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Breastfeeding and Attention Deficit Hyperactivity Disorder in Children Aged 2-5 Years
National Survey of Child Health, 2016-2017

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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Abstract

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Background: Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by difficulties sustaining attention and controlling hyperactivity and impulsive behavior often identified in preschool-aged children. While infant breastfeeding has been associated with lower risk of ADHD in a range of ages and world regions, results among preschool-aged children in the U.S. have been mixed. Given a wide range of negative outcomes for young children diagnosed with ADHD and the lack of consistent findings on the relationship between breastfeeding and subsequent diagnosis of ADHD, this study aims to clarify current understanding of the breastfeeding-ADHD relationship among a national sample of 2-5-year-olds from the U.S.

Methods: This thesis uses cross-sectional analysis of the 2016-2017 National Survey of Children's Health (NSCH). Descriptive analyses were conducted using Rao-Scott Chi-square and Wilson method 95% confidence intervals (CI). Logistic regression, prevalence odds ratios (PORs) and Wald 95% CIs were used to examine associations between exposure and outcome. Analyses were conducted using SAS 9.4, proc surveyfreq and proc surveylogistic to account for the complex survey design.

Results: Exposure and outcome data were available for 14,259 children aged 2-5 years. In the unadjusted analysis, children with any infant breastfeeding had prevalence odds of ADHD 65% lower than children with no breastfeeding (95% CI: 0.17, 0.70). Controlling for age, sex, race/ethnicity, household poverty, secondhand smoke, and parent mental health, prevalence odds of ADHD were 64% lower in children with 6-12 months breastfeeding (95% CI: 0.17, 0.84) compared to those with no breastfeeding. Although not statistically significant, prevalence odds of ADHD relative to children with no breastfeeding, children with less than 6 months and 12 or more months of breastfeeding were 26% (95% CI: 0.33-1.66) and 52% lower (95% CI: 0.17-1.34), respectively.

Conclusion: While initial findings seem to suggest that prevalence of ADHD is reduced among children with any breastfeeding compared to no breastfeeding, after adjusting for age, sex, race/ethnicity, household poverty, secondhand smoke, and parent mental health, prevalence odds of ADHD were statistically significant only for those who were breastfed for 6-12 months as infants. These results highlight the importance of further examining the duration and timing of breastfeeding in studies attempting to further understand the breastfeeding-ADHD association.

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Chapter I: Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder with onset in childhood and characterized by difficulties in sustaining attention and controlling hyperactivity and impulsive behavior (1). While prevalence estimates of ADHD vary due to sampling methodology, some meta-analytic results estimate an increasing worldwide prevalence of ADHD from 5.29% in 2004 (2) to 7.2% in 2015 (3). The 2016 National Survey of Children's Health (NSCH) estimated 9.4% or 6.1 million of United States (U.S.) children aged 2-17 years had ever received an ADHD diagnosis according to parent report (4).

Characterized as a chronic disorder, ADHD tends to be accompanied by functional impairment in behavioral, social, familial, and academic domains, often appearing early in life and extending well into adulthood (5,6). Children with ADHD are at increased likelihood of developing comorbidities such as learning disability, speech problems, epilepsy/seizures, Tourette syndrome, depression, anxiety, oppositional defiant disorder (ODD), conduct disorder, externalizing disorders, and other neurodevelopmental or psychiatric disorders in general (7–10). They also experience more accidental injuries than non-affected siblings and other children of similar demographics who have not been diagnosed with ADHD (11–13). Furthermore, associations have been found between early ADHD-like symptoms in preschool-aged children and risk for later academic, social, emotional, and behavioral impairment in adolescence, with early symptom severity and impairment predictive of later symptom severity, impairment, and persistence (14,15). In addition to functional impairment, injury, and the deleterious effects of comorbidities on clinical and functional outcomes, ADHD is also a quite costly public health concern from an economic standpoint. The most recent U.S. expenditure estimates for ADHD are available from the Bureau of Economic Analysis (BEA) Health Care Satellite Account (HCSA) and suggest that in 2015, individuals with ADHD spent an average $45.51 per episode of care and $2066.66 overall for the year (16,17).

Though the American Academy of Pediatrics has issued guidelines for diagnosis and treatment of ADHD in children aged 4-18 years (18), a burgeoning literature suggests that early symptoms may be identifiable in infant and toddler behavior (19–23), and that very young children may experience mental health disorders as older children and adolescents do, with similar disorder rates, core symptom presentation, and levels of disability (24–27). The preschool age is particularly vulnerable to emerging psychopathology which may disrupt critical periods of social and emotional development leading to persistent problems throughout childhood and adolescence (28–30). Given the early onset and often chronic impairment caused by ADHD, early identification and treatment is necessary to minimize the potential for negative clinical and functional outcomes (31). However, considering the significant burden of disease, early identification and treatment interventions alone are not enough to reduce incidence or curtail the functional and economic costs of this disorder. As a result, it would be beneficial to look at contributing factors that may moderate risk for ADHD and/or address areas of impairment.

Many studies in recent decades have examined how different aspects of nutrition are associated with ADHD, and several of them have found an association between infant breastfeeding and symptoms of ADHD or diagnosis of ADHD in samples across varying ages and settings (32,33). For example, two recently published meta-analyses reached complementary conclusions regarding the breast-feeding--ADHD association. In the 2019 meta-analysis of 11 studies by Tseng et al., results suggested that among children with ADHD the mean duration of breastfeeding was shorter than in children without ADHD by a mean difference of 2.44 months. Additionally, compared to children without ADHD, the likelihood of discontinuing breastfeeding before 3 months was significantly higher, and the likelihood of breastfeeding for 6 months or more was significantly lower (32). Similarly, the 2018 systematic review and meta-analysis of 12 studies by Zeng et al., found lower incidence of ADHD in those children who had any exposure to maternal breast milk compared to children with no exposure to maternal breast milk. However, there was a significant amount of heterogeneity. They also found a negative association between ADHD and breastfeeding duration of more than 1 month with no significant heterogeneity (33). Taken together, findings from these 14 studies reveal an association between breastfeeding and ADHD in samples with a variety of ages (3-18 years overall, with mean ages ranging from 7.4 years to 11.3 years) and representing multiple world regions that include the European Union, Middle East, Asia, Africa, and the U.S. (32,33). Though the scientific literature examining the relationship between breastfeeding and ADHD is growing overall, studies focusing specifically on the association between breastfeeding and ADHD within U.S. samples of preschool-aged children have been limited in number and have produced mixed findings (34,35). The purpose of this study is to examine the association between duration of breastfeeding and parent report of subsequent ADHD diagnosis in a U.S. sample of children, aged 2-5 years, using nationally representative population-based cross-sectional data from the NSCH, survey cycles 2016 and 2017. The primary aim is to determine if duration of breastfeeding or being fed breast milk as an infant is inversely associated with subsequent ADHD diagnosis in preschool-aged children in the U.S. In doing so, findings from this study are meant to further clarify the current understanding of how infant breastfeeding relates to ADHD diagnosis in a national sample of 2-5-year-old children from the U.S.

Chapter II: Review of the Literature

Introduction

In order to place the current study in context, it is necessary to review the historical background of ADHD as a disorder, as well as its current conceptualization, including the prevalence, cost, consequences, treatment options, etiology, risk factors, course of illness, and factors specific to ADHD in the preschool-age population. It is also necessary to fully examine the current literature on infant breastfeeding and its association with ADHD.

History of ADHD

Although the cluster of symptoms and outcomes currently termed as ADHD has been described since a German physician first attempted to capture its complexity in 1775, understanding of the disorder has evolved substantially from the pre-diagnostic era to early psychological and environmental frameworks to the current biopsychosocial conceptualization (36,37). This syndrome was characterized as "Hyperactive/Hyperkinetic Syndrome" and "Minimal Brain Dysfunction" prior to the development of reliable, operational diagnostic criteria in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) (36–38). Early theories included "brain damage" given the hallmark symptoms of hyperactivity and motor disturbance as well as neurochemical imbalance such as dopamine deficiency (36). More recent advances in neuroscience, brain imaging technology, and genetic research, has culminated in the current conceptualization of ADHD as a highly prevalent neurodevelopmental disorder, often with a chronic course and wide-ranging impairment (36,37).

ADHD Prevalence among children globally and in the U.S.

