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MAXIM KIKOLER BSc Hons MSc PGCert

EXPLORING RISK FACTORS FOR SUICIDALITY IN  
ADOLESCENTS WITH AUTISM SPECTRUM DISORDERS

Section A: Suicidality in children and adolescents with Autism  
Spectrum Disorders: A review of prevalence and risk factors

Word Count: 7990 (plus 297 additional words)

Section B: Suicidality in adolescents with Autism Spectrum  
Disorders: investigating Depression and Irritability as risk factors  
in a UK clinical population

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A thesis submitted in partial fulfilment of the requirements of  
Canterbury Christ Church University for the degree of  
Doctor of Clinical Psychology

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To my parents, thank you for supporting me, making it possible for me to pursue this path, but most importantly for never letting me give up on this dream – almost there!

To Jules, your love and support kept me going when submitting didn't look possible. Thank you for feeding, watering, and encouraging me via your instastory. You helped make this happen. Now this is in, I'll start cooking again.

## Summary of Major Research Project

**Section A** examines the prevalence and risk factors associated with suicidality in children and adolescents with Autism Spectrum Disorders (ASD). A systematic of the available research was conducted, yielding nine relevant papers. Findings indicated rates of suicidality in children and adolescents with ASD were being comparable to those reported for typically developing youth. The research suggested a range of psychological and sociodemographic risk factors to be potentially associated with suicidality in children and adolescents with ASD. Methodological issues hindering generalisability of findings are outlined. Implications for future research, as well as clinical practice, are discussed.

**Section B** is an empirical study investigating the role of depression, irritability, and specific depressive profiles as risk factors for suicidality in adolescents with ASD in a UK clinical cohort. Data from the electronic mental health records of 1314 adolescents diagnosed with ASD between 2008 and 2013 were analysed. Suicidality was the outcome of interest, with depression, irritability, and specific depressive profiles as exposure variables. Findings showed depression, irritability, and specific depressive profiles to be associated with suicidality in adolescents with ASD, alongside several sociodemographic risk factors. Strengths and limitations of the study are explored, as well as implications both clinical practice and future research.

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Maxim Kikoler BSc Hons MSc PGCert

Section A: Literature Review

**Suicidality in children and adolescents with Autism Spectrum Disorders: A review of prevalence and risk factors**

Word Count: 7990 (excluding abstracts, references, tables and figures)

A thesis submitted in partial fulfilment of the requirements of  
Canterbury Christ Church University for the degree of  
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APRIL 2018

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## **Abstract**

**Background & Objectives:** Suicidality, a collective term encompassing both suicidal ideation and suicidal behaviour, has been identified as a significant health concern for adults with Autism Spectrum Disorders (ASD). Emerging research suggests that suicidality is also a significant issue for children and adolescents with ASD. This review evaluated the published literature investigating prevalence of suicidality in youth with ASD and its risk factors.

**Method:** A systematic literature search of research from inception to December 2017 was conducted using three online databases. Nine studies investigating suicidality and the associated risk factors in children and adolescents with ASD were identified. Quality of study was evaluated individually.

**Results:** Rates of suicidality in children and adolescents with ASD were found to be comparable to those reported for typically developing youth, with a range of psychological and sociodemographic risk factors potentially associated with suicidality in youth with ASD.

**Limitations & Conclusions:** Generalisability of findings was limited due to several methodological issues, including inconsistency in suicidal phenomena investigated, non-UK samples, and heterogeneity in diagnosis of ASD between studies. Future studies should look to repeat with UK samples, as well as investigating specific risk factors to understand better the risk mechanisms associated with suicidality.

**Keywords:** ASD, suicidality, children, adolescents, risk factors

## Introduction

### Autism Spectrum Disorders (ASD)

ASD is a collective diagnostic label representing a range of neurodevelopmental disorders. These disorders are typically categorised by deficits in the domains of social communication, social interaction and sensory processing, alongside repetitive stereotyped behaviours, rigid thinking style and highly specific interests, the presence of which occurs early on in a person's development (American Psychiatric Association, 2013). With the publication of the Diagnostic and Statistical Manual 5th edition (American Psychiatric Association, 2013), ASD has become the collective term encompassing several specific diagnoses:

- *Autism/Autistic Disorder (AD)*: alongside the characteristics outlined above, individual receiving a diagnosis of AD will have also displayed clinically significant delay, prior to three years old, in a minimum of one of the following domains:
  - Social interaction
  - Language as a form of social communication
  - Imaginative/symbolic play
- *Asperger Syndrome (AS)*: unlike AD, individuals receiving a diagnosis of AS will have displayed no clinically significant delays in language, cognitive development, and adaptive behaviour.
- *Pervasive Development Disorder – Not Otherwise Specified (PDD-NOS)*: sometimes referred to as “atypical autism”, this diagnosis will have been given if an individual

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displays significant impairment akin to AD but doesn't meet full criteria for a diagnosis, or onset is after three years old.

In the UK, assessment is based on ICD-10 criteria and is typically conducted using diagnostic tools, such as the Autism Diagnostic Observation Schedule 2<sup>nd</sup> Edition (Lord et al., 2012).

Similar prevalence of ASD has been reported in adulthood and childhood. In the UK, Brugha et al.(2012) reported 1.1% of the adult population having a diagnosis of ASD, whilst Baron-Cohen et al.(2009) suggested ASD occurs in approximately 1% of the child population; however, Baron -Cohen et al.(2009) found a ratio of 2:3 when comparing known cases to undiagnosed cases, suggesting that rates may actually be higher than originally estimated.

With regards to gender, ASD diagnosis is currently more common amongst males, with a male to female ratio of 4:1 commonly cited (Halladay et al., 2015). However, in a recent systematic review by Loomes, Hull, and Mandy (2017), it was suggested that the gender ratio is actually closer to 3:1. Furthermore, it has been suggested that phenotypic presentation of ASD may differ between genders (Werling & Geschwind, 2013).

As well as the associated social communication difficulties, ASD is associated with increased risk of co-occurring psychiatric disorders. Simonoff et al.(2008) reported significantly higher rates of psychiatric disorders in youth with ASD compared to a similar study of rates within a general population sample, whilst Joshi et al.(2010) found, within a clinical population, youth with ASD suffered from significantly higher numbers of co-occurring psychiatric disorders than non-ASD controls. Kim, Szatmari, Bryson, Streiner, and Wilson (2000) found that children with high-functioning ASD were at greater risk of mood and anxiety problems than the general population. Level of risk of co-occurring disorders may even differ between different ASD diagnoses: Mukaddes, Hergüner, and Tanidir (2010) found that children and



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adolescents with AS were at greater risk of depression than individuals with diagnosis of HFA. Explanations for this increased prevalence remain unclear, but it has been suggested that the effects of presumed risks factor (both environmental and genetic) for psychiatric outcomes differ in children with neurodevelopmental disorders (Simonoff et al., 2013; Simonoff et al., 2008).

Research also suggests that psychiatric presentation in ASD may differ from the general population. Ghaziuddin (2005) posits that depression in ASD presents with “special features” (p.131); similarly, Magnuson and Constantino (2011) found that ASD-affected children may present with additional features, such as catatonia and mood lability. Depressive presentations may even vary between different ASD diagnoses (Pearson et al., 2006).

### **Suicidality**

The National Strategy for Suicide Prevention (Center for Mental Health Services (US) & Office of the Surgeon General (US), 2001) defines “suicidality” as the collective term for a range of suicidal phenomena:

- *Suicidal ideation*: thoughts pertaining to suicide/suicidal behaviour.
- *Suicidal plans*: thoughts around method of carrying out suicidal behaviour.
- *Suicidal attempt*: an unsuccessful attempt to engage in behaviour with intended outcome to die as a result of the act.
- *Completed suicide*: death occurring as a result of direct behaviour intended to end one’s life.

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Suicidality is globally recognised as a major public health issue. Suicide is one of the leading causes of death for 5- to 19-year olds in the UK (Office of National Statistics, 2016), and the second leading cause of death globally amongst 10- to 24-year olds (Hawton, Saunders, & O'Connor, 2012). Thus far, research has focused predominantly on adolescent suicide, and not childhood trends. A review by McLoughlin, Gould and Malone (2015) on global trends in adolescent suicide reported lifetime prevalence of suicidal ideation and suicide attempts ranging from 12.1%-29.9% and 4.1%-10.5%, respectively. Risk factors for suicidality within typically-developing youth have been widely researched, identifying a range of factors:

- *Psychological disorder*: depression, anxiety disorders, substance use disorder (Fergusson, Woodward, & Horwood, 2000)
- History of sexual and/or physical abuse (Bruffaerts et al., 2010; Martin, Dykxhoorn, Afifi, & Colman, 2016)
- Exposure to marital disruption/divorced parents (Fergusson et al., 2000; Fuller-Thomson & Dalton, 2011)
- Socioeconomic adversity (Dupéré, Leventhal, & Lacourse, 2009; Fergusson et al., 2000)

There have been a range of psychological theories proposed in an attempt to identify and explain the causal mechanisms that might lead to suicidal phenomena being expressed or experienced. According to Barzilay and Apter (2014), theoretical models can be categorised into the following:

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- Psychological Pain theories: suicidality occurring as a response to significant emotional pain and the desire to escape distress (e.g. “Suicide as escape from self”, Baumeister, 1990).
- Cognitive theories: suicidality occurring as a result of maladaptive thinking styles and negative attentional biases (e.g. Cognitive Model, Wenzel & Beck, 2008).
- Stress-Diathesis theories: suicidality occurring as a result of an interaction between pre-existing vulnerability characteristics and an external stressor (e.g. Interpersonal Theory of Suicide, Joiner, 2007).

### **ASD & Suicidality**

Suicidality within ASD populations is still a relatively new area of study. Research into adults with ASD has shown suicidality also to be a significant health concern within this population. Paquette-Smith, Weiss and Lunsky (2014), examining suicidality in adults with AS in a Canadian sample, found that 35% of their sample reported history of attempted suicide, significantly higher than lifetime prevalence of 4.6% reported by the general population, identifying depression and severity of AS presentation as risk factors. Cassidy et al.(2014) found that 66% of their sample of adults with AS reported lifetime experience of suicidal ideation, and 35% reporting historical planned/attempted suicide, the former of which was nine times greater than rates observed in the general population. Similar to reports by Paquette-Smith et al.(2014), Cassidy et al.(2014) found depression and high levels of autistic traits as risk factors for suicidality.

Several case studies have also highlighted the relationship between suicidality and ASD in adults. Spencer et al.(2011), outlined the case of a 44-year old man who presented to hospital

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after attempting to take his life through cutting his wrists, subsequently admitted to a psychiatric inpatient unit. During admission, he was diagnosed with depression and ASD, the former of which resulted from difficulties in social interaction, which the authors posited to be related to core features of ASD. Mikami, Ohya, Akaska, and Matsumoto (2006) described the case of a 23-year old male with a diagnosis of AS, who had attempted suicide through burning himself and had a history of two suicide attempts by hanging. Through examination of predisposing factors, they identified low self-esteem stemming from relationship difficulties and resultant feelings of isolation, with difficulties in his relationship with his parents contributing to feelings of isolation. Mikami et al. (2006) posited that core elements of tension between the young man and his parents were AS characteristics, such as lacking in emotional reciprocity and being unreasonably insistent on restrictive thinking, and his parents' lack of comprehension of AS. Both studies drew similar conclusions, emphasizing the importance of ASD diagnosis to assist formulation, and to focus intervention on both ASD presentation and predisposing psycho-social factors as part of suicide prevention.

In terms of suicidality in youth diagnosed with ASD, a case study by Mikami, Onishi, & Matsumoto (2014) described the case of a 17-year old male admitted to hospital after attempting suicide by jumping, fracturing his lumbar spine. During his admission he was diagnosed with ASD and adjustment disorder. The authors formulated that the young man's suicide attempt was related to low self-esteem stemming from pervasive difficulties in developing interpersonal relationships and consequent feelings of isolation, as well as poor communication with his parents since infancy due to his ASD presentation. Furthermore, they suggested that delay in ASD diagnosis may have played a significant role in the extent of relationship difficulties and feelings of isolation, as well as expediting development of poor communication with his parents. Mikami et al. (2014) described the effective use of

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psychosocial intervention in preventing suicide reattempt, causing positive change in the patient's parents' attitude towards him, not only resulting in reduced feelings of low self-esteem and social isolation but also a cessation in suicidal ideation. As with adult cases, they concluded that diagnosis of ASD, especially early diagnosis, is vital in suicide prevention, and that clinicians should hold in mind, alongside ASD traits, the impact of psychosocial predisposing factors for suicide when developing intervention.

However, given the novelty of this topic, research on suicidality in individuals with ASD and the relationship with risk factors identified in the general population is currently limited.

### **Aims of the Review**

Current literature, albeit sparse, suggests suicidality to be a significant issue for youth with ASD. Therefore, this review aimed to explore and summarise the research investigating suicidality in children and adolescents with diagnoses of ASD, guided by the following research questions:

1. How prevalent is suicidality amongst children and adolescents with ASD?
2. What does the research tell us about the risk factors associated with suicidality in this population?

### **Methodology**

#### **Literature Search**

A systematic review of the literature was conducted guided by the Preferred Reporting Items for Systematic Reviews and Meta Analyses statement (Moher, Liberati, Tetzlaff, Altman, &

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Prisma Group, 2009). An electronic search was conducted using PsychInfo, Medline and Web of Science databases from inception to December 31<sup>st</sup> 2017.

Search terms were elaborated to improve search strategy (see Appendix A). Search terms for the construct ‘ASD’ were elaborated to include those with a diagnosis of autism/autistic disorder (AD), Asperger’s Syndrome (AS), Pervasive Development Disorder (PDD), and Pervasive Developmental Disorder – Not otherwise specified (PDD-NOS), as informed by Richa, Fahed, Khoury and Mishara (2014), Segers and Rawana (2014), and Zahid and Upthegrove (2017). Elaborated search terms for the construct of ‘suicide’ were informed by Chan et al.(2016), and Evans et al.(2005). Search terms for constructs of ‘child’ and ‘adolescent’ were informed by Rosing, Schmidt, Wedderkopp and Baguley (2016) (see Figure 1.).

### **Inclusion Criteria**

- English Language
- Peer reviewed journal
- Quantitative study
- Suicidality is an outcome variable of interest
- ASD cohort consisting of people with formal diagnosis of ASD including ASD, AS, PDD and PDD-NOS
- Children and/or adolescents (3-19yo) included in sample – this age range is to reflect the depiction within current literature, as well as reflecting the current culture in

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which 19 years old is a threshold at which young people often transition to adult services from children and young people services (NHS England, 2015).

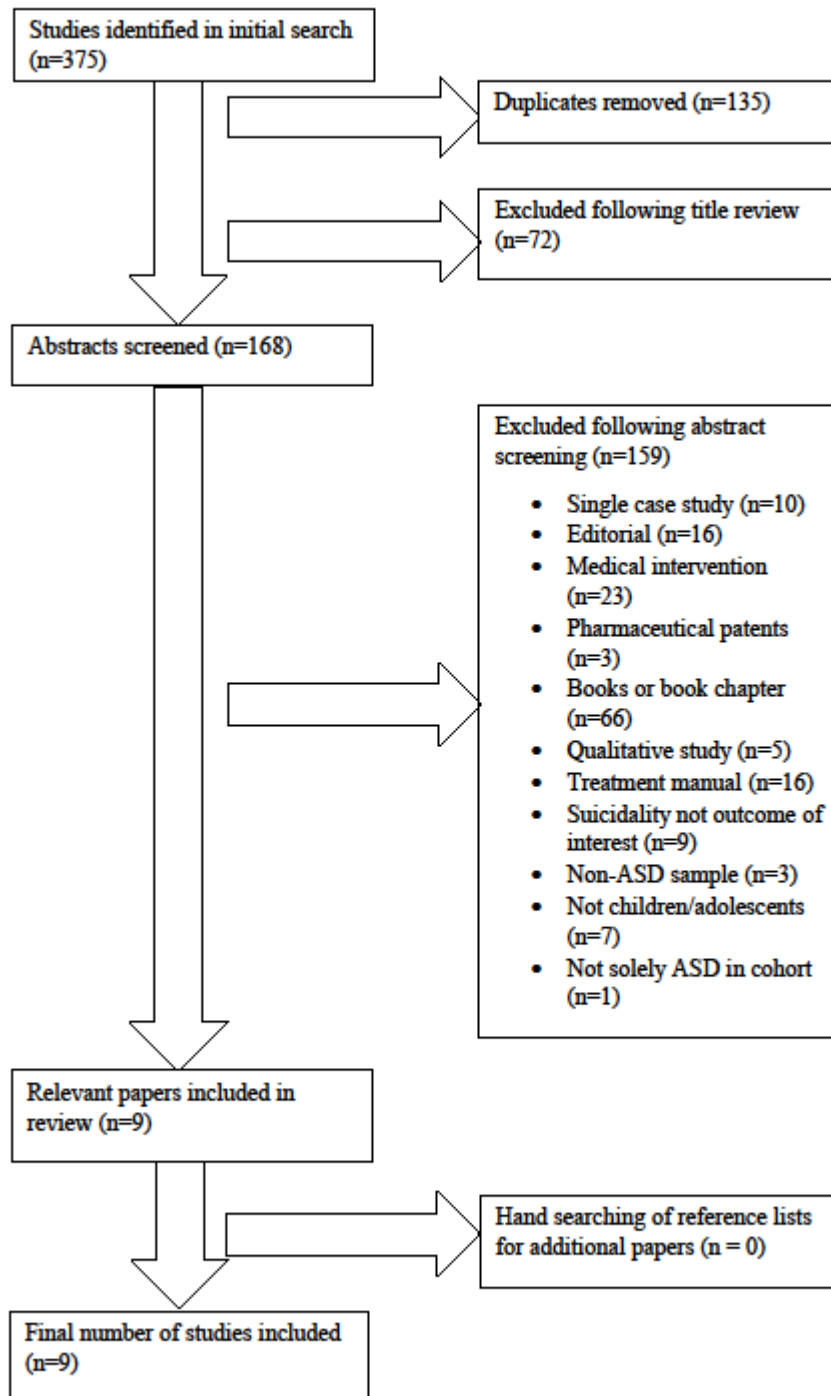
### **Exclusion Criteria**

- Qualitative studies
- Case studies
- Autism defined solely by measure of autistic traits, without presence/indication of formal diagnosis within sample
- Adult-only samples
- Books/chapters
- Evaluation of psychopharmacological intervention
- Editorials

### **Quality of Evidence**

Quality of studies was reviewed using the critical appraisal template for cohort studies, a quality assessment tool from the Critical Appraisal Skills Programme (CASP, 2017; see Appendix B). Rather than using numerical ratings of study quality, which have been shown to have poor validity and reliability (Booth, Sutton, & Papaioannou, 2016), the CASP checklist was selected as it provides a clear structure to systematically critique and evaluate quality of research studies.

**Figure 1.** Literature Search Strategy.





## Literature Review

### Overview of Studies

The search protocol yielded nine studies which met the inclusion criteria. Basic study information, including demographic and sample information, is presented in Table 1.

**Location.** Of these studies, five were from the United States of America, two from Turkey, one from Japan, and the last from Taiwan.

**Setting.** Two studies were conducted in hospitals, three conducted in outpatient clinics, two via mail and websites, one conducted in a university, and one using a national health insurance research database. Of the two hospital studies, one was conducted in an inpatient unit, the other in an advanced critical care centre.

**Design.** Seven studies utilised cross-sectional study design. The remaining two used prospective cohort study design, varying in length of study with follow-up periods ranging collectively from 1-15 years.

**Suicidality Definition.** Studies varied on the aspect of suicidality investigated: four studies investigated both suicidal ideation and suicidal attempts, three studies investigated suicidal ideation only, and two studies explored suicidal attempt only.

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**Table 1. Basic Study Information Including Demographic and Sample Information**

| Study              | Purpose   | Location | Design          | Study duration | Setting   | Sample            |   |                          |               |                |            |                        |                          |                |     |
|--------------------|---|----------|-----------------|----------------|---|-------------------|---|--------------------------|---------------|----------------|------------|------------------------|--------------------------|----------------|-----|
|                    |   |          |                 |                |   | Total Sample size | ASD Sample  |                          |               |                |            | Comparison Sample      |                          |                |     |
|                    |   |          |                 |                |   |                   | Sample Characteristics  | Size (% of total sample) | ASD Diagnosis | Gender (%male) | Age        | Sample Characteristics | Size (% of total sample) | Gender (%male) | Age |
| Shtayermman (2007) | To examine the level of suicidal ideation and co-occurring disorders in adolescents and young adult with Asperger's syndrome. | USA      | Cross-sectional | N/A            | Community: self-administered mail questionnaire and web-based questionnaire | 10                | Adolescents/young adults diagnosed with AS who had participated in a previous study.            | 10 (100%)                | Asperger's    | 90%            | 19.7 (3.0) | N/A                    | N/A                      | N/A            | N/A |
|                    |   |          |                 |                |   |                   | Advertised to parents of adolescents/young adults diagnosed with AS on Autism-related websites. |                          |               |                |            |                        |                          |                |     |
| Shtayermman (2008) | To examine the level of suicidal ideation and co-occurring disorders in adolescents and young adult with Asperger's syndrome. | USA      | Cross-sectional | N/A            | Community: self-administered mail questionnaire and web-based questionnaire | 10                | Adolescents/young adults diagnosed with AS who had participated in a previous study.            | 10 (100%)                | Asperger's    | 90%            | 19.7 (3.0) | N/A                    | N/A                      | N/A            | N/A |
|                    |   |          |                 |                |   |                   | Advertised to parents of adolescents/young adults diagnosed with AS on Autism-related websites. |                          |               |                |            |                        |                          |                |     |

# SUICIDALITY IN YOUTH WITH ASD: A REVIEW

| Study                   | Purpose  | Location | Design          | Study duration | Setting  | Sample            |  |                          |                               |                |            |                        |                          |                |            |
|-------------------------|--|----------|-----------------|----------------|--|-------------------|--|--------------------------|-------------------------------|----------------|------------|------------------------|--------------------------|----------------|------------|
|                         |  |          |                 |                |  | Total Sample size | ASD Sample   |                          |                               |                |            | Comparison Sample      |                          |                |            |
|                         |  |          |                 |                |  |                   | Sample Characteristics   | Size (% of total sample) | ASD Diagnosis                 | Gender (%male) | Age        | Sample Characteristics | Size (% of total sample) | Gender (%male) | Age        |
| Mikami et al. (2009)    | To examine the frequency and clinical features of pervasive developmental disorder relative to suicide attempts. | Japan    | Cross-sectional | N/A            | Hospital: advanced critical care centre of university hospital | 94                | Consecutive sample of adolescents (<20yo) who had been hospitalised for inpatient treatment following suicide attempts (i.e. intentionally inflicted self-injury with suicidal ideation) between October 2004 and July 2007. | 12 (12.8%)               | Asperger's (6)<br>PDD-NOS (6) | 41.7%          | 17.1 (1.6) | Typical development    | 82 (87.2%)               | 45.4%          | 16.9 (1.6) |
| Mukaddes & Fateh (2010) | Report on the rates of co-occurring psychiatric disorders in individuals with Asperger's disorder.               | Turkey   | Cross-sectional | 1-5 years      | Clinic: private psychiatry clinic                              | 37                | Children and adolescents referred to the clinic from December 2002 to February 2007.<br><br>Inclusion criteria:<br>• Diagnosis of Asperger's disorder according to DSM-IV criteria;<br>• Full IQ score >89 on WISC-R         | 37 (100%)                | Asperger's                    | 86.5%          | 10.9 (4.5) | N/A                    | N/A                      | N/A            | N/A        |

SUICIDALITY IN YOUTH WITH ASD: A REVIEW

| Study  | Purpose   | Location | Design          | Study duration | Setting  | Sample            |   |                          |                        |                |                   |  |                          |                |            |
|--|---|----------|-----------------|----------------|--|-------------------|---|--------------------------|------------------------|----------------|-------------------|--|--------------------------|----------------|------------|
|  |   |          |                 |                |  | Total Sample size | ASD Sample  |                          |                        |                | Comparison Sample |  |                          |                |            |
|  |   |          |                 |                |  |                   | Sample Characteristics  | Size (% of total sample) | ASD Diagnosis          | Gender (%male) | Age               | Sample Characteristics   | Size (% of total sample) | Gender (%male) | Age        |
| Mayes, Gorman, Hillwig-Garcia, & Syed (2013) | To examine the frequency of suicidal ideation and suicide attempts in children with Autism. | USA      | Cross-sectional | N/A            | Clinic: outpatient psychiatric diagnostic clinic | 1012              | Children and adolescents with ASD evaluated in an outpatient psychiatric diagnostic clinic. | 791 (78.2%)              | HFA (537)<br>LFA (254) | 84.1%          | 6.6 (3.1)         | Non-autistic children with diagnosis of MDD or dysthymic disorder.   | 35(1.7%)                 | 25.7%          | 13.0 (2.3) |
|  |   |          |                 |                |  |                   |   |                          |                        |                |                   | Typically developed children and adolescents who had participated in a previous general population epidemiologic study on the prevalence of sleep disorders in children. | 186(18.4%)               | 43.5%          | 8.7 (1.7)  |

