



# The differential associations of positive and negative symptoms with suicidality

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## ARTICLE INFO

### Keywords:

Schizophrenia  
Positive symptoms  
Negative symptoms  
Suicidal ideation  
Suicide attempt

## ABSTRACT

**Background:** Suicide is one of the leading causes of death in people with schizophrenia. Identifying risk factors for suicide in schizophrenia is therefore an important clinical and research priority.

**Method:** A cross-sectional secondary analysis was conducted on the DNA Polymorphisms in Mental Illness Study (DPIM) data. Suicidality data was extracted, and the number of positive and negative symptoms were established for a total of 1494 participants. Logistic and negative binomial regression analyses were conducted to assess for associations between positive or negative symptoms and suicidal ideation, attempt, or number of attempts, whilst adjusting for potential confounders.

**Results:** Negative symptoms were associated with a reduction in the risk of suicidal ideation (odds ratio [OR]: 0.83; 95 % CI: 0.75–0.91) and suicide attempt (OR: 0.79; 95 % CI: 0.71–0.88) after adjusting for age and sex. Positive symptoms were associated with an increased risk of suicidal ideation (OR: 1.06; 95 % CI: 1.03–1.09), suicide attempt (OR: 1.04; 95 % CI: 1.00–1.07) and number of suicide attempts (incidence rate ratio [IRR]: 1.05; 95 % CI: 1.01–1.08). Further adjusting for depressive symptoms slightly increased the magnitude of associations with negative symptoms but attenuated associations between positive symptoms and suicidality to the null.

**Conclusions:** Negative symptoms are associated with a reduced risk of suicidality, whilst positive symptoms are associated with an increased risk of suicidality. Depressive symptoms may confound or mediate these associations.

## 1. Introduction

It is estimated that, worldwide, over 800,000 people die by suicide every year (World Health Organization, 2014). Approximately 14.1 % of global suicides are accounted for by individuals with schizophrenia (Bachmann, 2018). Schizophrenia is a multifactorial psychiatric disorder with a large global disease burden and an estimated life expectancy of 20 years less than the general population (Laursen et al., 2014). Suicide is a key contributor to this excess mortality, with approximately 24–50 % of individuals with schizophrenia experiencing suicidal ideation (Breier et al., 1991; Harvey et al., 2018) and 26.8 % attempting to end their own lives (Lu et al., 2020; Rahman and Lauriello, 2016). Despite the known risk, suicide attempts are extremely difficult to predict, and efficacious evidence-based interventions are limited.

Numerous risk factors have been postulated as important predictors of suicidality in schizophrenia (note: the term suicidality covers suicidal

ideation, plans and attempts). Depressed mood is a robustly established risk factor (Hawton et al., 2005), although it remains unclear whether the clinical symptoms of schizophrenia itself lead to suicidality. A systematic review found that those with unipolar psychotic major depression, consisting of predominantly hallucinations and delusions, had over twice the odds of attempting suicide than those with depression absent from psychotic features (Gournellis et al., 2018). Further, studies have shown that the risk of subsequent suicidal ideation, attempts and death was over two, three and four times higher, respectively, among those with sub-clinical psychotic experiences compared to those without (Honings et al., 2016; Yates et al., 2019). Therefore, this is indicative that suicidality in schizophrenia may indeed be driven by the manifestation of positive symptoms.

Research has explored this concept in those with a clinical diagnosis of schizophrenia and found specific types of hallucinations, namely command hallucinations, positively correlate with suicidality (Kjelby

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et al., 2015; Ventriglio et al., 2016). Command hallucinations may contain suicidal orders, driving an individual to harm oneself (Rogers et al., 2002). Evidence regarding delusions, however, has been mixed (Freeman et al., 2019; Kjelby et al., 2015; Madsen and Nordentoft, 2012). A number of these studies had relatively small sample sizes which may account for these inconsistencies.

