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# BMJ Open

## Using natural language processing to extract self-harm and suicidality data from a clinical sample of patients with eating disorders: a retrospective cohort study

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8 **Using natural language processing to extract**  
9 **self-harm and suicidality data from a**  
10 **clinical sample of patients with eating**  
11 **disorders: a retrospective cohort study**  
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50 electronic health records, natural language processing  
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52 **Word count:** 3827  
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## Abstract

**Aim:** This study's aim was to determine risk factors for those diagnosed with eating disorders who report self-harm and suicidality.

**Method:** This study was a retrospective cohort study within a secondary mental health service, South London & Maudsley NHS Trust. All patients diagnosed with an F50 diagnosis of eating disorder from 01/2009-09/2019 were included. Electronic health records (EHRs) for these patients were extracted and natural language processing tools were used to determine documentation of either self-harm or suicidality in their clinical notes. These tools were validated manually for attribute agreement scores within this study.

**Results:** The attribute agreements for precision of positive mentions of self-harm were  $>0.90$  and for suicidality were  $>0.80$ ; this demonstrates a 'strong' and 'near perfect' agreement and highlights the reliability of the tools in identifying the EHRs reporting self-harm or suicidality. There were 7434 patients with EHRs available and diagnosed with eating disorders included in the study from the dates 01/2007 to 09/2019. Of these, 4591 (61.8%) had a mention of self-harm within their records and 4764 (64.0%) had a mention of suicidality; 3899 (52.4%) had mentions of both. Patients reporting either self-harm or suicidality were more likely to have a diagnosis of anorexia nervosa (self-harm, AN OR=3.44, 95% CI 1.05-11.3,  $p=0.04$ ; suicidality, AN OR=8.20, 95% CI 2.17-30.1;  $p=0.002$ ). They were also more likely to have a diagnosis of borderline personality disorder ( $p<0.001$ ), bipolar disorder ( $p<0.001$ ) or substance misuse disorder ( $p<0.001$ ).

**Conclusion:** A high percentage of patients ( $>60\%$ ) diagnosed with eating disorders report either self-harm or suicidal thoughts. Relative to other eating disorders, those diagnosed with anorexia nervosa were more likely to report either self-harm or suicidal thoughts. Psychiatric comorbidity, in particular borderline personality disorder and substance misuse were also associated with an increase risk in self-harm and suicidality. Therefore, risk assessment amongst patients diagnosed with eating disorders is crucial.

### Article Summary: Strengths and Limitations of this study

1. The size of the cohort is over 7400 patients
2. Long period of follow up (12.5 years)
3. Limited number of study designs (most cross sectional) reporting on suicidal behaviour amongst those with EDs
4. The tools used to detect self-harm and suicidality are not able to consider the temporality in relation to the ED diagnosis; therefore, the suicidal behaviour could have been detected prior to diagnosis

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3 5. The clinical records are routine clinical data not  
4 primarily collected for research therefore rely on  
5 clinician documentation.  
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## 12 **Introduction**

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14 Patients diagnosed with eating disorders (EDs), including  
15 anorexia nervosa (AN), bulimia nervosa (BN) and eating  
16 disorder not otherwise specified (EDNOS)<sup>1</sup> are at a greater risk  
17 of mortality compared to the general population (1, 2). A  
18 major contribution to this increased mortality rate is the  
19 higher risk of completed suicide in patients with EDs (3).  
20 Individuals with a lifetime diagnosis of AN and BN are 18 and  
21 7 times more likely to die from suicide compared to age-  
22 matched general population controls, respectively (4, 5).  
23 Those with a diagnosis of EDNOS are 4 times more likely to  
24 complete suicide (6). Therefore, given the elevated risk of  
25 suicide amongst patients diagnosed with EDs, it is of utmost  
26 importance that factors associated with this risk are  
27 determined (7).  
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30 Self-harm and suicidal ideation are both strong  
31 predictors of subsequent suicide (8). Self-harm can be defined as  
32 'self-injurious behaviour characterised by deliberate harm to  
33 the body in the absence of an intent to die' (9) and suicidal  
34 ideation can be defined as 'thoughts about killing oneself,  
35 which may or may not include a plan' (10). It has been  
36 determined that a common antecedent for completed suicide in  
37 the general population, is previous self harm, with up to 60%  
38 of people who complete suicide having previously self-harmed,  
39 the majority within one year prior to the attempt (11, 12).  
40 Lifetime suicidal ideation is also associated with attempted  
41 suicide (up to 30%); those with a plan have an increased risk  
42 of completed suicide (up to 55%) and the majority of attempts  
43 occur within the first year of the onset of suicidal ideation  
44 (13). Therefore, identifying patients who report either  
45 lifetime suicidal ideation and self-harm is an important  
46 clinical marker for those at risk of later suicide.  
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49 Previous studies have demonstrated the association  
50 between suicidality, self-harm and EDs (14-17). Our previous  
51 study focusing on suicide attempts, demonstrated the  
52 cumulative 10-year incidence of suicide attempts in a  
53 population of patients with EDs as 6.8% (17). Rates of self-  
54 harm have been reported as high as 42% for AN, up to 55% for  
55 bulimia nervosa BN (18) and 26% for EDNOS (19). A recent meta-  
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59 <sup>1</sup> The DSM-V now refers to 'Otherwise specified feeding or eating disorder' (OFSED); but the studies and data  
60 included in this paper used the DSM-IV equivalent term of EDNOS.

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3 analysis summarised that 22% of patients with AN and 33% of  
4 patients with BN reported lifetime self-harm (20).

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6 Studies have reported mixed findings in terms of suicide  
7 attempts across ED diagnostic categories (21-24), with many  
8 showing no difference in suicide attempts between ED subtypes,  
9 some demonstrated higher rates of suicide attempts and self-  
10 harm in AN compared to BN (17, 23, 25, 26) and others reported  
11 more frequent suicide attempts and ideation in BN compared to  
12 AN (24, 27). Furthermore, binge eating disorder (BED), a  
13 relatively new diagnostic category, has also been associated  
14 with increased suicidality (22). In other studies it appears  
15 that binge eating and purging are particularly associated with  
16 increased risks of attempted suicide, due to their association  
17 with impulsivity (26, 28). Some of these heterogenous findings  
18 have been attributed to differences in patient settings  
19 (outpatient or inpatient) (21), diagnostic subtyping (e.g.  
20 restricting vs binge-purging AN) (28) or the methods used for  
21 determining suicide attempts (26).

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24 Some studies have focused on risk factors for developing  
25 suicidal behaviour amongst those with EDs. A number of risk  
26 factors have been identified, such as younger age of ED onset,  
27 specific personality traits, comorbid disorders, negative life  
28 events and substance misuse (17, 26, 29). However, there are  
29 limitations with a number of past studies in terms of low  
30 numbers of suicidal behaviour within the study population,  
31 resulting in low power (5). One possibility to improve this  
32 problem is to use longitudinal psychiatric case records, such  
33 as electronic health records (EHRs). This captures a large  
34 enough population manifesting suicidal behaviour, to ensure a  
35 sufficiently powered study (30).

36  
37 The increasing use of EHRs in hospital care systems,  
38 alongside the growth of health informatics allows us to  
39 develop computational tools that can analyse these large  
40 clinical datasets (31). Natural language processing (NLP)  
41 tools allow us to determine information about symptomatology  
42 from information written in free-text EHRs (32). Previous  
43 research has shown that using NLP applications increases the  
44 positive predictive value of detecting patient-level  
45 suicidality (33). This is of particular use for suicidal  
46 behaviour, as both positive and negated mentions of  
47 suicidality and self-harm are routinely reported within free  
48 text during psychiatric assessments and follow-up (31, 34, 35).

