

## University of Groningen

### On edge: night and day. Understanding the association between poor sleep and aggression van Veen, Maaike

DOI:  
[10.33612/diss.248586077](https://doi.org/10.33612/diss.248586077)

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*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2022

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*  
van Veen, M. (2022). *On edge: night and day. Understanding the association between poor sleep and aggression*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen.  
<https://doi.org/10.33612/diss.248586077>

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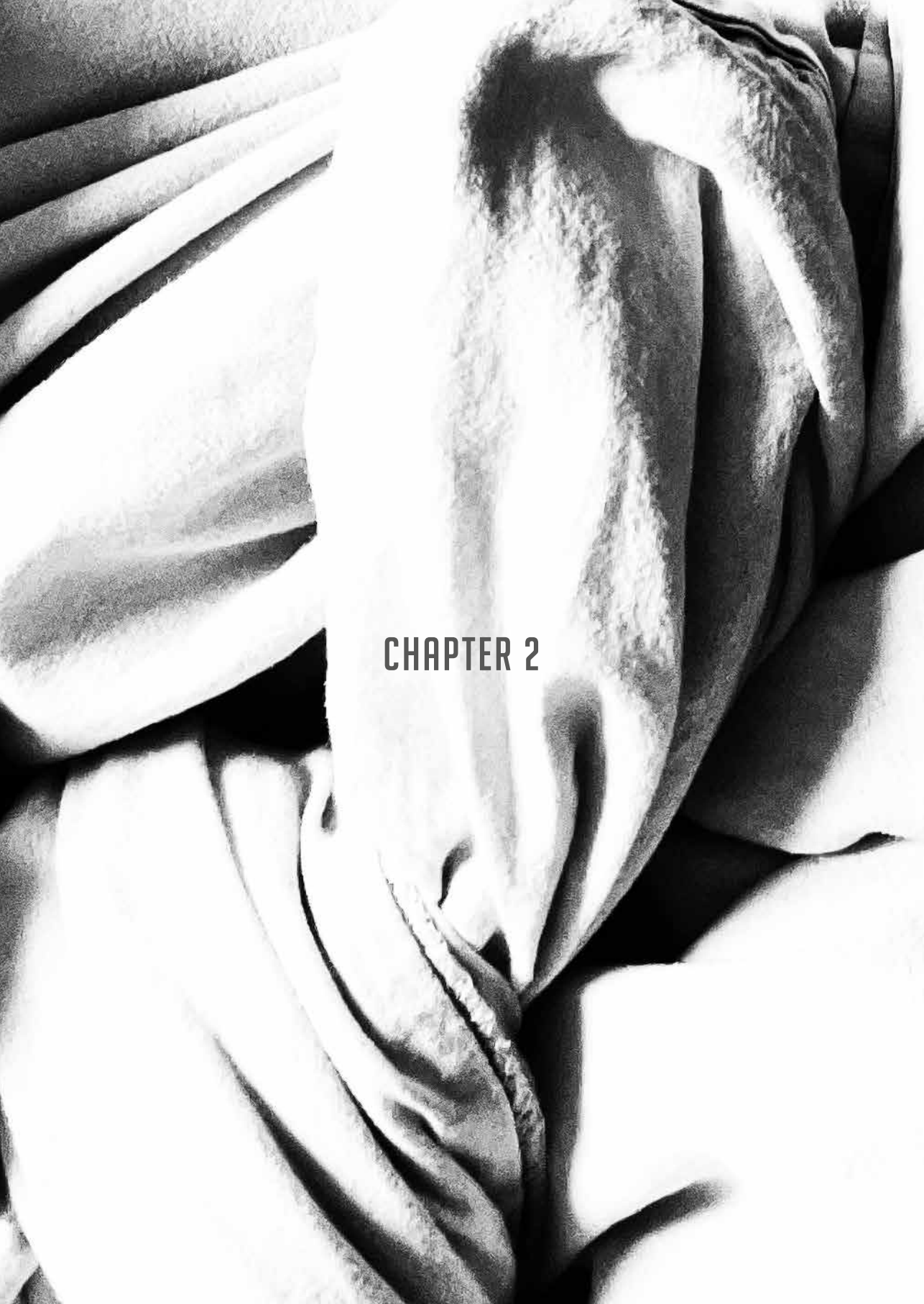
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## CHAPTER 2

### THE ASSOCIATION OF SLEEP QUALITY AND AGGRESSION: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

Published as:

Van Veen MM, Lancel M, Beijer E, Remmelzwaal S, Rutters F. The association of sleep quality and aggression: a systematic review and meta-analysis of observational studies. *Sleep Medicine Reviews*. 2021 May 12:101500

## SUMMARY

Poor sleep quality is closely related to aggression, but despite the promise of new therapeutic possibilities, a systematic synthesis of observational research on the association between sleep quality and aggression is lacking. This systematic review and meta-analysis examined the association between sleep quality and aggression, using the academic databases PubMed and PsycINFO. Subjective and objective measures of sleep quality were included, as well as multiple measures of aggression, assessing aggressive and externalizing behavior, anger, hostility and irritability. Ninety-two observational articles, containing 96 studies, encompassing a total of 58.154 children, adolescents and adults were sourced out of 7161 references identified. Methodological quality was moderate or strong in 76% of studies. Data for meta-analysis was available from 74 studies. Poorer sleep quality was associated with higher aggression in 80.8% of studies. Pooled results showed a correlation of 0.28 (95%CI 0.25-0.31;  $I^2=90.1\%$ ) and odds ratio of 3.61 (95%CI 1.13-11.51;  $I^2=88.3\%$ ). Effect estimates and heterogeneity varied according to population type and measurement instruments, but not according to article quality or age group. Our findings confirm that poor sleep quality is consistently associated with higher aggression. As most evidence is cross-sectional, more prospective and high-quality experimental evidence is required to elucidate cause-effect and optimize prevention and treatment of aggression.

## INTRODUCTION

Sleep plays an essential role in psychological well-being [1]. Over the last decades, a growing body of research has demonstrated that disturbed sleep impairs neurocognitive functioning [2-4], as well as the experience and regulation of emotions [3, 5]. It is therefore understandable that sleep disturbances are associated with various forms of psychopathology, such as developmental, affective, psychotic and personality disorders [6-8]. More specifically, sleep has been suggested to be a relevant factor in aggression, as disturbed sleep attenuates the control over cognition, emotion and subsequent behavior [4, 5]. Multiple experimental and epidemiological studies found disturbed sleep to be associated with different aspects of aggression, such as increased hostility, higher tendencies to blame others, anger and increased occurrence of verbal or physical aggression [9]. Some of this previous work indicates that especially sleep quality is closely related to aggression, stronger than sleep quantity [10, 11]. Narrative reviews on this topic confirm the association between poorer sleep quality and more aggressive or externalizing behavior [12, 13].

When examining the association between sleep quality and aggression, it is important to realize that both constructs have a broad definition. Poor sleep quality can be interpreted in multiple ways, varying from sleep disorders, such as insomnia disorder, to alterations in objective measures of sleep (polysomnography or actigraphy) as well as subjective reports of poor quality of sleep. Aggression is usually defined as the intentional act to harm another who is motivated to avoid that harm. Several conceptual frameworks try to incorporate the processes relevant to aggressive tendencies and actual aggressive behavior in humans. The General Aggression Model is the most comprehensive and widely used framework, and provides an integrative view of many, more specific, theories [14]. It describes the interplay between numerous personal and situational factors influencing internal state, encompassing arousal and affective or cognitive aspects such as anger and hostility, and factors influencing appraisal and decision, such as attribution bias and level of self-control. These factors combined eventually result in actual aggressive behavior. Considering the extensive effects of disturbed sleep on many of these factors that play a role in aggression, targeting sleep may be a previously overlooked point of intervention in preventing or reducing the risk of aggression.

Studies on the association of poor sleep with aggression reflect the complexity of the aggression construct, assessing a variety of aspects of aggression including (physical or verbal) aggressive behavior, externalizing behavior (including both aggression and rule-breaking), anger, irritability and hostility. In their valuable narrative review on this topic, Krizan and Herlache [15] describe three potential pathways, based on the General Aggression Model, through which poor sleep can lead to a higher tendency toward aggression; via amplification of negative affect, increase of hostile perception and impairment of impulse control. Of course, a reverse pathway must also be considered. It is likely that aggressive thoughts or behaviors during the day could negatively influence sleep quality by increased physiological arousal and stress [15]. In other words, the association between sleep quality and aggression is hypothesized to be bidirectional. However, thus far the evidence for aggressive or externalizing behavior negatively influencing sleep quality is much less conclusive than the other way around [16, 17].

Despite previous research indicating that sleep quality is associated with aggression, and thus poses a great opportunity as a possible target for interventions, a systematic synthesis of the current observational evidence on the association between sleep quality and aggression is lacking. The current study aims to assess the association between sleep quality and measures of aggression in a systematic review and meta-analysis of observational studies. We deliberately chose to keep a broad scope, both considering diverse measures of sleep quality and aggression, to provide a comprehensive overview on the association. We hypothesize that poor sleep quality is associated with increased aggression.

## METHODS

### Data sources and search strategy

A systematic review and meta-analysis were conducted in accordance with the guidelines on Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) [18] as well as the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines for observational studies [19]. The protocol of this review was registered in the PROSPERO database under number CRD42019106966. In short, we conducted a comprehensive search of the literature in MEDLINE (PubMed) and PsycINFO from inception up until October 1<sup>st</sup> 2019, in collaboration with a librarian. Reference lists of included studies were searched manually for additional studies. Search terms included controlled terms (MeSH in PubMed and thesaurus terms in PsycINFO) as well as free text terms. The search strategy focused on a combination of these terms and their synonyms related to night-time sleep duration and sleep quality. The full search strategy is provided in Supplemental File S1. For aggression, the following terms were used: aggression, explicit aggression, reactive aggression, externalizing behavior, irritability, hostility, hostile behavior, violence, violent, eager, impulsiveness, anger, anger temper and anger tendencies. Although impulsiveness as sole outcome was not further assessed in this review, we included this (and closely related) term(s) to enable detection of studies on impulsive aggression and / or externalizing behavior. For the purpose of the current study, we solely reviewed the studies on sleep quality, either assessed as sleep efficiency - percentage of actual sleep of total time in bed, measured by polysomnography or actigraphy - or as subjective reports of sleep quality or sleep problems, including insomnia, assessed by questionnaires or diaries. The studies on the association between sleep duration measures and aggression will be addressed in a separate paper, as sleep quality and sleep duration are regarded as two separate domains in relation to emotional and behavioral problems (see for example, Kosticova et al. 2020 [20]).

### Study selection

Studies were included if (1) the population consisted of humans, including children (aged four years or older), young adolescents (aged twelve years or older) or adults (aged eighteen years or older); (2) the article was available full text; and (3) the article was written in English, German or Dutch. Studies were excluded if (1) poor sleep quality was defined

as sleep-related breathing disorder or sleep-related movement disorder; (2) sleep quality was defined as fatigue or day time sleeping, i.e. napping and daytime sleepiness, or when defined as sleep timing preference, i.e. chronotype; (3) aggression was solely defined as delinquency, delinquent behavior, criminal activity, conduct problems or antisocial behavior; (4) sleep quality was regarded as the dependent variable and no uncorrected correlation coefficient could be extracted. When results from a study were reported more than once, the most recent article was used.

### Study screening and data extraction

All studies identified in the literature search were screened for eligibility on title and abstract by two of three reviewers (OS and FR or MV), using Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at [www.covidence.org](http://www.covidence.org)). The full text versions of potentially eligible studies were independently assessed for inclusion by two reviewers. The mean positive proportion and negative proportion of agreement between the reviewers for title/abstract screening was 49% and 91%, respectively. For full-text screening, the mean positive proportion and negative proportion of agreement was 86% and 84%, respectively. Discrepancies were resolved through discussion, consulting the third reviewer.