The relationship between negative symptoms and suicidality is even less established. One study found that negative symptoms increase the risk for suicidality (Ventriglio et al., 2016), whilst others found an inverse relationship (Gómez-Durán et al., 2012; Hor and Taylor, 2010; Huang et al., 2018; Kjelby et al., 2015) and some found no association (Cassidy et al., 2018; Jahn et al., 2016). Many studies in this area lean towards the premise that negative symptoms protect against suicidal ideation and attempts. Ventriglio et al. (2016) however, focused on the early stages of schizophrenia where suicide risk is notably higher, potentially explaining this contrast in evidence. Diminished drive and social withdrawal have been shown to protect against suicidal behaviour (Fenton et al., 1997), whilst blunted affect has been found to both increase (Grigoriou et al., 2018) and decrease risk for suicidality (Fenton et al., 1997; Gómez-Durán et al., 2012; Tarrier et al., 2007). Although social withdrawal is more commonly associated with an increase in suicidality, in the context of schizophrenia solitude may have protective effects by eliciting an escape from sensory overload (Seeman, 2017). People with schizophrenia have demonstrated higher levels of introversion (Berenbaum and Fujita, 1994; Nilsson et al., 2016) and prefer spending time alone. Those with more negative symptoms, in particular, have shown less desire for social belonging (Oorschot et al., 2013) and therefore experience greater satisfaction in solitude and less risk of suicidal ideation. In addition, lethargy and inactivity may lead to reduced motivation and energy required to carry out a suicide attempt.

Despite prior observations of the association between psychotic symptoms and suicidality, it remains unclear whether negative symptoms protect against suicidal ideation and behaviour. Consequently, the relationship between suicidality and the symptoms of schizophrenia warrants further investigation in a clinical sample of sufficient size. Identifying schizophrenia symptoms that are associated with suicidality may be informative for suicide prevention strategies, potentially leading to a more focused approach and improving early detection of suicide risk.

The aim of the study was to examine whether positive and negative symptoms of schizophrenia were associated with suicidal outcomes. We tested the following a priori hypotheses: (1) negative symptoms would be associated with a decrease in suicidal ideation and suicide attempts and (2) positive symptoms would be associated with an increase in suicidal ideation and attempts.

## 2. Methods

### 2.1. Data source

We performed a secondary analysis of cross-sectional data on participants with schizophrenia from the University College London (UCL), DNA Polymorphisms in Mental Illness Study (DPIM) (Al Eissa et al., 2018; Arican et al., 2019). In total, 2204 participants with schizophrenia were recruited to DPIM between 1994 and 2015. Suicide attempt data from a subset of this sample has previously been analysed as part of large meta-analyses studying the genetic architecture of suicidal behaviour (Mullins et al., 2019, 2022).

Participants with a diagnosis of schizophrenia, as classified by the International Classification of Disease version 10 (ICD-10), were recruited through the National Institute for Health Research (NIHR) funded Mental Health Research Network and 32 NHS services by psychiatrists or clinicians trained in the assessments. The clinical settings and referral pathways will therefore not be consistent across the sample. Written informed consent was obtained, and diagnosis was confirmed by interview using the Schedule for Affective Disorders and Schizophrenia

– Lifetime version (SADS-L). The SADS-L has high test-retest reliability ( $r = 0.91$ ) and internal consistency ( $\alpha = 0.87$ ) (Endicott and Spitzer, 1978). Data from SADS-L interviews were supplemented by information from clinical records. The Operational Criteria Checklist for Psychotic Disorders (OPCRIT) (McGuffin et al., 1991) was also administered. This is a standardised 90-item checklist of psychiatric symptoms, primarily applied in research settings to generate diagnoses, and has good inter-rater reliability (mean kappa = 0.69) (Brittain et al., 2013).

### 2.2. Dataset for analysis

Data cleaning and quality checking procedures were performed; implausible values were checked against the case report forms to eliminate previous data entry errors. Participants were excluded where data for all OPCRIT psychotic symptoms (Supplementary Table 1) and both suicidality outcomes (ideation or attempts) was missing. The final sample for analysis consisted of 1494 participants (Supplementary Fig. 1).

### 2.3. Measures

#### 2.3.1. Suicidal ideation

Suicidal ideation, regardless of intent, was measured using an item from the OPCRIT, defined as: “preoccupation with thoughts of death including thinking of attempting suicide or wishing to be dead” across the lifetime. Scores range from 0 to 3, where 1 and 2 indicate duration in number of weeks and 3 signifies presence for one month or longer. This was transformed into a binary variable, indicating presence or absence.

#### 2.3.2. Suicide attempts

Suicide attempts, regardless of perceived lethality, were assessed as part of the SADS-L interview. Participants were asked by a psychiatrist whether they had made discrete suicidal gestures or attempts through the course of their illness, specifically “have you ever tried to kill yourself or done anything that could have killed you?”. A discussion was held to determine presence of intent, and answers were either coded as; yes, no or no information. If the answer was yes, participants were asked about the number of gestures or attempts, ranging from 1 to 8 + .