49  
50 The aim of this study was to evaluate two NLP approaches  
51 that identify both self-harm and suicidality in the clinical  
52 records for a cohort of ED patients. To achieve this, we  
53 compared the performance of the NLP tools against a gold-  
54 standard set of manually annotated documents, using previously  
55 defined coding rules. We then used the tools to identify  
56 positive mentions of either self-harm or suicidality on a  
57 patient level, to evaluate the incidence of self-harm and  
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3 suicidality in patients diagnosed with eating disorders over a  
4 12-year period.  
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## 6 **Methods**

### 7 **Study Design and Setting**

8  
9 This study is a retrospective cohort study using data  
10 obtained from South London and Maudsley National Health  
11 Service Foundation trust (SLaM). This is a mental health  
12 service serving an estimated population of 2 million residents  
13 of southeast London. Patients come from the London boroughs of  
14 Croydon, Southwark, Lambeth, Lewisham, Bromley, Bexley and  
15 Greenwich. SLaM has had fully electronic records since 2006  
16 and the National Institute for Health Research funded  
17 Biomedical Research Centre supports the infrastructure for  
18 rendering its anonymised records available for research.  
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### 22 **Inclusion criteria and exposures**

23 The analysed cohort was extracted via the Clinical Record  
24 Interactive Search (CRIS) system (36) and comprised of  
25 individuals who received an International Classification of  
26 Diseases, 10<sup>th</sup> Revision (ICD-10) (37) diagnosis of an ED  
27 (F50.0-F50.9) within the 12-year observation period of 1  
28 January 2007 to 31 September 2019. These patients were  
29 extracted using two methods available within the EHRs. First,  
30 structured information on diagnosis was extracted from drop  
31 down fields in the source record. Second, data were extracted  
32 from open text fields using a bespoke algorithm generated by  
33 the Generalised Architecture for Text Engineering (GATE)  
34 software. The comorbidity exposures of interest were diagnoses  
35 of substance misuse (F10-F19), bipolar disorder (F31), anxiety  
36 disorders, depression (F32 and F33) and personality disorder  
37 (F60) determined by structured information on the EHRs in the  
38 drop-down fields in the source record.  
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### 44 **Primary outcomes**

45 The outcomes of interest were a patient reporting at  
46 least one positive mention of self-harm or one positive  
47 mention of suicidality. Information on these outcomes was  
48 extracted using NLP applications that have been previously  
49 developed and used within similar datasets (31, 34, 35). The  
50 first application assessed for positive mentions of self-harm  
51 (SH), this included historic and current episodes, but did not  
52 include self-harm ideation. The second application included  
53 suicidal ideation (SUI) of both a passive and active nature;  
54 both of these were recorded as a binary outcome.  
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### 60 **Workflow for validating the NLP tools**

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3 **Figure 1** shows the workflow for validating the NLP tools  
4 to determine the primary outcomes. All F50 diagnoses between  
5 1<sup>st</sup> Jan 2007 and 31<sup>st</sup> March 2019 were included in the  
6 validation; this period of time was 6 months shorter than the  
7 final analysis due to the lag time between the validation and  
8 final statistical analysis. In total, 7,188 patients met the  
9 inclusion criteria, of which 6,972 had at least one EHR  
10 document available. Overall, **1,054,640** documents were  
11 available for these patients. For all 6,972 patients, the NLP  
12 tools were used to search for mentions of both suicidality and  
13 self-harm. In total, 5,456 patients had positive mentions of  
14 either SH or SUI, 4741 had any mention of SH, 4528 had any  
15 mention of SUI, and 3813 patients had both SH and SUI  
16 mentioned. Manual annotations were compared to the NLP tool  
17 annotations and attribute agreements were calculated (38).

18  
19 From these patients, a sample of documents was randomly  
20 extracted. This was achieved by firstly restricting the  
21 patients to those who had a number of EHR documents within the  
22 1<sup>st</sup> and 3<sup>rd</sup> quartiles, to eliminate outliers with very few  
23 documents or with excessive documentation. This resulted in  
24 2923 patients in total with positive mentions of either SH or  
25 SUI (**135,317** documents), 2431 patients with a positive mention  
26 of SH (**114,962** documents), 2294 patients with a positive  
27 mention of SUI (**110,399** documents), and 1802 patients with a  
28 positive mention of both SH and SUI (**90,044** documents). Each  
29 patient had a minimum of 17 documents and maximum of 99  
30 documents.

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32 A randomised sample of 500 documents was taken for manual  
33 review: 100 with a positive mention of suicidality only, 100  
34 with a positive mention of self-harm only, 100 with a mention  
35 of both self-harm and suicidality and 200 with no mention of  
36 either. Three manual coders, including one clinically trained  
37 psychiatrist (CC, AS, AV), were assigned either suicidality  
38 (AS, 400 documents), self-harm (AV, 400 documents) or both  
39 (CC, 500 documents) for review. The sets were independently  
40 classified with 300 of them crossing over and classified by  
41 all three authors.

42  
43 For the suicidality documents, two coders (CC and AS)  
44 independently labelled each document as suicidal, non-suicidal  
45 or uncertain. Inter-rater agreement was measured using Cohen's  
46 Kappa and the F1 statistic on a document level to determine  
47 interrater reliability (38). Any discrepancies were discussed  
48 and clarified to develop a 'gold standard' set of documents.  
49 The same principle was applied to mentions of self-harm within  
50 the documents, determined by two coders (CC, AV). Any mention  
51 of self-harm within the document was coded as positive,  
52 negative and whether relevant, non-relevant, for example the  
53 mention was about a friend or family member that was not  
54 relevant to the patient, or uncertain (see Figure 1).

## 55 56 57 58 59 60 **Testing the Algorithms**

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3 The performance of each NLP tool was tested by comparing  
4 the output of the application against the 'gold standard' set  
5 of manual annotations and calculating precision (positive  
6 predictive value; PPV) and recall (sensitivity) statistics.  
7 Good inter-rater agreement between the NLP output and gold-  
8 standard was indicated by a Cohen's kappa of 0.80 for  
9 identifying both suicidality and self-harm. Scores > 0.80  
10 demonstrate a 'strong' level of agreement and reliable data,  
11 scores > 0.90 are 'almost perfect' agreement and scores > 0.60  
12 were considered 'moderate' in agreement (38).  
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### 17 **Figure 1: Workflow for validation of both NLP tools**

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#### 21 **Covariates**

22 The year and month of birth, gender, ethnicity,  
23 deprivation score and marital status were retrieved from the  
24 CRIS database. Age in years was calculated from the  
25 individual's first eating disorder diagnosis in the  
26 observation window or from January 2007 if the diagnosis  
27 preceded the observation period.  
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#### 30 **Patient and Public involvement**

31 There was no patient and public involvement in the development  
32 of the manuscript.  
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34

#### 35 **Statistical analysis**

36 Analysis was completed using Stata software. All patients  
37 were eligible for analysis. Descriptive statistics were used  
38 to characterise the patients. Logistic regression was used to  
39 calculate odd ratios with 95% confidence intervals with self-  
40 harm or suicidality as the 'outcome' and the comorbid  
41 psychiatric diagnoses as exposure. ED diagnoses were  
42 categorised into AN (both restricting and purging types), BN,  
43 and all other F50 diagnoses. For those with multiple  
44 diagnoses, a diagnostic hierarchy of AN>BN>other was used. The  
45 observation period started from the first date of diagnosis or  
46 1 Jan 2007 if the diagnosis was made prior to this date and  
47 the ended on the 31 September 2019. Univariate logistic  
48 regression was used to estimate the effect of the primary ED  
49 diagnosis, demographic characteristics and psychiatric  
50 comorbidities on each of the outcomes of interest (SH and  
51 SUI). Next, multivariable analyses were performed to calculate  
52 the adjusted odds ratio (OR) and 95% confidence interval (CI)  
53 for each comorbid psychiatric diagnosis, whilst controlling  
54 for demographics and the ED diagnosis. the effect of the  
55 psychiatric comorbidities and demographics.  
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## Results

### Descriptive Statistics

A total of 7434 patients with ED diagnoses were identified by the CRIS system between 1 Jan 2007 and 31 September 2019; 4591 (61.8%) had a mention of self-harm and 4764 (64.0%) had a mention of suicidality; 3899 (52.4%) had mentions of both. Of the 7434 patients, 2553 (34.3%) had a diagnosis of AN, 1572 (21.2%) a diagnosis of BN, and 3298 (44.4%) a diagnosis of other EDs (including binge eating disorder, EDNOS, otherwise unspecified) and 11 (<1%) had no information about the type of ED diagnosis. The mean age was 26.0 (SD 11; range 10-90) (see Table 1).