## SUICIDALITY IN YOUTH WITH ASD: A REVIEW

| Study  | Purpose   | Location | Design                              | Study duration | Setting  | Sample            |   |                          |  |                |                     |                        |                          |                |     |
|--|---|----------|-------------------------------------|----------------|--|-------------------|---|--------------------------|--|----------------|---------------------|------------------------|--------------------------|----------------|-----|
|  |   |          |                                     |                |  | Total Sample size | ASD Sample  |                          |  |                | Comparison Sample   |                        |                          |                |     |
|  |   |          |                                     |                |  |                   | Sample Characteristics  | Size (% of total sample) | ASD Diagnosis  | Gender (%male) | Age                 | Sample Characteristics | Size (% of total sample) | Gender (%male) | Age |
| Storch et al. (2013)                               | To investigate the phenomenology and clinical correlates of suicidal thoughts and behaviours in you with ASD.                                       | USA      | Cross-sectional                     | N/A            | University:<br>Department of Psychiatry & Neuroscience<br>Department of Paediatrics<br>Department of Disability and Psychoeducation<br>1 Studies | 102               | Children and adolescents with ASD diagnoses and co-occurring anxiety problems.<br><br>Exclusion criteria:<br>• IQ<70 (9 excluded)<br>• Diagnosis of bipolar disorder (None excluded)<br>• Active psychotic symptoms (None excluded)   | 102 (100%)               | Autism (28)<br><br>Asperger's (39)<br><br>PDD-NOS (35) | 77%            | 10.55 (2.31)        | N/A                    | N/A                      | N/A            | N/A |
| Karakoc Demirkaya, Tutkunkardas, & Mukaddes (2016) | To assess the rate of suicidality (suicidal ideation, behaviours and attempts) and associated risk factors for suicidality in high-functioning ASD. | Turkey   | Longitudinal:<br>Prospective Cohort | 1-15 years     | Clinic: outpatient psychiatry clinic of university hospital  | 55                | Children and adolescents attending the Autism Clinic of Child and Adolescent Psychiatry department of university hospital.<br><br>Inclusion criteria:<br>• capability of reading, writing and speaking;<br>• no intellectual disability (IQ>=70)<br>• no history of chronic neurological or physical disorder;<br>• presence of data about suicidality. | 55 (100%)                | AD (24)<br><br>Asperger's (26)<br><br>PDD-NOS (5)      | 89%            | 13.61 (range: 7-20) | N/A                    | N/A                      | N/A            | N/A |

# SUICIDALITY IN YOUTH WITH ASD: A REVIEW

| Study                  | Purpose   | Location | Design                           | Study duration | Setting   | Sample            |  |                          |               |                |  |   |                          |                |  |
|------------------------|---|----------|----------------------------------|----------------|---|-------------------|--|--------------------------|---------------|----------------|--|---|--------------------------|----------------|--|
|                        |   |          |                                  |                |   | Total Sample size | ASD Sample   |                          |               |                | Comparison Sample  |   |                          |                |  |
|                        |   |          |                                  |                |   |                   | Sample Characteristics   | Size (% of total sample) | ASD Diagnosis | Gender (%male) | Age  | Sample Characteristics  | Size (% of total sample) | Gender (%male) | Age  |
| Chen et al. (2017)     | To investigate the risk of suicide attempts among adolescents and young adults with ASD, and the roles of co-occurring psychiatric disorders as potential risk factors. | Taiwan   | Longitudinal: Prospective Cohort | 2-10 years     | Population: National Health Insurance Research Database | 28090             | ASD cohort: adolescents and young adults diagnosed with ASD between January 1st 2001 and December 31st 2009 with no history of suicide attempt prior to diagnosis.   | 5618 (20%)               | ASD           | 78.2%          | 17.2 (4.58); Adolescents (range: 12-17), young adults (range: 18-29) | Matched controls: adolescents & young adults without ASD diagnosis, and no previous history of suicide attempt. | 22472 (80%)              | 78.2%          | 17.2 (4.58); Adolescents (range: 12-17), young adults (range: 18-29) |
| Horowitz et al. (2017) | To examine the prevalence of thoughts of death or suicide in youth with ASD and associated co-occurring psychiatric diagnoses.  | USA      | Cross-sectional                  | N/A            | Hospital: Specialised inpatient psychiatric units       | 107               | Children and adolescents with ASD diagnosis admitted specialized inpatient psychiatry units for youth with ASD and other developmental disorders.<br><br>Inclusion criteria:<br>• 10yo or older<br>• Non-verbal IQ of 55 or greater<br>• Parent response on CASI question about suicidal ideation<br><br>Exclusion criteria:<br>• caregiver lack of proficiency in English<br>• youth having prisoner status | 107 (100%)               | ASD           | 77%            | 13.63(2.26)  | N/A   | N/A                      | N/A            | N/A  |

## SUICIDALITY IN YOUTH WITH ASD: A REVIEW

**Demographics.** The majority of participants with ASD were male (88.1%). The average age was 14.33 years (range = 1-29). However, sample composition varied greatly: five studies used a mix of child and adolescent participants (1-19 years), three had combined samples of adolescents and young adults (12-29 years), and one had adolescent participants only (<20 years).

**ASD Diagnosis.** Samples consisted of a variety of diagnostic labels: autistic disorder (0.77%), Asperger's Syndrome (1.90%), PDD-NOS (0.68%), ASD (84.92%), high functioning autism (HFA; 7.96%), low functioning autism (LFA; 3.77%). The range of ASD diagnoses characterising the samples varied between studies. Three studies investigated cohorts with diagnoses of AS only, and two had cohorts composed only of those with a diagnosis of ASD. Of the remaining five studies, four studied samples composed of multiple ASD diagnoses, with two studies using samples with combined compositions of participants with diagnoses of AD, AS and PDD-NOS, one study dividing the cohort by level of functioning (High-Functioning Autism vs. Low-Functioning Autism), and one study using a sample consisting of participants with diagnoses of AS and PDD-NOS. Only two papers included external controls as part of their study: one study included both a group of children with depression and a typically-developed group with no identified psychological disorders, whilst the second study used matched-controls based on age, sex, and date of enrolment into study which was defined by date of ASD diagnosis of ASD participant.

## SUICIDALITY IN YOUTH WITH ASD: A REVIEW

**ASD Measures.** A range of measures to assess ASD were used. Three studies used diagnostic assessment instruments, two used measures to assess ASD severity only, three used clinical interview based on approved diagnostic criteria, and one study used both clinical interview and a measure of ASD severity. No study using clinical interview reported whether they used validated diagnostic instruments, or whether assessment was based on the clinical judgement of the assessor.

**Suicidality measures.** Only three studies administered measures specifically designed to assess suicidality, completed by the young people themselves. Of the remaining six studies, three studies utilised measures of psychological difficulties including a component assessing suicidality, two assessed via clinical interview, and one reviewed patient records. Of the three studies using measures of psychological difficulties, no study used young person report only: one study used report from the young person as well as the parent, whilst the other two relied solely on parental ratings.

**Psychological Disorder Assessment Measures.** Seven studies used standardised measures to assess for depression and other co-occurring psychological disorders: of these studies, two studies used parental report only, two studies used only young person report, and three administered to both parent and young person. The two remaining studies used clinical interview guided by diagnostic criteria.



## SUICIDALITY IN YOUTH WITH ASD: A REVIEW

**Study focus.** Of the nine papers, four investigated prevalence and incidence of suicidality only, with three examining rates of suicidality within the ASD cohort, and one investigating rates of ASD in a suicidal cohort. All four studies investigated prevalence of co-occurring psychological disorders, with two also including peer victimisation as a variable of interest. The remaining five studies, alongside examining prevalence, investigated potential psychological and demographic risk factors for suicidality in ASD samples: four examined predictors of reporting suicidality, the remaining study investigating predictors of subsequent suicide attempt. Of these five, three investigated differences in suicidality presentation (i.e. ideation vs behaviours/attempts); however, only one investigated the relationship between potential risk factors and each individual suicidal presentation.

**Statistical analysis.** Statistical analyses employed varied between papers. One study reported descriptive statistics only, and three studies reported significance of association between factors and outcome variable. The remaining five tested for strength of association alongside significance, of which two used correlational analysis, one used odds ratios (OR), another Cohen's *d* and explained variance, and the last used hazard ratios (HR).

**Repeated testing.** Two studies analysed participants from the same cohort (Shtayermman, 2007; 2008); however, whilst there is overlap in variables, there are also factors unique to each paper. Therefore, duplicated analyses have been condensed and will be reported as a single finding.

### Overview of Findings

An overview of findings around prevalence of suicidality and risk factors is presented in Table 2.

### **Prevalence of Suicidality in ASD**

Eight papers reported prevalence of suicidality in ASD, of which two examined suicidal ideation and suicide attempt as separate outcome variables. According to Mayes, Gorman, Hillwig-Garcia, and Syed (2013), mothers of children with ASD reported rates of suicidal ideation and suicide attempt of 10.9% and 7.2%, respectively. Karakoc Demirkaya, Tutkunkardas, and Mukaddes (2016) found within their sample 16.3% reporting suicidal ideation, and 12.7% having attempted suicide.

Three studies examined suicidal ideation only within ASD. Shtayermann (2007; 2008) found 50% of its sample experienced suicidal ideation. Horowitz et al. (2017) found 22.4% of youth with ASD in a psychiatric inpatient unit reported by their parent/guardian to have periods of frequently talking about suicide or death.

Chen et al. (2017) examined only suicide attempt in ASD, finding 3.9% of their ASD cohort had attempted suicide during the course of the study.

The remaining two papers examined ideation and attempt combined into a single outcome variable. Mukaddes and Fateh (2010) found 16% of their sample of youth diagnosed with Asperger's reported a history of suicidality. Storch et al. (2013) reported 20% of their participants disclosed either having suicidal thoughts, thinking a lot about death/dying, or a history of suicide attempt; furthermore, suicidality was observed in 11% of their sample, determined by endorsement of questionnaire items measuring suicidal thoughts, suicide planning, or previous suicide attempts.

SUICIDALITY IN YOUTH WITH ASD: A REVIEW

**Table 2. Overview of findings: Suicidality, ASD and associated factors**

| Study              | Suicidality investigated | Data Sources                  | Measures for Suicidality        | Measures for ASD | Measure for psychological disorders | Other measures/data collected                                  | Data analysis          | Prevalence of suicidality in ASD sample | Prevalence of ASD in suicidal sample | Psychological Disorders identified in study  | Rates of Psychological disorders in ASD suicidal sample | Rates of Psychological disorders identified in ASD sample  | Findings   |  |  |
|--------------------|--------------------------|-------------------------------|---------------------------------|------------------|-------------------------------------|--|------------------------|---|--------------------------------------|--|---|--|--|--|--|
|                    |                          |                               |                                 |                  |                                     |  |                        |   |                                      |  |   |  | Suicidality  | Psychological Disorders  | Socio-Demographic Factors                    |
| Shtayermman (2007) | Suicidal ideation        | Questionnaires (young person) | Suicidal Ideation Questionnaire | KADI             | PHQ-A                               | Peer victimization (SEQ)                                       | Correlational analysis | 50.0%                                   | N/A                                  | <ul style="list-style-type: none"> <li>• MDD</li> <li>• GAD</li> <li>• Additional psychiatric diagnoses (bipolar disorder, OCD)</li> </ul> | Not reported  | <ul style="list-style-type: none"> <li>• MDD (20%)</li> <li>• GAD (30%)</li> <li>• Additional psychiatric diagnoses (bipolar disorder, OCD) (67%)</li> </ul> | 50% reported suicidal ideation.  | Significant negative correlation between level of suicidal ideation and severity of AS presentation.         | 38% reported experiencing peer victimisation |
|                    |                          |                               |                                 |                  |                                     | 20% met criteria for MDD. (21.4% reported depressive symptoms) |                        |   |                                      |  |   |  |  |  |  |
|                    |                          |                               |                                 |                  |                                     | 30% met criteria for GAD. (21.4% reported anxiety symptoms)    |                        |   |                                      |  |   |  | Positive but not significant correlations between level of suicidal ideation and level of anxiety symptoms, depressive symptoms. | Positive but not significant correlation between level of suicidal ideation and level of peer victimisation. |  |

# SUICIDALITY IN YOUTH WITH ASD: A REVIEW

| Study               | Suicidality investigated   | Data Sources      | Measures for Suicidality                          | Measures for ASD  | Measure for psychological disorders               | Other measures/data collected  | Data analysis   | Prevalence of suicidality in ASD sample | Prevalence of ASD in suicidal sample | Psychological Disorders identified in study  | Rates of Psychological disorders in ASD suicidal sample   | Rates of Psychological disorders identified in ASD sample  | Findings  |  |                           |
|---------------------|--|-------------------|---|---|---|--|---|---|--------------------------------------|--|---|--|---|--|---------------------------|
|                     |  |                   |   |   |   |  |   |   |                                      |  |   |  | Suicidality   | Psychological Disorders  | Socio-Demographic Factors |
| Shtayermman (2008)  | Suicidal ideation  | YP Questionnaires | Suicidal Ideation Questionnaire                   | KADI  | PHQ-A   | Current age, age at first diagnosis, professional who gave AS diagnosis, additional psychiatric diagnoses, whether AS was first diagnosis given, medication status, number of services received, educational setting, highest level of education, living situation, employment status, number of hours a week worked at paying in job in the last month, does volunteer work, number of hours a week of volunteer activity in past month amongst those who volunteer | Correlational analysis                                | 50.0%                                   | N/A                                  | <ul style="list-style-type: none"> <li>• MDD</li> <li>• GAD</li> <li>• Additional psychiatric diagnoses (bipolar disorder, OCD)</li> </ul> | Not reported  | <ul style="list-style-type: none"> <li>• MDD (20%)</li> <li>• GAD (30%)</li> <li>• Additional psychiatric diagnoses (bipolar disorder, OCD) (67%)</li> </ul> | 50% reported suicidal ideation.                         | <p>Significant negative correlation between level of suicidal ideation and severity of AS presentation.</p> <p>20% met criteria for MDD. (21.4% reported depressive symptoms)</p> <p>30% met criteria for GAD. (21.4% reported anxiety symptoms)</p> <p>Positive but not significant correlations between level of suicidal ideation and level of anxiety symptoms, depressive symptoms.</p> |                           |
| Mikami et al (2009) | Suicide Attempt: Emergency room patients who inflicted serious self-harm with suicidal ideation. | Hospital records  | Psychiatric interview based on DSM-IV-TR criteria | Clinical judgement on basis of DSM-IV-TR criteria<br>AQ-J | Clinical judgement on basis of DSM-IV-TR criteria | <p>IQ (WAIS-R; WISC-III)</p> <p>Method of attempted suicide: overdose, jumping, hanging, stabbing, poisoning, carbon monoxide poisoning</p>  | chi-square/ Fisher's Exact tests; Mann-Whitney U test | 100.0%                                  | 12.8%                                | <ul style="list-style-type: none"> <li>• Mood disorder</li> <li>• Anxiety disorder</li> <li>• Adjustment disorder</li> </ul>               | <ul style="list-style-type: none"> <li>• Mood disorder (8.3%)</li> <li>• Anxiety disorder (8.3%)</li> <li>• Adjustment disorder (8.3%)</li> </ul> | N/A  | 12.8% individuals diagnosed with PDD (PDD-NOS=6; AS=6). | Participants with PDD were significantly less likely to have a mood disorder or anxiety disorder than non-PDD participants.  |                           |

# SUICIDALITY IN YOUTH WITH ASD: A REVIEW

| Study  | Suicidality investigated  | Data Sources  | Measures for Suicidality                         | Measures for ASD  | Measure for psychological disorders                 | Other measures/data collected                           | Data analysis   | Prevalence of suicidality in ASD sample                         | Prevalence of ASD in suicidal sample | Psychological Disorders identified in study   | Rates of Psychological disorders in ASD suicidal sample  | Rates of Psychological disorders identified in ASD sample  | Findings  |   |   |
|--|---|---|--|---|---|---|---|---|--------------------------------------|---|--|--|---|---|---|
|  |   |   |  |   |   |   |   |   |                                      |   |  |  | Suicidality   | Psychological Disorders   | Socio-Demographic Factors   |
| Mukaddes & Fateh (2010)                      | Suicidal behaviours (ideation, attempt)   | Child assessment/interview<br>Parent assessment/interview | Clinical interviews of patients & their parents. | Clinical judgment and diagnostic interview in accordance with DSM-IV criteria | K-SADS-PL Clinical assessment using DSM-IV criteria | WISC-R<br><br>Age, gender, developmental history        | Descriptive (frequency)   | 16% total sample (42% of adolescents age 12–20; 0% in children) | N/A                                  | <ul style="list-style-type: none"> <li>Anxiety Disorders (OCD, specific phobia)</li> <li>Mood disorders (MDD, BP)</li> <li>Disruptive Behaviour disorders (ADHD, ODD, CD)</li> <li>Tic Disorders</li> </ul> | MDD only (100%)  | <ul style="list-style-type: none"> <li>Anxiety Disorders (OCD, specific phobia; 54%)</li> <li>Disruptive Behaviour disorders (ADHD, ODD, CD; 48%)</li> <li>Mood disorders (MDD and BP; 37%)</li> <li>Tic Disorders (18%)</li> </ul>                              | 16% reported suicidality.   | All patients reporting suicidal ideation or behaviours met DSM criteria for major depressive disorder.  | All patients reporting suicidal ideation or behaviours were adolescents (12-20 years).  |
| Mayes, Gorman, Hillwig-Garcia, & Syed (2013) | Suicidal ideation (“talks about harm or killing self”); Suicide attempts (“deliberately harms oneself or attempts suicide”) | Parent assessment/interview                               | Pediatric Behavior Scale (rated by mothers)      | CASD  | Pediatric Behavior Scale                            | Demographics, parental occupation/socio-economic status | Chi-square test; Cohen’s d/ explained variance; stepwise binary logistic regression | 13.8% (suicide attempt: 7.2%; suicidal ideation: 10.9%)         | 82%                                  | <ul style="list-style-type: none"> <li>MDD</li> <li>Behaviour problems</li> <li>Mood dysregulation</li> <li>Impulsive</li> <li>Anxiety</li> <li>Somatic complaints</li> <li>Sleep disturbance</li> </ul>    | <ul style="list-style-type: none"> <li>MDD (26.4%)</li> <li>Behaviour problems (23.5%)</li> <li>Mood dysregulation (19.6%)</li> <li>Impulsive (15.7%)</li> <li>Anxiety (18.2%)</li> <li>Somatic complaints (29.5%)</li> <li>Sleep disturbance (18.6%)</li> </ul> | <ul style="list-style-type: none"> <li>MDD (40.2%)</li> <li>Behaviour problems (41.0%)</li> <li>Mood dysregulation (65.1%)</li> <li>Impulsive (87.6%)</li> <li>Anxiety (66.8%)</li> <li>Somatic complaints (14.2%)</li> <li>Sleep disturbance (44.8%)</li> </ul> | 13.8% reported suicidality:<br><br><ul style="list-style-type: none"> <li>10.9% reported suicidal ideation</li> <li>7.2% reported attempts</li> </ul> | Psychological predictors of suicidal ideation or behaviour in children with autism:<br><br><ul style="list-style-type: none"> <li>Depression</li> <li>Behaviour problems (oppositional, aggressive, angry, explosive, impulsive)</li> <li>Bullied by peers</li> </ul> | Demographic predictors of suicide behaviour in children with autism:<br><br><ul style="list-style-type: none"> <li>Male</li> <li>10yo or older</li> <li>Black or Hispanic</li> <li>Lower SES</li> </ul>                                 |
|  |   |   |  |   |   |   |   |   |                                      |   |  |  | Suicide behaviour (ideation or attempts) in children with autism was 28 times more common than in typical children, but less than depressed sample.   | Protective psychological factors against suicidal ideation or behaviour in children with autism:<br><br><ul style="list-style-type: none"> <li>no impulsiveness</li> <li>no mood dysregulation</li> <li>no behaviour problems</li> </ul>                              | Protective demographic factors against suicidal ideation or behaviour in children with autism:<br><br><ul style="list-style-type: none"> <li>Female</li> <li>White/Asian</li> <li>Higher SES</li> <li>Younger than 10 years;</li> </ul> |

# SUICIDALITY IN YOUTH WITH ASD: A REVIEW

| Study                                      | Suicidality investigated   | Data Sources  | Measures for Suicidality  | Measures for ASD                                  | Measure for psychological disorders    | Other measures/data collected  | Data analysis  | Prevalence of suicidality in ASD sample | Prevalence of ASD in suicidal sample | Psychological Disorders identified in study   | Rates of Psychological disorders in ASD suicidal sample   | Rates of Psychological disorders identified in ASD sample   | Findings  |   |  |   |  |
|--|--|---|---|---|--|--|--|---|--------------------------------------|---|---|---|---|---|--|---|--|
|  |  |   |   |   |  |  |  |   |                                      |   |   |   | Suicidality   | Psychological Disorders   | Socio-Demographic Factors  |   |  |
| Storch et al (2013)                        | Suicidal Ideation ("thoughts of death or dying"; "thought about killing him/herself"; "thought of a way to kill him/herself"); Suicide attempt ("tried to kill him/herself") | Child assessment/interview<br>Parent assessment/interview | Anxiety Disorder Interview Schedule - Child and Parent Versions | ADOS; ADI-R                                       | ADIS-IV-CP; PARS; CBCL; MASC-P; CIS-PV | Demographics, medication status  | Chi-square tests; Cramers V; Cohen's d; Kruskal-Wallis test; Mann-Whitney tests; Logistic Regression | 11.0%                                   | N/A                                  | <ul style="list-style-type: none"> <li>Social phobia</li> <li>GAD</li> <li>Specific phobia</li> <li>DBD</li> <li>Separation anxiety disorder</li> <li>OCD</li> <li>MDD/dysthymia</li> <li>PTSD</li> </ul>                                       | <ul style="list-style-type: none"> <li>Social phobia (100%)</li> <li>GAD (90.9%)</li> <li>Specific phobia (72.7%)</li> <li>DBD (63.6%)</li> <li>Separation anxiety disorder (27.3%)</li> <li>OCD (54.5%)</li> <li>MDD/dysthymia (36.4%)</li> <li>PTSD (27.3%)</li> </ul>                                      | <ul style="list-style-type: none"> <li>Social phobia (86.3%)</li> <li>GAD (74.5%)</li> <li>Specific phobia (62.7%)</li> <li>DBD (56.8%)</li> <li>Separation anxiety disorder (41.2%)</li> <li>OCD (35.2%)</li> <li>MDD/dysthymia (13.7%)</li> <li>PTSD (5.8%)</li> </ul>  | 11% reported suicidality.   | Children with autism are more likely to have suicidal thoughts/behaviors than those with Asperger's disorder. | Suicidality predicted when presence of co-occurring diagnosis of <ul style="list-style-type: none"> <li>Depression</li> <li>PTSD</li> </ul>  |   |  |
| Demirkaya, Tutkunkardas, & Mukaddes (2016) | Suicidal Ideation; Suicide Attempt   | Child assessment/interview<br>Parent assessment/interview | Eskin's Suicide Screening Questionnaire                         | Clinical judgement on basis of DSM-IV-TR criteria | K-SADS-PL                              | Sociodemographic data form: detailed developmental history, history of behavioral, emotional and physical problems, detailed medical history (drugs, co-occurring diseases, hospitalizations, emergency visits), family history of suicidal behaviors and attempts, alcohol-substance use disorder, other psychiatric disorders, aggressive behaviors of the patients toward others and self | Chi-square tests; Pearson, Fisher's Exact, McNemar   | 29% (ASD:43.8%; AS:50%; PDD-NOS:6.2%)   | N/A                                  | <ul style="list-style-type: none"> <li>Depression</li> <li>Bipolar disorder</li> <li>GAD</li> <li>Separation Anxiety disorder</li> <li>OCD</li> <li>Social Phobia</li> <li>Specific phobia</li> <li>ADHD</li> <li>Psychotic features</li> </ul> | <ul style="list-style-type: none"> <li>Depression (18.7%)</li> <li>Bipolar disorder (12.5%)</li> <li>GAD (6.2%)</li> <li>Separation Anxiety disorder (0%)</li> <li>OCD (12.5%)</li> <li>Social Phobia (6.2%)</li> <li>Specific phobia (6.2%)</li> <li>ADHD (50%)</li> <li>Psychotic features (25%)</li> </ul> | <ul style="list-style-type: none"> <li>Depression (18.1%)</li> <li>Bipolar disorder (5.4%)</li> <li>GAD (5.4%)</li> <li>Separation Anxiety disorder (1.8%)</li> <li>OCD (18.1%)</li> <li>Social Phobia (5.4%)</li> <li>Specific phobia (7.2%)</li> <li>ADHD (65.5%)</li> <li>Psychotic features (9.1%)</li> </ul> | 29% reported suicide: <ul style="list-style-type: none"> <li>ASD (43.8%)</li> <li>AS (50%)</li> <li>PDD-NOS (6.2%)</li> </ul> | Suicidality associated with presence of psychotic features  | Psychological disorders identified: <ul style="list-style-type: none"> <li>mood disorders (23.6%)</li> <li>anxiety disorders (43.6%)</li> <li>disruptive behaviours (65.4%)</li> </ul> | Suicidality associated with presence of family history of completed suicide | Suicidality associated with presence of family history of lethal and nonlethal suicidal behaviours |

# SUICIDALITY IN YOUTH WITH ASD: A REVIEW

| Study                 | Suicidality investigated  | Data Sources  | Measures for Suicidality                                 | Measures for ASD                           | Measure for psychological disorders        | Other measures/data collected  | Data analysis   | Prevalence of suicidality in ASD sample | Prevalence of ASD in suicidal sample | Psychological Disorders identified in study   | Rates of Psychological disorders in ASD suicidal sample   | Rates of Psychological disorders identified in ASD sample   | Findings                                       |   |                           |
|-----------------------|---|---|--|--|--|--|---|---|--------------------------------------|---|---|---|--|---|---------------------------|
|                       |   |   |  |  |  |  |   |   |                                      |   |   |   | Suicidality                                    | Psychological Disorders   | Socio-Demographic Factors |
| Chen et al (2017)     | Suicide Attempt (as coded by emergency room physicians, psychiatrists, internal medicine, and surgeons) | National Health Insurance Research Database (NHIRD) | Patient records  | Clinical judgment and diagnostic interview | Clinical judgment and diagnostic interview | Demographics, age at first suicide attempt, time between ASD diagnosis and first suicide attempt, level of urbanisation, income-related insured amount | t-tests; Pearson chi-squared; Cox regression models; sensitivity analysis | 3.9%                                    | 58.7%                                | <ul style="list-style-type: none"> <li>• Unipolar Depression</li> <li>• Bipolar disorder</li> <li>• Anxiety disorders</li> <li>• ADHD</li> <li>• Disruptive behaviour disorders</li> <li>• Alcohol use disorder</li> <li>• Substance use disorder</li> <li>• Intelligence disability</li> </ul> | Not reported  | <ul style="list-style-type: none"> <li>• Unipolar Depression (16.0%)</li> <li>• Bipolar disorder (8.4%)</li> <li>• Anxiety disorders (11.2%)</li> <li>• ADHD (25.3%)</li> <li>• Disruptive behaviour disorders (6.6%)</li> <li>• Alcohol use disorder (1.2%)</li> <li>• Substance use disorder (1.5%)</li> <li>• Intelligence disability (42.8%)</li> </ul> | 3.9% reported suicide attempts.                | <p>Significantly higher rates in ASD cohort of:</p> <ul style="list-style-type: none"> <li>• Unipolar Depression</li> <li>• Bipolar Disorder</li> <li>• Anxiety disorders</li> <li>• ADHD</li> <li>• DBD</li> <li>• Intelligence disability</li> </ul> <p>ASD is significant risk factor for suicide attempts amongst both adolescents and adults.</p> <p>Increased probability of suicidality across total adolescent sample associated with:</p> <ul style="list-style-type: none"> <li>• Unipolar Depression</li> <li>• Substance use disorder</li> </ul> <p>Substance use disorder and Alcohol use disorder increase likelihood of suicidality in males only.</p> |                           |
| Horowitz et al (2017) | Suicidal ideation   | Parent assessment/interview                         | Child and Adolescent Symptom Inventory-5 (parent rating) | ADOS-2                                     | CASI-5                                     | VABS-II; Leiter-3<br><br>Demographics, non-verbal IQ (NVIQ)  | Spearman Correlation analysis; Ordered logistic regression models         | 22.4%                                   | N/A                                  | <ul style="list-style-type: none"> <li>• Mood disorder</li> <li>• Anxiety disorder</li> <li>• DBD</li> <li>• ADHD</li> </ul>  | <ul style="list-style-type: none"> <li>• Mood disorder (42%)*</li> <li>• Anxiety disorder (58%)*</li> <li>• DBD (33%)</li> <li>• ADHD (29%)*</li> </ul> | <ul style="list-style-type: none"> <li>• Mood disorder (29%)</li> <li>• Anxiety disorder (42%)</li> <li>• DBD (39%)</li> <li>• ADHD (40%)</li> </ul>  | 22.4% reported talking about death or suicide. | <p>Increased likelihood of talking about death or suicide associated with:</p> <ul style="list-style-type: none"> <li>• Mood disorder</li> <li>• Anxiety disorder</li> </ul> <p>Reduced likelihood of talking about death or suicide associated with ADHD.</p>  |                           |

Mikami et al. (2009) was the only study to report method of attempt within their ASD sample. They found subjects engaged in drug overdose (58.3%), jumping (25%), carbon monoxide poisoning (8.35%), and poisoning (8.35%).