#### 2.3.3. Positive and negative symptoms

Presence or absence of schizophrenia symptoms was measured using the OPCRIT. This produced 23 binary and categorical variables. All categorical variables were transformed into binary and summed to produce a positive and negative symptom score for each participant. The symptoms were classified according to a phenomenological analysis by Leonenko et al. (2018) (Supplementary Table 1).

#### 2.3.4. Demographic variables

Age, sex, age of illness onset, marital status and employment status were measured using OPCRIT items. Education was measured using an item from the SADS-L, which asked for highest completed school grade. Age of illness onset was cut off at 8 to 70 years. Illness duration was calculated by subtracting age of illness onset from age at interview.

#### 2.3.5. Substance abuse

Substance abuse was assessed using an item from the OPCRIT, which rated whether the participant had experienced alcohol or drug abuse during the year prior to illness onset, and produced a binary measure. The coding schedule states: “alcohol abuse where quantity is excessive, where alcohol related complications occur” and “drug abuse where non-prescribed drugs are repeatedly taken or prescribed drugs are used in excessive quantities and without medical supervision”.

#### 2.3.6. Depressive symptoms

A proxy was generated using 12 OPCRIT items (dysphoria, irritable mood, excessive self-reproach, loss of energy, reduced need for sleep,

loss of pleasure, diminished libido, excessive sleep, poor appetite, weight loss, increased appetite and weight gain), which were transformed into binary variables and then summed to produce a lifetime depressive symptom score. We calculated the Cronbach's alpha score for this measure which shows high internal consistency ( $\alpha = 0.80$ ).

## 2.4. Statistical analyses

### 2.4.1. Main analyses

The following pre-specified analyses were performed. We investigated the association between positive symptoms and suicidal ideation using unadjusted logistic regression with suicidal ideation as the outcome and number of positive symptoms as the main exposure. A second model adjusted for age and sex as a priori confounders, while further models adjusted additionally for other potential confounders (age of illness onset, education, marital status, employment status, substance abuse and depressive symptoms). The same model building process was carried out for the other two outcomes, using logistic regression for the binary suicide attempt outcome and negative binomial models for number of suicide attempts. This was then replicated for all outcomes using number of negative symptoms as the main exposure. We calculated sensitivity, specificity and positive predictive values for the fully adjusted regression model. All statistical analyses were performed using Stata 14.

### 2.4.2. Exploratory analyses

Univariable logistic regression analyses were carried out to establish which individual symptoms of schizophrenia were associated with suicidality. A univariable ordinal logistic regression analysis was performed with number of positive symptoms as the predictor and number of negative symptoms as the outcome. To assess whether the association between positive symptoms and the outcome was modified by negative symptoms (and vice versa), we fitted a logistic regression model for suicidal ideation and suicide attempt, and a negative binomial model for number of suicide attempts with number of positive and negative symptoms and their interaction as explanatory variables.

### 2.4.3. Sensitivity analyses

Based on the findings from initial exploratory analyses, which indicated that bizarre delusions produced a low odds ratio in comparison to other positive symptoms, we generated a positive symptom score excluding bizarre delusions and re-ran the main analyses to determine how this would influence the results. For the main analyses, we additionally adjusted for suicidal ideation in the models with suicide attempt as the outcome variable.

### 2.4.4. Missing data

To ensure that symptom scores were not unduly influenced by missing data, the overall score was set as missing if there was not an adequate amount of OPCRIT data available for each participant. Participants were required to have data for 10 or more (out of 19) positive symptoms and three or more (out of 4) negative symptoms. For the OPCRIT depressive symptom score, participants were required to have data for 7 symptoms (out of 12).

## 3. Results

### 3.1. Characteristics of study sample

A total of 1494 participants with a diagnosis of schizophrenia were included in the final analysis, 1081 (72 %) of whom were male. All participants were white Caucasian of British ancestry. The mean age of the sample was 44 (standard deviation [SD]: 13) and the majority were single (78 %) and unemployed (73 %), with a mean illness duration of 21 years (SD: 13). Median negative symptom score was 1 (interquartile range [IQR]: 0 to 2) and median positive symptom score was 6 (IQR: 4 to

9). Overall, 811 participants (54 %) experienced suicidal ideation and 540 (36 %) had attempted suicide. Demographic and clinical characteristics are presented in Table 1. Supplementary Fig. 2 illustrates the distribution of positive and negative symptom scores.