**Table 1: Summary of all diagnoses by age group** (11 patients had no detailed information about the diagnosis other than 'F50')

Age group Years, (n)% total	AN	BN	EDNOS
<10 (39) <1%	4 (<1%)	0	35 (1.1%)
10-19 (2572) 34.6%	1250 (49.0%)	320 (20.4 %)	1002 (30.4%)
20-29 (2720) 36.6%	807 (31.6%)	714 (45.4 %)	1199 (36.4%)
30-39 (1233) 16.6%	276 (10.8%)	354 (22.5 %)	603 (18.3%)
40-49 (527) 7.10%	118 (4.62%)	122 (7.76 %)	287 (8.70%)
50+ (332) 4.47%	98 (3.84%)	62 (3.94 %)	172 (5.22%)
<b>TOTAL</b> n= 7423 (11 missing detailed diagnosis)	<b>2553</b>	<b>1572</b>	<b>3298</b>

### Self-harm and Suicidality amongst patients

The attribute agreements for the final corpus of documents on self-harm and suicidality are displayed below in

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Table 2. The three attributes include 'positive' ie there is a mention of either self-harm or suicidality, 'negative or non' ie there is a denial of self-harm or suicidality and 'relevant' i.e. the mention is relevant to the patient and not a family member or friend. A summary of those reporting self-harm or suicidality by age are displayed in Table 3.

**Table 2: Attribute agreements:** attribute agreements reflect the comparison of the NLP tool output to the gold standard set of manually annotated documents.

	Positive suicidal ity	Relevant document s for suicidal ity	Non- suicida l documen ts	Positi ve for self- harm	Relevan t documen ts for self- harm	Negati ve for self- harm
Precisi on	0.80	0.98	0.58	0.96	0.89	0.59
Recall	0.82	0.91	0.87	0.91	0.72	0.79
F1- score	0.81	0.95	0.70	0.94	0.80	0.68

**Table 3: Self harm and suicidality reported amongst patients by age**

Age group, years	Self- harm present during follow up period, n (%)	Suicidality present, n (%)
<10	16 (<1%)	15 (<1%)
10-19	1914 (41.7%)	1928 (40.5%)
20-29	1489 (32.4%)	1553 (32.6%)
30-39	675 (14.7%)	722 (15.2%)
40-49	310 (6.75%)	168 (6.75%)
50+	187 (4.1%)	134 (5.38%)

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<b>TOTAL</b>	<b>4591</b>	<b>4520</b>
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### Self-harm-reported amongst patients with eating disorders

Patients who reported self-harm (past or present) were more likely to be younger in age (OR = 0.98, 95% CI 0.97-0.98; P<0.001), less likely to be female (OR = 0.67, 95% CI 0.58-0.79; P<0.001) more likely to be of white ethnicity (OR = 1.40, 95% CI 1.10-1.78; p=0.006), and more likely to have a diagnosis of AN (OR = 3.44, 95% CI 1.05-11.3; p=0.04). They were also more likely to have a comorbid diagnosis; in particular a diagnosis of borderline personality disorder (BPD; OR = 54.2, 95% CI 24.2-121.4; p<0.001), bipolar disorder (OR = 9.57, 95% CI 5.57-15.4; p<0.001) and substance misuse (OR = 7.22, 95% CI 2.94- 18.3; p<0.001); as displayed in Table 4.

**Table 4: Univariable logistic regression to determine the effect of demographics, primary ED diagnosis, and psychiatric comorbidities on risk of self-harm**

Variables	Number (%) Age=Mean +/- SD	Self harm n (% of group)	Unadjusted Odds Ratio	P value
<b>Age (years)</b>	26.0 (11.0)	4591	0.98 (0.97-0.98)	<0.001
<b>Gender</b>	6635	4252	ref	
Female	(91.5%)	(58.6%)		
Male	613 (8.5%)	334 (4.6%)	0.67 (0.58-0.79)	<0.001
<b>Marital Status</b>				
Single	5081 (70.1%)	3,341 (46.0%)	ref	
Married/partner	724 (9.98%)	429 (5.91%)	0.76 (0.65 -0.89)	P=0.001
Separate/divorced/widow	200 (2.76%)	122 (1.68%)	0.81 (0.61-1.1)	P=0.17
Not known	1248 (17.7%)	699 (9.64%)	n/a	n/a
<b>Ethnicity</b>				
White	6,008 (84.5%)	3752 (53.8%)	1.40 (1.10-1.78)	0.006
Black	344 (4.84%)	239 (3.50%)	1.26 (0.94-1.68)	0.12
South Asian	219 (3.1%)	149 (2.17%)	1.06 (0.86-.1.30)	0.59
Mixed and other	428 (6.0%)	273 (3.97%)	0.81 (0.53-1.25)	0.34
Unknown	115 (1.6%)	51 (<1%)	n/a	n/a
<b>Deprivation Score</b>				

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Group 1	2001 (26.9%)	1240 (27.0%)	ref	
Group 2	2897 (39.0%)	1778 (38.7%)	0.88 (0.83-1.11)	0.83
Group 3	2514 (33.8%)	1559 (34.0%)	1.00 (0.88-1.13)	0.99
Not known	22 (<1%)	14 (<1%)	1.34 (0.52-3.51)	0.54
<b>Primary ED diagnosis</b>				
AN	2553 (34.4%)	1876 (40.9%)	3.44 (1.05-11.3)	0.04
BN	1572 (21.2%)	973 (21.2%)	2.28 (0.69-7.52)	0.17
EDNOS	3298 (44.4%)	1737 (37.8%)	1.40 (0.43-4.59)	0.55
Unknown/other?	181 (2%)	5 (<1%)	n/a	n/a
<b>All substance misuse</b>				
None	2644 (99.3%)	4398 (95.8%)	ref	
Alcohol	13 (<1%)	132 (2.89%)	6.10 (3.44-10.8)	<0.001
Substance misuse	5 (<1%)	61 (1.33%)	7.22 (2.94- 18.3)	<0.001
<b>Depression</b>				
No	2532 (95.1%)	3777 (82.3%)	ref	
Yes	130 (4.89%)	814 (17.7%)	4.20 (3.46-5.01)	<0.001
<b>Anxiety disorders</b>				
No	2642 (99.3%)	4503 (98.1%)	ref	
Yes	20 (<1%)	88 (1.92%)	2.58 (1.58-4.21)	<0.001
<b>Borderline Personality Disorder</b>				
No	2656 (99.8%)	4090 (89.1%)	ref	
Yes	6 (<1%)	501 (10.9%)	54.2 (24.2-121.4)	<0.001
<b>Other Personality Disorder</b>				
No	2649 (99.5%)	3939 (85.8%)	ref	
Yes	13 (<1%)	652 (14.2%)	33.7 (19.4-58.5)	<0.001
<b>Bipolar Disorder</b>				
No	2648 (99.5%)	4370 (95.2%)	ref	
Yes	14 (<1%)	221 (4.81%)	9.57 (5.57-15.4)	<0.001

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### Suicidality reported amongst patients with eating disorders

Patients who reported suicidality were more likely to be younger (OR = 0.98, 95% CI 0.97-0.99;  $p < 0.001$ ), of white ethnicity (OR=1.59, 95% CI 1.23-2.10;  $p < 0.001$ ), less likely to be married or with a partner (OR=0.76, 95% CI 0.65-0.90;  $p = 0.001$ ) and have a diagnosis of AN (OR=8.20, 95% CI 2.17-30.1;  $p = 0.002$ ). They were also more likely to have a comorbid diagnosis, in particular BPD (OR = 26.2, 14.4-47.7;  $p < 0.001$ ), bipolar disorder (OR = 9.31, 95% CI 5.31-16.3;  $P < 0.001$ ) and alcohol misuse (OR = 6.59, 95% CI 3.56-12.2;  $p < 0.001$ ), as seen in Table 5.