Two studies compared suicidality prevalence between ASD and typically-developed controls. Mayes et al. (2013) found that rates of suicidal ideation or suicide attempt in children with ASD was 28 times greater than in typically-developing controls, but three times less frequent than in the depressed sample. Similarly, Chen et al. (2017) reported that adolescents and young adults with ASD were five times more likely to attempt suicide in later life compared to non-autistic controls.

### **Prevalence of ASD in Suicidality**

Three studies investigated percentage of ASD diagnoses within the larger sample of youth presenting with suicidality; however, rates varied greatly. Mikami et al. (2009) reported 12.8% of their suicidal sample was diagnosed with ASD; in contrast, both Mayes et al. (2013) and Chen et al. (2017) reported much higher rates of 82% and 58.7% of their respective suicidal samples having a diagnosis of ASD. It should be noted that the high rate of ASD within suicidal sample reported by Mayes et al. (2013) may not be representative, as their ASD sample made up 78.2% of their entire sample; however, rates reported in the other two papers evidence that youth with ASD make up a significant fraction of the overall sample of suicidal youth (Chen et al., 2017; Mikami et al., 2009).

### **Prevalence of Psychological Disorders in ASD**

All papers reported prevalence of psychological disorders. Six papers reported rates specifically within suicidal contingent of their ASD cohort; however, specific individual disorders investigated varied greatly amongst studies. Depression was most commonly



included, with four papers reporting rates ranging from 18.7% to 100% (Karakoc Demirkaya et al., 2016; Mayes et al., 2013; Mukaddes & Fateh, 2010; Storch et al., 2013), followed by anxiety, reported in three papers rates ranging from 6.2% to 90.9% (Karakoc Demirkaya et al., 2016; Mayes et al., 2013; Storch et al., 2013). Two studies (Karakoc Demirkaya et al., 2016; Storch et al., 2013) reported prevalence of: social phobia 6.2%-100%; separation anxiety 0%-27.3% ; specific phobia 6.2%-72.7%(Karakoc Demirkaya et al., 2016; Storch et al., 2013); OCD 12.5%-54.5% (Karakoc Demirkaya et al., 2016; Storch et al., 2013) . No more than two studies reported prevalence of: ADHD 29%-50% (Horowitz et al., 2017; Karakoc Demirkaya et al., 2016); DBD 33%-63.6% (Horowitz et al., 2017; Storch et al., 2013).

There were four studies which were sole investigators of specific presentations. Mayes et al. (2013) was the only study to report rates of sleep disturbance (18.6%), somatic complaints (29.5%), mood dysregulation (19.6%), and impulsivity (15.7%). Mikami et al. (2009) reported 83% having a diagnosis of adjustment disorder, whilst Storch et al. (2013) found that 27.3% had a diagnosis of PTSD. Karakoc Demirkaya et al. (2016) found 25% of their suicidal sample reported having psychotic experiences, and 12.5% had a diagnosis of bipolar disorder. Two studies (Horowitz et al., 2017; Mikami et al., 2009) used umbrella terms grouping together multiple diagnoses: “anxiety disorders” (phobias, separation anxiety, generalized anxiety, Post-traumatic Stress Disorder; PTSD), ranging from 8.3% to 58%, and “mood disorders” (Bipolar disorder, Major Depressive Disorder), ranging from 8.3% to 42%.

### **Risk Factors Associated with Suicidality In ASD**

**ASD Presentation.** Five papers compared the relationship between suicidality and different ASD presentations. Shtayermann (2007; 2008) looked at level of AS traits, finding that suicidal ideation was negatively correlated with ratings of severity of AS presentation. Of the three papers which compared rates of suicidality between different ASD diagnoses (Karakoc Demirkaya et al., 2016; Mayes et al., 2013; Storch et al., 2013) only one reported significant results. Storch et al. (2013) found that children with Autism were more likely to report suicidal ideation or attempt than those with Asperger's Syndrome.

**Suicidal Ideation.** Mayes et al. (2013) were the only researchers to investigate the relationship between different phenomena of suicidality. Investigating suicidal ideation as a potential risk factor for suicidal attempt, when entered into a stepwise linear regression analysis with multiple demographic and co-occurring psychological factors, suicidal ideation emerged as the strongest single predictor of suicidal attempt.

**Psychological Disorder Diagnosis.** Six studies reported on the role of depression within suicidality (Chen et al., 2017; Mayes et al., 2013; Mukaddes & Fateh, 2010; Shtayermman, 2007; Shtayermman, 2008; Storch et al., 2013), of which four reported significant results. Mukaddes and Fateh (2010), the only study not involving statistical tests, reported frequency only, but found that all participants reporting suicidality had a co-occurring diagnosis of MDD. Of the five papers that employed significance testing, three reported significant positive associations. Mayes et al. (2013) found depression not only to be a significant risk factor for suicidal ideation or attempt in children with autism but was also the strongest single predictor of suicidal ideation in their sample; similarly, Storch et al. (2013) reported that suicidal thoughts and behaviours were associated with depression. Chen et al. (2017), the only study to investigate the temporal relationship between suicidality and depression, found that unipolar depression was associated with increased probability of suicidality across both the total adolescent sample, and the sample as a whole. Shtayermann (2007; 2008) reported positive correlations between level of suicidal ideation and depressive symptoms, but these were not statistically significant.

Of the six studies reporting on the role of anxiety in the suicidality phenomena (Karakoc Demirkaya et al., 2016; Mayes et al., 2013; Mukaddes & Fateh, 2010; Shtayermman, 2007; Shtayermman, 2008; Storch et al., 2013), there was no significant association discovered. Shtayermann (2007; 2008) reported positive correlations between level of suicidal ideation and anxiety symptoms, but again these were not statistically significant.

Storch et al. (2013) was the only paper to investigate PTSD as a risk factor for suicidality, reporting suicidal thoughts and behaviours to be associated with PTSD.

Of the four studies including ADHD within their analysis (Chen et al., 2017; Horowitz et al., 2017; Karakoc Demirkaya et al., 2016; Mukaddes & Fateh, 2010) one study reported significant results: Horowitz et al. (2017) found that ADHD was negatively associated with talking about death or suicide within their sample.

There were several studies that were sole investigators of specific psychological disorders and phenomena. Mukaddes and Fateh (2010) was the only study reporting on Oppositional Defiant Disorder within their sample but found that none of the suicidal individuals met criteria for said diagnosis.

Karakoc Demirkaya et al. (2016) was the only study to examine psychotic features as a potential risk factor, finding suicidality to be positively associated with the presence of psychotic features; they were also the only study to include bipolar disorder in their analysis, but this was not found to be significant.

Mayes et al. (2013) were the investigators of the role of different behavioural profiles as risk factors, finding that behavioural problems (oppositional, aggressive, angry, explosive, impulsive) were risk factors for suicidal ideation or attempt. Furthermore, before suicidal ideation, mood dysregulation was the stronger predictor of suicidal attempt.

Chen et al. (2017) investigated the relationship between suicidality and both substance-use disorder and alcohol-use disorder, reporting an increased likelihood of subsequent suicide attempt in males associated with both disorders; however, it should be noted that this is in reference to the entire sample, and not the ASD cohort specifically.

Two studies used the umbrella term “mood disorders” to refer to multiple different diagnoses, with one study investigating its role as a risk factor (Horowitz et al., 2017), the other comparing rates with non-ASD controls (Mikami et al., 2009). Horowitz et al. (2017), the

only study to define the diagnoses included under this label (Bipolar 1, Unspecified Bipolar, Major Depressive Disorder, Unspecified Depression), found mood disorders to be positively associate with talking about death or suicide. Mikami et al. (2009) reported that there were significantly lower rates of mood disorders in their PDD group than the non-PDD controls; however, the size of the PDD cohort was a quarter of that of the comparison group, so the fact that the groups were unbalanced may have had an impact on the results and should therefore be held in mind before drawing any definitive conclusions about differences between ASD and non-ASD populations.

Three studies used the umbrella term “anxiety disorders” to refer to multiple different diagnoses: two studies investigating its role as a risk factor (Chen et al., 2017; Horowitz et al., 2017), the other comparing rates with non-ASD controls (Mikami et al., 2009). Of the two investigating risk factors, only Horowitz et al. (2017), the only study to define the diagnoses included under this label (phobias, separation anxiety, generalized anxiety, Post-traumatic Stress Disorder), found anxiety disorders to be positively associate with talking about death or suicide. Mikami et al. (2009) reported that there were significantly lower rates of anxiety disorders in their PDD group than the non-PDD controls: once again, given the unbalanced group sizes, one should be cautious before drawing any definitive conclusions about differences between ASD and non-ASD populations.

**Socio-Demographic characteristics.** Mayes et al. (2013) was the only paper to examine gender, finding that being male was a significant predictor of suicidal ideation or attempt.

Two studies reported on the relationship between suicidality and age (Mayes et al., 2013; Mukaddes & Fateh, 2010). Mukaddes and Fateh (2010) reported that all participants who had

reported suicidality were in adolescence (12-20 years). Mayes et al. (2013), the only study of the two to analyse the relationships statistically, found that being 10 years old or older was a predictor of suicidal ideation or attempt. Mayes et al. (2013) also looked at ethnicity and socioeconomic status (SES), reporting that being, black, Hispanic, and from a lower SES were predictors of suicidality.

The only study to examine family characteristics, Karakoc Demirkaya et al. (2016) reported suicidality to be associated with both family history of lethal and nonlethal suicidal behaviours, and familial history of completed suicide.

Both Mikami et al. (2009) and Mayes et al. (2013) reported significant associations between suicidality and factors pertaining to social relationships. Mikami et al. (2009), found that 75% of PDD group reported personal relationship conflict, such as being bullied, to be the precipitating event of suicide attempts; similarly, Mayes et al. (2013) reported being teased as a significant risk factor for suicidality within their sample.

### **Protective factors in ASD**

Mayes et al. (2013) was the only study to highlight factors associated with significantly lower likelihood of suicidality, identifying a combination of demographic and psychological factors. They found that participants who were female, white, Asian, and from a higher socio-economic status reported no instances of suicidality; furthermore, children reported not to display any mood dysregulation, behavioural problems, or impulsivity significantly less likely to display any type of suicidality.

## **Methodological Issues**

**Design.** Seven studies utilised cross-sectional designs (Horowitz et al., 2017; Mayes et al., 2013; Mikami et al., 2009; Mukaddes & Fateh, 2010; Shtayermman, 2007; Shtayermman, 2008; Storch et al., 2013), which can be effective in both determining prevalence of an outcome, and identifying significant associations between factors and outcomes. However, a disadvantage of this design is that one cannot infer causality between factors and outcomes; therefore, it can only be concluded that a given factor is significantly associated with the presence of suicidality, giving no indication of whether it preceded suicidality as a potential cause/contributing factor.

The remaining two studies used prospective longitudinal designs (Chen et al., 2017; Karakoc Demirkaya et al., 2016), which unlike cross-sectional studies, allows for clearer understanding of the direction of the temporal relationship between risk factors and suicidality i.e. assessing whether a risk factor preceded suicidality; however only Chen et al. (2017) conducted analysis investigating the temporal relationship between risk factors and subsequent suicide attempt. However, a disadvantage of this design is that, due to its observational approach, it is difficult to control for potential confounding variables. Chen et al. (2017) sought to account for this by including matched controls as their comparison group; whilst this can help control for confounding variables, it risks selection bias, resulting in controls not being representative of the general population.

**Sample size.** Six studies boasted large sample sizes (Chen et al., 2017; Horowitz et al., 2017; Karakoc Demirkaya et al., 2016; Mayes et al., 2013; Storch et al., 2013), an advantage of which is that larger sample sizes increase the power of statistical tests in detecting significant differences, reducing the probability of wrongly rejecting the research hypothesis. The smaller sample sizes reported in the remaining four papers (Mikami et al., 2009; Mukaddes & Fateh, 2010; Shtayermman, 2007; 2008) mean that the statistical power of the analyses was diminished, therefore making it difficult to test associations and draw conclusions with confidence: three studies acknowledge this limitation (Mikami et al., 2009; Mukaddes & Fateh, 2010; Shtayermman, 2007). Whilst large sample sizes can improve the probability of detecting statistically significant differences, they offer little information on practical or clinical significance of observed differences, which the calculation and reporting of effect sizes can remedy.

**Statistical analysis.** Within observational research, the use of certain statistical tests, such as logistic regression providing odds ratios reporting magnitude and direction of differences, help to illustrate practical or clinical significance of observed differences. Five studies utilised such tests, reporting different measures of effect size: two providing correlations (Shtayermman, 2007; 2008), one providing ORs (Horowitz et al., 2017), one providing Cohen's  $d$  and explained variance (Mayes et al., 2013), the last providing HRs (Chen et al., 2017). Additionally, confidence intervals were provided by two of the aforementioned studies (Chen et al., 2017; Horowitz et al., 2017), allowing further assessment of the precision of the results.



**Participant Characteristics.** Given that none of these studies were carried out in the UK, generalising findings to a UK population should be done cautiously as there may be significant cultural differences, such as the impact of a different socioeconomic climate, or population ethnicity composition. Similarly, these studies being carried out in several different countries results in culturally heterogeneous samples, meaning that generalisation of findings amongst these studies should be done tentatively as they may also be vulnerable to the same potential sociodemographic differences, and thus potential confounding variables, highlighted above.

**Unequal Sample Sizes.** Whilst a strength of three papers was that they helped control for confounding variables by including control subjects (Chen et al., 2017; Mayes et al., 2013; Mikami et al., 2009), none of these studies reported balanced group sizes; the drawback of this being it can affect the power of statistical analysis testing for group difference, increasing risk of both “false-positives” and “false-negatives”, depending on how the groups are weighted. Mikami et al. (2009) reported a PDD group four times smaller than the comparison group, whilst the ASD cohort reported by Mayes et al. (2013) was almost four times that of the two comparison groups combined; therefore, caution should be taken in inferring definitive conclusions. However, despite reporting an ASD cohort four times smaller than the non-ASD controls, the use of matched-controls by Chen et al. (2017) should have controlled for unequal group sizes.

**Recruitment.** Several studies note that the nature of recruitment sources and applied inclusion criteria increased the risk of selection bias, which could impact on the generalisability of findings as the samples may not been representative of the wider population of youth with ASD. Seven studies used clinical samples (Chen et al., 2017; Horowitz et al., 2017; Karakoc Demirkaya et al., 2016; Mayes et al., 2013; Mikami et al., 2009; Mukaddes & Fateh, 2010; Storch et al., 2013); therefore, it is unclear whether risk factors identified for these samples correlate to those present in non-clinical samples.

**Data Sources and Collection.** Whilst it could be argued that a strength shared amongst the studies is that they all clearly describe their data sources, there are limitations in the description of the data collection process which hinder drawing substantive conclusions from the findings. Firstly, two studies gathered data on both suicidality and psychological disorder diagnosis via review of clinical records (Chen et al., 2017; Mikami et al., 2009). Whilst this can be beneficial in terms of amount of data available, clinical records tend to be more subject to opinion and therefore at higher risk of reporting bias. Furthermore, none of these studies makes any mention of who was involved in the data collection process; therefore, it is not clear how, if at all, reliability and consistency in data interpretation were assessed, meaning bias cannot confidently be ruled out in the interpretation of the data in these studies.

**Assessing Suicidality and Psychological Disorder.** Seven studies utilised standardised measures to assess for suicidality and psychological disorder (Horowitz et al., 2017; Karakoc Demirkaya et al., 2016; Mayes et al., 2013; Mukaddes & Fateh, 2010; Shtayermman, 2007; Shtayermman, 2008; Storch et al., 2013), helping in both ensuring consistency in the identification and measurement of variables, and in the generalisability of findings; however, the exact measures included vary between the studies, meaning that consistency cannot be assumed between the studies, hampering any generalisability of findings.

Another issue concerns suitability of the measures administered. Karakoc Demirkaya et al. (2016) reported that the measures employed in their study were originally designed for typically-developing populations. None of the other studies collecting data from young people, and not solely parental report, appeared to have employed measures designed for ASD populations, so whilst they may have been shown to be valid and reliable with non-ASD samples, they may not be appropriately sensitive in assessing for psychological disorders with this population.

Lastly, studies varied regarding who made reports of suicidality. Of the eight studies employing measures or clinical interview, three studies used young person report of suicidality only, with the remaining five using either a combination of child- and parent-report or parent-report only. This brings into question reliability of report of suicidality in these five studies, because, as Horowitz et al. (2017) remarked, it is unclear “which reporter, or potentially a combination of the two, will prove to be most meaningful and predictive”, increasing the risk of either under-reporting or over-reporting, as it has been suggested that suicidal phenomena amongst people with ASD can often be overlooked (Fitzgerald, 2007),

potentially due to the high prevalence of non-suicidal self-injury precluding recognition (Hannon & Taylor, 2013).

**ASD Diagnosis.** The heterogeneity of ASD diagnosis characterising samples limits the generalisability of findings across the wider ASD population; given the differences between diagnostic presentations, it is not possible to conclude from these studies whether certain risk factors are specific to certain ASD diagnoses, or whether they are relevant across the diagnostic spectrum.

**Assessing ASD.** A crucial component of ASD research is the confirmation that all participants actually meet criteria for a diagnosis, a task made robust through the use of recognised reliable and validated assessment tools. Within this review, only two studies employed the “gold standard” ASD diagnostic assessment tool (Horowitz et al., 2017; Storch et al., 2013); of the remaining seven, four used different measures of ASD (Mayes et al., 2013; Mikami et al., 2009; Shtayermman, 2007; 2008), the rest relying on clinical judgement based on DSM criteria (Chen et al., 2017; Karakoc Demirkaya et al., 2016; Mukaddes & Fateh, 2010).

Therefore, inconsistency in diagnostic assessment tools employed between studies adds to the difficulty in generalising findings resulting from heterogeneity of ASD presentations, as there has been limited scope to control for severity of ASD presentation, and consequently the relationship between presentation and suicidality. Of the studies, only Shtayermann (2007; 2008) included severity of presentation within their studies.

**Difference in Study Focus and Risk Factors of Interest.** Given that the aspect of suicidality investigated differed between studies, it is therefore difficult to generalise the role of risk factors across all types of suicidality; for example, it could be that a significant factor associated with suicidal ideation has no significant association with suicidal behaviour. Furthermore, despite much overlap across studies, no study matches another exactly in terms of factors investigated. For example, not only did the range of psychological disorders investigated vary, they also differed in how they were included in the analysis: whilst some studies investigated depression, anxiety and ADHD as individual factors, others investigated them as members of collections of psychological disorders, mood disorders, anxiety disorders and disruptive behaviour disorders, respectively. In some cases, factors for which significant associations were observed were included in one particular study e.g. psychotic features and family history (Karakoc Demirkaya et al., 2016). Investigation of socio-demographic factors was also limited, with only two studies including factors above gender and age.

The lack of consistency in variables of interest between studies means that the level of control of potential confounding variables varied between studies, and therefore it is not possible to rule out the role of variables of interest from one study being unaccounted for as confounding variables in another. Consequently, due to the potential impact of unaccounted confounding variables, one should be cautious in generalising these findings.

## **Discussion**

### **Summary of findings of the Review**

This review appraised the research investigating suicidality in children and adolescents with ASD, guided by the following research questions:

1. How prevalent is suicidality amongst children and adolescents with ASD?

2. What does the research tell us about the risk factors associated with suicidality in this population?

In total, nine papers were identified and included in this review. In terms of prevalence of suicidality within ASD specifically, presence of any suicidal phenomenon ranged from 3.9% to 50%, broken down between suicidal ideation (10.9% to 50%), and suicidal behaviour/attempt (3.9% and 12.7%): these rates are comparable to those identified in the population-based adolescent studies, with rates of suicidal ideation and attempt within this population reported to be 20-30% and 10%, respectively (Evans et al., 2005). These findings indicate that risk of suicidality in individuals with ASD is not isolated to adults, and that young people with ASD are at a similar level of risk of suicidality as their typically-developed counterparts.

With regards to associated risk factors, the research suggests a range of psychological and sociodemographic factors may be associated with increased risk of suicidality in youth with ASD; however, due to inconsistency between studies in factors investigated and assessment measures, generalisability of findings is dubious and therefore any conclusions drawn should be tentative. Additionally, given only Chen et al. (2017) investigated any temporal relationship between suicidality and risk factors, it is not possible to reliably infer conclusions about causal relationships between suicidality and any of the associated factors identified.

### **Factors Associated with Suicidality in ASD**

**ASD Presentation.** The research suggests that suicidality may vary between different diagnoses along the autistic spectrum. children with Autism were found more likely to report suicidality than those with Asperger's (Storch et al, 2013); however, this was only reported in a single study and therefore is difficult to generalise.

**Psychological Disorders.** In terms of psychological disorders, significant associations were identified with:

- Depression
- PTSD
- Substance-use disorder
- Alcohol-use disorder
- Mood disorders
- Anxiety disorders
- Psychotic features
- Behavioural problems

Of these, depression was the most widely identified risk factor, and was shown to have a temporal relationship with subsequent suicide attempts in adolescents, as did substance-use disorder (Chen et al., 2017).

**Socio-demographic factors.** Several socio-demographic factors were identified as potential risk factors: gender, low SES and ethnicity (Mayes et al., 2013); age (Mayes et al., 2013; Mukaddes & Fateh, 2010); family history of lethal and nonlethal suicidal behaviours and family history of completed suicide (Karakoc Demirkaya et al., 2016). It was also suggested that relationship conflict, such as bullying or teasing, may also be associated with suicidality (Mayes et al., 2013; Mikami et al., 2009).

Only one study carried out analysis to test for a causal or temporal relationship; furthermore, none of the studies in this review ran a comparison against non-ASD controls to test whether any of the aforementioned factors were specific to ASD, or whether ASD might act as a moderating factor, with the relationships between factors and suicidality being more or less significant within ASD populations. Consequently, it is not currently possible to confidently infer conclusions about these associations, highlighting the need for further research in this area.

### **Limitations of the Review**

This review focused solely on quantitative studies into suicidality in children and adolescents with ASD, excluding both qualitative studies and case studies. It is possible that these particular methodologies, given their ability to focus more on an individual and their experience, may be helpful and more adept at identifying mechanisms and processes associated with particular risk factors. Therefore, omitting these studies may have limited the extent of possible conclusions able to be inferred in this review.

### **Clinical Implications**

As none of these studies were conducted with UK samples, generalisability and implications of these findings for clinical practice in the UK are tentative. However, there are several



potential avenues arising from these findings for development of clinical practice. Firstly, whilst inferring definitive conclusions should be done cautiously, these findings could help inform the development of service protocols geared towards minimising either risk of, or preventing escalation of, suicidality in adolescents with ASD. Those identified to be at higher risk of suicidality may benefit from more frequent risk assessment in order to reduce the likelihood that suicidality goes unnoticed and therefore potentially escalates to engagement in life-threatening behaviours. This type of early identification could help ensure that those requiring intervention do not get overlooked and receive appropriate support in a timely manner. Secondly, better understanding of associated risk factors could help inform the development of preventative interventions tailored to address specific factors, such as difficulties related to psychological disorders, social communication difficulties, or difficulties within peer relationships.