Meta-analytic results have estimated a worldwide prevalence of ADHD among children and adolescents aged 18 or younger as 5.29% in 2004 (2) and 7.2% in 2015 (3). As with worldwide estimates, prevalence of ADHD among children and adolescents within the U.S. appears to have increased over time based on parent reports. In fact, data from the 2003, 2007, and 2011 National Survey of Children's Health (NSCH) indicate that parent report of children aged 4-17 with ADHD increased from 7.8% in 2003 to 9.5% in 2007, representing a 21.8% increase, and then increased further from 9.5% to 11% in 2011, a 16.7% increase (39,40). Whether such increases reflect true increase in ADHD incidence or are a product of changing diagnostic approaches is not known.

Due to changes in survey methodology between the 2011 and 2016 cycles, it is not possible to analyze trends occurring between them (41). Based on parent reports, NSCH results from 2016 indicate that 6.1 million (9.4%) of children between the ages of 2-17 years old were reported as having ever received a diagnosis of ADHD, with 5.4 million of them continuing to have ADHD on the date of survey completion (4). Among those with current ADHD, 62.0% were currently taking medication for ADHD, 46.7% had received behavioral treatment for ADHD in the preceding 12 months, and 59.9% had received behavioral treatment or any treatment from a mental health provider in the previous 12 months (4). Focusing on preschool children aged 2-5 years old, 2.4% were reported as having ever received a diagnosis of ADHD, with 2.1% continuing to have a diagnosis of ADHD at survey completion., Among those with current ADHD, 18.2% were currently taking medication for ADHD, 59.5% had received behavioral treatment for ADHD in the previous 12 months, and 62.9% had received behavioral treatment or any treatment from a mental health provider in the preceding 12 months (4).

ADHD Clinical Features: Impairment, Comorbidity, and Cost

In general, ADHD has been found to be more strongly associated with being male than female (26,31,42–44), and tends to be accompanied by functional impairment that extends well into adulthood (5). Such impairments have been found early on in life as one study has demonstrated that preschoolers diagnosed with ADHD exhibited more deficits in behavioral, social, familial, and academic domains than those without ADHD (6). Also, children with ADHD have been found to experience more accidental injuries than non-affected siblings (59) and other children of similar demographics without ADHD (11–13). Furthermore, children with ADHD appear to be at greater risk for developing comorbid diagnoses, including learning disability, speech problems, epilepsy/seizures, Tourette syndrome, depression, anxiety, oppositional defiant disorder (ODD), conduct disorder, externalizing disorders, and neurodevelopmental or psychiatric disorders in general (7–10).

Findings of early comorbidity are demonstrated by a study of preschoolers (3-5.5 years old) with moderate-to-severe ADHD Hyperactive/Impulsive or Combined type. In brief, 69.6% had comorbid disorders, with the most common including ODD, communication disorder, and anxiety (45). These results are complementary to those of a large community study of preschoolers in Norway in that 46.2% of children with ADHD had at least one other psychiatric disorder (46). More specifically, those children also met criteria for ODD (20.8%), conduct disorder (14.4%), anxiety (5.9%), or depression (22.4%) (46). Highlighting the importance of considering the impact of the aforementioned comorbidities, preschoolers in the U.S. who have symptoms of both ADHD and anxiety have also been found to have more severe ADHD symptom presentations than those with ADHD alone (9).

As a function of associated behavioral impairment, injury, and the deleterious effects of comorbidities and clinical outcomes, ADHD is a quite costly public health concern from an economic standpoint. One study examining U.S. healthcare spending over time used BEA HCSA data from 2000-2014 and found ADHD to be one of the top 30 fastest growing medical conditions accounting for 42% of per capita spending growth observed during that period (47). Specifically, rates of growth in spending for ADHD from 2000-2014 were 3.82 in spending per capita, 1.70 in spending per case and 2.24 in treated prevalence. This growth is attributed to both increasing prevalence and cost of treatment (47). Healthcare costs specific to children with ADHD have also been studied. In 2012, a systematic literature review of ADHD-related costs found reports of excess health care costs due to increased use of services for children and adolescents with ADHD ranging from $621 to $2,720 (48). One children's health care expenditure study acquired data from the Agency for Healthcare Research and Quality (AHRQ)'s 2006 and 2011 Healthcare Cost and Utilization Project (HCUP) which uses the Nationwide Inpatient

Sample (NIS) and Nationwide Emergency Department Sample (NEDS) databases, and on AHRQ's pooled 2006 to 2011 Medical Expenditure Panel Survey (MEPS). That study demonstrated that children presenting at hospitals to address mental health issues have, on average, about 3.6 hospital visits compared to 1.6 hospital visits for children presenting with other, non-mental health conditions (49). The same study also found a 20.6% increase from 2006-2011 in emergency room visits that were attributed to mental health causes among children aged 1-4 years (49).

The economic burden of ADHD is incurred not only directly in the health care sector, but also indirectly in the work force, educational settings, and criminal justice system. In fact, individuals with high levels of hyperactivity while in preschool have been shown to incur higher long-term costs in each of these settings (50). For example, requisite specialized educational services for children with ADHD have been shown to impacts costs in the education sector. Furthermore, analysis of service utilization and costs in preschool children demonstrated that preschoolers with ADHD were significantly more likely than those without ADHD to use any service, including speech and language therapy, occupational therapy, and physical therapy (51). Moreover, preschool children with ADHD also used two to four times the services of preschool children without ADHD, culminating in individual costs at two to six times higher for the ADHD group (51). Finally, the work force sector is affected by absenteeism and productivity losses resulting from both adults with ADHD and parents of children with ADHD. For example, parents of children with ADHD report working reduced hours, changing jobs, lessening job responsibilities, and quitting or being fired (52). When controlling for intellectual functioning, ODD symptoms, and conduct problems, the he total economic burden of ADHD (including both indirect and direct costs) over the course of child development is substantial and estimated to be $15,036 per child relative to $2,848 per child without ADHD (52).

Given the early onset of ADHD and the challenges faced by individuals with this disorder, early identification and treatment is necessary to minimize impairment and economic burden (31). Current treatment regimens for ADHD include stimulant medication, behavioral therapy, or a combination of medication and therapy (53), with the use of stimulant medication in preschool aged children with ADHD not uncommon (54,55). However, considering the apparent increasing prevalence and significant costs, discussed previously, these interventions are not sufficient for reducing incidence or curtailing the functional and economic costs of this disorder. As a result, it would be beneficial to look at contributing factors that may moderate risk for ADHD and/or address areas of impairment. Careful consideration of factors at play both within the etiology of ADHD and the functional impairments that are associated with it may illuminate areas for early intervention.

ADHD Etiology

As with many other psychiatric illnesses, ADHD is thought to be a heterogeneous disorder potentially developing by way of multiple developmental pathways from etiological factors to behavioral symptoms, such that different combinations of factors confer risk on different groups of people (56–58). Many researchers acknowledge that

ADHD may be the result of many diverse and complex developmental mechanisms and that diagnosis in childhood can lead to dissimilar outcomes in adolescence and adulthood (5,59). Although the full etiology of ADHD is not yet understood, recent research suggests a strong genetic component with a 76% estimate of heritability (60).

The neurodevelopmental model of psychiatric illness hypothesizes that inherited genes confer vulnerability to ADHD and interact with diverse biological and environmental factors within critical periods of neurodevelopment. Several lines of research offer ideas about components that may be involved this model's application in ADHD. For example, neurobiological studies reveal significant variations in brain anatomy, structures, and function, as well as in neurophysiological activity and neurochemical factors for individuals with ADHD relative to controls (56). Furthermore, research in neuroendocrinology suggests that disruptions in the natural biological processes during childbirth and in the post-partum period, such as hormone disrupting pharmacologic interventions, caesarian section, mother-infant separation, etc., may result in increased risk for cognitive or emotional disorders in the infant (61).

Key prenatal and postnatal risk factors have been implicated, including preterm birth, (59,62–64), low birth weight, (59,62–66), maternal stress (62,67), prenatal exposure to nicotine (59,62,63,68,69), alcohol (62,63,68), illicit drugs (62,63), polychlorinated biphenyls (PCBs) (62,70), lead (62,63,70), mercury and organophosphate pesticides (62), and postnatal exposure to second-hand smoke (71). Similarly, ADHD has also been associated with a variety of individual outcomes and behavioral characteristics including socioeconomic disadvantage and psychosocial adversity (65,69,72,73), having a non-intact family (59), young maternal age at birth (43,59), paternal childhood/adolescent antisocial behaviors and maternal depression at infants at the age of 5 months (59), childhood head trauma (63,68), difficult temperament (59,74), sleep disturbances (74,75), epilepsy, abdominal trauma during pregnancy, Cesarean section, unwanted pregnancy, history of abortion, and use of formula rather than breastfeeding (68).

