionnaires will also be used to ask about your child's symptoms and their severity.
- If you are interested please contact us to see if your child is eligible and schedule an appointment.

Nationwide Children's Hospital
Leanna Perez, Program Coordinator
Phone: 614-292-4772
E-mail: Leanna.Perez@nationwidechildrens.org



Nationwide Children's — When your child needs a hospital, everything matters.
Ohio State University Medical Center

RESEARCH OPPORTUNITY

Dr. Barbara Gracious of Nationwide Children's Hospital and The Ohio State University is conducting a research study. The study is looking at the relationship between nutrition and depression severity. The study will include two meetings with the study research team at Nationwide Children's Hospital. There will be payment for each meeting for families who join the study.

Would you like to be contacted with more information about the research study?

Agree Disagree

If you AGREE to be contacted by the research team, please complete the following information:

Child's Name: _____ Child's Birthdate: _____

Telephone Number: _____ Alternative Number: _____

Parent/Guardian name (Please PRINT): _____

Parent/Guardian signature: _____ Date: _____

Participation in the study is strictly voluntary. Choosing not to participate at any time will not affect any present or future care at Nationwide Children's Hospital.

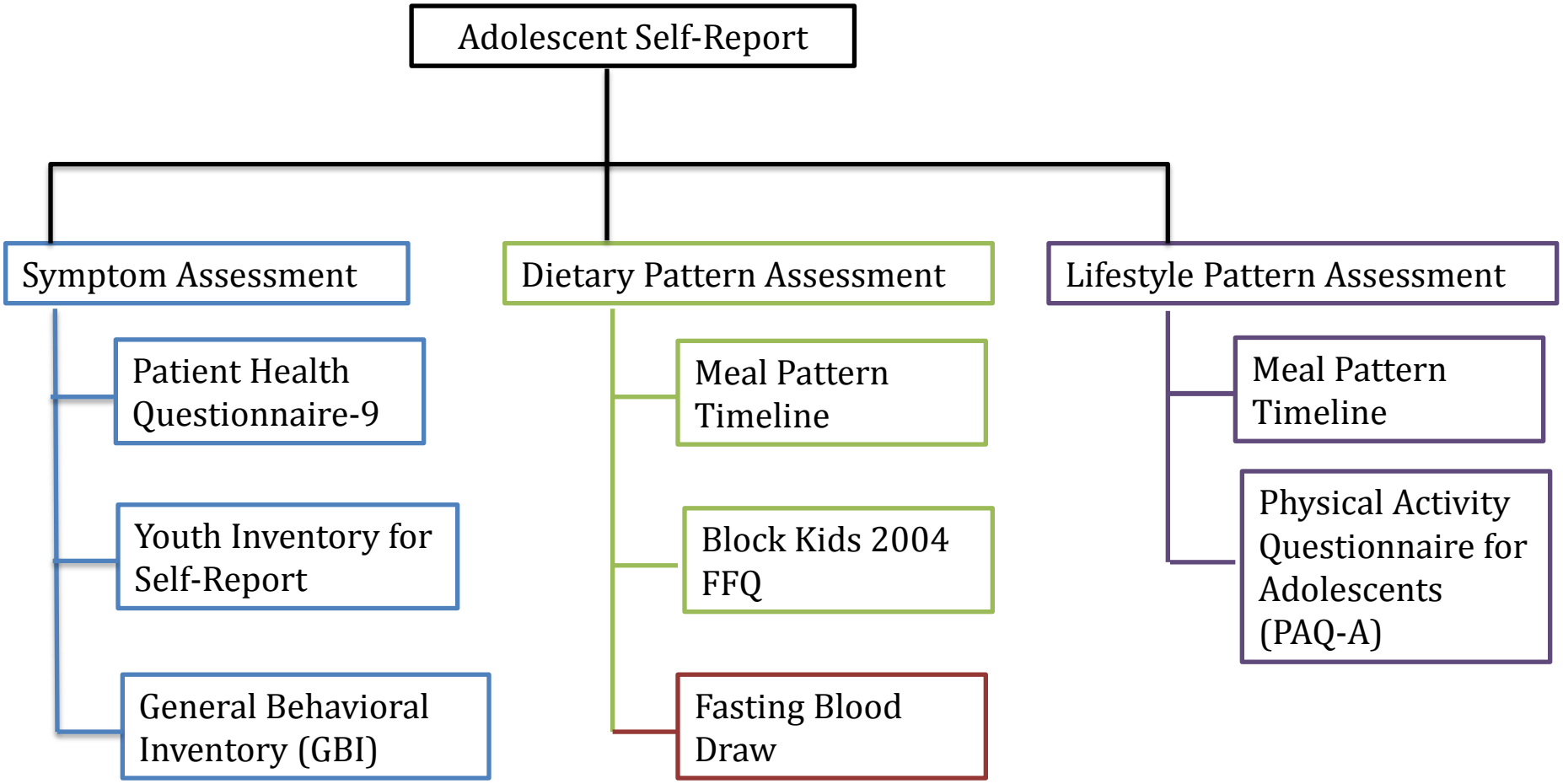
Questions? Please call Leanna Perez (614-292-4772) or email at Leanna.Perez@nationwidechildrens.org

****Please return forms to Dr. Barbara Gracious,
(NCH: JWest 4th Floor; OSU: 2nd floor mailbox) ****

Place MR sticker here:

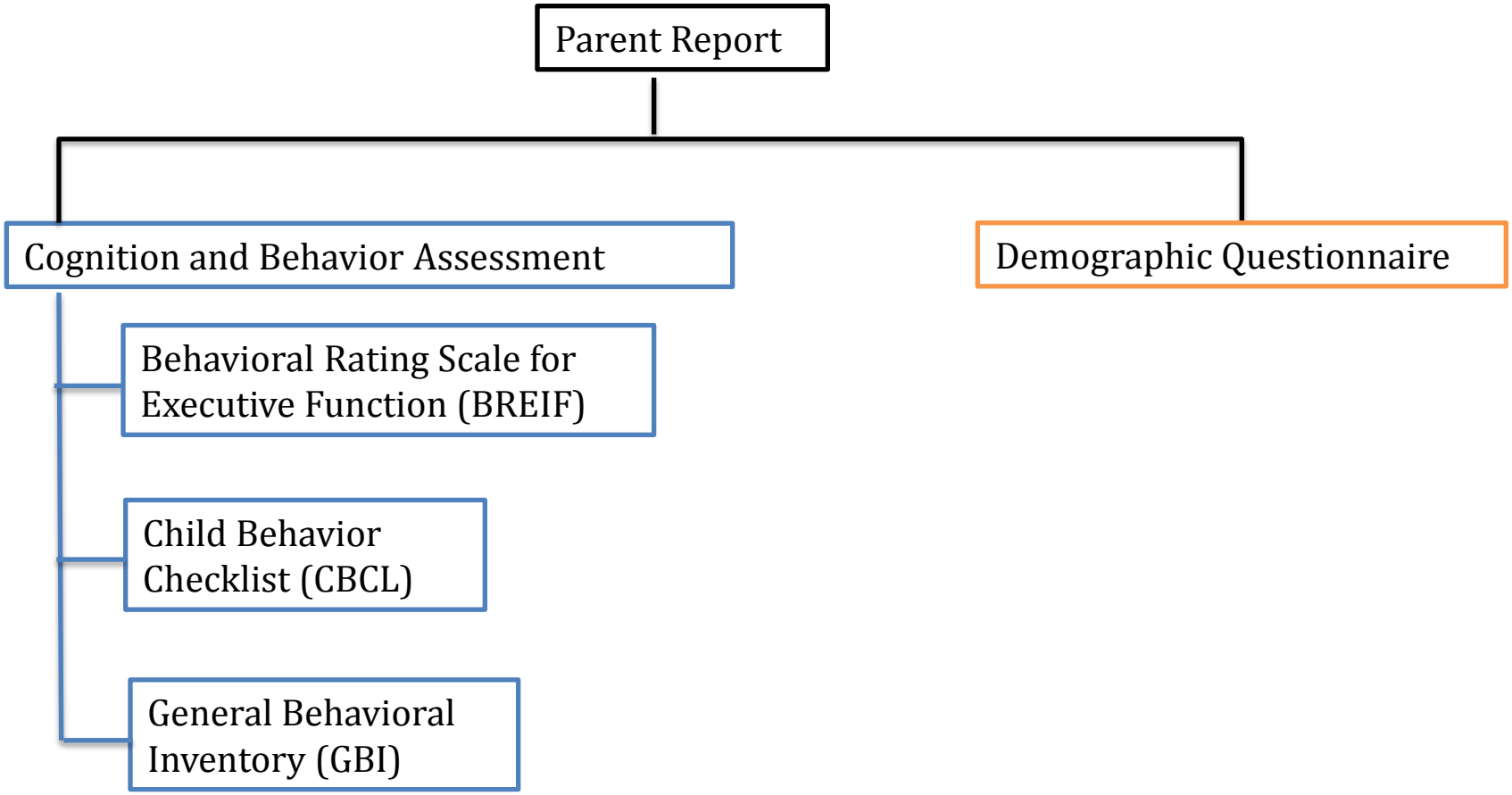
700 Children's Drive | Columbus, Ohio 43205 | 614.722.2000 | NationwideChildrens.org

