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Research Review: A systematic review and meta-analysis of infant and toddler temperament as predictors of childhood attention-deficit/hyperactivity disorder

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Background: Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder with onset as early as preschool and impairment across the lifespan. Temperament factors, specifically those that theoretically map onto ADHD symptoms, may be early markers of risk for developing later childhood ADHD that could be identifiable in infancy or toddlerhood. This meta-analysis examined the associations between these early temperamental factors and later symptoms and diagnosis of ADHD and mapped early temperament constructs onto the three ADHD symptom dimensions. **Methods:** A systemic review of the literature was conducted to identify prospective longitudinal studies that included theoretically relevant temperament constructs (sustained attention, activity level, inhibition, and negative emotionality) examined from birth to 36 months old and ADHD (symptoms or diagnosis) in preschool or childhood. The association between each temperament construct and ADHD outcomes was examined using pooled standardized estimates in meta-analyses. **Results:** Forty-eight articles (n = 112,716 infants/toddlers) prospectively examined temperament and the relation to childhood ADHD symptoms or diagnosis. Activity level (k = 18) in infancy and toddlerhood was moderately associated with childhood ADHD (r = .39, CI = 0.27, 0.51, p < .001). Moderate effect sizes were also observed for sustained attention (k = 9; r = −.28, CI = −0.42, −0.12, p < .001) and negative emotionality (k = 33; r = .25, CI = 0.16, 0.34, p < .001) with ADHD. The specificity of each temperament construct for later ADHD symptom dimensions was such that activity level and negative emotionality were predictive of all three symptom dimensions (i.e., inattention, hyperactivity/impulsivity, and combined), whereas sustained attention was only associated with combined symptoms. **Conclusions:** Infant and toddler temperament is an early risk factor for the development of childhood ADHD that could be utilized for early intervention identification. Yet, this systematic review found that relatively few prospective longitudinal studies have examined sustained attention (k = 9) and inhibition (k = 15) in infancy and toddlerhood in relation to later ADHD highlighting the need for further research. **Keywords:** ADHD; infant; temperament; activity level; attention; impulsivity; negative emotionality.

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder with an estimated worldwide prevalence of 5% (Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007). Children with ADHD are most often identified for evaluation and treatment at school age, after impairment in social and academic functioning has become apparent (Visser et al., 2014). Longitudinal studies of children treated for ADHD have found continued adverse outcomes in adulthood including lower educational achievement, greater occupational difficulties, interpersonal conflict, more frequent motor vehicle accidents and traffic violations, substance use problems, and suicide (Barkley, 2014; Chronis-Tuscano et al., 2010; Molina et al., 2009; Shaw et al., 2012). More recently, it has been suggested that individuals with childhood ADHD have a 9–13-year reduction in healthy life expectancy (Barkley, 2018; Schiavone et al., 2022). Given the significant negative long-term outcomes of ADHD, there is a growing interest in identifying early signals of risk for ADHD before the full onset of the disorder. These signals of risk could inform targets for early prevention and interventions to delay or prevent the onset of ADHD diagnosis, associated impairments, and the development of comorbidity.

The neurodevelopmental nature of ADHD, with onset as young as preschool-age, suggests that the disorder begins early in life and markers of risk for developing ADHD could be identifiable even in infancy or toddlerhood (Nigg, Sibley, Thapar, & Karalunas, 2020; Schmidt & Petermann, 2009). One potential early emerging marker of ADHD is temperament. Temperament is characterized as individual differences in behavior in response to the environment, that is relatively stable beginning at 4 months of age, and is driven by neurophysiological underpinnings (Carranza, González-Salinas,

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& Ato, 2013; Rothbart & Bates, 2006). Thus, temperament is one possible early marker of risk for later development of childhood ADHD (Nigg et al., 2020). Nigg, Blaskey, Stawicki, and Sachek (2004) have conceptualized a theoretical model with impaired regulation and reactivity as temperamental risk factors for developing ADHD.

Attention develops rapidly in infancy with the capacity for sustained attention (attending to a stimulus while ignoring distractors for an extended period) emerging by the second half of the first year of life (Hendry et al., 2018; Putnam, Gartstein, & Rothbart, 2006; Rothbart, 1981). Individual differences in attention during infancy and toddlerhood have been found to be moderately stable and are associated with later cognitive abilities suggesting a potential predictive value of early developing attention to later childhood outcomes of interest to ADHD (Bornstein & Sigman, 1986; Colombo, 1993; Sigman, Cohen, & Beckwith, 1997). Moreover, infants and toddlers at high familial risk for ADHD have been noted to have less sustained attention as early as 7 months of age as compared to infants and toddlers without a familial history of ADHD (Auerbach, Atzaba-Poria, Berger, & Landau, 2004; Miller et al., 2020). Thus, difficulty with sustained attention in the first 2 years of life may be an early signal of risk for developing childhood ADHD. Yet, only a few longitudinal studies have examined sustained attention or attention problems in infancy or toddlerhood as predictors of later symptoms of ADHD and with mixed results. For example, Papageorgiou et al. (2014) found that greater sustained attention, eye-tracking generated mean duration of fixation, at 7 months of age was associated with fewer ADHD symptoms at age 3.5 years, whereas Frick, Forslund, & Brocki, (2019) reported that 10-month sustained attention, measured via behaviorally coded attention during toy play, did not predict inattentive or hyperactive symptoms at age 3. These mixed findings may indicate that the measurement method of sustained attention is important, such that some measures of sustained attention may be more sensitive to differences than others.

Activity level as a temperament trait is the child's natural tendency toward more or less motor activity. High activity levels are described as frequently moving arms and legs, squirming, kicking, or rolling in infancy (Gartstein & Rothbart, 2003) and being full of energy or exuberant in toddlerhood (Putnam et al., 2006). These behaviors emulate hyperactivity, a core symptom of ADHD. Thus, it is of no surprise that activity level has been examined as a possible early predictor of childhood ADHD. The meta-analysis by Kostyrka-Allchorne, Wass, and Sonuga-Barke (2020) found a small but significant correlation between parent reported infant activity level and later symptoms of ADHD. Age was a significant moderator such that activity level was more strongly associated with childhood ADHD when measured later in infancy (13–24 months). This moderation effect may be in part due to greater recognition of a child's activity level by parents as mobility increases into the second year of life. It is possible that the predictive value of activity level could continue to increase into toddlerhood. Additionally, despite the increased cost relative to parent report measures, observational methods may be important in more precisely quantifying early motor activity. Interestingly, activity level assessed multiple times across the first 2 years of life was consistently significantly associated with hyperactivity/impulsivity, but not attention problems at age 7 (Shephard et al., 2019). Therefore, activity level in infancy and toddlerhood may have greater predictive power for hyperactivity/impulsivity symptoms than the inattentive symptoms of childhood ADHD.

Inhibition is often characterized as the ability to control, regulate, or inhibit approach and avoidance behaviors (Rothbart, 1989), sometimes referred or including effortful control. The temperamental construct of inhibition shares conceptual similarities to the construct of impulsivity underlying ADHD, along with self-regulation which is also examined via affective constructs such as negative emotionality (discussed below). Early emerging inhibitory control deficits have been associated with the development of ADHD (e.g., Gewirtz, Stanton-Chapman, & Reeve, 2009; Jacobson, Schneider, & Mahone, 2018), with most studies examining cross-sectional and longitudinal designs of school-age children through adolescence. The literature on infant and toddler inhibition and later ADHD outcomes is limited, with only a handful of studies examining early childhood inhibition measured using behavioral observations and parent-report as a predictor of later ADHD, resulting in mixed findings. For example, studies by Frick and colleagues did not identify a significant relation between early inhibition (measured starting at 10 and 12 months) and later ADHD (measured at 3 and 6 years) in typically developing samples (Frick, Bohlin, Hedqvist, & Brocki, 2019; Frick, Forslund, & Brocki, 2019). On the other hand, several others have found early inhibition to be associated with later ADHD and related symptoms. In a sample of same-sex twins, Gagne, Asherson, and Saudino (2020) found that early inhibition was related to later ADHD, although much of the covariance was accounted for by genetic variance. Inhibition may have some specificity regarding the development of ADHD, as inhibition in infancy and toddlerhood has been shown to be predictive of ADHD symptoms, but not autism or anxiety symptoms (Shephard et al., 2019). Furthermore, early inhibition has been associated with later attention problems and as a mediator in the relation between preterm birth and later attention problems (Jaekel, Eryigit-Madzwamuse, & Wolke, 2016). However, there is limited research examining the specificity of early

inhibition on attention versus hyperactive impulsive dimensions of ADHD.

Negative emotionality is a temperament profile often characterized by high rates of negative affect and reactivity such as anger, distress, or irritability (Rothbart & Bates, 2006). Infants with intensified negative emotionality are often described by parents as "difficult" and at times described and measured in the literature as difficult temperament. Predictively, higher levels of negative emotionality have been associated with poorer emotional and behavioral outcomes and often considered a transdiagnostic risk factor for psychopathology, with several studies supporting the link between negative emotionality and ADHD. Infant and toddler negative emotionality has been associated with higher rates of ADHD diagnosis, hyperactivity, inattention, as well as increasing trajectories of symptoms (Galéra et al., 2011) through to age 10, with most studies focusing on outcomes in young children, 3–7-years-old (Becker, Holtmann, Laucht, & Schmidt, 2004; Lawson & Ruff, 2004a; Miller, Hane, Degnan, Fox, & Chronis-Tuscano, 2019; Williams, Nicholson, Walker, & Berthelsen, 2016). However, some studies have not found a significant association between negative emotionality and ADHD, in predominately typically developing samples (Arnett, Macdonald, & Pennington, 2013; Elberling et al., 2014; Jorm et al., 2001). These mixed findings may highlight the overlap of negative emotionality as an underlying factor among multiple disorders, including ADHD, oppositional defiant disorder, and depression, as well as some normative variations throughout early childhood.

