Development and Psychopathology (2020), **32**, 791–802
doi:10.1017/S0954579419001135

CAMBRIDGE UNIVERSITY PRESS

Regular Article

Early life predictors of attention deficit/hyperactivity disorder symptomatology profiles from early through middle childhood

Michael T. Willoughby[1], Jason Williams[1,2], W. Roger Mills-Koonce[3] and Clancy B. Blair[4]

[1]Education & Workforce Development, RTI International, Research Triangle Park, NC, USA; [2]Substance Use, Prevention, Evaluation and Research Program, RTI International, Research Triangle Park, NC, USA; [3]School of Education, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA and [4]Department of Applied Psychology, New York University, New York, NY, USA

Abstract

This study used repeated measures data to identify developmental profiles of elevated risk for ADHD (i.e., six or more inattentive and/or hyperactive-impulsive symptoms), with an interest in the age at which ADHD risk first emerged. Risk factors that were measured across the first 3 years of life were used to predict profile membership. Participants included 1,173 children who were drawn from the Family Life Project, an ongoing longitudinal study of children's development in low-income, nonmetropolitan communities. Four heuristic profiles of ADHD risk were identified. Approximately two thirds of children never exhibited elevated risk for ADHD. The remaining children were characterized by early childhood onset and persistent risk (5%), early childhood limited risk (10%), and middle childhood onset risk (19%). Pregnancy and delivery complications and harsh-intrusive caregiving behaviors operated as general risk for all ADHD profiles. Parental history of ADHD was uniquely predictive of early onset and persistent ADHD risk, and low primary caregiver education was uniquely predictive of early childhood limited ADHD risk. Results are discussed with respect to how changes to the age of onset criterion for ADHD in DSM5 may affect etiological research and the need for developmental models of ADHD that inform ADHD symptom persistence and desistance.

Keywords: age-of-onset criterion, attention deficit hyperactivity disorder, etiology, latent class analysis

(Received 11 September 2018; accepted 6 May 2019)

Attention deficit/hyperactivity disorder (ADHD) has long been conceptualized as an early onset disorder. Beginning with DSM-5 (American Psychiatric Association, 2013), children must have exhibited several ADHD symptoms before age 12. The rationale for expanding the age-of-onset criterion from age 7 to age 12 was twofold. First, a systematic review of 31 studies concluded that children who exhibited clinically elevated levels of ADHD symptoms were similarly impaired across multiple domains of functioning, irrespective of whether their symptoms emerged before age 7 versus age 12 (Kieling et al., 2010). Second, increasing the age-of-onset criterion also facilitated diagnostic decision-making for clinicians who worked with adolescents and adults who were often unable to definitively document ADHD symptom onset before age 7 (Barkley & Biederman, 1997). A potentially unintended consequence of increasing the age-of-onset criterion for ADHD was to increase etiologic heterogeneity of the disorder. Although children who exhibit elevated ADHD symptomatology are typically impaired in multiple domains of current functioning, irrespective of whether their symptoms emerged before age 7 versus age 12, it is not clear that developmental precursors of ADHD symptoms differ depending on the age at which symptoms first emerged. That is, similarities in children's current ADHD symptomatology may obscure important differences in the etiological processes that contributed to those symptoms.

Questions that focus on the age of ADHD symptom onset are best addressed using studies that involve prospective longitudinal designs, which overcome the challenges inherent in obtaining reliable retrospective reports of the age of ADHD symptom onset. Numerous prospective longitudinal studies have documented profiles of ADHD symptomatology. One set of studies has focused on profiles of ADHD symptoms that first emerged in early childhood (see O'Neill, Rajendran, Mahbubani, & Halperin, 2017 for a review of recent studies). Whereas some children exhibit an early childhood limited profile of ADHD symptoms (i.e., early symptom onset that dissipates during the transition to school), others exhibit an early childhood persistent profile (i.e., early symptom onset that persists into elementary school). These studies are consistent with long-standing notions of ADHD as an early onset disorder, but they also highlight individual differences in symptom persistence.

Another set of studies has focused on profiles of ADHD symptoms across early and middle childhood, generally including children 5–12 years of age. Four profiles of ADHD symptomatology have been described, including stable low, stable high, increasing, and decreasing symptom groups (Pingault et al., 2011; Robbers et al., 2011; Romano, Tremblay, Farhat, & Côté, 2006; Sasser,

Author for Correspondence: Michael T. Willoughby, RTI International, Post Office Box 12194, 3040 Cornwallis Road, Research Triangle Park, NC 27709-2194. E-mail: mwilloughby@rti.org

Cite this article: Willoughby MT, Williams J, Mills-Koonce WR, Blair CB (2020). Early life predictors of attention deficit/hyperactivity disorder symptomatology profiles from early through middle childhood. *Development and Psychopathology* **32**, 791–802. https://doi.org/10.1017/S0954579419001135

Beekman, & Bierman, 2015). Notably, these studies used large unselected (and in some cases representative) samples, which guard against the complications that result from trying to make generalizable inferences from clinic-referred samples. These studies have repeatedly identified a group of children who exhibit elevated levels of ADHD symptomatology for the first time during elementary school, which is consistent with the modification of the ADHD age-of-onset criterion from 7 to 12 years of age in the DSM-5. The first goal of this study was to empirically identify profiles of children who exhibited elevated ADHD symptomatology between age 3 (arguably the youngest age at which ADHD can be reliably assessed) and age 12 (the upper limit of the DSM-5 age-of-onset criterion).

Many studies that focused on developmental profiles of ADHD have considered the predictive validity of profile membership (e.g., see Pingault, Côté, Galéra, et al., 2013; Pingault, Côté, Lacourse, et al., 2013; Pingault et al., 2014; Pingault et al., 2011) or sought to identify ongoing factors that distinguish persistent from desisting symptom profiles (e.g., see Rajendran, O'Neill, Marks, & Halperin, 2015; Rajendran et al., 2013; Sasser, Beekman, et al., 2015; Sasser, Kalvin, & Bierman, 2016). Fewer studies have tested whether early life risk factors are differentially associated with developmental profiles of ADHD symptomatology. The second goal of this study was to test whether early life risk factors for ADHD were differentially related to membership in ADHD symptom profile groups.

Early life risk factors for ADHD span the prenatal period (e.g., pregnancy complications), the perinatal period (e.g., low birth weight, delivery complications), and the early postnatal period (e.g., household poverty, psychosocial adversity) (Das Banerjee, Middleton, & Faraone, 2007; Froehlich et al., 2011; Russell, Ford, Rosenberg, & Kelly, 2014; Sciberras, Mulraney, Silva, & Coghill, 2017; Thapar, Cooper, Jefferies, & Stergiakouli, 2012). These risk factors are assumed to interact with genetic susceptibility and/or to initiate epigenetic processes that lead to disruptions to neural and cognitive development that underlie ADHD (Nigg, 2012a, 2012b; Thapar, Cooper, Eyre, & Langley, 2013). Virtually all studies that have investigated early life risk factors for ADHD have ignored variations in the age of ADHD symptom onset.

The idea that etiological risk factors may vary as a function of the age of onset of ADHD symptoms has been raised with respect to distinguishing child- versus adult-onset cases of ADHD (Shaw & Polanczyk, 2017). Here, we are raising that same question with respect to children who meet the DSM-5 age of onset criterion. Many risk factors that are predictive of ADHD are evident early in life (e.g., family history of ADHD, low birth weight, pregnancy and delivery complications). It stands to reason that these risk factors would be particularly prominent among children with symptoms that emerge in early childhood. There is growing evidence that socioeconomic risk factors (e.g., household income, caregiver education) are also related to ADHD (Russell et al., 2014). Socioeconomic risk factors are a proxy for a host of macroenvironmental (e.g., neighborhood safety and cohesion; school quality) and microenvironmental experiences (e.g., household chaos; caregiving environment) that are relatively stable over time (Evans, 2004; Russell et al., 2014). As such, it is less clear whether socioeconomic risks would be differentially related to the ADHD profiles that included earlier versus later onset.

In addition to early life risk factors, including socioeconomic risks, we also tested whether variations in parent–child interaction quality were predictive of ADHD symptom profile groups. Historically, most of the research on parent–child interaction quality in ADHD has involved children or adolescents who were already diagnosed with ADHD. These studies documented that parents of children with ADHD exhibited more harsh-intrusive and coercive behaviors, and fewer warm and sensitive behaviors, toward their children relative to parents with typically developing children. Moreover, these behaviors were characteristic of a broader set of family stressors among families with ADHD youth (Johnston & Mash, 2001). The conventional wisdom is that children with ADHD evoke many of these nonoptimal parenting behaviors. Indeed, parenting behaviors have improved when children were medicated for ADHD behavior (Barkley, Karlsson, Strzelecki, & Murphy, 1984; Danforth, Anderson, Barkley, & Stokes, 1991).