Data extraction was performed independently by two reviewers (EB and FR or MV). A standardized, pre-piloted form was used to extract data from the included studies. Data extraction included: author, year of publication, study design, study population, number of participants, mean age, sleep quality measures and aggression measures. In case of multiple categories of sleep quality, the outcome data from adjacent categories were used for extraction, rather than the data of the most extreme categories (e.g. "poor" vs "good", rather than "very poor" vs "very good" sleep quality). In this way, overestimation of the association between sleep quality and aggression is avoided, as choosing extremes of the sleep quality spectrum may lead to an overestimation of the association with aggression. Furthermore, the extreme categories often contain very low numbers of participants per group, attenuating the statistical robustness of results. If papers described both cross-sectional and prospective associations, the data from the cross-sectional analyses were used. If studies reported multiple outcomes of aggression, the overall aggression outcome was extracted, and, if not available, the outcome measure most closely representing actual aggressive behavior (e.g. physical or verbal aggression over psychological aggression). For a number of publications, data extraction and / or pooling was not possible for several reasons, such as missing information to enable pooling (e.g. no standard error or confidence interval) or unsuitable analyses for pooling (e.g. highly corrected data or advanced (growth) models). In total, 45 first authors were contacted by email to request additional information, in the form of unadjusted correlations, which resulted in 18 authors (40%) providing additional data. If no unadjusted effects were obtained, studies were included in the qualitative synthesis. Discrepancies identified during the duplicate data extraction were resolved through discussion, if necessary, consulting the third reviewer.

## Quality assessment

An adaptation of the standard Quality Assessment Tool for Quantitative Studies, as developed by the Effective Public Health Practice Project (EPHPP), was used for assessment of the methodological quality of the included studies [21]. Mackenbach et al. adapted this to a 19-item tool suitable for assessing the methodological quality of studies of observational and experimental design. This tool describes eight domains of quality: 1) study design; 2) blinding; 3) representativeness with regard to selection bias; 4) representativeness with regard to withdrawals/dropouts; 5) confounders; 6) data-collection; 7) data-analysis; and 8) reporting. The ratings of some domains are less straight forward and are therefore further explained. Confounding was scored as ‘weak’ when data were not corrected for confounders; a ‘moderate’ score was attributed to studies that corrected for age or sex; and ‘strong’ was attributed to studies correcting for age and sex, possibly including additional relevant variables as well. Data-collection was scored as ‘weak’ when no information on reliability or validity of measurement instruments was provided in the study itself or in the design paper. Limited information on measurements instruments was scored ‘moderate’ and inclusion of specific information on reliability or validity, or reference to validation papers, resulted in a ‘strong’ rating for data-collection. Data-analysis was scored as ‘weak’ when data was not or inappropriately tested and ‘strong’ for multivariable analysis. All included studies were assessed independently by two reviewers (EB/OS, MV or FR) for methodological quality. The mean proportion of initial agreement between reviewers was 79%. The ratings of each domain and the overall ratings were compared between the reviewers to reach consensus.

## Data synthesis

A meta-analysis was conducted by using a model of random-effects (because of differences in the methodology of studies) by pooling data, if at least three or more studies described the same determinant, outcomes and reported similar effect measures. Effect measures of group differences (standardized mean differences) were re-calculated to correlations [22]. The results were sorted according to effect measures; correlations or odds ratio. All types of sleep quality and aggression measures were pooled to provide overall estimates of their association. Subsequently, the results were stratified based on the aggression construct measured, resulting in 7 categories: 1) aggression composite that includes emotional, cognitive and behavioral aspects of aggression combined in an overall score, 2) aggressive behavior that assesses actual aggressive behavior, such as physical or verbal aggression and violence, 3) externalizing behavior that includes aggression and rule-breaking, 4) irritability, 5) hostility, 6) anger and 7) anger control. Statistical heterogeneity was evaluated with the  $I^2$  statistic, reflecting the percentage of total variance that can be explained by heterogeneity. A score of 0% is generally considered as no heterogeneity in contrast to 100 %, indicating high heterogeneity [23]. In sensitivity analyses, the influence of methodological quality, age groups, population type and type of measurement instrument for sleep or aggression on the pooled estimates and heterogeneity was explored. Pooled estimates were considered to differ significantly if no overlap in 95% confidence intervals was present. Visual inspection of multiple funnel plots was used to assess asymmetry. All analyses and plots were performed using the Metafor package in RStudio version 3.4.2.

## RESULTS

### Description of included studies

The systematic literature search identified 7324 articles. After screening titles and abstracts, 265 potentially eligible articles were read full text. In total, 84 papers met the inclusion criteria for this current systematic review on sleep quality (see Figure 1). Additionally, we identified 8 articles in the grey literature search meeting the criteria, leading to a total of 92 included articles describing results from 96 studies. A total number of 58.154 participants from both general (n=57) and clinical populations (psychological vulnerability n=32; medical condition n=7) were included. Study designs were cross-sectional (69.8%), mixed cross-sectional and prospective (20.8%) or prospective (9.4%). Studies involved either adults (n=31), children (n=29), adolescents (n=8) or elderly (n=3), the remainder of studies involving multiple age groups in varying and overlapping compositions (n=25). An overview of study characteristics is provided in Table 1.

The included studies assessed different aspects of sleep quality: sleep quality (n=38), sleep problems measured continuously (n=32) or dichotomous (n=4), sleep efficiency (n=8), sleep disturbances (n=6), insomnia symptoms or disorder (n=6), sleep disorder (n=1) and trouble sleeping (n=1). Measurement instruments most frequently used to assess sleep quality were the Pittsburgh Sleep Quality Index (PSQI) [112] (n=23), Child Sleep Hygiene Questionnaire (CSHQ) [113] (n=10), Child Behavior Checklist (CBCL) [114] (n=7) and actigraphy [115] (n=8).

The included studies assessed different aggression constructs: aggression composite (n=28), aggressive behavior (n=16), externalizing behavior (n=28), irritability (n=8), hostility (n=3), anger (n=12) and anger control (n=1). Measurement instruments most frequently used to assess aggression were the Child Behavior Checklist (CBCL) [116] (n=18) or Youth Self Report (YSR) [117] (n=6), Strengths and Difficulties Questionnaire (SDQ) [118] (n=6) and Aggression Questionnaire (AQ) [119] (n=5).

Finally, 74 studies could be included in the quantitative analysis. Of these, 3 studies provided data for 2 separate participant groups, making extraction possible for 77 effect estimates. The remaining 22 studies were included in the qualitative analysis. An overview of the methodological quality assessment per domain per study for all included studies is provided in Supplemental Table 2. Methodological quality was considered strong in 24 studies, moderate in 49 studies and weak in 23 studies. Important reasons for downgrading methodological quality were less representativeness of the population and inadequate correction for confounders.

### Sleep quality and aggression

Of the eligible studies, the majority (80.8 %) showed significant associations between poor sleep quality and measures of aggression. The remaining studies (19.2%) either reported a non-significant association in the same direction or no association. No studies found evidence for an inverse association, i.e. poorer sleep quality to be related to lower aggression. The overall pooled correlation estimate of the association between sleep

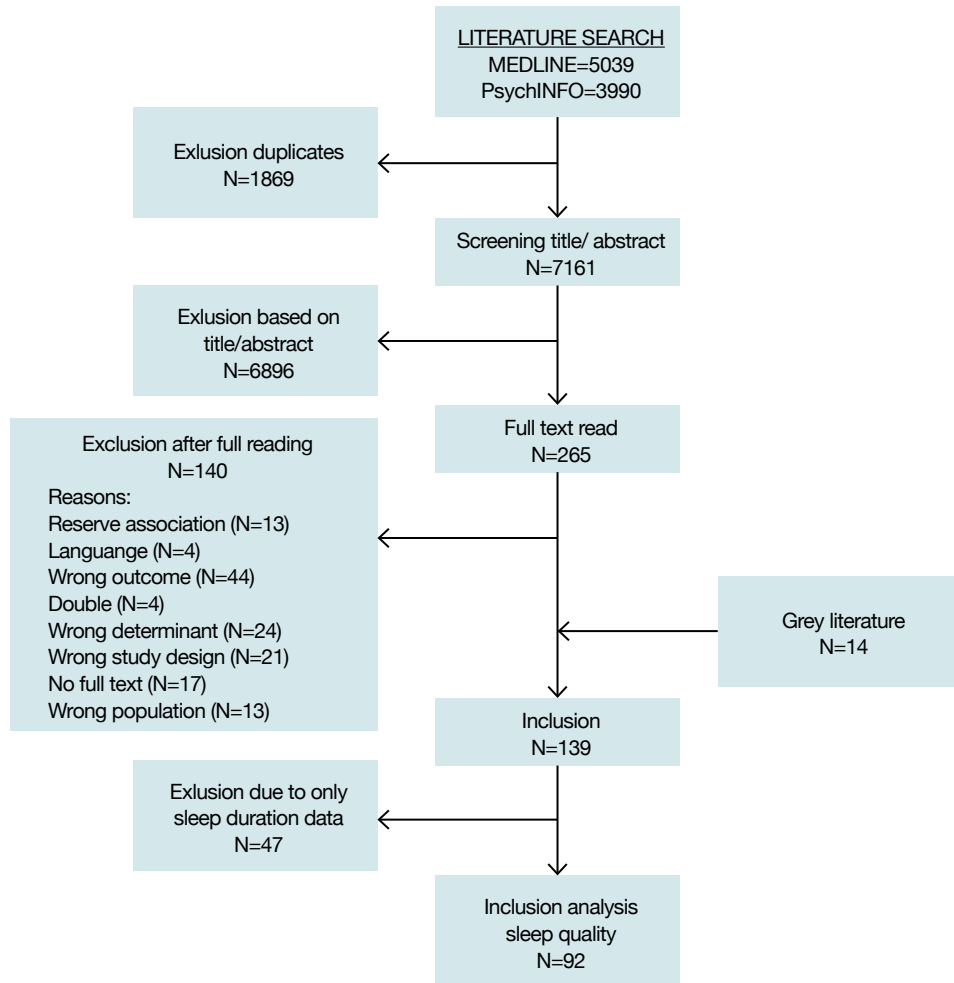


Figure 1. Flow-chart of the search and selection process.

quality and aggression was 0.28 (95%CI 0.25-0.31;  $I^2=90.1\%$ ) (Fig.2). The pooled odds ratio estimate was 3.61 (95%CI 1.13-11.51;  $I^2=88.3\%$ ) (Fig.3). In the following section, we will present the meta-analyzed results of the estimates of the association between sleep quality and aggression per outcome category, as well as the qualitative results per outcome category.

**The association between sleep quality and aggression per outcome category**

In total, 26 studies investigated the association between sleep quality and aggression composite score. Nineteen correlations from 17 studies [24, 38, 39, 42, 52, 68, 69, 75, 79,

80, 83, 91, 94, 98, 104, 111] were meta-analyzed (Fig.2) and provided a pooled correlation estimate of 0.26 (95% CI 0.21-0.32), indicating a significant association between sleep quality and aggression composite score, with a high heterogeneity ( $I^2=82.3\%$ ). Two studies providing odds ratios [97, 101] both showed a significant association between sleep quality and aggression composite score (Fig. 3). Seven studies could not be included in the meta-analysis; qualitative analysis showed that four studies observed statistically significant associations between poor sleep quality and higher aggression [16, 47, 92, 102], whereas three studies showed no statistically significant association [43, 55, 62].