**Table 5: Univariable logistic regression to determine the effect of demographics, primary ED diagnosis, and psychiatric comorbidities on risk of suicidality**

Variables	Number (%) Age=Mean +/- SD	Suicidality n (% of group)	Unadjusted Odds Ratio	P value
<b>Age (years)</b>	26.1 (11.0)		0.98 (0.97-0.99)	<0.001
<b>Gender %</b>	6635	4364 (65.8%)	ref	
Female	(91.5%)			
Male	613 (8.5%)	395 (64.4%)	0.94 (0.79-1.12)	
<b>Marital Status</b>				
Single	5081 (70.1%)	3476 (72.3%)	ref	
Married/partner	724 (9.98%)	451 (9.47%)	0.76 (0.65 -0.90)	P=0.001
Separate/divorced/widow	200 (2.76%)	131 (2.75%)	0.88 (0.65-1.18)	P=0.39
Not known	1248 (17.7%)	706 (14.8%)	n/a	n/a
<b>Ethnicity</b>				
White	6,008 (84.5%)	3907 (84.3%)	1.59 (1.23-2.10)	<0.001
Black	344 (4.84%)	255 (5.5%)	1.03 (0.77-1.37)	0.84
South Asian	219 (3.1%)	145 (3.13%)	0.97 (0.79-1.20)	0.80
Mixed and other	428 (6.0%)	276 (5.95%)	0.76 (0.49-1.17)	0.21
Unknown	115 (1.6%)	52 (1.12%)	n/a	n/a
<b>Deprivation Score</b>				
Group 1	2001 (26.9%)	1300 (27.3%)	ref	
Group 2	2897 (39.0%)	1829 (38.9%)	0.93 (0.83-1.06)	0.27
Group 3	2514 (33.8%)	1623 (34.1%)	0.98 (0.86-1.11)	0.75
Not known	22 (<1%)	12 (<1%)	0.76 (0.31-1.87)	0.54
<b>Presence of eating Disorder</b>				
AN	2553 (34.4%)	1909 (75.5%)	8.20 (2.17-30.1)	0.002
BN	1572 (21.2%)	1005 (67.7%)	4.49 (1.48-21.2)	0.01

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EDNOS	3298 (44.4%)	1847 (57.2%)	3.57 (0.94-13.47)	0.06
unknown	11 (<1%)	3 (<1%)	n/a	n/a
<b>All substance misuse</b>				
None	2472 (99.3%)	4570 (95.9%)	ref	
Alcohol	11 (<1%)	134 (2.81%)	6.59 (3.56-12.2)	<0.001
Substance misuse	6 (<1%)	60 (1.26%)	5.41 (2.33-12.5)	<0.001
<b>Depression</b>				
No	2383 (95.7%)	3926 (82.4%)	ref	
Yes	106 (4.26%)	838 (17.6%)	4.80 (3.90-5.91)	<0.001
<b>Borderline Personality Disorder</b>				
No	2478 (99.6%)	4268 (89.6%)	ref	
Yes	11 (<1%)	496 (10.4%)	26.2 (14.4-47.7)	<0.001
<b>Bipolar Disorder</b>				
No	2476 (99.5%)	4542 (95.3%)	ref	
Yes	13 (<1%)	222 (4.67%)	9.31 (5.31-16.3)	<0.001
<b>Anxiety</b>				
No	2476 (99.5%)	4669 (98.0%)	ref	
Yes	13 (<1%)	95 (2.0%)	3.88 (2.17-6.93)	<0.001
<b>Other Personality Disorder</b>				
No	2472 (99.3%)	4116 (86.4%)	ref	
Yes	17 (<1%)	648 (13.6%)	22.9 (14.1 -37.1)	<0.001

### **Multivariable analysis of the effect of comorbid psychiatric diagnoses on self-harm and suicidality**

When adjusting for demographics and the primary ED diagnosis, depression, bipolar disorder, other PD, substance misuse and alcohol use disorder remained significantly associated with suicidal behaviour. However, after adjusting for the demographics BPD remained only associated with self-harm (OR 2.84, 0.84-9.68, p=0.09) and not with suicidality (OR =1.52, 0.51-4.50, p=0.45). Anxiety disorders remained associated with suicidality (OR =1.93, 95% CI 1.01-3.69, p=0.05) but not self-harm (OR =1.47, 95% CI 0.81-2.65, p=0.20).

**Table 6 (i) Multivariable logistic regression examining the association between psychiatric comorbidities and self-harm; adjusted for demographics & ED diagnosis**

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Comorbid diagnosis	Adjusted Odds Ratio (95% CI)	P Value
Borderline Personality Disorder	2.84 (0.84-9.64)	0.09
Anxiety disorders	1.47 (0.81-2.65)	0.20
Depression	3.38 (2.72-4.21)	<0.001
Bipolar disorder	5.49 (2.97-10.2)	<0.001
Other PD	13.3 (5.72-30.8)	<0.001
Alcohol	5.26 (2.67-10.3)	<0.001
Substance misuse	4.35 (1.65-11.5)	0.003

**Table 6 (ii) Multivariable logistic regression examining the association between psychiatric comorbidities and suicidality: adjusted for demographics & ED diagnosis**

Comorbid diagnosis	Adjusted Odds Ratio (95% CI)	P Value
Borderline Personality Disorder	1.52 (0.51-4.50)	0.45
Anxiety disorders	1.93 (1.01-3.69)	0.05
Depression	3.62 (2.87-4.57)	<0.001
Bipolar disorder	5.07 (2.69-9.56)	<0.001
Other PD	11.6 (4.94-26.5)	<0.001
Alcohol use disorder	5.75 (2.73-12.1)	<0.001
Substance misuse	2.84 (1.16-6.98)	0.02

## Discussion

### Accuracy of the NLP output

The attribute agreements for precision of positive mentions of self-harm were >0.90 and for suicidality were >0.80; this demonstrates a 'strong' and 'near perfect' agreement and when compared to manual annotations (38) demonstrating the validity of the tool. However, negative polarity appeared less accurate for both tools, which demonstrates that the NLP tools were better at picking up positive and relevant mentions of both self-harm and suicidality within the clinical notes, than negative mentions.

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3 As we are relying on at least one positive mention to  
4 ascertain those with any past or current history of suicidal  
5 behaviour, this is unlikely to significantly impact the  
6 validity of the results.  
7

### 8 **Discussion of clinical findings**

10  
11 This study highlights the high lifetime prevalence (>60%)  
12 of both self-harm and suicidality reported amongst those  
13 diagnosed with eating disorders in both inpatient and  
14 outpatient settings. One explanation for the high rates of  
15 suicidal behaviour is that patients with EDs are at an  
16 increased risk of psychiatric comorbidities (1, 2),  
17 particularly mood disorders, substance misuse and personality  
18 disorders (29, 39). It is well documented that patients with  
19 comorbidities are more likely to self-harm and attempt suicide  
20 (40, 41). However, studies have demonstrated that even when  
21 adjusted for comorbid disorders, the risk of suicidal  
22 behaviour remains higher in patients with EDs than in the  
23 general population and comorbid disorders just elevate that  
24 risk further (17, 39, 42).  
25

26  
27 In our study, psychiatric comorbidity was associated with  
28 increased suicidal behaviour. In particular, BPD was  
29 associated with highly elevated odds of self-harm and suicidality, prior to adjustment.  
30 When adjusted, BPD increased the odds of self-harm, but interestingly not suicidality;  
31 although this adjusted association could reflect a lack of statistical power, as the cell size was  
32 small and CIs wide. This is consistent with previous studies as BPD presents with emotional  
33 dysregulation and impulsivity; associated with self-harm and ED symptoms such as bingeing  
34 or purging (18, 43). Furthermore, psychotherapies aimed at supporting those diagnosed with  
35 BPD and self-harm have been shown to be effective at also supporting patients with a  
36 diagnosis of ED (44, 45).  
37

38  
39 Similarly, those with a diagnosis of alcohol or substance misuse had an elevated odds  
40 of reporting self-harm and suicidality. Substance and alcohol misuse are associated with  
41 impulsivity; impulsivity is associated with behaviours such as bingeing and purging and  
42 suicidal behaviour (46-48) which has been shown to increase risk of completed suicide (49,  
43 50). Bipolar Disorder was also significantly associated with a five-fold increase in odds of  
44 suicidal behaviour when adjusted for demographics and the primary ED diagnosis. This is  
45 consistent with previous studies demonstrating an increased risk of hospitalised suicide  
46 attempts in ED patients with bipolar disorder compared to those without (17).  
47

48  
49 Relative to BN and other EDs, AN presented with the highest risk of suicidal  
50 behaviour, particularly suicidality. This is consistent with previous studies reporting a higher  
51 prevalence of suicide attempts and completed suicide in individuals with AN compared to  
52 those with BN or other EDs (5, 17, 23). However, it is important to  
53 consider the number of studies reporting suicidal behaviour  
54 most prevalent in BN (24, 48, 51). One explanation for the  
55 difference between our results and the above findings is that  
56 the current study used a diagnostic hierarchy of AN>BN>EDNOS  
57 to assign a primary ED diagnosis to patients; we know there is  
58 a well-established diagnostic crossover between EDs, with 50%  
59 of patients initially being diagnosed with AN being re-  
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3 diagnosed with BN or AN-binge purge subtype (52). Evidence also  
4 indicates that individuals experiencing diagnostic cross-over may be at particularly elevated  
5 risk of suicidality (53). Therefore, there could be a subtype of particular interest; future  
6 investigations should focus on diagnostic flux and whether the suicidal behaviour risk  
7 correlates to fluctuating ED symptoms (26).  
8

