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Relationship Between Prenatal Maternal Smoking and Drinking and Subtypes of ADHD in Two Population Based Samples of Missouri Twins

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Introduction

- The etiology of attention-deficit/hyperactivity disorder (ADHD) is currently unknown.
- However, family, twin, and adoption studies have confirmed the familiarity of ADHD.
- Although genetic factors have been shown to be important in some forms of ADHD, maternal drinking and smoking during pregnancy have been postulated to be an environmental risk factor for the development of ADHD symptoms.

Objectives

- To examine the associations between maternal alcohol drinking and smoking during pregnancy and variously defined subtypes of ADHD:
 - Any DSM-IV ADHD
 - Three DSM-IV subtypes:
 - Primarily inattentive type
 - Primarily hyperactive-impulsive type
 - Combined inattentive and hyperactive-impulsive type
 - Eight ADHD subtypes defined by latent class analysis (LCA)

Samples Used for Analyses

Twin births identified from MO birth registry

MOTWINS

- Two-stage sampling design:
 - Parent or best informant screening interview about their twins
 - If parent endorsed 3+ inattentive symptoms about a twin, families invited to complete a comprehensive interview (MAGIC).
- Aged 7-19 years at time of interview. Average age 12.96 years (std=3.23 years).
- 14.85% African American
- 1569 twins:
 - MZ pairs: 60 female, 141 male
 - DZ pairs: 67 female, 173 male; 340 opposite sex
 - Singletons: 1 MZ (1 male); 6 DZ (4 females, 2 males)

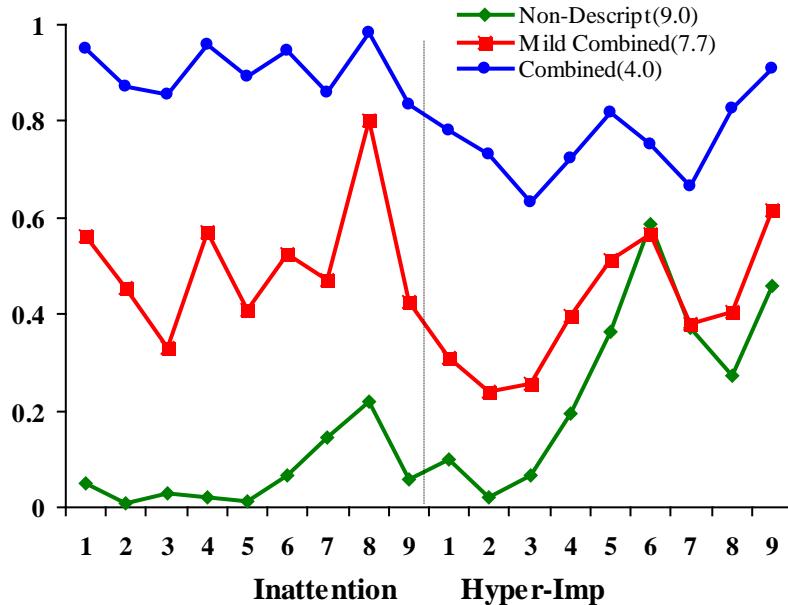
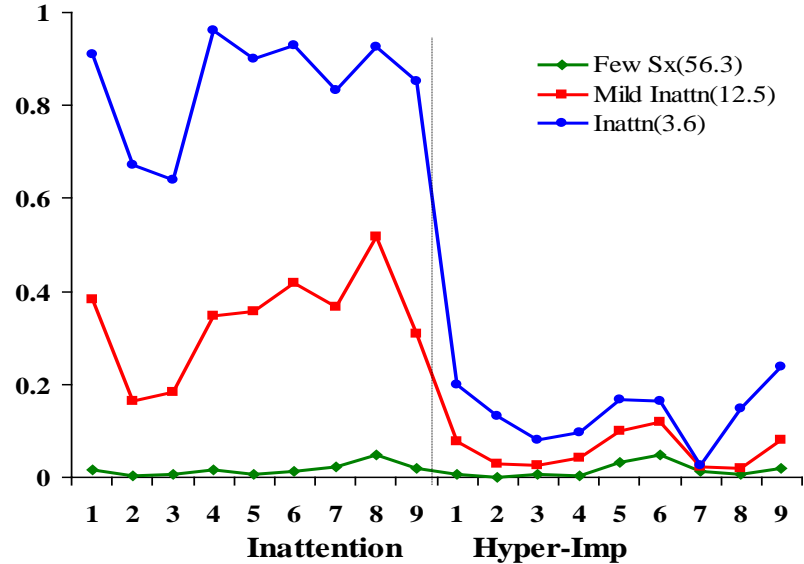
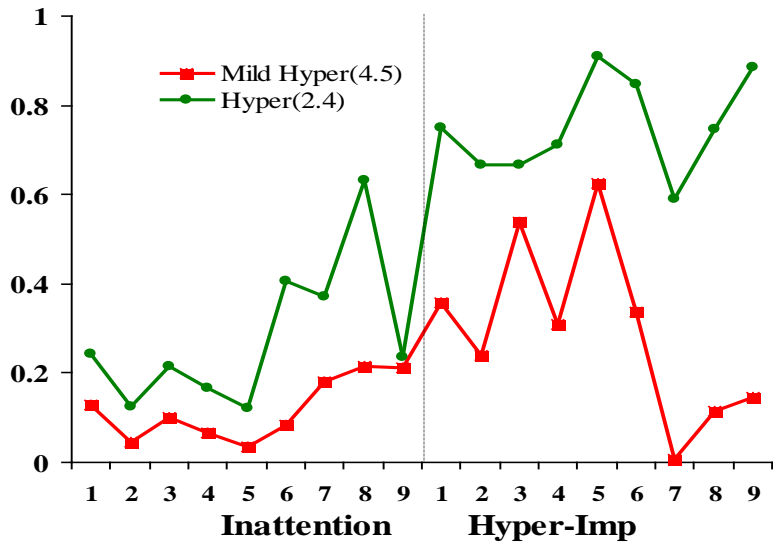
MARC