## 3.2. Main analyses

### 3.2.1. Negative symptoms

We found evidence that for each additional negative symptom, the odds of experiencing suicidal ideation decreases by 19 % (OR: 0.81; 95 % CI: 0.74 to 0.89;  $p < 0.001$ ) and the odds of a suicide attempt decreases by 21 % (OR: 0.79; 95 % CI: 0.71 to 0.87;  $p < 0.001$ ). We found evidence that for each additional negative symptom, the number of suicide attempts decreases by 10 % (IRR: 0.90; 95 % CI: 0.81 to 1.00;  $p = 0.046$ ).

These associations remained unchanged after adjustment for age and sex, but further adjustment for depressive symptoms increased the magnitude of associations with all three outcomes. This increase was particularly marked for number of suicide attempts (IRR: 0.82; 95 % CI: 0.74 to 0.91;  $p < 0.001$ ), but less so for suicidal ideation (OR: 0.78; 95 % CI: 0.69 to 0.86;  $p < 0.001$ ) and suicide attempt (OR: 0.76; 95 % CI: 0.68 to 0.85;  $p < 0.001$ ). Adjusting for the remaining covariates did not materially affect the results.

### 3.2.2. Positive symptoms

We found evidence that for each additional positive symptom, the odds of experiencing suicidal ideation increases by 6 % (OR: 1.06; 95 % CI: 1.03 to 1.09;  $p < 0.001$ ) and the odds of a suicide attempt increases by 4 % (OR: 1.04; 95 % CI: 1.00 to 1.07;  $p = 0.031$ ). We likewise found evidence that for each additional positive symptom the number of suicide attempts increases by 5 % (IRR: 1.05; 95 % CI: 1.01 to 1.08;  $p = 0.006$ ).

These associations remained unchanged after adjustment for age and sex, but further adjustment for depressive symptoms attenuated all three associations to the null ( $p = 0.119$ ,  $p = 0.411$  and  $p = 0.079$  respectively). Adjusting for the remaining covariates did not materially affect the results. Main findings are presented in Table 2. Sensitivity, specificity and positive predictive values for the fully adjusted model are presented in Supplementary Table 4.

**Table 1**  
Demographic and clinical characteristics.

	Summary statistic	Missing observations (N = 1494)
Age (years) – mean (SD)	44 (13)	8 (1 %)
Age of illness onset (years) – mean (SD)	23 (8)	22 (1 %)
Illness duration (years) – mean (SD)	21 (13)	53 (4 %)
Sex		
Male	1081 (72 %)	54 (4 %)
Level of education		
Graduate	51 (3 %)	233 (16 %)
In or completed college or sixth form	323 (22 %)	
Year 10/11 or completed school	782 (52 %)	
Up to 9 years of school	105 (7 %)	
Marital status		
Single	1165 (78 %)	16 (1 %)
Married	313 (21 %)	
Employment status		
Unemployed	1087 (73 %)	29 (2 %)
Alcohol or drug abuse within one year of onset	467 (31 %)	62 (4 %)
Suicidal ideation	811 (54 %)	26 (2 %)
Suicide attempt	540 (36 %)	197 (13 %)
Number of suicide attempts – median (IQR)	0 (0 to 1)	292 (20 %)
Negative symptom score – median (IQR)	1 (0 to 2)	38 (3 %)
Positive symptom score – median (IQR)	6 (4 to 9)	25 (2 %)
Depressive symptom score – median (IQR)	2 (0 to 5)	67 (4 %)

Statistics are n (%) unless otherwise specified. SD = standard deviation. IQR = interquartile range. Median (IQR) is reported where data are skewed.

**Table 2**

Main analyses investigating associations between negative or positive symptom score and suicidal ideation, suicide attempt and number of suicide attempts.

	Unadjusted			Adjusting for age and sex			Adjusting for age, sex and depressive symptoms		
	OR	95 % CI	p	OR	95 % CI	p	OR	95 % CI	p
<b>Suicidal ideation</b>									
Negative symptom score	0.81	0.74 to 0.89	<0.001	0.83	0.75 to 0.91	<0.001	0.78	0.69 to 0.86	<0.001
Positive symptom score	1.06	1.03 to 1.09	<0.001	1.06	1.03 to 1.09	<0.001	1.03	0.99 to 1.06	0.119
<b>Suicide attempt</b>									
Negative symptom score	0.79	0.71 to 0.87	<0.001	0.79	0.71 to 0.88	<0.001	0.76	0.68 to 0.85	<0.001
Positive symptom score	1.04	1.00 to 1.07	0.031	1.04	1.00 to 1.07	0.034	1.01	0.98 to 1.05	0.411
<b>Number of suicide attempts</b>									
Negative symptom score	0.90	0.81 to 1.00	0.046	0.90	0.81 to 1.00	0.049	0.82	0.74 to 0.91	<0.001
Positive symptom score	1.05	1.01 to 1.08	0.006	1.05	1.01 to 1.08	0.006	1.03	1.00 to 1.06	0.079