**Table 1.** Characteristics of included studies.

Author	Year	Study design	Study population	N	Age: mean ( $\pm$ SD or range) (yrs)	Determinant: Sleep quality	Outcome: Aggression	Outcome: Category	Sleep quality measurement	Aggression measurement	Qualitative analysis
Abdoli [24]	2018	C	Substance-abusing adult male traffic offenders	360	30.97 $\pm$ 9.51	Sleep quality	Aggression	AC	PSQI	AQ	no
Adams [25]	2014	C	Children and adolescents with ASD	144 vs 111	No sleep problem: 7.96 $\pm$ 3.48 Severe sleep problem: 7.52 $\pm$ 3.33 yrs	Sleep problems	Externalizing behavior	EB	ASD-CC (1 item)	ASD-BPC	MIP
Adrian [26]#	2019	P	Adolescent and adult soldiers	1698	65% aged 17-19	Sleep problems	Anger	ANG	ISI (modified, 4 items)	Anger reactions (4 items)	no
Arbunaga [27]#	2019	C	Adult university students	1252	23.58 $\pm$ 3.28	Sleep quality	Anger	ANG	PSQI	STAXI	no
Armstrong [28]	2014	C	Children	142 vs 254	4.5	Insomnia symptoms	Hostile / aggressive behavior	AB	CSHQ	PBQ	no
Aronen [29]	2000	C	Healthy children	49	9.37 $\pm$ 1.39	Sleep efficiency	Externalizing behavior	EB	Actigraphy	CBCL	NDP
Aronen [30]	2014	CP	Children with CD/ODD	30	9.8 $\pm$ 1.4	Sleep efficiency	Externalizing behavior	EB	Actigraphy	CBCL	HCD

Barclay [31]#	2011	C	Adult twins	1556	20 (range 18 - 27)	Sleep quality	Externalizing behavior	EB	PSQI	ASR	no
Barker – study 1 [10]	2016	C	Adult prisoners	95	35.25 $\pm$ 10.9	Sleep quality	Aggression	AB	PSQI	Revised DIPC	MIP
Barker – study 2 [10]	2016	C	Adolescent and adult prisoners	141	19.15 $\pm$ 1.24	Sleep quality	Aggression	AB	PSQI	RPQ	no
Becker [32]#	2014	C	Children and adolescents	175	9.61 $\pm$ 1.88	Sleep problems	Aggression	AB	SSR	Dodge and Cole's measure of aggression	no
Becker [33]#	2015	CP	Children and young adolescents with ADHD	81	12.20 $\pm$ 0.95	Sleep problems	Externalizing behavior	EB	CBCL	SSIS	no
Biggins [34]	2018	C	Adult athletes	36 vs 33	22.7 $\pm$ 4.1	Sleep quality	Anger / Hostility	ANG	PSQI	POMS	NPT
Brandt [35]	2017	C	Adolescents and adult athletes	28 vs 294	22 $\pm$ 6.8	Sleep perception	Anger	ANG	BRUMS	BRUMS	no
Brylewski [36]	1999	C	Adults living in health- or social-services-managed community housing	79 vs 121	46.8 (21 – 83)	Sleep problems	Aggression	AB	Simonds & Parraga Sleep Questionnaire	ABC	no
Catrett [37]	2009	CP	Adolescents	4353	13.18 $\pm$ 0.80	Possible insomnia	Violence	AB	Trouble sleeping / morning tiredness (2 items)	Several items on use of violence / fighting	HCD
Cepuch [38]	2017	C	Adolescents and adults suffering from CF	70	14-25	Insomnia symptoms	Aggression	AC	AIS	HADS	no

Chester – study 1 [39]	2020	CP	Undergraduate students	388	19.58 ± 2.39	Sleep quality	Aggression	AC	PSQI	V DAT	no
Chester – study 2 [39]	2020	CP	Adult employees	317	33.15 ± 11.18	Sleep quality	Aggression	AC	PSQI	V DAT	no
Chester – study 3 [39]	2020	CP	Undergraduate students	379	19.15 ± 2.79	Sleep quality	Aggression	AC	PSQI	V DAT	no
Cohen [40]	2018	CP	Children, adolescents and adults with low-functioning autism	37	12.91 ± 3.32	Sleep efficiency	Aggression	AB	Nightly observations of sleep by caregivers	CBI	ADM
Cohen-Mansfield [41]	1990	P	Adult nursing home residents	408	85 (70-99)	Sleep disturbances	Aggression	AB	Nurse's Sleep Rating Questionnaire	CMAI	HCD
Coto [42]	2018	C	Children with externalizing behavior problems	148	5.06 (3.78-6.05)	Sleep problems	Aggression	AC	CSHQ	DBRS-PV	no
Coulombe [43]	2011	C	Adolescents	980	13.88 ± 1.41	Sleep problems	Aggression	AC	YSR	YSR (aggression subscale)	HCD
Dahl [44]	1995	C	Children with AD	59	8.0 ± 2.3	Sleep problems	Irritability	IRR	CSBS	CSBS	NPT
Denis, study 1 [45]#	2017	C	Adult twins	1156	20.3 ± 1.76	Sleep quality	Externalizing behavior	EB	PSQI	ASR	no
Denis, study 2 [45]#	2017	C	Adults	338	23.5 ± 8.2	Sleep quality	Externalizing behavior	EB	PSQI	ASR	no
Didden [46]	2002	C	Children, adolescents and adults with mild to profound ID	286	8.3 ± 4.1	Sleep problems	Irritability	IRR	Simonds & Parraga Sleep Questionnaire	ABC	NPT

Elison [47]	2019	C	Adult veterans with PTSD	143	40.87 ± 11.79	Insomnia	Aggression	AC	ISI	ROAS	HCD
Elrafifi-Feireira [48]	2019	C	Children with nighttime fears	68	4.9 ± 0.9	Sleep problems	Externalizing behavior	EB	SHIPC	CBCL	no
El-Sheikh [49]	2007	C	Children	167	8.7 ± 0.3	Sleep efficiency	Aggression	AB	Actigraphy	SBS	no
El-Sheikh [50]#	2013	P	Children	251	8.23 ± 0.73	Sleep problems	Aggression	AC	SSHS	TSCC	no
El-Sheikh - females [51]	2015	C	Adult couples	135	Wives: 37 ± 0.5	Sleep efficiency	Aggression	AB	Actigraphy	Revised CTS	no
El-Sheikh – males [51]	2015	C	Adult couples	135	Husbands: 39 ± 0.6	Sleep efficiency	Aggression	AB	Actigraphy	Revised CTS	no
El-Sheikh [52]	2019	C	Adolescents	235	15.78 ± 0.8	Sleep quality	Aggression	AC	SSHS	YSR (aggression subscale)	no
Engin [53]	2010	C	Adults with insomnia sleep disorder	96 vs 96	Patients: 30.96 ± 9.15 Controls: 30.56 ± 8.63	Insomnia disorder	Anger	ANG	DSM-IV-TR diagnose by psychiatrist	TAAES	no
Erreygers [54]	2018	P	Adolescents	1746	13.55 ± 0.55	Sleep quality	Anger	ANG	Revised ASWS	Anger (1 item)	no
Fadini [55]	2015	C	Children and adolescents with ASD	101	9.7 ± 4.1	Sleep disorders	Aggression	AC	SDSC	CBCL (aggression subscale)	NDP



Fernandez-Mendoza [56]	2009	C	Adolescent and adult first year university students	1271	18.85 ± 1.45	Sleep quality	Anger	ANG	Self-developed (3 items on sleep quality)	Angry in class (1 item)	no
Franzen [57]	2010	P	Adult patients with hepatitis C	86	47.4 ± 12.4	Sleep quality	Anger / Irritability	ANG	PSQI	AIAQ	no
Freitag [58]	2017	C	Adults	200	29.3 ± 11.0	Sleep quality	Aggression	AB	PSQI	IPAS	no
Goodnight [59]	2007	CP	Children	556	5.0	Sleep problems	Externalizing behavior	EB	CBCL	TRF	no
Grano [60]	2008	CP	Adult hospital employees	4005	45.4 ± 8.6	Sleep disturbances	Hostility	HOS	4-item Jenkins Scale	FTSH	no
Gregory [16]	2002	P	Children and adolescents	490	Baseline: 3/4 Follow-up: 13-15	Sleep problems	Aggression	AC	CBCL	CBCL (aggression subscale)	HCD
Gregory [61]	2004	P	Twin children	4387	Baseline: 3/4 Follow-up: 7	Sleep problems	Externalizing behavior	EB	general sleep problem scale, 4 items	SDQ	HCD
Gregory [62]	2008	P	Children	2076	Baseline: 9.93 ± 3.75	Sleep problems	Aggression	AC	CBCL (1 item)	CBCL (aggression subscale)	NDP
Henderson [63]	2011	C	Children with ASD	58	9.0 ± 2.09	Sleep quality	Externalizing behavior	EB	CSWS	CBCL	no
Hisler [64]	2017	C	Adults	436	56.91 ± 11.49	Sleep quality	Anger	ANG	Sleep diary (1 item)	STAXI	no
Hoedlmoser [65]	2010	C	Children	330	9.52 ± 0.56	Sleep problems	Externalizing behavior	EB	CSHQ	SDQ	no

Ivanenko [66]	2006	C	Children and adolescents with psychiatric disorders	174	10.5 ± 3.6	Sleep problems	Externalizing behavior	EB	CSQ	BASC	no
Johnson [67]	2018	C	Children	52 vs 46	Good sleepers: 4.81 ± 1.07 Poor sleepers: 4.67 ± 1.23	Sleep disturbances	Irritability	IRR	CSHQ	ABC	no
Kamphuis [68]#	2014	C	Adult forensic psychiatric patients	109	36.9 ± 10.4	Sleep quality	Aggression	AC	PSQI	AQ	no
Kara – cases [69]#	2019	C	Children with psychiatric disease	317	4-6	Sleep problems	Aggression	AC	CSHQ	SCBE-30	no
Kara – controls [69]#	2019	C	Healthy children	151	4-6	Sleep problems	Aggression	AC	CSHQ	SCBE-30	no
Keller [70]	2014	C	Young adult women, university undergraduates	108	19.07 (18-24)	Sleep efficiency	Aggression	AB	Actigraphy	CPS	no
Keller [71]	2017	C	Predominantly white, middle-class, married adults	342	45.54 ± 14.65	Sleep quality	Aggression	AB	PSQI	Revised CTS	ADM
Kelly [17]	2014	CP	Children	176	8.68 ± 0.36	Sleep efficiency	Externalizing behavior	EB	Actigraphy	PIC	no
Kirwan [72]	2019	C	Adults	334	35.41 ± 11.08	Sleep quality	Aggression	AB	PSQI	AQ	no
LaMotte [73]	2017	C	Adults, returning veterans	103	33.73 ± 9.03	Sleep quality	Aggression	AB	PSQI	Revised CTS	no
Leppert [74]	2019	C	Preschool aged children	291	4.20 ± 0.80	Sleep quality	Irritability	IRR	Sleep quality (1 item)	ECI - Frequency of irritability / tantrums	no

Madrid-Vaiero [75]#	2019	C	Children	245 vs 1787	8.06 ± 1.45	Trouble sleeping	Aggression	AC	CBCL (1 item)	CBCL (aggression subscale)	no
Manini – spouses [76]	2018	C	Spouses of knee osteoarthritis patients	138	65.36 ± 11.54	Sleep quality	Anger	ANG	PSQI	Anger (1 item)	no
Manini – patients [76]	2018	C	Knee osteoarthritis patients	138	65.51 ± 9.60	Sleep quality	Anger	ANG	PSQI	Anger (1 item)	no
Mazurek [77]	2016	C	Children, adolescents and adults with ASD	81	10.3 ± 3.8	Sleep problems	Aggression	AB	CSHQ	CSHA	no
Meijer [78]#	2000	C	Children and adolescents	449	11.25 ± 0.67	Sleep quality	Aggression control	ACON	Self-developed questionnaire on children's sleep behavior	SPQ	no
Meijer [79]#	2010	CP	Adolescents	650	13.36 ± 0.55	Sleep quality	Aggression	AC	Self-developed questionnaire on children's sleep behavior	YSR (aggression subscale)	no
Meijers [80]#	2015	CP	Adult male prisoners with psychotic illness	19	33.2 ± 9.4	Sleep efficiency	Aggression	AC	Actigraphy	SDAS	no
Mulraney [81]	2016	CP	Children and adolescents with ADHD	270	10.1 ± 1.9	Sleep problems	Externalizing behavior	EB	CSHQ	SDQ	no
Muratori [82]#	2019	CP	Primary school children	227	7.9 ± 1.0	Sleep problems	Externalizing behavior	EB	SDSC	SDQ	no

Osgood [83]#	2019	C	Adult soldiers	2420	18-39	Sleep continuity disturbances	Aggression	AC	ISI (3 sleep continuity items)	Aggression (4 items)	no
Paavonen [84]	2009	C	Children	297	5-6	Sleep problems	Externalizing behavior	EB	SDSC	CBCL	no
Pieters [85]	2015	CP	Children and adolescents	555	13.96 ± 0.78	Sleep problems	Externalizing behavior	EB	Combined subscales from ASWS and ASHS	SDQ	no
Pitcher [86]	1997	C	Adults	30	20.9 ± 0.98	Sleep quality	Anger / Hostility	ANG	PSQI	POMS	no
Prinen [87]	2014	C	Children and adolescents diagnosed with IBD	157	15.4 ± 2.2	Sleep problems	Externalizing behavior	EB	SSR	YSR	no
Poon [88]	2019	C	Adult teachers	17	76.5% aged <40	Sleep quality	Irritability	IRR	Sleep diary (1 item)	Self-developed questionnaire (1 item)	no
Poznanski [89]	2018	C	Treatment-seeking anxious children, adolescents and adults	435	12.7 ± 3.0	Sleep problems	Irritability	IRR	Sleep problems composite: CBCL (5 items) / RCADS (4 items)	CBCL (3 items)	no
Quach [90]	2018	CP	Children	4983	4.7 ± 0.2	Sleep problems	Externalizing behavior	EB	BISQ	SDQ	no