It is also interesting to note that dietary and nutritional factors have also been linked to ADHD. For example, ADHD has been linked with low serum iron (63), vitamin D deficiency (76–78), diets consisting of high levels of sugar, fats, and processed foods, and low levels of fiber, lean protein, folate, and omega-3 fatty acids (79), and folate deficiency in the mother during pregnancy (80,81). Finally, intestinal microbiota has also been implicated in neurodevelopmental and psychiatric disorder etiology due to its connection to and influence on the nervous system (82,83). In fact, researchers are beginning to identify patterns of microbiota that may be linked to ADHD (84,85).

Breastfeeding and ADHD

The impact of breastfeeding on cognitive development has been much researched with mixed findings. Many studies have found positive associations between breastfeeding and cognitive development (35,86–88), but a 2013 systematic review of the literature suggests that the observed effects may be due to the presence of uncontrolled confounding factors (89). The World Health Organization (WHO) and American Academy of Pediatrics recommends 6 months of exclusive breastfeeding and continued mixed breastfeeding for at least 12 months (90). Although the Cochrane Collaboration 2012 review concurs that 6 months is the optimal duration for exclusive breastfeeding with continued mixed breastfeeding after 6 months, they did not find significant evidence for long-term effects on allergic disease, growth, obesity, cognitive ability, or behavior of the infant (91). However, it is plausible that breastmilk could have positive effects on neurodevelopment due to its composition of molecules essential to brain development, including long-chain polyunsaturated fatty acids which are components in neuronal membranes, oligosaccharides which function as immune modulators, amino acids which are the building blocks of proteins, and prebiotics which feed the beneficial gut microorganisms (92,93). In fact, in infants, the composition of the developing gut microbiome is greatly influenced by source of nutrition, with differences in diversity between the microbiota of breastfed and formula fed infants (82).

Several studies have examined the association between breastfeeding and ADHD, with a recent meta-analysis supporting an inverse association between breastfeeding and ADHD across samples of varying ages and settings (32,33). For example, a 2005 case-control study conducted by Kadziela-Olech and Piotrowska-Jastrzębska in Białystok, Poland, found that breastfeeding duration differed significantly between children aged 4-11 years old with and without ADHD, suggesting a link between shorter duration of breastfeeding and increased risk of ADHD (94). Then, in 2012, Shamberger published an ecological study in the U.S. examining average percentage of exclusive breastfeeding by state using 2001-2004 Centers for Disease Control and Prevention (CDC) data and state prevalence of ADHD using NSCH 2003 data, revealing an inverse relationship ADHD and exclusive breastfeeding (95). Similarly, in 2013, a study by Mimouni-Bloch and colleagues in Petach Tikya, Israel retrospectively examined prevalence of breastfeeding in children 6-12 years old who were diagnosed with ADHD and concluded they were more likely to have breastfed for shorter durations than their siblings without ADHD (96). Furthermore, a 2014 school-based study of children 8-11 years old from several Korean cities found a significant association between lack of breastfeeding as an infant and increased ADHD morbidity (86). Moreover, a retrospective case control study published in 2016, Stadler and colleagues examined the breastfeeding-ADHD association in case-control study of children 7-13 years old and concluded that mothers of children with ADHD were less likely to initiate and continue breastfeeding than mothers of children without ADHD (97). Finally, a Danish National Birth Cohort study also found significant inverse correlations between risk for later diagnosis of ADHD and both duration of exclusive breastfeeding and total duration of breastfeeding as reported by mothers of 6 months old infants and risk for later diagnosis of ADHD (74).

Contrary to previously discussed results, a 2017 multi-center birth cohort study in Spain found a positive association between duration of breastfeeding and overall cognition in 4 to 7-year-old children (98). However, no significant association between breastfeeding duration and attention or symptoms of ADHD remained after adjusting for parental education, social class, maternal age and country of birth, parity, and maternal smoking. Similarly, another 2017 study with inconsistent results examined formula feeding and ADHD in preschool children aged 3-5 years by comparing results of the NSCH 2007 to the 2011/12 survey. While they found a significant formula-ADHD association with the

2007 data, again no significant formula-ADHD association remained after adjusting for propensity scores in the 2011/12 data (34). Taken together, these results highlight the need for analyses that allow for controlling for potentially confounding factors on the relatedness of breast feeding and subsequent ADHD diagnosis preschool children.

Given the trend for increasing prevalence of preschool ADHD, the poor prognosis, and need for early intervention, and the potentially protective association between breastfeeding and ADHD, promotion of breastfeeding seems to have the potential to be an early intervention strategy for the prevention of subsequent ADHD diagnosis. Though the literature in this area is growing, less is known about the relationship between breastfeeding duration and diagnosis of ADHD in preschool-aged children. The aim of the current study is to examine the association between parent-reported duration of breastfeeding and subsequent diagnosis of ADHD in a national sample of children 2-5 years old, with the hypothesis that longer duration of breastfeeding will be associated with lower prevalence odds of ADHD diagnosis.

Chapter III: Methodology

Introduction

The data analyzed in the present study were collected as part of the 2016 and 2017 iterations of the NSCH, a survey of health, health care, family, neighborhoods, school, and social characteristics of non-institutionalized children ages 0-17 years in the United States. The NSCH is sponsored by The U.S. Department of Health and Human Services, Health Resources and Services Administration's Maternal and Child Health Bureau (41,98).

Data Sources

Both the 2016 and 2017 NSCH were administered by the U.S. Census Bureau using internet- and mail-based instruments (41,98–100). Invitations to complete an online screening questionnaire were mailed to households randomly selected from the Census Master Address File (MAF), a sample of 364,150 in 2016 and 170,726 in 2017 (41,98–100). The invitations and screening surveys requested responses from adults who were familiar with the health and health care of any household children aged 17 years or younger (41,98–100). Those opting to participate were referred immediately to one of three age-specific topical questionnaires: children aged 0-5, 6-11, or 12-17 years, according to the age of the selected child (41,98–100). Among families with multiple children under 18 years, the survey subject was randomly selected from the children within that household (41,98–100). Accommodations to improve response rates included the availability of paper copies of the screening questionnaire and the main topical questionnaire, Spanish-language versions of the questionnaires, mailings of reminders and paper screening questionnaires to non-responding households, as well as toll-free telephone assistance and cash incentives (99,100).

The NSCH uses a complex survey design with stratifications by state of residence and household, and weights reflecting annual populations. As a result, combining the 2016 and 2017 survey data requires use of a combined weight to accurately produce multi-year estimates (101). Though pre-2016 NSCH data cannot be combined with 2016 or later survey data due to changes in survey design, survey data collected after the 2016 redesign can be combined to provide the larger sample sizes necessary for analysis of rare outcomes (101–103). Weighted, overall NSCH response rates were 40.7% for the 2016 survey and 37.4% for 2017 (41,98). The majority of respondents were biological or adoptive parents, accounting for 91% of respondents in the 2016 survey and 90.3% in 2017 (41,98). Survey data were collected between June, 2016 and February, 2017 for the 2016 effort and between August, 2017 and February, 2018 for the 2017 survey (102,103).

Study Sample

As the present study concerns ADHD in preschool-aged children, the sample selected for analysis was limited to children of ages 2-5 years. Further selection criteria included availability of data for the primary exposure variable, duration of breastfeeding, and the outcome variable, ADHD. The survey design provided data on breastfeeding for children aged 0-5 years old, and ADHD data for children aged 0-17 years.

Outcome Variable

Lifetime ADHD diagnosis status was obtained using the Yes/No question, "Has a doctor or other health care provider EVER told you that this child has Attention Deficit Disorder or Attention Deficit/Hyperactivity Disorder, that is, ADD or ADHD," and current ADHD was assessed using the Yes/No follow up question, "If yes, does this child CURRENTLY have the condition," (104,105). A composite variable for current ADHD was created using these two variables in which individuals with a "No" response to ADHD ever were coded as "No" for current ADHD, and individuals with a "Yes" response to current ADHD were coded as "Yes" for the new current ADHD variable.

Exposure Variable

Breastfeeding information was available for children aged 0-5 years old, and, for those answering "Yes" to the Yes/No question, "Was this child EVER breastfed or fed breast milk," this additional questions addressing duration of breastfeeding was asked: "How old was this child when he or she COMPLETELY stopped breastfeeding or being fed breast milk," with answer options of number of days, number of weeks, number of months or still breastfeeding (104,105).