- Male twins plus their sibs
- Cohort sequential sampling design:
 - Identified 13, 15, 17, 19, 21 year old twins to be followed annually
 - Mother or best informant interviewed about their twins
- 10% African American
- 3648 twins and sibs:
 - Number MZ pairs: 772
 - Number DZ pairs: 667
 - Number Siblings: 770 (400 males, 370 females)

LCA Was Used to Define Subtypes of ADHD

- LCA is a statistical method to identify distinct subsets of observations based on multivariate categorical data. In this study the categorical data are the 18 DSM-IV ADHD defining symptoms
- Eight LCA subtypes were defined for further analyses. These classes can be understood by examining Figure 1

Figure 1: Item Prevalence by Latent Class (8 Class Solution)



Inattention Items

1. Fails to give close attention to details
2. Difficulty sustaining attention
3. Does not seem to listen
4. Does not follow through; fails to finish
5. Difficulty organizing tasks and chores
6. Reluctant to engage in tasks requiring sustained mental effort
7. Loses things necessary for tasks
8. Easily distracted by extraneous stimuli
9. Forgetful in daily activities

Hyperactivity Items

1. Fidgets with hands or feet
2. Leaves seat when remaining seated is expected
3. Runs about or climbs excessively
4. Has difficulty playing quietly
5. Often "on the go"
6. Often talks excessively

Impulsivity Items

7. Blurts out answers
8. Has difficulty awaiting turn
9. Interrupts or intrudes on others

Risk Factors for ADHD Used in the Analyses

- **Alcohol use during pregnancy:**
 - a. (Alc-entire) Drinking throughout pregnancy
 - b. (Alc-frq) Frequency of drinking alcohol, days per week
 - c. (Alc-max) Most drank at one time
- **Smoking during pregnancy:**
 - d. (Smk-entire) Smoked during entire pregnancy (y/n)
 - e. (Smk-frq) Frequency of smoking ,days per week
 - f. (Smk-n/day) Number of cigarettes smoked per day
- **Other Factors:**
 - g. (Prob_preg) Count of complications during pregnancy
 - h. (Brith Weight) Twin's birth weight, in grams
 - i. (Nwks-premature) Number of weeks premature
 - j. (Prob-del) Any problems at the delivery