Study Visit- Adolescent



Duration 1.5 hours

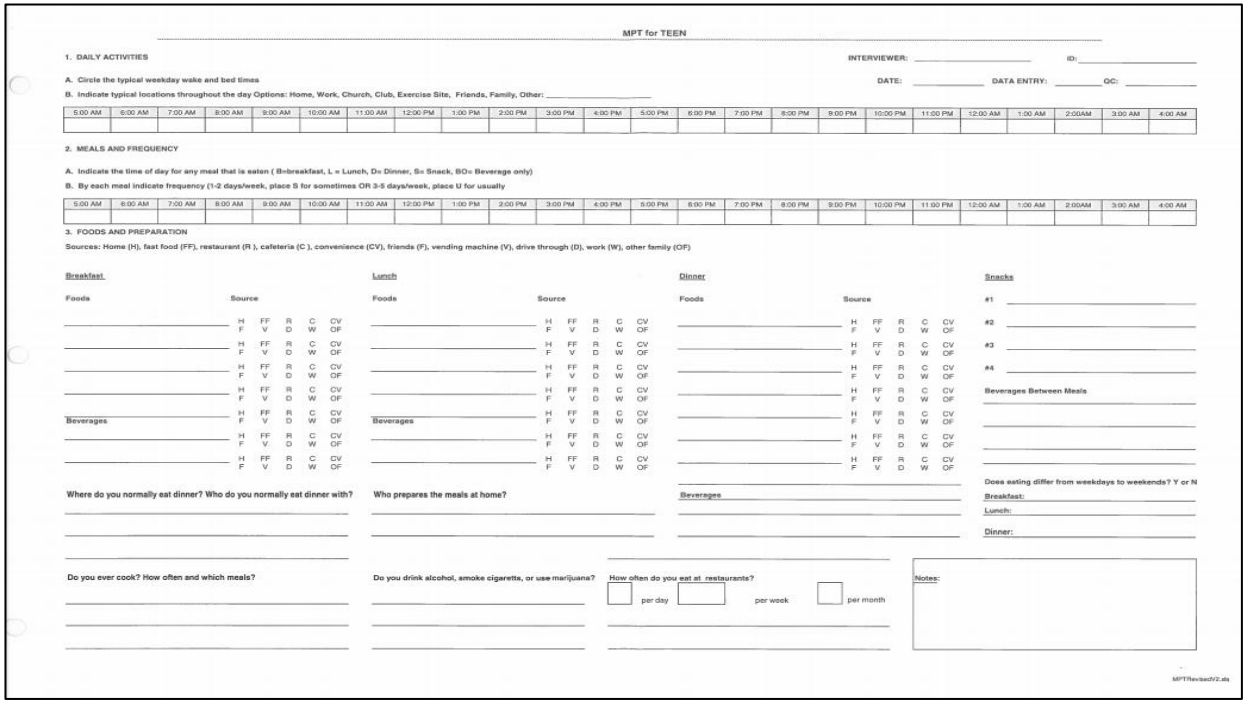
Study Visit- Parent



Meal Pattern Timeline

- The Meal Pattern Timeline (MPT) interview was administered to measure dietary and lifestyle pattern changes

- The MPT assessment is designed to describe and capture the relationships between routine lifestyle, activity, and diet behaviors.



MPT for TEEN

1. DAILY ACTIVITIES

INTERVIEWER: _____ ID: _____

A. Circle the typical weekday wake and bed times

DATE: _____ DATA ENTRY: _____ QC: _____

B. Indicate typical locations throughout the day Options: Home, Work, Church, Club, Exercise Site, Friends, Family, Other: _____

5:00 AM	6:00 AM	7:00 AM	8:00 AM	9:00 AM	10:00 AM	11:00 AM	12:00 PM	1:00 PM	2:00 PM	3:00 PM	4:00 PM	5:00 PM	6:00 PM	7:00 PM	8:00 PM	9:00 PM	10:00 PM	11:00 PM	12:00 AM	1:00 AM	2:00AM	3:00 AM	4:00 AM

2. MEALS AND FREQUENCY

A. Indicate the time of day for any meal that is eaten (B=breakfast, L = Lunch, D= Dinner, S= Snack, BO= Beverage only)

B. By each meal indicate frequency (1-2 days/week, place S for sometimes OR 3-5 days/week, place U for usually

5:00 AM	6:00 AM	7:00 AM	8:00 AM	9:00 AM	10:00 AM	11:00 AM	12:00 PM	1:00 PM	2:00 PM	3:00 PM	4:00 PM	5:00 PM	6:00 PM	7:00 PM	8:00 PM	9:00 PM	10:00 PM	11:00 PM	12:00 AM	1:00 AM	2:00AM	3:00 AM	4:00 AM

3. FOODS AND PREPARATION

Sources: Home (H), fast food (FF), restaurant (R), cafeteria (C), convenience (CV), friends (F), vending machine (V), drive through (D), work (W), other family (OF)

Breakfast

Foods | Source: H F, FF V, R D, C W, CV OF

Beverages

Lunch

Foods | Source: H F, FF V, R D, C W, CV OF

Beverages

Dinner

Foods | Source: H F, FF V, R D, C W, CV OF

Beverages

Snacks

#1 _____

#2 _____

#3 _____

#4 _____

Beverages Between Meals

Where do you normally eat dinner? Who do you normally eat dinner with?

Who prepares the meals at home?

Does eating differ from weekdays to weekends? Y or N

Breakfast: _____

Lunch: _____

Dinner: _____

Do you ever cook? How often and which meals?

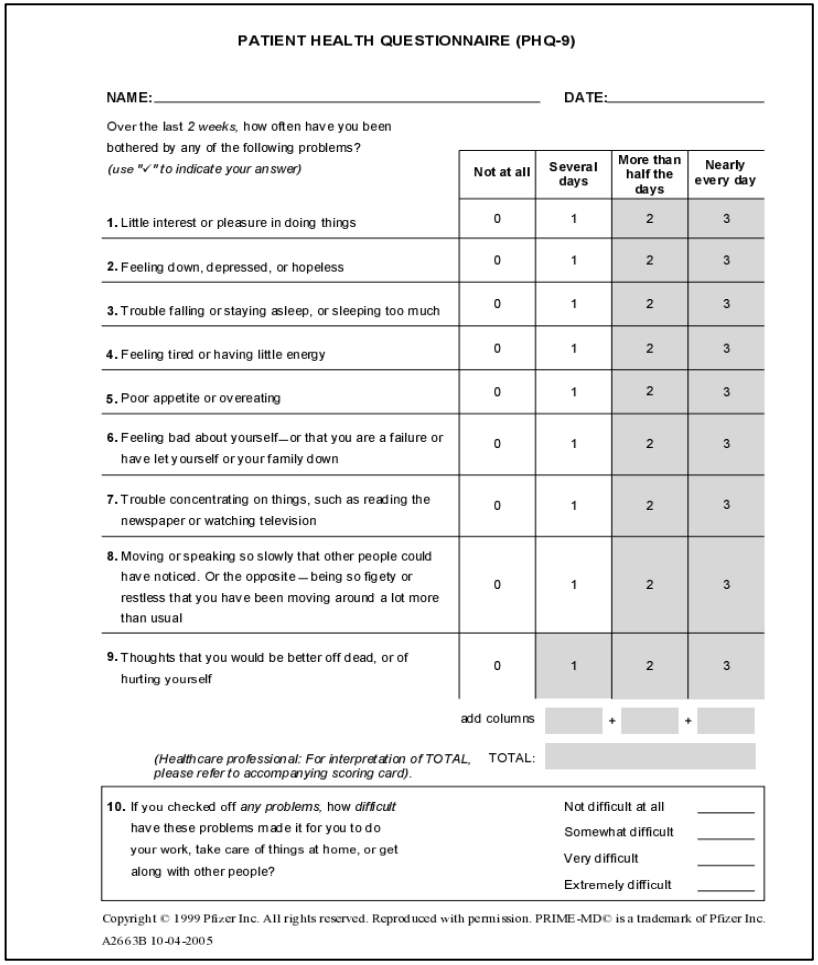
Do you drink alcohol, smoke cigarette, or use marijuana?

