# Association of self-harm and suicidality with psychiatric co-occurring conditions in autistic individuals: a systematic review and pooled analysis



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#### Summary

Background Autistic individuals frequently experience psychiatric co-occurring conditions, but the association with self-harm/suicidality according to these conditions was not yet elucidated. We aimed to summarize the association between self-harm/suicidality and psychiatric co-occurring conditions in autistic people.

Methods We systematically searched PubMed, Scopus, Embase, Web of Science, and Cochrane Database of Systematic Reviews until June 4, 2024 (PROSPERO registration number: CRD42023412860). Observational studies were included that provided information to calculate the odds ratio (OR) regarding the association between self-harm/suicidality and psychiatric co-occurring conditions in autistic individuals. We summarized the identified associations by presenting OR range or meta-analyzing when 7 or more estimates are available.

Findings The systematic search found 20 eligible studies with 301,841 participants. Our findings suggested that autistic individuals with any psychiatric disorder (k = 1; OR 3.55; 95% CI 1.27–9.98), ADHD (k = 3; OR range: 1.07–1.65), or mood disorder (k = 1; OR 1.26; 95% CI 1.05–1.51) may be associated with higher odds of self-harm than those without these conditions. We identified potential positive associations between suicidality and the following co-occurring conditions: any psychiatric disorder (k = 1; OR 11.65; 95% CI 10.68–12.71), psychotic disorder (k = 4; OR range: 1.95–10.97), mood disorder (k = 3; OR range: 1.75–9.82), bipolar disorder (k = 2; OR range: 2.55–4.95), depressive disorder (k = 10; pooled OR 2.29; 95% CI 1.39–3.77), trauma- and stress-related disorder (k = 2; OR range: 1.28–10.47), and adjustment disorder (k = 1; OR 3.52; 95% CI 2.89–4.28).

Interpretation We found psychiatric co-occurring conditions that may be associated with higher odds of self-harm/suicidality in autistic individuals. However, our findings should be interpreted with caution considering the limited number of included studies. We suggested that clinicians should remain vigilant for autistic individuals with psychiatric co-occurring conditions for their potentially higher likelihood of self-harm and suicidality.

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#### Introduction

Autism, according to the double empathy problem, is a neurodevelopmental difference where communication challenges arise from mutual misunderstandings between autistic and non-autistic individuals rather than deficits in the autistic person alone.<sup>1,2</sup> Due to the heterogeneous nature of autism and differences in methods to determine the prevalence, there have been significant variations in the reported prevalence. The US Centers for Disease Control and Prevention reported a

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#### Research in context

#### Evidence before this study

We systematically searched PubMed, Scopus, Embase, Web of Science, and Cochrane Database of Systematic Reviews until June 4, 2024, without any restrictions for identifying observational studies that investigated the association between self-harm/suicidality and psychiatric co-occurring conditions in autistic individuals. We used the following search terms in PubMed which were adequately modified for each database (Appendix p 10): ("autis\*" OR "Asperg\*" OR "pervasive developmental disorder") AND (("mortality" OR "death\*" OR "survival\*" OR "fatal\*") OR (("suicide" OR suicide) OR ("self-injurious behavior" OR ((self injur\*) AND behavior) OR (self injurious behavior\*) OR (self AND harm\*) OR (self harm\*) OR (self AND injur\*) OR (self injur\*)))) AND (epidemiology OR epidemiologic\* OR (cohort stud\*) OR (longitudinal stud\*) OR (case control stud\*)). We identified three systematic reviews with meta-analysis that reported self-harm and suicidality in the autistic population. Blanchard et al., 2019 found that autistic individuals were associated with approximately 3-fold increased odds of self-harm (odds ratio [OR] 3.18, 95% confidence interval [CI], 2.45-4.12) and suicidality (OR 3.32, 95% CI, 2.60-4.24). Newell et al., 2023 meta-analyzed the prevalence of suicidal ideation (0.34, 95% CI 0.28-0.40), suicide plan (0.22, 95% CI 0.13-0.30), and attempted suicide and behaviors (0.24, 95% CI 0.19-0.30) in autistic and possibly autistic people. Lastly, Huntjens et al., 2024 investigated the prevalence of suicidal ideation (12 months: 0.25, 95% CI 0.19-0.33; lifetime: 0.37, 95% CI 0.25-0.51) and attempted suicide (12 months: 0.14, 95% CI 0.07-0.25; lifetime: 0.15, 95% CI 0.10-0.24) in autistic individuals. However, none of these previous meta-analyses have reported summarized estimates on self-harm and suicidality based on autistic individuals' psychiatric co-occurring conditions.

#### Added value of this study

To the best of our knowledge, previous studies have primarily focused on the association between autism and self-harm and/or suicidality, while primary studies have yielded inconsistent results regarding the association of self-harm/

suicidality with individuals' psychiatric co-occurring conditions. This systematic review offered a more comprehensive insight into the relationship between self-harm/suicidality (including suicidal ideation, attempt, and mortality) and psychiatric co-occurring conditions within autistic individuals by summarizing up-to-date evidence. Our findings suggested that autistic individuals with any psychiatric disorder, ADHD, or mood disorder may be associated with higher odds of self-harm compared to those without these conditions. Regarding suicidality, our study has also identified potential positive associations between suicidality and the following co-occurring conditions in people on the autism spectrum: any psychiatric disorder, psychotic disorder, mood disorder, bipolar disorder, depressive disorder, trauma- and stress-related disorder, and adjustment disorder. Specifically, depressive disorder and psychotic disorder consistently showed significant associations across various outcomes on suicidality including suicidal ideation, attempts, and mortality.

#### Implications of all the available evidence

The findings from this systematic review inferred that healthcare professionals should remain attentive to autistic individuals' psychiatric co-occurring conditions because this population with a particular co-occurring condition could be at an increased likelihood of self-harm and/or suicidality than those without the condition. Given the high prevalence of psychiatric co-occurring conditions among autistic individuals, those with a particular co-occurring condition may require a focused interest concerning the possibly increased likelihood of self-harm or suicidality. However, our findings should be interpreted with caution due to the limited number of included studies. Although the hypothesized exacerbating role of autistic traits in self-harm and suicidality among individuals with a psychiatric co-occurring condition seemed to be plausible, further studies could offer valuable insights that compare the magnitude of effects among autistic individuals, non-autistic individuals, people with a specific psychiatric condition, and those on the autism spectrum with a specific psychiatric condition.

prevalence of one out of 36 in 2020.<sup>3</sup> The global age-standardized prevalence was estimated to be 788.3 per 100,000 according to the 2021 Global Burden of Disease study.<sup>4</sup>

One area of concern in autism is associated with the risk of self-harm and suicidality. A meta-analysis estimated the prevalence of suicidal ideation (0.34, 95% confidence interval [CI] 0.28–0.40), suicide plan (0.22, 95% CI 0.13–0.30), and attempted suicide and behaviors (0.24, 95% CI 0.19–0.30) in autistic and possibly autistic people. Moreover, the risk of self-harm and suicidality in this population was reported to be elevated compared to the general population. Previous

studies reported a 3-fold increased odds of self-harm and suicidality in autistic people.<sup>6,7</sup> The increased self-harm and suicidality observed in autistic individuals compared to non-autistic individuals appeared to be attributed to factors such as camouflaging behaviors, lack of adequate support, high prevalence of psychiatric co-occurring conditions, heightened feelings of burdensomeness, a sense of thwarted belonging, and greater exposure to trauma over their lifetime.<sup>8,9</sup>