Our questions differed from most previous studies in that we were interested in testing whether early life parenting behaviors contributed to emergence of ADHD symptomatology. Two studies by Sroufe and colleagues provided the first indication that caregiving behaviors in the first 3 years of life were prospectively associated with subsequent child distractibility and teacher-rated hyperactivity in elementary school (Carlson, Jacobvitz, & Sroufe, 1995; Jacobvitz & Sroufe, 1987). Specifically, maternal intrusiveness at 6 months of age and maternal overstimulating behavior at 3.5 years of age each uniquely predicted teacher reports of ADHD behaviors at 11 years of age, beyond the effects of earlier observed child distractibility. Notably, although earlier hyperactivity best predicted later ADHD behaviors, the early maternal caregiving behaviors predicted early hyperactivity and the maintenance of hyperactivity into the elementary school years. At around the same time, Campbell and colleagues also reported that family stress and insensitive parenting behaviors were common among "hard to manage" boys at age 3 years and predicted persistent behavioral difficulties (Campbell, 1995; Campbell, Breaux, Ewing, & Szumowski, 1986; Campbell, March, Pierce, Ewing, & Szumowski, 1991). Although neither the Sroufe nor Campbell studies had comprehensive measures of ADHD symptomatology, these studies were consistent with the idea that early caregiving behaviors contribute to the early emergence of multiple aspects of externalizing behaviors, including ADHD (Campbell, Shaw, & Gilliom, 2000; Patterson, DeGarmo, & Knutson, 2000). Nevertheless, these ideas have received surprisingly little attention in the recent literature, apart from studies that have linked children's early life experience of institutional care to later risk for ADHD behaviors and related neurocognitive functioning (Baptista, Belsky, Mesquita, & Soares, 2017; Kreppner, O'Connor, Rutter, & the English and Romanian Adoptees Study Team, 2001; Stevens et al., 2008; Tibu et al., 2016).

ADHD researchers have long distinguished between inattentive and hyperactive-impulsive symptomatology, including for purposes of subtyping youth to reduce heterogeneity within the disorder (Willcutt et al., 2012). However, longitudinal studies demonstrated that ADHD subtypes were unstable across time (Lahey, Pelham, Loney, Lee, & Willcutt, 2005; Todd et al., 2008). As such, beginning in DSM-5, children are no longer subtyped according to differences in inattentive and hyperactive-impulsive symptomatology. Instead, variations in inattentive and hyperactive-impulsive symptomatology are used to describe the current 'presentation' of the disorder, with an understanding that an individual's symptom presentation may vary across time (American Psychiatric Association, 2013). At the same time, a growing number of psychometrically oriented studies have questioned the merits of distinguishing inattentive and hyperactive-impulsive symptomatology (Arias, Ponce, Martinez-Molina, Arias, & Nunez, 2016; Sturm, McCracken, & Cai, 2017; Toplak et al., 2009; Ullebo, Breivik, Gillberg, Lundervold, & Posserud,

https://doi.org/10.1017/S0954579419001135 Published online by Cambridge University Press

2012; Wagner et al., 2016). These studies have consistently emphasized that a general propensity for ADHD underlies inattentive and hyperactive-impulsive symptoms and that little reliable variation remains in either dimension (especially hyperactive-impulsivity) after accounting for their shared variation. For these reasons, in this study, we focused on age-related variations in children's overall risk for ADHD, without consideration of inattentive and hyperactive-impulsive domains separately. Moreover, to better approximate diagnostic decision making, we defined ADHD risk as instances in which a child was reported to exhibit six or more inattentive and/or six or more hyperactive-impulsive symptoms. Developmental profiles of subthreshold levels of symptomatology were not of interest.

In sum, the first goal of our study was to characterize developmental profiles of elevated risk for ADHD in children from age 3 years through fifth grade. Consistent with previous studies, we hypothesized that four ADHD symptom profile groups would be evident: early childhood onset and persistent ADHD risk, early childhood limited ADHD risk, middle childhood onset ADHD risk, and no risk. The second goal was to test the unique contributions of a range of risk factors, all measured from birth to age 3 years, in the prediction of ADHD symptom profile groups. We hypothesized that pre- and perinatal risk factors would be more strongly associated with an early onset of ADHD risk, while socioeconomic risk factors would be equally strongly associated with ADHD risk, irrespective of the time of onset. Given the lack of directly comparable studies (especially those with comparable measurement of ADHD outcomes and relevant covariates), we considered the tests of parenting behaviors as risk factors to be exploratory, with sensitive and harsh-intrusive behaviors being considered as both main effects and possible moderators of early life risk factors.

Method

Participants and Procedures

The Family Life Project (FLP) was designed to study young children and their families who lived in two of the four major geographical areas of the United States with high poverty rates (Dill, 2001). Specifically, three counties in Eastern North Carolina (NC) and three counties in Central Pennsylvania (PA) were selected to be indicative of the Black South and Appalachia, respectively. The FLP adopted a developmental epidemiological design in which complex sampling procedures were employed to recruit a representative sample of 1,292 children whose families resided in one of the six counties at the time of the child's birth. Low-income families in both states and, in NC, African American families were oversampled; however, using weighted analyses, all of our inferences generalize back to the six-county study area as though participants were selected using simple random sampling. Detailed information on the study design and sampling plan were presented elsewhere (Vernon-Feagans, Cox, & the Family Life Project Key Investigators, 2013).

Of the 1,292 children whose families were enrolled in the main study, 1,173 were included in the current study if they had at least one (of the available 10) parent and/or teacher rating of ADHD symptoms. We retained children with as few as one assessment to avoid introducing selection bias (i.e., skewing the sample towards families who were able and interested in more assessments). Among participating children ($N = 1{,}173$), the mean number of available ADHD ratings was 8.1 and the median was 9 (4.4% of children had 1–2 ratings, 5.5% had 3–4 ratings, 6.7% had 5–6 ratings, 24.4% had 7–8 ratings, and 59.0% had 9–10 ratings). Participating children and families did not differ from nonparticipating children and families with respect to recruitment state (40% vs. 43% from Pennsylvania, $p = .53$), recruitment into the poor strata (78% vs. 75% poor, $p = .45$), child race (43% vs. 36% African American, $p = .14$), child sex (50% vs. 55% male, $p = .29$), primary caregiver education (80% vs. 78% had high school degree, $p = .56$), or (when applicable) secondary caregiver education (83% vs. 80% had high school degree, $p = .41$).

Following hospital screening, participants who were selected and agreed to participate were formally enrolled into the study by way of completion of a home visit when the target child was approximately 2 months old. Participating families were invited to participate in seven additional home visits when their child was 6, 15, 24, 36, 48, and 60 months old, and when their child was in first grade. At each visit, parents and children completed a variety of standardized tasks, observational procedures, interviews, and questionnaires. School visits occurred when children were in preschool, kindergarten through third grade, and fifth grade. Teacher ratings were collected in the spring of each year.

The reading subscale of the Kaufman Functional Academic Skills Test (K-FAST; Kaufman & Kaufman, 1994) was administered at the first home visit (and readministered if/when the primary caregiver associated with a target child changed). The reading subscale from the K-FAST correlates with the reading components of the Woodcock-McGrew-Werder Mini-Battery of Achievement and the Wide Range Achievement Test-3 (Flanagan, McGrew, Abramowitz, Lehner, Untiedt, Berger, & Armstrong, 1997); moreover, Flanagan and colleagues indicated that the K-FAST is most effective for determining an individual's ability to function outside of school. For our purposes, the K-FAST was administered to primary caregivers by trained data collectors, and a score of 16 was the reference point for determining if caregivers had the option of reading questionnaires on their own. Anyone scoring above a normed score of 16 (corresponding to a 16-year-old reading level) had the option of reading independently or having the items read for them by the home visitor. Anyone who scored 16 or below was not given the option for independent reading and had items read aloud to them. To promote the confidentiality of their responses when the items were read aloud, the participants had a keypad that they used to enter data so that their responses were recorded without the data collector being able to observer their answers. Based on these data, 19.2% of the primary respondents were not allowed to read items independently and instead had items read aloud to them.

Measures

Outcome: Attention deficit/hyperactivity disorder (ADHD) symptom ratings. Each of the 18 DSM symptoms for ADHD were rated on a four-point Likert scale (0 = *not at all*, 1 = *just a little*, 2 = *pretty much*, 3 = *very much*). Parent-rated data were available from the age 3, 4, and 5-year, as well as the first-grade, home visits. Teacher-rated data were available when children were in preschool, kindergarten, and first, second, third, and fifth grades. The confounding of informant and child age is a consequence of testing our questions in a study that was not designed specifically to investigate questions related to ADHD onset or persistence. Following convention for the use of this instrument and others like it (e.g., Pelham, Gnagy, Greenslade, & Milich, 1992), items that were rated as either "pretty much" or "very much" were considered an approximation for symptom endorsement. Following

https://doi.org/10.1017/S0954579419001135 Published online by Cambridge University Press

DSM conventions, we defined elevated risk for ADHD as six or more of inattentive and/or hyperactive-impulsive symptoms at each assessment (parent and teacher reports were considered separately).

Risk factor: Pregnancy and delivery complications. At the 2-month home visit, biological mothers of target children completed the pregnancy and delivery module of the Missouri Assessment of Genetics Interview for Children (Reich, Todd, Joyner, Neuman, & Heath, 2003). Reich and colleagues reported good short- and long-term reliability for self-reports of pregnancy behaviors using this instrument (Reich et al., 2003). For the Family Life Project, the biological mothers reported on the presence of a range of complications of pregnancy (e.g., heavy bleeding, excessive vomiting, emotional problems, high blood pressure) and delivery (e.g., induced labor, breech birth, evidence of fetal distress, surgery), which were summed to form an overall index of risk.

Risk factor: Low birth weight. As part of the 2-month interview, mothers reported the target child's birth weight in pounds and ounces. This weight was converted to grams, and children weighing less than or equal to 2,500 g were designated low birth weight.