9 This study highlights the importance of further understanding the shared mechanisms  
10 for suicidal behaviour and ED diagnosis. There are various explanations that  
11 have been hypothesised for the high risk of self-harm and  
12 suicidality; some studies have suggested there are shared  
13 genetic factors predisposing to both conditions (54, 55).  
14 Others suggest that emotional dysregulation is associated with  
15 EDs and others demonstrate that adjusting for comorbid  
16 psychiatric disorders weakens any association (22, 54, 55).  
17 Increased pain tolerance and fearlessness for death are other  
18 hypotheses for the increased risk amongst patients diagnosed  
19 with EDs (56). The interpersonal theory of suicide describes  
20 that a higher lethality attempt requires both a desire for  
21 death and capability for suicide; capability of suicide has  
22 been theorised as developing after gradual chronic exposure to  
23 painful ED behaviours and habituation to fear and pain (57,  
24 58). Therefore, extreme restrictive eating may differentiate  
25 AN from other EDs, increasing the capability of both self-harm  
26 and suicidality (58).  
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### 30 **Strengths and limitations**

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33 The main strengths of this study are the size of the  
34 cohort (>7400), the longitudinal study design and long period  
35 of time for follow up (12.5 years), facilitated by the use of  
36 the CRIS database. There is currently a limited body of  
37 research on correlates and risk factors for suicidal behaviour  
38 amongst ED patients and previous studies have small numbers  
39 and a high usage of cross-sectional studies as well as studies  
40 at risk of reporting bias (26). The NLP approach used to  
41 extract clinician documentation of self-harm and suicidality  
42 from narrative text in EHRs reduces the risk of reporting bias  
43 and allows access to detailed clinical information that would  
44 not be available from EHR structured fields (30, 35).  
45

46 The main limitation of this study is that the tools were  
47 not able to consider the timing of reported suicidality or  
48 self-harm relative to the ED diagnosis. Therefore, it is  
49 possible the reported suicidal behaviour was prior to ED  
50 diagnosis; an improvement of the NLP tool would be to include  
51 temporality to understand specific time periods of risk for  
52 self-harm or reported suicidality. Another consideration is  
53 that due to changing diagnostic codes between the follow up  
54 period of 2007-2020 and the introduction of the ICD-11 codes  
55 of binge eating disorder, we had to include all EDs aside from  
56 AN and BN into one heterogenous group of diagnoses 'Other  
57 EDs'. This was needed to ensure consistency over the time  
58 period and to avoid the problem of small group sizes in the  
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3 regression analysis. Finally, given that EHRs include routine  
4 clinical data not primarily collected for research purposes,  
5 the study relies on clinician documentation which could  
6 include non-grammatical errors, jargon and idiosyncratic  
7 abbreviations; all of these could increase the chance of NLP  
8 misclassification (35). However, this was mitigated by using  
9 all documents available for each patient. Therefore, there  
10 were multiple opportunities to capture suicidality information  
11 to compensate for lack of sensitivity of the tool.  
12  
13

### 14 **Clinical and research implications**

15 This study highlights the importance of risk assessment  
16 screening in all patients diagnosed with EDs, with a particular  
17 emphasis on those diagnosed with AN and ED patients with  
18 comorbid psychiatric diagnoses. This study also highlights the  
19 potential use of EHR databases to further suicidality and  
20 self-harm research by utilising NLP techniques. These tools  
21 could potentially have use with further development in risk  
22 prediction within ED services; their use along clinician  
23 reported decisions could help predict future suicidal  
24 behaviour in ED patients (13, 30).  
25  
26

27  
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29 grant, but the primary researcher CC was supported by an NIHR  
30 Academic Clinical Fellowship training post and with support  
31 from the Biomedical Research Centre at the IoPPN.  
32

33 **Competing interests:** nil

34 **Author's contribution:** CC led the project, conducted the data  
35 analysis and wrote the final manuscript; RD and US helped  
36 support the project title and review the final script; KV and  
37 AS conducted data analysis and supported the final manuscript;  
38 AB, SV and HS conducted data abstraction and expertise with  
39 NLP analysis.  
40

### 41 **Ethical Approval and Data Availability**

42 The CRIS database has received ethical approval for secondary analysis: Oxford REC C,  
43 reference 18/SC/0372. The data is made available under specific governance requirements:  
44 researchers need to have a contract with the South London and Maudsley NHS Trust, which  
45 can be applied for relevant research studies. Each research project is reviewed by a service-  
46 user led oversight committee of the National Institute of Health Research Biomedical  
47 Research Centre. On request, and after appropriate arrangements, the data and modelling  
48 employed in this study can be viewed within the secure system firewall.  
49  
50

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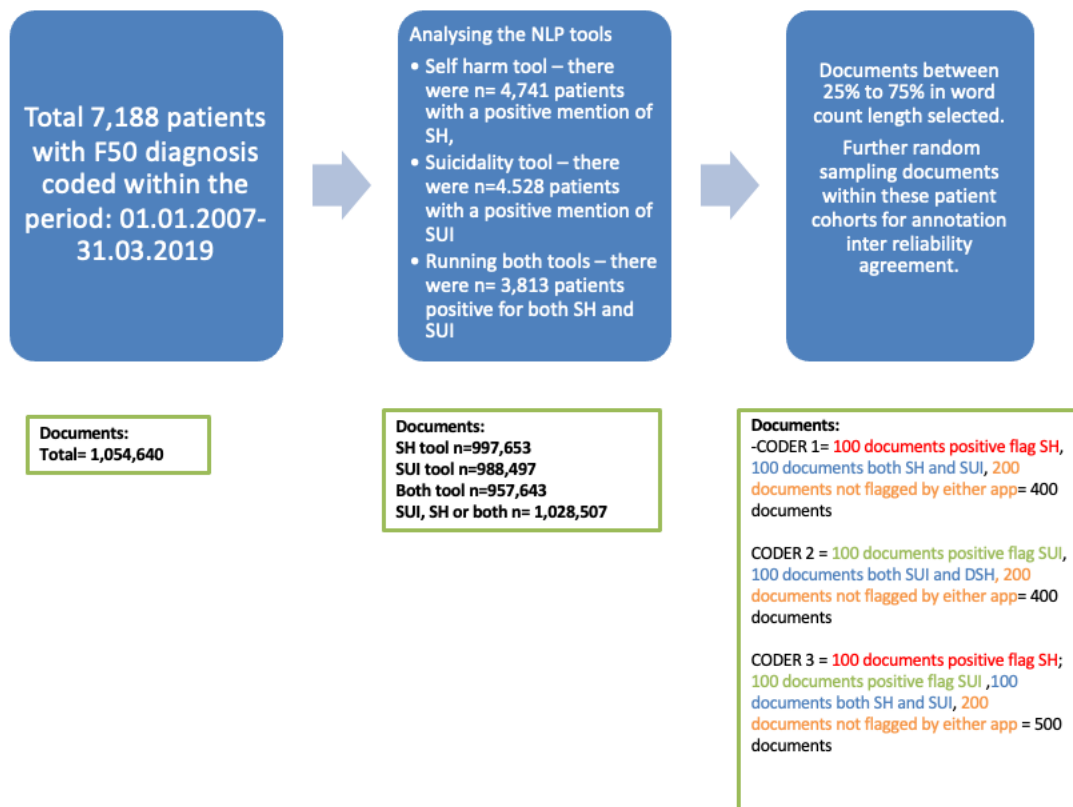
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Supplementary File Figure 1

**Figure 1: Workflow for validation of both NLP tools**



ew only



STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	2
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3
Bias	9	Describe any efforts to address potential sources of bias	4
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	5
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	5-6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	5-6
Outcome data	15*	Report numbers of outcome events or summary measures over time	7

1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5-7
2			(b) Report category boundaries when continuous variables were categorized	
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
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9	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5-7
10				
11	<b>Discussion</b>			
12				
13	Key results	18	Summarise key results with reference to study objectives	7-8
14	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8
15				
16	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
17				
18				
19	Generalisability	21	Discuss the generalisability (external validity) of the study results	8
20				
21	<b>Other information</b>			
22	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	9
23				
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\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

# BMJ Open

## Using natural language processing to extract self-harm and suicidality data from a clinical sample of patients with eating disorders: a retrospective cohort study