MOTWINS: Univariate Logistic Regression Results

Odds Ratios: Risk Factors* vs. ADHD Subtypes

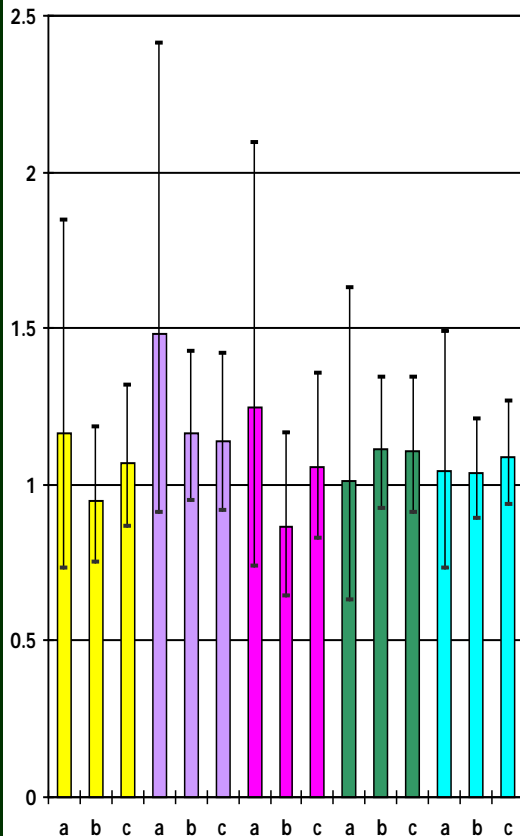
■ LC-Combined

■ LC-Inattn

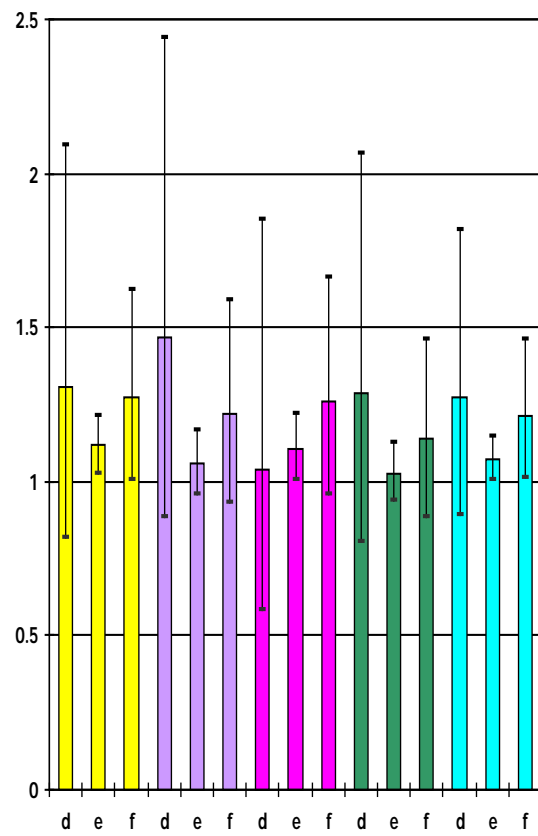
■ DSM-IV Combined

■ DSM-IV Inattn

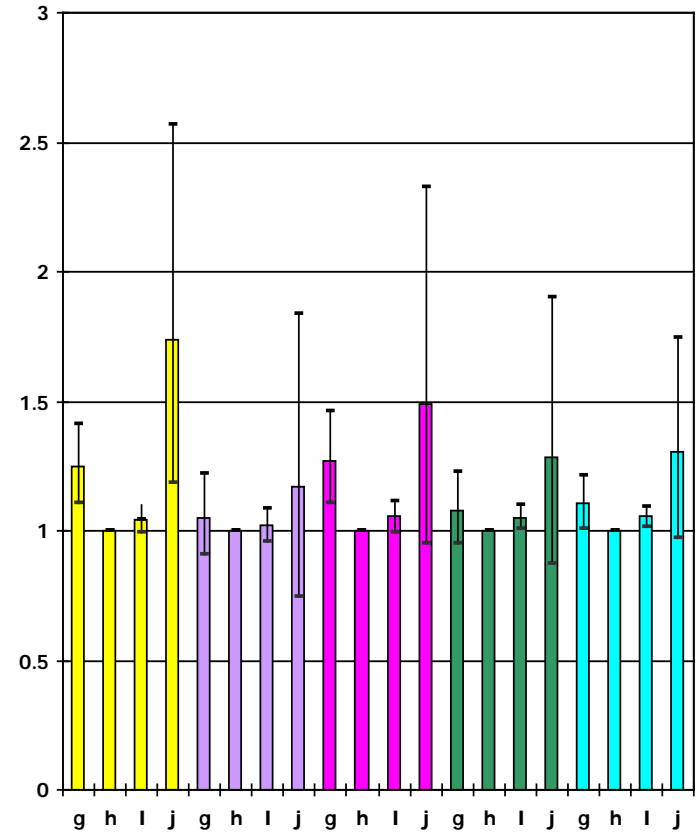
■ DSM-IV ADHD



Alcohol use during pregnancy



Smoking during pregnancy