Suicidal ideation and suicide attempt were analysed using logistic regression with number of negative or positive symptoms as the main explanatory variable. Number of suicide attempts was analysed using negative binomial regression with number of negative or positive symptoms as the main explanatory variable. OR = odds ratio, IRR = incidence rate ratio, CI = confidence interval.

### 3.3. Exploratory analyses

#### 3.3.1. Negative symptoms

Exploratory analyses were carried out on individual symptoms and their association with suicidality. We found evidence that negative formal thought disorder and blunted affect reduces the odds of suicidal ideation and suicide attempt by 33–45 %, whilst restricted affect reduced the odds of suicide attempt but not suicidal ideation.

#### 3.3.2. Positive symptoms

Delusions of guilt were most strongly associated with an increase in the odds of suicidal ideation and attempt. We also found evidence that abusive voices, non-affective auditory (command) hallucinations and non-affective hallucinations in any other modality increased the odds of suicidal ideation and attempt. Delusions of influence, primary delusional perception, other primary delusions, thought insertion, thought broadcast and nihilistic delusions were found to increase the odds of suicidal ideation but not suicide attempt. Bizarre delusions decreased the odds of suicidal ideation and suicide attempt. Results from exploratory analyses are presented in Table 3.

A univariable ordinal logistic regression analysis revealed evidence of an inverse association between number of positive and number of negative symptoms (proportional OR: 0.97; 95 % CI: 0.07 to 0.12;  $p < 0.001$ ). Interaction analyses did not provide any evidence that number of negative symptoms modifies the association between number of

positive symptoms and suicidal ideation ( $p = 0.376$ ), suicide attempts ( $p = 0.626$ ) or number of attempts ( $p = 0.496$ ).

### 3.4. Sensitivity analyses

Removing bizarre delusions from the positive symptom score marginally increased the magnitude of the association (Supplementary Table 2) but did not materially alter the results. We therefore present results from models including bizarre delusions as our main results. In sensitivity analyses with suicide attempt or number of suicide attempts as the outcome variable, further adjusting for suicidal ideation attenuated all associations to the null (Supplementary Table 3).

## 4. Discussion

### 4.1. Negative symptoms and suicidality

We found evidence to suggest that positive and negative symptoms are differentially associated with suicidality. As the number of negative symptoms increases, the odds of experiencing suicidal ideation and suicide attempts decreases. Our findings are consistent with the findings of Gómez-Durán et al. (2012), Hor and Taylor (2010), Kjelby et al. (2015) and the meta-analysis of Huang et al. (2018). Huang et al. (2018) found negative symptoms to reduce the odds of suicidality by 70 %. However, our findings are at variance with those of Ventriglio et al.

**Table 3**

Exploratory analyses investigating associations between individual schizophrenia symptoms and suicidal ideation or attempt.