The current study is a systematic review and meta-analysis that aimed to clarify the mixed findings in the literature by examining the longitudinal association between temperament (sustained attention, activity level, inhibition, and negative emotionality) in infancy and toddlerhood (0–36 months) and later development of childhood ADHD symptoms and/or diagnosis (3–13 years). Additionally, this meta-analysis aimed to examine the association between these early temperament constructs and the specific ADHD symptom dimensions which could potentially help disentangle the heterogenous developmental trajectories of ADHD. A recent meta-analysis examined temperament (negative emotionality, self-regulation, behavioral inhibition, surgency, and activity) as reported by parents in infancy (0–24 months) as predictors of later psychopathology (Kostyrka-Allchorne et al., 2020). They concluded that some temperament traits (i.e., negative emotionality) may confer transdiagnostic risk whereas others (e.g., activity level) may provide greater disorder specificity. Importantly, all associations were weak and concerns about shared method variance may arise, suggesting screening by parent report may have limited predictive power. Shephard et al. (2022) also conducted a systematic review and meta-analysis that aimed to identify all neurocognitive and behavioral measures examined between birth and 5 years of age among children at elevated risk for ADHD. However, this meta-analysis included studies of familial risk for ADHD as well as cross-sectional studies of children with ADHD, therefore limiting the interpretation of which of these markers measured in infancy and toddlerhood may be predictive of later development of ADHD. The current review builds upon this foundational work by (a) expanding the temperament traits measured to include sustained attention and inhibition given conceptual overlap with the inattention and hyperactivity/impulsivity, (b) extending the age of temperament assessment through toddlerhood, a period of development found to be important for maturation of self-regulation and early identification, (c) considering observational assessments of temperament, in addition to questionnaires, and (d) specifically focusing on prospective longitudinal designs to examine the predictive value of identifying early infant and toddler temperament on the development of ADHD or ADHD symptoms in childhood and adolescence.

This systematic review and meta-analysis focus on four temperament constructs that can be identified as early as 4 months that theoretically map onto ADHD symptom dimensions. We hypothesized that less sustained attention, more activity, poorer inhibition, and greater negative emotionality in the first 3 years of life would each predict later childhood ADHD symptoms and diagnosis. We tested the specificity of each temperament trait to (a) the three ADHD symptom dimensions (inattention, hyperactivity/impulsivity, and combined) and (b) ADHD symptoms versus ADHD diagnosis. We expected sustained attention to be related with inattention, inhibition, and activity level to be related with hyperactivity and negative emotionality to be related with combined symptom dimensions. Regarding ADHD symptom versus diagnosis, we hypothesized that all temperament constructs would be more strongly related to ADHD symptoms, given the increased variability of symptoms and limited range of diagnosis. Given the wide developmental age range of the ADHD outcome assessment, we examined age at ADHD outcome (i.e., preschool 3–5 vs. school-age 6–13) as a moderator between the relation of each temperament construct and later ADHD. We expected stronger effects for preschool ADHD outcomes given the temporal proximity of assessment between infancy/toddlerhood and preschool. However, given that the temperament constructs were assessed within a narrow range (0–36 months), we did not examine age at which temperament was collected as a moderator. Finally, we conducted two exploratory moderator analyses (a) reporter of the ADHD outcome variable and (b) percentage of the sample identified as male children.

Methods

This systematic review and meta-analysis was preregistered with PROSPERO (CRD42020158739). Comprehensive literature searches were performed in the PubMed, EMBASE.com, and PsycINFO (Ovid) electronic databases on May 6, 2020, and were re-run on December 17, 2021. Search strings for each database were developed by a health sciences librarian (JF), using controlled vocabulary (Medical Subject Headings, Emtree terms, Thesaurus of Psychological Index Terms) and natural language words or phrases to reflect the concepts of "attention deficit and hyperactivity disorder," "temperament," and "infancy/toddlerhood." The search strings are shown in the Appendix S1. The search was limited to English language studies only, humans only, and the publication years from 1980 to 2021. The beginning of the literature search was set to 1980 reflecting the publication of the 3rd edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III; American Psychiatric Association, 1980) which described the initial diagnostic criteria for attention deficit disorder. A total of 16,839 citations were retrieved from the three databases (Figure 1, Moher, Liberati, Tetzlaff, & Altman, 2009). Citations were exported from each database into EndNote and duplicates were removed by the librarian (JF) using the Bramer Method (Bramer, Giustini, de Jonge, Holland, & Bekhuis, 2016). The remaining citations were then uploaded to DistillerSR (DistillerSR, Evidence Partners, Ottawa, Canada). All search procedures in the current study followed rigorous standards for conducting systematic reviews and meta-analyses (Polanin, Pigott, Espelage, & Grotpeter, 2019).

Prospective longitudinal studies and retrospective studies that included archival data collected during infancy or toddlerhood (e.g., medical records) were included. All studies that relied on retrospective recall of infant and toddler temperament were excluded. Prospective longitudinal studies were eligible for inclusion if temperament was examined from birth to 36 months old and ADHD outcome was reported in preschool, childhood, or adolescence. The ADHD outcomes included ADHD diagnosis or ADHD symptoms such as attention problems, hyperactivity, and impulsivity. The temperament and ADHD data could be determined by a clinician, observation, task or as rated by a parent, caregiver, or teacher informant. All abstracts were independently reviewed by two authors for eligibility criteria. All articles meeting inclusion after abstract reviewer were full text reviewed by two authors and selected for inclusion based on consensus. Any disagreements were discussed with a third author. References of included manuscripts were then reviewed for additional papers to consider.

Adequacy of report and risk of bias was assessed for all included studies using the STROBE checklist for cohort, case control and cross-sectional studies (Von Elm et al., 2007). Funnel plots were used to assess the risk of publication bias, see Figures S1–S4.

For the primary analyses, a single effect size was obtained from each study for each temperament construct, ensuring the assumption of independence of effect sizes across studies. The effect size measure chosen for our primary analyses was correlation, specifically between early temperament constructs and later ADHD symptoms or diagnoses, as most of the included studies reported such associations using the correlation metric. When studies reported differences in means (i.e., the difference in mean early temperament between low and high ADHD symptom or diagnosis groups), the standardized mean difference (Cohen's *d*) was first computed using the pooled standard deviation. The standardized mean difference was then converted to the correlation metric using established methods (Borenstein, Hedges, Higgins, & Rothstein, 2021). For studies that reported odds ratios for the association between early temperament and later ADHD, the log odds ratio was computed and converted to a standardized mean difference, which was ultimately converted to a correlation (Borenstein et al., 2021). Correlations were interpreted using Cohen's *d* conventions $r = .10$ small, $r = .25$ medium, and $r = .50$ large. Once all effect sizes were converted to correlations, Fisher's *z*-transformation was employed as a variance-stabilizing transformation when performing the meta-analyses and combining effects across studies (Silver & Dunlap, 1987), see Figures S5–S8.

Random effects (RE) meta-analysis models were constructed and fitted via restricted maximum likelihood (REML) to estimate the mean of the distribution of effect sizes on the Fisher's *z*-scale (Hedges, 1983). Separate models were used to estimate the mean effect along with 95% confidence intervals (CIs) for each of the four temperament constructs. Results were back-transformed to the original correlation scale for ease of reporting and interpretation. Heterogeneity measures such as between-study variance (τ^2) and the proportion of total variability attributable to between-study variability (I^2) were calculated, and Cochran's *Q* heterogeneity statistics were used to formally test for heterogeneity. To investigate factors that may explain high between-study heterogeneity, we performed subgroup analyses based on ADHD symptom dimension (inattentive, hyperactive, and combined symptoms), ADHD symptom versus diagnosis, categorized age (preschool vs. school age), and rater of ADHD symptoms (parent vs. observer), separately for each temperament construct. Meta-regression was also performed to determine whether continuous age and percentage of male children were moderators that account for a significant portion of between-study heterogeneity, separately for each temperament construct. To test for small study effects and potential publication bias, regression-based Egger tests were performed using a RE meta-analysis model fit via REML while accounting for between-study heterogeneity by controlling for potential moderators (ADHD symptom vs. diagnosis, categorized age, reporter, ADHD symptom dimension, and percentage of male children). To provide publication bias-adjusted effect sizes, the trim-and-fill technique was employed using the linear (L_0) estimator for the number of potentially missing studies. Bias-adjusted effect sizes are reported when the number of imputed studies was greater than zero. Outliers were defined as effect sizes whose Fisher's *z*-transformed correlation was below the first quartile minus 1.5 times the interquartile range, or above the third quartile plus 1.5 times the interquartile range. All analyses were performed using Stata/SE 16.1 (StataCorp LLC, College Station, TX).

Results

Sample

Forty-eight articles including 112,716 infant and toddler participants followed longitudinally to childhood (3–13 years old) were included in the meta-analyses. Of the 48 studies, 33 evaluated negative emotionality, 18 reported on activity level, 15 assessed inhibition, 9 examined sustained attention in relation to later developing ADHD symptoms or diagnosis. Twelve studies obtained data from participants on multiple temperament constructs. Study characteristics are reported in Table 1. Outlier analyses identified two studies as outliers (one negative emotionality and one inhibition) and removal of these outliers did not change the significance of any results. Compliance with the STROBE statement for adequate reporting of observational studies was 83% (range 58%–97%) overall for the included studies.