### **Research Implications**

The findings of this review identify multiple potential risk factors for suicidality in youth with ASD. Further research is required to hone understanding of these risk factors, and the related mechanisms at play. Firstly, given no study investigated UK samples, UK-based research would help to ascertain whether these findings are generalisable to UK samples, or whether there are significant sociodemographic differences with the countries of origin which would dismiss any relevance. Given the majority of studies used cross-sectional analysis, with only one study employing a longitudinal approach, future research should use longitudinal analysis to assess for any causal relationships with suicidality.

Despite considerable overlap, factors, both psychological and sociodemographic, investigated varied greatly between studies, making it difficult to rule out influence of potential

confounding variables. Future studies should consolidate all factors investigated across these studies to help better control for confounding variables. Specifically, studies should aim to investigate individual psychological diagnoses, rather than collections, and also include a comprehensive range of socio-demographic factors:

- Ethnicity
- SES
- sexual orientation
- relational factors (e.g. peer victimisation)
- trauma history
- family history of suicidality
- family mental health history
- educational history
- family composition (e.g. number of siblings, age positioning within family)
- Treatment factors to be investigated:
  - Psychological intervention
  - Psychopharmacological intervention

Including these factors would help investigate cultural factors related specifically to the UK and control for potential cultural differences, enhancing generalisability of findings.

Additionally, alongside risk factors, identifying protective factors should be included as a future research aim.

Suicidal phenomenon investigated differed between studies, making it difficult to generalise the role of risk factors across all phenomenon. Future studies should investigate different aspects of suicidality as separate outcome variables when attempting to identify relevant risk factors.

Only one study investigated the relationship between different aspects of suicidality, reporting suicidal ideation to be the strongest single risk factor for suicide attempt.

Therefore, further research is needed to assess the relationship between existing/historical suicidality and later incidences, as this could shed light on the progression trajectory for suicidality.

Without comparison groups, it is difficult to make conclusions about any uniqueness of relationship between these factors and suicidality in ASD. Lack of control subjects within all but one study makes it impossible to conclude whether these factors are specific to ASD, or whether the strength of association is significantly different from non-ASD samples.

Furthermore, findings were mixed when comparing different ASD diagnoses, and no study investigated whether significance of associations differed between clinical and community samples. Future studies should include non-ASD controls, differential diagnoses, and both clinical and community samples. It could also be beneficial when comparing different ASD diagnosis samples to stratify samples in terms of age, given its potential association.

Once risk factors have been robustly investigated and causal relationships have been indicated, studies should investigate identified at-risk groups (e.g. depression) to develop

understanding of the risk mechanisms and processes explaining the relationship between risk factors and suicidality.

To reduce risk of reporting bias associated with subjective measures (e.g. clinical notes), studies should prioritise using objective and standardised measures, where possible, to investigate factors of interest.

No psychometric measure reported in this review was designed for use with an ASD population, bringing into question the reliability, sensitivity, and validity of using these measures with this population. Therefore, future studies should aim to use measures designed for use with ASD samples; should these be unavailable, development of such measures should be a priority to improve report and identification of psychological distress within this population. For example, individuals with ASD have the propensity to make literal interpretations of more figurative uses of language for literal understanding of language (Frith & Happe, 2005): updating the language used in measures to accommodate this tendency could reduce the possibility of misunderstanding or misinterpretation of questions when administering a measure, increasing the validity of the measure for use within an ASD population. However, in creating bespoke measures, there is a risk of emphasising differences associated with individuals with ASD, relative to the typically-developed population, and creating a sense of ‘othering’ within those diagnoses with ASD. Additionally, in creating and using of ASD-specific measures, there is the risk that characteristics shared between those with ASD and typically-developing individuals will be overlooked by such measures. Therefore, these issues should be considered when pursuing development of such measures.

Given the heterogeneity of presentation associated with respective psychological disorder labels, investigating specific characteristics associated with individual diagnoses would help

to improve understanding of the nature of the relationship between psychological factors and suicidality, potentially identifying mechanisms responsible for said relationships. This would be particularly relevant to ASD populations, as there can be additional characteristics present within children and adolescents with ASD, compared to non-ASD populations (Ghaziuddin, 2005; Magnuson & Constantino, 2011).

No study included psychological theory as part of their examination of suicidality within adolescents with ASD. Lack of attention to the investigation of theoretical models limits the available research to infer conclusions around the causal mechanisms at play between risk factors and suicidality; therefore, future research should endeavour to include psychological theory as part of studies to improve understanding of causal mechanisms behind suicidality within this population.

Moreover, further study should investigate the relationship between identified risk factors and variations in suicidal phenomenology; for example, whether is there a relationship between type of suicide methodology chosen and specific psychiatric diagnosis, or whether certain diagnoses are associated with higher frequency or greater severity of suicidality.

### **Conclusion**

This review aimed to explore the current state of research on suicidality in children and adolescents with diagnoses of ASD, examining prevalence and associated risk factors. From the nine papers identified, suicidality has consistently been shown to be a significant health issue in young people with ASD; however, findings regarding risk factors have been somewhat mixed and difficult to generalise across the wider youth ASD population, due to several methodological variations and issues (e.g. inconsistency in suicidal phenomena investigated, heterogeneity in diagnosis of ASD between studies). However, the review

suggests that there are a variety of psychological and socio-demographic risk factors associated with suicidality in children and adolescents with ASD.

Future studies should use UK samples to investigate the relationship between suicidality and youth with ASD including all factors investigated across these studies. Additionally, studies should look to investigate specific risk factors (e.g. depression) to identify the risk mechanisms pertaining to suicidality (e.g. specific profile of low mood with irritability).

Better understanding of risk factors could help identify at-risk individuals potentially requiring increased risk assessment and support, and in doing so hopefully both minimising likelihood of suicidality going unnoticed and improving possibility of timely intervention.

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Section B: Empirical Paper

**Suicidality in adolescents with Autism Spectrum Disorders:  
investigating Depression and Irritability as risk factors in a UK  
clinical population**

Word Count: 7784 (excluding abstracts, references, tables and  
figures)

A thesis submitted in partial fulfilment of the requirements of  
Canterbury Christ Church University for the degree of  
Doctor of Clinical Psychology

APRIL 2018

SALOMONS

CANTERBURY CHRIST CHURCH UNIVERSITY

### Abstract

**Background:** Suicidality, suicidal ideation and suicidal behaviour, is a significant health concern for adolescents with Autism Spectrum Disorders (ASD). Depression and Irritability have been identified as risk factors for suicidality in autistic adolescents. Autistic youth may have higher vulnerability to these factors than typically-developing adolescents. No study has compared the relationship between suicidality and different depressive profiles, nor used a UK clinical sample. This study investigated depression, irritability, and specific depressive profiles as risk factors for suicidality in adolescents with ASD within a UK clinical population. **Method:** This clinical cohort study used archival data extracted from an electronic mental health records database. The sample consisted of 1314 adolescents (13+ years) who received an ICD-10 ASD diagnosis between 2008 and 2013. Outcome measure was suicidality, with exposure variables of depression, irritability, and specific profiles (depression with co-occurring irritability (DWI), depression without co-occurring irritability (DNI), and irritability without co-occurring depression (IND)). **Results:** Cross-sectional analysis found depression to be associated with higher likelihood of suicidality. Irritability was found to be associated with higher likelihood of suicidality, even after controlling for depression. DWI was a more significant predictor of suicidality than IND, but no different from DNI. Psychosis, being female, antidepressant use, and caregiver mental health difficulties were also positively associated with suicidality, but significantly less likely in individuals diagnosed with ID. **Conclusions:** Results indicate multiple characteristics of adolescents with ASD at high-risk of suicidality. Early identification of high-risk individuals could help deliver timely intervention, potentially reducing both incidence and progression of suicidality.

**Keywords:** Suicidality, Adolescent, Depression, Irritability



## Introduction

### Autism Spectrum Disorders (ASD)

ASD is defined as a neurodevelopmental disorder, typically categorised by deficits in social communication, social interaction and sensory processing, with co-occurring repetitive stereotyped behaviours, rigid thinking style and highly specific interests, present from early on in a person's development (APA, American Psychiatric Association, 2013). The Diagnostic and Statistical Manual 5th edition (DSM-V; APA, 2013), employs ASD as the collective term encompassing several previous specific diagnoses: autism/autistic disorder, Asperger's syndrome, and pervasive developmental disorder-not otherwise specified.

In the UK, it is thought that ASD occurs in approximately 1% of the child population (Baron-Cohen et al., 2009); however, Baron -Cohen et al (2009) found a ratio of 2:3 when comparing known cases to undiagnosed cases, suggesting that rates may actually be higher than originally thought.

Research suggests a propensity towards a diagnosis of ASD amongst males, with a male to female ratio of 4:1 commonly cited (Halladay et al., 2015). However, a recent systematic review by Loomes, Hull, and Mandy (2017), suggested that the gender ratio is actually closer to 3:1. Furthermore, it has been suggested that presentation of ASD traits may differ between genders (Werling & Geschwind, 2013), differing in core ASD features: males with ASD are more likely to display externalising behavioural difficulties (e.g. hyperactivity, aggression), whereas females with ASD are more likely to present with internalising difficulties (e.g. depression, anxiety) (Mandy et al., 2012).

### **Suicidality in Adolescents with ASD**

Suicidality is globally recognised as a major public health issue. The National Strategy for Suicide Prevention (Center for Mental Health Services (US) & Office of the Surgeon General (US), 2001) defines “suicidality” as the collective term for a range of suicidal phenomena:

- *Suicidal ideation*: thoughts pertaining to suicide/suicidal behaviour.
- *Suicidal plans*: thoughts around method of carrying out suicidal behaviour.
- *Suicidal attempt*: an unsuccessful attempt to engage in behaviour with intended outcome to die as a result of the act.
- *Completed suicide*: death occurring as a result of direct behaviour intended to end one’s life.

Suicide is one of the leading causes of death in young adults in the UK (Office of National Statistics, 2016), and the second leading cause of death globally amongst 10- to 24-year olds (Hawton et al., 2012). With regards to those with ASD, a recent study found suicide to be a leading cause of premature death amongst this population (Hirvikoski et al., 2016).

Suicidality has been identified as a significant public health issue amongst typically-developing adolescents (Evans et al., 2005). Similarly, in a review on suicidality in youth with ASD, Kikoler (in preparation) found suicidality to pose significant risk to adolescents with ASD, citing prevalence of any suicidal phenomenon ranging from 3.9% to 50%, broken down between suicidal ideation (10.9% to 50%), and suicidal behaviour/attempt (3.9% and 12.7%), rates comparable to those identified in population-based typically-developed adolescent studies, indicating that young people with ASD are at a similar level of risk of suicidality as their typically-developed counterparts. Adolescence has also been identified as

## SUICIDALITY RISK FACTORS ADOLESCENTS WITH ASD

a period of increase for suicidality in individuals with ASD. For example, Mayes, Gorman, Hillwig-Garcia, and Syed (2013) found being older than 10 years to be a risk factor for suicidality in autistic youth older than 10 years, whilst Mukaddes and Fateh (2010) reported that all of their patients with AS who disclosed suicidal phenomena were adolescents.

### **Interpersonal-Psychological Theory of Suicide**

Whilst a range of theoretical models have been proposed to understand the causal mechanisms behind suicidality (Stress-diathesis Model, van Heeringen, 2012; Cognitive Model, Wenzel & Beck, 2008), thus far the application of such models to the ASD population has been limited; to the author's knowledge, the only model to have been tested with this population is the Interpersonal-Psychological Theory of Suicide (IPT: Joiner, 2007; Van Orden et al., 2010).

The IPTS model proposes an individual will engage in suicidal behaviours if the following two conditions are met: firstly, they have the desire to die, also referred to as suicidal ideation; secondly, they have the capability to carry out acts driven by said desire.

Furthermore, these conditions arise out of the interplay between three factors (see Figure 1):

1. Thwarted belongingness: characterised by self-reported feelings of loneliness or alienation, absence of reciprocal social relationship, limited social support, and social relationship breakdown.
2. Perceived burdensomeness: characterised by “the perception that one has become a hopeless burden on family and friends” (Pelton & Cassidy, 2017), and can be associated with unemployment, long-term physical illness, and low self-esteem.

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### 3. Acquired Capability for Suicide.

According to IPTS, it is the combination of Thwarted Belongingness and Perceived Burdensomeness that leads to suicidal ideation and the desire to die, developing from acquired feelings of hopelessness and belief that if they were dead their friends and/or family would be better off. Furthermore, it is the introduction of Acquired Capability for Suicide that leads to a person progressing from suicidal ideation to suicide attempt; IPTS posits this is acquired through someone overcoming their innate drive for self-preservation, resulting in reduced fear of death and increased pain tolerance (see Figure 2).

IPTS also claims suicidality presentation varies significantly between different psychological disorders due to the heterogeneity in difficulties. For example, depression is associated with increased likelihood of behaviours associated with both Thwarted Belongingness (e.g. due to increases in social withdrawal), and Perceived Burdensomeness (e.g. due to increases in low self-esteem), and therefore a higher risk of suicidal ideation; whereas Post-Traumatic Stress Disorder is associated with Acquired Capability for Suicide only; currently no single diagnosis has been found to be associated with all three factors in the model (Silva, Ribeiro, & Joiner, 2015).

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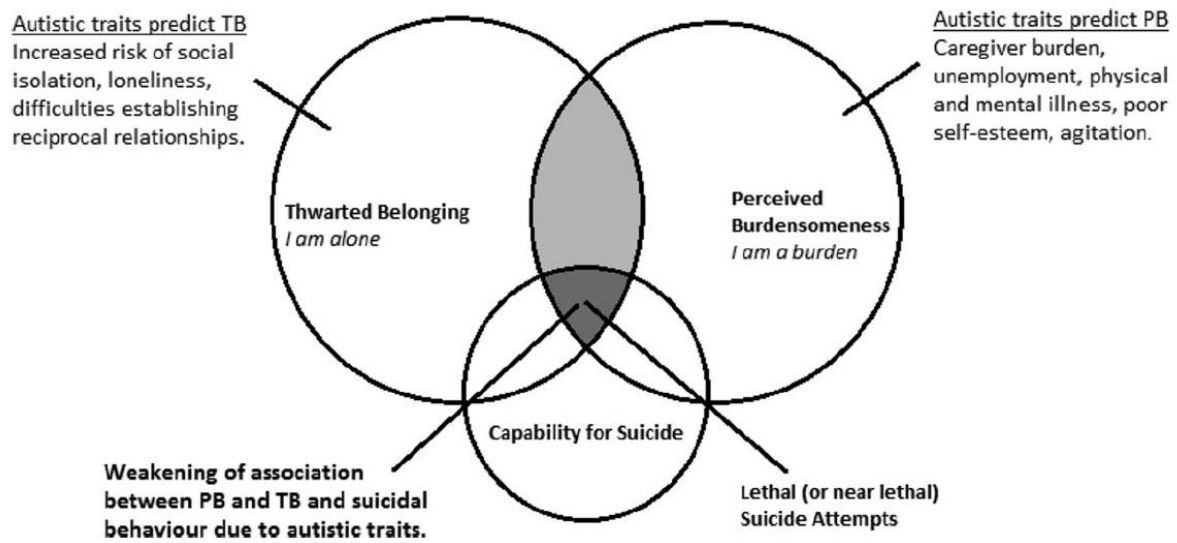


Figure 1. The interpersonal psychological theory of suicide and hypothesized interaction with autistic traits (adapted from Pelton & Cassidy, 2017).

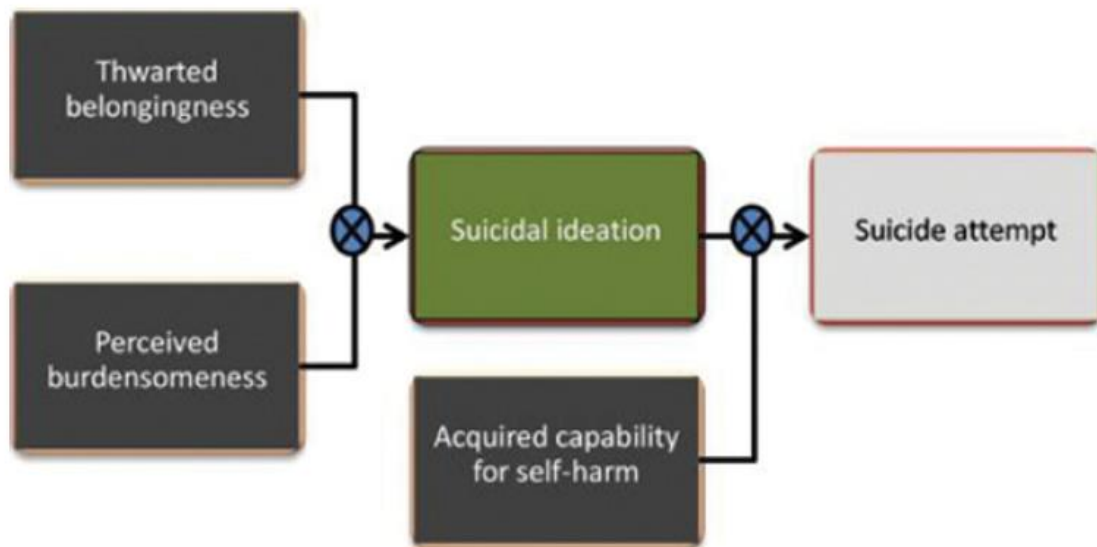


Figure 2. The interpersonal psychological theory of suicide (adapted from Stewart, Eaddy, Horton, Hughes, & Kennard, 2017).

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IPTS has been shown to have validity in explaining the causal mechanisms associated with suicidality in both adults (Van Orden, Witte, Gordon, Bender, & Joiner Jr, 2008), and adolescents (S. M. Stewart et al., 2017). To date, only one study has tested IPTS in the context of ASD. Pelton and Cassidy (2017) investigated the association between autistic traits and suicidality within a sample of young adults, finding a significant relationship between autistic traits and suicidality, mediated by both Thwarted Belongingness and Perceived Burdensomeness, and that autistic traits significantly predicted both Thwarted Belongingness and Perceived Burdensomeness, indicating validity of using IPTS with individuals with autistic traits. They postulated that behaviours suggestive of the presence of both Thwarted Belongingness (e.g. self-reported feelings of loneliness, limited social support), and Perceived Burdensomeness (e.g. unemployment, family burden), were also related to high levels of autistic traits, and therefore individuals with high autistic traits were at risk of suicidality due to increased likelihood of experiencing Thwarted Belongingness and Perceived Burdensomeness. Pelton and Cassidy (2017) also found depression to significantly predict both Thwarted Belongingness and Perceived Burdensomeness within their sample. They posited that depression may also be intensified by autistic traits, with the propensity for rigid thinking-styles, difficulty switching attentional focus, and repetitive behaviours increasing the possibility of engaging in ruminative thinking. Given that depression is associated with Thwarted Belongingness and Perceived Burdensomeness, and not Acquired Capability for Suicide, Pelton and Cassidy (2017) suggest that, in the presence of autistic traits, the association between suicidal ideation (i.e. Thwarted Belongingness and Perceived Burdensomeness) and suicidal behaviour (i.e. Acquired Capability for Suicide) is weakened.

### **Depression & Suicidality**

Depression has been consistently identified as a risk factor for suicidality amongst typically-

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developing adolescents (Fergusson et al., 2000; Kirkcaldy, Siefen, Urkin, & Merrick, 2006; Pelkonen & Marttunen, 2003; Strandheim et al., 2014). Similarly for adolescents with ASD, depression has been identified as a significant risk factor for suicidality (Mayes et al., 2013; Storch et al., 2013), and has even been found to have a temporal relationship with suicidality, increasing the likelihood of later suicide attempt (Chen et al., 2017).

Depression is typically characterised by low mood and anhedonia, amongst a combination of other difficulties (e.g. sleep disturbances, reduced appetite, fatigue), causing significant impairment to daily functioning (APA, 2013). Adolescence has been highlighted as a period of increased vulnerability to developing depression, when depressive symptoms significantly increase and first depressive episodes develop (Kim-Cohen et al., 2003), visible in the comparison of 12-month prevalence of depression in childhood with that in adolescence: childhood estimates range from 0.5% to 3% (Birmaher et al., 1996), but increased in adolescence to a range of 2% to 8% (Costello, Erkanli, & Angold, 2006). The increased emergence of depression in adolescence is thought to be due to the intense period of development, characterised by physical, social, cognitive and neural changes, associated with adolescence, changes which are considered likely to play an important role in the development of depression. Features include rapidly developing emotional and motivational systems, as well as increasing self-awareness and self-reflection, resulting in a mismatch between the need for increases in emotional regulation occurring at a rate faster than the responsible cognitive function can develop, not to mention significant changes in social environment. These characteristics have led to adolescence being akin to “starting the engine with an unskilled driver” (Dahl, 2004, p.17).

Like their typically-developing counterparts, there is significant, if not higher, risk of depression for adolescents with ASD: several studies have reported higher risk of depression

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amongst youth with ASD than typically-developing controls (Ghaziuddin, Ghaziuddin, & Greden, 2002; Gurney, McPheeters, & Davis, 2006; Stewart, Barnard, Pearson, Hasan, & O'Brien, 2006). The increased risk may be due to the impact of the changes associated with adolescence potentially exacerbated by core characteristics associated with ASD (Magnuson & Constantino, 2011). For example, changes in social environment and peer relationships may increase an autistic individual's awareness of their diagnosis and the way it makes them different from their typically-developing peers and has been associated with greater severity of depressive symptoms (Butzer & Konstantareas, 2003). Given this potential increased risk for developing depression, adolescents with ASD may therefore be at higher risk of suicidality as they might be more predisposed to developing this particular known risk factor.

However, 'Depression' is a "phenomenologically heterogeneous" label and encompasses a range of presentations (Leventhal, Pettit, & Lewinsohn, 2008), which has prompted the proposal of distinct depressive presentations to aid diagnosis and help inform treatment (Rush, 2007). With regards to ASD, as well as these proposed presentations, it has been posited that depression in ASD can present with special features, such as increased withdrawal and irritability (p.131; Ghaziuddin, 2005); similarly, Magnuson and Constantino (2011) found that depression in ASD-affected children can often be characterised by an "atypical presentation", as well as potentially presenting with additional features, such as catatonia and mood lability. Depressive presentations have even been found to vary significantly between different ASD diagnoses (Pearson et al., 2006).

To date, research into the relationship between depression and suicidality has tended to focus solely on diagnosis and not investigated difference in relationship between suicidality and distinct depressive profiles; therefore, it remains unclear whether specific depressive presentations are more associated than others with suicidality, and what aspects of such



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presentations are responsible for the increase in risk. Furthermore, given the further heterogeneity associated with adolescent depression in ASD, it is also unclear whether a depressive profile associated with suicidality within typically-developing adolescents would have a similar relationship with ASD, or whether the relevant risk factor is unique to ASD.

### **Irritability & Suicidality**

Whilst psychological risk factors have been ubiquitously investigated, several behavioural characteristics, such as irritability, have also been identified as having a significant association with suicidality. Irritability is characterised by the DSM-V as "easily annoyed and provoked to anger" (APA, 2013), and associated with poor emotional self-regulation. From a theoretical standpoint, IPTS proposes an association between emotional-regulation difficulties and suicidality: Silva et al. (2015) reported anger to be associated with both Thwarted Belongingness and Perceived Burdensomeness, increasing likelihood of suicidal ideation. Hawkins et al. (2013), found Perceived Burdensomeness mediated the relationship between anger and both suicidal ideation and past suicide attempts, positing that feelings of burdensomeness unto others may occur due to anger leading to negative emotional states (Tafra, Kassirer, Dundin, as cited in Hawkins et al., 2013). Irritability has been found to be associated with increased probability of suicide attempt in typically-developing adolescents (Dour, Cha, & Nock, 2011). Research also suggests that the association between irritability and suicidality carries over into autistic youth: Mayes et al. (2013) found mood dysregulation to significantly predict suicidality within their sample of children and adolescents with ASD, identified as one of the strongest predictors of suicide attempt, second only to suicidal ideation. Whilst not explicitly a diagnostic criterion, irritability is becoming increasingly identified as a characteristic endemic to those with ASD (Jahromi, Meek, & Ober-Reynolds, 2012; Samson, Wells, Phillips, Hardan, & Gross, 2015), proposed to be

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related to innate deficits in both temperament control and ability to be soothed (Samyn, Roeyers, & Bijttebier, 2011). As mentioned previously, Perceived Burdensomeness is associated with high levels of autistic traits (Pelton & Cassidy, 2017), and given the potential predisposition towards irritability, individuals with ASD may be at greater risk of suicidality than their typically-developing counterparts when it comes to the influence of this particular factor.

### **Depression & Irritability**

Whilst observed to be present in a range of psychological disorders in children and adolescents (McLaughlin, Hatzenbuehler, Mennin, & Nolen-Hoeksema, 2011), irritability has been identified to be particularly related to depression in youth to the extent that irritability can be substituted in place of low mood in the diagnosis of depression in children and adolescents (APA, 2013; Rao & Chen, 2009). Irritability has been identified as a characteristic highly likely to be observed in depressed youth with ASD (Magnuson & Constantino, 2011). Furthermore, depressive presentations with co-occurring irritability have been found to be associated with suicidality in autistic youth, with Mayes et al. (2013) reporting that irritability presenting alongside other depressive characteristics, such as anhedonia, was associated with increased likelihood of suicidality.

As highlighted earlier, depression is a diagnostic term representing a range of heterogeneous presentations, and to date, research into the relationship between depression and suicidality has tended to focus solely on depression as a collective label and not distinct profiles. It is therefore not clear what causal mechanisms are responsible for the relationship between depression and suicidality. Given the identification of irritability as a characteristic endemic to ASD, as well as the findings of Mayes et al. (2013), it may be that depression with co-

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occurring irritability is a depressive profile associated with a higher likelihood for suicidality in youth with ASD, perhaps more so than other depressive profiles, and therefore might be a better and more helpful indicator of those at higher risk of suicidality than looking at depression as a collective construct.