Co-variables

We examined the following variables in our study as co-factors in the association between breastfeeding and ADHD: the child's age (2-5 years), sex (male / female), race/ethnicity (black, white, Hispanic, or other), household percentage of the federal poverty level (<100% / 100-199% / 200-399% / >400%), birth weight (normal / low /

very low), preterm birth (yes / no), exposure to second-hand smoke (no / yes-outside / yes-inside), and parental mental health status (at least one parent reported to have fair or poor mental health: no / yes) (104,105).

Data Analysis

Descriptive analysis of the sample was conducted using Rao Scott chi-square test, a design-adjusted version of the Pearson chi-square test which provides a test of independence between row and column variables while accounting for the complex survey method of NSCH. Associations between exposures and outcome were examined using crude prevalence odds ratios (PORs) and 95% confidence intervals (CI) constructed using the Wilson method. Interaction was assessed for variables based on biological plausibility and included sex and preterm birth. Multivariate modeling was conducted using logistic regression and backward elimination of non-significant interaction terms, and non-confounding variables. All significance levels were set to 0.05 unless otherwise specified, and all analyses were conducted using SAS 9.4 (106). Due to the complex survey design, analyses were conducted using SAS proc surveyfreq and proc surveylogistic procedures to account the sample weights and multiple levels of stratification.

Chapter IV: Results

Sample

Among children between the ages of 2 and 5 years old, with complete data on infant breastfeeding duration and current ADHD status, 194 or 1.7% (260,342, weighted; 95% CI: 1.2-2.4) were reportedly told by a doctor at some point that they had ADHD, and 186, or 1.7% (256,717, weighted; 95% CI: 1.2-2.3%) currently had ADHD. The 8 subjects with "Yes" responses to ADHD ever and "No" to ADHD current were excluded from analyses leaving an overall sample size of 14,259 (Figure 1). Also, within the sample, 11,748 or 76.7% (95% CI: 74.9-78.5) were reported to have been breastfed or fed breast milk as infants. Of the subjects excluded, 56,968 were outside of the 2-5-year age range, 93 were missing outcome variable data, 8 had history of ADHD but no current ADHD, and 482 were missing exposure variable data (Figure 1).

Descriptive Analysis

Our descriptive analysis showed that among preschool children aged 2-5 years, breastfeeding duration, age, sex, race/ethnicity, household poverty level, exposure to second-hand smoke, parental mental health status, use of mental health services, and use of psychotropic medication differed significantly between those with ADHD and those without ADHD ($p < 0.05$) (Table 1). Characteristics of the sample by duration of infant breastfeeding showed that among preschool children aged 2-5, current ADHD diagnosis, age, race/ethnicity, household poverty level, and exposure to second-hand smoke differed significantly between subjects based on breastfeeding duration ($p < 0.05$) (Table 2).

Unadjusted Prevalence Odds Ratios

In our unadjusted analysis (Table 3), children with any infant breastfeeding had prevalence odds of ADHD at 65% lower than children with no breastfeeding (95% CI: 0.17, 0.70). Specifically, compared to children with no breastfeeding, prevalence odds of ADHD were 81% lower in those with 6-12 months breastfeeding (95% CI: 0.09-0.40), 78% lower in those with 12 or more months breastfeeding (95% CI: 0.09, 0.58) (Table 3). Among children with less than months breastfeeding, prevalence odds of ADHD were lower, but not statistically significant compared to children with no breastfeeding (POR: 0.52, 95% CI: 0.23-1.20).

Outside of the primary study hypothesis, ADHD was associated with age, sex, race/ethnicity, household poverty, second-hand smoke exposure, and parent mental health status. For the effect of age, when compared to 2-year-old children the prevalence odds of ADHD are 8.78 higher among 5-year-old children (95% CI: 2.31-33.4, Table 3). However, they are not statistically significant among children ages 3 and 4 years. A sex differences is also apparent in that the prevalence odds of ADHD were 3.28 in males than females (95% CI: 1.60-6.73). Racial group comparisons revealed that prevalence odds of ADHD were 3.0 times higher (95% CI: 1.16-7.73) in children who were black or African American alone than those who were white. For children who were Hispanic or other races, the race-ADHD association did not reach statistical significance (Hispanic POR: 1.96, 95% CI: 0.87-4.42; other race POR: 0.80, 95% CI: 0.42-1.54).

The association of the household poverty level as a percentage of the federal poverty level (%FPL) with ADHD was statistically significant on all levels. Compared to children in families with income 400%FPL, prevalence odds of ADHD was 2.15 higher in children living in households with income 200-399% FPL (95% CI: 1.14-4.07), 3.22 higher in in children living in households with income 100-199% FPL (95% CI: 1.30-7.97), and 5.31 higher in children living in households with income less than 100% FPL (95% CI: 2.67-10.5). Preterm birth (POR: 1.2, 95% CI: 0.63-2.40) was not a statistically significant predictor of current ADHD status in this sample. Household smoke exposure was a significant predictor of ADHD in this sample, with prevalence odds of ADHD 2.58 higher in children exposed to smoke outdoors only (95% CI: 1.07-6.25) and 5.24 higher in children exposed to smoke indoors (95% CI: 2.13-12.9) when compared to children living in households with no tobacco use. Children with at least one parent whose mental health status was reported as fair or poor had prevalence odds of ADHD 8.03 higher than children whose parent(s)'s mental health status was not reported as fair or poor (95% CI: 3.37-19.1).

Interaction Analysis

Modification of the breastfeeding-ADHD association was assessed for sex and preterm birth, controlling for age, sex, race, poverty, preterm birth, secondhand smoke, and parent mental health (Table 4). Neither cross-product term was statistically significant, (p=0.27 and p=0.14, respectively) and both were eliminated from further modeling.

Backward Elimination of Main Effects

Beginning with the fully adjusted model, including breastfeeding duration, age, sex, race/ethnicity, household poverty, preterm birth, secondhand smoke, and parent mental health, covariates were removed from the fully adjusted model, one at a time, to assess confounding in the breastfeeding duration PORs (Table 5). Evidence of confounding was identified for age, sex, race/ethnicity, household poverty, secondhand smoke exposure, and parent mental health, and those variables were retained in the final model. Upon removal of the variables for preterm birth and sex, the PORs for the breastfeeding-ADHD association were fairly stable and did not suggest a confounding effect, so preterm birth and sex were removed leaving the final model.

Final Adjusted Model

Table 6 summarizes the fully adjusted model containing breastfeeding duration and the potentially confounding variables of age, sex, race, poverty, preterm birth, secondhand smoke, and parent mental health, as well as the final adjusted model obtained from backward elimination of main effect terms. For the overall breastfeeding-parent mental health association with ADHD in the final model adjusted for the child's age, sex, race/ethnicity, household poverty level, smoke exposure, and parent mental health, patterns of results were similar to the crude and fully adjusted PORs among those with 6-12 months of breastfeeding: compared to children with no breastfeeding, prevalence odds of ADHD were 64% lower in those with 6-12 months breastfeeding (95% CI: 016-0.84). Although not significant, children with less than 6 months of breastfeeding and 12 or more months of breastfeeding also had lower prevalence odds of ADHD relative to those with no breastfeeding (<6M POR: 0.74, 95% CI: 0.33-1.66; ≥12M POR: 0.48 95% CI: 0.17-1.34). In addition to calculating PORs for the levels of each categorical variable, tests for overall variable significance across levels were also conducted for each model. Tests of main effects terms were statistically significant for age, household poverty level, and parent mental health in both the fully adjusted model and the final model.

Chapter V: Conclusions

Considering the primary aim of this study, to clarify the relationship between duration of breastfeeding during infancy and subsequent ADHD diagnosis, findings were mixed. While the unadjusted duration of infant breastfeeding was associated with a lower rate of subsequent ADHD diagnosis in U.S. children aged 2-5 years, after controlling for the child's age, race/ethnicity, household poverty, secondhand smoke exposure, and parent mental health, the variable for overall duration of breastfeeding was no longer statistically significant. However, in children breastfed for 6-12 months, the prevalence odds of ADHD were significantly lower relative to children with no breastfeeding (POR: 0.36, 95% CI: 0.16-0.84). Taken together, these results suggest a more complex relationship between breastfeeding and subsequent ADHD diagnosis than what has typically been found in previous studies, highlighting the importance of considering duration of breastfeeding in overall breastfeeding-ADHD association studies.