Rubens [91]	2017	C	Children in the 3 <sup>rd</sup> -5 <sup>th</sup> -grade of elementary school	285	not stated	Sleep quality	Aggression	AC	SSR	CEMS	no
Sadeh [92]	2002	C	Children and adolescents from the 2nd, 4th and 6th grade	110 vs 25	2nd grade: 7.9 ± 0.34 4th grade: 9.7 ± 0.30 6th grade: 11.8 ± 0.45	Sleep problems	Aggression	AC	Actigraphy	CBCL (aggression subscale)	MIP
Samatiene [93]	2013	C	Children with epilepsy	61	8.6 ± 1.6	Sleep problems	Externalizing behavior	EB	SDSC	CBCL	no
Semiz [94]	2008	C	Adolescent / adult male soldiers with APD	125	APD: 22.0 ± 2.4	Sleep quality	Aggression	AC	PSQI	AQ	no
Shimizu [95]	2019	C	Adolescent/ adult high school students	180	17.49 ± 0.62	Sleep problems	Externalizing behavior	EB	SSHS	YSR	no
Sikora [96]	2012	C	Children with ASD	555	4-10	Sleep quality	Externalizing behavior	EB	CSHQ	CBCL	MIP
Simola [97]	2014	P	Children	470	Baseline: 3-6 Follow-up: 7-11	Sleep problems	Aggression	AC	SDSC	CBCL (aggression subscale)	no
Sosnowski [98]	2016	CP	Middle-school children and adolescents	785	12.32 ± 0.51	Sleep problems	Aggression	AC	S/WBPS	PBFS	no
Taylor [99]#	2013	C	Adolescent / adult undergraduate psychology students	66	19.04 ± 1.57	Sleep quality	Hostility	HOS	PSQI	CMHo	no

Tsuchiyama [11]	2013	C	Adult hospital employees	61	27.3 ± 6	Sleep quality	Hostility	HOS	PSQI	CMHo	no
Valincetti-McDermott [100]	2019	C	Children and adolescents with ASD or developmental disabilities	100	ASD: 8.8 ± 3 Developmental disabilities: 9.2 ± 3	Sleep problems	Irritability	IRR	CSHQ	ABC	no
Vaughn [101]	2015	C	Adults	2499	16-65	Sleep problems	Aggression	AC	SSR	AQ	no
Velten-Schurian [102]	2010	C	Children with parent-perceived sleep problems	34	7.1 (5.2 - 10.9)	Sleep problems	Aggression	AC	Sleep diary	CBCL (aggression subscale)	HCD
Vernon [103]	2018	CP	Adolescents	1101	13.5	Sleep quality	Externalizing behavior	EB	SSHS	7 items on an 8-point Likert Scale	ADM
Vogler [104]	2014	C	Male adult prison inmates	16 vs 33	39.37 ± 13.95	Insomnia	Aggression	AC	SSR	ARGI	no
De Vrijer [105]	2014	C	Adolescents	339	16	Sleep quality	Externalizing behavior	EB	Sleep quality (7 items)	YSR	no
Wang [106]	2019	CP	Children and adolescents	2116	Baseline: 5	Sleep problems	Externalizing behavior	EB	CBCL	CBCL	no
Ward [107]	2014	C	Children with JIA	116	8.5 ± 1.9	Sleep disturbances	Externalizing behavior	EB	CSHQ	CBCL	no
Waters [108]	1993	C	Adolescent and adult undergraduate insomniacs	40	22.4 ± 6.7	Sleep quality	Anger	ANG	Sleep Diary	NAS-PI	no

Wong [109]	2009	CP	Children	490	3-5	Sleep problems	Externalizing behavior	EB	CBCL	CBCL	ADM
Xu [110]#	2018	C	Elderly patients with mild to moderate cognitive impairment	839	70.3 ± 6.3	Sleep disturbances	Irritability	IRR	NPI	NPI	no
Zschoche [111]	2015	C	Adolescents	93	15.97 ± 1.3	Sleep quality	Aggression	AC	PSQI	FEPAA	no

**Abbreviations Table 1:**

# unadjusted data provided by author contact  
 N = Number of participants, SD = standard deviation.  
 Study design: C = cross-sectional, CP = cross-sectional and prospective, P = prospective.  
 Study population: ADHD = Attention-Deficit Hyperactivity Disorder; AD = Atopic Dermatitis; AlzD = Alzheimer's disease; APD = Antisocial Personality Disorder; ASD = Autism Spectrum Disorder; CD = Conduct Disorder; CF = cystic fibrosis; ID = Intellectual Disability; JIA = Juvenile Idiopathic Arthritis; ODD = Oppositional Defiant Disorder; PTSD = Posttraumatic Stress Disorder.  
 Outcome category: AC = aggression composite, AB = aggressive behavior, ANG = anger, ACON = aggression control, EB = externalizing behavior, HOS = hostility, IRR = irritability.  
 Sleep quality measurement: AIS = Athens Insomnia Scale; ASD-CC = Autism Spectrum Disorders-Comorbidity for Children; ASHS = Adolescent Sleep Hygiene Scale; ASWS = Adolescent Sleep-Wake Scale; BISQ = Brief Infant Sleep Questionnaire; BRUMS = Brunel Mood Scale Questionnaire; CBCL = Child Behavior Checklist; CSBS = Child Sleep Behavior Scale; CSHQ = Children's Sleep Habits Questionnaire; CSWS = Children's Sleep-Wake Scale; CSQ = Childhood Sleep Questionnaire; ISI = Insomnia Severity Index; NPI = Neuropsychiatric Inventory; PSQI = Pittsburgh Sleep Quality Index; RCADS = Revised Child Anxiety and Depression Scale; SDSC = Sleep Disturbance Scale for Children; SHIPC = Sleep Habits Inventory for Preschool Children; SSHS = School Sleep Habits Survey; SSR = Sleep Self-Report; S/WBPS = Sleep/Wake Behavior Problems Scale.  
 Aggression measurement: AIAQ = Anger Irritability and Aggression Questionnaire; ABC = Aberrant Behavior Checklist; AQ = Buss-Perry Aggression Questionnaire; ARGI = Anger-Related Reactions and Goals Inventory; ASD-BPC = Autism Spectrum Disorder-Behavior Problems for Children; ASR = Adult Self-Report; BASC = Behavioral Assessment System for Children; BRUMS = Brunel Mood Scale Questionnaire; CBCL = Child Behavior Checklist; CBI = Challenging Behavior Index; CEMS = Children's Emotion Management Scale; CMAI = Cohen-Mansfield Agitation Inventory; CMHo = Cook-Medley Hostility Scale; CPS = Conflict and Problem Solving Scales; CSBS = Child Sleep Behavior Scale; CSHA = Children's Scale for Hostility and Aggression; CTS = Conflict Tactics Scale; DBRS-PV = Disruptive Behavior Disorders Rating Scale Parent Version; DJPC = Direct and Indirect Prisoner Checklist; ECI = Early Childhood Inventory; FEPAA = German Questionnaire for Assessment of Empathy, Prosociality and Aggression; FTSH = Finnish Twin Study Hostility; HADS = Hospital Anxiety and Depression Scale; IPAS = Impulsive Premediated Aggression Scale; NAS-PI = Novaco Anger Scale and Provocation Inventory; NPI = Neuropsychiatric Inventory; PBFS = Problem Behavior Frequency Scale; PBQ = Preschool Behavior Questionnaire; PIC = Personality Inventory for Children; POMS = Profile of Mood States Questionnaire; ROAS = Retrospective Overt Aggression Scale; RPO = Reactive-Proactive Questionnaire; SBS = Student Behavior Survey; SCBE-30 = Social Competence and Behavior Evaluation; SDAS = Social Dysfunction and Aggression Scale; SDQ = Strengths and Difficulties Questionnaire; SPO = School Perception Questionnaire; SSIS = Social Skills Improvement System; STAXI = State-Trait Anger Expression Inventory; TAAES = Trait Anger-Anger Expression Scale; TRF = Teacher Report Form; TSCC = Trauma Symptoms Checklist for Children; VAT = Voodoo Doll Aggression Test; YSR = Youth Self-Report.  
 Qualitative analysis: ADM = advanced data modelling; HCD = highly corrected data; MIP = missing information to enable pooling; NDP = no data provided; NPT = non-parametric test.

For externalizing behavior as outcome category, twenty-one correlations from 20 studies were available for pooling [17, 31, 33, 45, 48, 59, 63, 65, 66, 81, 82, 84, 85, 87, 90, 93, 95, 105-107] yielding a pooled estimate of 0.34 (95% CI 0.29-0.40), indicating a significant association between sleep quality and externalizing behavior, with a high heterogeneity ( $I^2=87.7\%$ ). Of seven studies that were assessed in qualitative analysis, six demonstrated statistically significant associations between poor sleep quality and higher externalizing behavior [25, 30, 61, 96, 103, 109] and one study showed no statistically significant association [29].

The pooled estimate from 11 studies [10, 28, 32, 36, 49, 51, 58, 70, 72, 73, 77] reporting 12 correlations between sleep quality and actual aggressive behavior (Fig.2) provided a pooled correlation estimate of 0.19 (95% CI 0.12-0.25), indicating a significant association between sleep quality and aggressive behavior, with moderate heterogeneity ( $I^2=54.9\%$ ). Five studies could not be included in the meta-analysis; qualitative analysis showed that four studies [10, 40, 41, 71] observed statistically significant associations between poor sleep quality and higher aggressive behavior, whereas one study did not [37].

In total, 12 studies investigated the association between sleep quality and anger. Eleven correlations from 10 studies [26, 27, 35, 53, 54, 57, 64, 76, 86, 108] were meta-analyzed (Fig.2) and provided a pooled correlation estimate of 0.27 (95% CI 0.20-0.35), indicating a significant association between sleep quality and anger, with a high heterogeneity ( $I^2=82.0\%$ ). One study providing an odds ratio showed a non-significant association between sleep quality and anger [56] (Fig. 3). One study could not be included in the meta-analysis; this study found no significant association between poor sleep quality and higher anger [34].

For irritability as outcome category, correlations from 6 studies [67, 74, 88, 89, 100, 110] were available for pooling. This yielded a pooled correlation estimate of 0.21 (95% CI 0.12-0.30), indicating a significant association between sleep quality and irritability, with moderate heterogeneity ( $I^2=54.6\%$ ). Two that were assessed in qualitative analysis showed significant associations between poor sleep quality and higher irritability [44, 46].

Correlations from 3 studies assessing the association between sleep quality and hostility [11, 60, 99] provided a pooled estimate of 0.32 (95% CI 0.10-0.55), indicating a significant association between sleep quality and hostility score, with a high heterogeneity ( $I^2=89.4\%$ ) (Fig.2).

Only one study assessed aggression control as outcome (Fig.2) [78]; showing a significant correlation between poor sleep quality and lower aggression control 0.24 (95% CI 0.15-0.33).

## Additional analyses

Sensitivity analysis (Supplemental Fig.S2a) showed that excluding studies with low methodological quality had no effect on the pooled correlation estimate or on heterogeneity ( $0.28$  (95%CI  $0.24-0.31$ ;  $I^2=89.8\%$ ). Sensitivity analysis of the effect of methodological quality on the pooled odds ratio could not provide an overall estimate, as only 2 out of 3 studies remained [97, 101].

For the overall correlation estimates of different age groups, only the correlation estimate for studies combining children and adolescents was slightly, but not significantly, higher ( $0.35$ ; 95%CI  $0.29-0.41$ ;  $I^2=76.8\%$ ) than for adults ( $0.24$ ; 95%CI  $0.19-0.29$ ;  $I^2=84.1\%$ ). However, estimates from studies including children ( $0.28$ ; 95%CI  $0.22-0.35$ ;  $I^2=92.9\%$ ) or adolescents ( $0.26$ ; 95%CI  $0.19-0.32$ ;  $I^2=63.6\%$ ) exclusively did not show marked differences with those in adults (Supplemental Fig.S2b).

Exploring the association between sleep quality and aggression in different populations showed stronger overall correlation estimates and lower heterogeneity for studies in participants with psychological vulnerabilities ( $0.33$ ; 95%CI  $0.28-0.37$ ;  $I^2=64.6\%$ ) or medical conditions ( $0.35$ ; 95%CI  $0.26-0.43$ ;  $I^2=38.1\%$ ), both estimates bordering on a statistically significant difference with the overall correlation estimate of studies in more general populations ( $0.25$ ; 95%CI  $0.21-0.28$ ;  $I^2=93.3\%$ ) (Supplemental Fig.S2c).