Notably, the presence of psychiatric co-occurring conditions has been suggested to largely moderate the observed association between autism and self-harm/suicidality. This potentially indicated that the

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reported 3-fold increased likelihood of self-harm and suicidality in autistic individuals may be compounded by varying estimates of co-occurring conditions, given the high prevalence of mental health conditions in people on the autism spectrum.<sup>12</sup> Indeed, the risk of self-harm and suicidality also varied based on different mental health conditions in the general population, influenced by underlying mechanisms.<sup>13</sup> Although understanding which psychiatric co-occurring conditions are more strongly associated with self-harm and suicidality could help focused support, to the best of our knowledge, none has systematically summarized the relationship between self-harm/suicidality and specific psychiatric co-occurring conditions in the autistic population.5,6,14 Some primary studies have provided estimates on these associations; however, they have reported inconsistent results with unclear magnitudes of association. For example, estimates on the association of anxiety with suicidal ideation have varied significantly, with odds ratios (OR) ranging from 0.53 to 4.67. 15-18 Given that the magnitudes of effects differed across various co-occurring conditions, indicating that autistic individuals with a specific condition might require focused interests and assessment regarding selfharm or suicidality risks, it seemed to be necessary to clarify the link between self-harm/suicidality and psychiatric co-occurring conditions in this population.

Herein, this study aimed to summarize the association of self-harm and suicidality with specific psychiatric co-occurring conditions in autistic individuals, using a systematic approach for up-to-date evidence. Our findings could offer a deeper understanding of the underlying mechanisms regarding self-harm and suicidality in autistic people. Moreover, the findings of this study will help alert clinicians to the heightened likelihood of self-harm/suicidality with a specific psychiatric co-occurring condition in autistic individuals, thereby enabling focused support and enhanced care strategies.

#### Methods

## Reporting guidelines and study protocol

We conducted the study in compliance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 guidelines (Appendix pp 3–6).<sup>19</sup> The present study was pre-registered with PROS-PERO (CRD42023412860). Protocol amendments were made during the study and revision process which were detailed in Appendix pp 7–9.

#### Search strategy and selection criteria

We systematically searched PubMed, Scopus, Embase, Web of Science, and Cochrane Database of Systematic Reviews until 4th June 2024, without any language limitations. We used the following search terms in PubMed, which were adequately modified for each database (Appendix p 10): ("autis\*" OR "Asperg\*" OR

"pervasive developmental disorder") AND (("mortality" OR "death\*" OR "survival\*" OR "fatal\*") OR (("suicide" OR suicide) OR ("self-injurious behavior" OR ((self injur\*) AND behavior) OR (self injurious behavior\*) OR (self AND harm\*) OR (self harm\*) OR (self AND injur\*) OR (self injur\*)))) AND (epidemiology OR epidemiologic\* OR (cohort stud\*) OR (longitudinal stud\*) OR (case control stud\*)). We also manually searched the references of related articles to further identify eligible articles. The screening tasks including title, abstract, and full-text selection were independently conducted by two authors (J.H.K. and J.L.). Any disagreements on eligibility were resolved by the discussion with the other author (K.A.C.).

The primary outcomes examined in this study were self-harm and suicidality. Note that suicidality encompasses outcomes related to suicidal ideation, attempts, and mortality, as per the previous meta-analysis.<sup>6</sup> Additionally, we investigated the subcategories of suicidality—suicidal ideation, attempts, and mortality—as secondary outcomes of interest. The definitions for these terms were based on the International Study of Definitions of English-Language Terms for Suicidal Behaviors.<sup>20</sup>

To select eligible articles, we applied the following inclusion criteria: observational studies; studies that included autistic individuals as participants; studies that reported OR for the association between outcomes of interests (self-harm, suicidality, suicidal ideation, attempts, or mortality) and any psychiatric condition, along with the standard error, 95% CI, or any statistic necessary for calculating standard error; (if OR and standard error are not provided) studies that provided sufficient data to calculate OR and standard error, which includes the number of autistic individuals who (1) had a psychiatric condition and were involved in any of the outcomes of interest, (2) had a psychiatric condition but were not involved in any outcomes of interest, (3) did not have a psychiatric condition but were involved in any outcomes of interest, and (4) did not have a psychiatric condition and were not involved in any outcomes of interest.

Studies that met the following criteria were excluded: non-primary studies; studies that did not report outcomes of interest in autistic individuals; studies that did not present enough data for re-analysis; and studies that did not provide the outcomes with information on co-occurring conditions; studies with inadequate comparison group. The operationalization of autism spectrum disorder was based on any version of the International Classification of Diseases (ICD) and the Diagnostic and Statistical Manual of Mental Disorders (DSM). This included criteria from DSM-III, DSM-IV, and ICD-10, where 'autism' may have been classified as 'autistic disorder' and did not encompass the entire autism spectrum. To gather a broad range of eligible studies, we also included studies that used the Autism

Diagnostic Interview (ADI), Autism Diagnostic Observation Schedule (ADOS), and other screening tools such as the Social Communication Questionnaire, and stated that enrolled patients were previously diagnosed with autism. This approach was intended to represent all individuals on the autism spectrum, not just those meeting the criteria for autistic disorder under earlier classifications.

#### Data extraction

Data extraction was primarily done by one author (J.L.) and subsequently verified by another author (J.H.K.). Extracted data included the name of the first author, publication year, the country where the study was conducted, operationalization method of autism, number of autistic individuals, mean age and standard deviation, percentage of men, specific outcome definitions; outcome of interests (OR and standard error for the association of self-harm, suicidality, suicidal ideation, attempts, or mortality with any psychiatric co-occurring condition). When pre-calculated estimates were presented, we included only maximally adjusted ones. This allowed us to potentially isolate the odds specifically associated with each co-occurring condition, as some estimates controlled for other co-occurring conditions such as depression. Regarding the methods for reporting sex, this study adopted 'sex assigned at birth' in accordance with the included eligible studies.

#### Study quality assessment

Study quality assessment was initially done by one author (J.L.) and then verified by another author (J.H.K.). The quality of the included studies was assessed using the Newcastle–Ottawa Scale (NOS), which is the commonly used tool for non-randomized studies.<sup>21</sup> As the original NOS was designed for cohort and case–control studies, we utilized the modified NOS for cross-sectional studies from a previous study.<sup>22</sup> The NOS evaluates the methodological quality of observational studies based on selection, comparability, and outcome/exposure criteria. The total score ranges from 0 to 9 for cohort and case–control studies, and from 0 to 10 for cross-sectional studies.

#### Data analysis

We calculated the OR and the corresponding 95% CI for each identified association using the extracted data when a primary study did not provide an estimate. Additionally, we presented a range of OR estimates along with all individual estimates to offer an overview of the published evidence for each association between self-harm/suicidality and psychiatric co-occurring conditions in autistic individuals.