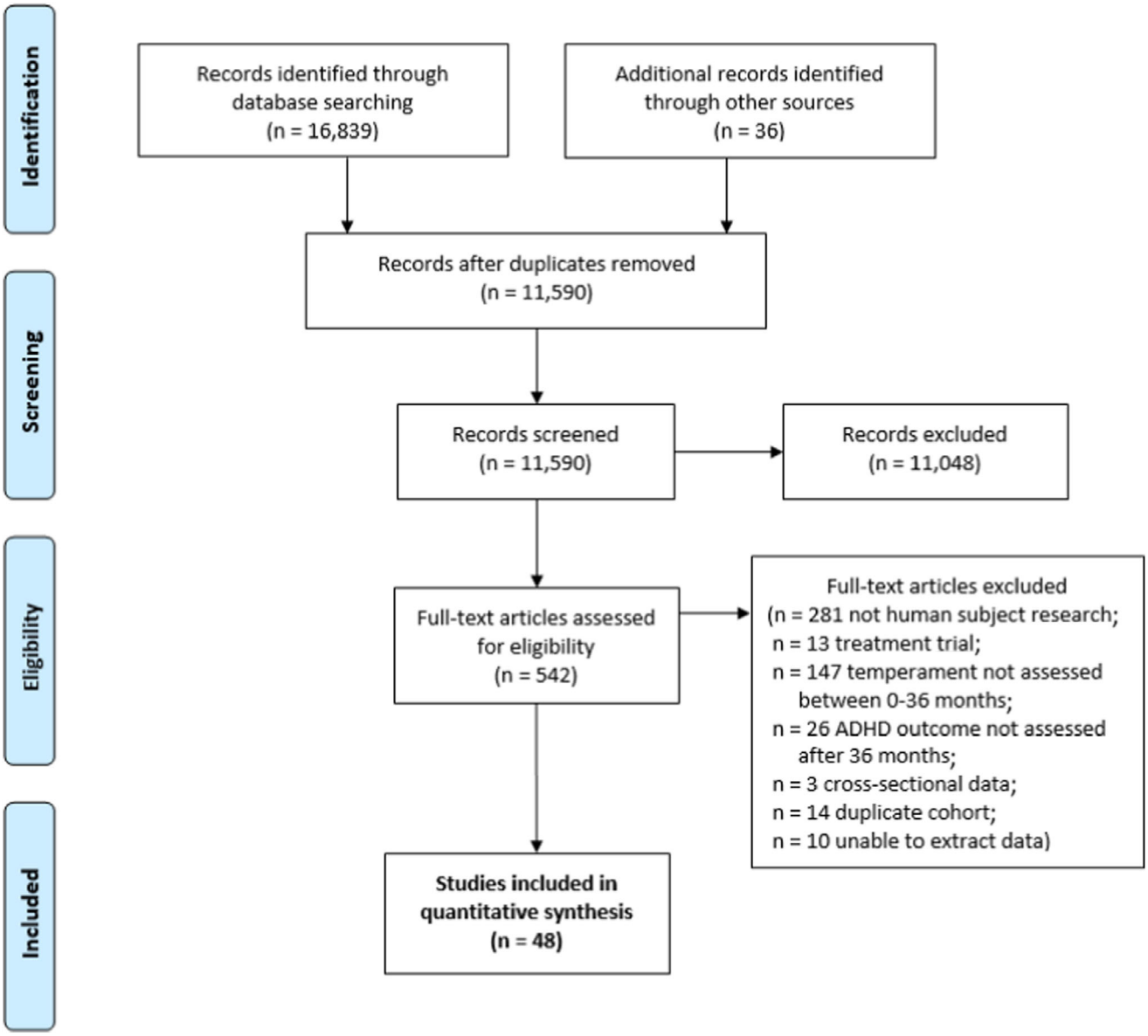

Figure 1 PRISMA flow diagram

Primary analyses

Table 2 presents the effect sizes for the associations between each temperament and later ADHD (symptoms and/or diagnosis) as well as the tests of heterogeneity. Sustained attention, activity level, and negative emotionality were significantly associated with later ADHD (Figures 2–4). The effect size was moderate for activity level, $r = .393$, CI [0.268, 0.505], sustained attention, $r = -.277$, CI [−0.420, −0.120], and negative emotionality, $r = .251$, CI [0.156, 0.342]. The relation between inhibition and ADHD was not significant, $r = .032$, CI [−0.200, 0.260] (Figure 5). There was significant heterogeneity for all temperament constructs based on Cochran's Q with 92%–99% of the variation across studies due to heterogeneity (Table 2). Egger tests revealed insufficient evidence to conclude significant small-study effects for all four temperament constructs (p-values between .127 and .737). The trim-and-fill technique detected no missing studies for sustained attention and activity level; however, two missing studies were identified and imputed for both negative emotionality and inhibition. Bias-adjusted effect sizes for negative emotionality and inhibition were $r_{adj} = .278$, CI [0.182, 0.367], and $r_{adj} = .123$, CI [−0.114, 0.348], respectively (Table 2). Thus, adjustment for publication bias produced negligible or nonexistent changes in effect sizes for all four temperaments.

Moderator analyses

ADHD symptom dimensions. The analyses for symptom dimension included symptom-level data and did not examine differences between diagnostic level specifier data as that was not available for most studies. The association between sustained attention in infancy and toddlerhood and later ADHD was only significant for the combined symptoms,

Table 1 Characteristics of included studies

ID	Author (Year)	*N*	Country	Temperament construct	Temperament assessment	ADHD outcome age	ADHD assessment	ADHD type	Rater
1.	Abulizi et al. (2017)	1,184	France	AL, NE	EAS	5.5	SDQ	COM	P
2.	Arnett et al. (2013)	1,016	US	NE	CITS	8	DBD	COM	P
3.	Becker et al. (2004)	319	Germany	NE	Interview, Behavioral Coding	11	MPI	COM	O
4.	Ben-Sasson, Soto, Heberle, Carter, and Briggs-Gowan (2017)	924	US	AL, AT	ITSEA	8	CBCL	COM	P
5.	Bilgin et al. (2020)	342	Germany	NE	Clinical Interview	6	CBCL	IN	P
6.	Bunford, Kujawa, Dyson, Olino, and Klein (2022)	354	US	NE	Behavioral Coding	9.12	K-SADS	IN/	
	HYP/COM	P							
7.	Davies, Sturge-Apple, and Cicchetti (2011)	201	US	NE	Behavioral Coding	3	CCQ	COM	O
8.	DeSantis, Coster, Bigsby, and Lester (2004)	28	US	NE	Daily Diary	5.5	CBCL	IN	P
9.	Einziger et al. (2018)	64	Israel	AL, IN, NE	CBQ	13.5	CPRS	IN/	
	HYP/COM	P							
10.	Elberling et al. (2014)	1,585	Denmark	AL, NE	Behavioral Coding	6	DAWBA	COM	O
11.	Flouri, Midouhas, and Narayanan (2016)	8,302	UK	NE	CITS	3	SDQ	COM	P
12.	Frick, Forslund, & Brocki, (2019)	47	Sweden	AL, IN	CCTI, Behavioral Coding	6	ADHD RS	IN	T
13.	Frick, Forslund, & Brocki, (2019)	112	Sweden	IN, AT, NE	Behavioral Coding, IBQ	3	ADHD RS	IN	P/T
14.	Gagne et al. (2020)	628	US	IN	Behavioral Coding	3	CBCL	COM	P
15.	Galéra et al. (2011)	2,057	Canada	NE	ICQ	8	ECBS	COM	P
16.	Goldsmith, Lemery-Chalfant, Schmidt, Arneson, and Schmidt (2007)	429	US	AL, IN, AT, NE	TBAQ	7	DISC	COM	P
17.	Goodwin et al. (2021)	113	UK	AL	IBQ, Behavioral Coding	3	CBCL	COM	P
18.	Gurevitz, Geva, Varon, and Leitner (2014)	116	Israel	NE	Behavioral Coding	8	Chart Review	COM	O
19.	Jaekel et al. (2016)	558	Germany	IN	Behavioral Coding	8	CBCL	IN	P
20.	Johnson et al. (2014)	136	UK	AL	Motion Tracking	7	DAWBA	COM	O
21.	Jorm et al. (2001)	660	Australia	NE	STSI	12	RPBQ	HYP	P
22.	Joseph, McKone, Molina, and Shaw (2021)	312	US	NE	Behavioral Coding	6	CBCL	IN	P
23.	Lawson and Ruff (2004a)	55	US	AT	Behavioral Coding	5	CPRS, CBCL	COM	P
24.	Lawson and Ruff (2004b)	75	US	NE	Behavioral Coding	3.5	CPRS	HYP	P
25.	Leblanc et al. (2008)	1,112	Canada	AL, IN	SBQ	5	SBQ	HYP	P
26.	Lemcke, Parner, Bjerrum, Thomsen, and Lauritsen (2016)	76,286	Denmark	AL, NE	Parent Interview	11	Chart Review	COM	O
27.	Levine and Woodward (2018)	156	New Zealand	IN	Behavioral Coding	4.5	SDQ	COM	P
28.	Meeuwsen, Perra, Van Goozen, and Hay (2019)	312	UK	AL, IN, AT, NE	IBQ, Behavioral Coding	7	PAPA	COM	O

(continues)

Table 1 (continued)

ID	Author (Year)	*N*	Country	Temperament construct	Temperament assessment	ADHD outcome age	ADHD assessment	ADHD type	Rater
29.	Miller, Iosif, Young, Hill, and Ozonoff (2018)	47	US	NE	Clinical Interview	10	CASI	COM	P/O
30.	Miller, Degnan, Hane, Fox, & Chronis-Tuscano, (2019)	291	US	AL, NE	Behavioral Coding	7.5	SNAP-IV	IN	P
31.	Miller, Hane, Degnan, Fox, & Chronis-Tuscano, (2019)	291	US	NE	Behavioral Coding	7	SNAP-IV	IN	P/T
32.	Miller et al. (2020)	145	US	AL, IN, AT, NE	Behavioral Coding	3	ADHD RS	COM	P
33.	Morrell and Murray (2003)	59	UK	NE	Behavioral Coding	8	RPBQ	HYP	P
34.	Olson, Bates, Sandy, and Schilling (2002)	89	US	NE	ICQ	8	Behavioral Coding	HYP	O
35.	Papageorgiou et al. (2014)	120	London	IN	ECBQ	3.5	SDQ	COM	P
36.	Rende (1993)[a]	91	US	NE, AL	CCTI	7	CBCL	IN	P
37.	Rende (1993)[a]	73	US	NE, AL	CCTI	7	CBCL	IN	P
38.	Robson and Pederson (1997)	85	Canada	AT	CITS	5.5	Behavioral Coding	IN	O
39.	Sanson, Smart, Prior, and Oberklaid (1993)	252	Australia	AL, NE	ITQ	6	CBQ	HYP	P
40.	Schmid and Wolke (2014)	1,120	Germany	NE	Clinical Interview	8.5	MPI	COM	O
41.	Shephard et al. (2019)	104	Britain	AL, IN, AT	IBQ, ECBQ	7	CPRS	IN/HYP	P
42.	Silberg et al. (2015)	624	US	NE	ICQ	3	DISC-YC	COM	O
43.	Silverman and Ragusa (1992)	69	US	AL, IN	EAS	4	YCI	COM	P
44.	Slinning (2004)	92	Norway	AT	CBCL	4.5	ADHD RS	COM	P/T
45.	Smarius et al. (2017)	3,389	Netherlands	NE	WQ	5	SDQ	COM	P
46.	Stephens, Elsayed, Reznick, Crais, and Watson (2021)	229	US	IN	FYI	4.5	ADHD RS	IN/HYP/COM	P
47.	Williams et al. (2016)	2,880	Australia	NE	ATS	6	SDQ	HYP	T
48.	Williams et al. (2016)	4,109	Australia	NE	ATS	7	SDQ	IN	P
49.	Willoughby, Gottfredson, and Stifter (2017)	1,074	US	AL, IN, AT, NE	Behavioral Coding	6	DBD	COM	P

ADHD RS, ADHD Rating Scale; AL, activity level; AT, attention; ATS, Australian Temperament Scale; CASI, Child and Adolescent Symptom Inventory; CBCL, Child Behavior Checklist; CBQ, Children's Behavior Questionnaire; CCQ, California Child Q-Set; CCTI, Colorado Childhood Temperament Inventory; CITS, Carey Infant Temperament Scale; COM, Combined ADHD Symptoms; CPRS, Conner's parent rating scale; DAWBA, Developmental and Well-Being Assessment; DBD, Disruptive Behavior Disorder Rating Scale; DISC-YC, Young Diagnostic Interview Schedule for Preschool Children; EAS, Emotionality Activity and Sociability; ECBQ, Early Childhood Behavior Questionnaire; ECBS, Early childhood behavior scale from the Canadian National Longitudinal Study of Children and Youth; FYI, First Year Inventory; Hyp, Hyperactivity Symptoms; IBQ, Infant Behavior Questionnaire; ICQ, Infant Characteristics Questionnaire; IN, Inhibition; ITQ, Infant Temperament Questionnaire; ITSEA, Infant Toddler Social and Emotional Assessment; MPI, Mannheim Parent Interview; NE, Negative Emotionality; PAPA, Preschool Age Psychiatric Assessment; RPBQ, Rutter Problem Behavior Questionnaire; SBQ, Social Behavior Questionnaire; SDQ, Strengths and Difficulties Questionnaire; SNAP-IV, Swanson, Nolan, and Pelham-IV; STSI, Short Temperament Scale for Infants; WQ, Wessel's Questionnaire; YCI, Yale Children's Inventory.