Risk factor: Biological parental history of attention deficit/hyperactivity disorder (ADHD). A single item was asked to establish whether either the biological mother or father of the target child had a childhood history of ADHD (i.e., "Has a doctor or other medical professional ever told you [him/her] that you [s/he] have [has] Attention Deficit Disorder?"). When the respondent was the biological mother of the target child, she answered the question about herself and the child's biological father. Likewise, when the respondent was the biological father of the target child, he answered the question about himself and the child's biological mother. When the respondent was not a biological parent of the target child, s/he answered the question with reference to the child's biological parents. Consistent with our previous work involving this sample (Willoughby, Gottfredson, Stifter, & Family Life Project Investigators, 2017), mother and father history was combined into a single index to accommodate the low base rates of these variables when considered separately.

Risk factor: Low educational attainment. As part of the 2-month interview, primary caregivers self-reported their educational attainment. A dummy variable was used to index those who had not completed a high school degree or general education diploma at the time of study recruitment.

Risk factor: Household poverty. Following the approach of Hanson, McLanahan, and Thomson (1997), household income was tallied for anyone who resided in the household, not just those related by blood, marriage, or adoption. Individuals were considered coresidents if they spent three or more nights per week in the household. Using this information, the total annual household income was divided by the yearly federal poverty threshold for a family of that size and composition to create an income/needs ratio. Given the highly stable nature of household income in this sample (Vernon-Feagans et al., 2013), the average income/needs ratio across the 6-, 15-, 24-, and 36-month assessments was used to index household poverty.

Risk factor: Observed parenting behaviors. Ten-minute videos that recorded parent–child interactions at 6, 15, 24, and 36 months were observed by trained and reliable coders and rated globally on the following dimensions of parenting behavior: sensitivity, detachment, intrusiveness, stimulation, positive regard, negative regard, and animation (Cox & Crnic, 2002; NICHD Early Child Care Research Network, 1999). Using Likert-type scales, coders gave a single rating for each code based on the overall quality of the entire interaction. Ratings ranged from 1 (*not at all characteristic*) to 5 (*highly characteristic*) at the 6- and 15-month assessments and from 1 to 7 at the 24- and 36-month assessments (these scores were rescaled to a 1–5 range for the current analyses). At least 30% of all interactions at each assessment were double coded for reliability; differences in scores were resolved between coders to create a final score for double-coded videos. Reliability was calculated using the intraclass correlation for the independent ratings made for the overlapping coding assignments. Reliability across subscales and composites was high (intraclass correlations > 0.80 for all subscales).

Individual codes were combined to form *sensitive parenting* and *harsh-intrusive parenting* composites at each assessment (Mills-Koonce et al., 2015). The sensitive parenting composite comprised the mean of sensitivity (level of responsiveness and support offered to the child contingent on the child's needs), positive regard (positive feelings and warmth directed toward the child), stimulation (developmentally appropriate language use), animation (level of facial and tonal affect), and detachment (reverse scored; degree to which the primary caregiver was disengaged). The harsh-intrusive parenting composite comprised the mean of intrusiveness (controlling, parent-agenda driven behaviors) and negative regard (hostile verbal and physical treatment of the child).

Building on previous research involving this sample (Mills-Koonce et al., 2016), the sensitivity and harsh-intrusive composites from each assessment (6, 15, 24, and 36 months) were used as indicators in a two-factor confirmatory factor analytic model that represented aggregate measures of observed sensitive and harsh-intrusive parenting behaviors from the 6- through 36-month assessments. The model was specified such that residual correlations were estimated between each pair of sensitive and harsh-intrusive indicators at each assessment (e.g., 6-month sensitivity was correlated with 6-month harsh-intrusiveness). This model fit the observed data well, χ^2 (15) = 77.9, $p < .0001$, root mean squared error of approximation (RMSEA) = 0.059, 90% confidence interval (CI) [0.046, 0.072], and comparative fit index (CFI) = 0.97. All the standardized factor loadings were of large magnitude (λs = 0.48–0.84) and statistically significant (ps < .001). Factor score estimates of aggregate levels of sensitive and harsh-intrusive parenting across the first 3 years of life were used as predictors of ADHD symptom profile groups.

Analytic Strategy

The first objective of this study was to characterize developmental profiles of elevated ADHD symptomatology from age 3 years through fifth grade. This was accomplished through the estimation of a series of conditional latent class analysis models. The ten dichotomous indicators of ADHD risk were the indicators. We incorporated two dichotomous indicators of whether a child was ever medicated for behavioral problems or ever had an individualized education plan (IEP) across the study period as covariates into the latent class model (i.e., we estimated *conditional* latent class models). We used summary variables because the rates of medication use and IEP status were small at individual assessments. We

https://doi.org/10.1017/S0954579419001135 Published online by Cambridge University Press

were motivated to include these predictors because they are ecologically valid indicators of ADHD-related impairment and because the incorporation of covariates into latent class models improves estimation and the assignment of children into classes (see e.g., Wurpts & Geiser, 2014; Lubke & Muthén, 2007). We fit a sequence of models in which the number of classes started at one and increased until model fit statistics (i.e., Bayesian information criterion; Lo-Mendell-Rubin likelihood ratio test) indicated the optimal number of classes had been reached (see Nylund, Asparouhov, & Muthén, 2008 for a rationale).

We used a three-step procedure to regress latent class membership onto early life risk factors (Asparouhov & Muthén, 2014). This approach involved estimating a multinomial regression of latent class membership onto predictors while acknowledging uncertainty in individual latent class membership and ensuring that class assignment did not change due to the inclusion of predictors. Initially, a series of univariate models were estimated (each risk factor considered alone). Next, a multivariate model was estimated (all risk factors considered together as main effects). Finally, we extended the multivariate model to include a series of two-way interactions (i.e., Each Risk Factor × Two Dimensions of Parenting). We culled nonsignificant interactions within each class and re-estimated the model as appropriate. Full information maximum likelihood estimation was used throughout to accommodate missing data.

Results

Descriptive Statistics

Children exhibited an average of three to four ADHD symptoms at each of the 10 assessments ($Ms = 2.4–4.2$; see Table 1). The standard deviation of symptom counts exceeded the mean values at each assessment, which was consistent with right-skewed distributions (most children exhibited no or few symptoms, but the full range of symptoms was present at every assessment). Although the rates of medication use for behavior problems were low at individual assessments, 18% of children were medicated at one or more assessments for behavior problems. Moreover, 24% of children had an IEP at some point during the study period.

With respect to risk factors, 8% of children met the threshold for low birth weight, and 6% had a biological parent with a history of ADHD. Primary caregivers reported an average of three pregnancy and delivery complications ($M = 2.8$, $SD = 2.0$). Consistent with the sampling design, 20% of primary caregivers did not have a high school diploma at the start of the study, and most household were considered low income (aggregated household income to needs ratio $M = 1.9$, $SD = 1.6$). Factor score estimates of observed sensitive and harsh-intrusive parenting behaviors were scaled to $M = 0$ and $SD = 1$, with substantial variation evident for both (see Table 1).

Latent Class Analysis

Children who exhibited six or more inattentive and/or hyperactive-impulsive symptoms at any assessment were defined as at risk for ADHD. These 10 ADHD risk indicators (i.e., one indicator per informant and assessment occasion) were used in a series of conditional latent class analysis models, in which we extracted one through five classes. The standard and sample-size-adjusted Bayesian information criteria were both minimized at the four-class solution, whereas the Lo-Mendell-Rubin test indicated two classes (see Table 2).

The four-class solution was substantively meaningful (see Figure 1). Most children were characterized as having no risk for ADHD (65%). However, approximately 5% of children were characterized by an early childhood onset and persistently elevated risk for ADHD, 10% by an early childhood limited risk for ADHD, and 19% by a middle childhood onset risk for ADHD. Compared with children in the no risk class, children in the early childhood persistent risk class (odds ratio [OR] = 35.3, $p < .001$), the early childhood limited class (OR = 7.4, $p < .001$), and the middle childhood onset classes (OR = 11.1, $p < .001$) were all more likely to have been medicated for behavior problems. Similarly, compared with children in the no risk class, children in the early childhood persistent risk class (OR = 6.4, $p < .001$) and the middle childhood onset class (OR = 3.4, $p < .001$), but not the early childhood limited class (OR = 2.1, $p = .11$), were more likely to have had an IEP at some point during the study period.

Predicting Latent Class Membership

We used a three-step approach to regress latent class membership on the full set of risk factors. This model is consistent with a multinomial regression in which probabilistic latent class membership is the outcome. We began by considering each risk factor separately (univariate models). We subsequently considered the full set of risk factors together, as well as testing whether observed parenting factors moderated any of the risk factors (multivariate models).

Univariate Prediction

As summarized in Table 3, children in the early childhood persistent class differed from their peers in the no-risk class on every risk factor considered. That is, when considered separately, low birth weight, more pregnancy and delivery complications, lower household income, parental history of ADHD, lower caregiver education, and less sensitive and more harsh-intrusive caregiving were all related to increased risk for membership in the early childhood onset relative to the no-risk class. Similarly, children in the early childhood limited and middle childhood onset classes also differed from children in the no-risk class on every risk factor except for low birth weight and parental history of ADHD (i.e., low birth weight and parental history of ADHD were only significantly related to early onset persistent risk class).

To more completely understand the contribution of individual risk factors, we also considered comparisons between the early onset limited and middle childhood onset groups with reference to the early childhood persistent group. None of the individual risk factors distinguished children in the early childhood limited versus early childhood persistent classes. Moreover, pregnancy and delivery complications (odds ratio [OR] = 0.79, $p = .002$) and parental history of ADHD (OR = 0.20, $p = .006$) were the only risk factors that distinguished children in the middle childhood onset versus the early childhood persistent classes (see rightmost columns of Table 3).