To obtain more robust evidence, we aimed to conduct a meta-analysis for data synthesis whenever a sufficient number of estimates were available. Considering the expected variability that originated from the innate heterogeneity of autism and the study settings, we planned to use a random-effect model as an appropriate strategy for meta-analysis. Random effects models assume that heterogeneity between studies is due to both sampling error variability and differences in studylevel characteristics. Since at least 7 estimates are required to produce reliable evidence from a randomeffects meta-analysis,23 we proceeded with the metaanalysis only when 7 or more estimates were available. When meta-analysis was performed, we also evaluated the heterogeneity between studies by estimating the  $I^2$ statistic and performing Cochrane's Q test which quantifies the significance. Conventionally, an  $I^2$  statistic greater than 50% is considered indicative of potential substantial heterogeneity, while an  $I^2$  statistic exceeding 75% is regarded as indicative of considerable heterogeneity. As mentioned above, note that suicidality was defined as the combination of outcomes related to suicidal ideation, attempt, and mortality. In the analysis for suicidality, we included all estimates in the analysis when separate estimates for suicidal ideation, attempt, or mortality were reported in a single study, following the previous meta-analysis with a similar subject.<sup>6</sup>

All statistical analyses were performed using R software (version 4.2.3) and RStudio (version 2023.09.1 + 494). We utilized the following R packages for analysis and figure generation: 'meta' (version 7.0.0), 'dmetar' (version 0.1.0), and 'ggplot2' (version 3.5.1). All statistical tests were two-sided and statistical significance was set at P < 0.05.

#### Role of the funding source

The funders had no role in the study design, data collection, data analysis, data interpretation, writing of the report, or decisions to submit the paper for publication. All researchers were independent of the funders, had access to the data, and accepted responsibility for the decision to submit for publication.

#### Results

#### Study selection and study characteristics

After removing duplicates, we screened 5219 citations for eligibility. Among these, 89 articles underwent full-text screening, of which 13 were deemed eligible for this study. Additionally, we manually searched for eligible articles through citation searching. Upon reviewing 70 articles, we identified 7 studies that met the selection criteria; 20 studies were included in total (Fig. 1).<sup>15–18,24–39</sup> The list of excluded studies with reasons during the full-text screening stage is provided in Appendix pp 11–19.

The characteristics of the included studies are summarized in Table 1. A total of 301,841 autistic individuals (median 577 per study, interquartile range [IQR] 98 to 9957, range 50–145,929) were included. In terms of study design, 5 studies (25.0%) were cohort, 2 (10.0%) were case—control, and 13 (65.0%) employed a

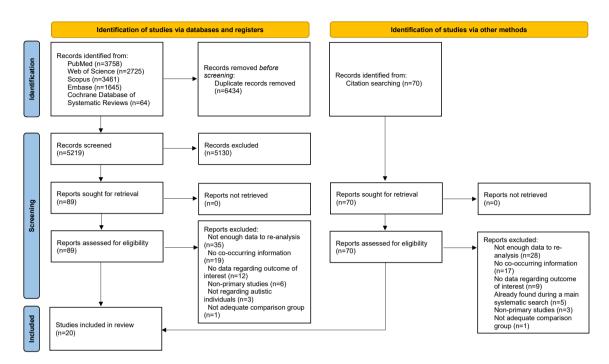


Fig. 1: Study selection flow.

cross-sectional design. Eligible studies were done in 9 countries between 2013 and 2024. Included studies were conducted in the USA (n=6); the United Kingdom (n=5); Canada and Sweden (n=2); India, Taiwan, Turkey, South Korea, and Netherlands (n=1). Among 20 included studies, 10 (50.0%) were available for the mean age of the sample for outcome estimation and the mean age of these studies was 20.05. Among the studies, 7 (35.0%) investigated self-harm and 13 (65.0%) examined suicidality.

### Association between self-harm and psychiatric cooccurring conditions in autistic individuals

Our systematic search found the following 5 psychiatric co-occurring conditions that were possibly associated with self-harm in people on the autism spectrum: any psychiatric disorder (the number of reported estimates [k] = 1), intellectual disability (k = 4), ADHD (k = 3), mood disorder (k = 1), and depressive disorder (k = 1). Meta-analysis was not performed due to the insufficient number of estimates.

Although derived from single studies, identified studies suggested that autistic individuals with any psychiatric disorder (the number of reported estimates [k] = 1, OR 3.55, 95% CI 1.27–9.98) or mood disorder (k = 1, OR 1.26, 95% CI 1.05–1.51) may be associated with higher odds of self-harm than those without these conditions. The association between self-harm and ADHD consistently demonstrated increased odds, as evidenced by three statistically significant estimates of

OR ranging from 1.07 to 1.65; however, the reported estimates of OR for intellectual disability largely varied, ranging from 0.44 to 2.03 (Table 2).

## Association between suicidality and psychiatric cooccurring conditions in autistic individuals Suicidality

From the systematic search, we identified the following 18 psychiatric co-occurring conditions that were possibly associated with suicidality in people on the autism spectrum: any psychiatric disorder (k = 1), intellectual disability (k = 7), ADHD (k = 9), psychotic disorder (k = 4), mood disorder (k = 3), bipolar disorder (k = 2), depressive disorder (k = 10), anxiety disorder (k = 10), generalized anxiety disorder (k = 2), social phobia (k = 1), specific phobia (k = 2), separation anxiety disorder (k = 1), obsessive-compulsive disorder (k = 3), trauma- and stress-related disorder (k = 2), adjustment disorder (k = 1), disruptive behavior disorders (k = 6), substance-related disorder (k = 1), and personality disorder (k = 2) (Table 2).

Among these conditions, meta-analysis was available for intellectual disability (k = 7, pooled OR 0.58, 95% CI 0.29 to 1.19), ADHD (k = 9, pooled OR 0.92, 95% CI 0.58–1.45), depressive disorder (k = 10, pooled OR 2.29, 95% CI 1.39–3.77), and anxiety disorder (k = 10, pooled OR 1.25, 95% CI 0.80–1.96), which suggested that autistic individuals with depressive disorder may be associated with increased odds of suicidality compared to those without this condition (Table 2). However,