How often do you eat at restaurants? ☐ per day ☐ per week ☐ per month

Notes:

MPTRevised\2.xls

Patient Health Questionnaire-9



PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME:_____ DATE:_____

Over the last *2 weeks*, how often have you been bothered by any of the following problems?
(use "√" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so figety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3
add columns		+	+	

(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card). TOTAL:

10. If you checked off *any problems*, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?

- Not difficult at all _____
- Somewhat difficult _____
- Very difficult _____
- Extremely difficult _____

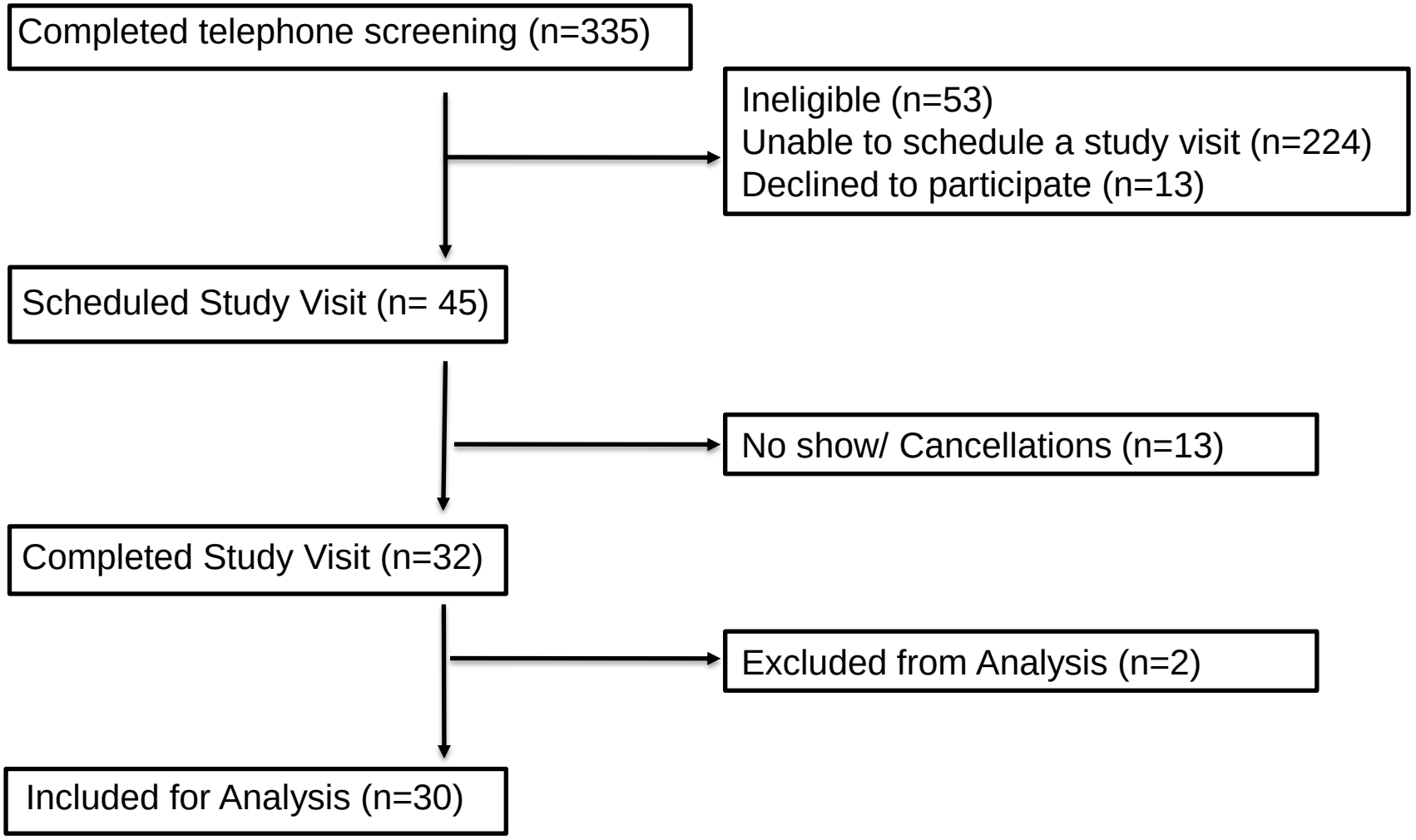
A2663B 10-04-2005

- Screen, diagnose, monitor, and measure the severity of depressive symptoms
- Participants were grouped according to PHQ-9 scores:
  - Range from minimal symptoms (0-4), Mild (5-9), Moderate (10-14), Moderate-severe (15-19), and Severe (20-27) depression categories
- In this sample the Minimal and Mild, as well as the Moderate-Severe and Severe groups, were condensed
- Resulting subgroups of:
  - Mild depression (1-9)
  - Moderate depression (10-14)
  - Severe depression (15-27)

Statistical Analysis

- MPT: Qualitatively analyzed
  - Categorical codes were developed from the range of MPT responses.
  - Matrices were constructed
  - Summary profiles were developed
- Quantitative analysis: assumptions of statistical tests were met
  - Log-transformations were applied where applicable on data not normally distributed.
  - Parametric and Nonparametric tests used as indicated
- A multinomial ordinal logistic regression analysis was also performed to investigate potential predictors for symptom severity.
- A p-value < 0.05 indicated statistical significance.

Results: Youth Categorization and Recruitment



Results: Demographics

	Mild (n= 3)	Moderate (n= 13)	Severe (n= 14)	P-value
		median (range)		
Age	15	17	16	0.28
	(15, 16)	(13, 18)	(13,18)	
BMI (kg/m^2)	28.6	25.5	25.9	0.93
	(22.32, 31.78)	(17.17, 46.99)	(18.68, 39.42)	
		n (%)[b]		
Gender				**0.05***
Male	2 (67%)	1 (8%)	2 (14%)	
Female	1 (33%)	12 (92%)	12 (86%)	
Race				0.17
Caucasian	2 (67%)	13 (100%)	12 (86%)	
AA, Hispanic, Asian	1 (33%)	0 (0%)	2 (14%)	
Family Income, past year				0.86
$10,000-$29,999	0 (0%)	1 (8%)	1 (7%)	
$30,000-$49,999	0 (0%)	2 (15%)	3 (21%)	
$50,000-$69,999	1 (33%)	2 (15%)	2 (14%)	
$70,000-$99,999	0 (0%)	2 (15%)	4 (29%)	
$100,000 or more	2 (67%)	4 (31%)	3 (21%)	