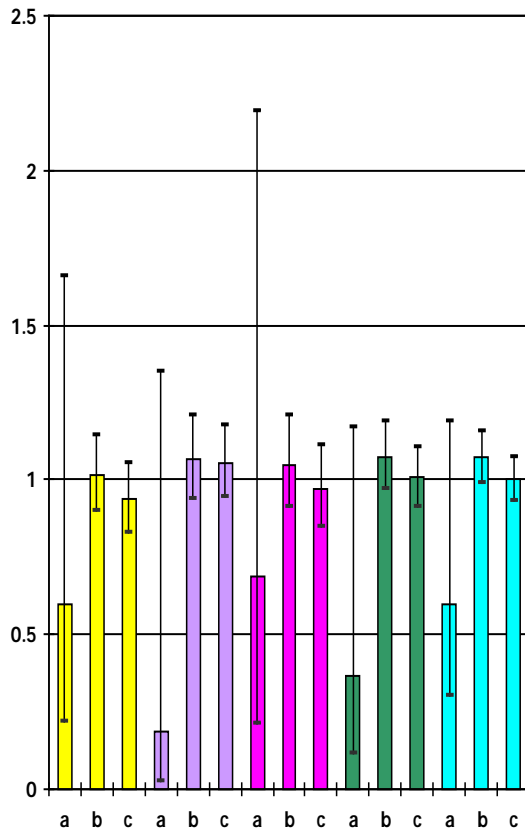
Other factors

* Risk factors defined on slide 7

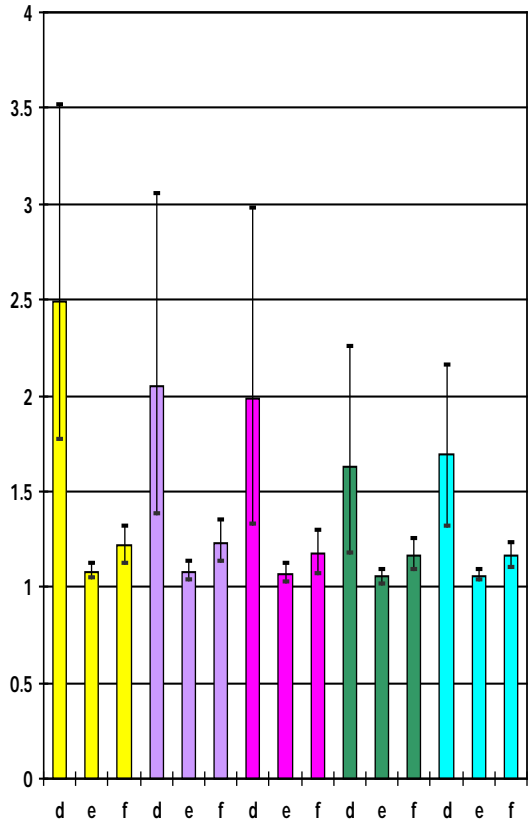
MARC: Univariate Logistic Regression Results

Odds Ratios: Risk Factors* vs. ADHD Subtypes

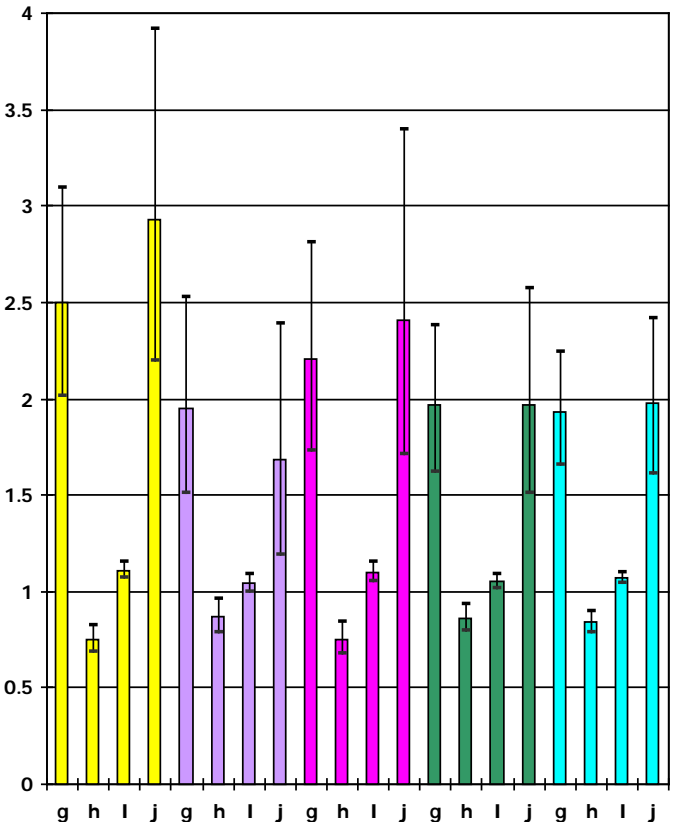
■ LC-Combined
 ■ LC-Inattn
 ■ DSM-IV Combined
 ■ DSM-IV Inattn
 ■ DSM-IV ADHD