[a]This manuscript reported separate correlations by child sex.

r = −.265, CI [−0.371, −0.153] and not for the hyperactive, CI [−0.143, 0.133], or inattentive, CI [−0.546, 0.130], symptom dimensions (Figure 6). The association between activity level and later ADHD was significant for the hyperactive symptom dimension, r = .390, CI [0.188, 0.561], inattention symptom dimension, r = .332, CI [0.133, 0.505], and combined symptom dimension, r = .381, CI [0.209, 0.531] (Figure 7). The association between inhibition and later ADHD was not significant for any of the three ADHD symptom dimensions: hyperactive symptoms, r = .033, CI [−0.214, 0.276], inattentive symptoms, r = .012, CI [−0.190, 0.213], and combined symptoms, r = .007, CI [−0.291, 0.303], Figure 8. The association between negative emotionality and later ADHD was significant for all three

Table 2 Meta-analyses results of overall association between infant/toddler temperament and childhood ADHD symptoms and/or diagnosis

Temperament	*K*	*N*	*r*	95% CI	r_{adj}	95% CI_{adj}	*Q*	I^2 (%)
Sustained attention	9	2,267	−.28*	−0.42, −0.12	–	–	87.87*	92.13
Activity level	18	88,306	.39*	0.27, 0.51	–	–	1,283.56*	99.12
Inhibition	14	4,939	.03	−0.20, 0.26	.12	−0.11, 0.35	585.22*	98.41
Negative emotionality	33	114,817	.25*	0.16, 0.34	.28*	0.18, 0.37	1,729.07*	99.37

All studies in Table 1 were included in these meta-analyses; r_{adj} is the bias-adjusted effect size.
*$p < .001$.

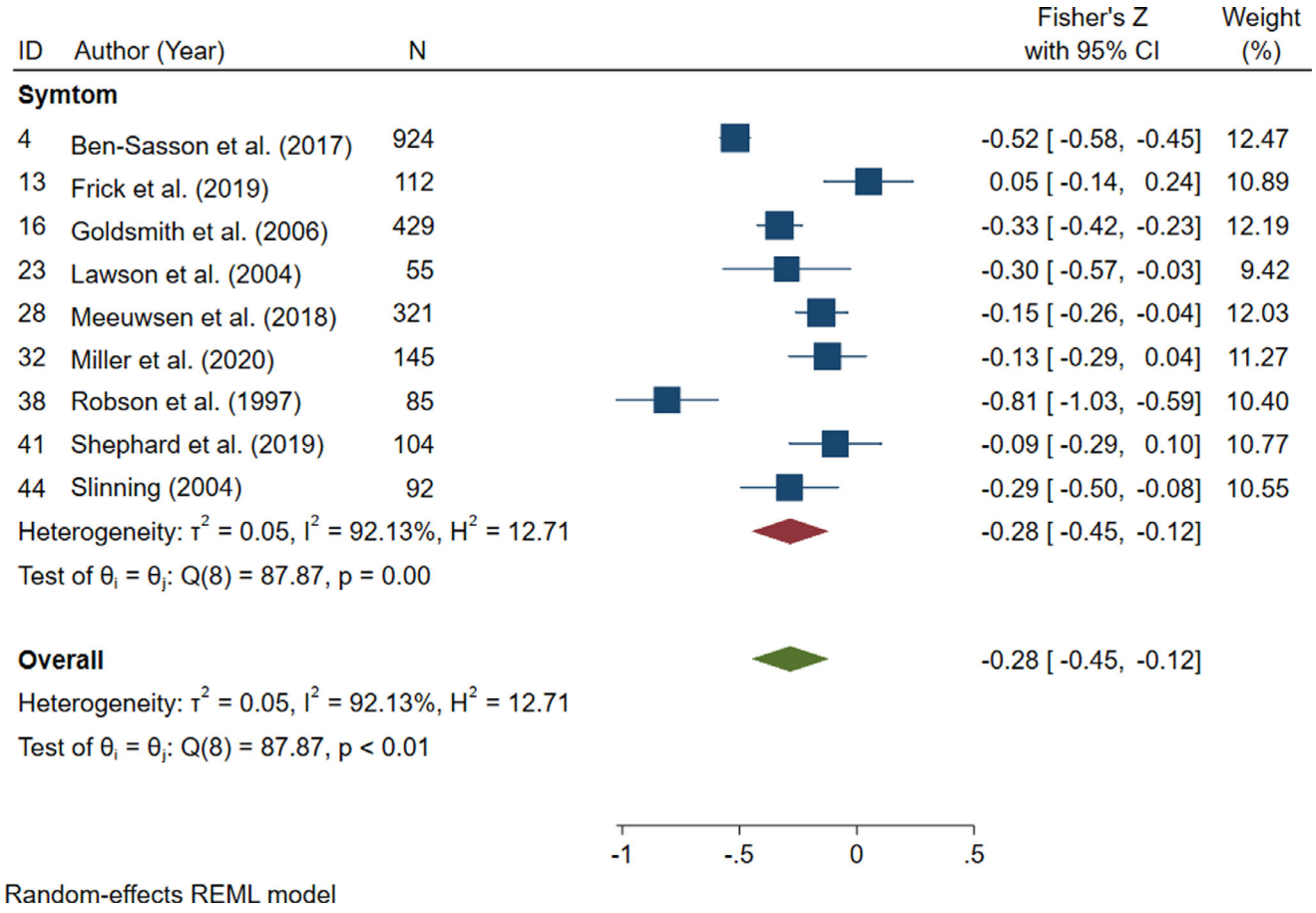

Figure 2 Forest plot of effect sizes of the association between sustained attention and later ADHD symptoms/diagnosis

symptom dimensions: hyperactive symptoms, $r = .257$, CI [0.105, 0.396], inattentive symptoms, $r = .321$, CI [0.141, 0.480], and combined symptoms, $r = .256$, CI [0.135, 0.369], Figure 9.

ADHD symptom versus diagnosis. In comparing ADHD symptoms versus ADHD diagnoses, activity level and negative emotionality remained significantly positively associated with both ADHD symptoms and diagnosis, see Figures 10 and 11. The strength of the relation for activity level and negative emotionality did not differ for later diagnosis compared to symptoms of ADHD. The effect size was moderate to large for the association between activity level with later symptoms of ADHD, $r = .388$, CI [0.246, 0.514] and later ADHD diagnosis, $r = .418$, CI [0.102, 0.658]. The effects were small to moderate for both the relations between negative emotionality with ADHD symptoms, $r = .255$, CI [0.145, 0.358] and diagnosis, $r = .237$, CI [0.029, 0.426]. No studies measuring sustained attention or inhibition in infancy and toddlerhood included ADHD diagnosis as an outcome so this could not be examined.

Age of outcome. The associations between sustained attention and later ADHD symptoms or diagnosis were significant when examining outcomes in preschool, $r = -.282$, CI [−0.518, −0.007], and childhood/adolescence, $r = -.277$, CI [−0.441, −0.094]. Activity level also remained significantly associated with later ADHD outcomes at both preschool-aged, $r = .293$, CI [0.070, 0.489], and childhood/adolescence, $r = 0.426$, CI [0.277, 0.555]. The association between inhibition and both the preschool-aged and childhood/adolescence ADHD

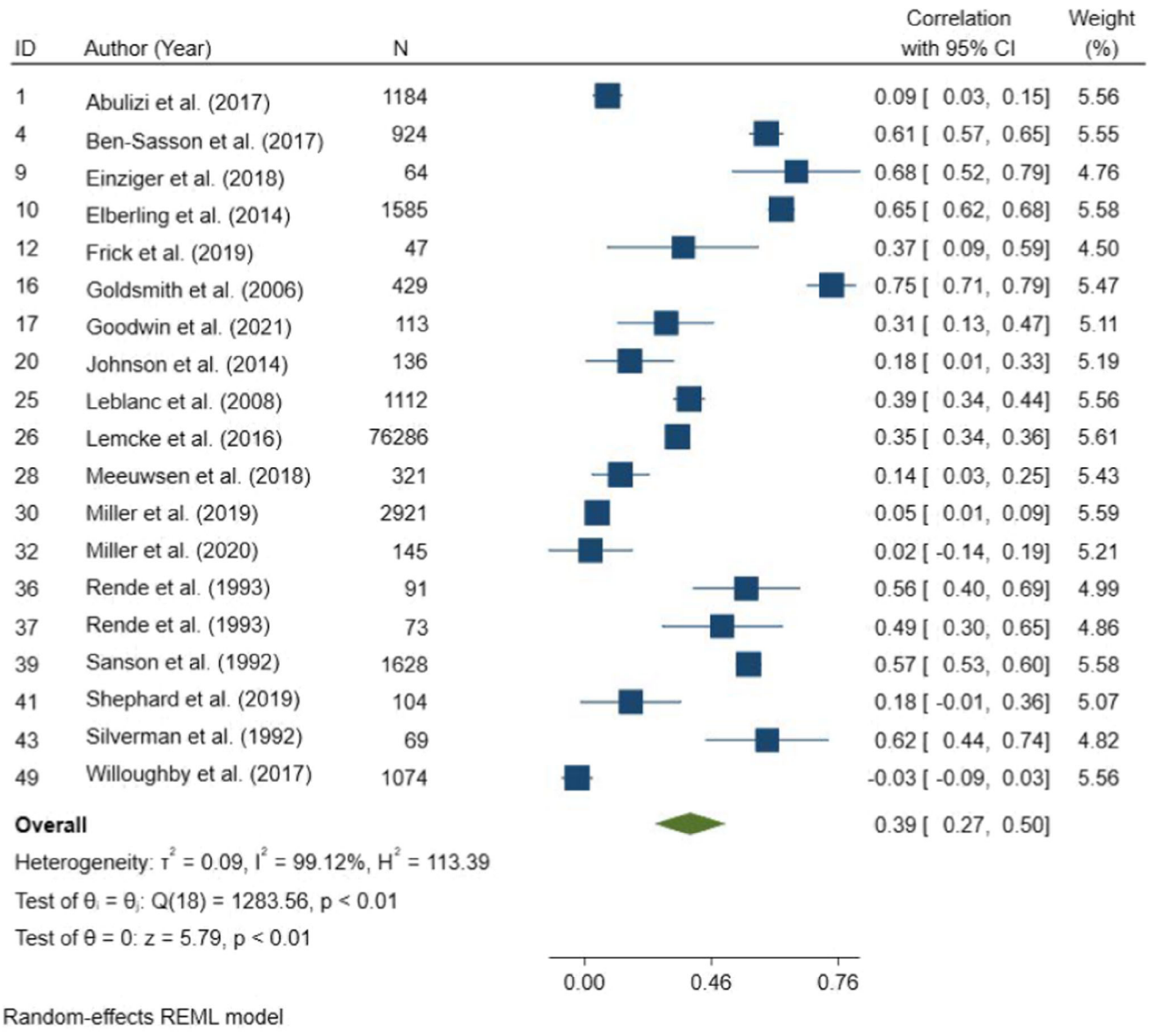

Figure 3 Forest plot of effect sizes of the association between activity level and later ADHD symptoms/diagnosis

outcomes were not significant, r = .084, CI [−0.338, 0.477] and r = −0.025, CI [−0.237, 0.189], respectively. The association with negative emotionality was significant for both preschool-aged ADHD outcomes, r = .184, CI [0.120, 0.246], and ADHD outcomes in childhood/adolescence, r = .274, CI [0.146, 0.393]. Age as a continuous variable was not a significant moderator of the associations between any of the temperament constructs and later ADHD, see Figures S9–S12.