Results: Medications and Psychiatric History

	Mild (n= 3)	Moderate (n= 13)	Severe (n= 14)	P-value
		mean (±SD)		
Total number of prescribed medications	1.33 (±3.33)	1.83 (±3.25)	1.85 (±3.31)	0.99
		median (range)		
Number of medications for mood disorders	1 (1, 2)	2 (1, 4)	1 (0, 4)	0.77
		n (%)		
Medication Type				
Antidepressants	2 (67%)	12 (92%)	11 (85%)	0.49
Antipsychotic	1 (7%)	3 (23%)	2 (16%)	0.76
Mood stabilizers	0 (0%)	3 (23%)	5 (38%)	0.36
Anti-anxiety	0 (0%)	1 (33%)	1 (8%)	0.88
Attention Deficit Hyperactivity Disorder (ADHD)	1 (7%)	1 (33%)	1 (8%)	0.39
Patient Psychiatric History				
Self-Harm History	3 (100%)	8 (62%)	10 (77%)	0.37
Suicidal Ideation History	2 (67%)	9 (69%)	10 (77%)	0.58
Emergency Room Psychiatric Visit History	2 (67%)	6 (46%)	7 (54%)	0.88
Suicide Attempt in last year	1 (33%)	4 (31%)	2 (16%)	0.62
Substance Abuse History	1 (33%)	4 (31%)	4 (31%)	0.99

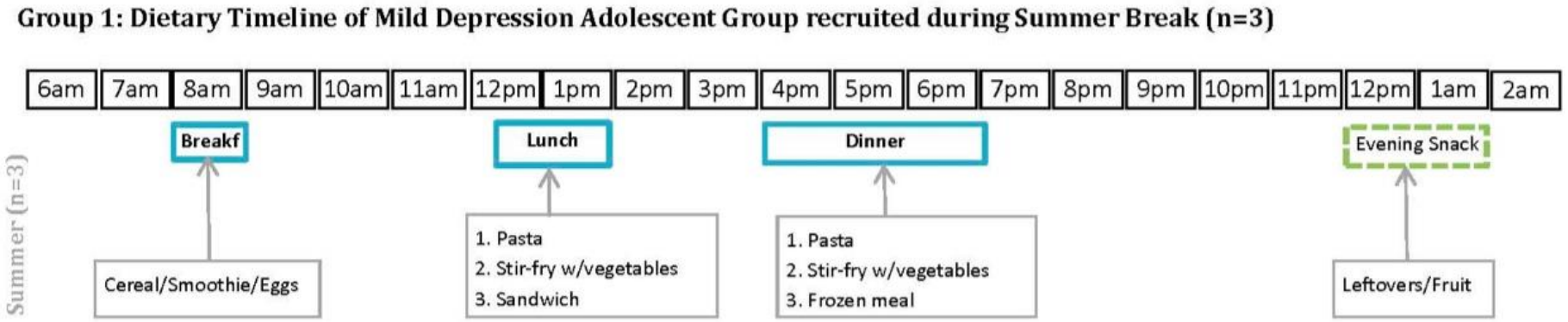
Results: Macronutrient Intake

	Mild (n= 3)	Moderate (n= 13)	Severe (n= 14)	P-value
		mean (±SD)		
Dietary Macronutrient				
Total energy intake (kcal)	1441.91 (±339.30)	1616.22 (±615.79)	960.96 (±310.30)	**0.01***
Fat (% energy)	31.59 (±6.58)	35.22 (±3.78)	33.04 (±5.53)	0.38
Carbohydrate (% energy)	58.68 (±9.24)	53.93 (±6.27)	56.04 (±7.25)	0.52
Protein (% energy)	12.14 (±2.19)	12.43 (±2.34)	12.92 (±2.28)	0.80
Omega 3 fatty acids (g/1000 kcal)	0.59 (±0.19)	0.76 (±0.18)	0.62 (±0.10)	0.04
Omega 6 fatty acids (g/1000 kcal)	7.30 (±2.71)	7.40 (±1.42)	6.74 (±2.05)	0.50
Myplate Dietary				
Non-whole grains (oz eq)	4.46 (±0.86)	5 (±1.97)	2.36 (±0.93)	**<0.01***
Total grains (oz eq.)	4.84 (±0.86)	5.62 (±2.24)	2.71 (±1.12)	**<0.01***
Discretionary fat (solid) (g)	27.12 (±20.05)	37.05 (±6.87)	19.44 (±9.77)	**<0.01***
Sugary beverages total (g)	101.70 (±59.70)	304.18 (±267.01)	189.09 (±229.24)	0.09

Results: Micronutrient Intake

	Mild (n= 3)	Moderate (n= 13)	Severe (n= 14)	P-value
		mean (±SD)		
Folate (mcg DFE/1000 kcal)	367.58 (±45.35)	254.67 (±50.19)	251.36 (±87.61)	**0.04***
Iron (mg /1000 kcal)	7.78 (±0.52)	6.90 (±1.16)	6.83 (±1.48)	0.51
Vitamin B12 (mcg /1000 kcal)	1.86 (±1.46)	1.71 (±0.69)	1.91 (±0.95)	0.85
Fortified Folate (mcg/1000 kcal)	143.82 (±43.72)	93.63 (±33.29)	90.80 (±47.18)	0.13
Food Folate (mcg)/1000 kcal	123.01 (±73.63)	95.51 (±27.28)	97.11 (±24.94)	0.65
Calcium (mg /1000 kcal)	468.61 (±116.16)	380.51 (±88.59)	387.99 (±127.37)	0.46
		median (range)		
Vitamin D (IU/kcal)	64.49 (1.21, 158.86)	57.24 (3.47, 77.21)	44.21 (7.64, 199.66)	0.93