### **Rationale & Aims**

Adolescence has been identified as a period of increased risk of suicidality in individuals with ASD. This is the first study to look at risk factors in a UK adolescent clinical sample.

Additionally, to date, no study has looked at the relationship between specific depressive profiles and suicidality in adolescents with ASD. The aim of the study was to identify risk factors for suicidality in a clinical sample of adolescents with ASD, specifically exploring the roles of depression and irritability as potential risk factors. Furthermore, this study compared the relationship between suicidality and individual depressive and irritability profiles. Based on current knowledge, the following hypotheses were made:

**Hypothesis 1.** Depression will be identified as a significant risk factor for suicidality in adolescents with ASD.

**Hypothesis 2.** Irritability will be identified as a significant risk factor for suicidality in adolescents with ASD.

**Hypothesis 3.** Part of the relationship, if not all, between irritability and suicidality will be explained by depression.

**Hypothesis 4.** Depression with co-occurring irritability will be a stronger predictor for suicidality in adolescents with ASD than both depression without co-occurring irritability and irritability without co-occurring depression.

## **Method**

### **Design**

This study was a clinical cohort study, using retrospective collection of data from electronic health records.

### **Sample**

Participants were selected from an open clinical cohort (entering and exiting the study at different times) of children and adolescents aged 5-17, referred to South London and Maudsley NHS Foundation Trust (SL&M) Child and Adolescent Mental Health services (CAMHS), who received, according to criteria outlined in International Statistical Classification of Diseases and Related Health Problems – 10<sup>th</sup> revision (ICD-10, World Health Organization, 1992), a diagnosis of ASD (F84.0, F84.1, F84.5, F84.9) between 1<sup>st</sup> January 2008 and 31<sup>st</sup> December 2013.

### **Inclusion Criteria**

In order to be included in the adolescent cohort, an individual had to be at least 13 years of age at time of first contact with services. This age was selected as it has been identified as an age of overlap between the end of the early adolescence, characterised by initial biological changes, and the start of adolescence, characterised by significant psychosocial change (Curtis, 2015); therefore, 13 years old appears to be the minimum age where all developmental changes associated with adolescence begin to occur simultaneously.

### **Procedure**

All study data were collected from an anonymised record database consisting of electronic

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mental health records for children and adolescents referred to SL&M CAMHS between 1<sup>st</sup> January 2008 and 31<sup>st</sup> December 2013, held in the UK National Institute for Health Research Biomedical Research Centre for Mental Health (Perera et al., 2016). The Clinical Record Interactive Search (CRIS) system was used to extract the deidentified dataset for analysis in this project. The dataset extracted consisted of clinician-recorded responses on standardised proforma structures, as well as unstructured data from “free text” input (e.g. progress notes, clinic letters, etc.), the latter achieved using Generalised Architecture for Text Engineering (GATE), a natural language processing (NLP) program (Cunningham, 2002).

### **Measures**

#### **Outcome Variable: Suicidality**

Suicidality outcome data were extracted from free text fields using an NLP program adapted specifically for and found to be accurate in screening for presence of suicidality within electronic health records, of which the author was part of the validation process (see Downs et al., 2017). The NLP program initially identifies mentions of suicidality in two ways: variations in “suicid\*” (e.g. suicidal, suicide), as well as associated phrases (e.g. “kill myself/herself/himself/themselves”, “want to die”, “take their own life”) and methods of suicidality (e.g. “overdose”, “hanging”). The program then differentiates between negative mentions of suicidality (e.g. “denies suicidal ideation”, “not suicidal” “risk of suicide: low”), and positive mentions of suicidality (e.g. “reported suicidal thoughts”, “with suicidal intent”, “XXX had contemplated suicide”); for full details of the NLP program protocol see Downs et al. (2017)

#### **Exposure Variable: Depression, Irritability & Individual Profiles**

Exposure variable data were extracted from structured fields and free text within CRIS.

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Exposure to depression was identified by clinician report in structured fields outlining a diagnosis of depressive disorder according to ICD-10 criteria (F32.0). Data on irritability were extracted from clinical notes using NLP, the method for which has been published previously and shown to be valid with this database (Jackson et al., 2018; Jackson et al., 2017). Individuals were allocated to the irritability cohort if there had been at least one positive mention of irritability, identified by the presence of a variation on “irrit\*” (e.g. “irritability”, “irritable”) within the free text (e.g. progress notes, clinical letters, etc.).

Three distinct profile variables were created using the data extracted for depression and irritability from the data as exposure variables. Of these three, two were depressive profiles: depression with co-occurring irritability (DWI), and depression with no co-occurring irritability (DNI). In order to be included in the DWI sample, an individual had to have a diagnosis of depression as well as a mention of irritability within a 28-day period either side of receiving their depression diagnosis; any mentions of irritability outside of that window were considered ineligible to be identified as co-occurring with depression. All remaining individuals with depression diagnoses were allocated to the DNI group. The remaining profile, irritability without co-occurring depression (IND), consisted of those with identified irritability but never having received a diagnosis of depression.

### **Covariates**

A range of clinical and demographic variables was extracted and included in the analysis as covariates. Demographic variables included sex, age at ASD diagnosis, age at first contact with CAMHS, age of first suicidal event. Data on ethnicity (‘White’, ‘Black’ ‘Asian’, ‘Mixed’, ‘Other/Not stated’; as outlined by UK Office of National Statistics), level of neighbourhood deprivation based on UK census data, divided into three tiers (‘Least

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deprived’, ‘Moderately deprived’, ‘Most deprived’), and caregiver mental health status were also extracted. Clinical data were collected regarding both co-occurring psychiatric disorders based on ICD-10 diagnostic criteria, and co-occurring neurodevelopmental disorders of attention deficit hyperactivity disorder (ADHD; ICD-10, F90), and intellectual disability (ID; ICD-10, F70-79). Information around prescription of psychotropic medications (antidepressants, antipsychotics) was also extracted. Baseline level of adaptive functioning was collected, measured by scores on the Children’s Global Assessment Scale (CGAS, Shaffer et al., 1983).

### **Ethical Approval**

Ethical approval for this study fell under an existing approval for use of the CRIS database for empirical study, granted by the Oxfordshire Ethics Committee, as part of a wider study using the CRIS database (ref: 08/H0606/71+5, see Appendix C). Approval for this project specifically was sought and granted by CRIS ethics committee (ref: 15-104, see Appendix D).

### **Data Analysis**

Statistical analysis was conducted using STATA version 13 (Statacorp, 2013). Following extraction from CRIS, the raw datasets had to be combined and cleaned prior to analysis being possible. Sample characteristics were analysed, with group differences tested using chi-square tests of independence for comparison of frequencies, and independent t-tests were conducted to test for difference in means. A series of multivariate binary logistic regression analyses were conducted to explore variables as potential risk factors for suicidality, with Odds Ratios (OR) calculated as measure of effect size.

### Results

An initial sample of 1950 youth with ASD was identified. After screening for exclusion criteria, 636 were removed; the final sample consisted of 1314 adolescents with ASD.

#### Sample Characteristics

Sample characteristics for the total sample was presented in Table 1. The sample consisted of 1314 adolescents with an ASD diagnosis, and was predominantly male (78.4%), with the gender ratio of approximately 4:1 appearing representative of that in reported in community ASD populations. The mean age at first contact with services was 15.27 (SD=1.43, range =13.01-17.94); mean age at ASD diagnosis was 14.98 (SD=1.80, range 6.65-17.95). Individuals came from a variety of ethnicities, with ‘White’ the most common (56.23%), followed by ‘Black’ (19.77%). The sample was evenly split in terms of level of neighbourhood deprivation, and 22.88% of the sample had caregivers with identified mental health difficulties. Several types of psychotropic medication prescriptions were identified, the most common of which were antipsychotics (21.23%), followed by antidepressants (14.84%). A range of psychological disorders were identified amongst the sample: depression (9.36%); anxiety (2.36%); psychotic disorder (8.37%); conduct disorder (10.27%); eating disorder (1.22%); tic disorder (1.52%); obsessive-compulsive disorder (5.48%). Diagnoses of co-occurring neurodevelopmental disorders of Attention Deficit Hyperactivity Disorder (ADHD; 20.62%) and Intellectual Disability (ID; 28.46%); 36.53% were also reported to have displayed irritability. The mean score on the CGAS, measuring level of baseline function, was 46.55 (SD=15.08, range=4-92), scoring within the “obvious problems” range.



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Table 1

*Sociodemographic and Clinical Characteristics of total sample.*

| Sample Characteristic                         | Total Sample<br>(n=1314) |
|---|--------------------------|
| Sex   |                          |
| Male  | 686 (78.4)               |
| Female  | 189 (21.6)               |
| Age at ASD diagnosis, mean (SD)               | 14.85 (1.90)             |
| Age of first contact with services, mean (SD) | 15.28 (1.43)             |
| Ethnicity                                     |                          |
| White   | 492 (56.23)              |
| Black   | 173 (19.77)              |
| Asian   | 40 (4.57)                |
| Mixed   | 78 (8.91)                |
| Other or Not stated                           | 92 (10.51)               |
| Level of neighbourhood deprivation            |                          |
| Least deprived                                | 319 (39.33)              |
| Moderately deprived                           | 240 (29.59)              |
| Most deprived                                 | 252 (31.07)              |
| Caregiver mental health difficulties          | 253 (22.88)              |
| Medication                                    |                          |
| Antidepressant                                | 195 (14.84)              |
| Antipsychotic                                 | 279 (21.23)              |
| Co-occurring Psychological Disorders          |                          |
| Depression                                    | 123 (9.36)               |
| Anxiety Disorder                              | 31 (2.36)                |
| Psychosis                                     | 110 (8.37)               |
| Conduct Disorder                              | 135 (10.27)              |
| Eating Disorder                               | 16 (1.22)                |
| Tic Disorder                                  | 20 (1.52)                |
| OCD   | 72 (5.48)                |
| Irritability                                  | 480 (36.53)              |
| Co-occurring Neurodevelopmental Disorders     |                          |
| ADHD  | 271 (20.62)              |
| Intellectual Disability                       | 249 (28.46)              |
| Baseline function                             |                          |
| CGAS Score, mean (SD)                         | 46.55 (15.08)            |

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### **Suicidality**

Sample characteristics are presented for the non-suicidal and suicidal samples in Table 2. Of the sample, 50.17% reported suicidality at least once during their time in contact with services. In comparison to the non-suicidal sample, the suicidal group had a higher proportion of females ( $\chi^2 (1) = 40.00, p < .001$ ), and higher mean age at ASD diagnosis ( $t (1312) = -3.79, p < .001$ ). Sample ethnicity was significantly different, with the suicidal sample having higher proportions of individuals from 'white' and 'mixed' backgrounds ( $\chi^2 (4) = 20.67, p < .001$ ), as well as a higher percentage of youth with caregivers with mental health difficulties ( $\chi^2 (1) = 19.67, p < .001$ ). There were significantly higher rates in the suicidal sample of both antidepressants ( $\chi^2 (1) = 84.43, p < .001$ ), and antipsychotics ( $\chi^2 (1) = 23.35, p < .001$ ). In terms of psychological disorders, the suicidal sample showed higher rates of depression ( $\chi^2 (1) = 96.43, p < .001$ ), psychotic disorder ( $\chi^2 (1) = 46.38, p < .001$ ), and OCD ( $\chi^2 (1) = 11.07, p = 0.001$ ); a higher proportion of irritability was also reported for the suicidal sample ( $\chi^2 (1) = 108.19, p < .001$ ). Of the neurodevelopmental disorders identified, there was a significantly lower proportion of ID in the suicidal sample ( $\chi^2 (1) = 45.68, p < .001$ ); the suicidal sample also showed significant higher score on the CGAS at baseline ( $t (1174) = -1.78, p = 0.08$ ).

### **Risk factors for Suicidality**

Unless mentioned otherwise, all associations reported are positive.

### **Hypothesis 1: Depression**

Sample Characteristics for the Depression sample are presented in Table 3. Of the depression cohort, 73.17% reported suicidality. The first analysis assessed the role of depression as a

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Table 2

*Sociodemographic and Clinical Characteristics of suicidal and non-suicidal cohorts.*

| Sample Characteristic                            | Total Sample (n=1314)       |                         | Test statistic value (df) | p-value |
|--|-----------------------------|-------------------------|---------------------------|---------|
|  | Non-Suicidal Sample (n=875) | Suicidal Sample (n=439) |                           |         |
| <b>Sex</b>                                       |                             |                         |                           |         |
| Male   | 686 (78.4)                  | 272 (61.96)             | $\chi^2$ (1)=40.00        | <.001   |
| Female   | 189 (21.6)                  | 167 (38.04)             |                           |         |
| Age at ASD diagnosis, mean (SD)                  | 14.85 (1.90)                | 15.24 (1.55)            | $t$ (1312) = -3.79        | <.001   |
| Age of first contact with services, mean (SD)    | 15.28 (1.43)                | 15.25 (1.29)            | $t$ (916) = - 0.30        | 0.77    |
| Age at first report of suicidality, mean (SD)    | N/A                         | 15.45 (1.39)            |                           |         |
| <b>Ethnicity</b>                                 |                             |                         |                           |         |
| White  | 492 (56.23)                 | 288 (65.6)              | $\chi^2$ (4)=20.67        | <.001   |
| Black  | 173 (19.77)                 | 66 (15.03)              |                           |         |
| Asian  | 40 (4.57)                   | 20 (4.56)               |                           |         |
| Mixed  | 78 (8.91)                   | 45 (10.25)              |                           |         |
| Other or Not stated                              | 92 (10.51)                  | 20 (4.56)               |                           |         |
| <b>Level of neighbourhood deprivation</b>        |                             |                         |                           |         |
| Least deprived                                   | 319 (39.33)                 | 180 (43.06)             | $\chi^2$ (2)=2.28         | 0.32    |
| Moderately deprived                              | 240 (29.59)                 | 124 (29.67)             |                           |         |
| Most deprived                                    | 252 (31.07)                 | 114 (27.27)             |                           |         |
| Caregiver mental health difficulties             | 131 (18.63)                 | 122 (30.27)             | $\chi^2$ (1)=19.67        | <.001   |
| <b>Medication</b>                                |                             |                         |                           |         |
| Antidepressant                                   | 74 (8.46)                   | 121 (27.56)             | $\chi^2$ (1)=84.43        | <.001   |
| Antipsychotic                                    | 152 (17.37)                 | 127 (28.93)             | $\chi^2$ (1)=23.35        | <.001   |
| <b>Co-occurring Psychological Disorders</b>      |                             |                         |                           |         |
| Depressive Disorder                              | 33 (3.77)                   | 90 (20.5)               | $\chi^2$ (1)=96.43        | <.001   |
| Anxiety Disorder                                 | 15 (1.71)                   | 16 (3.64)               | $\chi^2$ (1)=4.73         | 0.03    |
| Psychosis  | 41 (4.69)                   | 69 (15.72)              | $\chi^2$ (1)=46.38        | <.001   |
| Conduct Disorder                                 | 82 (9.37)                   | 53 (12.07)              | $\chi^2$ (1)=2.34         | 0.13    |
| Eating Disorder                                  | 9 (1.03)                    | 7 (1.59)                | $\chi^2$ (1)=0.78         | 0.38    |
| Tic Disorder                                     | 12 (1.37)                   | 8 (1.82)                | $\chi^2$ (1)=.40          | 0.53    |
| OCD  | 35 (4.00)                   | 37 (8.43)               | $\chi^2$ (1)=11.07        | 0.001   |
| Irritability                                     | 234 (26.74)                 | 246 (56.04)             | $\chi^2$ (1)=108.19       | <.001   |
| <b>Co-occurring Neurodevelopmental Disorders</b> |                             |                         |                           |         |
| ADHD   | 182 (20.8)                  | 89 (20.27)              | $\chi^2$ (1)=.05          | 0.82    |
| Intellectual Disability                          | 249 (28.46)                 | 52 (11.85)              | $\chi^2$ (1)=45.68        | <.001   |
| <b>Baseline function</b>                         |                             |                         |                           |         |
| CGAS Score, mean (SD)                            | 45.98 (16.29)               | 47.61 (12.51)           | $t$ (1174)=-1.78          | 0.08    |

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Table 3

*Sociodemographic and Clinical Characteristics of depression cohort.*

| Sample Characteristic                            | Total Sample (n=123)       |                        | Test statistic value (df) | p-value | Percentage of Total Cohort |
|--|----------------------------|------------------------|---------------------------|---------|----------------------------|
|  | Non-Suicidal Sample (n=33) | Suicidal Sample (n=90) |                           |         |                            |
| <b>Sex</b>                                       |                            |                        |                           |         |                            |
| Male   | 25 (75.76)                 | 43 (47.78)             | $\chi^2 (1)=7.65$         | 0.006   | 9.91%                      |
| Female   | 8 (24.24)                  | 47 (52.22)             |                           |         | 29.10%                     |
| Age at ASD diagnosis, mean (SD)                  | 15.24 (1.65)               | 15.59 (1.42)           | $t (121) = -1.14$         | 0.27    |                            |
| Age of first contact with services, mean (SD)    | 15.29 (1.38)               | 15.50 (1.29)           | $t (115) = -0.73$         | 0.47    |                            |
| Age at first report of suicidality, mean (SD)    | N/A                        | 15.50 (1.36)           |                           |         |                            |
| <b>Ethnicity</b>                                 |                            |                        |                           |         |                            |
| White  | 22 (66.67)                 | 60 (66.67)             | $\chi^2 (4)=6.35$         | 0.17    | 17.89%                     |
| Black  | 4 (12.12)                  | 18 (20)                |                           |         | 12.72%                     |
| Asian  | 2 (6.06)                   | 5 (5.56)               |                           |         | 17.50%                     |
| Mixed  | 3 (9.09)                   | 7 (7.78)               |                           |         | 12.82%                     |
| Other or Not stated                              | 2 (6.06)                   | 0 (0)                  |                           |         | 2.17%                      |
| <b>Level of neighbourhood deprivation</b>        |                            |                        |                           |         |                            |
| Least deprived                                   | 13 (43.33)                 | 36 (42.86)             | $\chi^2 (2)=2.30$         | 0.89    | 15.36%                     |
| Moderately deprived                              | 10 (33.33)                 | 25 (29.76)             |                           |         | 14.58%                     |
| Most deprived                                    | 7 (23.33)                  | 23 (27.38)             |                           |         | 11.90%                     |
| Caregiver mental health difficulties             | 11 (35.48)                 | 30 (34.09)             | $\chi^2 (1)=0.02$         | 0.89    | 16.21%                     |
| <b>Medication</b>                                |                            |                        |                           |         |                            |
| Antidepressant                                   | 13 (39.39)                 | 53 (58.89)             | $\chi^2 (1)=3.69$         | 0.055   | 33.85%                     |
| Antipsychotic                                    | 14 (42.42)                 | 25 (27.78)             | $\chi^2 (1)=2.39$         | 0.12    | 13.98%                     |
| <b>Co-occurring Psychological Disorders</b>      |                            |                        |                           |         |                            |
| Anxiety Disorder                                 | 4 (12.12)                  | 3 (3.33)               | $\chi^2 (1)=3.47$         | 0.06    | 22.58%                     |
| Conduct Disorder                                 | 4 (12.12)                  | 7 (7.78)               | $\chi^2 (1)=0.56$         | 0.46    | 10.00%                     |
| Psychosis  | 6 (18.18)                  | 21 (23.33)             | $\chi^2 (1)=0.37$         | 0.54    | 20.00%                     |
| Eating Disorder                                  | 0 (0)                      | 2 (2.22)               | $\chi^2 (1)=0.75$         | 0.39    | 12.50%                     |
| Tic Disorder                                     | 1 (3.03)                   | 0 (0)                  | $\chi^2 (1)=2.75$         | 0.10    | 5.00%                      |
| OCD  | 4 (12.12)                  | 5 (5.56)               | $\chi^2 (1)=1.53$         | 0.22    | 12.50%                     |
| Irritability                                     | 19 (57.58)                 | 65 (72.22)             | $\chi^2 (1)=2.39$         | 0.12    | 17.50%                     |
| <b>Co-occurring Neurodevelopmental Disorders</b> |                            |                        |                           |         |                            |
| ADHD   | 8 (24.24)                  | 9 (10.00)              | $\chi^2 (1)=4.11$         | 0.043   | 6.27%                      |
| Intellectual Disability                          | 8 (24.24)                  | 7 (7.78)               | $\chi^2 (1)=6.11$         | 0.013   | 6.02%                      |
| <b>Baseline function</b>                         |                            |                        |                           |         |                            |
| CGAS Score, mean (SD)                            | 44.03 (12.63)              | 50.34 (11.01)          | $t (119) =-1.78$          | 0.009   |                            |

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risk factor for suicidality in adolescents with ASD. A multivariate binary logistic regression analysis was conducted, undergoing four iterations: Model 1 included depression as a sole predictor; Model 2 adjusted for sociodemographic factors; Model 3 further adjusted for both psychological and neurodevelopmental disorders; Model 4 was the final iteration, including psychotropic medications (see Table 4).

After adjusting for sociodemographic factors, co-occurring diagnoses and psychotropic medication, depression remained significantly associated with suicidality (OR 3.18, 1.94-5.21). In terms of sociodemographic factors, there was a significant association identified with gender (OR 0.56, 0.41-0.77), with females more likely to report suicidality; additionally, having a caregiver with mental health difficulties was also significantly associated with suicidality (OR 1.54, 1.10-2.14). Psychotic disorder was the only other psychological disorder found to be associated with suicidality (OR 2.15, 1.25-3.68), whilst ID was found to have a negative association (OR 0.33, 0.22-0.49) with individuals significantly less likely to be in the suicidal group. Lastly, individuals were more likely to be in the suicidal sample if taking antidepressants (OR 2.08, 1.39-3.11), or antipsychotics (OR 1.56, 1.06-2.30).

### **Hypothesis 2: Irritability**

Sample Characteristics for the Irritability sample are presented in Table 5. Of the irritability cohort, 51.25% reported suicidality. The second analysis assessed the role of irritability as a risk factor for suicidality. A multivariate binary logistic regression analysis was conducted, undergoing four iterations: Model 1 included irritable as a sole predictor; Model 2 adjusted for sociodemographic factors; Model 3 adjusted for all, bar depression, co-occurring diagnoses; Model 4 adjusted for psychotropic medications (see Table 6).