Reporter of ADHD outcome. The associations between infant/toddler temperament and observer versus parent reported childhood ADHD symptoms or diagnosis were examined, see Figures S13 and S14. Sustained attention in infancy/toddlerhood was significantly associated with parent report of ADHD symptoms, r = −.234, CI [−0.369, −0.090]. Activity level in infancy/toddlerhood continued to be moderately associated with childhood ADHD symptoms and/or diagnoses when determined by observation and parent report, r = .354, CI [0.083, 0.576] and r = .406, CI [0.250, 0.542], respectively. The strength of the association between negative emotionality in infancy/toddlerhood and childhood ADHD symptoms and/or diagnosis varied by reporter such that the association was small when ADHD outcome was determined by an observer, r = .168, CI [0.025, 0.304], and moderate when reported by parent, r = .293, CI [0.174, 0.404]. Infant and toddler inhibition was not significantly associated with parent report of childhood ADHD symptoms, CI [−0.252, 0.280]. Too few studies of sustained attention (2 studies) and inhibition (1 study) included observer report to conduct meta-analyses.

Child sex. The percent of the sample identified as male children was not a significant moderator of the associations between any of the temperament constructs and later ADHD.

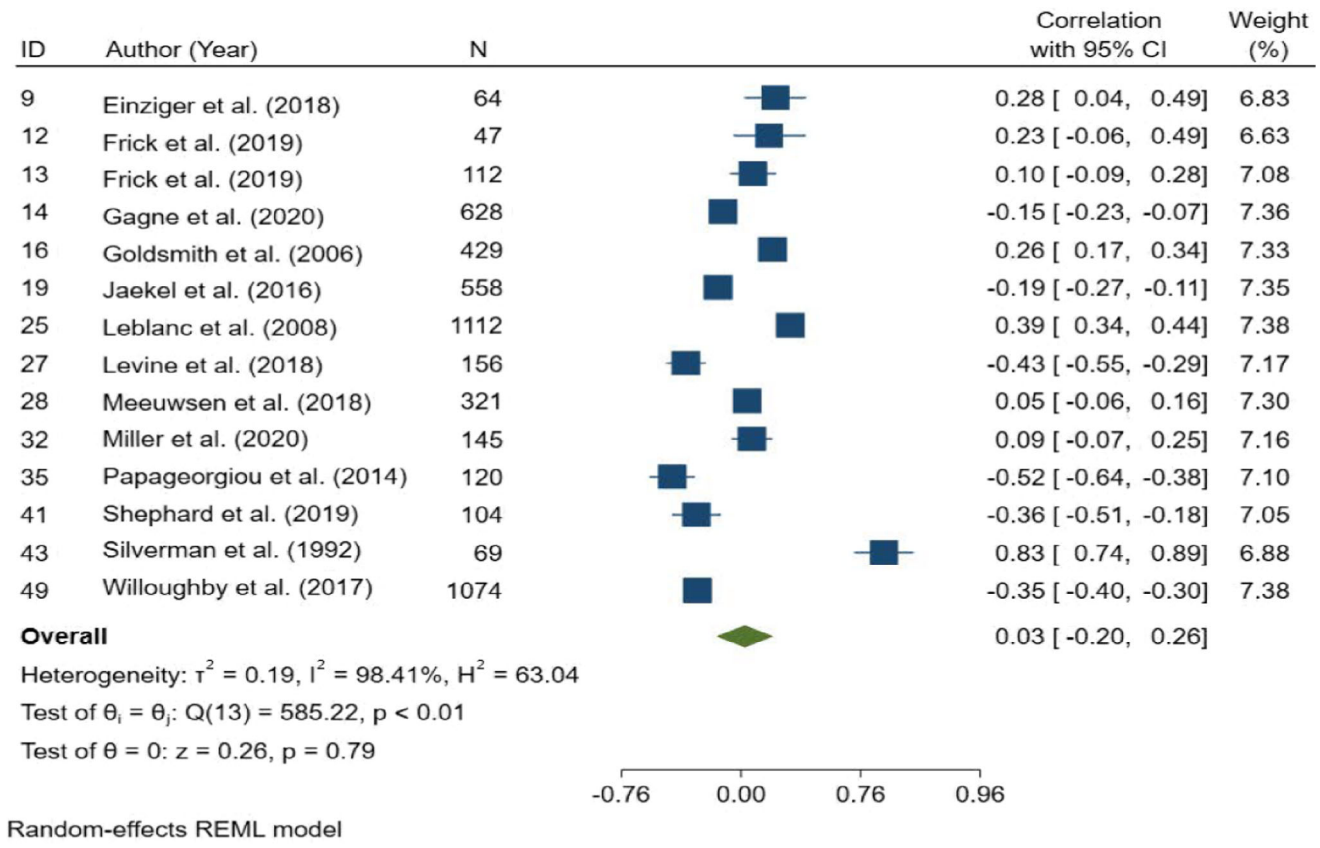

Figure 4 Forest plot of effect sizes of the association between inhibition and later ADHD symptoms/diagnosis

Discussion

Identifying early temperamental precursors to ADHD could help connect children to early intervention services with the potential of improving the developmental trajectory of symptoms and impairment associated with ADHD and comorbid conditions. Given the potential benefits of early identification of risk factors for ADHD, the goal of the current study was to systematically examine the extent to which four theoretically derived temperament constructs identified in infancy and toddlerhood were associated with later ADHD. Focusing on prospective longitudinal designs to examine the developmental unfolding of ADHD, our systematic review revealed that several studies have demonstrated a link between early temperament and later ADHD, with negative emotionality being the most common temperament construct examined (k = 33) in the literature and few studies examining early attention (k = 9). The meta-analyses found a moderate effect size for the relation between activity level, sustained attention, and negative emotionality in infancy and toddlerhood and ADHD in childhood and adolescence. There was no significant effect for inhibition in infancy and toddlerhood on ADHD in childhood and adolescence.

Given the developmental trajectory of ADHD, with younger children displaying more hyperactive symptoms and older children displaying inattentive and/or combined symptoms, we examined the association between infant and toddler temperament constructs and ADHD symptom dimensions in childhood and adolescence, as well as differences between ADHD symptoms versus diagnosis. Infant and toddler activity level predicted all symptom dimensions of ADHD (i.e., hyperactivity, inattention, and combined). This finding aligns with the potential overlap or early presentation of hyperactive symptoms in early childhood. Additionally, activity level had moderate to large effect sizes for diagnosis and symptom level outcome of ADHD. These findings may suggest that activity level can be identified early, as it is probably more noticeable in young children and supports the idea of stability of hyperactivity beginning in infancy and toddlerhood.

Negative emotionality predicted hyperactivity, inattentive, and combined symptom dimensions. The small to moderate effect sizes of negative emotionality and effect on all symptom dimensions could suggest the possibility of negative emotionality as a predictor of other co-occurring disorders (e.g., anxiety, ODD; Kostyrka-Allchorne et al., 2020; Vogel, Jackson, Barch, Tillman, & Luby, 2019). High rates of negative emotionality have been demonstrated in children with ADHD but can overlap with constructs such as irritability or difficulties with emotion regulation which are often characterized as transdiagnostic factors of psychopathology. Additionally, there was a small to moderate effect of negative emotionality and both ADHD diagnosis and symptom level outcomes, suggesting that although it may