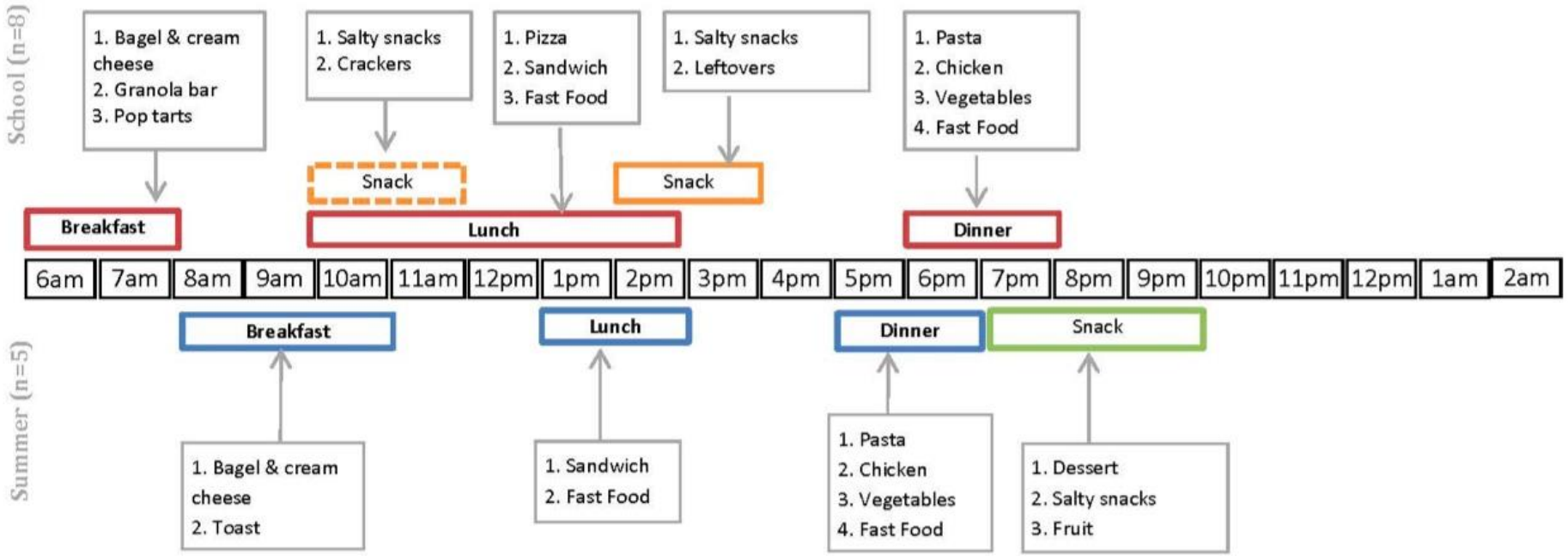
Results: Dietary Patterns



Mean total energy intake: 1441 kcal

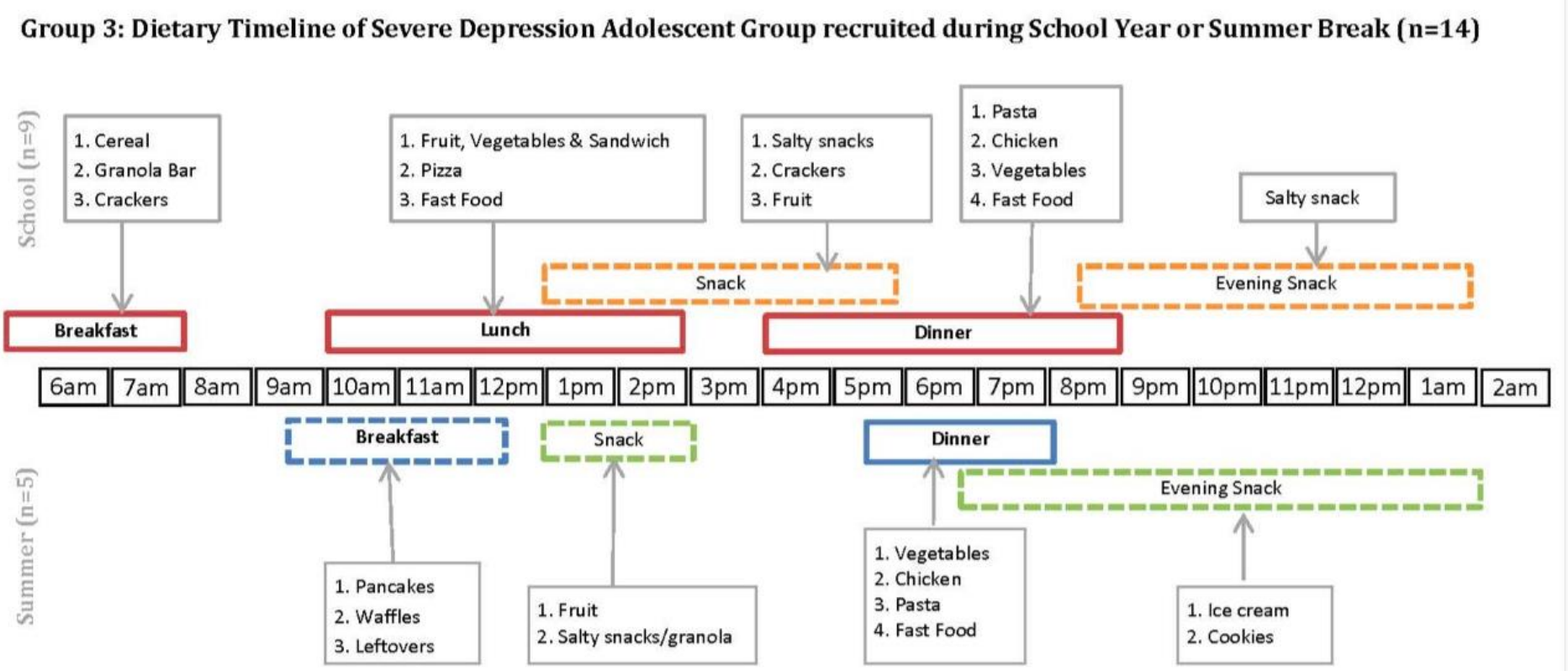
Results: Dietary Patterns

Group 2: Dietary Timeline of Moderate Depression Adolescent Group recruited during School Year or Summer Break (n=12)



Mean total energy intake: 1616 kcal

Results: Dietary Patterns



Mean total energy intake: 960 kcal

Results: Regression Analysis

- Folate DFE= Dietary Folate Equivalents
- Folate DFE intake negatively correlated with adolescent PH-Q-9 score (Spearman $p \leq 0.01$)
- A multinomial ordinal logistic regression test:
  - Controlling for age, race and gender, dietary folate DFE intake was a significant predictor for depression symptom severity

Folate DFE intake, controlling for age, race, and gender, is a significant predictor of youth self-report depression symptom severity

Co-variable	β1	P-value
Folate DFE intake	0.007	**0.005***
Age	0.186	0.518
Race	-0.044	0.951
Gender	-0.434	0.445

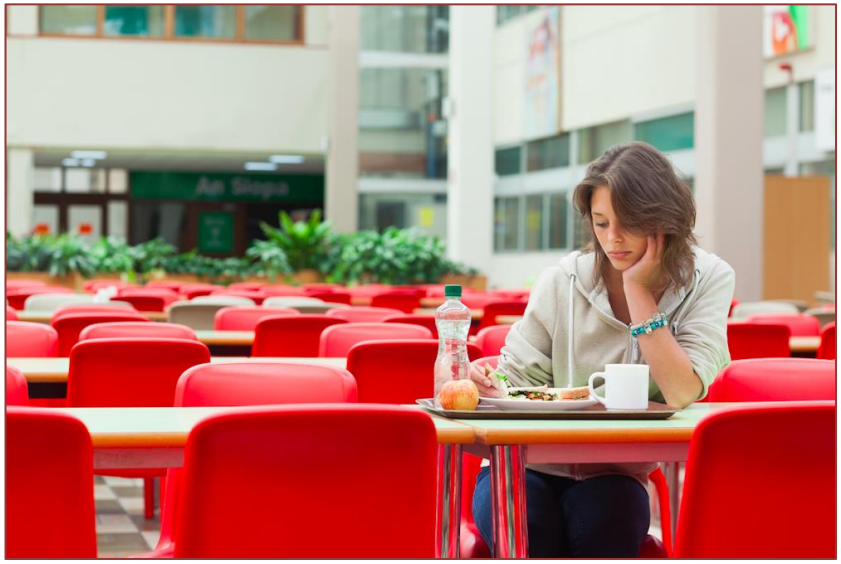
Summary of Results: Dietary patterns and Intake

- Habitual dietary patterns and intake varied between depression severity subgroups
  - > Habitual dietary patterns varied within depression severity subgroups by school-year versus summer break status
- Dietary intake falls short of meeting many essential dietary recommendations for their age as determined by the 2015-2020 US Dietary Guidelines
  - > Negative relationship between folate and depression symptom severity

Study 3: Prospective Assessment of Diet Patterns and Nutrient Intake in Youth Receiving Treatment for Depressive Disorders

Objectives

Prospectively identify correlations between real-time changes in the nutritional status of youth with depressive symptoms throughout their mood disorder treatment process



Study 3: Materials and Design

> Study population subset

> Same materials; Inclusion/Exclusion criteria and recruitment methods

> Repeated Measures Method

>Patient Health Questionnaire-9 used to assess monthly changes in depression symptom severity

** A baseline PHQ-9 score ≥ 10 was required for enrollment*

Indicator of Moderate Depression

Specific Aims

- **Aim 1:** Categorize adolescents with mood disorders by response to treatment.

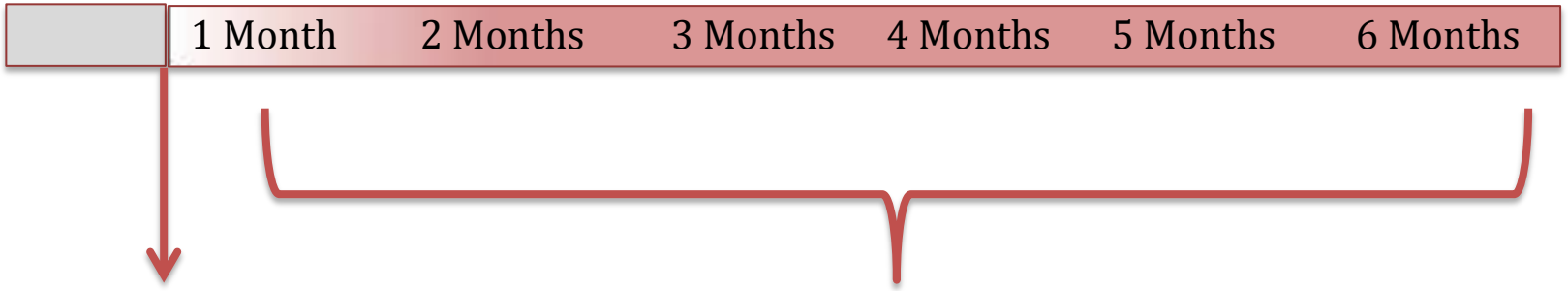
- **Aim 2:** Describe changes in lifestyle and dietary patterns in adolescents based on responder subgroup assignment.