# **Articles**

Author (year)	Country	Study design	Assessment tool/ criteria for autism	Mean age (SD)	Number of participants	Study outcome(s) and reported co-occurring condition(s)	Covariates adjustn adjusted variables	Covariates adjustment status and adjusted variables	Total NOS scoreª
Bal et al. (2022) <sup>15</sup>	South Korea	Cross-sectional	ASSQ, ADOS, ADI-R	8.9 (1.6)	98	Outcome: suicidal ideation Co-occurring conditions: anxiety, hyperactivity	Yes	Demographics, peer victimization, behavioral problems, depression, socioeconomic status	8/10
Cervantes et al. (2023) <sup>24</sup>	USA	Cohort	(CD-9	Ψ V	145,929	Outcomes: suicidal ideation or intentional self- inflicted Co-occurring conditions: any psychiatric concems, any ID, adjustment disorder, mood disorders, anxiety disorders, psychotic disorders	Yes	Age, sex, insurance type, median household income for patient's ZIP code, clinical factors, region of hospital, teaching status of hospital, ID	6/9
Demirkaya et al. (2016) <sup>28</sup>	Turkey	Cross-sectional	DSM-IV-TR	13.6 (2.9)	55	Outcome: suicidality Co-occurring conditions: ADHD, psychotic features, mood disorders (bipolar, depression), anxiety disorders (generalized anxiety disorder, separation anxiety disorder, obsessive compulsive disorder, social phobia, specific phobia)	° Z		8/10
Hand et al. (2020) <sup>25</sup>	NSA	Case-control	CD-9	۷ ۷	21,792	Outcomes: suicidal ideation, suicide attempt Co-occurring conditions: ID, unipolar depression	Yes	Years of age, female, race, dually eligible, comorbid conditions, number of psychiatric hospitalizations, number of psychiatric emergency department visits	6/8
Hirvikoski et al. (2019) <sup>26</sup>	Sweden	Case-control	ICD-9	ID: 21.0 (15.5) ADHD: 20.7 (13.9)	ID: 32,239 ADHD: 43,570	Outcomes: suicide attempts, death by suicide Co-occurring conditions: ID, ADHD	N <sub>O</sub>	ı	6/8
Holden et al. (2020) <sup>27</sup>	United Kingdom	Cohort	ICD-10, ADOS	15.2 (1.4)	089	Outcome: later suicidality Co-occurring conditions: ID, ADHD, psychosis, anxiety disorder	Yes	Bullied, sociodemographic factors, clinical factors, factors, factors, adaptive fuctors, adaptive function	6/6
Hooijer et al. (2020) <sup>18</sup>	Netherlands	Netherlands Cross-sectional	DSM-IV	Median age = 28.5 [IQR 23.0-42.3]	74	Outcomes: lifetime suicidal ideation, lifetime suicide attempt Co-occurring conditions: anxiety disorder, depressive disorder, obsessive-compulsive disorder, personality disorder, trauma and stress-disorder, substance use disorder	0	ı	7/10
Horowitz et al. (2018) <sup>16</sup>	USA	Cross-sectional	SCQ, ADOS-2	13.6 (2.3)	107	Outcome: "Talks about death or suicide" Co-occurring conditions: ADHD, mood disorder, anxiety disorder, disruptive behavior disorder	Yes	Sex, race, age, non-verbal IQ, comorbid diagnoses	7/10
Licence et al. (2020) <sup>29</sup>	United Kingdom	Cross-sectional	Previous diagnosis, SCQ	14.1 (6.2)	83	Outcome: self-harm Co-occurring conditions: mood, overactivity/ impulsivity	Yes	Comorbid conditions	7/10
Liu et al. (2023) <sup>30</sup>	Sweden	Cohort	ICD-9/10	ΝΑ	5291	Outcome: intentional self-harm Co-occurring condition: ID	Yes	Sex, birth year	6/6
Malhi et al. (2021) <sup>31</sup>	India	Cross-sectional	DSM-IV/5, CARS	Y Y	1252	Outcome: self-injurious behaviors Co-occurring conditions: ID, hyperactivity	° N	Ī	4/10
McDonnell et al. (2020) <sup>17</sup>	Canada	Cross-sectional	ADOS, ADI-R	Ψ.	474	Outcomes: "Talks about killing self", "Deliberately harms or tries to kill self" Co-occurring conditions: anxiety problems, ADHD problems, ODD problems, conduct problems	Yes	CBCL diagnostic scale total scores	8/10
Moseley et al. (2020) <sup>32</sup>	United Kingdom	Cross-sectional	Previous diagnosis	42.6 (14.0)	102	Outcome: self-harm Co-occurring condition: psychiatric comorbidities	§.	I	5/10
O'Nions et al. (2024) <sup>33</sup>	United Kingdom	Cohort	Previous diagnosis	NA A	22,112	Outcome: self-harm Co-occurring condition: ID	o N	ı	6/8
								(Table 1 continues on next page)	kt page

Author (year) Country	Country	Study design	Assessment tool/ criteria for autism	Mean age (SD)	Number of participants	Study outcome(s) and reported co-occurring condition(s)	Covariates adjustr adjusted variables	Covariates adjustment status and adjusted variables	Total NOS score <sup>a</sup>
(Continued from previous page)	previous page								
Paquette-Smith Canada et al. $(2014)^{34}$	Canada	Cross-sectional	AQ and formal diagnosis	34.4 (11.0)	50	Outcome: attempted suicide Co-occurring conditions: anxiety, depression	No		2/10
Soke et al. (2016) <sup>35</sup>	USA	Cross-sectional	DSM-IV-TR	NA	6012	Outcome: self-injurious behaviors Co-occurring condition: ID	No		8/10
Soke et al. (2018) <sup>36</sup>	USA	Cross-sectional	DSM-IV-TR, ADOS, ADI-R	NA	692	Outcome: ever self-injurious behaviors Co-occurring condition: child developmental conditions	NO NO		7/10
Stewart et al. (2023) <sup>37</sup>	United Kingdom	Cross-sectional	Autism Spectrum Traits questionnaire	63.0 (6.7)	276	Outcomes: suicidal ideation, suicide attempt Co-occurring condition: depression	No		7/10
Storch et al. (2013) <sup>38</sup>	USA	Cross-sectional	DSM-IV-TR	10.6 (2.3)	102	Outcome: suicidal thoughts/behavior Co-occurring conditions: social phobia, generalized anxiety disorder, specific phobia, separation anxiety disorder, obsessive-compulsive disorder, post- traumatic stress disorder, major depressive disorder/ dysthymia, disruptive behavior disorder	° N		4/10
Tsai et al. (2023) <sup>39</sup>	Taiwan	Cohort	ICD-9/10	NA	45,398	Outcome: suicide Co-occurring conditions: ID, ADHD, schizophrenia, bipolar disorder, major depressive disorder	Yes Sex, to of urt	Sex, birth year, income, level of urbanization, Charlson Comorbidity Index	6/6

Abbreviations: ADHD, Attention-Deficit/Hyperactivity Disorder; ADOS, Autism Diagnostic Observation Schedule; ADI, Autism Diagnostic Interview; AQ, Autism Spectrum Quotient questionnaire; ASSQ, Autism Spectrum Screening Questionnaire; CBCL, Child Behavior Checklist; CARS, Childhood Autism Rating Scale; DSM, Diagnostic and Statistical Manual of Mental Disorders; ICD, International Classification of Diseases; ID, Intellectual Disability; IQ, Intelligence Quotient, IQR, Interquartile Range; NA, Not Available; NOS, Newcastle-Ottawa Scale; ODD, Oppositional Defant Disorder; SCQ, Social Communication Questionnaire; SD, Standard Deviation. \*Total score of NOS is 9 for cohort and case-control and 10 for cross-sectional design.