Alcohol use during pregnancy



Smoking during pregnancy

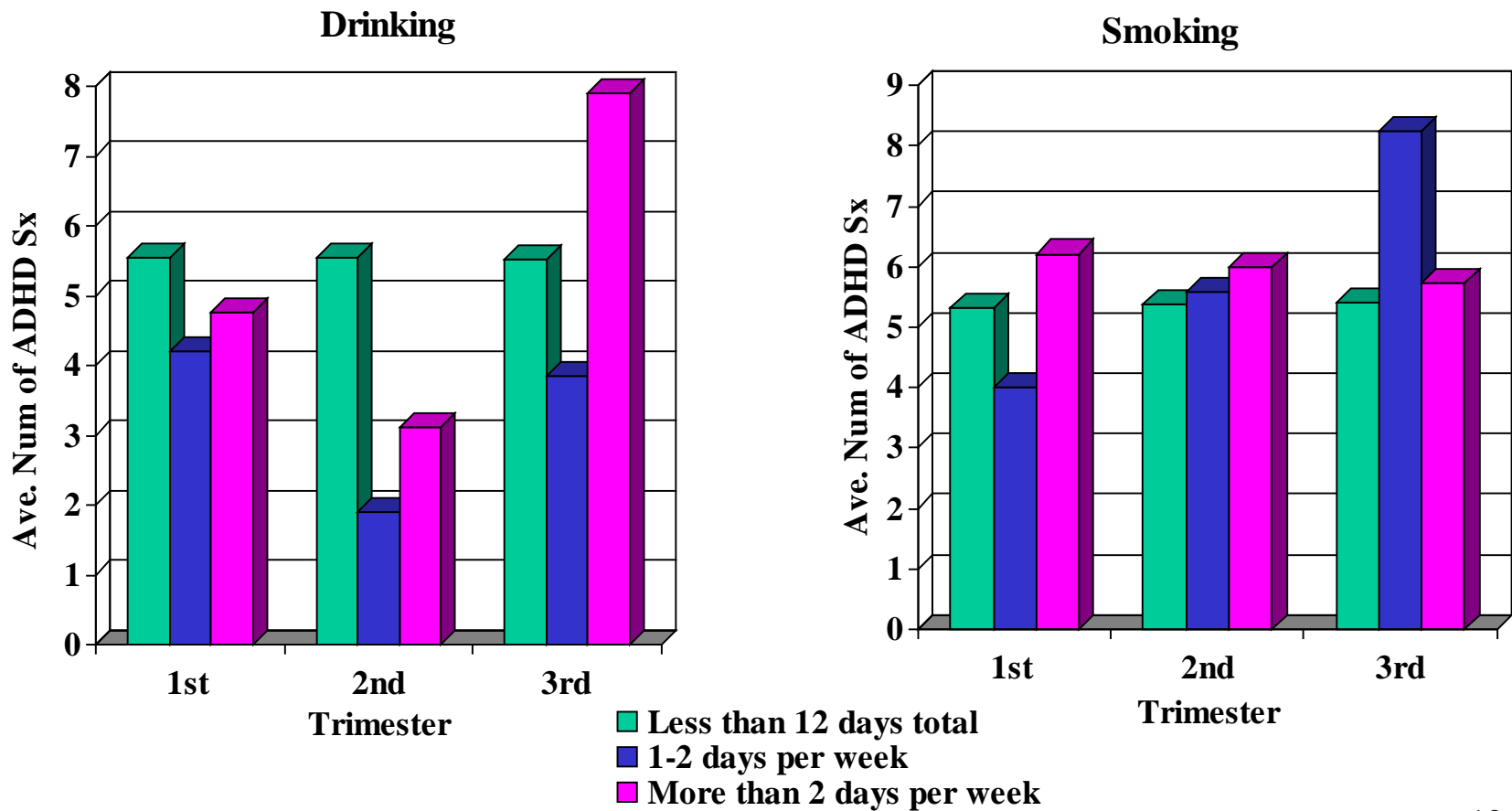


Other factors

* Risk factors defined on slide 7

MOTWINS

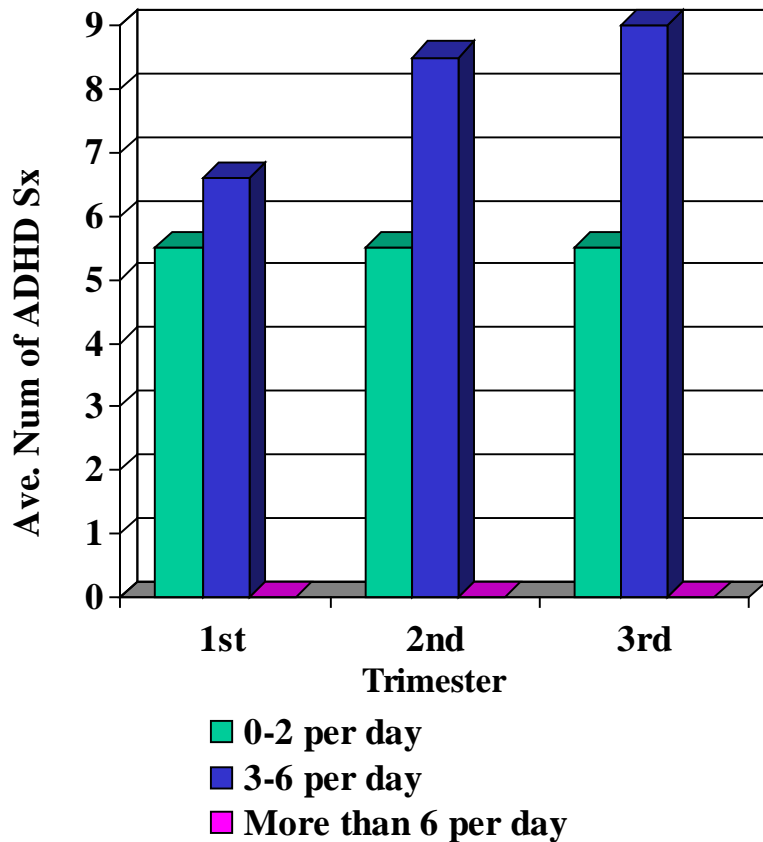
Average Number of ADHD Symptoms as a Function of the