Multiple Variable Prediction

As summarized in Table 4, when all risk factors were considered simultaneously, low birth weight, household income-to-needs ratio, and caregiver sensitivity were not uniquely related to membership in any of the ADHD classes, irrespective of the reference

https://doi.org/10.1017/S0954579419001135 Published online by Cambridge University Press

Table 1. Unweighted descriptive statistics

Risk Factor	*N*	%	Range
Parental history of ADHD	1,153	6	0–100
Low birthweight	1,171	8	0–100
PC education (high school degree)	1,173	80	0–100
Medicated for behavior problems (ever)	1,075	18	0–100
Individualized education plan (ever)	1,075	24	0–100
	N	*M (SD)*	Range
Pregnancy and delivery complications	1,171	2.8 (2.0)	0–12
Income/needs ratio•	1,146	1.9 (1.6)	0–16.5
PC sensitivity (factor score)•	1,159	0.0 (1.0)	−2.8–2.8
PC harsh-intrusiveness (factor score)•	1,159	0.0 (1.0)	−2.7–3.4
PC reported ADHD symptoms (age 3)	1,096	4.2 (4.7)	0–18
PC reported ADHD symptoms (age 4)	1,062	3.7 (4.4)	0–18
PC reported ADHD symptoms (age 5)	1,066	3.1 (4.3)	0–18
PC reported ADHD symptoms (1st grade)	1,086	3.2 (4.5)	0–18
Teacher reported ADHD symptoms (PreK)	816	2.4 (4.0)	0–18
Teacher reported ADHD symptoms (K)	984	3.2 (4.9)	0–18
Teacher reported ADHD symptoms (1st grade)	929	3.6 (5.2)	0–18
Teacher reported ADHD symptoms (2nd grade)	928	3.6 (5.1)	0–18
Teacher reported ADHD symptoms (3rd grade)	848	3.3 (4.7)	0–18
Teacher reported ADHD symptoms (5th grade)	703	2.9 (4.5)	0–18

Note: PC = primary caregiver; PreK = prekindergarten; K = kindergarten; • denotes values aggregated across 6- to 36-month assessments.

Table 2. Latent class analysis of parent- and teacher-reported ADHD symptomatology

Class	BIC	aBIC	LMR LR
1	9844.09	9799.62	—
2	8691.58	8602.64	0.000
3	8576.54	8446.31	0.232
4	**8559.68**	**8388.16**	0.929
5	8624.23	8411.42	0.901

Note: BIC = Bayesian information criterion; aBIC = sample size adjusted Bayesian information criterion; LMR LR = Lo-Mendell-Rubin likelihood ratio test *p* value.

group. Pregnancy and delivery complications (OR = 1.34, $p < .001$), parental history of ADHD (OR = 3.38, $p = .009$), and early harsh-intrusive parenting behaviors (OR = 2.02, $p = .005$) were all uniquely predictive of membership in the early childhood persistent class versus the no risk class. Pregnancy and delivery complications (OR = 1.20, $p = .036$) and low caregiver education (OR = 0.65, $p < .001$) were uniquely predictive of membership in the early childhood limited class relative to the no risk class (the contribution of early harsh-intrusive parenting behaviors approached significance, OR = 1.57, $p = .053$). Similarly, pregnancy and delivery complications (OR = 1.12, $p = .046$), low caregiver education (OR = 0.84, $p = .049$), and early harsh-intrusive parenting behaviors (OR = 1.53, $p = .019$) were uniquely predictive of membership in the middle childhood onset relative to the no risk class.

Next, we tested whether any of the risk factors differentiated the early childhood limited or middle childhood onset classes from the early childhood persistent class. Low caregiver education (OR = 0.69, $p = .032$) was the only unique predictor of membership in the early childhood limited class versus early childhood persistent class (children in the early childhood limited group had caregivers with lower education than those in the early childhood persistent group). Pregnancy and delivery complications (OR = 0.84, $p = .034$) and parental history of ADHD (OR = 0.22, $p =$ 012) were the only unique predictors of membership in the middle childhood onset class versus early childhood persistent class.

A final model tested whether either sensitive or harsh-intrusive caregiving behaviors moderated (i.e., augmented in the case of harsh-intrusive and mitigated in the case of sensitive behaviors) the influence of any of the risk factors on class membership. This involved extending the previous model to include two, two-way interactions for each risk factor (e.g., Sensitive × Family History, Harsh-Intrusive × Family History). None of these interactions was statistically significant after the nonsignificant terms had been removed.

Discussion

This study documented variations in the age of onset and persistence of risk for ADHD across early and middle childhood. Like previous studies, most children never exhibited elevated ADHD symptomatology. However, approximately one third of children exhibited elevated ADHD symptomatology during early childhood (i.e., age 3–6 years), middle childhood (i.e., age 7–12

https://doi.org/10.1017/S0954579419001135 Published online by Cambridge University Press

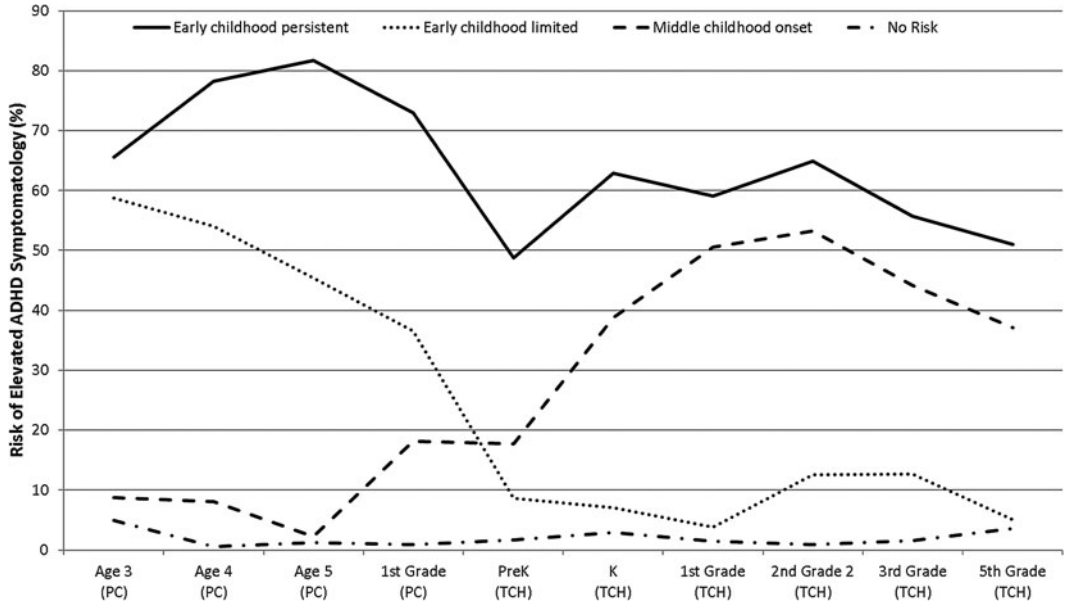

Figure 1. Developmental Profiles of caregiver- and teacher-reported ADHD symptoms from age 3 through fifth grade. *Note*: PC = primary caregiver informant; TCH = teacher informant.

Table 3. Univariate prediction of ADHD latent class membership (predictors considered separately)

	Class (No risk class is reference)			Class (EC-Persistent is reference)	
	EC-Persistent OR (95% CI)	EC-Limited OR (95% CI)	MC-Onset OR (95% CI)	EC-Limited OR (95% CI)	MC-Onset OR (95% CI)
Low birth weight	**3.9 (1.68, 9.05)****	1.15 (0.35, 3.84)	1.9 (0.92, 3.93)	0.30 (0.07, 1.29)	0.49 (0.18, 1.31)
PDCs	**1.43 (1.26, 1.64)*****	**1.19 (1.03, 1.38)***	**1.13 (1.02, 1.26)***	0.83 (0.69, 1.00)	**0.79 (0.68, 0.92)****
Income/needs ratio•	**0.70 (0.49, 1.00)***	**0.49 (0.26, 0.93)***	**0.56 (0.41, 0.76)*****	0.71 (0.32, 1.58)	0.80 (0.49, 1.30)
Parental ADHD	**6.07 (2.59, 14.22)*****	2.26 (0.78, 6.57)	1.23 (0.47, 3.18)	0.37 (0.10, 1.36)	**0.20 (0.06, 0.63)****
PC education (HS)	**0.68 (0.54, 0.86)****	**0.52 (0.40, 0.66)*****	**0.67 (0.58, 0.77)*****	0.76 (0.55, 1.04)	0.98 (0.77, 1.25)
PC sensitivity•	**0.39 (0.26, 0.57)*****	**0.37 (0.15, 0.90)*****	**0.39 (0.30, 0.50)*****	0.95 (0.59, 1.55)	1.01 (0.65, 1.56)
PC harsh-intrusiveness•	**3.24 (2.32, 4.52)*****	**2.93 (2.07, 4.15)*****	**2.74 (2.07, 3.62)*****	0.90 (0.60, 1.35)	0.85 (0.60, 1.19)

Note: $N = 1{,}173$; PDCs = Pregnancy and delivery complications; PC = primary caregiver; EC-Limited = early childhood limited class; MC-Onset = middle childhood onset class. $^{*}p \leq .05$ $^{**}p \leq .01$ $^{***}p \leq .001$.

years), or both periods. A subset of pre- and perinatal, socioeconomic, and early parenting risk factors was predictive of membership in ADHD classes. However, the specific patterns of prediction only partially supported our hypotheses. These results are elaborated in turn.