The present study differs from previous studies in several important ways. First, few existing studies have examined the breastfeeding-ADHD association in nationally representative samples within the U.S., and even fewer focus specifically on preschool children aged 2-5 years. In fact, to our knowledge, only one previously published study attempts to do this. More specifically, in 2017 Adesman and colleagues conducted a study using NSCH data from the 2007 and 2011/2012 survey cycles to assess the relationship between ADHD and formula feeding in children 3-5 years old by comparing results from the 2007 NSCH data to those obtained using 2011-2012 NSCH data (34).

While results revealed a significant formula-ADHD association with the 2007 data, there was no significant formula-ADHD association in the 2011/12 data. The difference in findings was hypothesized to be due reduced exposure to BPA after 2008 when concerns about the neurotoxic effects of BPA containing products prompted their discontinuation in the production of bottles typically used in formula feeding (34). However, despite having a similar sample age range a major difference between the study by Adesman et al. (2017) and the present study is our examination of how different categories of breastfeeding duration are associated with ADHD. More specifically, while they looked at breastfeeding dichotomously, with breastfed ever including any breastfeeding lasting two weeks or longer and never breastfed, or formula-fed, including those with a no response to the breastfed ever question, the current study looked at breastfeeding exposure categorized by duration, with no breastfeeding, any breastfeeding up to 6 months, from 6 months up to 12 months, and 12 months or longer duration of breastfeeding.

Strengths

Strengths of this study included use of a nationally representative sample to aid in producing results generalizable to the U.S. population for future health policy and public health research. With a large dataset such as the NSCH, there were many variables that could be considered for confounding along with the primary association, and this is important as many previous studies of breastfeeding and neurodevelopment have been affected by uncontrolled confounding. As a result, we were able to make use of the large amount of data available in this dataset to do more than examine the basic relationship between breastfeeding and ADHD. In fact, we were able to look at how different durations of breastfeeding related to ADHD, as well as statistically controlling for the potentially confounding variables of the child's age, sex, race, household poverty level, preterm birth, secondhand smoke exposure, and parent mental health status. Finally, this study is the first to consider the association of breastfeeding and ADHD since the redesign of the NSCH. As a result, it is an important first step in examining the most up-to-date data available for the breastfeeding-ADHD association in the U.S.

Limitations

Limitations of this study were largely methodological. First, some of the variables (e.g. secondhand smoke exposure and parent mental health status) used in the analyses as controls for confounding were proxies for intended measures and lacked specificity that may have improved precision. As an example, the parental mental health status variable was a proxy for parental mental illness in that it was a composite of survey items consisting of mental health quality ratings for up to two household adults instead of one or more questions about actual diagnostic status for the parent. Additionally, we were unable to further stratify by biological or adoptive parents in our study as NSCH publishes it as a combined category. Furthermore, the exposure to household smoking variable lacks information pertaining to the onset and duration of the exposure.

Second, parent report is subject to recall bias overall. For example, with regard to ADHD diagnosis, there may be less accuracy in reporting than verification of diagnosis for ADHD via medical record or clinical assessment would provide. For the latter, diagnosis can be further complicated by the fact that we cannot assume that practitioners diagnosing ADHD all use the same criteria for diagnosis. In fact, practitioners diagnosing ADHD often do not use structured scales or teacher input described in best practices for making ADHD diagnoses (107). Although some studies have demonstrated accuracy in maternal recall of breastfeeding after 20 years, with a median error of about 2 weeks (108), the potential still exists for recall bias in reporting for breastfeeding duration.

Finally, there are several important, potential confounders and effect modifiers from the literature available to date that are not considered in this study. More specifically, maternal toxemia, antepartum hemorrhage, maternal hypothyroidism, antenatal stress, maternal depression during pregnancy, parental postnatal anxiety and ADHD status, and exposure to environmental toxins were not included in the NSCH.

Implications and Conclusion

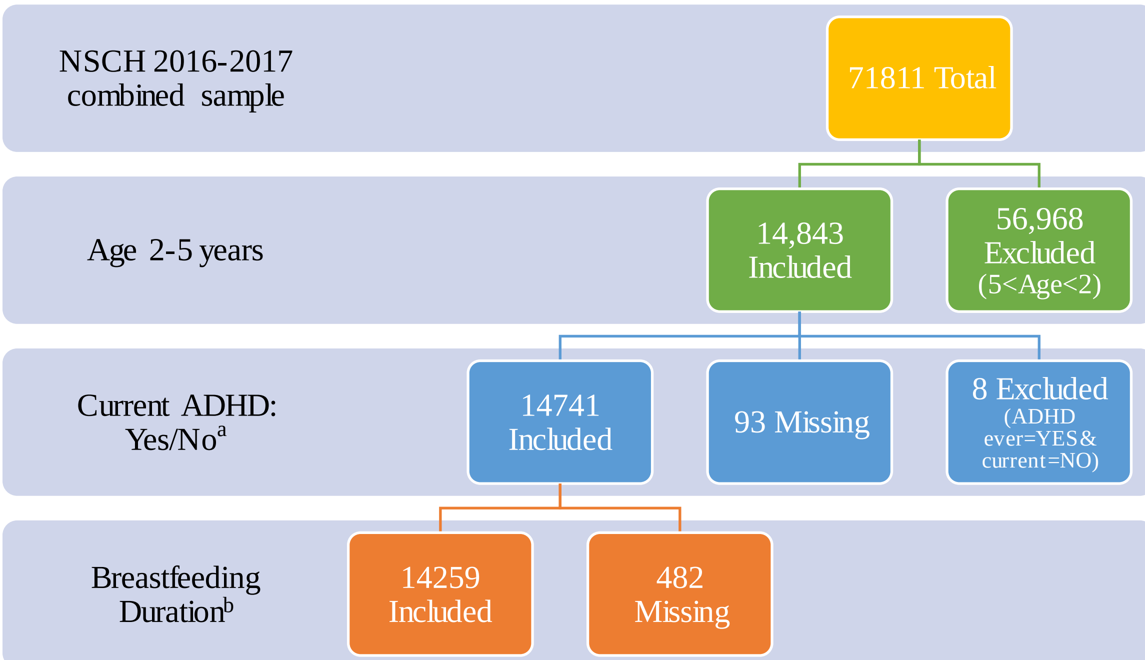
In summary, study results indicate 6-12 months of breastfeeding is associated with lower prevalence odds of subsequent ADHD diagnosis compared to no breastfeeding while controlling for the child's age, race/ethnicity, household poverty, secondhand smoke exposure, and parent mental health.

Taken together with study strengths and limitations considered above, these findings raise some important questions for further analyses. For example, why do we find decreased prevalence odds of ADHD only among children who were breastfed as infants for 6-12 months compared to children with no breastfeeding, but not in those with less than 6 months or 12 months or more of breastfeeding duration? Prior research suggests that the postnatal period is a critical time for infant brain development, and events occurring during this period can alter the developmental trajectory for children for better or worse (83). The infant gut microbiota and immune system are also developing during this period, and, like the brain, they are sensitive to environmental disturbances and may be linked to the development of mental disorders later in life (80,82). Early nutrition plays a significant role in the developmental processes occurring during the first year of life, and breastfeeding has been positively associated with development of the infant brain, gut microbiota, and immune system (80,82,109). These processes of development continue beyond the first year of life. In the current study, the lack of significantly lower odds of ADHD for children with less than 6 months of breastfeeding could be explained by insufficient duration of breastfeeding, and would not necessarily be inconsistent with prior research findings. However, lack of significance in the result for children with 12 months or more of breastfeeding is more puzzling given the result among children with 6 to 12 months of breastfeeding. Further research is needed to address the new questions raised by these results.

In conclusion, this current study is an important first step in illuminating the potential relationship between breastfeeding and subsequent ADHD diagnosis in preschool children in the U.S. who were breastfed until 6 to 12 months of age. Consideration of the potential mechanisms influencing the breastfeeding-ADHD association and how they apply to specific developmental phases and stages will need to be examined further in future studies. Such studies should include samples sizes that provide sufficient power for detecting significant differences in complicated statistical modelling analyses. When possible, they also should attempt to include more robust variables for key variables of interest. In short, studies that build on these results and the discussion of them would have increased potential to help policy makers and providers implement and/or strengthen current early intervention efforts for the reduction of burden and negative outcomes for children who may or may not go on to develop ADHD.