Number of Days Drinking/Smoking During Pregnancy: Stratified by Trimester



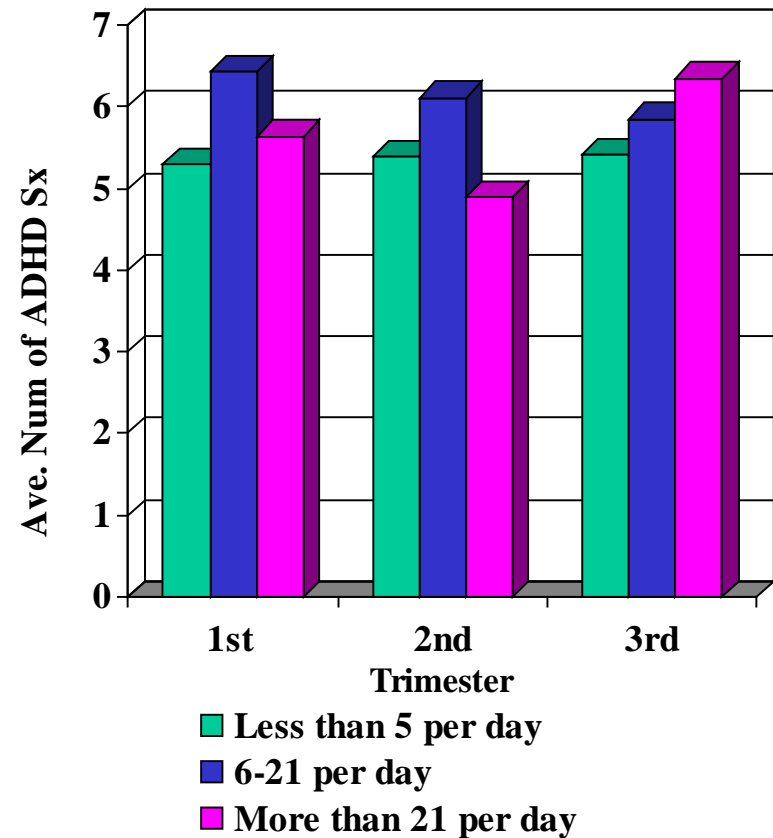
MOTWINS

Average Number of ADHD Symptoms as a Function of the Number of Drinks/Cigarettes Per Day During Pregnancy: Stratified by Trimester