We identified three heuristic profiles of ADHD risk. Approximately 5% of children were characterized by elevated risk for ADHD that was consistently evident from age 3 through age 12. This profile is consistent with "classic" characterizations of ADHD and its prevalence (e.g., Palfrey, Levine, Walker, & Sullivan, 1985). Approximately 10% of children were characterized by elevated risk for ADHD that was limited to parent reports when children were 3–5 years old. This profile underscores the developmental transience of even clinically elevated ADHD symptoms in young children and conforms to one of the hypothesized early pathways involving ADHD risk (see Sonuga-Barke, Auerbach, Campbell, Daley, & Thompson, 2005). Finally, approximately 20% of children were characterized by elevated risk for ADHD that was limited to teacher reports from first through fifth grade, although parental reports indicated somewhat elevated rates of ADHD risk in first grade.

We were surprised by the large number of children whose ADHD symptoms were elevated in middle childhood. A recent study that used a nationally representative sample of adolescents demonstrated that the expanded age-of-onset criterion resulted in a 46% increase in the proportion of children meeting diagnostic criteria for ADHD, from 7.38% to 10.84% (Vande Voort, He, Jameson, & Merikangas, 2014). Children with a later onset of ADHD symptoms in that study did not differ from their peers with earlier onset symptoms in terms of overall ADHD severity or comorbidity, but they were more likely to be from families that had lower income or were members of an ethnic minority. The relatively large numbers of children in the middle childhood onset group in the current study may have reflected the

https://doi.org/10.1017/S0954579419001135 Published online by Cambridge University Press

Table 4. Multiple predictor model of ADHD class membership (predictors considered simultaneously)

	Class (No risk class is reference)			Class (EC-Persistent is reference)	
	EC-Persistent OR (95% CI)	EC-Limited OR (95% CI)	MC-Onset OR (95% CI)	EC-Limited OR (95% CI)	MC-Onset OR (95% CI)
Low birth weight	1.58 (0.62, 4.05)	0.55 (0.18, 1.64)	0.92 (0.43, 1.95)	0.35 (0.09, 1.28)	0.58 (0.20, 1.69)
PDCs	**1.34 (1.14, 1.57)*** **	**1.20 (1.01, 1.42)***	**1.12 (1.00, 1.25)***	0.89 (0.72, 1.11)	**0.84 (0.71, 0.99)***
Income/needs ratio	1.02 (0.78, 1.34)	0.85 (0.52, 1.39)	0.79 (0.57, 1.10)	0.83 (0.79, 0.88)	0.77 (0.51, 1.18)
Parental ADHD	**3.38 (1.36, 8.37)****	1.22 (0.47, 3.18)	0.76 (0.29, 1.96)	0.36 (0.10, 1.25)	**0.22 (0.07, 0.72)***
PC education (HS)	0.93 (0.72, 1.21)	**0.65 (0.51, 0.82)*** **	**0.84 (0.71, 1.00)***	**0.69 (0.5, 0.97)***	0.91 (0.68, 1.21)
PC sensitivity	0.70 (0.37, 1.31)	0.72 (0.47, 1.09)	0.70 (0.48, 1.02)	1.03 (0.47, 2.26)	1.00 (0.48, 2.05)
PC harsh-intrusiveness	**2.02 (1.24, 3.3)****	1.57 (0.99, 2.48)	**1.53 (1.07, 2.17)***	0.77 (0.42, 1.42)	0.75 (0.45, 1.27)

Note: $N = 1{,}173$; PDCs = Pregnancy and delivery complications; PC = primary caregiver; EC-Limited = early childhood limited class; MC-Onset = middle childhood onset class. $^{*}p \leq .05$ $^{**}p \leq .01$ $^{***}p \leq .001$.

oversampling of low-income and African American families from lower income communities. The reasons for elevated rates of teacher-reported ADHD symptoms among long income and/or minority families is an area in need of more systematic research (Miller, Nigg, & Miller, 2009).

An overarching objective of this study was to consider whether early life risk factors for ADHD were differentially related to ADHD profile classes. We hypothesized that whereas pre- and perinatal risks would be predictive of early onset and persistent ADHD, socioeconomic risk factors would operate as general factors for ADHD that emerged at all ages. Our hypotheses were only partially supported. With respect to pre- and perinatal risks, in support of our hypotheses, positive parental history of ADHD was associated with increased risk for being in the early onset persistent class (relative to no risk) and decreased risk for being in the middle childhood onset class (relative to early onset persistent risk). Although parental history did not differentiate early onset persistent and early onset limited classes, this may have been to low statistical power to detect differences between these relatively small classes (we note that the point estimate was consistent with the idea that a positive parental history of ADHD was less common in the early childhood limited versus persistent classes). However, counter to our hypotheses, pregnancy and delivery complications were elevated in all ADHD classes (not unique to early childhood persistent symptoms). Conversely, low birth weight was not uniquely related to membership in any ADHD class. The lack of unique effects for low birth weight is likely due to the inclusion of more sensitive measures in the model (i.e., continuous measure of pregnancy and delivery complications). Indeed, when low birth weight was considered alone, it was elevated among children in the early childhood persistent group.

With respect to socioeconomic risks, although low household income was associated with increased likelihood of all ADHD classes when considered alone, it was not uniquely related to any ADHD class membership in the presence of other covariates. Poverty is a marker variable for a range of risks, including less sensitive and more harsh-intrusive parenting behaviors (Bradley, Corwyn, McAdoo, & García Coll, 2001; McLeod & Shanahan, 1993; McLoyd, 1998). Previous studies involving this sample have documented that poverty undermines children's behavioral and cognitive outcomes through its influence on caregiving behaviors (Mills-Koonce et al., 2016; Vernon-Feagans et al., 2012; Vernon-Feagans et al., 2016). Household income may not have uniquely predicted ADHD classes due to the inclusion of caregiving behaviors as covariates. This is consistent with the results of a nationally representative study of Canadian children in which household poverty was not uniquely related to ADHD risk in the presence of measures of parenting behaviors (Romano et al., 2006).

Low caregiver education was associated with increased likelihood of all ADHD classes when considered alone. However, in the presence of other predictors, low caregiver education was most consistently associated with membership in the early childhood limited class (low caregiver education uniquely distinguished children in the early onset limited class from both no risk and early childhood persistent classes). The unique contribution of low caregiver education to membership in the early childhood limited class is interesting because this class was identified exclusively defined by caregiver reports of ADHD risk. One possible interpretation of this finding is that some caregivers who have low educational attainment may have developmentally inappropriate expectations about normative behaviors for young children, which results in higher endorsements of ADHD behaviors than would otherwise be the case.

The unique effect of harsh-intrusive caregiving in the prediction of all ADHD classes is broadly consistent with findings from Carlson and colleagues (1995), who reported early intrusive caregiving and later overstimulation as predictors of early and consolidated ADHD behaviors. The association between early (i.e., birth–age 3 years) harsh and intrusive parenting and later (i.e., age 3–12 years) ADHD behaviors may be related to the disrupted development of child attention abilities when caregivers undermine children's self-directed active engagement with their environments. Intrusive caregiving involves the unnecessary imposition of a parental agenda onto the ongoing activity of the child. As such, harsh-intrusive and controlling or overstimulating parents can limit their children's normative experiences of sustained attention to objects or activities that are otherwise positively reinforcing the attention. To what degree this parent–child dynamic ultimately undermines attentional capacities and how that is related to later ADHD is not fully known; however, recent research has identified associations between harsh and intrusive caregiving and poor sustained attention (Graziano,

https://doi.org/10.1017/S0954579419001135 Published online by Cambridge University Press

Calkins, & Keane, 2011; Gueron-Sela et al., 2018) and has suggested that the association between intrusive caregiving in infancy and later attention capacity is partially mediated by neurological differences in children measured by left frontal electroencephalography power (Swingler, Perry, Calkins, & Bell, 2017). Although compelling, an equally tenable explanation of our results is that harsh-intrusive parenting was evoked by challenging behaviors in infancy and toddlerhood. Experimental designs in which early parenting behaviors are modified are essential for resolving these questions. Notably, we found no evidence that caregiving behaviors moderated the effects of early risk factors on the emergence of ADHD behaviors. Moreover, early harsh-intrusive caregiving behaviors were better characterized as a general risk for ADHD, not specific to the age of onset or persistence.

The results of this study have at least three implications for research and clinical practice. First, studies of ADHD that enroll school-aged samples risk mixing subpopulations of ADHD youth who have comparable levels of current ADHD symptomatology but who differ with respect to the age of onset of those symptoms. In this sample, parental history of ADHD, which is often used as a proxy for genetic risk factors, was uniquely associated with the early childhood persistent profile class. Our results raise the prospect that tests of Gene × Environment predictions of ADHD may benefit from defining youth based both on ADHD symptom level and age of onset (e.g., some Gene × Environment associations may be stronger for children with symptoms that emerged in early versus middle childhood). This idea is countered by our limited measurement of family history of ADHD. In the future, we hope to have detailed genetic information on children's genetic risk for ADHD (i.e., polygenic risk scores). When these data become available, we will be in a better opportunity to test this speculation.