After adjusting for sociodemographic factors, co-occurring diagnoses and psychotropic

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Table 4

## *Multivariate Binary Logistic Regression Analysis of the Association between Suicidality and Depression in adolescents with ASD.*

| Variable                                  | Model 1: Crude Model |                         |       |         | Model 2: Adjusting for Sociodemographic Factors |                         |      |         | Model 3: Adjusting for Co-occurring Diagnoses |                         |       |         | Model 4: Fully Adjusted Model |                         |       |         |
|---|----------------------|-------------------------|-------|---------|---|-------------------------|------|---------|---|-------------------------|-------|---------|-------------------------------|-------------------------|-------|---------|
|   | OR                   | 95% Confidence Interval |       | p-value | aOR   | 95% Confidence Interval |      | p-value | aOR   | 95% Confidence Interval |       | p-value | aOR                           | 95% Confidence Interval |       | p-value |
|   |                      | OR                      | Lower |         |   | Upper                   | OR   |         |   | Lower                   | Upper |         |                               | OR                      | Lower |         |
| Depression                                | 6.58                 | 4.33                    | 9.99  | <.001   | 4.86  | 3.08                    | 7.68 | <.001   | 4.08  | 2.54                    | 6.54  | <.001   | 3.18                          | 1.94                    | 5.21  | <.001   |
| Sex                                       |                      |                         |       |         |   |                         |      |         |   |                         |       |         |                               |                         |       |         |
| Female                                    |                      |                         |       |         | Reference                                       |                         |      |         | Reference                                     |                         |       |         | Reference                     |                         |       |         |
| Male                                      |                      |                         |       |         | 0.53  | 0.39                    | 0.71 | <.001   | 0.54  | 0.40                    | 0.73  | <.001   | 0.56                          | 0.41                    | 0.77  | <.001   |
| Age at ASD Diagnosis                      |                      |                         |       |         | 1.04  | 0.96                    | 1.13 | 0.36    | 1.02  | 0.94                    | 1.11  | 0.60    | 1.01                          | 0.93                    | 1.11  | 0.76    |
| Ethnicity                                 |                      |                         |       |         |   |                         |      |         |   |                         |       |         |                               |                         |       |         |
| White                                     |                      |                         |       |         | Reference                                       |                         |      |         | Reference                                     |                         |       |         | Reference                     |                         |       |         |
| Black                                     |                      |                         |       |         | 0.66  | 0.45                    | 0.96 | 0.031   | 0.70  | 0.47                    | 1.05  | 0.084   | 0.75                          | 0.50                    | 1.13  | 0.17    |
| Asian                                     |                      |                         |       |         | 0.89  | 0.47                    | 1.70 | 0.73    | 0.87  | 0.45                    | 1.70  | 0.69    | 0.91                          | 0.46                    | 1.79  | 0.78    |
| Mixed                                     |                      |                         |       |         | 0.95  | 0.60                    | 1.51 | 0.84    | 0.95  | 0.60                    | 1.53  | 0.85    | 1.02                          | 0.63                    | 1.64  | 0.94    |
| Other or Not stated                       |                      |                         |       |         | 0.45  | 0.23                    | 0.87 | 0.019   | 0.50  | 0.25                    | 0.99  | 0.048   | 0.55                          | 0.27                    | 1.10  | 0.09    |
| Level of neighbourhood deprivation        |                      |                         |       |         |   |                         |      |         |   |                         |       |         |                               |                         |       |         |
| Least deprived                            |                      |                         |       |         | Reference                                       |                         |      |         | Reference                                     |                         |       |         | Reference                     |                         |       |         |
| Moderately deprived                       |                      |                         |       |         | 0.84  | 0.60                    | 1.17 | 0.31    | 0.82  | 0.58                    | 1.16  | 0.26    | 0.83                          | 0.59                    | 1.18  | 0.30    |
| Most deprived                             |                      |                         |       |         | 0.91  | 0.65                    | 1.28 | 0.60    | 0.89  | 0.62                    | 1.27  | 0.52    | 0.95                          | 0.66                    | 1.36  | 0.77    |
| Family Characteristics                    |                      |                         |       |         |   |                         |      |         |   |                         |       |         |                               |                         |       |         |
| Caregiver Mental health difficulties      |                      |                         |       |         | 1.73  | 1.26                    | 2.37 | 0.001   | 1.53  | 1.11                    | 2.13  | 0.01    | 1.54                          | 1.10                    | 2.14  | 0.011   |
| Co-occurring Psychological Disorders      |                      |                         |       |         |   |                         |      |         |   |                         |       |         |                               |                         |       |         |
| Anxiety Disorder                          |                      |                         |       |         |   |                         |      |         | 1.43  | 0.61                    | 3.34  | 0.41    | 1.18                          | 0.49                    | 2.81  | 0.71    |
| Psychosis                                 |                      |                         |       |         |   |                         |      |         | 3.04  | 1.85                    | 5.00  | <.001   | 2.15                          | 1.25                    | 3.68  | 0.005   |
| Conduct Disorder                          |                      |                         |       |         |   |                         |      |         | 1.26  | 0.80                    | 2.00  | 0.32    | 1.11                          | 0.69                    | 1.80  | 0.66    |
| Tic Disorder                              |                      |                         |       |         |   |                         |      |         | 0.85  | 0.31                    | 2.36  | 0.76    | 0.84                          | 0.30                    | 2.36  | 0.75    |
| Eating Disorder                           |                      |                         |       |         |   |                         |      |         | 1.53  | 0.44                    | 5.34  | 0.50    | 1.55                          | 0.44                    | 5.47  | 0.50    |
| OCD                                       |                      |                         |       |         |   |                         |      |         | 1.65  | 0.91                    | 3.00  | 0.10    | 1.25                          | 0.67                    | 2.33  | 0.48    |
| Co-occurring Neurodevelopmental Disorders |                      |                         |       |         |   |                         |      |         |   |                         |       |         |                               |                         |       |         |
| ADHD                                      |                      |                         |       |         |   |                         |      |         | 0.90  | 0.63                    | 1.30  | 0.59    | 0.87                          | 0.60                    | 1.26  | 0.46    |
| Intellectual Disability                   |                      |                         |       |         |   |                         |      |         | 0.36  | 0.24                    | 0.52  | <.001   | 0.33                          | 0.22                    | 0.49  | <.001   |
| Psychotropic Medication                   |                      |                         |       |         |   |                         |      |         |   |                         |       |         |                               |                         |       |         |
| Antidepressant use                        |                      |                         |       |         |   |                         |      |         |   |                         |       |         | 2.08                          | 1.39                    | 3.11  | <.001   |
| Antipsychotic use                         |                      |                         |       |         |   |                         |      |         |   |                         |       |         | 1.56                          | 1.06                    | 2.30  | 0.025   |
| Pseudo r-square                           |                      | 5.40%                   |       |         |   | 8.71%                   |      |         |   | 13.10%                  |       |         |                               | 14.53%                  |       |         |
| Chi-square                                |                      | 90.34, df=1, p<.001.    |       |         |   | 118.82, df=10, p<.001.  |      |         |   | 177.99, df=18, p<.001.  |       |         |                               | 198.16, df=20, p<.001.  |       |         |

## SUICIDALITY RISK FACTORS ADOLESCENTS WITH ASD

Table 5

### *Sociodemographic and Clinical Characteristics of irritability cohort.*

| Sample Characteristic                            | Total Sample (n=480)        |                         | Test statistic value (df) | p-value | Percentage of Total Cohort |
|--|-----------------------------|-------------------------|---------------------------|---------|----------------------------|
|  | Non-Suicidal Sample (n=234) | Suicidal Sample (n=246) |                           |         |                            |
| <b>Sex</b>                                       |                             |                         |                           |         |                            |
| Male   | 181 (77.35)                 | 143 (58.13)             | $\chi^2(1)=20.20$         | <.001   | 47.23%                     |
| Female   | 53 (22.65)                  | 103 (41.87)             |                           |         | 82.54%                     |
| Age at ASD diagnosis, mean (SD)                  | 15.14 (1.75)                | 15.20 (1.63)            | $t(478)=-0.39$            | 0.69    |                            |
| Age of first contact with services, mean (SD)    | 15.32 (1.43)                | 15.23 (1.32)            | $t(400)=0.62$             | 0.53    |                            |
| Age at first report of suicidality, mean (SD)    | N/A                         | 15.42 (1.38)            |                           |         |                            |
| <b>Ethnicity</b>                                 |                             |                         |                           |         |                            |
| White  | 148 (63.25)                 | 168 (68.29)             | $\chi^2(4)=6.89$          | 0.14    | 64.23%                     |
| Black  | 47 (20.09)                  | 37 (15.04)              |                           |         | 48.55%                     |
| Asian  | 10 (4.27)                   | 12 (4.88)               |                           |         | 55.00%                     |
| Mixed  | 13 (5.56)                   | 21 (8.54)               |                           |         | 43.59%                     |
| Other or Not stated                              | 16 (6.84)                   | 8 (3.25)                |                           |         | 26.09%                     |
| <b>Level of neighbourhood deprivation</b>        |                             |                         |                           |         |                            |
| Least deprived                                   | 77 (35.32)                  | 96 (41.03)              | $\chi^2(2)=1.65$          | 0.44    | 54.23%                     |
| Moderately deprived                              | 73 (33.49)                  | 74 (31.62)              |                           |         | 61.25%                     |
| Most deprived                                    | 68 (31.19)                  | 64 (27.35)              |                           |         | 52.38%                     |
| Caregiver mental health difficulties             | 43 (22.16)                  | 73 (31.33)              | $\chi^2(1)=4.49$          | 0.034   | 45.85%                     |
| <b>Medication</b>                                |                             |                         |                           |         |                            |
| Antidepressant                                   | 40 (17.09)                  | 96 (39.02)              | $\chi^2(1)=28.40$         | <.001   | 69.74%                     |
| Antipsychotic                                    | 78 (33.33)                  | 102 (41.46)             | $\chi^2(1)=3.38$          | 0.07    | 64.52%                     |
| <b>Co-occurring Psychological Disorders</b>      |                             |                         |                           |         |                            |
| Depression                                       | 19 (8.12)                   | 65 (26.42)              | $\chi^2(1)=27.83$         | <.001   | 68.29%                     |
| Anxiety Disorder                                 | 6 (2.56)                    | 12 (4.88)               | $\chi^2(1)=1.78$          | 0.18    | 58.06%                     |
| Psychosis  | 19 (8.12)                   | 59 (23.98)              | $\chi^2(1)=22.18$         | <.001   | 70.91%                     |
| Conduct Disorder                                 | 29 (12.39)                  | 32 (13.01)              | $\chi^2(1)=0.04$          | 0.84    | 45.19%                     |
| Eating Disorder                                  | 3 (1.28)                    | 6 (2.44)                | $\chi^2(1)=0.87$          | 0.35    | 56.25%                     |
| Tic Disorder                                     | 2 (0.85)                    | 4 (1.63)                | $\chi^2(1)=0.58$          | 0.45    | 30.00%                     |
| OCD  | 14 (5.98)                   | 25 (10.16)              | $\chi^2(1)=2.81$          | 0.09    | 54.17%                     |
| <b>Co-occurring Neurodevelopmental Disorders</b> |                             |                         |                           |         |                            |
| ADHD   | 61 (26.07)                  | 56 (22.76)              | $\chi^2(1)=.71$           | 0.40    | 43.17%                     |
| Intellectual Disability                          | 74 (31.62)                  | 32 (13.01)              | $\chi^2(1)=24.15$         | <.001   | 42.57%                     |
| <b>Baseline function</b>                         |                             |                         |                           |         |                            |
| CGAS Score, mean (SD)                            | 43.07 (15.79)               | 47.29 (13.24)           | $t(448)=-1.78$            | 0.002   |                            |

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Table 6

## Multivariate Binary Logistic Regression Analysis of the Association between Suicidality and Irritability in adolescents with ASD.

| Variable                                  | Model 1: Crude Model  |                         |      |         | Model 2: Adjusting for Sociodemographic Factors |                         |      |         | Model 3: Adjusting for Co-occurring Diagnoses |                         |          |         | Model 4: Adjusting for Psychotropic medication |                         |      |         | Model 5: Full Model after adjusting for Depression |                         |      |         |
|---|-----------------------|-------------------------|------|---------|---|-------------------------|------|---------|---|-------------------------|----------|---------|--|-------------------------|------|---------|--|-------------------------|------|---------|
|   | OR                    | 95% Confidence Interval |      | p-value | aOR   | 95% Confidence Interval |      | p-value | aOR   | 95% Confidence Interval |          | p-value | aOR  | 95% Confidence Interval |      | p-value | aOR  | 95% Confidence Interval |      | p-value |
| Irritability                              | 3.49                  | 2.74                    | 4.44 | <.001   | 3.37  | 2.56                    | 4.44 | <.001   | 3.06  | 2.28                    | 4.097043 | <.001   | 2.61   | 1.92                    | 3.54 | <.001   | 2.47   | 1.82                    | 3.37 | <.001   |
| Sex                                       |                       |                         |      |         |   |                         |      |         |   |                         |          |         |  |                         |      |         |  |                         |      |         |
| Female                                    |                       |                         |      |         | Reference                                       |                         |      |         | Reference                                     |                         |          |         | Reference                                      |                         |      |         | Reference  |                         |      |         |
| Male                                      |                       |                         |      |         | 0.51  | 0.38                    | 0.68 | <.001   | 0.52  | 0.38                    | 0.70888  | <.001   | 0.55   | 0.40                    | 0.76 | <.001   | 0.57   | 0.41                    | 0.78 | <.001   |
| Age at ASD Diagnosis                      |                       |                         |      |         | 1.05  | 0.96                    | 1.14 | 0.30    | 1.03  | 0.94                    | 1.119124 | 0.56    | 1.02   | 0.93                    | 1.11 | 0.69    | 1.01   | 0.92                    | 1.10 | 0.84    |
| Ethnicity                                 |                       |                         |      |         |   |                         |      |         |   |                         |          |         |  |                         |      |         |  |                         |      |         |
| White                                     |                       |                         |      |         | Reference                                       |                         |      |         | Reference                                     |                         |          |         | Reference                                      |                         |      |         | Reference  |                         |      |         |
| Black                                     |                       |                         |      |         | 0.73  | 0.50                    | 1.08 | 0.11    | 0.74  | 0.49                    | 1.100628 | 0.14    | 0.77   | 0.51                    | 1.16 | 0.21    | 0.77   | 0.51                    | 1.16 | 0.21    |
| Asian                                     |                       |                         |      |         | 0.99  | 0.51                    | 1.90 | 0.97    | 0.93  | 0.48                    | 1.82019  | 0.83    | 0.97   | 0.49                    | 1.91 | 0.92    | 0.92   | 0.46                    | 1.84 | 0.81    |
| Mixed                                     |                       |                         |      |         | 1.17  | 0.73                    | 1.86 | 0.52    | 1.12  | 0.69                    | 1.805027 | 0.65    | 1.15   | 0.71                    | 1.86 | 0.58    | 1.15   | 0.71                    | 1.88 | 0.57    |
| Other or Not stated                       |                       |                         |      |         | 0.47  | 0.24                    | 0.95 | 0.034   | 0.50  | 0.25                    | 1.03     | 0.06    | 0.55   | 0.27                    | 1.11 | 0.10    | 0.56   | 0.28                    | 1.15 | 0.11    |
| Level of neighbourhood deprivation        |                       |                         |      |         |   |                         |      |         |   |                         |          |         |  |                         |      |         |  |                         |      |         |
| Least deprived                            |                       |                         |      |         | Reference                                       |                         |      |         | Reference                                     |                         |          |         | Reference                                      |                         |      |         | Reference  |                         |      |         |
| Moderately deprived                       |                       |                         |      |         | 0.77  | 0.55                    | 1.08 | 0.13    | 0.75  | 0.53                    | 1.060066 | 0.10    | 0.76   | 0.54                    | 1.09 | 0.13    | 0.77   | 0.54                    | 1.10 | 0.15    |
| Most deprived                             |                       |                         |      |         | 0.85  | 0.60                    | 1.21 | 0.37    | 0.81  | 0.57                    | 1.167489 | 0.26    | 0.87   | 0.60                    | 1.25 | 0.44    | 0.88   | 0.61                    | 1.27 | 0.51    |
| Family Characteristics                    |                       |                         |      |         |   |                         |      |         |   |                         |          |         |  |                         |      |         |  |                         |      |         |
| Caregiver Mental health difficulties      |                       |                         |      |         | 1.76  | 1.28                    | 2.41 | <.001   | 1.56  | 1.12                    | 2.168969 | 0.010   | 1.54   | 1.10                    | 2.15 | 0.01    | 1.48   | 1.05                    | 2.07 | 0.024   |
| Co-occurring Psychological Disorders      |                       |                         |      |         |   |                         |      |         |   |                         |          |         |  |                         |      |         |  |                         |      |         |
| Depression                                |                       |                         |      |         |   |                         |      |         |   |                         |          |         |  |                         |      |         | 2.83   | 1.71                    | 4.68 | <.001   |
| Anxiety Disorder                          |                       |                         |      |         |   |                         |      |         | 1.38  | 0.59                    | 3.21     | 0.46    | 1.12   | 0.47                    | 2.66 | 0.80    | 1.06   | 0.44                    | 2.54 | 0.89    |
| Psychosis                                 |                       |                         |      |         |   |                         |      |         | 2.41  | 1.45                    | 4.00     | <.001   | 1.96   | 1.13                    | 3.37 | 0.02    | 1.91   | 1.10                    | 3.32 | 0.023   |
| Conduct Disorder                          |                       |                         |      |         |   |                         |      |         | 1.13  | 0.70                    | 1.83     | 0.61    | 1.08   | 0.66                    | 1.77 | 0.76    | 1.10   | 0.68                    | 1.81 | 0.69    |
| Eating Disorder                           |                       |                         |      |         |   |                         |      |         | 1.23  | 0.35                    | 4.37     | 0.75    | 1.32   | 0.37                    | 4.72 | 0.67    | 0.94   | 0.33                    | 2.66 | 0.90    |
| Tic Disorder                              |                       |                         |      |         |   |                         |      |         | 1.24  | 0.34                    | 4.51     | 0.88    | 0.90   | 0.31                    | 2.58 | 0.84    | 1.29   | 0.35                    | 4.69 | 0.70    |
| OCD                                       |                       |                         |      |         |   |                         |      |         | 1.32  | 0.72                    | 2.40     | 0.37    | 1.05   | 0.56                    | 1.96 | 0.88    | 1.14   | 0.61                    | 2.14 | 0.69    |
| Co-occurring Neurodevelopmental Disorders |                       |                         |      |         |   |                         |      |         |   |                         |          |         |  |                         |      |         |  |                         |      |         |
| ADHD                                      |                       |                         |      |         |   |                         |      |         | 0.79  | 0.55                    | 1.15     | 0.22    | 0.79   | 0.54                    | 1.15 | 0.23    | 0.83   | 0.57                    | 1.21 | 0.34    |
| Intellectual Disability                   |                       |                         |      |         |   |                         |      |         | 0.33  | 0.22                    | 0.48     | <.001   | 0.33   | 0.22                    | 0.48 | <.001   | 0.34   | 0.23                    | 0.50 | <.001   |
| Medication                                |                       |                         |      |         |   |                         |      |         |   |                         |          |         |  |                         |      |         |  |                         |      |         |
| Antidepressant use                        |                       |                         |      |         |   |                         |      |         |   |                         |          |         | 2.12   | 1.43                    | 3.16 | <.001   | 1.71   | 1.13                    | 2.60 | 0.011   |
| Antipsychotic use                         |                       |                         |      |         |   |                         |      |         |   |                         |          |         | 1.23   | 0.83                    | 1.83 | 0.30    | 1.24   | 0.83                    | 1.86 | 0.28    |
| Pseudo r-square                           | 6.37%                 |                         |      |         | 10.53%  |                         |      |         | 14.52%  |                         |          |         | 15.68%   |                         |      |         | 16.95%   |                         |      |         |
| Chi-square                                | 106.67, df=1, p<.001. |                         |      |         | 143.70, df=10, p<.001.                          |                         |      |         | 198.11, df=18, p<.001.                        |                         |          |         | 213.94, df=20, p<.001.                         |                         |      |         | 231.16, df=21, p<.001.                             |                         |      |         |



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medication, irritability was found to be significantly associated with suicidality (OR 2.61, 1.92-3.54). In terms of sociodemographic factors, there was a significant association identified with gender (OR 0.55, 0.40-0.76), with females more likely to report suicidality; additionally, having a caregiver with mental health difficulties was also significantly associated with suicidality (OR 1.54, 1.10-2.15). Psychotic disorder was the only psychological disorder found to be associated with suicidality (OR 1.96, 1.13-3.37), whilst ID was found to have a negative association (OR 0.33, 0.22-0.48), with individuals significantly less likely to be in the suicidal group. Lastly, in terms of medication, only antidepressants were found to be associated with suicidality (OR 2.12, 1.43-3.16).

### **Hypothesis 3: Depression & Irritability**

Depression was added to the final model (Model 5; see Table 6), in order to establish whether irritability remained a significant predictor of suicidality after controlling for depression (see Table 6). Even after controlling for depression, irritability remained significantly associated with suicidality (OR 2.47, 1.82-3.37). Gender continued to have a significant association with suicidality (OR 0.57, 0.41-0.78), with suicidality more likely amongst females; caregiver mental health was also a significant predictor of suicidality (OR 1.48, 1.05-2.07). Psychotic disorder was the only psychological disorder found to have significant association (OR 1.91, 1.10-3.32), whilst ID was found to have a negative association (OR 0.33, 0.22-0.48), with the likelihood of suicidality being significantly lower for those with an ID diagnosis.

Antidepressants were also found to be associated with suicidality (OR 2.12, 1.43-3.16).

### **Hypothesis 4: Individual Profiles**

Sample characteristics are presented in Table 7. The final research question investigated the relationship between suicidality and the three distinct profiles: DWI, DNI, and IND. The

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analysis underwent two phases, the first examining the role of each profile as a predictor for suicidality, the second comparing each profile with the other. For the first phase, a multivariate binary logistic regression analysis was conducted, undergoing six iterations: Model 1 included DWI as a sole predictor; Model 2 adjusted for DNI; Model 3 adjusted for IND; Model 4 adjusted for sociodemographic factors; Model 5 adjusted for all other co-occurring diagnoses; Model 6 was the final iteration, including psychotropic medications (see Table 8).

Significant associations with suicidality were found for all three profiles: DNI (OR 7.51, 2.69-20.96), DWI (OR 4.53, 2.56-8.03), and IND (OR 2.70, 1.96-3.74). Of the sociodemographic factors, gender was found to be significant, with suicidality more likely amongst females (OR 0.57, 0.41-0.78), as well as caregiver mental health difficulties (OR 1.45, 1.03-2.03). Psychotic disorder was the only psychological disorder found to have significant association (OR 1.95, 1.12-3.39), whilst ID was found to have a negative association (OR 0.34, 0.23-0.50), with the likelihood of suicidality being significantly lower for those with an ID diagnosis. Antidepressant use was also found to be associated with suicidality (OR 2.12, 1.43-3.16).

In order to compare relationship to suicidality between profiles, a composite dummy variable was created using DWI as the reference group. The dummy variable was included in a multivariate binary logistic regression analysis, which underwent four iterations: Model 1 consisted of the profile composite variable only; Model 2 adjusted for sociodemographic factors; Model 3 further adjusted for the remaining disorders; Model 4 was the final iteration, including psychotropic medications (see Table 9).

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Table 7

*Sociodemographic and Clinical Characteristics of for each profile presentation.*

| Sample Characteristic                         | Depression with Co-occurring Irritability |                            |                           |         | Depression without Co-occurring Irritability |                             |                           |         | Irritability without Co-occurring Depression |               |                           |         |
|---|---|----------------------------|---------------------------|---------|--|-----------------------------|---------------------------|---------|--|---------------|---------------------------|---------|
|   | Total Sample (n=34)                       |                            | Test statistic value (df) | p-value | Total Sample (n=89)                          |                             | Test statistic value (df) | p-value | Total Sample (n=396)                         |               | Test statistic value (df) | p-value |
| Non-Suicidal Sample (n=6)                     | Suicidal Sample (n=28)                    | Non-Suicidal Sample (n=27) |                           |         | Suicidal Sample (n=62)                       | Non-Suicidal Sample (n=215) |                           |         | Suicidal Sample (n=181)                      |               |                           |         |
| Sex   |   |                            |                           |         |  |                             |                           |         |  |               |                           |         |
| Male  | 3 (50)                                    | 15 (53.57)                 | $\chi^2(1)=0.025$         | 0.87    | 22 (81.48)                                   | 28 (45.16)                  | $\chi^2(1)=10.08$         | 0.001   | 166 (77.21)                                  | 113 (62.43)   | $\chi^2(1)=10.31$         | 0.001   |
| Female  | 3 (50)                                    | 13 (46.43)                 |                           |         | 5 (18.52)                                    | 34 (54.84)                  |                           |         | 49 (22.79)                                   | 68 (37.57)    |                           |         |
| Age at ASD diagnosis, mean (SD)               | 14.71 (1.60)                              | 15.37 (1.65)               | $t(32)=-0.89$             | 0.38    | 15.36 (1.67)                                 | 15.68 (1.30)                | $t(87)=-0.99$             | 0.33    | 15.16 (1.76)                                 | 15.08 (1.67)  | $t(394)=0.42$             | 0.68    |
| Age of first contact with services, mean (SD) | 14.23 (1.08)                              | 15.28 (1.30)               | $t(30)=-1.69$             | 0.10    | 15.52 (1.35)                                 | 15.59 (1.28)                | $t(83)=-.22$              | 0.83    | 15.36 (1.44)                                 | 15.13 (1.31)  | $t(319)=1.47$             | 0.14    |
| Age at first report of suicidality, mean (SD) | N/A                                       | 15.26 (1.35)               |                           |         | N/A  | 15.60 (1.37)                |                           |         | N/A  | 15.40 (1.39)  |                           |         |
| Ethnicity                                     |   |                            |                           |         |  |                             |                           |         |  |               |                           |         |
| White   | 3 (50)                                    | 21 (75)                    | $\chi^2(3)=5.61$          | 0.13    | 19 (70.37)                                   | 39 (62.90)                  | $\chi^2(4)=3.53$          | 0.47    | 136 (63.26)                                  | 132 (67.96)   | $\chi^2(4)=5.92$          | 0.21    |
| Black   | 1 (16.67)                                 | 5 (17.86)                  |                           |         | 3 (11.11)                                    | 13 (20.97)                  |                           |         | 45 (20.93)                                   | 26 (14.36)    |                           |         |
| Asian   | 1 (16.67)                                 | 2 (7.14)                   |                           |         | 1 (3.70)                                     | 3 (4.84)                    |                           |         | 8 (3.72)                                     | 8 (4.42)      |                           |         |
| Mixed   | 0 (0)                                     | 0 (0)                      |                           |         | 3 (11.11)                                    | 7 (11.29)                   |                           |         | 11 (5.12)                                    | 16 (8.84)     |                           |         |
| Other or Not stated                           | 1 (16.67)                                 | 0 (0)                      |                           |         | 1 (3.70)                                     | 0 (0)                       |                           |         | 15 (6.98)                                    | 8 (4.42)      |                           |         |
| Level of neighbourhood deprivation            |   |                            |                           |         |  |                             |                           |         |  |               |                           |         |
| Least deprived                                | 3 (60)                                    | 11 (44)                    | $\chi^2(2)=1.51$          | 0.47    | 10 (40)                                      | 25 (42.37)                  | $\chi^2(2)=0.09$          | 0.96    | 70 (35.00)                                   | 72 (41.38)    | $\chi^2(2)=1.71$          | 0.42    |
| Moderately deprived                           | 2 (40)                                    | 8 (32)                     |                           |         | 8 (32)                                       | 17 (28.81)                  |                           |         | 66 (33.00)                                   | 54 (31.03)    |                           |         |
| Most deprived                                 | 0 (0)                                     | 6 (24)                     |                           |         | 7 (28)                                       | 17 (28.81)                  |                           |         | 64 (32.00)                                   | 48 (27.59)    |                           |         |
| Caregiver mental health difficulties          | 4 (80)                                    | 12 (42.86)                 | $\chi^2(1)=2.34$          | 0.13    | 7 (26.92)                                    | 18 (30.00)                  | $\chi^2(1)=.08$           | 0.77    | 36 (20.45)                                   | 53 (31.36)    | $\chi^2(1)=5.36$          | 0.021   |
| Medication                                    |   |                            |                           |         |  |                             |                           |         |  |               |                           |         |
| Antidepressant                                | 2 (33.33)                                 | 15 (53.57)                 | $\chi^2(1)=0.81$          | 0.37    | 11 (40.74)                                   | 38 (61.29)                  | $\chi^2(1)=3.21$          | 0.07    | 32 (14.88)                                   | 52 (28.73)    | $\chi^2(1)=11.27$         | 0.001   |
| Antipsychotic                                 | 2 (33.33)                                 | 10 (35.71)                 | $\chi^2(1)=0.01$          | 0.91    | 12 (44.44)                                   | 15 (24.19)                  | $\chi^2(1)=3.65$          | 0.06    | 68 (31.63)                                   | 78 (43.09)    | $\chi^2(1)=5.55$          | 0.018   |
| Co-occurring Psychological Disorders          |   |                            |                           |         |  |                             |                           |         |  |               |                           |         |
| Anxiety Disorder                              | 1 (16.67)                                 | 0 (0)                      | $\chi^2(1)=4.80$          | 0.028   | 3 (11.11)                                    | 3 (4.84)                    | $\chi^2(1)=1.18$          | 0.28    | 3 (1.40)                                     | 9 (4.97)      | $\chi^2(1)=4.28$          | 0.039   |
| Psychosis                                     | 2 (33.33)                                 | 10 (35.71)                 | $\chi^2(1)=0.01$          | 0.91    | 4 (14.81)                                    | 11 (17.74)                  | $\chi^2(1)=0.12$          | 0.74    | 13 (6.05)                                    | 40 (22.10)    | $\chi^2(1)=21.85$         | <.001   |
| Conduct Disorder                              | 0 (0)                                     | 2 (7.14)                   | $\chi^2(1)=0.46$          | 0.50    | 4 (14.81)                                    | 5 (8.06)                    | $\chi^2(1)=0.94$          | 0.33    | 27 (12.56)                                   | 26 (14.36)    | $\chi^2(1)=.28$           | 0.6     |
| Eating Disorder                               | 0 (0)                                     | 0 (0)                      |                           |         | 0 (0)  | 2 (3.23)                    | $\chi^2(1)=0.89$          | 0.35    | 3 (1.40)                                     | 4 (2.21)      | $\chi^2(1)=0.38$          | 0.54    |
| Tic Disorder                                  | 0 (0)                                     | 0 (0)                      | $\chi^2(1)=.40$           | 0.53    | 1 (3.70)                                     | 0 (0)                       | $\chi^2(1)=2.32$          | 0.13    | 2 (0.93)                                     | 4 (2.21)      | $\chi^2(1)=1.08$          | 0.3     |
| OCD   | 0 (0)                                     | 0 (0)                      | $\chi^2(1)=11.07$         | 0.001   | 4 (14.81)                                    | 5 (8.06)                    | $\chi^2(1)=0.94$          | 0.33    | 11 (5.12)                                    | 20 (11.05)    | $\chi^2(1)=4.79$          | 0.029   |
| Co-occurring Neurodevelopmental Disorders     |   |                            |                           |         |  |                             |                           |         |  |               |                           |         |
| ADHD  | 2 (33.33)                                 | 3 (10.71)                  | $\chi^2(1)=2.02$          | 0.16    | 6 (22.22)                                    | 6 (9.68)                    | $\chi^2(1)=2.54$          | 0.11    | 55 (25.58)                                   | 49 (27.07)    | $\chi^2(1)=.11$           | 0.74    |
| Intellectual Disability                       | 0 (0)                                     | 1 (.57)                    | $\chi^2(1)=0.22$          | 0.64    | 8 (29.63)                                    | 6 (9.68)                    | $\chi^2(1)=5.65$          | 0.017   | 70 (32.56)                                   | 28 (15.47)    | $\chi^2(1)=15.41$         | <.001   |
| Baseline function                             |   |                            |                           |         |  |                             |                           |         |  |               |                           |         |
| CGAS Score, mean (SD)                         | 45.00 (4.24)                              | 52.33 (12.60)              | $t(31)=-1.39$             | 0.17    | 43.81 (13.93)                                | 49.47 (10.23)               | $t(86)=-2.12$             | 0.037   | 43.23 (15.99)                                | 45.97 (13.65) | $t(365)=-1.76$            | 0.08    |

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predictor for suicidality, the second comparing each profile with the other. For the first phase, a multivariate binary logistic regression analysis was conducted, undergoing six iterations: Model 1 included DWI as a sole predictor; Model 2 adjusted for DNI; Model 3 adjusted for IND; Model 4 adjusted for sociodemographic factors; Model 5 adjusted for all other co-occurring diagnoses; Model 6 was the final iteration, including psychotropic medications (see Table 8).