Drinking

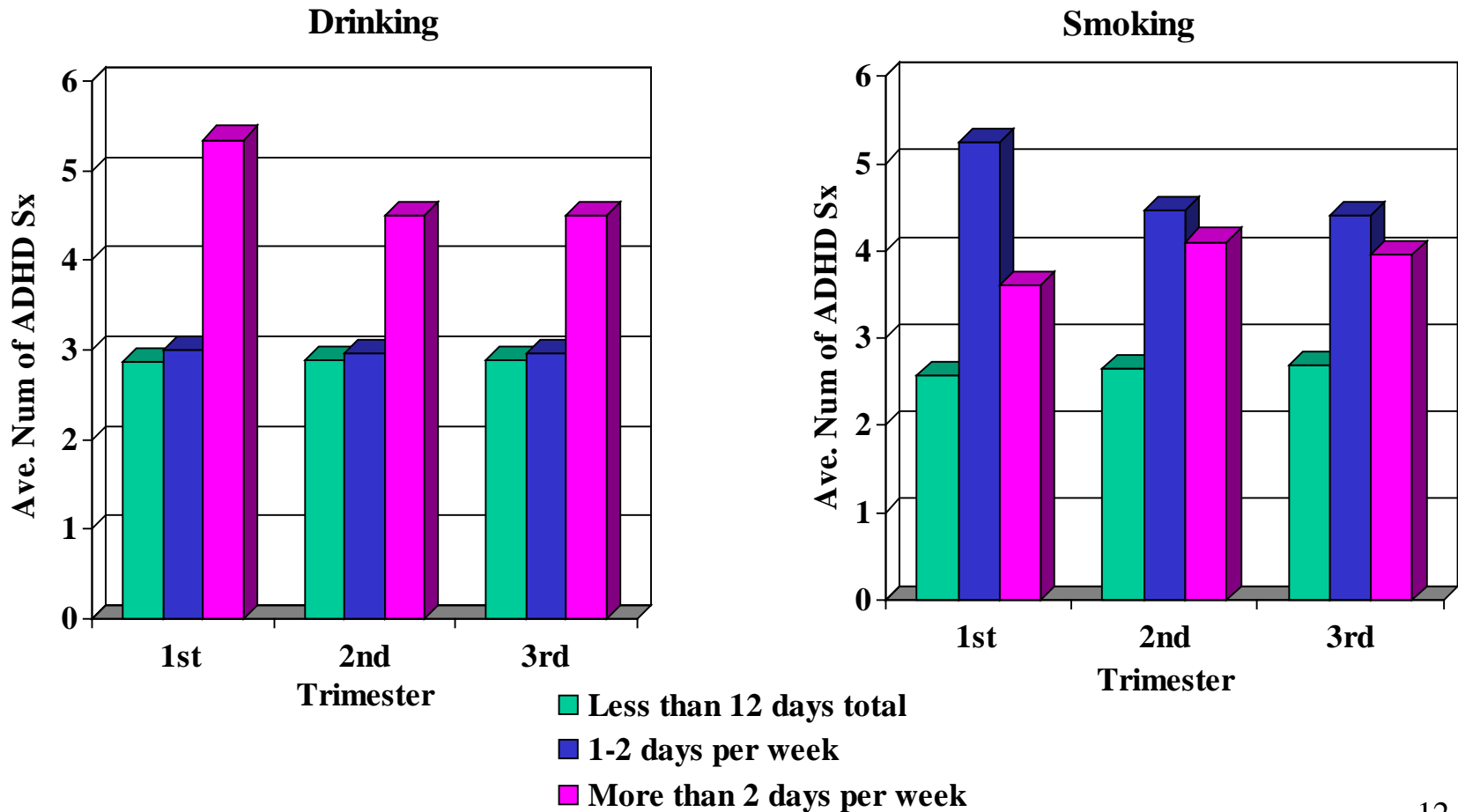


Smoking



MARC

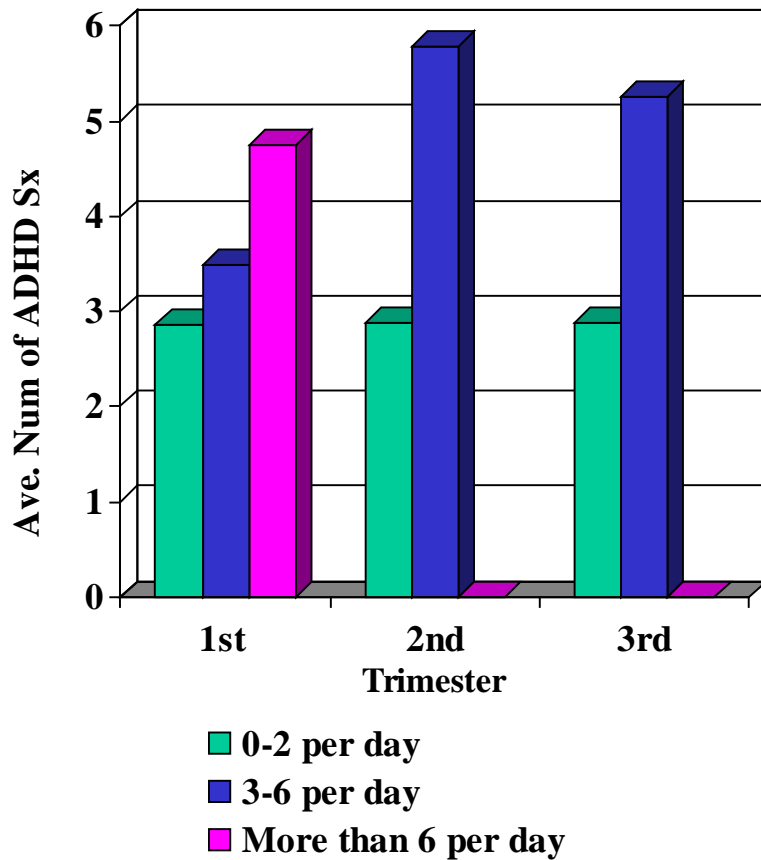
Average Number of ADHD Symptoms as a Function of the Number of Days Drinking/Smoking During Pregnancy: Stratified by Trimester