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<b>Primary Subject Heading</b>:	Mental health
Secondary Subject Heading:	Health informatics
Keywords:	Eating disorders < PSYCHIATRY, Suicide & self-harm < PSYCHIATRY, BIOTECHNOLOGY & BIOINFORMATICS, EPIDEMIOLOGY

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9 **Using natural language processing to extract self-harm and**  
10 **suicidality data from a clinical sample of patients with eating**  
11 **disorders: a retrospective cohort study**  
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19 Charlotte Cliffe<sup>1</sup>, Aida Seyedsalehi<sup>1</sup>; Katerina Vardavoulia<sup>1</sup>, Andre Bittar<sup>1</sup>, Sumithra  
20 Velupillai<sup>1</sup>, Hitesh Shetty<sup>1</sup>, Ulrike Schmidt<sup>1</sup>, Rina Dutta<sup>1</sup>  
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**Key words:** self-harm, suicidality, eating disorders, electronic health records, natural  
language processing

**Word count:** 3827

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4 3 Using natural language processing to extract self-harm and suicidality data from a  
5 4 clinical sample of patients with eating disorders: a retrospective cohort study  
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9 6 Charlotte Cliffe, Aida Seyedsalehi, Katerina Vardavoulia, Andre Bittar, Sumithra Velupillai,  
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11 7 Ulrike Schmidt, Rina Dutta

12 8 **Abstract**  
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15  
16 10 **Objectives:** The objective of this study was to determine risk factors for those diagnosed with  
17 11 eating disorders who report self-harm and suicidality.

18  
19 12 **Design & Setting:** This study was a retrospective cohort study within a secondary mental  
20 13 health service, South London & Maudsley NHS Trust. **Participants:** All diagnosed with an  
21 14 F50 diagnosis of eating disorder from 01/2009-09/2019 were included. **Intervention and**  
22 15 **measures:** Electronic health records (EHRs) for these patients were extracted and two natural  
23 16 language processing tools were used to determine documentation of self-harm and suicidality  
24 17 in their clinical notes. These tools were validated manually for attribute agreement scores  
25 18 within this study.

26 19 **Results:** The attribute agreements for precision of positive mentions of self-harm were 0.96  
27 20 and for suicidality were 0.80; this demonstrates a 'strong' and 'near perfect' agreement and  
28 21 highlights the reliability of the tools in identifying the EHRs reporting self-harm or  
29 22 suicidality. There were 7434 patients with EHRs available and diagnosed with eating  
30 23 disorders included in the study from the dates 01/2007 to 09/2019. Of these, 4591(61.8%)  
31 24 had a mention of self-harm within their records and 4764 (64.0%) had a mention of  
32 25 suicidality; 3899 (52.4%) had mentions of both. Patients reporting either self-harm or  
33 26 suicidality were more likely to have a diagnosis of anorexia nervosa (self-harm, AN  
34 27 OR=3.44, 95% CI 1.05-11.3, p=0.04; suicidality, AN OR=8.20, 95% CI 2.17-30.1; p=0.002).  
35 28 They were also more likely to have a diagnosis of borderline personality disorder (p<0.001),  
36 29 bipolar disorder (p<0.001) or substance misuse disorder (p<0.001).

37  
38 30 **Conclusion:** A high percentage of patients (>60%) diagnosed with eating disorders report  
39 31 either self-harm or suicidal thoughts. Relative to other eating disorders, those diagnosed with  
40 32 anorexia nervosa were more likely to report either self-harm or suicidal thoughts. Psychiatric  
41 33 comorbidity, in particular borderline personality disorder and substance misuse were also  
42 34 associated with an increase risk in self-harm and suicidality. Therefore, risk assessment  
43 35 amongst patients diagnosed with eating disorders is crucial.  
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## Article Summary: Strengths and Limitations of this study

1. The size of the cohort is over 7400 patients
2. Long period of follow up (12.5 years)
3. Limited number of study designs (most cross sectional) reporting on suicidal behaviour amongst those with EDs
4. The tools used to detect self-harm and suicidality are not able to consider the temporality in relation to the ED diagnosis; therefore, the suicidal behaviour could have been detected prior to diagnosis
5. The clinical records are routine clinical data not primarily collected for research therefore rely on clinician documentation.

Word count: 3827

## Introduction

Patients diagnosed with eating disorders (EDs), including anorexia nervosa (AN), bulimia nervosa (BN) and eating disorder not otherwise specified (EDNOS)<sup>1</sup> are at a greater risk of mortality compared to the general population (1, 2). A major contribution to this increased mortality rate is the higher risk of completed suicide in patients with EDs (3). Individuals with a lifetime diagnosis of AN and BN are 18 and 7 times more likely to die from suicide compared to age-matched general population controls, respectively (4, 5). Those with a diagnosis of EDNOS are 4 times more likely to complete suicide (6). Therefore, given the elevated risk of suicide amongst patients diagnosed with EDs, it is of utmost importance that factors associated with this risk are determined (7).

Self-harm and suicidal ideation are both strong predictors of subsequent suicide (8). Self-harm can be defined as 'self-injurious behaviour characterised by deliberate harm to the body in the absence of an intent to die'(9) and suicidal ideation can be defined as 'thoughts about killing oneself, which may or may not include a plan'(10). It has been determined that a common antecedent for completed suicide in the general population, is previous self harm, with up to 60% of people who complete suicide having previously self-harmed, the majority

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<sup>1</sup> The DSM-V now refers to 'Otherwise specified feeding or eating disorder' (OFSED); but the studies and data included in this paper used the DSM-IV equivalent term of EDNOS.

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4 70 within one year prior to the attempt (11, 12). Lifetime suicidal ideation is also associated with  
5 71 attempted suicide (up to 30%); those with a plan have an increased risk of completed suicide  
6 72 (up to 55%) and the majority of attempts occur within the first year of the onset of suicidal  
7 73 ideation (13). Therefore, identifying patients who report either lifetime suicidal ideation and  
8  
9 74 self-harm is an important clinical marker for those at risk of later suicide.

10  
11  
12 75 Previous studies have demonstrated the association between suicidality, self-harm and  
13 76 EDs (14-17). Our previous study focusing on suicide attempts, demonstrated the cumulative  
14  
15 77 10-year incidence of suicide attempts in a population of patients with EDs as 6.8% (17).  
16  
17 78 Rates of self-harm have been reported as high as 42% for AN, up to 55% for bulimia nervosa  
18  
19 79 BN (18) and 26% for EDNOS (19). A recent meta-analysis summarised that 22% of patients  
20  
21 80 with AN and 33% of patients with BN reported lifetime self-harm (20).

22 81 Studies have reported mixed findings in terms of suicide attempts across ED  
23  
24 82 diagnostic categories (21-24), with many showing no difference in suicide attempts between  
25  
26 83 ED subtypes, some demonstrated higher rates of suicide attempts and self-harm in AN  
27  
28 84 compared to BN (17, 23, 25, 26) and others reported more frequent suicide attempts and  
29  
30 85 ideation in BN compared to AN (24, 27). Furthermore, binge eating disorder (BED), a  
31  
32 86 relatively new diagnostic category, has also been associated with increased suicidality (22).  
33  
34 87 In other studies, it appears that binge eating and purging are particularly associated with  
35  
36 88 increased risks of attempted suicide, due to their association with impulsivity (26, 28). Some  
37  
38 89 of these heterogenous findings have been attributed to differences in patient settings  
39  
40 90 (outpatient or inpatient) (21), diagnostic subtyping (e.g. restricting vs binge-purging AN) (28)  
41  
42 91 or the methods used for determining suicide attempts (26).

43  
44 92 Some studies have focused on risk factors for developing suicidal behaviour amongst  
45  
46 93 those with EDs. A number of risk factors have been identified, such as younger age of ED  
47  
48 94 onset, specific personality traits, comorbid disorders, negative life events and substance  
49  
50 95 misuse (17, 26, 29). However, there are limitations with a number of past studies in terms of  
51  
52 96 low numbers of suicidal behaviour within the study population, resulting in low power (5).  
53  
54 97 One possibility to improve this problem is to use longitudinal psychiatric case records, such  
55  
56 98 as electronic health records (EHRs). This captures a large enough population manifesting  
57  
58 99 suicidal behaviour, to ensure sufficient power (30).