Appendix

Figure 1. Inclusion/Exclusion of Subjects



[a] Current ADHD:

- Coded "Yes" for subjects with responses of "Yes" to both ADHD Ever and Current ADHD
- Coded "No" for subjects with responses of "No" to ADHD Ever
- Subjects with responses of "Yes" to ADHD Ever and "No" to Current ADHD are excluded

[b] Breastfeeding Duration:

- Subjects with responses of "No" to Breastfed Ever, were coded "0" (no breastfeeding)
- For subjects with responses of "Yes" to Breastfed Ever, the sum of days, weeks, months for age when breastfeeding stopped was calculated for duration
- 152 missing Breastfed Ever and 330 missing Breastfeeding Duration

Table 1. Characteristics of Children Aged 2-5 Years (n=14,259[a]), With and Without Current ADHD, NSCH 2016-2017

Characteristic	ADHD (186)				No ADHD (14,073)						Total (14,259[a])			
	Freq.	Weighted	%	95% CI [b]	Freq.	Weighted	%	95% CI [b]	X^2 (DF)[c,d]	p-value	Freq.	Weighted	%	95% CI [b]
Breastfeeding Duration									18.67 (3)	*<0.001*				
No breastfeeding	76	118,066	*46.0%*	*(30.2-62.6)*	2435	3,456,430	*22.9%*	*(21.0-24.7)*			2,511	3,574,496	*23.3%*	*(21.4-25.1)*
0 - < 6 Months	66	93,658	*36.5%*	*(21.8-54.1)*	5043	5,225,959	*34.6%*	*(32.8-36.3)*			5,109	5,319,618	*34.6%*	*(32.8-36.3)*
6 - < 12 Months	26	21,410	*8.3%*	*(4.63-14.5)*	3403	3,335,717	*22.1%*	*(20.5-23.7)*			3,429	3,357,127	*21.8%*	*(20.2-23.4)*
≥ 12 Months	18	23,582	*9.2%*	*(4.22-18.8)*	3192	3,095,319	*20.5%*	*(18.9-22.0)*			3,210	3,118,901	*20.3%*	*(18.8-21.8)*
Age of child (years)									45.54 (3)	*<0.001*				
2	12	19,642	*7.7%*	*(2.44-21.5)*	3894	3,843,253	*25.4%*	*(23.8-27.1)*			3,906	3,862,895	*25.3%*	*(23.7-26.9)*
3	24	21,276	*8.3%*	*(4.36-15.1)*	3455	3,806,109	*25.2%*	*(23.5-26.9)*			3,479	3,827,386	*24.7%*	*(23.1-26.4)*
4	57	55,164	*21.5%*	*(13.6-32.2)*	3405	3,883,528	*25.7%*	*(24.0-27.4)*			3,462	3,938,692	*25.6%*	*(23.9-27.2)*
5	93	160,635	*62.6%*	*(47.8-75.2)*	3319	3,580,534	*23.7%*	*(22.0-25.4)*			3,412	3,741,169	*24.5%*	*(22.8-26.2)*
Sex of child									11.81 (1)	*<0.001*				
Female	46	58,661	*22.9%*	*(12.8-37.2)*	6840	7,447,742	*49.3%*	*(47.3-51.2)*			6,886	7,506,403	*48.8%*	*(46.8-50.7)*
Male	140	198,056	*77.1%*	*(62.7-87.1)*	7233	7,665,682	*50.7%*	*(48.7-52.6)*			7,373	7,863,738	*51.2%*	*(49.2-53.1)*
Race/Ethnicity of child									9.06 (3)	*0.029*				
White	106	95,258	*37.1%*	*(24.4-51.7)*	9817	8,037,900	*53.2%*	*(51.2-55.1)*			9,923	8,133,157	*52.9%*	*(50.9-54.8)*
Black/African American	27	61,596	*24.0%*	*(11.3-43.7)*	757	1,733,957	*11.5%*	*(10.2-12.8)*			784	1,795,553	*11.7%*	*(10.4-13.0)*
Hispanic	31	83,032	*32.3%*	*(17.9-51.1)*	1516	3,575,496	*23.7%*	*(21.5-25.8)*			1,547	3,658,528	*23.8%*	*(21.7-25.9)*
Other	22	16,831	*6.6%*	*(3.60-11.6)*	1983	1,766,072	*11.7%*	*(10.6-12.8)*			2,005	1,782,903	*11.6%*	*(10.5-12.7)*
Household Poverty (%FPL)									13.85 (3)	*0.003*				
< 100%	53	105,458	*41.1%*	*(25.8-58.1)*	1414	3,156,744	*20.9%*	*(18.9-22.9)*			1,467	3,262,202	*21.2%*	*(19.3-23.2)*
100-199%	37	66,027	*25.7%*	*(12.6-45.1)*	2192	3,252,695	*21.5%*	*(19.7-23.3)*			2,229	3,318,722	*21.6%*	*(19.8-23.4)*
200-399%	50	56,911	*22.2%*	*(12.9-35.2)*	4562	4,206,495	*27.8%*	*(26.3-29.4)*			4,612	4,263,405	*27.7%*	*(26.2-29.3)*
≥ 400%	46	28,321	*11.0%*	*(6.93-17.0)*	5905	4,497,490	*29.8%*	*(28.2-31.3)*			5,951	4,525,812	*29.4%*	*(27.9-30.9)*
Preterm Birth									0.35[d] (1)	*0.556[d]*				
No	153	220,606	*86.5%*	*(77.4-92.2)*	12587	13,319,771	*88.6%*	*(86.9-90.0)*			12,740	13,540,378	*88.6%*	*(86.9-90.0)*
Yes	30	34,519	*13.5%*	*(7.76-22.5)*	1396	1,712,861	*11.4%*	*(9.94-13.0)*			1,426	1,747,380	*11.4%*	*(9.99-13.0)*
Missing	*3*				*90*						*93*			
Household Secondhand Smoke									12.73[d] (2)	*0.002[d]*				
None	127	172,248	*67.6%*	*(49.8-81.3)*	12088	12,737,146	*85.6%*	*(84.1-86.8)*			12,215	12,909,394	*85.3%*	*(83.8-86.5)*
Outdoor exposure	44	67,378	*26.4%*	*(13.5-45.1)*	1676	1,928,861	*13.0%*	*(11.7-14.3)*			1,720	1,996,239	*13.2%*	*(11.9-14.5)*
Indoor exposure	13	15,363	*6.0%*	*(2.77-12.5)*	147	216,709	*1.5%*	*(1.12-1.88)*			160	232,072	*1.5%*	*(1.19-1.96)*
Missing	*2*				*162*						*164*			
Fair-Poor Parent Mental Health Status									31.77[d] (1)	*<0.001[d]*				
No	129	143,016	*67.6%*	*(47.7-82.6)*	12599	13,061,121	*94.4%*	*(93.5-95.0)*			*12,728*	*13,204,137*	*94.0%*	*(93.0-94.7)*
Yes (for at least 1 parent)	34	68,577	*32.4%*	*(17.3-52.2)*	827	780,094	*5.6%*	*(4.92-6.44)*			861	848,671	*6.0%*	*(5.25-6.93)*
Missing	*23*				*647*						*670*			
Mental Health Services in Past 12 Months									328.21[d] (2)	*<0.001[d]*				
Yes	69	85,925	*34.1%*	*(21.5-49.3)*	246	224,671	*1.5%*	*(1.13-1.95)*			315	310,597	*2.0%*	*(1.61-2.54)*
No, but needed	23	56,058	*22.2%*	*(9.49-43.7)*	85	100,678	*0.7%*	*(0.42-1.05)*			108	156,736	*1.0%*	*(0.64-1.61)*
No	92	110,245	*43.7%*	*(28.1-60.5)*	13691	14,738,732	*97.8%*	*(97.2-98.2)*			13,783	14,848,978	*96.9%*	*(96.2-97.5)*
Missing	*2*				*51*						*53*			
Psychotropic Medication Use in Past 12 Months									760.02[d] (1)	*<0.001[d]*				

No	128	179,493	*71.4%*	*(52.6-84.7)*	13841	14,821,356	*99.8%*	*(99.6-99.8)*	13,969	15,000,849	*99.3%*	*(98.8-99.5)*
Yes	55	72,072	*28.6%*	*(15.2-47.3)*	32	33,553	*0.2%*	*(0.13-0.36)*	87	105,625	*0.7%*	*(0.41-1.17)*
Missing	*3*				*200*				*203*			

Abbreviations: Freq., Frequency; CI, Confidence Interval; DF, Degrees of Freedom; %FPL, Percentage of the Federal Poverty Level;
[a] Sample includes children aged 2-5 years with data available for the primary exposure and outcome variables
[b] Wilson method 95% Confidence Interval for Percent
[c] Rao-Scott Chi-Square test
[d] Chi-square test excludes missing data