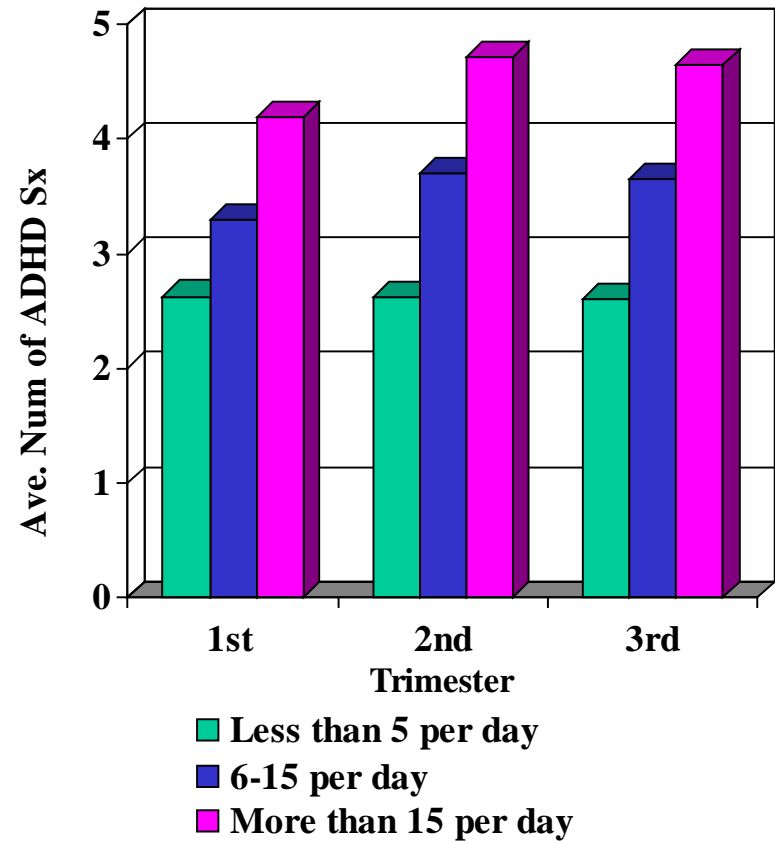
MARC

Average Number of ADHD Symptoms as a Function of the Number of Drinks/Cigarettes Per Day During Pregnancy: Stratified by Trimester

Drinking



Smoking



Summary (I)

- Although both datasets were population based, with the MOTWINS dataset over sampled for inattention symptoms, differences were seen between the MARC and MOTWINS results.
- The associations with maternal smoking during pregnancy were strongest in the MARC dataset:
 - Latent class combined and inattentive classes
 - All DSM-IV subtypes
- Alcohol items did not show a significant associations with any ADHD subtypes in either dataset.
- Other factors showing strong associations in both datasets were problems during pregnancy/delivery.

Summary (II)

The mean number of ADHD symptoms in offspring were positively correlated with trimester of pregnancy for:

- Number of drinks per day during pregnancy: ADHD SX highest for drinking in 2nd and 3rd trimesters (MARC and MOTWINS)
- Number of cigarettes per day during pregnancy: ADHD SX high for any smoking throughout pregnancy (MOTWINS) and high for heavy smoking throughout pregnancy for MARC data.
- Number of days drinking during pregnancy: ADHD SX highest for heavy drinking in 3rd trimester (MOTWINS)
- Number of days smoking during pregnancy: ADHD SX elevated for heavy smoking in the 3rd trimester (MARC).

Additional Comments

- The associations between the risk factors during pregnancy and ADHD subtypes were not consistent across the two datasets. Additional analyses are necessary to understand these variations.
- Future work will also include multivariate analysis and conditional analysis on drinkers and smokers only.