	Suicidal ideation				Suicide attempt			
	n/N (%)	OR	95 % CI	p	n/N (%)	OR	95 % CI	p
<b>Negative symptoms</b>								
Negative formal thought disorder	189/418 (45 %)	0.57	0.45 to 0.71	<0.001	117/370 (32 %)	0.55	0.43 to 0.71	<0.001
Restricted affect	256/490 (52 %)	0.85	0.68 to 1.06	0.15	157/422 (37 %)	0.77	0.61 to 0.98	0.037
Blunted affect	245/504 (49 %)	0.67	0.54 to 0.84	<0.001	146/429 (34 %)	0.62	0.49 to 0.79	<0.001
<b>Positive symptoms</b>								
Delusions of influence	406/697 (58 %)	1.27	1.03 to 1.56	0.025	261/602 (43 %)	1.15	0.92 to 1.44	0.21
Bizarre delusions	404/795 (51 %)	0.67	0.54 to 0.82	<0.001	267/701 (38 %)	0.73	0.58 to 0.91	0.006
Primary delusional perception	170/275 (62 %)	1.39	1.06 to 1.82	0.017	106/230 (46 %)	1.26	0.94 to 1.68	0.12
Other primary delusions	234/393 (60 %)	1.28	1.01 to 1.61	0.043	153/338 (45 %)	1.24	0.96 to 1.60	0.093
Thought insertion	327/541 (60 %)	1.41	1.14 to 1.75	0.002	202/461 (44 %)	1.17	0.93 to 1.47	0.19
Thought broadcast	305/514 (59 %)	1.29	1.04 to 1.61	0.021	193/438 (44 %)	1.18	0.93 to 1.49	0.18
Delusions of guilt	116/150 (77 %)	3.11	2.09 to 4.62	<0.001	79/126 (63 %)	2.65	1.81 to 3.88	<0.001
Nihilistic delusions	68/101 (67 %)	1.74	1.13 to 2.67	0.012	41/84 (49 %)	1.38	0.89 to 2.15	0.16
Abusive voices	517/840 (62 %)	1.78	1.43 to 2.21	<0.001	347/737 (47 %)	1.66	1.32 to 2.10	<0.001
Non-affective auditory (command) hallucinations	459/765 (60 %)	1.52	1.23 to 1.88	<0.001	314/676 (46 %)	1.52	1.21 to 1.91	<0.001
Non-affective hallucination in any other modality	441/728 (61 %)	1.54	1.25 to 1.90	<0.001	313/661 (47 %)	1.63	1.30 to 2.05	<0.001

Univariable logistic regression analyses examining associations between presence (vs. absence) of each symptom and suicidal ideation or suicide attempt. OR = odds ratio, CI = confidence interval. n/N is number of people who experience suicidal ideation or suicide attempt out of those with each OPCRIT schizophrenia symptom.

(2016). The aforementioned study explored first episode psychosis (Ventriglio et al., 2016), where suicide risk is substantially elevated. The chronicity of our sample is reasonably high, as is the spread of data for years of illness. Therefore, the present findings are more generalisable to individuals across multiple stages of the disease. Exploratory analyses indicated a sizeable reduction in the odds of suicidality for those who experienced blunted affect or negative formal thought disorder compared to those who did not. Blunted affect has previously been shown to both decrease (Gómez-Durán et al., 2012) and increase (Grigoriou et al., 2018) suicide risk. This inconsistency may be because Grigoriou et al. (2018) investigated schizoaffective disorder, hence the mood symptoms may drive the suicidal outcomes.

In multivariable analyses adjusting for depressive symptoms increased the magnitude of the associations with suicidality, although changes in risk were marginal. Some evidence indicates a symptomatology overlap, generating a diagnostic dilemma through the misattribution of negative symptoms to depressed mood (Bosanac and Castle, 2013). In this instance, we would expect depressive symptoms to attenuate the association rather than strengthen it. However, according to a dimensional model, this overlap only occurs with specific symptoms which were not included in our symptom score (Krynicky et al., 2018). Alternatively, this may be a temporal artefact based on our measurement of lifetime depressive symptoms. Antidepressant use has been associated with a reduced risk of suicidality (Khan et al., 2018), therefore there may be an indirect relationship between lifetime depressive symptoms, antidepressant use and a subsequent reduction in suicidality. Accordingly, antidepressant use may mediate the relationship between negative symptoms and suicidality.

Despite the strong statistical significance of the fully adjusted model with negative symptom score as the main exposure variable and the additional variables within it, its sensitivity, specificity and positive predictive value falls below that of clinical utility. However, the aim of this paper is not to build a risk prediction model but to determine the association between an exposure and outcome variable whilst controlling for confounders.

Our findings illustrate a potentially protective nature of negative symptoms. It is plausible that this is a consequence of severe emotion expressivity deficits, leading to an inability to become emotionally distressed and experience suicidal ideation. Indeed, cognitive models indicate that those who experience more negative symptoms have a reduced potential to activate suicide schemas (Tarrrier et al., 2007), resulting from decreased emotional reactivity. Furthermore, diminished drive, amotivation and lethargy may result in an inability to plan and ultimately attempt suicide. Negative symptoms highly correlate with cognitive deficits such as poor planning ability (Leanza et al., 2018), thereby potentially lessening the risk of a planned suicide attempt. Moreover, the interpersonal theory of suicide suggests thwarted belongingness may increase the risk of suicidality (Joiner, 2005). Negative symptoms reduce the desire for social belonging (Kring et al., 2013) and therefore minimise suicidality through this mechanism.