# **Articles**

	Number of reported estimate(s)	Number of participants	Range of OR estimate(s)	Meta-analyzed estimate (pooled OR, 95% CI) <sup>a</sup>	Findings on the association bewteen self-harm/suicidality and co-occurring conditions (OR, 95% CI) <sup>b</sup>	Mean NOS score
Self-harm						
Any psychiatric disorder	1	102	3.55		Increased odds (1) - Moseley et al. (2020) <sup>32</sup> : <b>3.55 (1.27–9.98)</b>	5
Intellectual disability	4	34,667	0.44-2.03		Increased odds (2)  - Malhi et al. (2021) <sup>31</sup> : <b>2.03 (1.48-2.78)</b> - Soke et al. (2016) <sup>35</sup> : <b>1.46 (1.30-1.64)</b> Decreased odds (2)  - Liu et al. (2023) <sup>30</sup> : <b>0.44 (0.37-0.53)</b> - O'Nions et al. (2024) <sup>32</sup> : <b>0.65 (0.61-0.70)</b>	7.25
ADHD	3	2027	1.07-1.65		Increased odds (3)  - Malhi et al. (2021) <sup>31</sup> : <b>1.65 (1.20-2.27)</b> - Licence et al. (2020) <sup>29</sup> : <b>1.07 (1.02-1.13)</b> - Soke et al. (2018) <sup>36</sup> : <b>1.55 (1.14-2.10)</b>	6
Mood disorder	1	83	1.26		Increased odds (1) - Licence et al. (2020) <sup>29</sup> : <b>1.26 (1.05-1.51)</b>	7
Depressive disorder	1	276	2.04		Increased odds (1) - Stewart et al. (2023) <sup>37</sup> : 2.04 (0.68-3.41)	7
Suicidality						
Any psychiatric disorder	1	145,929	11.65		Increαsed odds (1) - Cervantes et al. (2023) <sup>24</sup> : <b>11.65 (10.68-12.71)</b>	6
Intellectual disability	7	246,038	0.25-1.92	0.58 (0.29-1.19)	Increased odds (1)  - Hand et al. (2019) <sup>25</sup> : <b>1.92 (1.64-2.24)</b> No effect (1)  - Cervantes et al. (2023) <sup>24</sup> : 1.00 (0.88-1.13) Decreased odds (5)  - Hand et al. (2019) <sup>25</sup> : <b>0.76 (0.64-0.90)</b> - Hirvikoski et al. (2019) <sup>25</sup> : 0.68 (0.63-0.73), <b>0.26 (0.23-0.31)</b> - Holden et al. (2020) <sup>27</sup> : <b>0.32 (0.18-0.58)</b> - Tsai et al. (2023) <sup>39</sup> : <b>0.25 (0.19-0.32)</b>	8
ADHD	9	90,370	0.17-1.79	0.92 (0.58-1.45)	Increased odds (3)  - Hirvikoski et al. (2019) <sup>26</sup> : <b>1.57 (1.42-1.73)</b> - Holden et al. (2020) <sup>27</sup> : <b>1.34 (0.84-2.13)</b> - Tsai et al. (2023) <sup>39</sup> : <b>1.79 (1.14-2.81)</b> No effect (1)  - McDonnell et al. (2020) <sup>17</sup> : 1.00 (0.89-1.12)  Decreased odds (5)  - Bal et al. (2022) <sup>15</sup> : <b>0.17 (0.04-0.74)</b> - Demirkaya et al. (2016) <sup>28</sup> : 0.40 (0.12-1.38)  - Hirvikoski et al. (2019) <sup>26</sup> : <b>0.68 (0.56-0.82)</b> - Horowitz et al. (2018) <sup>16</sup> : <b>0.45 (0.21-0.96)</b> - McDonnell et al. (2020) <sup>17</sup> : 0.89 (0.78-1.01)	8.1
Psychotic disorder	4	192,062	1.95-10.97		Increased odds (4)  - Cervantes et al. (2023) <sup>24</sup> : <b>2.20 (1.95–2.48)</b> - Demirkaya et al. (2016) <sup>28</sup> : 10.98 (0.72–168.20)  - Holden et al. (2020) <sup>27</sup> : <b>2.98 (1.46–6.08)</b> - Tsai et al. (2023) <sup>39</sup> : <b>1.95 (1.76–2.15)</b>	8
Mood disorder	3	146,091	1.75-9.82		Increased odds (3) - Cervantes et al. (2023) <sup>24</sup> : <b>9.82 (9.14-10.55)</b> - Demirkaya et al. (2016) <sup>28</sup> : 1.75 (0.45-6.85) - Horowitz et al. (2018) <sup>16</sup> : <b>2.71 (1.12-6.55)</b>	7
Bipolar disorder	2	45,453	2.55-4.95		Increased odds (2) - Demirkaya et al. (2016) <sup>18</sup> : 4.95 (0.37-163.71) - Tsai et al. (2023) <sup>39</sup> : <b>2.55 (1.35-4.82)</b>	8.5
Depressive disorder	10	67,747	1.08-8.54	2.29 (1.39-3.77)	Increased odds (10)  - Demirkaya et al. (2016) <sup>28</sup> : 1.08 (0.22–5.29)  - Hand et al. (2019) <sup>25</sup> : <b>8.54 (7.12–10.24), 1.78 (1.52–2.08)</b> - Hooijer et al. (2020) <sup>18</sup> : 1.13 (0.34–3.79), 1.30 (0.33–5.14)  - Paquette-Smith et al. (2014) <sup>34</sup> : 2.59 (1.00–6.71)  - Stewart et al. (2023) <sup>37</sup> : 1.71 (0.63–4.64), 2.21 (0.40–12.10)  - Storch et al. (2013) <sup>38</sup> : <b>4.57 (1.06–19.72)</b> - Tsai et al. (2023) <sup>39</sup> : <b>1.67 (1.49–1.87)</b>	7