A sensitivity analysis exploring different measurement instruments of sleep quality, showed a pooled correlation estimate of  $0.13$  (95%CI  $0.04-0.23$ ;  $I^2=39.0\%$ ) in studies with objectively measured sleep quality, i.e. sleep efficiency assessed by actigraphy (Supplemental Fig.S2d). The correlation estimates for questionnaires were higher, for PSQI ( $0.26$ ; 95%CI  $0.21-0.31$ ) or CSHQ ( $0.29$ ; 95%CI  $0.23-0.35$ ), and also showed higher heterogeneity ( $I^2=72.8\%$  and  $I^2=51.3\%$ , respectively).

A sensitivity analysis looking at different measurement instruments of aggression, showed higher pooled correlation estimates of studies using questionnaires measuring externalizing behavior, such as CBCL ( $0.38$ ; 95%CI  $0.28-0.48$ ;  $I^2=91.8\%$ ) and SDQ ( $0.36$ ; 95%CI  $0.28-0.45$ ;  $I^2=81.3\%$ ), bordering on a statistically significant difference with combined miscellaneous studies using other aggression measures ( $0.24$ ; 95%CI  $0.20-0.28$ ;  $I^2=84.9\%$ ) (Supplemental Fig.S2e). Heterogeneity was high for all instruments.

## Publication bias

No considerable asymmetry was observed in the funnel plot of correlations (Supplemental Fig.S4a). Egger's test confirmed the absence of asymmetry ( $p = 0.10$ ). This test is sometimes regarded as a publication bias test, but is of limited value in this highly heterogeneous observational data set [120]. For odds ratios, no further interpretation or test of asymmetry is considered appropriate, since only 3 studies were involved.

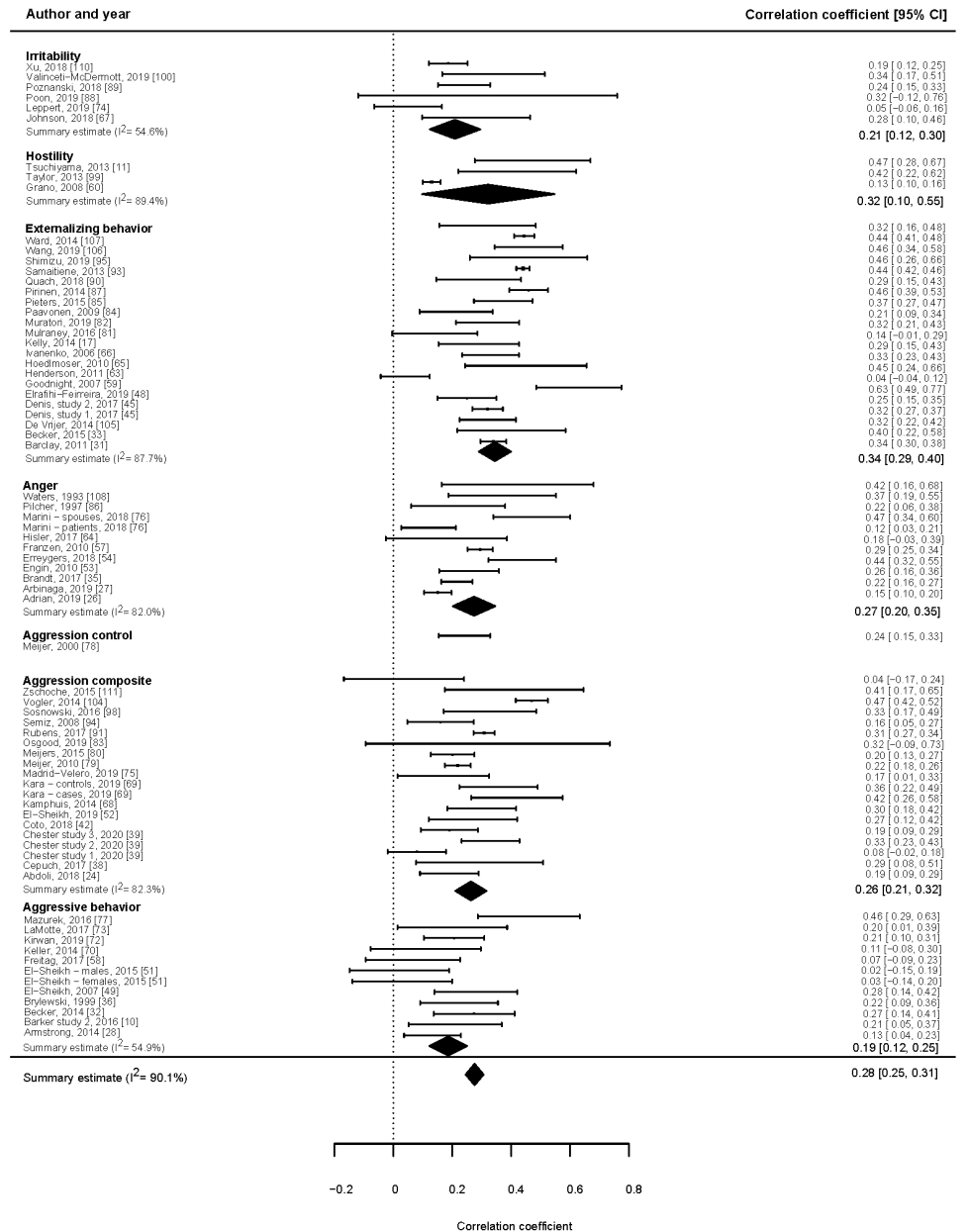
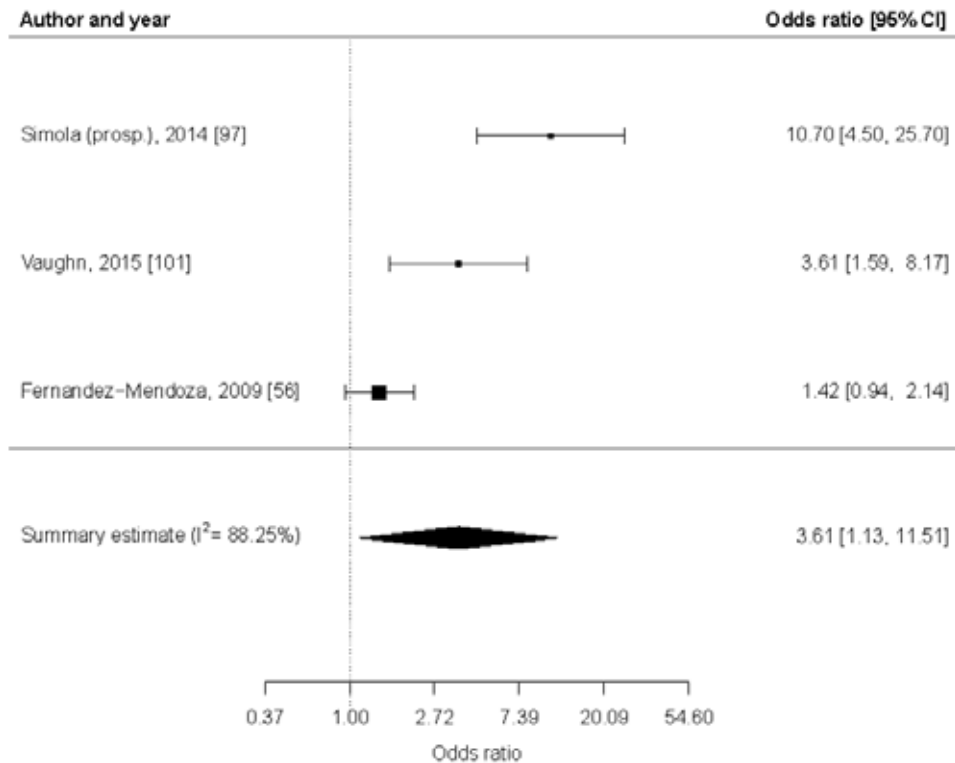


Fig. 2. Forest plot of the overall correlation estimate of the association of sleep quality with aggression.

CH1

CH2



**Fig. 3.** Forest plot of the overall odds ratio estimate of the association of sleep quality with aggression.

## DISCUSSION

The current study aimed to assess the overall association between sleep quality and measures of aggression in a systematic review and meta-analysis of observational studies. In accordance with our hypothesis, the systematic synthesis of available evidence showed a consistent association of poor sleep quality with increased aggression. In the quantitative data analysis, the pooled estimates of the association between sleep quality and measures of aggression were all in the same direction, indicating poorer sleep quality to be associated to higher aggression. Most studies included in the qualitative analysis (64%) also showed a statistically significant association, which indicates that the qualitative analysis supported the quantitative analysis. The quality of this combined evidence is regarded to be moderate; although this review encompasses only studies with observational designs, the results are consistent, a large number of participants from different populations is included and most studies were of moderate to strong individual quality. Our study is the first systematic evaluation on this topic, and our findings substantiate previous non-systematic and qualitative reviews [12, 13] confirming that poor sleep quality is indeed associated with increased aggression in both general and clinical populations.

### Broad scope

By applying a broad definition of both sleep quality and aggression, we aimed to provide a comprehensive overview of all the available literature. Keeping a broad scope in a meta-analysis of observational studies is topic of discussion, and could enhance its relevance but also contribute to increased bias [121]. We would like to emphasize that our work is intended to generate an overall impression of the current body of evidence and order of magnitude of the association, rather than offer a definite and precise estimate. By doing so, we attempt to represent the diversity of available research in this field, without imposing too many limitations. Heterogeneity was high for most pooled estimates and is presumably a direct consequence of the broad scope of this review. We included studies with substantial differences in defining the constructs of sleep quality and/or aggression, used several types of measurement instruments (e.g. self-report and objective measurement; varying categorization or cut-off points), study designs and populations (both variable in age as in health status), as well as divergent statistical approaches.

When looking at different outcome categories, externalizing behavior yielded a considerably stronger pooled correlation estimate than aggressive behavior and irritability, whereas heterogeneity in the latter two categories was lower. A limited number of possible factors of influence and sources of heterogeneity was explored in the sensitivity analyses. The stronger correlation for externalizing behavior was confirmed by the sensitivity analysis of different aggression measurement instruments; showing similarly high pooled correlation estimates in studies measuring externalizing behavior using the CBCL and SDQ. However, aggression measurement instruments were not a source of heterogeneity. In addition, excluding studies with a low methodological quality did not substantially influence the effect estimates nor heterogeneity. Different age categories did not display clear differences in

either effect estimate or heterogeneity. Although it is possible that the association between sleep and aggression or externalizing behavior is somewhat more pronounced in children and adolescents, for example because of vulnerability of the developing brain, the current results do not provide proof of this assumption.

A striking finding was the observed trend in correlation estimates for different populations, with studies in participants with psychological vulnerabilities or medical conditions showing stronger correlations between poor sleep and aggression, with lower heterogeneity, compared to studies in the general population. Although the difference in correlation estimates bordered on significance, it is conceivable that participants with psychological or medical conditions are more vulnerable to the negative effects of poor sleep quality, for example because of increased psychological stress or physical pain, or that their perception of sleep quality and aggressive features differs from those in the general population. An alternative theory may be that sleep disturbances, aggression and certain psychological or medical conditions are manifestations of a common underlying vulnerability. Another interesting result was that pooling studies using actigraphy to assess sleep quality (i.e. sleep efficiency) showed a significantly lower pooled correlation estimate, with much lower heterogeneity, than other sleep measures. This is in line with previous research suggesting that the subjective perception of sleep quality is more prominently related to aggression than objective measures of sleep quality [10, 11].

### **Mechanisms linking sleep quality to aggression**

Several possible mechanisms may link poor sleep to higher aggression; for example via amplification of negative affect, increasing negative evaluations and hostile interpretations of others' behavior, and impairment of self-inhibitory mechanisms [15]. One important underlying theory is that poor sleep attenuates prefrontal cortical functioning, especially its inhibitory control over emotions and aggressive impulses, thus lowering the threshold for aggressive behavior [12]. Other theories encompass individual variations in the central serotonergic system and the hypothalamic-pituitary-adrenal-axis, influencing the vulnerability for amplified aggressive responses induced by disturbed sleep. Genetic studies even suggest that the association could be explained by common genes, possibly affecting serotonergic activity and/or hypothalamic-pituitary-adrenal axis functioning [75]. This implies a shared vulnerability for both sleep disturbances and aggression, with additional environmental factors further modulating their association. Although reciprocal effects between poor sleep and aggression are plausible, as described in the introduction, there currently is more evidence for poor sleep quality negatively influencing aggressive or externalizing behavior than vice versa [16, 17].