- **Aim 3:** Assess biochemical measures across responder subgroups.

Study Design

Enrollment

Monitoring Phase (up to 6 months post baseline)



Baseline Measure

Questionnaires/Interview
- Dietary Patterns
- Lifestyle Patterns
- Additional psychological/behavioral questionnaires

Blood Draw
- Dietary biomarkers

Final Assessment

> Adolescents will be screened monthly with the PHQ-9 to monitor depressive symptom severity.

> If a clinically significant improvement in symptom severity is achieved (equal to a ≥ 50% reduction in PHQ-9 scores from baseline scores), adolescent will return for the final assessment.

Questionnaires/Interview
- Dietary Patterns
- Lifestyle Patterns
- Additional psychological/behavioral questionnaires

Blood Draw
- Dietary biomarkers

Study Design: Responder Groups

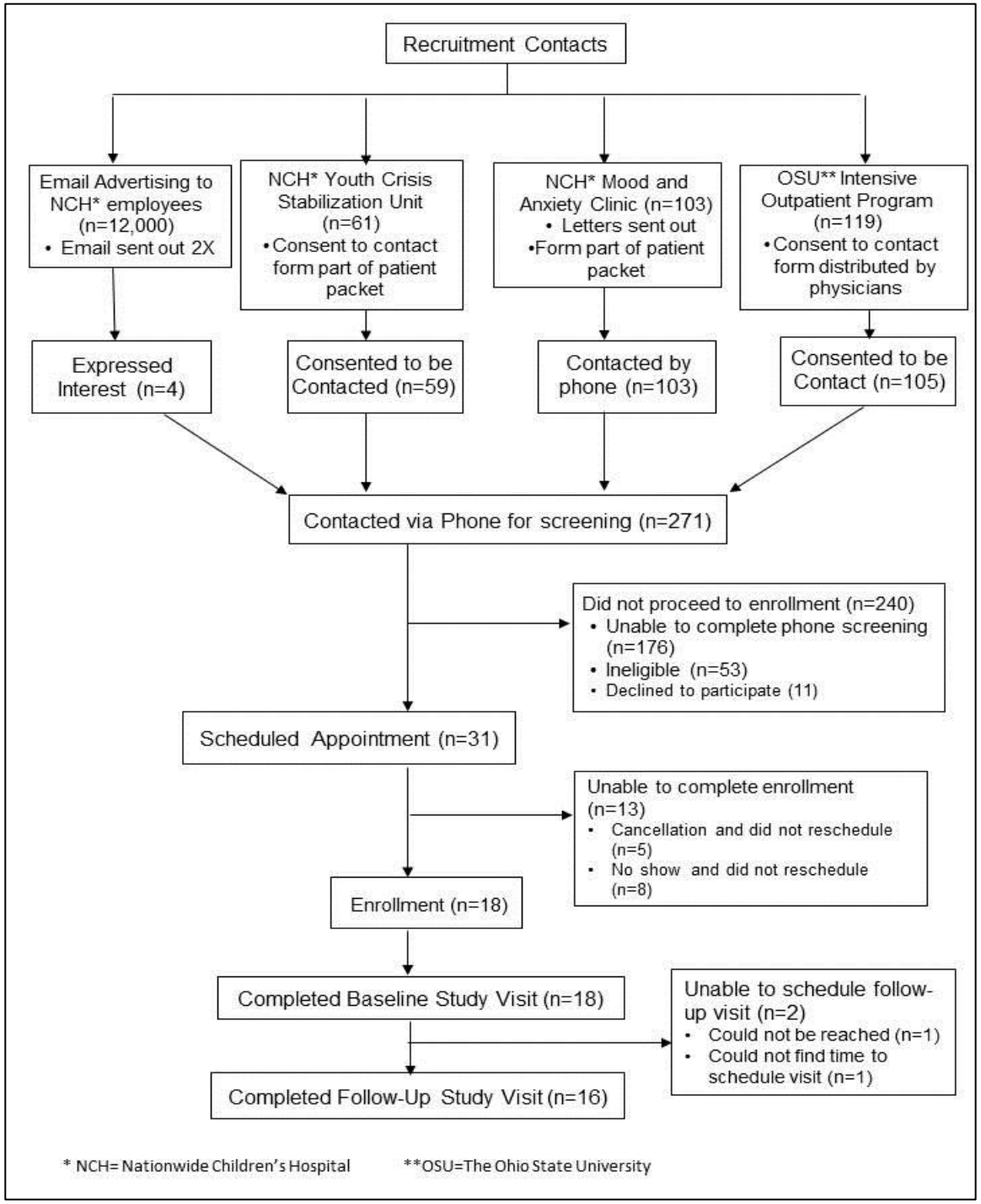
Quick Responders

Responders

Non-Responders

Statistical Analyses

- MPT: Qualitatively analyzed
  - Categorical codes were developed from the range of MPT responses.
  - Matrices were constructed
  - Summary profiles were developed
- Quantitative analysis: assumptions of statistical tests were met; Log-transformations were applied where applicable on data not normally distributed.
  - Parametric and Nonparametric tests used as indicated
- A multinomial logistic regression analysis was also performed to investigate potential predictors for treatment response time.
- A p-value < 0.05 indicated statistical significance.



Consort Flow

1. Electronic and on-site ads:

- Email advertisement to hospital employees
- Letters/postcards
- Flyers on-site, with a section for the family to provide contact information if interested