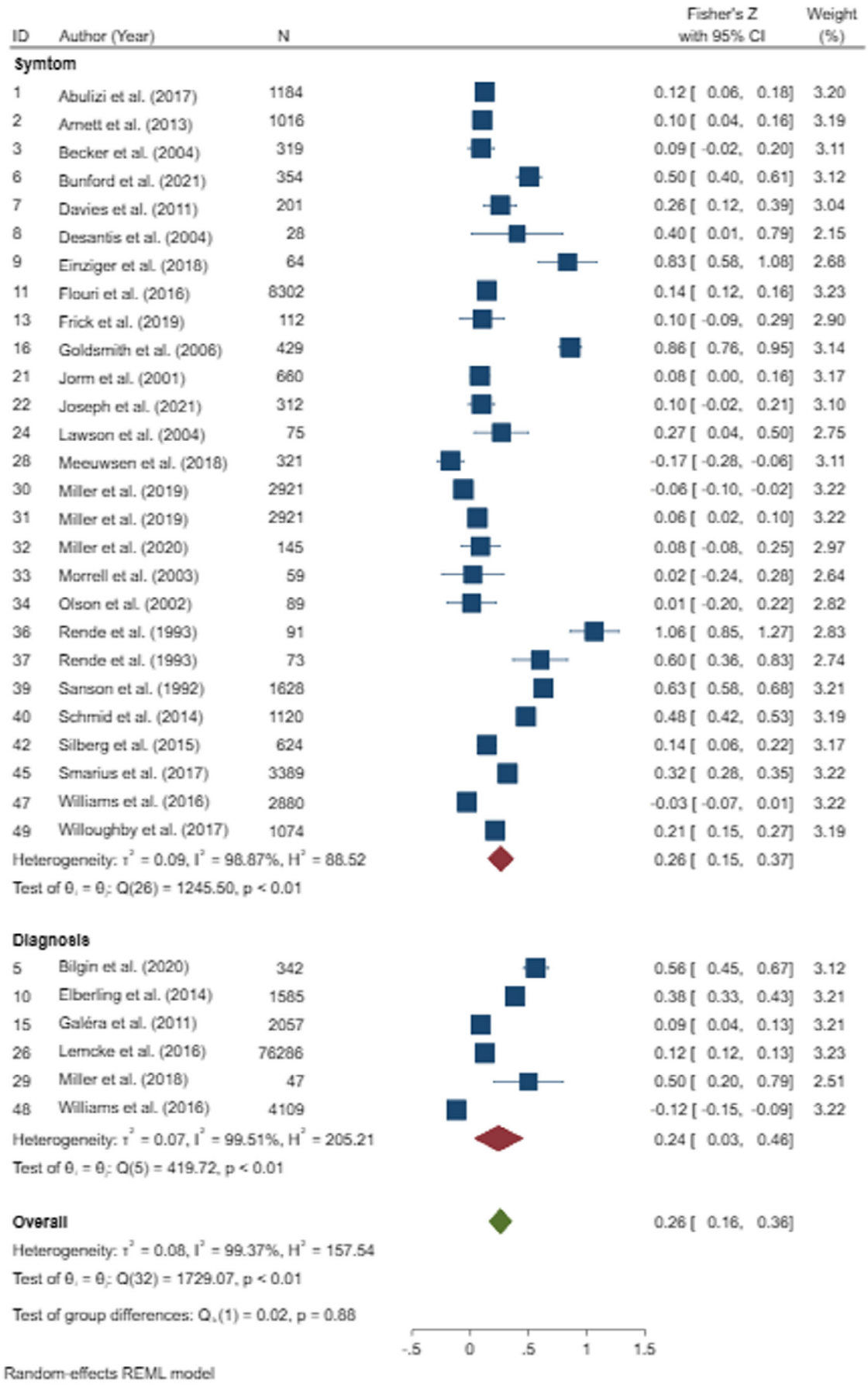

Figure 5 Forest plot of effect sizes of the association between negative emotionality and later ADHD symptoms/diagnosis

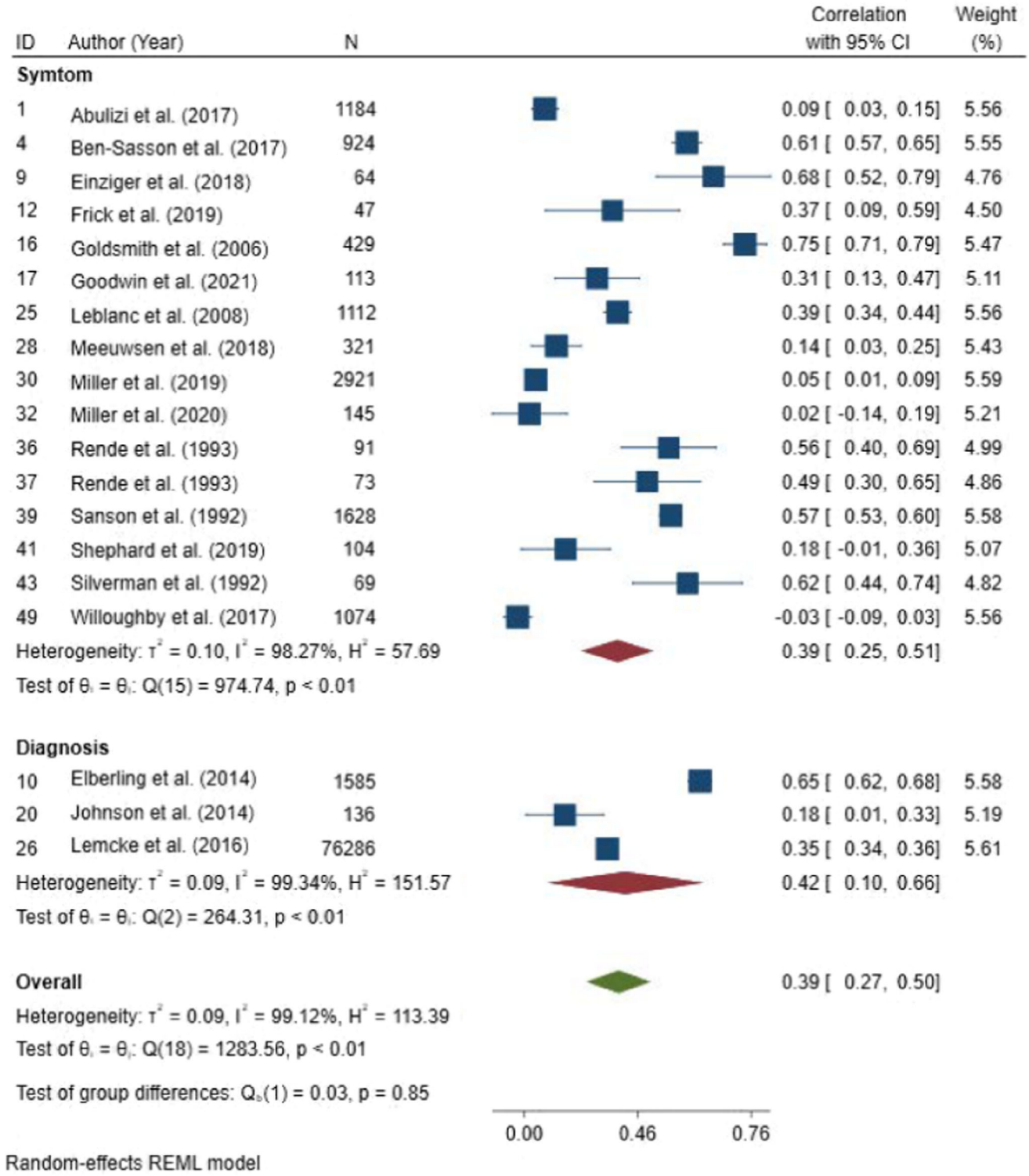

Figure 6 Forest plot of effect sizes for activity level associations with symptoms versus diagnosis of ADHD

help identify early risk for ADHD, it may also predict other common co-occurring disorders.

Sustained attention in infancy and toddlerhood only predicted later combined symptom dimension of ADHD ($k = 7$). It may be that the combined symptoms dimension captures more of the variability in ADHD symptoms and account for the heterogenous nature of ADHD. It is also possible that there may not have been enough power to detect significant associations with inattentive ($k = 4$) or hyperactive/impulsive symptoms ($k = 3$) individually given that only a few studies examined these symptom dimensions. Sustained attention, as suggested by Barkley (Barkley, 1997), is at the core of ADHD, impacting one's ability to maintain focus and ignore distractions. However, in our extensive review of literature, there was still a limited number of studies examining either sustained attention in infancy and toddlerhood as a predictor of ADHD. Additionally, none of the studies measuring sustained attention in infancy

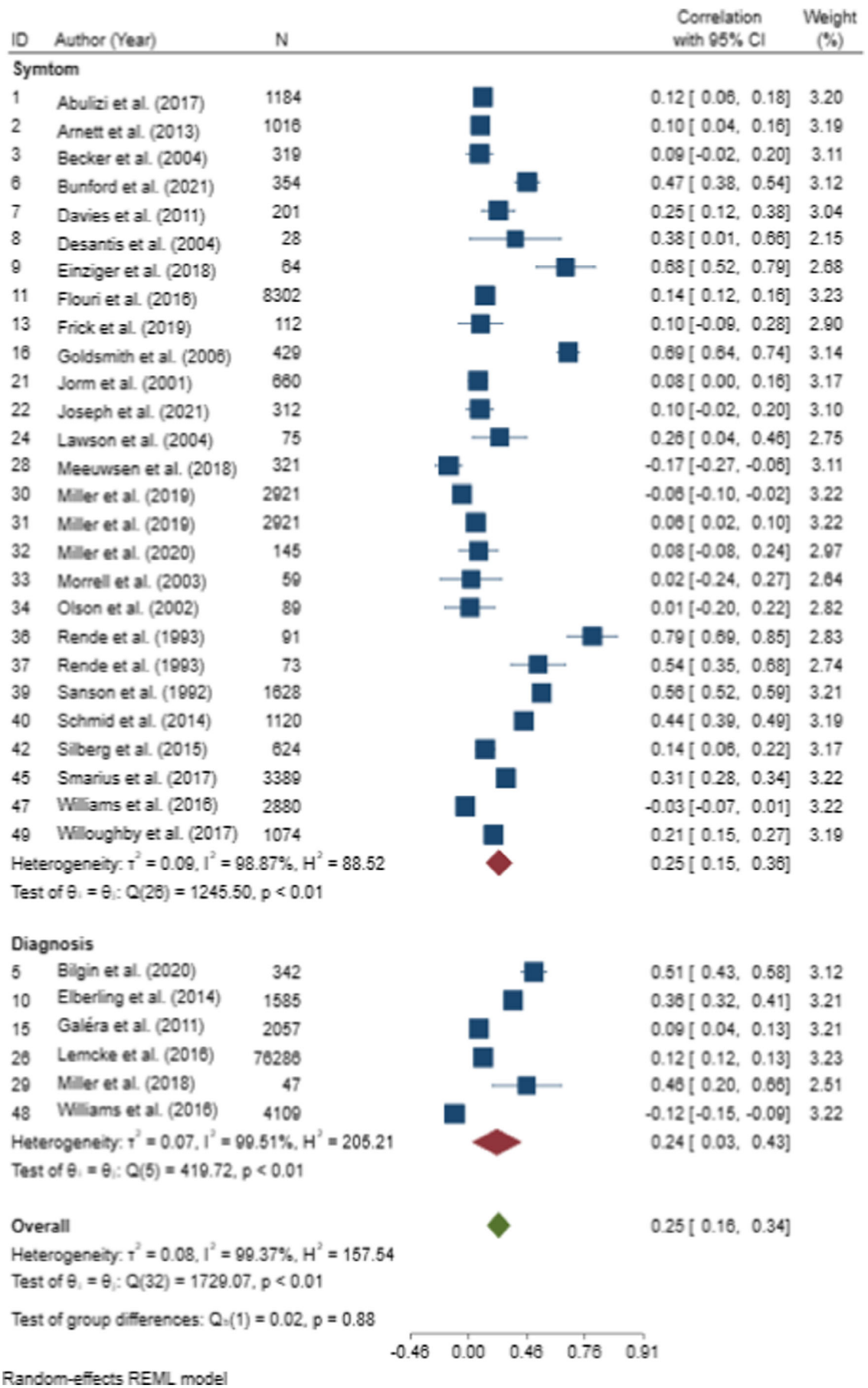

Figure 7 Forest plot of effect sizes for negative emotionality associations with symptoms versus diagnosis of ADHD