Second, among those children who exhibited elevated ADHD symptomatology in early childhood, only a minority continued to demonstrate elevated risk for ADHD into middle childhood. This outcome differed from clinical samples, where most children with early onset ADHD symptoms have continued to exhibit elevated ADHD into middle childhood (e.g., Bunte, Schoemaker, Hessen, van der Heijden, & Matthys, 2014; Lahey et al., 2016). The rates of early onset ADHD symptom persistence and desistance may have implications for treatment planning. Although clinical best practice advocates for parent management training as a first line of treatment and pharmacotherapy as a second line of treatment of ADHD for preschool-aged children, many clinicians do not appear to follow this practice (Chung, Tchaconas, Meryash, & Adesman, 2016). In 2011–2012, approximately 40% of preschool-aged children who were diagnosed with ADHD in the United States were medicated for their behavior (Danielson et al., 2017). In our sample, 24% of children in the early childhood limited group were medicated at some point during the study period for behavior problems. The transient nature of even clinically elevated levels of ADHD symptoms in early childhood raises serious questions about the overuse of medication in young children. An important direction for future research involves the identification of dynamic predictors that can predict which individual children with elevated ADHD in early childhood will have symptoms that persist or desist into middle childhood. Similar challenges face investigators who wish to predict which children in middle childhood with ADHD will have symptoms that persist or desist during the transition to adolescence and adulthood (see Franke et al., 2018 for a selective review). Developmentally informed models of ADHD will be essential for identifying the experiences and mechanisms that explain persistence versus desistance of ADHD symptoms at key transition periods.

Third, this study represents one of the largest efforts to date to test whether caregiving behaviors that were observed across the first 3 years of life were uniquely associated with ADHD risk. Most studies of parenting and ADHD have focused on considerably older children who were already diagnosed. Although early caregiving behaviors conveyed risk for ADHD that was independent of more commonly used pre- and perinatal and socioeconomic risk factors, there was little specificity in prediction (harsh-intrusive caregiving was a predictor all three ADHD classes relative to the no risk class but did not meaningfully differ across classes). Moreover, neither sensitive nor harsh-intrusive caregiving behaviors moderated (augmented or mitigated) the effects of other risk factors. Studies that experimentally manipulate early life parenting behaviors among children at high risk for ADHD are needed. The results of these studies have implications for whether and what role parenting behaviors play in preventing or mitigating the burden of subsequent ADHD (Sonuga-Barke & Halperin, 2010).

The study had at least five limitations. First, the Family Life Project was not designed to be a prospective study of ADHD. As such, we were limited to the timing and types of data that were available. Our early childhood reports of ADHD were derived entirely from parents, while our middle childhood reports of ADHD were derived mostly from teachers (first grade was the only assessment period with combined parent and teacher reports of ADHD). This near complete confounding of informant with assessment period may have undermined our developmental interpretation of study results. We are collecting parent-reported ADHD data, using structured psychiatric interviews, for these children in middle school and high school. These future data will help to adjudicate whether the ADHD classes are best conceived of as developmental phenomena or an artifact of the confounding of informant with assessment period. Second, ADHD profile classes were defined based on the presence of clinically elevated levels of ADHD symptoms—not on impairments related to ADHD symptoms. Although this situation is true of most ADHD research, it limits the translational utility of ADHD profile classes as proxies for clinical diagnosis. Third, even though our study began with 1,292 families and retained 1,173 children for ADHD symptom profile classes, the numbers of children who were characterized by different ADHD profiles were modest (5% to 19% of the sample). Although small subsamples are inevitable for studies that use community samples to test questions about ADHD, the relatively smaller number of children in the ADHD classes undoubtedly limited our statistical power to detect small but potentially meaningful differences between classes. Fourth, this study involved a representative sample of children from six low-wealth, nonmetropolitan counties in eastern North Carolina and central Pennsylvania. It was not a representative study of all children living in poverty. Moreover, it is unclear how these results could be generalized to suburban or urban settings. Fifth, we primarily tested the unique contributions of risk factors as main effects (the exception was the consideration of caregiving behaviors as moderators). In the future, it will be important to consider early life risk factors in conjunction with genetic risks to more fully inform questions regarding the different etiologies of ADHD (Nigg, Nikolas, & Burt, 2010).

Broadly considered, the results of this study underscore the value of using prospective longitudinal data to characterize both the severity and timing of ADHD symptomatology. Although

https://doi.org/10.1017/S0954579419001135 Published online by Cambridge University Press

the decision to expand the ADHD age-of-onset criterion in the DSM-5 from 7 to 12 years had many merits, it may have had the unintended consequence of obscuring risk factors that are associated with differential timing of ADHD symptom onset, which may ultimately influence thinking about treatment development. Large-scale community-based studies that oversample children who are at risk for ADHD, that involve prospective longitudinal data collection, that include neurodevelopmental outcomes from infancy forward, and that include a range of genetic and experiential risk factors for ADHD will be essential for delineating multiple developmental pathways into and out of the disorder.

Acknowledgments. The Family Life Project Key Investigators in the second phase of the study included Lynne Vernon-Feagans, Martha Cox, Clancy Blair, Peg Burchinal, Linda Burton, Keith Crnic, Patricia Garrett-Peters, Mark Greenberg, Roger Mills-Koonce, and Michael Willoughby.

Financial Support. Support for this research was provided by the Eunice Kennedy Shriver National Institute of Child Health and Human Development grant P01 HD39667, with co-funding from the National Institute on Drug Abuse, and more recently from the National Institute of Health Environmental Influences on Child Health Outcomes (1UG3OD023332-01).

References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders, fifth edition (DSM-5)*. Washington, DC: Author.

Arias, V. B., Ponce, F. P., Martinez-Molina, A., Arias, B., & Nunez, D. (2016). General and specific attention-deficit/hyperactivity disorder factors of children 4 to 6 years of age: An exploratory structural equation modeling approach to assessing symptom multidimensionality. *Journal of Abnormal Psychology*, *125*, 125–137. doi:10.1037/abn0000115

Asparouhov, T., & Muthén, B. (2014). Auxiliary variables in mixture modeling: Three-step approaches using Mplus. *Structural Equation Modeling*, *21*, 329–341. https://doi.org/10.1080/10705511.2014.915181

Baptista, J., Belsky, J., Mesquita, A., & Soares, I. (2017). Serotonin transporter polymorphism moderates the effects of caregiver intrusiveness on ADHD symptoms among institutionalized preschoolers. *European Child & Adolescent Psychiatry*, *26*, 303–313. https://doi.org/10.1007/s00787-016-0890-x

Barkley, R. A., & Biederman, J. (1997). Toward a broader definition of the age-of-onset criterion for attention-deficit hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*, 1204–1210. https://doi.org/10.1097/00004583-199709000-00012

Barkley, R. A., Karlsson, J., Strzelecki, E., & Murphy, J. V. (1984). Effects of age and Ritalin dosage on the mother–child interactions of hyperactive children. *Journal of Consulting and Clinical Psychology*, *52*, 750–758. https://doi.org/10.1037/0022-006X.52.5.750

Bradley, R. H., Corwyn, R. F., McAdoo, H. P., & García Coll, C. (2001). The home environments of children in the United States part I: Variations by age, ethnicity, and poverty status. *Child Development*, *72*, 1844–1867. https://doi.org/10.1111/1467-8624.t01-1-00382

Bunte, T. L., Schoemaker, K., Hessen, D. J., van der Heijden, P. G., & Matthys, W. (2014). Stability and change of ODD, CD and ADHD diagnosis in referred preschool children. *Journal of Abnormal Child Psychology*, *42*, 1213–1224. https://doi.org/10.1007/s10802-014-9869-6

Campbell, S. B. (1995). Behavior problems in preschool children: A review of recent research. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *36*, 113–149. https://doi.org/10.1111/j.1469-7610.1995.tb01657.x

Campbell, S. B., Breaux, A. M., Ewing, L. J., & Szumowski, E. K. (1986). Correlates and predictors of hyperactivity and aggression: A longitudinal study of parent-referred problem preschoolers. *Journal of Abnormal Child Psychology*, *14*, 217–234. https://doi.org/10.1007/BF00915442

Campbell, S. B., March, C. L., Pierce, E. W., Ewing, L. J., & Szumowski, E. K. (1991). Hard-to-manage preschool boys: Family context and the stability of externalizing behavior. *Journal of Abnormal Child Psychology*, *19*, 301–318. https://doi.org/10.1007/BF00911233

Campbell, S. B., Shaw, D. S., & Gilliom, M. (2000). Early externalizing behavior problems: Toddlers and preschoolers at risk for later maladjustment. *Development and Psychopathology*, *12*, 467–488. https://doi.org/10.1017/S0954579400003114

Carlson, E. A., Jacobvitz, D., & Sroufe, L. A. (1995). A developmental investigation of inattentiveness and hyperactivity. *Child Development*, *66*, 37–54. https://doi.org/10.2307/1131189

Chung, J., Tchaconas, A., Meryash, D., & Adesman, A. (2016). Treatment of attention-deficit/hyperactivity disorder in preschool-age children: Child and adolescent psychiatrists' adherence to clinical practice guidelines. *Journal of Child and Adolescent Psychopharmacology*, *26*, 335–343. https://doi.org/10.1089/cap.2015.0108

Cox, M. J., & Crnic, K. A. (2002). *Qualitative ratings for parent–child interaction at 3–12 months of age*. Unpublished manuscript. Chapel Hill, NC.