Significant associations with suicidality were found for all three profiles: DNI (OR 7.51, 2.69-20.96), DWI (OR 4.53, 2.56-8.03), and IND (OR 2.70, 1.96-3.74). Of the sociodemographic factors, gender was found to be significant, with suicidality more likely amongst females (OR 0.57, 0.41-0.78), as well as caregiver mental health difficulties (OR 1.45, 1.03-2.03). Psychotic disorder was the only psychological disorder found to have significant association (OR 1.95, 1.12-3.39), whilst ID was found to have a negative association (OR 0.34, 0.23-0.50), with the likelihood of suicidality being significantly lower for those with an ID diagnosis. Antidepressant use was also found to be associated with suicidality (OR 2.12, 1.43-3.16).

In order to compare relationship to suicidality between profiles, a composite dummy variable was created using DWI as the reference group. The dummy variable was included in a multivariate binary logistic regression analysis, which underwent four iterations: Model 1 consisted of the profile composite variable only; Model 2 adjusted for sociodemographic factors; Model 3 further adjusted for the remaining disorders; Model 4 was the final iteration, including psychotropic medications (see Table 9).

After adjusting for covariates, the analysis found that the only significant difference in relationship to suicidality between profiles was between DWI and IND, with those with

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Table 8

## Multivariate Binary Logistic Regression Analysis of the Association between Suicidality and Individual Profiles in adolescents with ASD.

| Variable   | Model 1: Crude Model |                         |         | Model 2: Adjusting for Depression without Co-occurring Irritability |                         |         | Model 3: Adjusting for Irritability without Co-occurring Depression |                         |         | Model 4: Adjusting for Sociodemographic Factors |                         |         | Model 5: Adjusting for All Co-occurring Diagnoses |                         |         | Model 6: Fully Adjusted Model |                         |         |       |       |           |      |       |       |
|--|----------------------|-------------------------|---------|---|-------------------------|---------|---|-------------------------|---------|---|-------------------------|---------|---|-------------------------|---------|-------------------------------|-------------------------|---------|-------|-------|-----------|------|-------|-------|
|  | OR                   | 95% Confidence Interval | p-value | aOR   | 95% Confidence Interval | p-value | aOR   | 95% Confidence Interval | p-value | aOR   | 95% Confidence Interval | p-value | aOR   | 95% Confidence Interval | p-value | aOR                           | 95% Confidence Interval | p-value |       |       |           |      |       |       |
| <b>Profiles</b>                                  |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               |                         |         |       |       |           |      |       |       |
| Depression with Co-occurring Irritability        | 9.87                 | 4.05                    | 24.02   | <.001   | 11.26                   | 4.62    | 27.43   | <.001                   | 17.42   | 7.10  | 42.75                   | <.001   | 13.49   | 4.97                    | 36.56   | <.001                         | 9.37                    | 3.41    | 25.75 | <.001 | 7.51      | 2.69 | 20.96 | <.001 |
| Depression without Co-occurring Irritability     |                      |                         |         |   | 5.54                    | 3.47    | 8.85  | <.001                   | 8.57    | 5.29  | 13.89                   | <.001   | 6.66  | 3.93                    | 11.28   | <.001                         | 5.75                    | 3.34    | 9.91  | <.001 | 4.53      | 2.56 | 8.03  | <.001 |
| Irritability without Co-occurring Depression     |                      |                         |         |   |                         |         |   |                         | 3.14    | 2.42  | 4.08                    | <.001   | 3.19  | 2.36                    | 4.29    | <.001                         | 3.01                    | 2.20    | 4.11  | <.001 | 2.70      | 1.96 | 3.74  | <.001 |
| <b>Sex</b>                                       |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               |                         |         |       |       |           |      |       |       |
| Female   |                      |                         |         |   |                         |         |   |                         |         |   |                         |         | Reference   |                         |         |                               | Reference               |         |       |       | Reference |      |       |       |
| Male   |                      |                         |         |   |                         |         |   |                         | 0.54    | 0.40  | 0.73                    | <.001   | 0.55  | 0.40                    | 0.76    | <.001                         | 0.57                    | 0.41    | 0.78  | <.001 | 0.57      | 0.41 | 0.78  | <.001 |
| Age at ASD Diagnosis                             |                      |                         |         |   |                         |         |   |                         | 1.02    | 0.94  | 1.12                    | 0.59    | 1.01  | 0.92                    | 1.10    | 0.84                          | 1.01                    | 0.92    | 1.10  | 0.84  | 1.01      | 0.92 | 1.10  | 0.91  |
| <b>Ethnicity</b>                                 |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               |                         |         |       |       |           |      |       |       |
| White  |                      |                         |         |   |                         |         |   |                         |         |   |                         |         | Reference   |                         |         |                               | Reference               |         |       |       | Reference |      |       |       |
| Black  |                      |                         |         |   |                         |         |   |                         | 0.72    | 0.49  | 1.06                    | 0.10    | 0.74  | 0.49                    | 1.11    | 0.15                          | 0.77                    | 0.51    | 1.16  | 0.21  | 0.77      | 0.51 | 1.16  | 0.21  |
| Asian  |                      |                         |         |   |                         |         |   |                         | 0.94    | 0.48  | 1.85                    | 0.87    | 0.90  | 0.45                    | 1.80    | 0.77                          | 0.94                    | 0.47    | 1.87  | 0.85  | 0.94      | 0.47 | 1.87  | 0.85  |
| Mixed  |                      |                         |         |   |                         |         |   |                         | 1.19    | 0.74  | 1.91                    | 0.48    | 1.16  | 0.71                    | 1.89    | 0.55                          | 1.19                    | 0.73    | 1.94  | 0.49  | 1.19      | 0.73 | 1.94  | 0.49  |
| Other or Not stated                              |                      |                         |         |   |                         |         |   |                         | 0.50    | 0.25  | 1.00                    | 0.05    | 0.53  | 0.26                    | 1.08    | 0.08                          | 0.56                    | 0.27    | 1.14  | 0.11  | 0.56      | 0.27 | 1.14  | 0.11  |
| <b>Level of neighbourhood deprivation</b>        |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               |                         |         |       |       |           |      |       |       |
| Least deprived                                   |                      |                         |         |   |                         |         |   |                         |         |   |                         |         | Reference   |                         |         |                               | Reference               |         |       |       | Reference |      |       |       |
| Moderately deprived                              |                      |                         |         |   |                         |         |   |                         | 0.78    | 0.56  | 1.11                    | 0.17    | 0.76  | 0.54                    | 1.09    | 0.14                          | 0.77                    | 0.54    | 1.11  | 0.16  | 0.77      | 0.54 | 1.11  | 0.16  |
| Most deprived                                    |                      |                         |         |   |                         |         |   |                         | 0.88    | 0.62  | 1.25                    | 0.48    | 0.85  | 0.59                    | 1.22    | 0.37                          | 0.89                    | 0.61    | 1.28  | 0.52  | 0.89      | 0.61 | 1.28  | 0.52  |
| <b>Family Characteristics</b>                    |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               |                         |         |       |       |           |      |       |       |
| Caregiver Mental health difficulties             |                      |                         |         |   |                         |         |   |                         | 1.61    | 1.16  | 2.23                    | <.001   | 1.44  | 1.03                    | 2.02    | 0.033                         | 1.45                    | 1.03    | 2.03  | 0.034 | 1.45      | 1.03 | 2.03  | 0.034 |
| <b>Co-occurring Psychological Disorders</b>      |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               |                         |         |       |       |           |      |       |       |
| Anxiety Disorder                                 |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               | 1.26                    | 0.53    | 3.00  | 0.60  | 1.11      | 0.46 | 2.65  | 0.82  |
| Psychosis  |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               | 2.33                    | 1.39    | 3.90  | <.001 | 1.95      | 1.12 | 3.39  | 0.018 |
| Conduct Disorder                                 |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               | 1.17                    | 0.72    | 1.88  | 0.53  | 1.11      | 0.68 | 1.81  | 0.69  |
| Eating Disorder                                  |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               | 0.94                    | 0.33    | 2.68  | 0.90  | 0.92      | 0.32 | 2.63  | 0.88  |
| Tic Disorder                                     |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               | 1.26                    | 0.35    | 4.54  | 0.72  | 1.32      | 0.37 | 4.74  | 0.67  |
| OCD  |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               | 1.39                    | 0.75    | 2.56  | 0.29  | 1.16      | 0.62 | 2.18  | 0.64  |
| <b>Co-occurring Neurodevelopmental Disorders</b> |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               |                         |         |       |       |           |      |       |       |
| ADHD   |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               | 0.84                    | 0.58    | 1.23  | 0.37  | 0.83      | 0.57 | 1.21  | 0.34  |
| Intellectual Disability                          |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               | 0.34                    | 0.23    | 0.51  | <.001 | 0.34      | 0.23 | 0.50  | <.001 |
| <b>Medication</b>                                |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               |                         |         |       |       |           |      |       |       |
| Antidepressant use                               |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               |                         |         |       |       | 1.73      | 1.14 | 2.62  | 0.010 |
| Antipsychotic use                                |                      |                         |         |   |                         |         |   |                         |         |   |                         |         |   |                         |         |                               |                         |         |       |       | 1.24      | 0.83 | 1.85  | 0.29  |
| Pseudo r-square                                  | 2.12%                |                         |         | 5.52%   |                         |         | 9.99%   |                         |         | 13.17%  |                         |         | 16.64%  |                         |         | 17.26%                        |                         |         |       |       |           |      |       |       |
| X-square   | 35.56, df=1, p<.001. |                         |         | 92.48, df=2, p<.001.  |                         |         | 167.20, df=3, p<.001.   |                         |         | 179.59, df=12, p<.001.                          |                         |         | 226.96, df=20, p<.001.                            |                         |         | 235.42, df=22, p<.001.        |                         |         |       |       |           |      |       |       |

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Table 9

*Multivariate Binary Logistic Regression Analysis comparing strength of Association between Suicidality and Individual Profiles in adolescents with ASD.*

| Variable   | Model 1: Crude Model |                         |         | Model 2: Adjusting for Sociodemographic Factors |                         |         | Model 3: Adjusting for All Co-occurring Diagnoses |                         |         | Model 4: Fully Adjusted Model |                         |         |      |      |       |       |
|--|----------------------|-------------------------|---------|---|-------------------------|---------|---|-------------------------|---------|-------------------------------|-------------------------|---------|------|------|-------|-------|
|  | OR                   | 95% Confidence Interval | p-value | aOR   | 95% Confidence Interval | p-value | aOR   | 95% Confidence Interval | p-value | aOR                           | 95% Confidence Interval | p-value |      |      |       |       |
| <b>Profiles</b>                                  |                      |                         |         |   |                         |         |   |                         |         |                               |                         |         |      |      |       |       |
| Depression with Co-occurring Irritability        | Reference            |                         |         | Reference                                       |                         |         | Reference   |                         |         | Reference                     |                         |         |      |      |       |       |
| Depression without Co-occurring Irritability     | 0.49                 | 0.18                    | 1.33    | 0.16  | 0.48                    | 0.16    | 1.46  | 0.20                    | 0.60    | 0.20                          | 1.86                    | 0.38    | 0.59 | 0.19 | 1.84  | 0.37  |
| Irritability without Co-occurring Depression     | 0.18                 | 0.07                    | 0.45    | <.001   | 0.23                    | 0.08    | 0.63  | <.001                   | 0.30    | 0.11                          | 0.85                    | 0.023   | 0.34 | 0.12 | 0.98  | 0.047 |
| <b>Sex</b>                                       |                      |                         |         |   |                         |         |   |                         |         |                               |                         |         |      |      |       |       |
| Female   | Reference            |                         |         | Reference                                       |                         |         | Reference   |                         |         | Reference                     |                         |         |      |      |       |       |
| Male   |                      |                         |         | 0.44  | 0.28                    | 0.69    | <.001   | 0.51                    | 0.32    | 0.81                          | <.001                   | 0.54    | 0.34 | 0.86 | 0.01  |       |
| Age at ASD Diagnosis                             |                      |                         |         | 0.95  | 0.83                    | 1.08    | 0.41  | 0.91                    | 0.80    | 1.04                          | 0.18                    | 0.91    | 0.79 | 1.04 | 0.17  |       |
| <b>Ethnicity</b>                                 |                      |                         |         |   |                         |         |   |                         |         |                               |                         |         |      |      |       |       |
| White  | Reference            |                         |         | Reference                                       |                         |         | Reference   |                         |         | Reference                     |                         |         |      |      |       |       |
| Black  |                      |                         |         | 0.91  | 0.51                    | 1.62    | 0.75  | 0.89                    | 0.48    | 1.63                          | 0.71                    | 0.97    | 0.52 | 1.78 | 0.91  |       |
| Asian  |                      |                         |         | 1.04  | 0.40                    | 2.75    | 0.93  | 1.02                    | 0.38    | 2.76                          | 0.97                    | 1.11    | 0.40 | 3.04 | 0.84  |       |
| Mixed  |                      |                         |         | 1.60  | 0.70                    | 3.69    | 0.27  | 1.69                    | 0.71    | 4.03                          | 0.24                    | 1.73    | 0.71 | 4.17 | 0.23  |       |
| Other or Not stated                              |                      |                         |         | 0.35  | 0.11                    | 1.09    | 0.07  | 0.36                    | 0.11    | 1.14                          | 0.08                    | 0.38    | 0.12 | 1.22 | 0.10  |       |
| <b>Level of neighbourhood deprivation</b>        |                      |                         |         |   |                         |         |   |                         |         |                               |                         |         |      |      |       |       |
| Least deprived                                   | Reference            |                         |         | Reference                                       |                         |         | Reference   |                         |         | Reference                     |                         |         |      |      |       |       |
| Moderately deprived                              |                      |                         |         | 0.73  | 0.44                    | 1.19    | 0.21  | 0.73                    | 0.44    | 1.22                          | 0.23                    | 0.74    | 0.44 | 1.24 | 0.25  |       |
| Most deprived                                    |                      |                         |         | 0.95  | 0.57                    | 1.59    | 0.84  | 0.95                    | 0.56    | 1.64                          | 0.86                    | 0.99    | 0.57 | 1.72 | 0.98  |       |
| <b>Family Characteristics</b>                    |                      |                         |         |   |                         |         |   |                         |         |                               |                         |         |      |      |       |       |
| Caregiver Mental health difficulties             |                      |                         |         | 1.55  | 0.97                    | 2.46    | 0.07  | 1.35                    | 0.83    | 2.19                          | 0.22                    | 1.31    | 0.80 | 2.14 | 0.28  |       |
| <b>Co-occurring Psychological Disorders</b>      |                      |                         |         |   |                         |         |   |                         |         |                               |                         |         |      |      |       |       |
| Anxiety Disorder                                 |                      |                         |         |   |                         |         |   | 1.18                    | 0.39    | 3.52                          | 0.77                    | 1.08    | 0.36 | 3.27 | 0.89  |       |
| Psychosis  |                      |                         |         |   |                         |         |   | 2.72                    | 1.44    | 5.16                          | <.001                   | 2.37    | 1.16 | 4.83 | 0.018 |       |
| Conduct Disorder                                 |                      |                         |         |   |                         |         |   | 0.98                    | 0.51    | 1.91                          | 0.96                    | 0.98    | 0.50 | 1.95 | 0.96  |       |
| Eating Disorder                                  |                      |                         |         |   |                         |         |   | 1.24                    | 0.26    | 5.96                          | 0.79                    | 1.34    | 0.28 | 6.48 | 0.71  |       |
| Tic Disorder                                     |                      |                         |         |   |                         |         |   | 1.07                    | 0.21    | 5.50                          | 0.94                    | 1.04    | 0.21 | 5.28 | 0.96  |       |
| OCD  |                      |                         |         |   |                         |         |   | 1.27                    | 0.58    | 2.75                          | 0.55                    | 1.02    | 0.46 | 2.27 | 0.97  |       |
| <b>Co-occurring Neurodevelopmental Disorders</b> |                      |                         |         |   |                         |         |   |                         |         |                               |                         |         |      |      |       |       |
| ADHD   |                      |                         |         |   |                         |         |   | 1.00                    | 0.59    | 1.68                          | 0.99                    | 0.98    | 0.58 | 1.67 | 0.95  |       |
| Intellectual Disability                          |                      |                         |         |   |                         |         |   | 0.42                    | 0.25    | 0.70                          | <.001                   | 0.41    | 0.24 | 0.72 | <.001 |       |
| <b>Medication</b>                                |                      |                         |         |   |                         |         |   |                         |         |                               |                         |         |      |      |       |       |
| Antidepressant use                               |                      |                         |         |   |                         |         |   |                         |         |                               |                         |         | 1.86 | 1.13 | 3.07  | 0.015 |
| Antipsychotic use                                |                      |                         |         |   |                         |         |   |                         |         |                               |                         |         | 1.11 | 0.66 | 1.85  | 0.70  |
| Pseudo r-square                                  | 4.38%                |                         |         | 7.74%   |                         |         | 11.42%  |                         |         | 12.48%                        |                         |         |      |      |       |       |
| X-square   | 31.49, df=2, p<.001. |                         |         | 46.23, df=11, p<.001.                           |                         |         | 68.26, df=19, p<.001.                             |                         |         | 74.61, df=21, p<.001.         |                         |         |      |      |       |       |

After adjusting for covariates, the analysis found that the only significant difference in relationship to suicidality between profiles was between DWI and IND, with those with IND significantly less likely to be report suicidality than their DWI counterparts (OR 0.34, 0.12-0.98). Gender continued to be significant (OR 0.54, 0.34-0.86); however, caregiver mental health was no longer significant (OR 1.31, 0.80-2.14). Psychotic disorder remained the only other psychological disorder to be associated with suicidality (OR 2.37, 1.16-4.83), whilst ID was negatively associated with suicidality (OR 0.41, 0.24-0.72). Antidepressant use was associated with suicidality (OR 1.86, 1.13-3.07).

### **Discussion**

The aim of the study was to identify risk factors for suicidality in adolescents with ASD, specifically exploring the roles of depression and irritability as potential risk factors. Furthermore, this study compared the relationship between suicidality and individual depressive and irritability profiles. The key findings are presented and interpreted below, followed by discussion of the study's strengths and limitations, and the implications, both research and clinical, of the findings.

## Summary and Interpretations of Key Findings

### **Hypothesis 1. Depression is a risk factor for suicidality in adolescents with ASD.**

As expected, depression was found to be associated with suicidality, with an increased likelihood of suicidality for adolescents with ASD and co-occurring depression. This finding is in keeping with the current research on suicidality in adolescents with ASD (Chen et al., 2017; Mayes et al., 2013; Storch et al., 2013). It is also consistent with the findings of Pelton and Cassidy (2017), and the relationship between depression and suicidality proposed by IPTS (Silva et al., 2015).

**Hypothesis 2. Irritability is a significant risk factor for suicidality in adolescents with ASD.** As predicted, irritability was found to have association with suicidality, with those reported with irritability more likely to report suicidality, which is consistent with Mayes et al. (2013), who found behavioural difficulties associated with poor emotional regulation to be a significant risk factor for suicidality in youth with ASD. This finding is also consistent with IPTS, proposing labile mood to be associated with both thwarted belongingness and perceived burdensomeness (Silva et al., 2015).

**Hypothesis 3. Part of the relationship, if not all, between irritability and suicidality will be explained by depression.** After controlling for depression in the regression model, the effect size for irritability reduced, but the association with suicidality remained significant. This suggests that, whilst a proportion of initial association between irritability and suicidality was explained by depression, irritability may be a significant risk factor for suicidality in its own right.



**Hypothesis 4. Depression with co-occurring irritability (DWI) will be a stronger predictor for suicidality in adolescents with ASD than both depression without co-occurring irritability (DNI) and irritability without co-occurring depression (IND).** This is the first study to investigate specific depressive and behavioural profiles as potential risk factors for suicidality in adolescents with ASD. Analysis showed that both depressive profiles, DWI and DNI, were significant risk factors for suicidality, as was IND. However, when comparing magnitude of respective effect sizes, DWI was only found to be significantly different than IND, with likelihood of suicidality significantly higher amongst individuals with DWI than IND. There are several possible interpretations of these results. Firstly, the finding that individuals with DWI were significantly more likely than irritability without co-occurring depression to be suicidal suggests the presence of depression might intensify and increase the strength of association between irritability and suicidality. Secondly, the lack of difference found between DWI and DNI may indicate that DWI is not a stronger risk factor for suicidality than other depressive profiles; however, the DNI group was almost triple the size of the DWI cohort, and it is possible that the imbalance in group sizes may have impacted the analysis and obscured an actual difference that may have been visible had the groups matched in number.

The analysis also identified significant associations between several of the covariates included. Psychotic disorder was found to be significantly associated with suicidality throughout all statistical analyses after controlling for all other covariates. Furthermore, the results suggest that its inclusion, alongside other psychological disorders, reduced the effect size of both depression and irritability, suggesting that some of their effect was partially explained by the presence of psychotic disorder. Whilst no study has investigated psychotic disorder as a risk factor within this population, Karakoc Demirkaya, Tutkunkardas, and

Mukaddes (2016) reported significantly higher rates of psychotic features within their ASD suicidal sample. Within the context of IPTS, Silva et al. (2015) found psychotic disorders to be associated with suicidality, predicting both perceived burdensomeness and Acquired Capability for Suicide.

Surprisingly, the analysis found that female adolescents within the sample were almost twice as likely as male counterparts to report suicidality, which is contrary to the findings of Mayes et al. (2013), who reported being female to act as a protective factor against suicidality within their sample. A possible explanation for this is around increased vulnerability to depression: in typically-developing adolescents, the ratio of females to males affected by depression is 2:1 (Birmaher et al., 1996), whilst females with ASD are more likely to display internalising difficulties, like depression (Mandy et al., 2012). With its strong association with suicidality, it may be that being at higher risk of depression increases likelihood of suicidality in female adolescents with ASD due to greater probability of exposure to said risk factor.

Adolescents with co-occurring diagnoses of ID were significantly less likely to engage in suicidality. To the best of the author's knowledge, no previous study has reported a significant relationship between ID and suicidality in adolescents with ASD; however, Hardan and Sahl (1999) reported of their cohort of youth with developmental disorders, in which ASD was included, significantly lower rates of suicidality amongst those diagnosed with severe/profound mental retardation. Shtayermann (2007) reported severity of AS presentation to be negatively correlation with both suicidal ideation and peer victimisation, positing that individuals with more severe presentations might be more likely to receive support and supervision from teachers, reducing incidence of peer victimisation, and due its potential role as a proximal risk factor, reducing the likelihood of suicidal ideation.