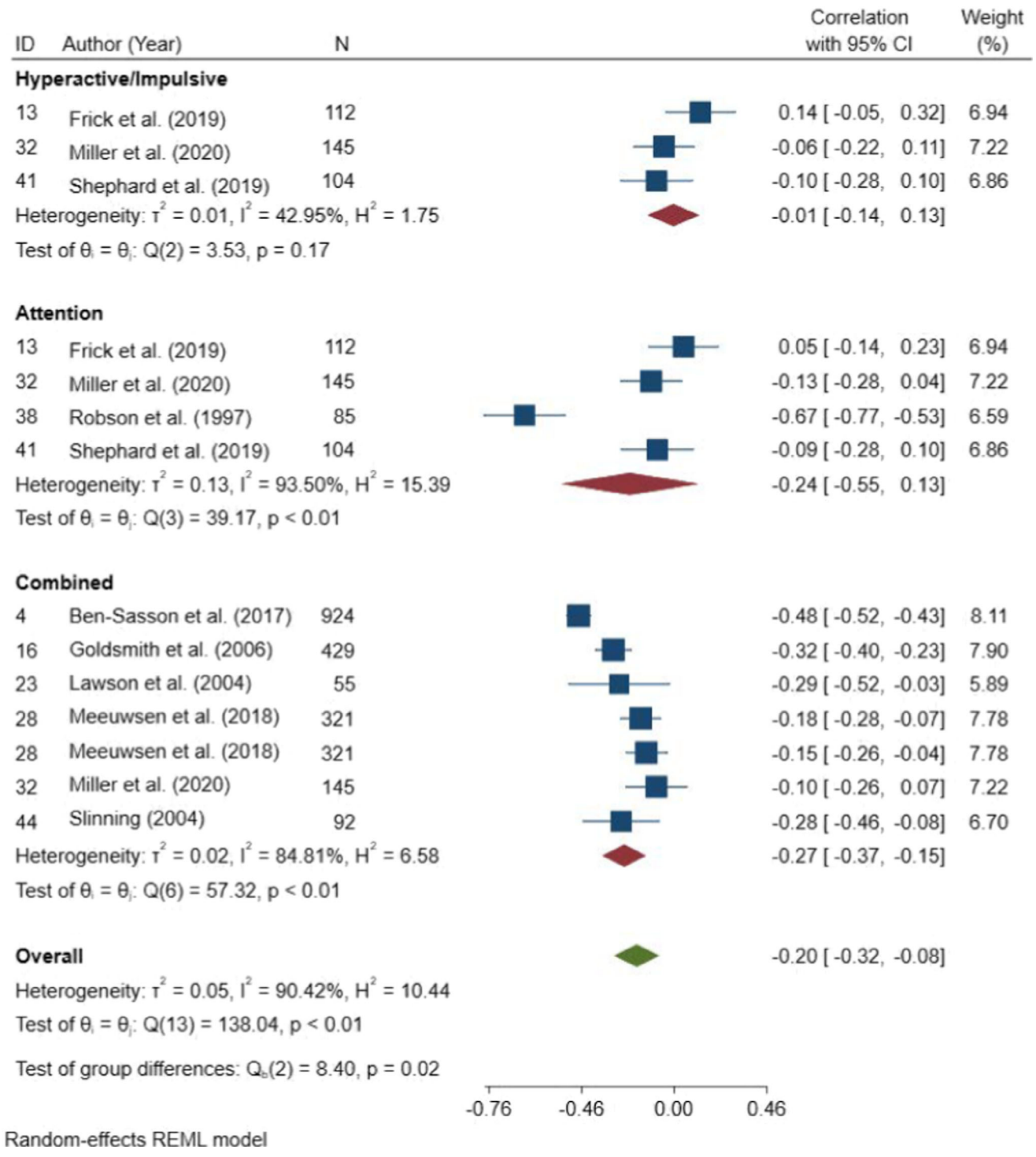

Figure 8 Forest plot of effect sizes for sustained attention associations by ADHD symptom dimensions

and toddlerhood examined ADHD diagnosis as an outcome and were all with community samples, suggesting a large gap in the literature and promising avenues for future research. Lastly, inhibition was not significantly associated with ADHD, including all subanalyses examining child age at the ADHD outcome measurement. Given the limited number of studies examining inhibition and varied measurement methods (e.g., different coding of behavioral tasks), it is possible that inhibition is a risk factor for ADHD that requires further investigation.

Moderation analyses revealed similar associations when comparing preschool age outcomes to the school age outcomes. Specifically, small to moderate effects were found for negative emotionality across both age groups, Additionally, a moderate effect was found for activity level and preschool age outcomes and moderate to large effect was found for childhood and adolescent age outcomes. Given the developmental trajectory of ADHD symptom dimensions and reliability of identifying children in preschool for ADHD,

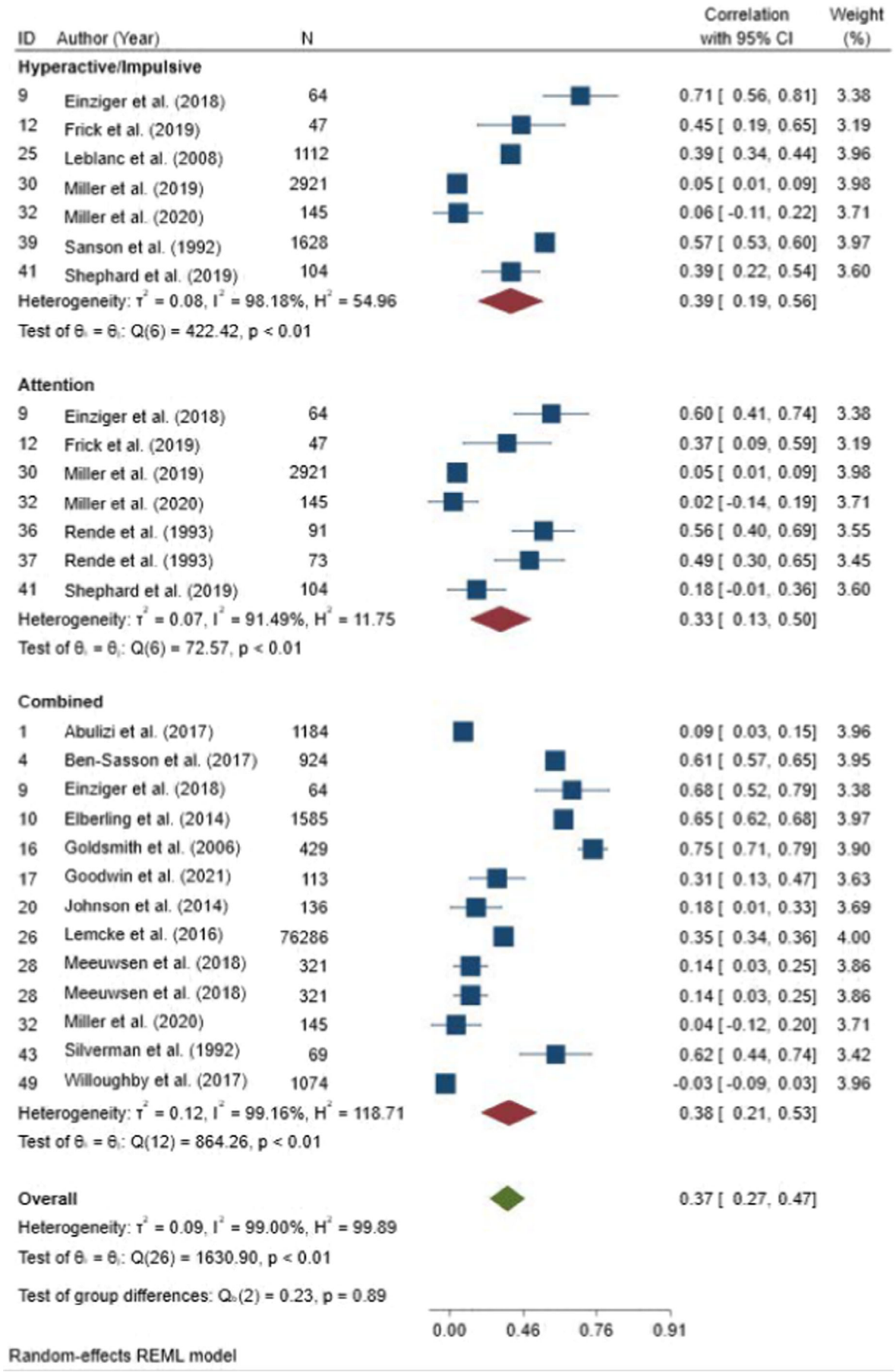

Figure 9 Forest plot of effect sizes for activity level associations by ADHD symptom dimensions

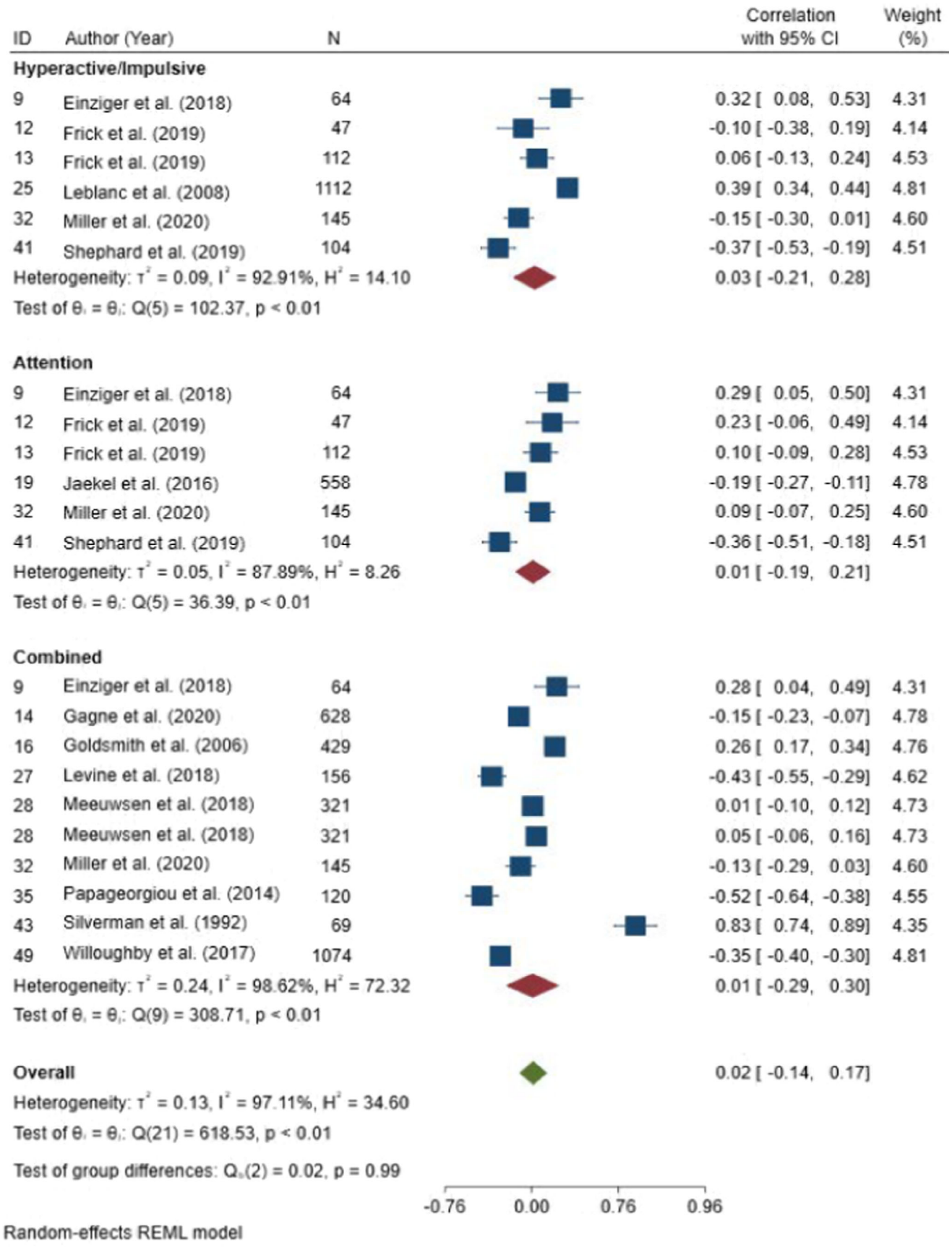

Figure 10 Forest plot of effect sizes for inhibition associations by ADHD symptom dimensions