59 100 The increasing use of EHRs in hospital care systems, alongside the growth of health  
60  
61 101 informatics allows us to develop computational tools that can analyse these large clinical  
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63 102 datasets (31). Natural language processing (NLP) tools allow us to determine information  
64  
65 103 about symptomatology from information written in free-text EHRs (32). Previous research

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4 104 has shown that using NLP applications increases the positive predictive value of detecting  
5 105 patient-level suicidality (33). This is of particular use for suicidal behaviour, as both positive  
6  
7 106 and negated mentions of suicidality and self-harm are routinely reported within free text  
8  
9 107 during psychiatric assessments and follow-up (31, 34, 35).

10  
11 108 The aim of this study was to evaluate two NLP tools, one that identifies mentions of  
12 109 self-harm (36), and the other that identifies suicidality (35) for a cohort of ED patients. To  
13  
14 110 achieve this, we compared the performance of the NLP tools against a gold-standard set of  
15 111 manually annotated documents, using previously defined coding rules. We then used the tools  
16  
17 112 to identify positive mentions of either self-harm or suicidality on a patient level, to evaluate  
18  
19 113 the incidence of self-harm and suicidality in patients diagnosed with eating disorders over a  
20  
21 114 12-year period.

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## 23 116 **Methods**

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### 25 118 **Study Design and Setting**

26  
27  
28 119 This study is a retrospective cohort study using data obtained from South London and  
29 120 Maudsley National Health Service Foundation trust (SLaM). This is a mental health service  
30  
31 121 serving an estimated population of 2 million residents of southeast London. Patients come  
32  
33 122 from the London boroughs of Croydon, Southwark, Lambeth, Lewisham, Bromley, Bexley  
34  
35 123 and Greenwich. SLaM has had fully electronic records since 2006 and the National Institute  
36  
37 124 for Health Research funded Biomedical Research Centre supports the infrastructure for  
38  
39 125 rendering its anonymised records available for research. We analysed the data as ‘event  
40  
41 126 notes’ in the electronic health records (EHRs), irrespective whether they were created during  
42  
43 127 an inpatient stay, during follow-up or a telephone appointment.

44 128

### 45 129 **Patient and public involvement**

46 130 No patient involved.

47 131

### 48 132 **Inclusion criteria and exposures**

49  
50  
51 133 The analysed cohort was extracted via the Clinical Record Interactive Search (CRIS)  
52 134 system (37) and comprised of individuals who received an International Classification of  
53  
54 135 Diseases, 10<sup>th</sup> Revision (ICD-10) (38) diagnosis of an ED (F50.0-F50.9) within the 12-year  
55  
56 136 observation period of 1 January 2007 to 31 September 2019. These patients were identified  
57  
58 137 using two data sources available within the EHRs. First, structured information on diagnosis  
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4 138 from drop down fields in the source record. Second, structured variables which are routinely  
5 139 extracted from open text fields using a bespoke algorithm generated by the Generalised  
6  
7 140 Architecture for Text Engineering (GATE) software (39). The comorbidity exposures of  
8  
9 141 interest were diagnoses of substance misuse (F10-F19), bipolar disorder (F31), anxiety  
10  
11 142 disorders, depression (F32 and F33) and personality disorder (F60) determined by structured  
12  
13 143 information on the EHRs in the drop-down fields in the source record.  
14  
15 144  
16 145

### 17 146 **Primary outcomes**

18  
19 147 The outcomes of interest were a patient reporting at least one positive mention of self-  
20  
21 148 harm or one positive mention of suicidality. Information on these outcomes was extracted  
22  
23 149 using NLP applications that have been previously developed and used within similar datasets  
24  
25 150 (31, 34, 35). The first application used rule-based linguistic processing to identify positive  
26  
27 151 mentions of self-harm (SH) in clinical texts, this included historic and current episodes, but  
28  
29 152 did not include self-harm ideation. The second application, also rule-based and using lexical  
30  
31 153 resource, included suicidal ideation (SUI) of both a passive and active nature; both of these  
32  
33 154 were recorded as a binary outcome. A detailed description of the development of both NLP  
34  
35 155 tools used to identify mentions of self-harm and suicidality are described in previous studies  
36  
37 156 (35, 36).  
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### 40 160 **Workflow for validating the NLP tools**

41 161 **Figure 1** shows the workflow for validating the NLP tools to determine the primary  
42  
43 162 outcomes. All F50 diagnoses between 1<sup>st</sup> Jan 2007 and 31<sup>st</sup> March 2019 were included in the  
44  
45 163 validation; this period of time was 6 months shorter than the final analysis due to the lag time  
46  
47 164 between the validation and final statistical analysis. In total, 7,188 patients met the inclusion  
48  
49 165 criteria, of which 6,972 had at least one EHR document available. Overall, **1,054,640**  
50  
51 166 documents were available for these patients. For all 6,972 patients, the NLP tools were used  
52  
53 167 to search for mentions of both suicidality and self-harm. In total, 5,456 patients had positive  
54  
55 168 mentions of either SH or SUI, 4741 had any mention of SH, 4528 had any mention of SUI,  
56  
57 169 and 3813 patients had both SH and SUI mentioned. Manual annotations were compared to  
58  
59 170 the NLP tool annotations and attribute agreements were calculated (40).

58 171 From these patients, a sample of documents was randomly extracted. This was  
59  
60 172 achieved by firstly restricting the patients to those who had a number of EHR documents

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4 173 within the 1<sup>st</sup> and 3<sup>rd</sup> quartiles, to eliminate outliers with very few documents or with  
5 174 excessive documentation. This resulted in 2923 patients in total with positive mentions of  
6  
7 175 either SH or SUI (135,317 documents), 2431 patients with a positive mention of SH (114,962  
8  
9 176 documents), 2294 patients with a positive mention of SUI (110,399 documents), and 1802  
10 177 patients with a positive mention of both SH and SUI (90,044 documents). Each patient had a  
11  
12 178 minimum of 17 documents and maximum of 99 documents.

13  
14 179 A randomised sample of 500 documents was taken for manual review: 100 with a  
15 180 positive mention of suicidality only, 100 with a positive mention of self-harm only, 100 with  
16 181 a mention of both self-harm and suicidality and 200 with no mention of either. Three manual  
17 182 coders, including one clinically trained psychiatrist (CC, AS, AV), were assigned either  
18  
19 183 suicidality (AS, 400 documents), self-harm (AV, 400 documents) or both (CC, 500  
20 184 documents) for review. The sets were independently classified with 300 of them crossing  
21  
22 185 over and classified by all three authors.

23  
24  
25 186 For the suicidality documents, two coders (CC and AS) independently labelled each  
26 187 document as suicidal, non-suicidal or uncertain. Inter-rater agreement was measured using  
27 188 Cohen's Kappa and the F1 statistic on a document level to determine interrater reliability  
28  
29 189 (40). Any discrepancies were discussed and clarified to develop a 'gold standard' set of  
30 190 documents. The same principle was applied to mentions of self-harm within the documents,  
31  
32 191 determined by two coders (CC, AV). Any mention of self-harm within the document was  
33  
34 192 coded as positive, negative and whether relevant or non-relevant, for example a positive code  
35 193 refers to the note referring to an act of self-harm by the individual, negative refers to a denial  
36  
37 194 or negated act of self-harm. If the mention was about a friend or family member that was not  
38  
39 195 relevant to the patient non-relevant was coded. (see Figure 1).  
40  
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42 196

### 43 197 **Testing the Algorithms**

44  
45 198 The performance of each NLP tool was tested by comparing the output of the  
46 199 application against the 'gold standard' set of manual annotations and calculating precision  
47 200 (positive predictive value; PPV) and recall (sensitivity) statistics. Good inter-rater agreement  
48  
49 201 between the NLP output and gold-standard was indicated by a Cohen's kappa of 0.80 for  
50 202 identifying both suicidality and self-harm. Scores > 0.80 demonstrate a 'strong' level of  
51  
52 203 agreement and reliable data, scores > 0.90 are 'almost perfect' agreement and scores > 0.60  
53  
54 204 were considered 'moderate' in agreement (40).  
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## 207 **Figure 1: Workflow for validation of both NLP tools**

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### 211 **Covariates**

212 The year and month of birth, gender, ethnicity, deprivation score and marital status  
213 were retrieved from the CRIS database. Age in years was calculated from the individual's  
214 first eating disorder diagnosis in the observation window or from January 2007 if the  
215 diagnosis preceded the observation period. The deprivation score was grouped into tertiles  
216 (33<sup>rd</sup> percentiles) and converted into a categorical variable. Previous studies have used this  
217 method of categorical definition using the same data source (2).