Several of the analyses suggested that caregiver mental health difficulties may also be a risk factor for suicidality within this population. This is the first study to the author's knowledge to include caregiver mental health within the analysis; Karakoc Demirkaya et al. (2016) included both family history of lethal and nonlethal suicidal behaviours, and familial history of completed suicide, finding significantly higher rates within their suicidal sample, suggesting the role of family characteristics as risk factors. A possible explanation for this finding is that caregiver mental health may increase probability of an individual developing mental health difficulties which have already been identified as risk factors for suicidality in their own rights. For example, within typically-developing samples, adolescents with a depressed parent are more likely develop depression by three to four times (Rice & Rawal, 2011).

Medication was consistently found to be related to suicidality, with taking antidepressants associated with increased likelihood of suicidality. Furthermore, the inclusion of medication as a covariate appeared to reduce the size of effect for depression, irritability and psychotic disorder. Whilst a potential interpretation is that antidepressant use increases probability of suicidality, it may be that any effect of medication observed is better explained by alternative, already existing risk factors. For example, depressed individuals may be more likely to be prescribed antidepressants, and, given the role of depression as a risk factor for suicidality, part of the effect of antidepressants may actually be better explained by depression.

However, it remains a possibility that there is a unique relationship between antidepressant use and suicidality, separate to any associated psychological disorder: whilst found to reduce incidence of suicidality in adult samples, antidepressants have been associated with an increased risk of suicidality in children and adolescents (Nischal, Tripathi, Nischal, & Trivedi, 2011).

## **Strengths and Limitations**

A strength of this study was the large sample size, which increased the power of statistical tests in detecting significant differences, reducing the probability of wrongly rejecting any of the research hypotheses. Moreover, using data from the CRIS database allowed for rich variety of variables to be included and controlled for within the study, contributing to greater precision of analysis. However, the study was also impacted by several limitations.

Firstly, the construct of suicidality investigated in this study was a collective term encompassing suicidal ideation, behaviour and attempt. Whilst using such a definition is arguably clinically useful, the inability to distinguish between different suicidal phenomena makes it difficult to fully generalise the role of the risk factors identified across all types of suicidality; for example, a risk factor associated with suicidal ideation may only be related to ideation, and thus have no association with suicidal behaviour whatsoever. Mayes et al. (2013) found depression to be the single strongest predictor for suicidal ideation, but for suicide attempt the strongest predictors were suicidal ideation and mood dysregulation. Consequently, this study is limited by its use of suicidality as a collective term, as it is not possible to conclude from these results whether any of the associations found apply across all types of suicidality, or whether they relate to specific suicidal phenomena.

This study employed a cross-sectional design: whilst effective in both determining prevalence of an outcome, and identifying significant associations between factors and outcomes, a limitation of this design is that it is impossible to infer causality between risk factors and outcomes (i.e. suicidality). Consequently, it limits the conclusions able to be drawn from these findings. In the cases of the relationship between suicidality and all psychological risk factors identified, it is possible that suicidal adolescents with ASD are more likely to develop

such phenomena; conversely, it may be that adolescents with these characteristics are more likely to present with some element of suicidality. This study's design means that conclusions around such questions cannot be inferred from these results, and therefore requires further longitudinal analysis to examine any temporal relationships.

Whilst the richness of information available from the CRIS database was a strength of this study, it also acted as a potential limitation in terms of quality of data available. A significant proportion of data extracted came from clinical records (progress notes, clinical correspondence, etc.), and whilst beneficial in terms of amount of data available, clinical records tend to be more subject to opinion and therefore at higher risk of reporting bias. Furthermore, this study investigated suicidality within a clinical population, and therefore it is unclear whether these findings can be generalised to community samples of autistic adolescents.

Additionally, whilst the vast amount of data available allowed for the inclusion of multiple covariate variables, a limitation of cohort studies is that their observational nature makes it difficult to control for the influence of unaccounted confounding variables. Given that the highest proportion of variance accounted for by any of the statistical models analysed was 17.26%, this suggests that there are still several unaccounted variables which may influence the relationship between ASD and suicidality in adolescents.

This study employed an epidemiological approach, focusing on establishing both prevalence of suicidality and associated risk factors. Whilst this can be clinically useful, a limitation of this approach is that, in focusing solely on describing a population's characteristics, it provides no insight into the causal processes mediating between risk factors and suicidality, which psychological theory seeks to explain. Consequently, a limitation of this study is that

its findings offer little contribution to theoretical literature on suicidality. Furthermore, testing of psychological theory within this study was limited by the data available: sample size and limited availability of qualitative data prevented the possibility of conducting qualitative analysis, which could be helpful in identifying causal processes.

### **Research implications**

This study's findings suggest several avenues for further research. Firstly, the associations identified between suicidality and depression, irritability, and psychotic disorder, as well as depressive profiles, should be tested longitudinally using Cox Regression Analysis with Hazard Ratios for measures of effect size. This study's use of cross-sectional design, precludes inference of any causal relationship between these risk factors and suicidality, making longitudinal analysis essential to provide insight into the direction of relationship between factors and outcome e.g. whether depression precedes suicidality, or whether suicidal individuals are more likely to become depressed.

The use of suicidality as a collective term encompassing both suicidal ideation and behaviour prevents both differentiation between risk factors specifically for ideation and those associated with behaviour, and establishment of shared risk factors between the two phenomena. Future studies should investigate different aspects of suicidality as separate outcome variables to establish the nature of association between risk factors and individual suicidality presentations. Isolating ideation and behaviour as separate outcome variables could also help test the validity of IPTS in explaining suicidal phenomena in this population, and a prospective cohort design would probably best suit this research goal.

Future research should look at suicidal ideation as a possible risk factor for later suicidal behaviour. Mayes et al. (2013) found suicidal ideation to be the strongest single risk factor

for suicide attempt amongst their sample of youth with ASD; therefore, it could be helpful to investigate, as part of a longitudinal analysis, suicidal ideation as a possible mediator between risk factors identified in this study and subsequent suicidal behaviour.

Future study should aim to enhance understanding of causal mechanisms mediating relationships between risk factors and suicidality. Further investigation into individual profiles, both depressive and psychotic, and their relationship with suicidality could shed light on such mechanisms. Furthermore, future studies could attempt to investigate score profiles on validated psychometric measures and see how they may map onto different behavioural/psychological profiles to assist identification for such studies.

Despite its efficacy in identifying risk factors, epidemiological approaches provide little insight into such mechanisms. Theory-driven research could complement findings of epidemiological studies and further aid understanding of such mechanisms. For example, testing IPTS with individuals identified in this study as high-risk (e.g. depressed adolescents), and investigating the roles of Thwarted Belongingness, Perceived Burdensomeness and Acquired Capability for Suicide could help improve understanding of possible causal mechanisms between risk factors and suicidality. This could be accomplished using a prospective longitudinal design, with multiple check-in points, to improve appropriateness and quality of data collected; moreover, a smaller cohort size should be used to allow for gathering and analysis of both quantitative and qualitative data.

Another potential avenue could be specifically to investigate high-risk groups identified within this study (e.g. adolescents with ASD and co-occurring depression, irritability or psychotic disorder; individuals with caregivers with mental health difficulties), to further contribute to understanding of the causal processes mediating suicidality and psychological

factors.

Lastly, given the target population were adolescents, it is unclear whether these findings would be applicable for younger children with ASD: risk factors for suicidality may differ in a younger cohort, and therefore future study could benefit from including children alongside an adolescent sample.

### **Clinical implications**

These findings identify several areas for development of clinical practice. Firstly, these findings could help inform development of existing risk assessment protocol with the aim of minimising either risk of, or preventing escalation of, suicidality in adolescents with ASD. Those identified to be at high risk for suicidality (e.g. depressed adolescents) may benefit from more frequent risk assessment by services in order to reduce the likelihood of suicidality going unnoticed and therefore potentially escalating to engagement in life-threatening behaviours. Additionally, those noted to have increased irritability may benefit from psychological assessment, given its association with a range of psychological disorders in children and adolescents (McLaughlin et al., 2011), as well as impromptu risk screening. This type of early identification could help ensure that those requiring intervention do not get overlooked and receive appropriate support in a timely manner. Increased contact could also help gather more information about an individual's situation, which could add to their formulation and better inform development of appropriate person-centred intervention; should this process identify caregiver mental health difficulties, clinicians could consider including psychological support for caregivers as part of an intervention centred on the young person.

Identifying high-risk individuals would also be useful as it would allow for those involved in



an individual's care, professionals and family members alike, to be provided training in both identifying and managing the emergence of and/or increases in levels of risk or suicidality, hopefully reducing opportunity for escalation.

These findings could help inform development of interventions targeting suicidality. Using frameworks such as IPTS to understand the nature of the relationship between risk factors and suicidality could help inform the development of more bespoke interventions; for example, if depression is associated with Thwarted Belongingness and Perceived Burdensomeness, an intervention designed to reduce the likelihood of these experiences could be instrumental in reducing the likelihood of suicidality for autistic adolescents with co-occurring depression.

### **Conclusion**

In conclusion, the aim of this study was to identify risk factors for suicidality in adolescents with ASD. Specifically, it sought to understand the roles of depression and irritability as potential risk factors for suicidality with this population. This was the first study to investigate suicidality and ASD in a UK adolescent clinical cohort. It was also the first study to compare different profiles (DWI, DNI, IND) and the potential associations with suicidality. Cross-sectional analysis indicated a positive association between suicidality and depression, as well as with irritability even after controlling for the effect of depression. With regards to difference between individual profiles, a difference was identified between depression with co-occurring irritability and irritability without co-occurring depression only, with depression with co-occurring irritability increasing likelihood of suicidality. The results also suggested that psychotic disorders are associated with increased likelihood of suicidality, as well as being female, having a caregiver with mental health difficulties, and taking

antidepressants, whilst a diagnosis of ID was found to be negatively associated with suicidality. The findings also appear to provide preliminary support for the use of the IPTS model in understanding the suicidality in adolescents with ASD. Future research may wish to repeat this study using a longitudinal design in order to better understand the nature of the temporal relationship between risk factors and suicidality. Furthermore, studies may wish to explore the relationship between suicidality and distinct profiles, as well as investigating the high-risk groups identified here, to increase knowledge around causal mechanisms at play. Lastly, these findings have implications for clinical practice, informing both the review of existing risk management protocols, as well as the development of specific interventions designed to prevent or minimise risk of suicidality in adolescent with ASD.

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**Section C**  
**Appendices of Supporting Material**

## Appendix A: Search terms using in Review

PsychInfo:

1. autism\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
2. asd.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
3. autistic disorder.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
4. asperger\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
5. autistic spectrum disorder.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
6. pervasive developmental disorder.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
7. pdd-nos.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
8. (pervasive developmental disorder not otherwise specified).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
9. asperger's syndrome.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]

10. aspergers syndrome.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. suicid\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
13. exp Drug Overdoses/
14. parasuicid\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
15. overdos\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
16. drug overdos\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
17. self poison\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
18. ligature\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
19. exp Suicide/
20. exp Suicidal Ideation/
21. exp Attempted Suicide/

22. selfpoison\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
23. hanging\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
24. 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25. child\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
26. adolescen\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
27. youth.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
28. (young adj (people or person)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
29. teen\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
30. p?ediatric.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
31. young adult\*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
32. 25 or 26 or 27 or 28 or 29 or 30 or 31

Medline:

1. child\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
2. adolescen\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
3. youth.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
4. (young adj (people or person)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
5. teen\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
6. p?ediatric.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]



7. Young Adult/
8. young adult\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. autism\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
11. asd.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
12. autistic disorder.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
13. asperger\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
14. autistic spectrum disorder.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

15. pervasive developmental disorder.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
16. pdd-nos.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
17. (pervasive developmental disorder not otherwise specified).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
18. asperger's syndrome.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
19. aspergers syndrome.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
20. autistic disorder.sh.
21. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22. suicid\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

23. exp Drug Overdoses/
24. parasuicid\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
25. overdos\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
26. drug overdos\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
27. self poison\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
28. ligature\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
29. exp Suicide/
30. exp Suicidal Ideation/
31. exp Attempted Suicide/

32. selfpoison\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

33. hanging\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

34. suicide.sh.

35. 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33

36. 9 and 21 and 35

#### Web of Science:

1. TS=(child\* OR adolescen\* OR youth OR young person OR young people OR teen\* OR pediatric OR paediatric OR young adult)

*DocType=All document types; Language=All languages*

2. TS=(autis\* OR autism OR asd OR autistic disorder OR asperger\* OR autistic spectrum disorder OR pervasive developmental disorder OR pdd-nos OR pervasive developmental disorder not otherwise specified OR aspergers syndrome OR asperger's syndrome)

*DocType=All document types; Language=All languages;*

3. TS=(suicid\* OR drug overdos\* OR overdos\* OR parasuicid\* OR self poison\* OR self-poison\* OR selfpoison\* OR ligature\* OR suicidal ideation OR suicide attempt\* OR hanging\*)

*DocType=All document types; Language=All languages;*

4. #1 AND #2 AND #3

**Appendix B: CASP Framework for cohort studies (CASP, 2017)**

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## **Appendix C: NHS Ethics Approval**

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## **Appendix D: CRIS Ethics Application & Approval**

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## **Appendix E: End of study report**

### **Suicidality in adolescents with Autism Spectrum Disorders: investigating Depression and Irritability as risk factors in a UK clinical population**

#### **Introduction**

Suicidality, suicidal ideation and suicidal behaviour, is a significant health concern for adolescents with Autism Spectrum Disorders (ASD). Depression and Irritability have been identified as risk factors for suicidality in autistic adolescents. Autistic youth may have higher vulnerability to these factors than typically-developing adolescents. No study has compared the relationship between suicidality and different depressive profiles, nor used a UK clinical sample.

#### **Aims**

The aim of the study was to identify risk factors for suicidality in a clinical sample of adolescents with ASD, specifically exploring the roles of depression and irritability as potential risk factors. Furthermore, this study compared the relationship between suicidality and individual depressive and irritability profiles. Based on current knowledge, the following hypotheses were made:

**Hypothesis 1.** Depression will be identified as a significant risk factor for suicidality in adolescents with ASD.

**Hypothesis 2.** Irritability will be identified as a significant risk factor for suicidality in adolescents with ASD.

**Hypothesis 3.** Part of the relationship, if not all, between irritability and suicidality will be explained by depression.

**Hypothesis 4.** Depression with co-occurring irritability will be a stronger predictor for suicidality in adolescents with ASD than both depression without co-occurring irritability and irritability without co-occurring depression.

## Method

This clinical cohort study used archival data extracted from UK National Institute for Health Research Biomedical Research Centre for Mental Health records database. The sample consisted of 1314 adolescents (13+ years) who received an ICD-10 ASD diagnosis between 2008 and 2013. The study investigated the following variables:

- **Outcome Variable:** Suicidality (suicidal ideation and/or suicidal behaviour)
- **Main Exposure Variables:**
  - Depression,
  - Irritability
  - Specific profile presentations:
    - Depression with co-occurring irritability (DWI)
    - Depression without co-occurring irritability (DNI)
    - Irritability without co-occurring depression (IND)

## Results

Cross-sectional analysis found depression to be associated with higher likelihood of suicidality. Irritability was found to be associated with higher likelihood of suicidality, even after controlling for depression. DWI was a more significant predictor of suicidality than IND, but no different from DNI. Psychosis, being female, antidepressant use, and caregiver mental health difficulties were also positively associated with suicidality, but significantly less likely in individuals diagnosed with an intellectual disability.

## Conclusions

Results indicate multiple characteristics of adolescents with ASD at high-risk of suicidality. Early identification of high-risk individuals could help deliver timely intervention, potentially reducing both incidence and progression of suicidality.

## **Appendix F: Author guidelines of journal chosen for submission of empirical paper**

### **Research in Autism Spectrum Disorders – Guide for Authors**

#### **Editorial Process**

All submissions will first be checked against the Aims and Scope and Guide for Authors by the Editor-in-Chief. Papers found to conform, in principle, to the journal's remit and standards will be assigned to a handling Editor (an Associate Editor or the Editor-in-Chief) for further evaluation. If a paper meets the journal's criteria a minimum of two independent reviewers will be invited to comment on the paper's methodological rigour and significance. Based on these comments and additional opinions if necessary, the handling Editors will make a decision. All accepted papers will therefore have received comments from a minimum of two independent reviewers and be reviewed by one or more editors. **Please note that RASD currently operates single-blinded peer review.**

#### **Human and Animal Rights**

If the work involves the use of animal or human subjects, the author should ensure that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans <http://www.wma.net/en/30publications/10policies/b3/index.html>; EU Directive 2010/63/EU for animal experiments [http://ec.europa.eu/environment/chemicals/lab\\_animals/legislation\\_en.htm](http://ec.europa.eu/environment/chemicals/lab_animals/legislation_en.htm); Uniform Requirements for manuscripts submitted to Biomedical journals <http://www.icmje.org>. Authors should include a statement in the manuscript that informed consent was obtained for experimentation with human subjects. The privacy rights of human subjects must always be observed. All animal studies need to ensure they comply

with the ARRIVE guidelines. More information can be found

at <http://www.nc3rs.org.uk/page.asp?id=1357>

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### ***Elsevier Researcher Academy***

[Researcher Academy](#) is a free e-learning platform designed to support early and mid-career researchers throughout their research journey. The "Learn" environment at Researcher Academy offers several interactive modules, webinars, downloadable guides and resources to guide you through the process of writing for research and going through peer review. Feel

free to use these free resources to improve your submission and navigate the publication process with ease.

## **MANUSCRIPT PREPARATION & SUBMISSION**

### **Use of word processing software**

Files must be saved in the native format of the word processor and the text should be in 10-point Arial font, single-column format, double spaced, with standard 1 inch page margins (2.54 cm). Please keep the layout of the text as simple as possible, as most formatting codes will be replaced on processing the article. In particular, do not use the options to justify text or hyphenate words. However, do use bold face, italics, subscripts, superscripts etc. Note that source files of figures and text graphics will be required whether or not you embed them in the text. See also the section on Electronic artwork below for details on preparing figures and graphics.

### **Language (usage and editing services)**

Please write your text in good English (American or British usage is accepted, but not a mixture of these). Authors who feel they require support in editing to eliminate possible grammatical or spelling errors and to conform to correct scientific English may wish to use the English Language Editing service available from Elsevier's WebShop (<http://webshop.elsevier.com/languageediting/>).

In relation to terminology, we prefer authors to refrain from using the terms 'low-functioning' or 'high-functioning' to describe individuals with ASD who either have additional intellectual or language impairments or not (see Kenny et al., 2015;

<http://aut.sagepub.com/content/early/2015/06/10/1362361315588200.abstract>). Instead authors should consider whether it may be appropriate to provide details about their

participants in terms of the severity specifiers of the DSM-5 (American Psychiatric Association, 2013).

## **Types of Articles**

Research in Autism Spectrum Disorders publishes the following types of manuscripts:

**Brief reports:** Papers of no more than 2,500 words that report an original piece of research of limited scope and/or that serves as proof-of principle for larger-scale studies.

**Regular Articles:** Papers of up to 6,000 words that report a substantive piece of research that makes a significant contribution and has clear implications for practice. Manuscripts reporting the results of randomized trials or interventions must demonstrate adherence to the CONSORT guidelines (<http://www.consort-statement.org/>) and include the relevant flow diagram and completed checklist.

**Reviews:** Papers of up to 10,000 words that provide a comprehensive overview of a significant area of research. Quantitative (e.g., meta-analyses) and qualitative reviews are welcome as long as they go beyond a mere description of the available literature and synthesise new knowledge with clear implications for future directions and practice. For systematic reviews and meta-analyses, authors must demonstrate adherence to the PRISMA guidelines ([www.prisma-statement.org](http://www.prisma-statement.org)) and include the relevant flow diagram and checklist.

**Commentaries:** We welcome brief commentaries of no more than 1,000 words that offer new insights on papers published in RASD or elsewhere. Commentaries on government policy and/or items in the media are also welcome.

NOTE: Word limits do not include the title page, abstract, figure legends, tables and reference list.

## **Submission**

Our online submission system guides authors stepwise through the submission process. The system converts article files to a single PDF file used in the peer–review process. Editable files (e.g., Word, LaTeX) are required to typeset your article for final publication. All correspondence, including notification of the Editor's decision and requests for revision, is sent by e–mail.

Elsevier accepts electronic supplementary material such as supporting applications, high resolution images, background datasets, sound clips and more. These will be published online alongside the electronic version of your article in Elsevier Web products, including ScienceDirect: <http://www.sciencedirect.com>. For further information, please visit our artwork instruction pages at <http://www.elsevier.com/artworkinstructions>

The journal also encourages authors to submit an AudioSlides presentation with their published article. AudioSlides are brief, webinar-style presentations that are shown next to the online article on ScienceDirect, giving authors the opportunity to showcase their work more readily. More information and examples are available at <http://www.elsevier.com/audioslides>. Authors of articles in this journal will automatically receive an invitation e–mail to create an AudioSlides presentation after acceptance of their paper.

To increase the transparency of editorial information within the framework of single/ double blind peer review, RASD displays the number of unique reviewer reports received in the first round of review with each published article. This policy will be in place for original research articles submitted from 1 January 2016 that are accepted for publication.

## **Manuscript Format**

All manuscripts must include a Title, Abstract and Highlights on separate pages, followed by the main manuscript text. The main manuscript text of brief reports, regular articles and quantitative reviews should include subsections carrying the headings Introduction, Methods, Results, Discussion & Implications. Reviews may deviate from this structure but must include a methods section that provides details on how the relevant literature was searched. The structure of commentaries is at the discretion of authors.

## **Essential Title Page Information**

**Title:** Titles must be concise and informative and should have no more than 20 words. Titles are often used in information–retrieval systems. Avoid abbreviations and formulae where possible.

**Author names and affiliations:** Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. Present the author's affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lowercase superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e–mail address of each author.

**Corresponding author:** Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. **Ensure that the e–mail address is given and that contact details are kept up to date by the corresponding author.**

**Present/permanent address:** If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the



work must be retained as the main affiliation address. Superscript Arabic numerals are used for such footnotes.

### **Abstract & Keywords**

The abstract page must include a structured abstract of no more than 250 words that includes the following subsections:

**Background**: A brief summary of the research question and rationale for the study.

**Method**: A concise description of the methods employed to test the stated hypotheses, including details of the participants where relevant.

**Results**: A brief description of the main findings.

**Conclusions**: This section must include a clear statement about the implications of the findings for practice.

Immediately after the abstract, a maximum of 6 keywords should be provided, avoiding general and plural terms and multiple concepts (for example, avoid 'and', 'of'). Be sparing with abbreviations: only abbreviations firmly established in the field may be eligible (e.g., ADOS, ASD, etc). These keywords will be used for indexing purposes.

### **Graphical Abstract**

Graphical abstracts are optional but encouraged to draw more attention to the online article.

The graphical abstract should summarize the contents of the article in a concise, pictorial form designed to capture the attention of a wide readership. Graphical abstracts should be submitted as a separate file in the online submission system. Please provide an image with a minimum of 531 X 1328 pixels (h X w) or proportionally more. The image should be readable at a size of 5 X13 cm using a regular screen resolution of 96 dpi. Preferred file types include TIFF, EPS, PDF or MS Office files.

See <http://www.elsevier.com/graphicalabstracts> for examples. Authors can make use of Elsevier's Illustration and Enhancement service to ensure the best presentation of their images.

<http://webshop.elsevier.com/illustrationservices/>

## **Introduction**

The introduction should develop a clear rationale for the presented work on the basis of a concise overview of the relevant literature. Detailed literature reviews should be avoided.

## **Methods**

This section will typically include sub-headings for a description of the Participants, Materials & Design, Procedures and Analysis. However, alternative sub-headings may be used to suit particular research approaches (e.g., case-studies, meta-analyses, imaging studies etc.)

The participants section should provide demographic information (age, sex, ethnicity, socio-economic status, etc.), and include details on where and how participants were recruited and how relevant clinical diagnoses were verified. Additional clinical information (e.g., intellectual functioning, co-morbidities, use of medication etc.) is desired and may be necessary for some research designs. Sample sizes should be justified by suitable power calculations although it is appreciated that it is not always feasible to obtain desired numbers of participants.

The materials, design and procedures must be described in sufficient detail for the work to be replicable. Authors must also include a statement confirming that the work was carried out in accordance with the ethical standards of the responsible committee on human

experimentation (institutional and national) and with the Declaration of Helsinki as revised in 2000. In this context confirmation should also be given that participant or guardian informed consent was obtained where appropriate.

The analysis section should provide details of the statistical methods used including information on the significance thresholds and the methods used to correct for multiple comparisons where necessary. Information on inter-rater reliability and any data filtering / transformation that was applied should also be included here.

## **Results**

The results should be set out transparently and in full and should conform to the formatting style of the American Psychological Association (<http://www.apastyle.org/>). Effect sizes must be reported for all significant and non-significant effects, and sufficient descriptive statistics must be provided for the effect size calculations to be replicated.

## **Tables**

Please submit tables as editable text and not as images. Tables can be placed either next to the relevant text in the article, or on separate page(s) at the end. The formatting of tables should conform to APA guidelines (<http://www.apastyle.org/>).

## ***Figures & Artwork***

### **General points**

- Make sure you use uniform lettering and sizing of your original artwork.
- Embed the used fonts if the application provides that option.
- Aim to use the following fonts in your illustrations: Arial, Courier, Times New Roman, Symbol, or use similar fonts.

- Number the illustrations according to their sequence in the text.
- Use a logical naming convention for your artwork files.
- Provide captions to illustrations separately.
- Size the illustrations close to the desired dimensions of the published version.
- Submit each illustration as a separate file.

For Vector drawings, the recommended file format is EPS or PDF (embed all used fonts).

For all other artwork, please use TIFF or JPEG file formats with the following resolutions:

- Colour or grayscale photographs (halftones): 300 dpi
- Pure black & white line drawings: 1000 dpi
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