	Number of reported estimate(s)	Number of participants	Range of OR estimate(s)	Meta-analyzed estimate (pooled OR, 95% CI) <sup>a</sup>	Findings on the association bewteen self-harm/suicidality and co-occurring conditions (OR, 95% CI) <sup>b</sup>	Mean NOS score
Continued from previous	s page)					_
Anxiety disorder	10	147,455	0.45-4.67	1.25 (0.80-1.96)	Increased odds (8)  - Bal et al. (2022) <sup>15</sup> : <b>4.67 (1.14-19.15)</b> - Cervantes et al. (2023) <sup>24</sup> : <b>1.99 (1.84-2.16)</b> - Demirkaya et al. (2016) <sup>28</sup> : 1.01 (0.30-3.37)  - Holden et al. (2020) <sup>27</sup> : 1.62 (0.58-4.55)  - Horowitz et al. (2018) <sup>16</sup> : <b>2.30 (1.08-4.90)</b> - Paquette-Smith et al. (2014) <sup>34</sup> : 1.89 (0.75-4.81)  - McDonnell et al. (2020) <sup>17</sup> : 1.11 (0.98-1.25), 1.05 (0.94-1.18)  Decreased odds (2)  - Hooijer et al. (2020) <sup>27</sup> : 0.53 (0.27-1.04), <b>0.45 (0.22-0.94)</b>	7
Generalized anxiety disorder	2	157	1.30-3.35		Increased odds (2) - Demirkaya et al. (2016) <sup>28</sup> : 1.30 (0.04-17.20) - Storch et al. (2013) <sup>38</sup> : 3.35 (0.58-86.04)	6
Social phobia	1	55	1.30		Increased odds (1) - Demirkaya et al. (2016) <sup>28</sup> : 1.30 (0.04–17.20)	8
Specific phobia	2	157	0.87-1.61		Increased odds (1) - Storch et al. (2013) <sup>38</sup> : 1.61 (0.42–8.18) Decreased odds (1) - Demirkaya et al. (2016) <sup>28</sup> : 0.87 (0.03–8.16)	6
Separation anxiety disorder	1	102	0.52		Decreased odds (1) - Storch et al. (2013) <sup>38</sup> : 0.52 (0.10-1.97)	4
Obsessive- compulsive disorder	3	231	0.40-2.41		Increased odds (1) - Storch et al. (2013) <sup>38</sup> : 2.41 (0.65-9.25)  Decreased odds (2) - Demirkaya et al. (2016) <sup>28</sup> : 0.58 (0.07-2.80) - Hooijer et al. (2020) <sup>18</sup> : 0.40 (0.00-1.21)	6.7
Trauma- and stress- related disorder	2	176	1.28-10.47		Increased odds (2) - Hooijer et al. (2020) <sup>18</sup> : 1.28 (0.00–4.41) - Storch et al. (2013) <sup>38</sup> : <b>10.47 (1.58–70.50)</b>	6
Adjustment disorder	1	145,929	3.52		Increased odds (1) - Cervantes et al. (2023) <sup>24</sup> : <b>3.52 (2.89–4.28)</b>	6
Disruptive behavior disorders	6	581	0.95-1.69		Increased odds (5) - Horowitz et al. (2018) <sup>16</sup> : 1.69 (0.74–3.87) - Storch et al. (2013) <sup>38</sup> : 1.35 (0.34–5.28) - McDonnell et al. (2020) <sup>17</sup> : 1.18 (0.99–1.41), <b>1.10 (1.01–1.19)</b> , <b>1.13 (1.04–1.23)</b> Decreased odds (1) - McDonnell et al. (2020) <sup>17</sup> : 0.95 (0.81–1.12)	6.3
Substance-related disorder	1	74	4.25		Increased odds (1) - Hooijer et al. (2020) <sup>18</sup> : 4.25 (0.00–12.19)	8
Personality disorder	2	74	0.61		Decreased odds (2) - Hooijer et al. (2020) <sup>18</sup> : 0.61 (0.00–1.75), 0.61 (0.00–1.99)	8

Abbreviations: ADHD, Attention-Deficit/Hyperactivity Disorder; CI, Confidence Interval; NOS, Newcastle–Ottawa Scale; OR, Odds Ratio. <sup>a</sup>Random-effect meta-analysis for data synthesis was performed only when 7 or more estimates were available. <sup>b</sup>Statistically significant estimates were highlighted with bold.

Table 2: Summarized evidence on the association between self-harm/suicidality and psychiatric co-occurring conditions in autistic individuals.

considerable heterogeneity was observed in the association between suicidality and depressive disorder with  $I^2$  of 96.3% (P < 0.0001), which was potentially due to diverse study settings, definitions of depressive disorder, and variations in the measurement and reporting of suicidality across the included studies. Forest plots and funnel plots for each meta-analysis were displayed in Appendix pp 22–25.

Although derived from single studies, autistic individuals with any psychiatric disorder (OR 11.65, 95% CI 10.68–12.71) or adjustment disorder (OR 3.52, 95% CI 2.89–4.28) were found to be possibly associated with higher odds of suicidality than those without these conditions. Also, identified studies consistently reported

increased odds of suicidality among autistic individuals with co-occurring psychotic disorder (k = 4, OR range: 1.95–10.97), mood disorder (k = 3, OR range: 1.75–9.82), bipolar disorder (k = 2, OR range: 2.55–4.95), and trauma- and stress-related disorder (k = 2, OR range: 1.28–10.47). Reports on other co-occurring conditions presented estimates that were either inconsistent or not statistically significant (Table 2).

Subcategories of suicidality (suicidal ideation, attempt, and mortality)

Regarding suicidal ideation, identified studies indicated that autistic individuals with intellectual disability (k = 1, OR 0.76, 95% CI 0.64–0.90) or ADHD (k = 4, OR range:

0.17–0.89) were potentially associated with decreased odds of suicidal ideation compared to those without these conditions. Conversely, autistic individuals who had co-occurring psychotic disorder (k = 1, OR 10.98, 95% CI 1.36–320.13), mood disorder (k = 2, OR range: 1.75–2.71), or depressive disorder (k = 4, OR range: 1.08–8.54) were reported to be possibly associated with higher odds of suicidal ideation than those without these conditions. Reports on other co-occurring conditions presented estimates that were either inconsistent or not statistically significant (Table 3).

Regarding suicide attempts, identified studies showed that autistic individuals with depressive disorder (k = 4, OR range: 1.30–2.59) were possibly related to increased odds of suicide attempts compared to those without this condition. Reports on other co-occurring conditions presented estimates that were either inconsistent or not statistically significant (Table 3).

Regarding suicide mortality, identified studies reported that autistic individuals with intellectual disability (k = 2, OR range: 0.25–0.26) were potentially associated with decreased odds of suicide mortality compared to those without this condition; however, psychotic disorder (k = 1, OR 1.95, 95% CI 1.77–2.15), bipolar disorder (k = 1, OR 2.55, 95% CI 1.35–4.82), and depressive disorder (k = 1, OR 1.67, 95% CI 1.49–1.88) showed reversed association (Table 3).

#### Study quality assessment

The quality assessment using the NOS resulted in a median score of 8 per study (IQR 6.75–8, range 2–9) (Table 1). Five cohort studies had a median score of 9/9 (IQR 8–9, range 6–9); both case–control studies scored 8/9; and 13 cross-sectional studies had a median score of 7/10 (IQR 5–8, range 2–8). Detailed rationales for the NOS scoring are displayed in Appendix pp 20–21.

#### Discussion

This systematic review aimed to summarize the association between self-harm/suicidality and specific psychiatric co-occurring conditions in autistic individuals. A total of 20 eligible studies with 301,841 participants were included in this study. Our study suggested that autistic individuals with any psychiatric disorder, ADHD, or mood disorder were possibly associated with higher odds of self-harm than those without these conditions. For suicidality, results from a meta-analysis indicated that autistic individuals with depressive disorder may be associated with increased odds of suicidality compared to those without this condition. Previous literature also reported potential positive associations between suicidality and the following cooccurring conditions: any psychiatric disorder, psychotic disorder, mood disorder, bipolar disorder,

trauma- and stress-related disorder, and adjustment disorder.