### **Strengths and limitations**

This study is the first systematic review on this topic, including quantitative and qualitative methods. We used rigorous review methods, with duplicate assessment at every stage, and included a large total sample. Plus, the broad scope of this review enables a comprehensive overview of the available observational evidence in several different populations and age groups.

Of course, several limitations of this review must be discussed. First, because the majority of studies included in this review were cross-sectional, we cannot make causal inferences about the relationship between poor sleep quality and aggression. Second, while many studies do not correct for confounders or a diverse set of confounders, we only included unadjusted estimates, to meta-analyze the results with a meaningful and comparable outcome. However, by using unadjusted estimates, we introduced bias as no corrections for age and general levels of psychopathology or stress are made. This could generate an under- as well as an overestimation of the association under study. In some studies, correction for important confounders strengthens the association between sleep and aggression (for example [30, 122]), as opposed to other studies in which adjustment results in a weakening of the association and / or loss of significance (for example [43, 62]). While the adjusted results from high quality studies were not included in the quantitative analysis, it is worth mentioning that several of these studies present extensively adjusted, and still significant, associations between poor sleep quality and aggressive behavior (for example [85, 95]).

Third, we excluded studies in which aggression was solely defined as delinquency, delinquent behavior, criminal activity, conduct problems or antisocial behavior, as these constructs at least partly imply some form of callousness or premeditation. In previous studies, callousness has been shown not to be associated with poor sleep quality (for example [45]), as opposed to more emotional or impulsive forms of aggression. However, a complete distinction between these constructs cannot be made in the current meta-analysis, as several studies incorporated both aggression features and conduct problems or rule-breaking as elements that together constitute aggressive or externalizing behavior. In addition, aspects of impulsiveness or self-control, apart from aggression control, were not incorporated in this overview. Although self-control mechanisms are strongly influenced by disturbed sleep and considered a key factor contributing to aggression [12, 15], we chose to focus on outcomes most directly related to aggression and aggressive behavior.

Finally, after careful deliberation we decided to exclude studies on sleep-disordered breathing, sleep-related movement disorders and circadian rhythm sleep disturbances. All these disorders affect sleep quality but have distinct underlying physiological conditions. The only sleep disorder included was insomnia (disorder or symptoms thereof). We feel the association of different physiological sleep disorders with aggression deserves a separate review, zooming in on disorder-specific alterations in sleep quality and their association to psychopathology, especially aggression and externalizing behavior (for example [123]).

### **Clinical implications**

Since this is the first study systematically describing the association between poor sleep quality and aggression our findings hold important clinical relevance. Although the strength of the correlation between poor sleep quality and aggression is considered weak to moderate, in the intricate framework of the many factors that play a part in aggression every individual factor, albeit small, could be of importance. Furthermore, as poor sleep quality is shown to be related to multiple aspects of aggression, such as anger and hostility,

modest single associations might add up to a clinically relevant effect. In addition to cross-sectional studies, poor sleep quality has been longitudinally associated with higher levels of aggression in several populations [16, 17, 122], supporting a causal relation. Our review stresses the importance of disturbed sleep as a factor contributing to aggression.

The fact that the association between poor sleep and aggression was moderately strong in populations with psychological or medical vulnerabilities stresses the possible impact that treating disturbed sleep may have in clinical practice. Specifically targeting sleep disturbances both in preventive and clinical care may significantly reduce aggression, similar to the effects seen in affective symptoms [124]. We particularly encourage future intervention studies focused on improving sleep quality to assess aggression or externalizing behavior as outcome measures in populations dealing with poor sleep quality and high risk of aggression, such as prisoners or (forensic) psychiatric patients [12]. Although treatment studies in this field are still scarce, several yield promising results showing a decrease in aggressive behavior or irritability following enhanced sleep quality (for example [125, 126]).

Further prospective work is needed to explore how distinct forms of disturbed sleep impact different aspects of aggression. Based on current observations, we advise to use homogeneous statistical approaches and well-established measurement instruments. Considering the repeatedly observed differences in the association of subjective and objective evaluations of sleep quality with aggression, both types of measurements should preferably be incorporated. In addition, it is essential to properly adjust for possible confounders, especially for psychopathological and medical comorbidity, to disentangle more general vulnerability effects from a specific disturbed sleep effect. Finally, studying large groups to identify how the impact that poor sleep has on aggression varies between individuals, for example depending on gender, comorbid conditions or pre-existent level of impulsiveness or hostility, may identify those most at risk.

## CONCLUSION

In conclusion, poor sleep quality is associated with increased aggression. These results emphasize the need for awareness of disrupted sleep as a possible risk factor for aggression and for targeting sleep in treatment of specifically vulnerable populations, such as patients with psychological vulnerabilities or medical conditions. More prospective and high-quality experimental evidence is required to elucidate etiological mechanisms and optimize prevention and treatment of aggression.

## RESEARCH AGENDA

Future research on the association of sleep quality with aggression needs to:

- examine how distinct features of sleep quality impact different aspects of aggression, preferably using prospective designs and specific focus on the comparison between subjectively and objectively obtained measures.
- examine how duration and / or timing of sleep impact different aspects of aggression
- examine how disturbed sleep impacts self-control mechanisms in clinical populations
- adjust results for several confounding factors, especially psychopathological and medical comorbidity.
- focus on conducting high quality experimental studies to assess the effects of enhancing sleep quality on multiple aspects of aggression.
- establish the effect of early screening, diagnosing and treating sleep disturbances to prevent the development of aggressive and externalizing behavior.

## PRACTICE POINTS

This review highlights the association of poor sleep quality with aggression.

- standardized assessment of sleep quality should be integrated in both preventative and clinical care, especially in populations with high risk of aggression.
- specifically targeting disturbed sleep may improve aggressive features and actual aggressive behavior.



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\* denotes key references

**Supplemental File 1.** Search strategy.

## PubMed

("Sleep"[Mesh] OR sleep\*[tiab] OR insomnia[tiab] OR "Sleep Initiation and Maintenance Disorders"[Mesh]) AND ("Aggression"[Mesh] OR aggress\*[tiab] OR externalizing behavior[tiab] OR externalizing behaviour[tiab] OR irritability[tiab] OR hostile\*[tiab] OR impulsive\*[tiab] OR violent\*[tiab] OR eager\*[tiab] OR anger[tiab])

## PsycInfo

(DE "Napping" OR DE "Sleep Disorders" OR DE "Hypersomnia" OR DE "Insomnia" OR DE "Sleep" OR DE "Sleep Deprivation" OR DE "Sleepiness" OR TI (sleep\* OR insomnia) OR AB (sleep\* OR insomnia)) AND (DE "Aggressiveness" OR DE "Aggressive Behavior" OR DE "Attack Behavior" OR DE "Bullying" OR DE "Conduct Disorder" OR DE "Cruelty" OR TI (aggress\* OR externalizing behavior OR externalizing behaviour OR irritability OR hostile\* OR impulsive\* OR violent\* OR eager\* OR anger) OR AB (aggress\* OR externalizing behavior OR externalizing behaviour OR irritability OR hostile\* OR impulsive\* OR violent\* OR eager\* OR anger))

**Supplemental Table 2.** Methodological quality rating per domain per study.

Author	Year	SD	BL	RSB	RWD	CF	DC	DA	RP	OVER-ALL QR
Abdoli	2018	M	NR	M	NR	M	S	M	S	M
Adams	2014	M	NR	W	NR	W	S	M	M	M
Adrian	2019	M	NR	W	S	M	S	M	M	M
Arbinaga	2019	M	NR	M	M	S	S	S	S	S
Armstrong	2014	M	NR	S	S	S	S	S	S	S
Aronen	2000	M	NR	M	M	S	M	S	S	M
Aronen	2014	M	NR	W	NR	W	S	M	M	W
Barclay	2011	M	NR	W	NR	M	S	M	M	M
Barker	2016	M	NR	W	NR	W	S	M	W	M
Becker	2014	M	NR	M	NR	S	S	S	M	M
Becker	2015	M	NR	S	NR	S	S	S	S	S
Biggins	2018	M	NR	W	NR	W	M	M	M	W
Brandt	2017	M	NR	M	NR	S	S	S	S	S
Catrett	2009	M	NR	W	NR	W	S	M	S	W
Cepuch	2017	M	NR	W	NR	M	W	M	M	M
Chester, study 1	2020	M	NR	W	NR	S	M	S	S	M
Chester, study 2	2020	M	NR	W	NR	S	M	S	S	M

Chester, study 3	2020	M	NR	W	NR	S	M	S	S	M
Cohen	2018	M	NR	M	NR	W	S	M	S	M
Cohen-Mansfield	1990	M	NR	W	NR	W	S	M	M	W
Coto	2018	M	NR	M	NR	W	M	M	M	M
Coulombe	2011	M	NR	S	NR	W	S	S	S	M
Dahl	1995	M	NR	M	NR	S	S	S	S	S
Denis, study 1	2017	M	NR	M	S	S	S	S	M	S
Denis, study 2	2017	M	NR	W	NR	M	S	M	S	M
Didden	2002	M	NR	M	NR	S	S	S	S	S
Ellison	2019	M	NR	W	NR	W	S	M	M	W
Elrafihi-Feirreira	2019	M	NR	M	NR	W	S	M	S	M
El-Sheikh	2007	M	NR	M	S	S	S	S	M	S
El-Sheikh	2013	M	NR	M	NR	S	S	S	S	S
El-Sheikh	2015	M	NR	W	NR	W	M	M	S	M
El-Sheikh	2019	M	NR	S	NR	S	S	S	S	S
Engin	2010	M	NR	M	NR	S	S	S	S	S
Erreygers	2018	M	NR	W	NR	W	S	W	S	W
Fadini	2015	M	NR	M	NR	W	M	M	S	M
Fernandez-Mendoza	2009	M	NR	W	NR	W	S	M	M	W

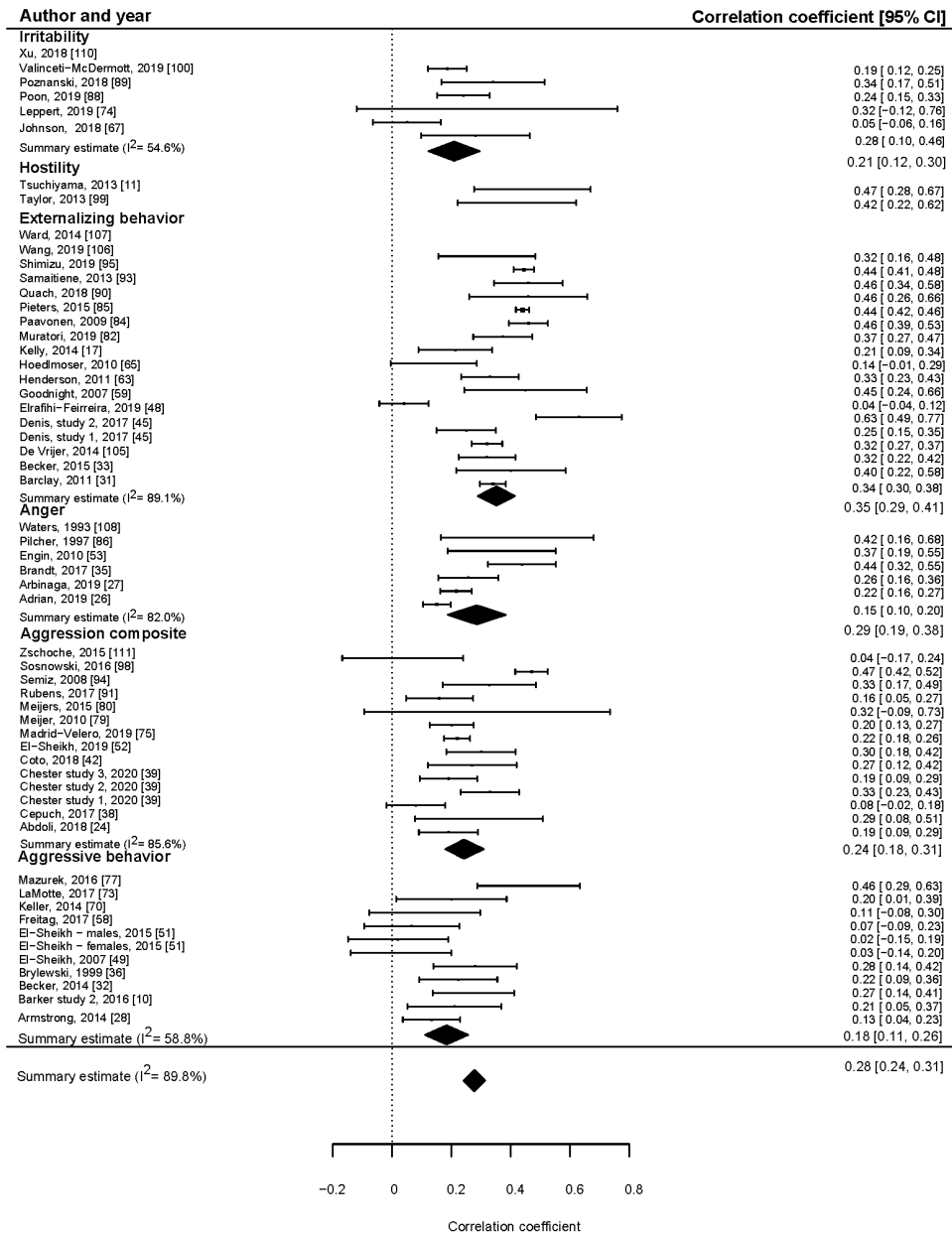
Franzen	2010	M	NR	W	NR	W	S	M	S	W
Freitag	2017	M	NR	S	NR	M	S	M	M	M
Goodnight	2007	M	NR	S	NR	S	S	S	S	S
Grano	2008	M	NR	W	NR	W	M	M	M	W
Gregory	2002	M	NR	S	NR	S	S	S	S	S
Gregory	2004	M	NR	M	NR	W	S	M	S	M
Henderson	2011	M	NR	S	M	S	S	S	S	S
Hisler	2017	M	NR	W	NR	W	S	M	S	W
Hoedlmoser	2010	M	NR	S	M	W	S	M	S	M
Ivanenko	2006	M	NR	W	NR	W	S	M	M	W
Johnson	2018	M	NR	S	NR	W	S	M	S	M
Kamphuis	2014	M	NR	W	NR	W	S	M	W	W
Kara	2019	M	NR	W	NR	W	S	M	S	W
Keller	2014	M	NR	M	W	W	M	M	S	W
Keller	2017	M	NR	W	NR	M	S	M	M	M
Kelly	2014	M	NR	M	NR	S	S	S	S	S
Kirwan	2019	M	NR	W	NR	W	S	M	S	W
LaMotte	2017	M	NR	W	NR	S	S	S	S	M
Leppert	2019	M	NR	W	NR	S	S	S	M	M