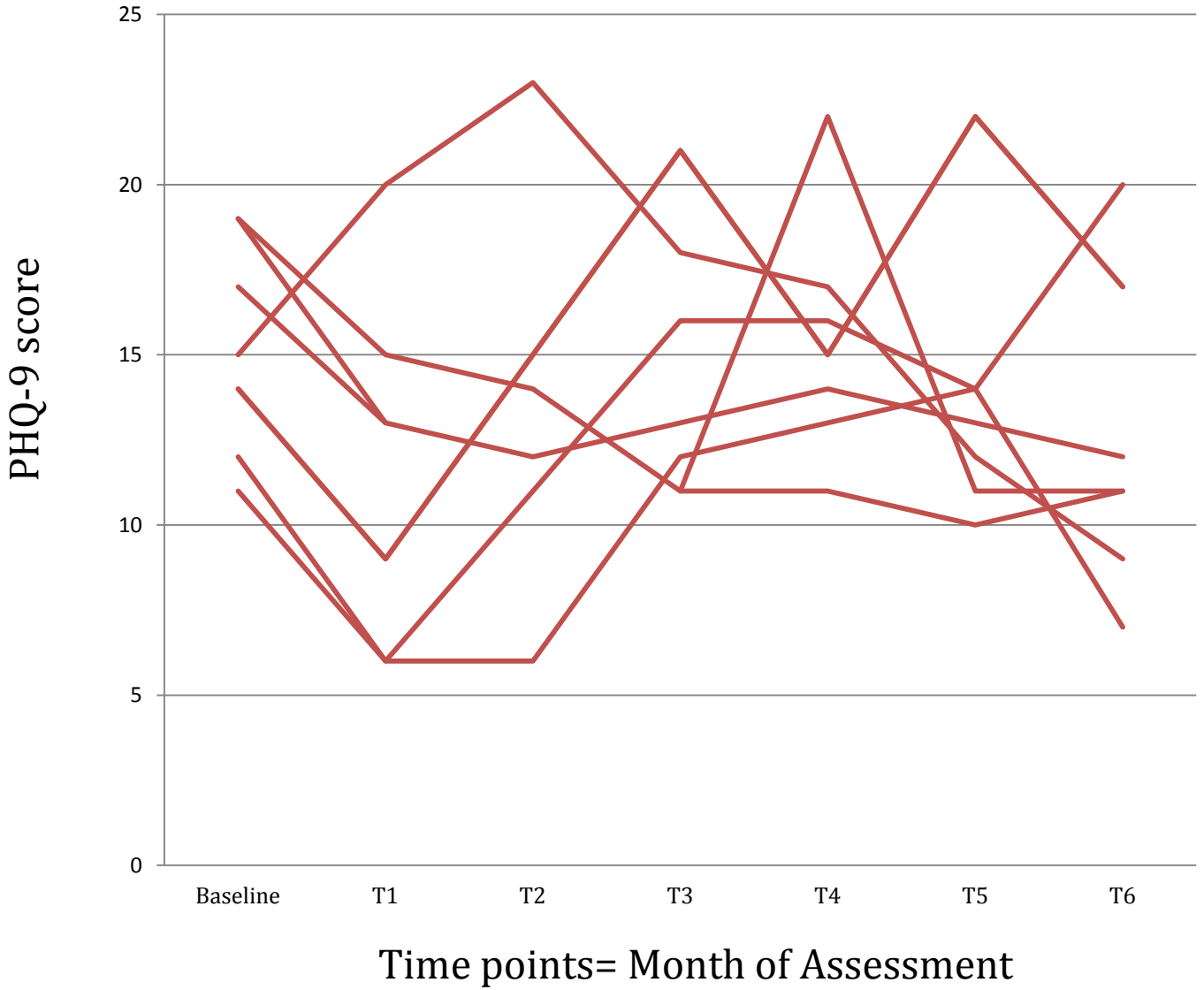
1. Electronic Medical Record Screening

1. Assessed for eligibility by telephone or an online survey

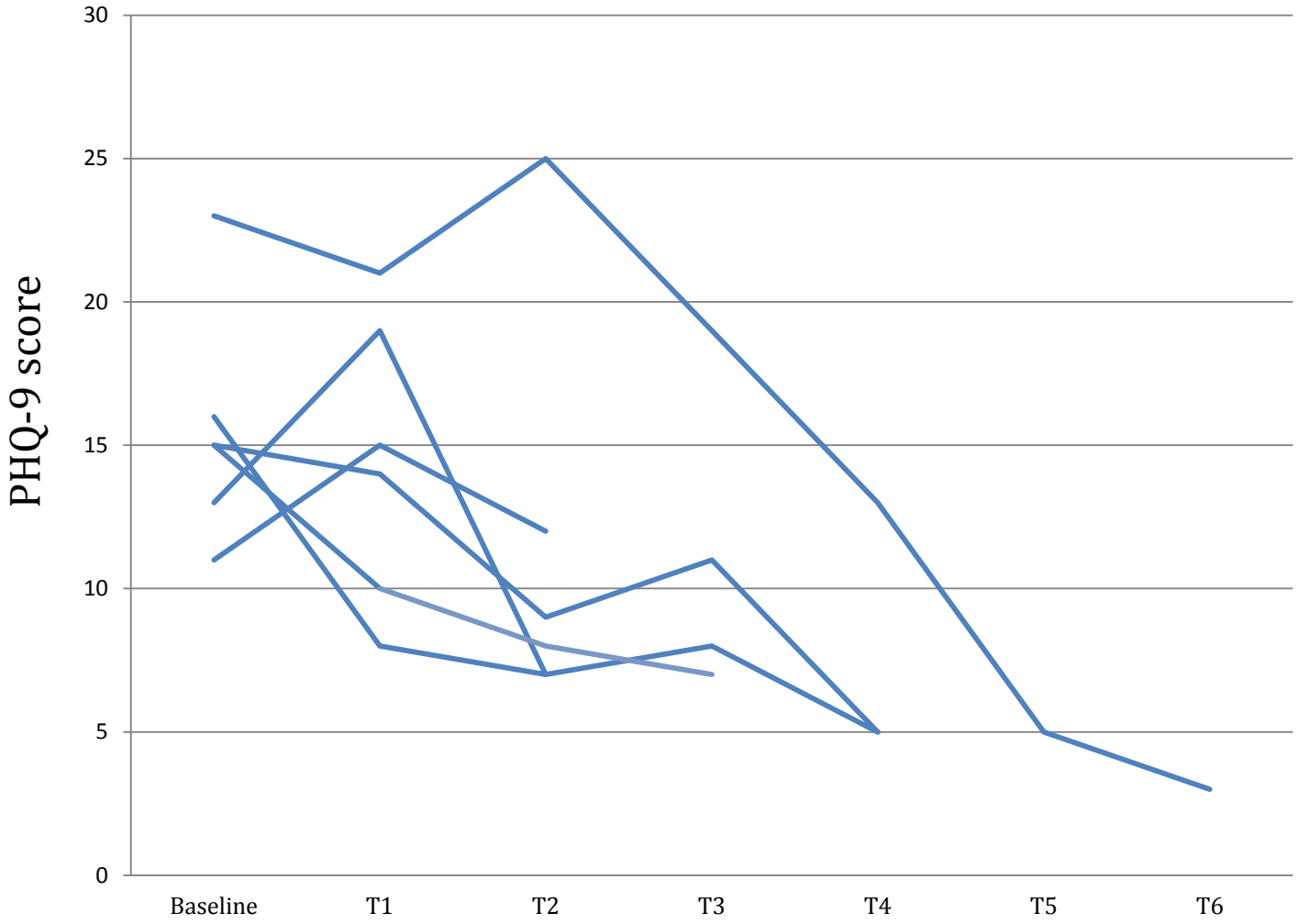
Results: Demographics

	Non Responders (n=7)	Responders (n=6)	Quick Responder (n=3)	P-value
		mean (±SD)		
Age	16.14 (±1.57)	16 (±1.67)	15.33 (±2.52)	0.80
BMI (kg/m^2)	24.86(±5.59)	32.56 (±9.86)	20.26 (±4.53)	0.07
		n%		
Gender				
Female	7 (100%)	2 (33%)	3(100%)	**0.01***
Male	0 (0%)	4 (67%)	0 (0%)	
Race				
Caucasian	7 (100%)	5 (83%)	3 (100%)	0.41
Hispanic, African American	0 (0%)	1 (17%)	0 (0%)	
Guardian married				
Never married	0 (0%)	1 (17%)	0 (0%)	0.47
Married	6 (86%)	2 (33%)	1 (17%)	
Separated/Divorced	1 (14%)	1 (17%)	1 (17%)	
Widowed	0 (0%)	1 (17%)	0 (0%)	
Guardian Income				
Less than $10,000	0 (0%)	0 (0%)	0 (0%)	0.41
$10,000 to $29,999	1 (14%)	0 (0%)	0 (0%)	
$30,000 to $49,999	0 (0%)	1 (17%)	1 (17%)	
$50,000 to $69,999	1 (14%)	2 (33%)	0 (0%)	
$70,000 to $99,999	4 (57%)	1 (17%)	0 (0%)	
$100,000 or more	1 (14%)	1 (17%)	1 (17%)	

Non-Responders: Patient Health Questionnaire (PHQ-9)



Responders: Patient Health Questionnaire (PHQ-9)



Results: Macronutrients

	Non Responder (n=7)	**Responders (n=6)**	**Quick Responder (n=3)**	
	Change Score	Change Score	Change Score	
	mean (±SD)	*mean* (±SD)	*mean* (±SD)	P-value
Total Energy (kcals)	75.29 (±468.10)	-276.45 (±627.32)	-151.24 (±188.65)	0.47
Total Fat (% energy)	1.60 (±3.77)	-4.39 (±6.14)	5.08 (±6.10)	**0.05***
Total Carbohydrates (% energy)	-1.86 (±4.22)	2.38 (±8.79)	-7.21 (±3.26)	0.13
Total Protein (% energy)	0.31 (±1.58)	1.57 (±2.01)	2.44 (±1.80	0.22
Saturated Fat (% energy)	-5.13 (±8.79)	-2.56 (±25.65)	2.16 (±1.27)	0.83
Polyunsaturated Fat (% energy)	15.36 (±27.77)	-23.23 (±26.12)	21.64 (±34.24)	**0.05***
Monounsaturated Fats (% energy)	0.27 (±1.50)	-1.63 (±2.31)	2.30 (±2.51)	**0.04***
Trans Fats (% energy)	0.44 (±12.25)	-5.97 (±18.71)	2.12 (±5.80)	0.65
Fiber (grams/1000 kcal)	0.26 (±1.12)	-0.31 (±2.66)	-0.51 (±0.49)	0.78