Table 2. Characteristics of Children Aged 2-5 Years by Breastfeeding Duration, NSCH 2016-2017

Characteristic	Not breastfed as infant *(2,511)*			0 - < 6 Months *(5,109)*			6 - < 12 Months *(3,429)*			≥ 12 Months *(3210)*				
	Freq.	*%*	*95% CI [a]*	Freq.	*%*	*95% CI [a]*	Freq.	*%*	*95% CI [a]*	Freq.	*%*	*95% CI [a]*	X^2 (DF)[b,c]	*p-value*
ADHD Current													18.67 (3)	*<0.001*
No	2,435	96.7%	(94.5-98.0)	5,043	98.2%	(96.7-99.0)	3,403	*99.36%*	(98.9-99.6)	3,192	*99.24%*	(98.4-99.6)		
Yes	76	3.3%	(1.97-5.48)	66	1.8%	(0.95-3.21)	26	*0.64%*	(0.37-1.07)	18	*0.76%*	(0.35-1.59)		
Age of child (years)													22.72 (9)	*0.007*
2	549	*23.6%*	(19.7-27.9)	1,336	*24.5%*	(22.0-27.1)	984	*23.07%*	(20.3-26.0)	1,037	*30.17%*	(26.6-33.9)		
3	566	*20.7%*	(17.7-23.9)	1,259	*26.2%*	(23.6-28.9)	841	*26.74%*	(22.8-31.0)	813	*25.51%*	(21.7-29.6)		
4	674	*26.9%*	(22.9-31.2)	1,237	*25.0%*	(22.6-27.6)	841	*27.61%*	(24.0-31.4)	710	*23.07%*	(20.0-26.4)		
5	722	*28.8%*	(24.5-33.5)	1,277	*24.3%*	(21.8-26.8)	763	*22.58%*	(19.4-26.0)	650	*21.24%*	(17.9-24.9)		
Sex of child													2.84 (3)	*0.416*
Female	1,186	*47.3%*	(42.6-51.9)	2,436	*48.9%*	(45.9-51.8)	1,656	*47.53%*	(43.5-51.5)	1,608	*51.89%*	(47.7-55.9)		
Male	1,325	*52.7%*	(48.0-57.3)	2,673	*51.1%*	(48.1-54.0)	1,773	*52.47%*	(48.4-56.4)	1,602	*48.11%*	(44.0-52.2)		
Race/Ethnicity of child													74.35 (9)	*<0.001*
White	1,592	*43.0%*	(38.8-47.3)	3,514	*51.5%*	(48.5-54.4)	2,528	*59.57%*	(55.1-63.8)	2,289	*59.44%*	(55.0-63.6)		
Black/African American	312	*19.6%*	(16.5-23.0)	265	*11.4%*	(9.27-13.9)	117	*8.40%*	(6.26-11.1)	90	*6.60%*	(4.67-9.24)		
Hispanic	313	*28.6%*	(23.3-34.4)	633	*24.9%*	(21.9-28.0)	303	*19.15%*	(15.2-23.7)	298	*21.46%*	(17.3-26.2)		
Other	294	*8.7%*	(7.06-10.7)	697	*12.2%*	(10.4-14.1)	481	*12.87%*	(10.2-16.1)	533	*12.50%*	(10.6-14.6)		
Household Poverty (%FPL)													140.55 (9)	*<0.001*
< 100%	533	*34.8%*	(30.1-39.8)	506	*20.6%*	(17.6-23.8)	198	*13.16%*	(9.69-17.6)	230	*15.41%*	(12.3-19.0)		
100-199%	519	*26.2%*	(21.8-31.0)	845	*20.8%*	(18.4-23.3)	390	*17.32%*	(14.3-20.7)	475	*22.23%*	(18.0-27.0)		
200-399%	741	*22.8%*	(19.8-26.0)	1,704	*29.2%*	(26.7-31.6)	1,143	*30.36%*	(27.0-33.9)	1,024	*28.14%*	(24.8-31.6)		
≥ 400%	718	*16.1%*	(13.8-18.7)	2,054	*29.5%*	(27.1-31.9)	1,698	*39.16%*	(35.3-43.0)	1,481	*34.21%*	(30.9-37.6)		
Preterm Birth													3.85[c] (3)	*0.278[c]*
No	2,161	*87.0%*	(83.1-90.1)	4,476	*87.4%*	(85.2-89.2)	3,146	*91.14%*	(87.2-93.9)	2,957	*89.56%*	(85.0-92.8)		
Yes	320	*13.0%*	(9.83-16.8)	605	*12.6%*	(10.7-14.7)	260	*8.86%*	(6.05-12.7)	241	*10.44%*	(7.15-14.9)		
Missing	*30*			*28*			*23*			*12*				
Household Secondhand Smoke													104.57[c] (6)	*<0.001[c]*
None	1,883	*76.4%*	(72.6-79.7)	4,232	*83.8%*	(81.6-85.8)	3,143	*91.46%*	*(88.7-93.5)*	2,957	*91.24%*	*(87.6-93.8)*		
Outdoor exposure	487	*19.3%*	(16.2-22.8)	784	*15.2%*	(13.2-17.3)	238	*7.82%*	*(5.81-10.4)*	211	*8.55%*	*(5.91-12.1)*		
Indoor exposure	93	*4.3%*	(3.07-5.97)	47	*1.0%*	(0.67-1.39)	*10*	*0.72%*	*(0.30-1.69)*	*10*	*0.21%*	*(0.08-0.54)*		
Missing	*48*			*46*			*38*			*32*				
Fair-Poor Parent Mental Health Status													5.07[c] (3)	*0.167[c]*
No	2,008	*92.6%*	(90.4-94.3)	4,566	*93.5%*	(91.8-94.7)	3,199	*94.69%*	(92.2-96.3)	2,955	*95.24%*	(93.8-96.3)		
Yes (for at least 1 parent)	166	*7.4%*	(5.64-9.54)	344	*6.5%*	(5.22-8.15)	152	*5.31%*	(3.63-7.70)	199	*4.76%*	(3.67-6.15)		
Missing	*337*			*199*			*78*			*56*				
Mental Health Services in Past 12 Months													32.21[c] (6)	*0.900[c]*
Yes	85	*2.6%*	(1.77-3.93)	110	*1.9%*	(1.32-2.75)	64	*1.93%*	(1.02-3.60)	56	*1.62%*	(1.02-2.54)		
No, but needed to	34	*1.0%*	(0.54-1.74)	37	*1.2%*	(0.49-2.78)	18	*0.81%*	(0.36-1.76)	19	*1.03%*	(0.36-2.90)		
No	2,376	*96.4%*	(94.9-97.4)	4,947	*96.9%*	(95.3-97.9)	3,335	*97.26%*	(95.4-98.3)	3,125	*97.35%*	(95.6-98.3)		
Missing	*16*			*15*			*12*			*10*				
Psychotropic Medication Use in Past 12 Months													6.22[c] (3)	*0.101[c]*
No	2,422	*98.9%*	(98.1-99.3)	5,010	*99.1%*	(97.5-99.6)	3,379	*99.63%*	(99.1-99.8)	3,158	*99.76%*	(99.4-99.9)		
Yes	40	*1.1%*	(0.67-1.82)	27	*0.9%*	(0.32-2.49)	12	*0.37%*	(0.16-0.80)	8	*0.24%*	(0.09-0.58)		
Missing	*49*			*72*			*38*			*44*				

Abbreviations: NSCH, National Survey of Child Health; Freq., Frequency; CI, Confidence Interval; DF, Degrees of Freedom; %FPL, Percentage of the Federal Poverty Level;
[a] Wilson method 95% Confidence Interval for Percent
[b] Rao-Scott Chi-Square test
[c] Chi-square test excludes missing data

Table 3. Logistic Regression: Unadjusted Associations of Characteristics in Children Aged 2-5 and ADHD, NSCH 2016-2017