significant predictors in infancy and toddlerhood of preschool and childhood ADHD would provide a unique opportunity to intervene early to prevent reduce the significant cascade of negative familial, social, and academic outcomes of children with ADHD.

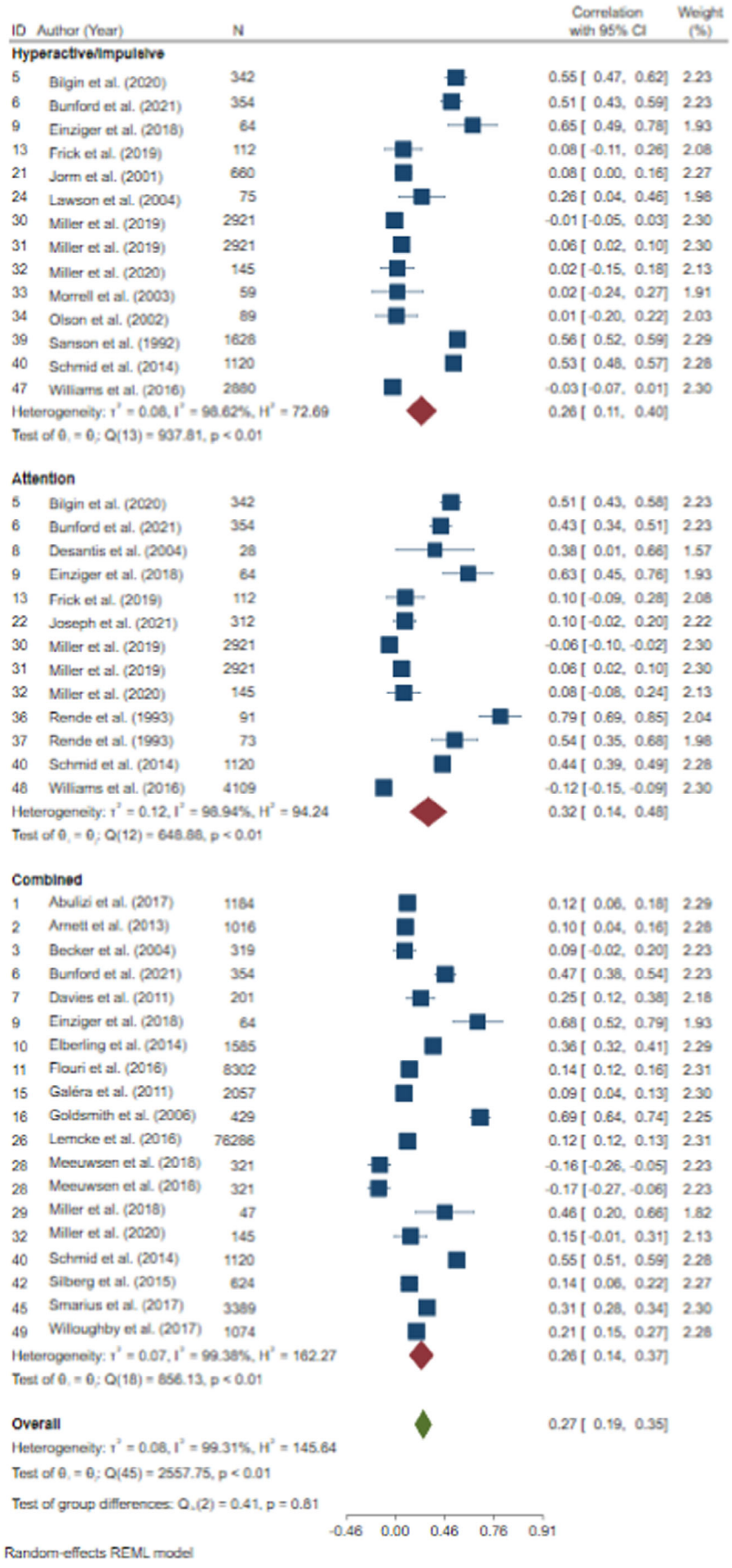

Figure 11 Forest plot of effect sizes for negative emotionality associations by ADHD symptom dimensions

In line with previous work, including recent reviews (Kostyrka-Allchorne et al., 2020; Shephard et al., 2022), the current systematic review and meta-analysis found significant associations between infant and toddler temperament constructs and child and adolescent ADHD. Specifically, the findings support associations between infant and toddler negative emotionality and child/adolescent activity level. Furthermore, the current study extends our understanding of infant and toddler temperament constructs by specifically focusing on prospective longitudinal designs to highlight the developmental trajectory beyond concurrent associations or cross-sectional designs. Additionally, the examination and findings associating infant and toddler sustained attention and inhibition with child and adolescent ADHD symptoms emphasizes other unique temperament profiles that can help increase early identification of ADHD. Lastly, the current study contributes to our knowledge on the specificity of these early risk markers to identify the unique and well-known heterogenous profiles of ADHD by examining the unique relations between the infant and toddler temperament constructs and the inattentive and hyperactive/impulsive symptom dimensions of ADHD.

Despite the strengths of the current study, we also acknowledge its limitations, which highly overlap with systematic reviews and meta-analytic designs. First, the findings may have limited generalizability given that most studies included either did not specify race/ethnicity and/or socioeconomic status (SES), and those that did largely relied on predominantly well-educated, mid- high SES samples. Future work should include more representative samples to encompass diversity in participant race/ethnicity, SES, and education. Additionally, measurement of constructs varied significantly ranging from observation to different reporters which makes it difficult to ascertain consistency between studies. We attempted to examine measurement based on reporter and found no moderation effects. However, infant negative emotionality demonstrated a small effect size for observed outcomes and a small-moderate effect size for parent report outcomes. Too few studies examined teacher reported outcomes of ADHD to be included in the moderator analyses. Second, unlike the recently published systematic review (Kostyrka-Allchorne et al., 2020; Shephard et al., 2022) who found limited variation due to heterogeneity, our findings suggest significant variation due to heterogeneity between studies. These findings highlighting the need for development of more refined measures of temperament and behavior. Third, although we aimed to examine more specificity regarding temperament constructs and ADHD, we did not examine individual-level data and therefore may not capture the heterogeneity of the samples included in each study. Although it would be a taxing and challenging task, a meta-analysis with individual level data could strengthen the current findings and emphasize the associations between the early temperament constructs and ADHD symptom dimensions. Consequently, given the focus on ADHD, we were unable to examine the heterogeneity of the infant and toddler temperament constructs beyond ADHD (e.g., ODD, depression, anxiety). Fourth, several studies have been published since the last date of search and are therefore not included in the current study. Lastly, there are several factors that may have moderated the associations that we were unable to examine given that there were either not enough studies that examined each factor (e.g., measurement method, parental psychopathology) or they were measured differently (e.g., parenting). Future research should consider examining factors such as parental psychopathology which can influence the heritability of ADHD, as well as parenting that may impact the developmental unfolding of ADHD symptoms.

There are several clinical implications of the current findings. Specifically, findings support temperament constructs (i.e., sustained attention, activity level, inhibition, negative emotionality) that can be identified early in infancy and toddlerhood as risk factors for ADHD. Early identification of these temperament constructs can help to identify at high risk for ADHD prior to the development of more serious behaviors, potentially leading to early interventions to help reduce the known long-term negative outcomes associated with ADHD. The findings suggest that activity level may be the most prominent or at least most easily identifiable and specific risk factor in infancy and toddlerhood, although further research is needed to examine attention and inhibition. It is important to note that given the significant heterogeneity, that future research is needed and that the associations imply risk, not causality.

Although we do not yet have normative temperament scores, information on infant/toddler temperament can aid in identifying those who could benefit from further assessment and monitoring. Based on these findings, families could be informed on how to monitor the temperament and providers could support parents with positive parenting skills (praise, positive reinforcement) as an early prevention method. Tracking and monitoring behavior is a great first step for families who may eventually need further behavioral and mental health supports for themselves and their child. Furthermore, several parenting interventions have demonstrated support for changing early toddler behavior including Incredible Years and Parent Child Interaction Therapy (PCIT), as well as research support for intervention strategies targeting self-regulation in preschool (see Graziano & Hart, 2016).

In conclusion, the current study provides additional and extended support for utilizing infant and toddler temperament as an early risk factor for the development of ADHD which provides an avenue for

early identification. Furthermore, our systematic review highlights the need for further research on several temperamental constructs and the need to examine longer term outcomes into adolescence and adulthood. Given the neurodevelopmental nature, stability, and associated negative long-term outcomes associated with ADHD, it is imperative to understand early individual differences that can be easily identified and reliably assessed.

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Key points

- ADHD is a prominent neurodevelopmental disorder with onset as early as preschool. Certain types of temperament in infancy and toddlers are associated with subsequent ADHD.
- The current systematic review and meta-analysis included 48 prospective longitudinal studies included temperament in infancy and toddlerhood as a predictor of later ADHD, suggesting high interest in early predictors of ADHD.
- Activity level measured in infancy and toddlerhood had a moderate effect size on later ADHD symptoms and diagnosis. Fewer studies examined inhibition and sustained attention in infancy and toddlerhood as predictors of childhood ADHD.
- Given the cascade of negative outcomes for children with ADHD, early identification and monitoring of child temperament may provide a valuable early indicator for early intervention and prevention.

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