Dysregulated hypothalamic-pituitary-adrenal axis activity, measured by flattened cortisol levels, is another potential risk factor for suicidality (McGirr et al., 2010). Studies have shown elevated basal cortisol levels in people with more depressive symptoms (Pruessner et al., 2003), more negative symptoms and fewer positive symptoms (Altamura et al., 1989; Shirayama et al., 2002), illustrating a plausible explanatory pathway for our findings from a neurobiological perspective.

As our sample is predominantly male, sex differences may influence our findings such that males are more likely to experience a greater number of negative symptoms and have a lower incidence rate of suicide attempts compared to females (Thorup et al., 2014). To account for this, we adjusted for sex in multivariate analyses and this did not impact our findings.

#### 4.2. Positive symptoms and suicidality

Number of positive symptoms was associated with an increase in the odds of suicidality. This association remained when adjusting for age and sex but was attenuated to the null when further adjusting for depressive symptoms. Our findings echo prior literature that psychotic experiences are associated with an increased risk for suicidality (Bornheimer, 2019; Honings et al., 2016; Yates et al., 2019) and confirms the presence of this relationship within a clinical sample.

Delusions of guilt were most strongly associated with an increase in risk for suicidality. Guilt is often a precursor to suicidal behaviour outside of delusional experiences (Hastings et al., 2002), therefore experiencing such beliefs alongside distressing clinical symptoms may exacerbate suicidal thoughts. Bizarre delusions, defined as “fantastic delusions whose content may be magical”, were the only positive symptom to decrease the odds of suicidality. Based on the OPCRIT definition, this appears to be less unpleasant than other positive symptoms (McGuffin et al., 1991). Therefore, delusional content may directly influence suicidal outcomes.

Similar explanations may exist for hallucinations. Positive associations have been found between command hallucinations and suicidality (Hor and Taylor, 2010; Kjelby et al., 2015; Wong et al., 2013), in line with our findings. Evidence suggests compliance rates to command hallucinations range from 39.2 to 88.5 % (Hersh and Borum, 1998), therefore hallucinations consisting of suicidal demands may drive suicidal behaviour.

Positive symptoms may directly affect risk of suicidality or act via other indirect mechanisms. The divergence of bizarre delusions may reflect florid psychosis and disorganisation, which has been linked to neurocognitive deficits (Nieuwenstein et al., 2001), whilst other positive symptoms may indicate greater cognitive stability. Indeed, poorer cognitive functioning has demonstrated protective effects against suicidal ideation (Richard-Devantoy et al., 2014; Villa et al., 2018). Cognitive impairment may also inhibit one's ability to plan and coordinate a suicide attempt. Similarly, insight has been shown to mediate the relationship between positive symptoms and suicidal ideation, such that individuals who experience fewer positive symptoms have less insight into their illness and therefore a lower risk of depression or suicidal ideation (Bornheimer et al., 2021; Murri et al., 2015). Factors such as internalised stigma, illness perception and recovery attitudes are all mediators of the association between insight and depression (Murri et al., 2015). This association may therefore be explained by denial or lack of awareness of their symptoms.

Based on multivariable analyses, it is evident that lifetime depressive symptoms may confound or mediate the association between positive symptoms and suicidality. The impact of depression on this association has previously been highlighted in a population-based sample (Bornheimer et al., 2019). Beck's cognitive theory of suicide postulates that individuals ascribe meaning to events, which largely influences behaviour. The perceived reality generated by hallucinations and delusions may trigger a negative mood reaction, resulting in suicidal responses (Wenzel and Beck, 2008).

Lack of adherence to antipsychotic medication provides another potential pathway of influence. Clozapine is primarily used to target positive symptoms and is associated with reduced suicide risk (Meltzer et al., 2003). However, some evidence suggests the depressogenic side effects of antipsychotics may contribute to suicidality (Sher and Kahn, 2019). Despite the apparent association between positive symptoms and suicidality, it is evident the relationship is multifaceted. Additionally, due to the nature of our lifetime measure of depressive symptoms, it is difficult to determine whether depressive symptoms confound or mediate the associations.

Sensitivity analyses revealed further adjusting for suicidal ideation in the main analyses with suicide attempt as the outcome attenuated all associations to the null. We believe this occurred because suicidal ideation is a mediator, not a confounder, for the association between

positive or negative symptoms and suicide attempt. Methodological studies have shown adjusting for a mediator can produce biased conclusions (Richiardi et al., 2013; Wang et al., 2017) and may reduce the effect of the predictor (Babyak, 2009). We therefore present our main findings without adjustment for suicidal ideation.