Our study found that autistic individuals may be associated with higher odds of self-harm when they have an additional psychiatric co-occurring condition such as any psychiatric disorder, ADHD, or mood disorder when compared to those without these conditions. Previous studies have demonstrated that both ADHD and mood disorders themselves were associated with an increased likelihood of self-harm.40-42 Specifically, ADHD-related problems (psychosocial adversities such as bullying and peer victimization, poor executive function, low selfesteem, etc.) and mood disorder-related problems (negative self-perception, psychological distress, impaired cognitive function, etc.) were reported to be significantly related to self-harm. 43,44 Yet, the potential exacerbating role of autism in self-harm remains unclear, as our findings were constrained to establishing an association. We hypothesized that autistic traits might aggravate the risk of self-harm by deepening the abovementioned problems related to ADHD or mood disorder. Autistic individuals tend to experience cognitive inflexibility,45 rigidity, 46 and challenges in comprehending the order and duration of events,47 leading to an alternative perception of social situations. They may become ensnared in distressing thought patterns, which may prompt them to engage in self-harm to escape from what they perceive as overwhelming hardship. Given that both ADHD and mood disorders are common co-occurring mental health conditions in individuals on the autism spectrum and self-harm is significantly associated with suicidality, it may be essential for clinical practice to pay a focused interest to the potential risk of self-harm in autistic individuals with either of these conditions. 12,42,48

Regarding suicidality, meta-analytic findings showed that autistic individuals with depressive disorder may be associated with increased odds of suicidality compared to those without this condition. Systematic evidence also suggested that autistic individuals with any of the following conditions—any psychiatric disorder, psychotic disorder, mood disorder, bipolar disorder, trauma- and stress-related disorder, or adjustment disorder-potentially have higher odds of suicidality than those without these conditions. Specifically, depressive disorder and psychotic disorder consistently showed significant associations across various outcomes on suicidality including suicidal ideation, attempts, and mortality. While both depressive and psychotic disorders are risk factors for suicidality,49 autistic traits may further explain these associations. According to the interpersonal theory of suicide, depressive and psychotic disorders are positively associated with thwarted belonging and perceived burdensomeness.<sup>13</sup> Given that (1) autistic individuals often experience greater thwarted belonging and perceived burdensomeness than non-autistic individuals and (2) autistic traits affect suicidality through these factors, autistic traits may contribute to the significant association between suicidality and these

		estimate(s)	suicidality (suicidal ideation, attempt, and mortality) and co- occurring conditions (OR, 95% CI) <sup>a</sup>	score
1	21,792	0.76	Decreased odds (1) - Hand et al. (2019) <sup>25</sup> : <b>0.76 (0.64-0.90)</b>	8
4	722	0.17-0.89	Decreased odds (4)  - Bal et al. (2022) <sup>15</sup> : <b>0.17 (0.04-0.74)</b> - Demirkaya et al. (2016) <sup>28</sup> : 0.40 (0.12-1.38)  - Horowitz et al. (2018) <sup>16</sup> : <b>0.45 (0.21-0.96)</b> - McDonnell et al. (2020) <sup>17</sup> : 0.89 (0.78-1.01)	7.8
1	55	10.98	Increased odds (1) - Demirkaya et al. (2016) <sup>28</sup> : <b>10.98 (1.36–320.13)</b>	8
2	162	1.75-2.71	Increased odds (2) - Demirkaya et al. (2016) <sup>28</sup> : 1.75 (0.43–6.64) - Horowitz et al. (2018) <sup>16</sup> : <b>2.71 (1.12–6.55)</b>	7.5
1	55	4.95	Increased odds (1) - Demirkaya et al. (2016) <sup>28</sup> : 4.95 (0.37–163.71)	8
4	22,197	1.08-8.54	Increased odds (4)  - Demirkaya et al. (2016) <sup>28</sup> : 1.08 (0.22–5.29)  - Hand et al. (2019) <sup>25</sup> : <b>8.54 (7.12–10.24</b> )  - Hooijer et al. (2020) <sup>18</sup> : 1.13 (0.34–3.79)  - Stewart et al. (2023) <sup>37</sup> : 1.71 (0.63–4.64)	7.8
5	796	0.53-4.67	Increased odds (4)  - Bal et al. (2022) <sup>15</sup> : <b>4.67 (1.14-19.15)</b> - Demirkaya et al. (2016) <sup>28</sup> : <b>1.01</b> (0.30-3.37)  - Horowitz et al. (2018) <sup>16</sup> : <b>2.30 (1.08-4.90)</b> - McDonnell et al. (2020) <sup>17</sup> : <b>1.11</b> (0.98-1.25)  Decreased odds (1)  - Hooijer et al. (2020) <sup>18</sup> : 0.53 (0.27-1.04)	7.8
1	55	1.30	Increased odds (1) - Demirkaya et al. (2016) <sup>28</sup> : 1.30 (0.04–17.20)	8
1	55	1.30	Increased odds (1) - Demirkaya et al. (2016) <sup>28</sup> : 1.30 (0.04–17.20)	8
1	55	0.87	Decreased odds (1) - Demirkaya et al. (2016) <sup>28</sup> : 0.87 (0.03–8.16)	8
2	129	0.40-0.58	Decreased odds (2) - Demirkaya et al. (2016) <sup>28</sup> : 0.58 (0.07–2.80) - Hooijer et al. (2020) <sup>18</sup> : 0.40 (0.00–1.21)	8
3	581	1.10-1.69	Increased odds (3) - Horowitz et al. (2018) <sup>16</sup> : 1.69 (0.74-3.87) - McDonnell et al. (2020) <sup>17</sup> : 1.18 (0.99-1.41), <b>1.10 (1.01-1.19)</b>	7.5
1	74	0.61	Decreased odds (1) - Hooijer et al. (2020) <sup>18</sup> : 0.61 (0.00–1.75)	8
2	54,031	0.68–1.92	Increased odds (1) - Hand et al. (2019) <sup>25</sup> : <b>1.92 (1.64–2.24)</b> Decreased odds (1) - Hirvikoski et al. (2019) <sup>26</sup> : <b>0.68 (0.61–0.75)</b>	8
2	44,044	1.00-1.57	Increased odds (1) - Hirvikoski et al. (2019) <sup>26</sup> : <b>1.57 (1.47-1.66)</b> No effect (1) - McDonnell et al. (2020) <sup>17</sup> : 1.00 (0.90-1.13)	8
4	22,192	1.30-2.59	Increased odds (4)  - Hand et al. (2019) <sup>25</sup> : <b>1.78 (1.52-2.08)</b> - Hooijer et al. (2020) <sup>18</sup> : 1.30 (0.33-5.14)  - Paquette-Smith et al. (2014) <sup>34</sup> : 2.59 (1.00-6.71)  - Stewart et al. (2023) <sup>37</sup> : 2.21 (0.40-12.10)	6.3
3	598	0.45-1.89	Increased odds (2)  - McDonnell et al. (2020) <sup>17</sup> : 1.05 (0.94–1.18)  - Paquette-Smith et al. (2014) <sup>34</sup> : 1.89 (0.75–4.81)  Decreased odds (1)  - Hooijer et al. (2020) <sup>18</sup> : <b>0.45 (0.22–0.94)</b>	6
1	74	1.28	Increased odds (1) - Hooijer et al. (2020) <sup>18</sup> : 1.28 (0.00–4.41)	8
	4  1  2  1  1  1  1  2  3  1  4  3	4 722  1 55 2 162 1 55 4 22,197  5 796  1 55 1 55 2 129 3 581 1 74 2 54,031 2 44,044 4 22,192	4 722 0.17-0.89  1 55 10.98 2 162 1.75-2.71 1 55 4.95 4 22,197 1.08-8.54  5 796 0.53-4.67  1 55 1.30 1 55 0.87 2 129 0.40-0.58 3 581 1.10-1.69 1 74 0.61 2 54,031 0.68-1.92 2 44,044 1.00-1.57 4 22,192 1.30-2.59	Hand et al. (2019)** 0,76 (0.64-0.90)