Danforth, J. S., Anderson, L. P., Barkley, R. A., & Stokes, T. F. (1991). Observations of parent–child interactions with hyperactive children: Research and clinical implications. *Clinical Psychology Review*, *11*, 703–727. https://doi.org/10.1016/0272-7358(91)90127-G

Danielson, M. L., Visser, S. N., Gleason, M. M., Peacock, G., Claussen, A. H., & Blumberg, S. J. (2017). A national profile of attention-deficit hyperactivity disorder diagnosis and treatment among US children aged 2 to 5 years. *Journal of Developmental and Behavioral Pediatrics*, *38*, 455–464. https://doi.org/10.1097/DBP.0000000000000477

Das Banerjee, T., Middleton, F., & Faraone, S. V. (2007). Environmental risk factors for attention-deficit hyperactivity disorder. *Acta Paediatrica (Oslo, Norway)*, *96*, 1269–1274. https://doi.org/10.1111/j.1651-2227.2007.00430.x

Dill, B. T. (2001). Rediscovering rural America. In J. R. Blau (Ed.), *Blackwell companion to sociology* (pp. 196–210). Malden: Blackwell.

Evans, G. W. (2004). The environment of childhood poverty. *The American Psychologist*, *59*, 77–92. https://doi.org/10.1037/0003-066X.59.2.77

Flanagan, D.P., McGrew, K.S., Abramowitz, E., Lehner, L., Untiedt, S., Berger, D., Armstrong, H. (1997). Improvement in academic screening instruments? A concurrent validity investigation of the K-FAST, MBA, and WRAT-3. *Journal of Psychoeducational Assessment*, *15*, 99–112. https://doi.org/10.1177/073428299701500201

Franke, B., Michelini, G., Asherson, P., Banaschewski, T., Bilbow, A. , Buitelaar, J. K., … Reif, A. (2018). Live fast, die young? A review on the developmental trajectories of ADHD across the lifespan. *European Neuropharmacology*, *28*, 1059–1088.

Froehlich, T. E., Anixt, J. S., Loe, I. M., Chirdkiatgumchai, V., Kuan, L., & Gilman, R. C. (2011). Update on environmental risk factors for attention-deficit/hyperactivity disorder. *Current Psychiatry Reports*, *13*, 333–344. https://doi.org/10.1007/s11920-011-0221-3

Graziano, P. A., Calkins, S. D., & Keane, S. P. (2011). Sustained attention development during the toddlerhood to preschool period: Associations with toddlers' emotion regulation strategies and maternal behavior. *Infant and Child Development*, *20*, 389–408. https://doi.org/10.1002/icd.731

Gueron-Sela, N., Camerota, M., Willoughby, M. T., Vernon-Feagans, L., & Cox, M. J., & the Family Life Project Key Investigators. (2018). Maternal depressive symptoms, mother-child interactions, and children's executive function. *Developmental Psychology*, *54*, 71–82. https://doi.org/10.1037/dev0000389

Hanson, T. L., McLanahan, S., & Thomson, E. (1997). Economic resources, parental practices, and children's well-being. In G. Duncan & J. Brooks-Gunn (Eds.), *Consequences of growing up poor* (pp. 190–221). New York: Russell Sage Foundation.

Jacobvitz, D., & Sroufe, L. A. (1987). The early caregiver-child relationship and attention-deficit disorder with hyperactivity in kindergarten: A prospective study. *Child Development*, *58*, 1496–1504.

Johnston, C., & Mash, E. J. (2001). Families of children with attention-deficit/hyperactivity disorder: Review and recommendations for future research. *Clinical Child and Family Psychology Review*, *4*, 183–207. https://doi.org/10.1023/A:1017592030434

Kaufman, A. S., & Kaufman, N. L. (1994). *Kaufman Functional Academic Skills Test (K-FAST)*. Circle Pines, MN: American Guidance Service.

Kieling, C., Kieling, R. R., Rohde, L. A., Frick, P. J., Moffitt, T., Nigg, J. T., … Castellanos, F. X. (2010). The age at onset of attention deficit hyperactivity disorder. *The American Journal of Psychiatry*, *167*, 14–16. https://doi.org/10.1176/appi.ajp.2009.09060796

Kreppner, J. M., O'Connor, T. G., & Rutter, M., & the English and Romanian Adoptees Study Team. (2001). Can inattention/overactivity be an institutional deprivation syndrome? *Journal of Abnormal Child Psychology*, *29*, 513–528. https://doi.org/10.1023/A:1012229209190

Lahey, B. B., Lee, S. S., Sibley, M. H., Applegate, B., Molina, B. S. G., & Pelham, W. E. (2016). Predictors of adolescent outcomes among 4–6-year-old children with attention-deficit/hyperactivity disorder. *Journal of Abnormal Psychology*, *125*, 168–181. https://doi.org/10.1037/abn0000086

Lahey, B. B., Pelham, W. E., Loney, J., Lee, S. S., & Willcutt, E. (2005). Instability of the DSM-IV subtypes of ADHD from preschool through elementary school. *Archives of General Psychiatry*, *62*, 896–902.

Lubke, G., and Muthén, B. O. (2007). Performance of factor mixture models as a function of model size, covariate effects, and class-specific parameters. *Structural Equation Modeling 14*, 26–47. doi:10.1207/s15328007sem1401_2

McLeod, J., & Shanahan, M. (1993). Poverty, parenting, and children's mental health. *American Sociological Review*, *58*, 351–366. https://doi.org/10.2307/2095905

McLoyd, V. C. (1998). Socioeconomic disadvantage and child development. *The American Psychologist*, *53*, 185–204. https://doi.org/10.1037/0003-066X.53.2.185

Miller, T. W., Nigg, J. T., & Miller, R. L. (2009). Attention deficit hyperactivity disorder in African American children: What can be concluded from the past ten years? *Clinical Psychology Review*, *29*, 77–86. doi:10.1016/j.cpr.2008.10.001

Mills-Koonce, W. R., Willoughby, M. T., Garrett-Peters, P., Wagner, N., & Vernon-Feagans, L., & the Family Life Project Key Investigators. (2016). The interplay among socioeconomic status, household chaos, and parenting in the prediction of child conduct problems and callous-unemotional behaviors. *Development and Psychopathology*, *28*, 757–771. https://doi.org/10.1017/S0954579416000298

Mills-Koonce, W. R., Willoughby, M. T., Zvara, B., Barnett, M., Gustafsson, H., & Cox, M. J., & the Family Life Project Key Investigators. (2015). Mothers' and fathers' sensitivity and children's cognitive development in low-income, rural families. *Journal of Applied Developmental Psychology*, *38*, 1–10. https://doi.org/10.1016/j.appdev.2015.01.001

NICHD [U.S. National Institute for Child Health and Human Development] Early Child Care Research Network. (1999). Child care and mother-child interaction in the first 3 years of life. *Developmental Psychology*, *35*, 1399–1413. https://doi.org/10.1037/0012-1649.35.6.1399

Nigg, J. (2012a). Environment, developmental origins, and attention-deficit/hyperactivity disorder [Editorial]. *Archives of Pediatrics and Adolescent Medicine*, *166*, 387–388. https://doi.org/10.1001/archpediatrics.2011.905

Nigg, J. T. (2012b). Future directions in ADHD etiology research. *Journal of Clinical Child and Adolescent Psychology*, *41*, 524–533. https://doi.org/10.1080/15374416.2012.686870

Nigg, J., Nikolas, M., & Burt, S. A. (2010). Measured gene-by-environment interaction in relation to attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *49*, 863–873. https://doi.org/10.1016/j.jaac.2010.01.025

Nylund, K. L., Asparouhov, T., & Muthén, B. O. (2008). Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. *Structural Equation Modeling: A Multidisciplinary Journal*, *14*, 535–569. https://doi.org/10.1080/10705510701575396

O'Neill, S., Rajendran, K., Mahbubani, S. M., & Halperin, J. M. (2017). Preschool predictors of ADHD symptoms and impairment during childhood and adolescence. *Current Psychiatry Reports*, *19*, 95. https://doi.org/10.1007/s11920-017-0853-z

Palfrey, J. S., Levine, M. D., Walker, D. K., & Sullivan, M. (1985). The emergence of attention deficits in early childhood: A prospective study. *Journal of Developmental and Behavioral Pediatrics*, *6*, 339–348. https://doi.org/10.1097/00004703-198512000-00004

Patterson, G. R., DeGarmo, D. S., & Knutson, N. (2000). Hyperactive and antisocial behaviors: Comorbid or two points in the same process? *Development and Psychopathology*, *12*, 91–106. https://doi.org/10.1017/S0954579400001061

Pelham Jr., W. E., Gnagy, E. M., Greenslade, K. E., & Milich, R. (1992). Teacher ratings of DSM-III-R symptoms for the disruptive behavior disorders. *Journal of the American Academy of Child and Adolescent Psychiatry*, *31*, 210–218. https://doi.org/10.1097/00004583-199203000-00006

Pingault, J. B., Côté, S. M., Galéra, C., Genolini, C., Falissard, B., Vitaro, F., & Tremblay, R. E. (2013). Childhood trajectories of inattention, hyperactivity and oppositional behaviors and prediction of substance abuse/dependence: A 15-year longitudinal population-based study. *Molecular Psychiatry*, *18*, 806–812. https://doi.org/10.1038/mp.2012.87

Pingault, J. B., Côté, S. M., Lacourse, E., Galéra, C., Vitaro, F., & Tremblay, R. E. (2013). Childhood hyperactivity, physical aggression and criminality: A 19-year prospective population-based study. *PLoS One*, *8*, e62594. https://doi.org/10.1371/journal.pone.0062594