Madrid-Valero	2019	M	NR	S	NR	W	S	M	S	M
Marini	2018	M	NR	W	NR	W	S	M	S	W
Mazurek	2016	M	NR	M	M	S	S	S	S	S
Meijer	2000	M	NR	W	NR	W	S	M	S	W
Meijer	2010	M	NR	W	NR	S	S	S	M	M
Meijers	2015	M	NR	S	M	W	S	M	S	M
Mulraney	2016	M	NR	W	NR	W	S	M	M	W
Muratori	2019	M	NR	W	NR	S	S	S	M	M
Osgood	2019	M	NR	W	NR	W	S	M	M	W
Paavonen	2009	M	NR	M	NR	W	S	M	S	M
Pieters	2015	M	NR	S	M	S	S	S	S	S
Pilcher	1997	M	NR	M	M	W	S	M	M	M
Pirinen	2014	M	NR	W	NR	W	S	M	S	W
Poon	2019	S	W	W	S	W	S	M	W	S
Poznanski	2018	M	NR	S	S	S	S	S	S	M
Quach	2018	M	NR	S	S	W	S	M	M	M
Rubens	2017	M	NR	W	NR	W	S	M	W	M
Sadeh	2002	M	NR	W	NR	W	S	M	W	M
Samaitiene	2013	M	NR	M	NR	W	S	M	S	M
Semiz	2008	M	NR	M	S	S	S	S	S	S

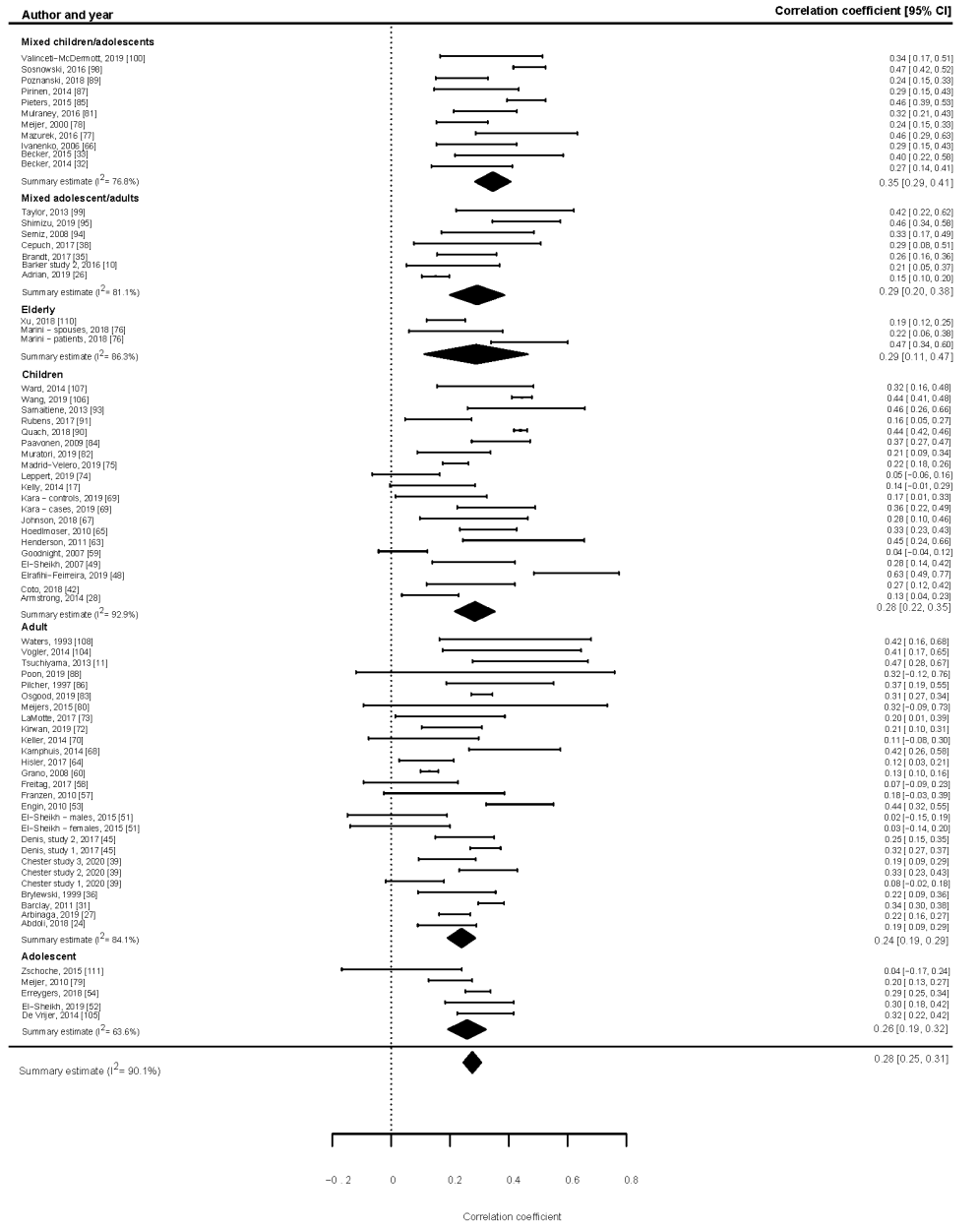
Shimizu	2019	M	NR	S	S	M	S	M	S	S
Sikora	2012	M	NR	W	W	W	S	M	M	W
Simola	2014	M	NR	S	NR	W	S	M	M	M
Sosnowski	2016	M	NR	W	NR	S	S	S	S	M
Taylor	2013	M	NR	M	M	S	M	S	S	M
Tsuyama	2013	M	NR	M	NR	W	M	M	M	M
Valincetti-McDermott	2019	M	NR	W	NR	W	S	M	S	M
Vaughn	2015	M	NR	M	S	W	M	M	M	M
Velten-Schurian	2010	M	NR	W	W	S	S	S	M	W
Vernon	2018	M	NR	M	NR	W	S	M	M	M
Vogler	2014	M	NR	M	NR	W	S	M	S	W
De Vrijer	2014	M	NR	M	NR	S	S	S	M	S
Wang	2019	M	NR	W	NR	M	M	M	S	M
Ward	2014	M	NR	M	M	S	S	S	S	S
Waters	1993	M	NR	S	M	W	S	M	M	M
Wong	2009	M	NR	S	NR	W	M	M	M	M
Xu	2018	M	NR	W	NR	W	S	M	W	M
Zschoche	2015	M	NR	S	NR	S	S	S	S	M

Abbreviations: SD= study design; BL= blinding; RSB= representativeness with regard to selection bias; RWD= representativeness with regard to withdrawals/dropouts; CF= confounding; DC= data-collection; DA= data-analysis; RP= reporting; W=weak; M= moderate; S=strong; NR= no rating.