	Number of reported estimate(s)	Number of participants	Range of OR estimate(s)	Findings on the association bewteen subcategories of suicidality (suicidal ideation, attempt, and mortality) and co- occurring conditions (OR, 95% CI) <sup>a</sup>	Mean NOS score
Continued from previous page)					
Disruptive behavior disorders	2	474	0.95-1.13	Increased odds (1)  - McDonnell et al. (2020) <sup>17</sup> : <b>1.13 (1.04–1.23)</b> Decreased odds (1)  - McDonnell et al. (2020) <sup>17</sup> : 0.95 (0.81–1.12)	8
Personality disorder	1	74	0.61	Decreased odds (1) - Hooijer et al. (2020) <sup>18</sup> : 0.61 (0.00-1.99)	8
Substance use disorder	1	74	4.25	Increased odds (1) - Hooijer et al. (2020) <sup>18</sup> : 4.25 (0.00–12.19)	8
Suicide mortality					
Intellectual disability	2	77,637	0.25-0.26	Decreased odds (2) - Hirvikoski et al. (2019) <sup>26</sup> : 0.26 (0.11–2.30) - Tsai et al. (2023) <sup>39</sup> : <b>0.25 (0.19–0.32)</b>	8.5
ADHD	2	88,968	0.68–1.79	Increased odds (1)  - Tsai et al. (2023) <sup>39</sup> : <b>1.79 (1.15–2.81)</b> Decreased odds (1)  - Hirvikoski et al. (2019) <sup>26</sup> : <b>0.68 (0.49–0.87)</b>	8.5
Psychotic disorder	1	45,398	1.95	Increased odds (1) - Tsai et al. (2023) <sup>39</sup> : <b>1.95 (1.77–2.15)</b>	8
Bipolar disorder	1	45,398	2.55	Increased odds (1) - Tsai et al. (2023) <sup>39</sup> : <b>2.55 (1.35–4.82)</b>	8
Depressive disorder	1	45,398	1.67	Increased odds (1) - Tsai et al. (2023) <sup>29</sup> : <b>1.67 (1.49–1.88)</b>	8

Table 3: Summarized evidence on the association between sub-categories of suicidality (suicidal ideation, attempt, and mortality) and psychiatric co-occurring conditions in autistic individuals.

mental health conditions.9 Furthermore, the challenges that autistic individuals encounter in society—such as victimization, discrimination, concealment, and internalized stigma-may directly explain the link between selfharm/suicidality and autism (since these challenges are themselves connected to self-harm/suicidality) and indirectly (because these challenges are associated with mental health conditions that could increase the risk of self-harm/ suicidality).50,51 On the other hand, the effect of cooccurring conditions, including depressive and psychotic disorders, could also be discussed. A previous study suggested that the presence of both autism and psychotic symptoms, which have shared genetic liability, might contribute to challenges in emotional communication, thereby leading to feelings of hopelessness, depression, and suicidal thoughts. 52,53 In clinical practice, it may be important to screen autistic individuals for their depressive and psychotic symptoms to address the potential risk of suicidality. Addressing these symptoms could also be an effective strategy for reducing the possible risk of suicidality in people on the autism spectrum.

Since our study only investigated comparisons of autistic individuals with and without a certain cooccurring condition, the potential amplifying effect of autistic traits on self-harm and suicidality in relation to psychiatric co-occurring conditions remains unclear even though the hypothesized exacerbating role seemed to be plausible. A previous nationwide cohort study in Denmark with 6,559,266 participants reported an adjusted incidence rate ratio of suicide attempts and suicide mortality for the following four groups for each psychiatric diagnosis: no autism and certain disorder, autism only, certain disorder only, and both autism and certain disorder. Their results suggested that autism might have a potential amplifying effect on suicide mortality but not on suicide attempts. However, similar observations regarding self-harm and suicidal ideation have not yet been elucidated. Further studies could offer valuable insights that compare the magnitude of effects among autistic individuals, non-autistic individuals, people with specific psychiatric conditions, and those on the autism spectrum with specific psychiatric conditions for each outcome of interest.

Our findings should be interpreted in light of several limitations. First, the small number of included studies restricted the generalizability of the results. Among the 49 associations identified from our systematic search, the median number of reported estimates was 2 (IQR 1–3, range 1–10). Also, only 4 associations (8.2%) had enough data for meta-analysis, with 7 or more estimates available. Therefore, our findings should be cautiously interpreted. Second, our results should be interpreted with caution because all included studies had an observational design. Since observational evidence cannot establish causality, the identified associations between self-harm/suicidality and psychiatric co-occurring conditions should not be addressed indicating that co-occurring conditions

increase the risk of self-harm/suicidality in individuals on the autism spectrum. Third, our study did not address the fact that mental disorders are often experienced differently by individuals, frequently misdiagnosed, and that the measurement properties and diagnostic categories used for non-autistic people may not be applicable to autistic individuals. Fourth, we included studies that utilized not only standardized diagnostic criteria/tools (ICD, DSM, ADI, and ADOS) but also less stringent ones to ensure a sufficient number of eligible articles. This approach led to variability in the quality and consistency of the diagnostic measures used, potentially affecting the reliability and comparability of the findings. Fifth, the identified cooccurring conditions might not be independent. That is, when considering autistic individuals do not necessarily experience a single co-occurring condition, the estimated effects might have been affected by those with two or more co-occurring conditions. Sixth, this study based on systematic review inevitably addressed participants' sex as binary (woman/man) because the included eligible studies used this approach.

This systematic review explored the association between self-harm/suicidality and specific psychiatric cooccurring conditions in autistic individuals. We found that autistic individuals with either any psychiatric disorder, ADHD, or mood disorder may be associated with increased odds of self-harm compared to those without these conditions. Regarding suicidality, our study has also identified potential positive associations between suicidality and the following co-occurring conditions in people on the autism spectrum: any psychiatric disorder, psychotic disorder, mood disorder, bipolar disorder, depressive disorder, trauma- and stress-related disorder, and adjustment disorder. However, our findings should be interpreted in light of limitations, especially the limited number of included studies, which warrant further studies to establish robust evidence. We suggested that clinicians should remain vigilant for autistic individuals who also have a psychiatric co-occurring condition, since they may be at a higher risk of selfharm and suicidality.

#### Contributors

JHK and JH equally contributed to this study as co-first authors. JHK, JL, and KAC contributed to the study concept and design. JHK and JH independently reviewed studies. JL extracted data and JHK checked them. JHK did the statistical analyses. JHK, JL, SS, and KAC analyzed and interpreted the data. JHK and JL drafted the manuscript. SS and KAC contributed to the critical revision of the manuscript for intelectual content. KAC supervised the overall process of this study. All authors had full access to the study data and the corresponding authors had the final responsibility for the decision to submit for publication.

#### Data sharing statement

The data used for this study can be shared by contacting the corresponding author (Keun-Ah Cheon; kacheon@yuhs.ac). The R code used in this study can be found at https://github.com/hello-jaehan/association-

of-self-harm-and-suicidality-with-specific-psychiatric-co-occurring-conditions-in-autism. git.

#### Declaration of interests

The authors have no competing interests to declare relevant to any content of this manuscript.

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#### Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102863.

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