Pingault, J. B., Côté, S. M., Vitaro, F., Falissard, B., Genolini, C., & Tremblay, R. E. (2014). The developmental course of childhood inattention symptoms uniquely predicts educational attainment: A 16-year longitudinal study. *Psychiatry Research*, *219*, 707–709. https://doi.org/10.1016/j.psychres.2014.06.022

Pingault, J. B., Tremblay, R. E., Vitaro, F., Carbonneau, R., Genolini, C., Falissard, B., & Côté, S. M. (2011). Childhood trajectories of inattention and hyperactivity and prediction of educational attainment in early adulthood: A 16-year longitudinal population-based study. *The American Journal of Psychiatry*, *168*, 1164–1170. https://doi.org/10.1176/appi.ajp.2011.10121732

Rajendran, K., O'Neill, S., Marks, D. J., & Halperin, J. M. (2015). Latent profile analysis of neuropsychological measures to determine preschoolers' risk for ADHD. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *56*, 958–965. https://doi.org/10.1111/jcpp.12434

Rajendran, K., Trampush, J. W., Rindskopf, D., Marks, D. J., O'Neill, S., & Halperin, J. M. (2013). Association between variation in neuropsychological development and trajectory of ADHD severity in early childhood. *The American Journal of Psychiatry*, *170*, 1205–1211. https://doi.org/10.1176/appi.ajp.2012.12101360

Reich, W., Todd, R. D., Joyner, C. A., Neuman, R. J., & Heath, A. C. (2003). Reliability and stability of mothers' reports about their pregnancies with twins. *Twin Research*, *6*, 85–88. https://doi.org/10.1375/136905203321536209

Robbers, S. C., van Oort, F. V., Polderman, T. J., Bartels, M., Boomsma, D. I., Verhulst, F. C., … Huizink, A. C. (2011). Trajectories of CBCL attention problems in childhood. *European Child and Adolescent Psychiatry*, *20*, 419–427. https://doi.org/10.1007/s00787-011-0194-0

Romano, E., Tremblay, R. E., Farhat, A., & Côté, S. (2006). Development and prediction of hyperactive symptoms from 2 to 7 years in a population-based sample. *Pediatrics*, *117*, 2101–2110. https://doi.org/10.1542/peds.2005-0651

Russell, G., Ford, T., Rosenberg, R., & Kelly, S. (2014). The association of attention deficit hyperactivity disorder with socioeconomic disadvantage: Alternative explanations and evidence. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *55*, 436–445. https://doi.org/10.1111/jcpp.12170

Sasser, T. R., Beekman, C. R., & Bierman, K. L. (2015). Preschool executive functions, single-parent status, and school quality predict diverging trajectories of classroom inattention in elementary school. *Development and Psychopathology*, *27*, 681–693. https://doi.org/10.1017/S0954579414000947

Sasser, T. R., Kalvin, C. B., & Bierman, K. L. (2016). Developmental trajectories of clinically significant attention-deficit/hyperactivity disorder (ADHD) symptoms from grade 3 through 12 in a high-risk sample: Predictors and outcomes. *Journal of Abnormal Psychology*, *125*, 207–219. https://doi.org/10.1037/abn0000112

Sciberras, E., Mulraney, M., Silva, D., & Coghill, D. (2017). Prenatal risk factors and the etiology of ADHD: Review of existing evidence. *Current Psychiatry Reports*, *19*, 1. https://doi.org/10.1007/s11920-017-0753-2

Shaw, P., & Polanczyk, G. V. (2017). Combining epidemiological and neurobiological perspectives to characterize the lifetime trajectories of ADHD. *European Child and Adolescent Psychiatry*, *26*, 139–141. https://doi.org/10.1007/s00787-017-0944-8

Sonuga-Barke, E. J., Auerbach, J., Campbell, S. B., Daley, D., & Thompson, M. (2005). Varieties of preschool hyperactivity: Multiple pathways from risk to

disorder. *Developmental Science*, *8*, 141–150. https://doi.org/10.1111/j.1467-7687.2005.00401.x

Sonuga-Barke, E. J. S., & Halperin, J. M. (2010). Developmental phenotypes and causal pathways in attention deficit/hyperactivity disorder: Potential targets for early intervention? *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *51*, 368–389. https://doi.org/10.1111/j.1469-7610.2009.02195.x

Stevens, S. E., Sonuga-Barke, E. J., Kreppner, J. M., Beckett, C., Castle, J., Colvert, E., … Rutter, M. (2008). Inattention/overactivity following early severe institutional deprivation: Presentation and associations in early adolescence. *Journal of Abnormal Child Psychology*, *36*, 385–398. https://doi.org/10.1007/s10802-007-9185-5

Sturm, A., McCracken, J. T., & Cai, L. (2017). Evaluating the Hierarchical Structure of ADHD Symptoms and Invariance Across Age and Gender. *Assessment*. *26*, 508–523. doi:10.1177/1073191117714559

Swingler, M. M., Perry, N. B., Calkins, S. D., & Bell, M. A. (2017). Maternal behavior predicts infant neurophysiological and behavioral attention processes in the first year. *Developmental Psychology*, *53*, 13–27. https://doi.org/10.1037/dev0000187

Thapar, A., Cooper, M., Eyre, O., & Langley, K. (2013). Practitioner review: What have we learnt about the causes of ADHD? *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *54*, 3–16. https://doi.org/10.1111/j.1469-7610.2012.02611.x

Thapar, A., Cooper, M., Jefferies, R., & Stergiakouli, E. (2012). What causes attention deficit hyperactivity disorder? *Archives of Disease in Childhood*, *97*, 260–265. https://doi.org/10.1136/archdischild-2011-300482

Tibu, F., Sheridan, M. A., McLaughlin, K. A., Nelson, C. A., Fox, N. A., & Zeanah, C. H. (2016). Reduced working memory mediates the link between early institutional rearing and symptoms of ADHD at 12 years. *Frontiers in Psychology*, *7*, Article 1850, 1–9. https://doi.org/10.3389/fpsyg.2016.01850

Todd, R. D., Huang, H., Todorov, A. A., Neuman, R. J., Reiersen, A. M., Henderson, C. A., & Reich, W. C. (2008). Predictors of stability of attention-deficit/hyperactivity disorder subtypes from childhood to young adulthood. *Journal of the American Academy of Child and Adolescent Psychiatry*, *47*, 76–85. doi:10.1097/chi.0b013e31815a6aca

Toplak, M. E., Pitch, A., Flora, D. B., Iwenofu, L., Ghelani, K., Jain, U., & Tannock, R. (2009). The unity and diversity of inattention and hyperactivity/impulsivity in ADHD: Evidence for a general factor with separable dimensions. *Journal of Abnormal Child Psychology*, *37*, 1137–1150. doi:10.1007/s10802-009-9336-y

Ullebo, A. K., Breivik, K., Gillberg, C., Lundervold, A. J., & Posserud, M. B. (2012). The factor structure of ADHD in a general population of primary school children. *Journal of Child Psychology and Psychiatry*, *53*, 927–936. doi:10.1111/j.1469-7610.2012.02549.x

Vande Voort, J. L., He, J. P., Jameson, N. D., & Merikangas, K. R. (2014). Impact of the DSM-5 attention-deficit/hyperactivity disorder age-of-onset criterion in the US adolescent population. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*, 736–744. https://doi.org/10.1016/j.jaac.2014.03.005

Vernon-Feagans, L., & Cox, M., & the Family Life Project Key Investigators (Eds.). (2013). *The Family Life Project: An epidemiological and developmental study of young children living in poor rural communities*. Special issue of *Monographs of the Society for Research in Child Development*, 78, 1–23. https://doi.org/10.1111/mono.12047

Vernon-Feagans, L., Garrett-Peters, P., Willoughby, M., Mills-Koonce, R., & the Family Life Project Key Investigators. (2012). Chaos, poverty, and parenting: Predictors of early language development. *Early Childhood Research Quarterly*, *27*, 339–351. https://doi.org/10.1016/j.ecresq.2011.11.001

Vernon-Feagans, L., Willoughby, M., & Garrett-Peters, P., & the Family Life Project Key Investigators. (2016). Predictors of behavioral regulation in kindergarten: Household chaos, parenting, and early executive functions. *Developmental Psychology*, *52*, 430–441. https://doi.org/10.1037/dev0000087

Wagner, F., Martel, M. M., Cogo-Moreira, H., Maia, C. R., Pan, P. M., Rohde, L. A., & Salum, G. A. (2016). Attention-deficit/hyperactivity disorder dimensionality: The reliable 'g' and the elusive 's' dimensions. *European Child & Adolescent Psychiatry*, *25*, 83–90. doi:10.1007/s00787-015-0709-1

Willcutt, E. G., Nigg, J. T., Pennington, B. F., Solanto, M. V., Rohde, L. A., Tannock, R., … Lahey, B. B. (2012). Validity of DSM-IV attention deficit/hyperactivity disorder symptom dimensions and subtypes. *Journal of Abnormal Psychology*, *121*, 991–1010. doi:10.1037/a0027347

Willoughby, M. T., Gottfredson, N. C., Stifter, C. A., & Family Life Project Investigators. (2017). Observed temperament from ages 6 to 36 months predicts parent- and teacher-reported attention-deficit/hyperactivity systems in fist grade. *Development and Psychopathology*, *29*, 107–120.

Wurpts, I. C., & Geiser, C. (2014). Is adding more indicators to a latent class analysis beneficial or detrimental? Results of a Monte-Carlo study. *Frontiers in Psychology*, *5*. doi:10.3389/fpsyg.2014.00920