This study has several limitations which may affect the generalisability of the findings. Firstly, both suicidality and symptoms were measured cross-sectionally, therefore our ability to infer direction of causality is restricted. Although schizophrenia is a consistently supported antecedent of suicidality, there is potential for a bidirectional association. Preliminary evidence exists to support this novel suicidal drive hypothesis (Murphy et al., 2018), where suicide attempt predisposes the development of visual hallucinations. This is based on the premise that psychosis emerges from intrusive and distressing mental events (i.e., suicidal ideation) as a means of threat externalisation and protection. For example, command hallucinations may contain commentaries instructing a person to harm oneself. Attributing this threat to a source other than themselves provides psychological protection from harm or death. However, evidence in support of this hypothesis is scarce. Secondly, despite efforts to reduce this, there was a substantial amount of missing data for suicide attempts (13 %). This level of missing data represents a partial view of the overall picture and may produce biased estimates. Despite this, firm conclusions regarding suicidal ideation can still be made as missing data was minimal (2 %). Thirdly, we combined multiple positive symptoms that individually increase or decrease suicidality, as revealed in exploratory analyses. To account for this, we investigated the effect of excluding bizarre delusions, but this did not impact our overall findings materially. Finally, the subjective nature of our suicidality and symptom measures may be influenced by the participants' perception of their experiences and retrospective recall may precipitate memory bias. To minimise this, the interviews were supplemented by information from clinical records and were completed by psychiatrists or trained clinicians. Further, the lack of shared nomenclature surrounding suicide-related terminology is problematic in this field, therefore future studies should seek to alleviate this by investigating lethality and level of intent.

Future prospective studies with clearly defined suicide-related outcome measures should explore the precise content of delusions and hallucinations and the exact mechanisms involved in their complex relationship with suicidality. The extent to which command hallucinations contain suicidal orders, for example, warrants further investigation. Whilst measuring symptoms subjectively, additional variables which may influence the associations should be considered. Namely, internalised stigma, illness perception and recovery attitudes.

Currently, there is a drive to identify efficacious treatments for negative symptoms, as antipsychotics are less effective at targeting these symptoms (Millan et al., 2014; Remington et al., 2016). Negative symptoms can severely affect functional outcomes and quality of life, but it appears they are potentially protective for suicide. It will be important to understand the mechanism behind this reduced risk so that treatments to ameliorate negative symptoms can be introduced safely.

Suicide risk assessment in patients with schizophrenia still requires much improvement (Large et al., 2016). Whilst our study highlights the complex nature of suicidality in schizophrenia, we believe our findings are of clinical utility. Given the influence of depressive symptoms on suicidality, our findings argue for enhanced exploration of both lifetime and current symptoms of depression when assessing suicide risk in people experiencing a greater number of positive symptoms. Suicidality is positively associated with number of positive symptoms and elucidation of depressive symptomology may be most challenging in florid psychosis. To guard against potential diagnostic overshadowing for people with a diagnosis of non-affective psychosis, we advocate careful consideration of lifetime depressive symptomology and a low threshold for treatment and risk management.

Although the precise aetiology of suicidality in schizophrenia remains elusive, our study has shed light on the differential association of

positive and negative symptoms with suicidal ideation and suicide attempt and the effect of depressive symptoms on these associations.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.schres.2022.07.016>.

## Funding sources

Data collection was supported by the Neuroscience Research Charitable Trust, Camden and Islington NHS Foundation Trust and ten other NHS Mental Health Trusts, and the Stanley Center for Psychiatric Research at the Broad Institute. AM and NJB are supported by the University College London Hospitals NHS Foundation Trust NIHR Biomedical Research Centre (BRC; Mental Health Theme).

## CRedit authorship contribution statement

**Laura E. Grover:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing – original draft, Writing – review & editing. **Rebecca Jones:** Validation, Writing – review & editing. **Nicholas J. Bass:** Funding acquisition, Supervision, Validation, Writing – review & editing. **Andrew McQuillin:** Funding acquisition, Supervision, Validation, Writing – review & editing.

## Declaration of competing interest

None.

## Acknowledgments

This paper is dedicated to the memory of Dr. Rebecca Jones. Rebecca was a highly valued colleague. We thank Rebecca for her contributions to the statistical analyses in this research paper. We will miss working with Rebecca.

We thank all the participants in the study and the clinical and research staff at the recruitment centres. Participant recruitment was made possible by collaboration with the NIHR Mental Health Research Network.

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