Results: My Plate Servings

	Non Responders (n=7)	**Responders (n=6)**	**Quick Responders (n=3)**	
	Change Score	Change Score	Change Score	
	mean (±SD)	*mean* (±SD)	*mean* (±SD)	P-Value
Total Vegetables (cups)	0.10 (±0.56)	-0.29 (±0.76)	0.26 (±0.39)	0.39
Total Dairy (milk-equivalent servings)	-0.24 (±0.78)	0.45 (±0.74)	0.06 (±0.55)	0.31
Milk (cups)	-0.28 (±0.53)	0.45 (±0.49)	0.08 (±0.24)	**0.06***
Discretionary Fat from Oil (grams)	6.25 (±11.53)	-14.62 (±21.53)	-0.26 (±16.42)	0.12
Discretionary Fat from Solids (grams)	-0.18 (±9.99)	-1.57 (±17.33)	-2.53 (±6.93)	0.96
Added Sugar (teaspoon-equivalents)	-0.33 (±5.29)	-4.50 (±7.96)	0.01 (±2.90)	0.44
Sugar Sweetened Beverage Intake (kcals)	-1.50 (±65.30)	-117.72 (±125.48)	64.25 (±51.29)	**0.03**
Total Grains (oz-equivalents)	0.45 (±1.85)	-0.54 (±2.88)	-1.89 (±2.97)	0.23

Results: Micronutrients

	Non-Responder (n=7)	**Responder (n=6)**	**Quick Responders (n=3)**	
	Change Score	Change Score	Change Score	
	mean (±SD)	*mean* (±SD)	*mean* (±SD)	P-value
Omega-3 fatty-acids (g/1000kcal)	0.05 (±0.21)	-0.07 (±0.21)	0.17 (±0.06)	0.23
Omega 6 fatty-acids (g/1000kcal)	1.17 (±3.10)	-2.50 (±2.79)	2.14 (±3.75)	**0.05***
Calcium (mg/1000kcal)	-33.53 (±83.99)	152.52 (±156.91)	26.37 (±99.21)	**0.04***
Vitamin D (IU/1000kcal)	-23.09 (±36.63)	55.41 (±45.60)	22.25 (±36.24)	**0.01***
Dietary Vitamin B12 (mcg/1000kcal)	-0.21 (±0.79)	0.72 (±0.58)	0.36 (±0.82)	0.10
Folate (mcg DFE/1000kcal)	14.36 (±70.05)	19.11 (±74.45)	-39.32 (±86.45)	0.75

Regression Analysis

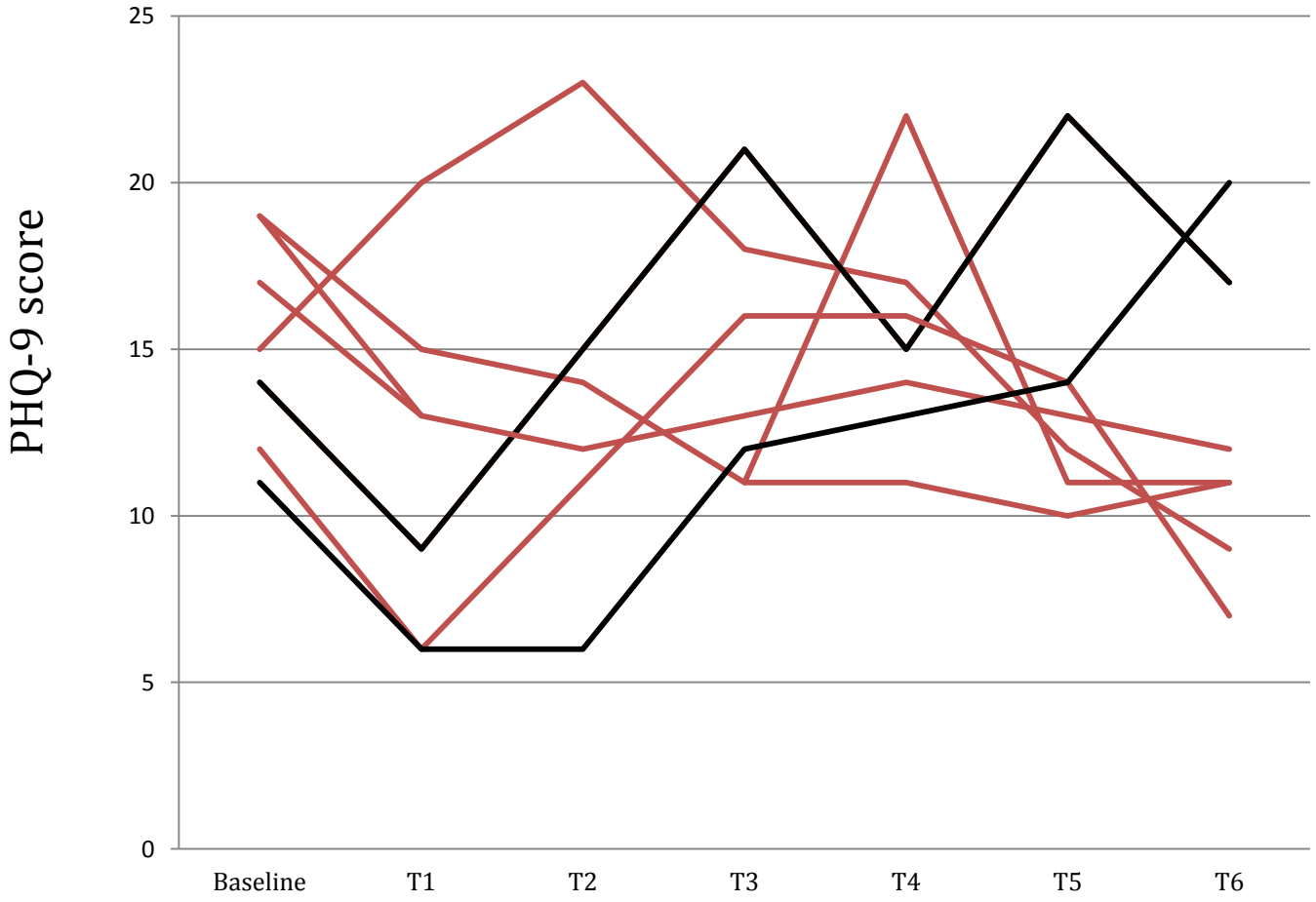
- Multinominal Logistic Regression:
  - Two *non-responders* were removed from analysis, since their PHQ-9 scores were shown to strongly increase across the study duration.
  - The remainder of the *non-responder* group (n=5) showed decreases in their PHQ-9 scores, indicating that they were showing signs of responding, but without reaching significance as defined by our study parameters

**** The *non-responder* group could be referred to as "***Partial Responders***"

Baseline depression symptom severity and change in dietary folate intake as predictors for youth partially responding or significantly responding to treatment within 6-months

Co-variable	Estimate	Likelihood Ratio Chi-Square	P-value
Phq9 baseline score	35.03	10.54	<0.001
Folate DFE change score	-0.14	7.11	0.99
Folate DFE change score*phq9 baseline score	0.41	13.29	<0.001

Non-Responders: Patient Health Questionnaire (PHQ-9)



Time points= Month of Assessment

Regression Analysis

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  - Two *non-responders* were removed from analysis, since their PHQ-9 scores were shown to strongly increase across the study duration.
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Co-variable	*Estimate*	*Likelihood Ratio Chi-Square*	*P-value*
Phq-9 baseline score	35.03	10.54	<0.001
Folate DFE change score	-0.14	7.11	0.99
Folate DFE change score*Phq-9 baseline score	0.41	13.29	<0.001

Study 3: Summary

- Changes in macro and micronutrients intake between and within response to treatment subgroups.
  - Mono/Polyunsaturated fats
  - Omega 6 fatty acids
  - Vitamin D & Calcium
  - Milk, Sugar sweetened beverage intake
- Relationships between nutrient intake and treatment response may be affected by depression severity at baseline
  - Folate DFE intake

Strengths & Limitations

Strengths

- Study Design
- Attrition low
- Careful characterization of the sample

Limitations

- Sample size!
- Supplementation Assessment
- Variance in Treatment time

Future Directions

- Replication of a study with similar design in a larger sample of depressed youth to see if these trends hold consistent.
- Study design should include recruiting those who are relapsing and subgroup by type of depression.
- To date, few studies exist to assess causality in the relationship between nutrition and depression → Additional need for RCT's
- Importance of subgroup identification

Thank You!

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