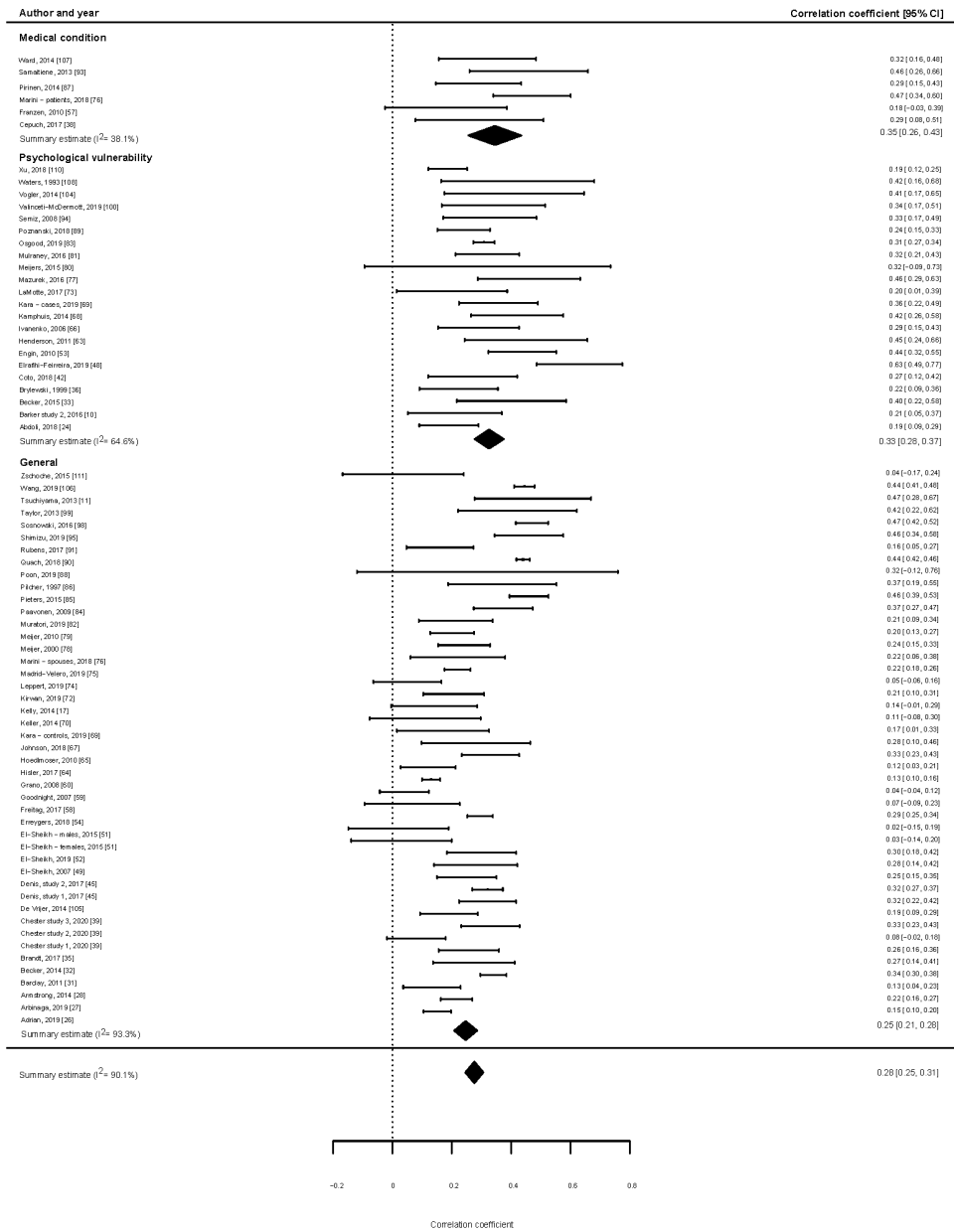




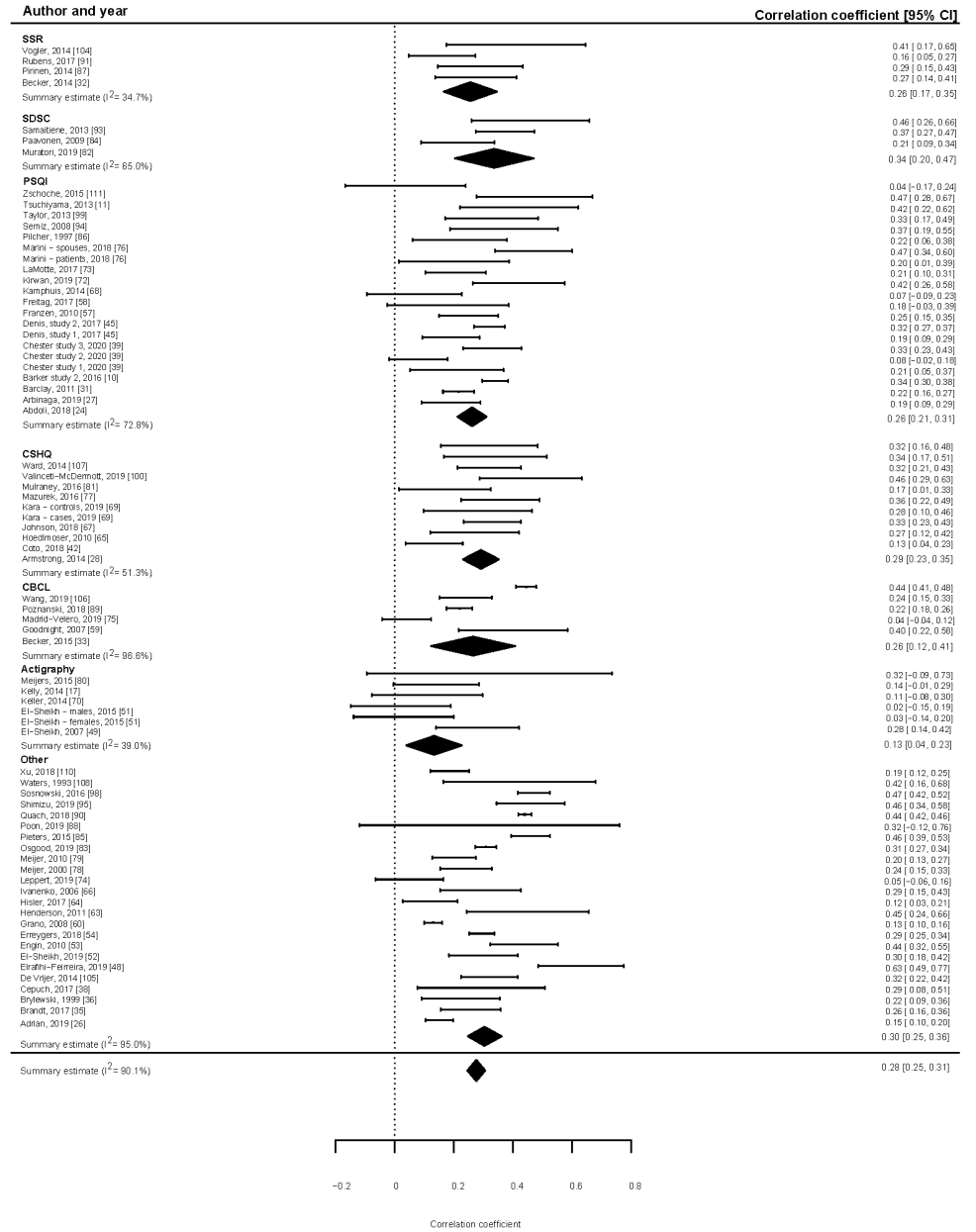
Supplemental FigS2a. Forest plot of the overall correlation estimate of the association of sleep quality with aggression, excluding studies with low methodological quality.



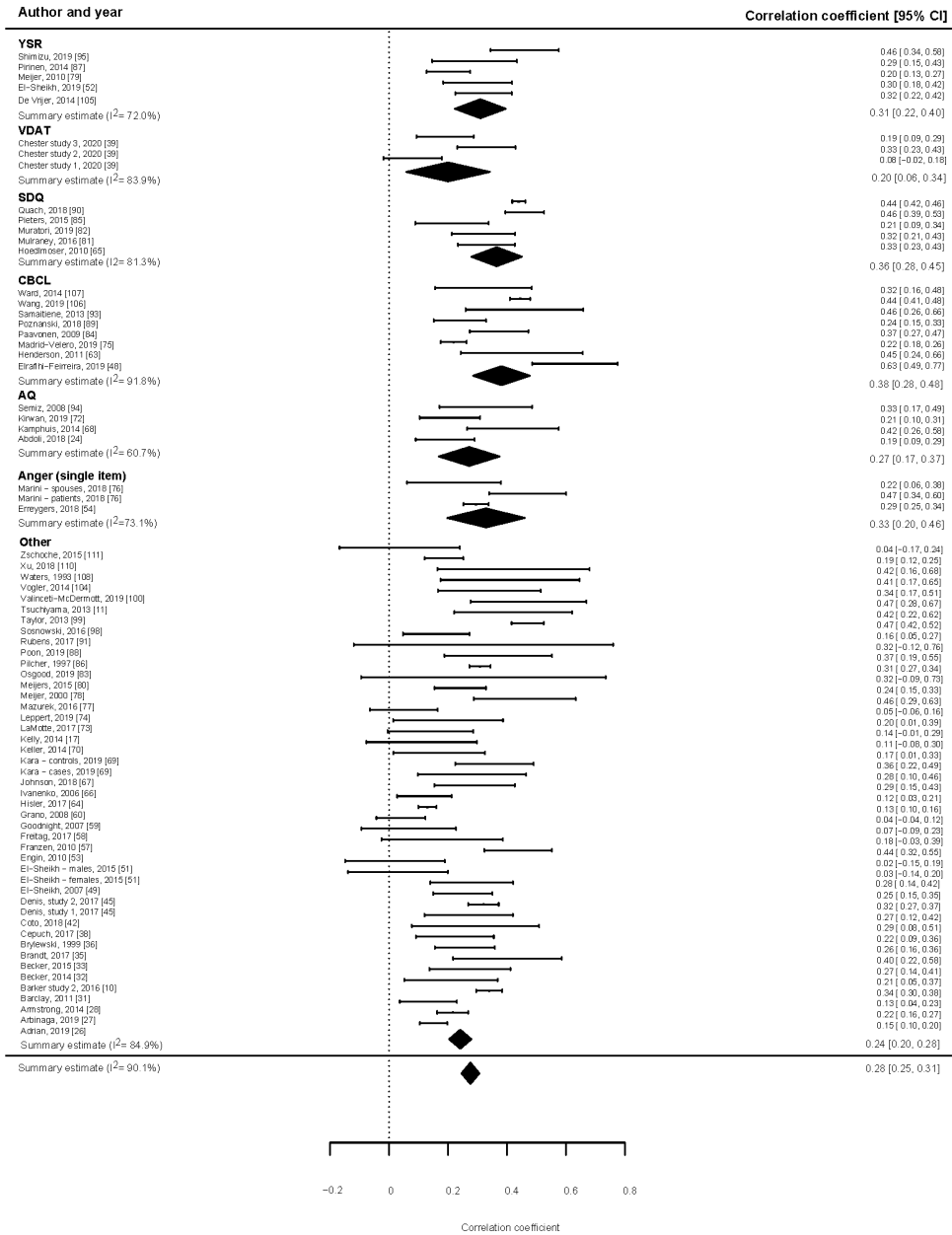
Supplemental Fig.S2b. Forest plot of the overall correlation estimate of the association of sleep quality with aggression, by age category.



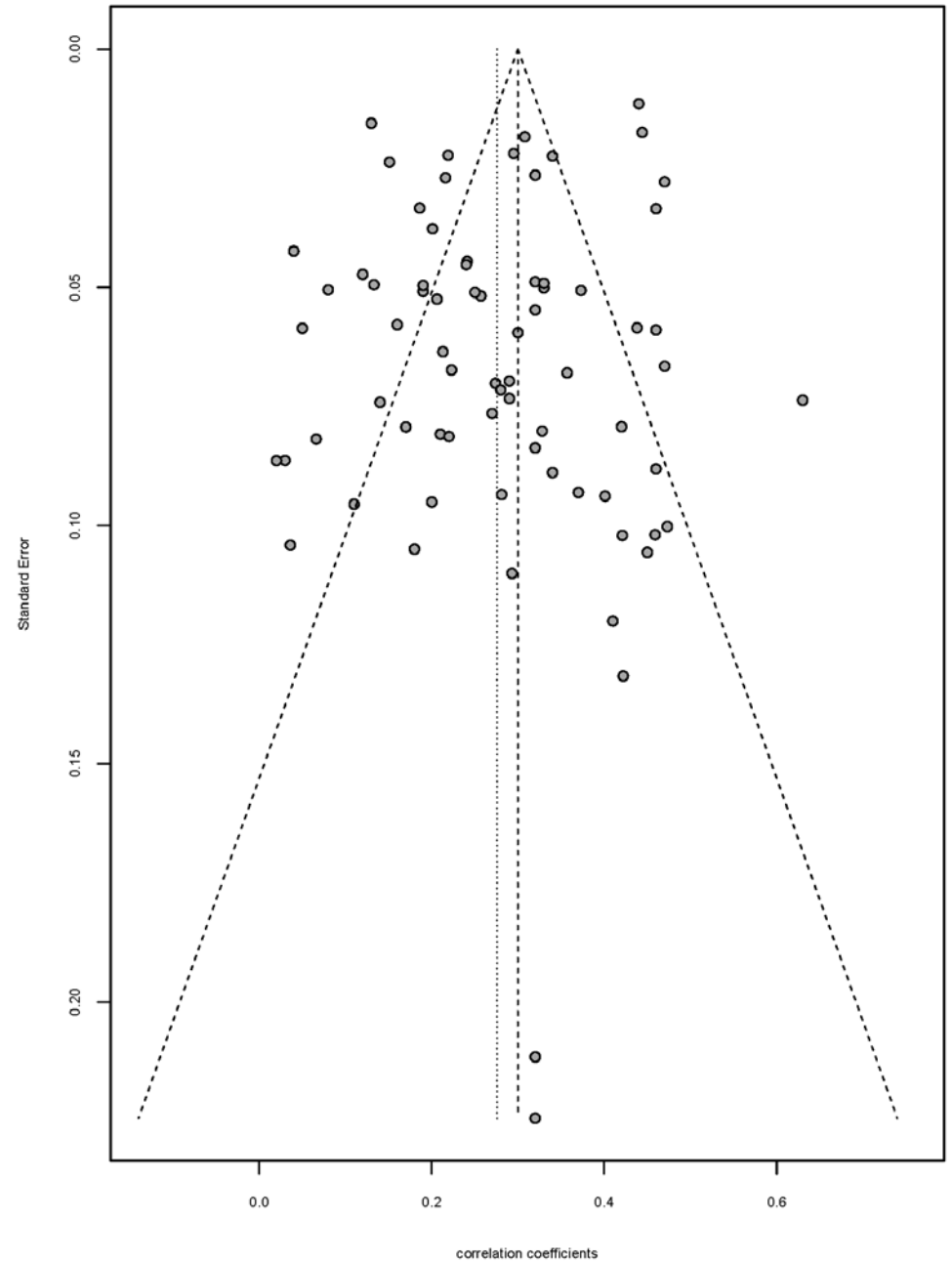
Supplemental Fig.S2c. Forest plot of the overall correlation estimate of the association of sleep quality with aggression, by population category.



Supplemental Fig.S2d. Forest plot of the overall correlation estimate of the association of sleep quality with aggression, by sleep measurement instrument.



**Supplemental Fig.S2e.** Forest plot of the overall correlation estimate of the association of sleep quality with aggression, by aggression measurement instrument.



**Supplemental Fig.S4a.** Funnel plot of correlation estimates in the meta-analysis of the association of sleep quality with aggression.