Characteristic		POR	Unadjusted 95% C.I. [a]	*p-value* [b]
Breastfed Ever				*<0.01*
(Unadjusted n=14,259)	No	1		
	Yes	0.35	(0.17-0.70)	
Breastfeeding Duration				0.07
(Unadjusted n=14,259)	No breastfeeding	1	--	
	0 - < 6 Months	0.52	(0.23-1.20)	
	6 - < 12 Months	0.19	(0.09-0.40)	
	≥ 12 Months	0.22	(0.09-0.58)	
Age:				*<0.01*
(Unadjusted n=14,259)	2	1		
	3	1.09	(0.28-4.32)	
	4	2.78	(0.76-10.1)	
	5	8.78	(2.31-33.4)	
Sex:				*<0.01*
(Unadjusted n=14,259)	Female	1		
	Male	3.28	(1.60-6.73)	
Race/Ethnicity				*0.03*
(Unadjusted n=14,259)	White	1		
	Black/African American	3.00	(1.16-7.73)	
	Hispanic	1.96	(0.87-4.42)	
	Other	0.80	(0.42-1.54)	
Household Poverty (% FPL)				*<0.01*
(Unadjusted n=14,259)	≥400%	1		
	200-399%	2.15	(1.14-4.07)	
	100-199%	3.22	(1.30-7.97)	
	< 100%	5.31	(2.67-10.5)	
Preterm Birth				*0.56*
(Unadjusted n=14,166)	No	1		
	Yes	1.22	(0.63-2.34)	
Household Tobacco Exposure				*<0.01*
(Unadjusted n=14,095)	No exposure	1		
	Outdoors only	2.58	(1.07-6.25)	
	Indoors	5.24	(2.13-12.9)	
Parent Mental Health is Fair/Poor				*<0.01*
(Unadjusted n=13,589)	No	1		
	Yes (at least 1 parent)	8.03	(3.37-19.1)	

Abbreviations: ADHD, Attention Deficit/Hyperactivity Disorder; NSCH, National Survey of Child Health; POR, Prevalence Odds Ratio; CI, Confidence Interval; %FPL, Percentage of the Federal Poverty Level;

[a] Wald 95% Confidence interval

[b] Test of the equality of cell means at the reference level of the other component main effects

Table 4. Adjusted[a] Prevalence Odds Ratios for Breastfeeding Duration and ADHD with Potential Effect Modifiers, Among Children Aged 2-5 Years, NSCH 2016-2017

Interaction with	**Breastfeeding Duration Prevalence Odds Ratios** 0 - <6M | No BF **POR**	**95% CI [b]**	6 - <12M | No BF **POR**	**95% CI [b]**	≥ 12M | No BF **POR**	**95% CI [b]**	**p-value [c]**
No Interaction (n=14,259)	0.77	*(0.34-1.74)*	0.35	*(0.15-0.82)*	0.52	*(0.18-1.49)*	
Sex (n=14,259)							0.27
Female	1.49	*(0.36-6.25)*	0.82	*(0.23-2.96)*	1.62	*(0.36-7.30)*	
Male	3.74	*(1.48-9.44)*	1.58	*(0.55-4.51)*	1.73	*(0.56-5.36)*	
Preterm Birth (n=13,439)							0.14
No	0.66	*(0.27-1.58)*	0.27	*(0.10-0.69)*	0.48	*(0.15-1.47)*	
Yes	1.13	*(0.37-3.43)*	0.91	*(0.27-3.08)*	0.47	*(0.05-4.14)*	

Abbreviations: ADHD, Attention Deficit/Hyperactivity Disorder; NSCH, National Survey of Child Health; M, Months; BF, breastfeeding; POR, Prevalence Odds Ratio; CI, Confidence Interval;

[a] Models adjusted for breastfeeding duration, age, sex, race, poverty, preterm birth, secondhand smoke, parent mental health

[b] Wald 95% confidence interval

[c] Homogeneity p-value is the Wald chi-square test for the significance of the combined cross-product terms

Table 5: Manual Backward Elimination of Main Effects Terms

Fully Adjusted Model
BREASTFEEDING DURATION ODDS RATIOS
n=13439

	FULLY ADJUSTED PORs
No breastfeeding	
0 - < 6 Months	0.77
6 - < 12 Months	0.35
≥ 12 Months	0.52

Main Effects Term Removed
PRETERM BIRTH
n=13516

	ADJUSTED PORs	% CHANGE
No breastfeeding		
0 - < 6 Months	0.76	-2%
6 - < 12 Months	0.34	-2%
≥ 12 Months	0.50	-2%

Remove or retain?
REMOVE

Main Effects Term Removed
RACE
n=13516

	ADJUSTED PORs	% CHANGE
No breastfeeding		
0 - < 6 Months	0.72	-7%
6 - < 12 Months	0.31	-11%
≥ 12 Months	0.46	-11%

Remove or retain?
RETAIN

Main Effects Term Removed
SMOKE
n=13589

	ADJUSTED PORs	% CHANGE
No breastfeeding		
0 - < 6 Months	0.72	-6%
6 - < 12 Months	0.32	-8%
≥ 12 Months	0.46	-11%

Remove or retain?
RETAIN

Main Effects Term Removed
PARENTMH
n=14095

	ADJUSTED PORs	% CHANGE
No breastfeeding		
0 - < 6 Months	0.78	1%
6 - < 12 Months	0.31	-10%
≥ 12 Months	0.44	-14%

Remove or retain?
RETAIN

Main Effects Term Removed
POVCAT
n=13516

	ADJUSTED PORs	% CHANGE
No breastfeeding		
0 - < 6 Months	0.73	-6%
6 - < 12 Months	0.30	-13%

Remove or retain?	≥ 12 Months	0.44	-14%
RETAIN			

Main Effects Term Removed		**ADJUSTED PORs**	**% CHANGE**
SEX	No breastfeeding		
n=13516	0 - < 6 Months	0.74	-4%
	6 - < 12 Months	0.36	5%
Remove or retain?	≥ 12 Months	0.48	-8%
REMOVE			

Main Effects Term Removed		**Adjusted PORs**	**% CHANGE**
AGE	No breastfeeding		
n=13516	0 - < 6 Months	0.79	2%
	6 - < 12 Months	0.38	11%
Remove or retain?	≥ 12 Months	0.45	-13%
RETAIN			

Table 6: Logistic Regression: Adjusted Models of Breastfeeding Duration and Odds of ADHD Among Children Aged 2-5 Years, NSCH 2016-2017

Model Variables		Fully Adjusted Model *(n=13,439)*			Final Model *(n=13,516)*		
		POR	**95% C.I.** [a]	***p-value*** [b]	**POR**	**95% C.I.** [a]	***p-value*** [b]
Breastfeeding Duration				*0.07*			*0.07*
	No breastfeeding	1			1		
	0 - < 6 Months	0.77	(0.34-1.74)		0.74	(0.33-1.66)	
	6 - < 12 Months	0.35	(0.15-0.82)		0.36	(0.16-0.84)	
	≥ 12 Months	0.52	(0.18-1.49)		0.48	(0.17-1.34)	
Age:				*<0.01*			*<0.01*
	2	1			1		
	3	1.02	(0.23-4.50)		1.06	(0.24-4.71)	
	4	2.40	(0.58-9.89)		2.50	(0.61-10.29)	
	5	5.90	(1.49-23.4)		6.00	(1.52-23.67)	
Sex:				*<0.01*			
	Female	1					
	Male	2.77	(1.34-5.70)				
Race/Ethnicity				*0.42*			*0.29*
	White	1			1		
	Black/African American	1.84	(0.76-4.46)		2.04	(0.81-5.10)	
	Hispanic	1.13	(0.53-2.41)		1.14	(0.54-2.39)	
	Other	0.79	(0.35-1.75)		0.73	(0.33-1.62)	
Household Poverty (%FPL)				*0.02*			*0.03*
	≥400%	1			1		
	200-399%	1.85	(0.90-3.79)		1.68	(0.82-3.43)	
	100-199%	1.30	(0.58-2.95)		1.26	(0.57-2.78)	
	< 100%	2.85	(1.47-5.51)		2.70	(1.41-5.18)	
Preterm Birth				*0.68*			
	No	1					
	Yes	1.16	(0.56-2.43)				
Household Tobacco Exposure				*0.14*			*0.18*

	No exposure	1			1		
	Outdoors only	1.48	(0.74-2.96)		1.56	(0.78-3.13)	
	Indoors	2.49	(0.95-6.50)		2.26	(0.83-6.11)	
Parent Mental Health is Fair/Poor				*<0.01*			*<0.01*
	No	1			1		
	Yes (at least 1 parent)	5.52	(2.73-11.18)		5.76	(2.88-11.52)	

Abbreviations: ADHD, Attention Deficit/Hyperactivity Disorder; NSCH, National Survey of Child Health; POR, Prevalence Odds Ratio; CI, Confidence Interval; %FPL, Percentage of the Federal Poverty Level;

[a] Wilson method 95% confidence interval

[b] Test of the equality of cell means at the reference level of the other component main effects

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