218

### 219 **Statistical analysis**

220 Analysis was completed using Stata software. All patients were eligible for analysis.  
221 Descriptive statistics were used to characterise the patients. Logistic regression was used to  
222 calculate odd ratios with 95% confidence intervals with self-harm or suicidality as the  
223 'outcome' and the comorbid psychiatric diagnoses as exposure. ED diagnoses were  
224 categorised into AN (both restricting and purging types), BN, and all other F50 diagnoses.  
225 For those with multiple diagnoses, a diagnostic hierarchy of AN>BN>other was used. The  
226 observation period started from the first date of diagnosis or 1 Jan 2007 if the diagnosis was  
227 made prior to this date and the ended on the 31 September 2019. Univariate logistic  
228 regression was used to estimate the effect of the primary ED diagnosis, demographic  
229 characteristics and psychiatric comorbidities on each of the outcomes of interest (SH and  
230 SUI). Next, multivariable analyses were performed to calculate the adjusted odds ratio (OR)  
231 and 95% confidence interval (CI) for each comorbid psychiatric diagnosis, whilst controlling  
232 for demographics and the ED diagnosis. the effect of the psychiatric comorbidities and  
233 demographics.

234

### 235 **Ethical Approval**

236 The CRIS database has received ethical approval for secondary analysis: Oxford REC  
237 C, reference 18/SC/0372.

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### 242 **Results**

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244 **Descriptive Statistics**

245 Table 1 summarises the different types of ED diagnosis by age. The mean age was

246 26.0 (SD 11; range 10-90)

247

248 **Table 1: Summary of all diagnoses by age group** (11 patients had no detailed information  
249 about the diagnosis other than 'F50')

250

Age group Years , (n)% total	AN	BN	EDNOS
<10 (39) <1%	4 (<1%)	0	35 (1.1%)
<b>10-19 (2572) 34.6%</b>	1250 (49.0%)	320 (20.4 %)	1002 (30.4%)
<b>20-29 (2720) 36.6%</b>	807 (31.6%)	714 (45.4 %)	1199 (36.4%)
<b>30-39 (1233) 16.6%</b>	276 (10.8%)	354 (22.5 %)	603 (18.3%)
<b>40-49 (527) 7.10%</b>	118 (4.62%)	122 (7.76 %)	287 (8.70%)
<b>50+ (332) 4.47%</b>	98 (3.84%)	62 (3.94 %)	172 (5.22%)
<b>TOTAL n= 7423 (11 missing detailed diagnosis)</b>	<b>2553</b>	<b>1572</b>	<b>3298</b>

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257 **Self-harm and Suicidality amongst patients**

258 The attribute agreements for the final corpus of documents on self-harm and

259 suicidality are displayed below in Table 2. The three attributes include 'positive' ie there is a

260 mention of either self-harm or suicidality, 'negative or non' ie there is a denial of self-harm

261 or suicidality and 'relevant' i.e. the mention is relevant to the patient and not a family

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262 member of friend. A summary of those reporting self-harm or suicidality by age are displayed  
263 in Table 3.

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267 **Table 2 ; Attribute agreements:** attribute agreements reflect the comparison of the NLP tool

268 output to the gold standard set of manually annotated documents. Annotations are document-

269 level for suicidality and mention-level for self-harm.

270

	Positive document for suicidality	Non-relevant document for suicidality	Non-suicidal documents	Positive mention of self-harm	Relevant mention of self-harm	Negative mention of self-harm
Precision	0.80	0.98	0.58	0.96	0.89	0.59
Recall	0.82	0.92	0.87	0.91	0.72	0.79
F1-score	0.81	0.95	0.70	0.94	0.80	0.68
Number of documents / mentions	114	106	55	528	385	86

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272

273 **Table 3: Self harm and suicidality reported amongst patients by age**

274

Age group, years	Self- harm present during follow up period, n (%l)	Suicidality present, n (%)
<10	16 (<1%)	15 (<1%)
10-19	1914 (41.7%)	1928 (40.5%)
20-29	1489 (32.4%)	1553 (32.6%)

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<b>30-39</b>	675 (14.7%)	722 (15.2%)
<b>40-49</b>	310 (6.75%)	168 (6.75%)
<b>50+</b>	187 (4.1%)	134 (5.38%)
<b>TOTAL</b>	<b>4591</b>	<b>4520</b>

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### 278 Self-harm-reported amongst patients with eating disorders

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280 Patients who reported self-harm (past or present) were more likely to be younger in age (OR  
 281 = 0.98, 95% CI 0.97-0.98; P<0.001), less likely to be female (OR = 0.67, 95% CI 0.58-0.79;  
 282 P<0.001) more likely to be of white ethnicity (OR = 1.40, 95% CI 1.10-1.78; p=0.006), and  
 283 more likely to have a diagnosis of AN (OR = 3.44, 95% CI 1.05-11.3; p=0.04). They were  
 284 also more likely to have a comorbid diagnosis; in particular a diagnosis of borderline  
 285 personality disorder (BPD; OR = 54.2, 95% CI 24.2-121.4; p<0.001), bipolar disorder (OR =  
 286 9.57, 95% CI 5.57-15.4; p<0.001) and substance misuse (OR =7.22 , 95% CI 2.94- 18.3;  
 287 p<0.001); as displayed in Table 4.

288

289 **Table 4: Univariable logistic regression to determine the effect of demographics,  
 290 primary ED diagnosis, and psychiatric comorbidities on risk of self-harm**

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292

Variables	Number (%) Age=Mean +/- SD	Self harm n (% of group)	Unadjusted Odds Ratio	P value
<b>Age (years)</b>	26.0 (11.0)	4591	0.98 (0.97-0.98)	<0.001
<b>Gender</b>	6635	4252	ref	
Female	(91.5%)	(58.6%)		
Male	613 (8.5%)	334 (4.6%)	0.67 (0.58-0.79)	<0.001
<b>Marital Status</b>				
Single	5081 (70.1%)	3,341 (46.0%)	ref	
Married/partner	724 (9.98%)	429 (5.91%)	0.76 (0.65 -0.89)	P=0.001
Separate/divorced/widow	200 (2.76%)	122 (1.68%)	0.81 (0.61-1.1)	P=0.17
Not known	1248 (17.7%)	699 (9.64%)	n/a	n/a
<b>Ethnicity</b>				

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White	6,008 (84.5%)	3752 (53.8%)	1.40 (1.10-1.78)	0.006
Black	344 (4.84%)	239 (3.50%)	1.26 (0.94-1.68)	0.12
South Asian	219 (3.1%)	149 (2.17%)	1.06 (0.86-1.30)	0.59
Mixed and other	428 (6.0%)	273 (3.97%)	0.81 (0.53-1.25)	0.34
Unknown	115 (1.6%)	51 (<1%)	n/a	n/a
<b>Deprivation Score</b>				
Group 1	2001 (26.9%)	1240 (27.0%)	ref	
Group 2	2897 (39.0%)	1778 (38.7%)	0.88 (0.83-1.11)	0.83
Group 3	2514 (33.8%)	1559 (34.0%)	1.00 (0.88-1.13)	0.99
Not known	22 (<1%)	14 (<1%)	1.34 (0.52-3.51)	0.54
<b>Primary ED diagnosis</b>				
AN	2553 (34.4%)	1876 (40.9%)	3.44 (1.05-11.3)	0.04
BN	1572 (21.2%)	973 (21.2%)	2.28 (0.69-7.52)	0.17
EDNOS	3298 (44.4%)	1737 (37.8%)	1.40 (0.43-4.59)	0.55
Unknown/other?	181 (2%)	5 (<1%)	n/a	n/a
<b>All substance misuse</b>				
None	2644 (99.3%)	4398 (95.8%)	ref	
Alcohol	13 (<1%)	132 (2.89%)	6.10 (3.44-10.8)	<0.001
Substance misuse	5 (<1%)	61 (1.33%)	7.22 (2.94- 18.3)	<0.001
<b>Depression</b>				
No	2532 (95.1%)	3777 (82.3%)	ref	
Yes	130 (4.89%)	814 (17.7%)	4.20 (3.46-5.01)	<0.001
<b>Anxiety disorders</b>				
No	2642 (99.3%)	4503 (98.1%)	ref	
Yes	20 (<1%)	88 (1.92%)	2.58 (1.58-4.21)	<0.001
<b>Borderline Personality Disorder</b>				
No	2656 (99.8%)	4090 (89.1%)	ref	
Yes	6 (<1%)	501 (10.9%)	54.2 (24.2-121.4)	<0.001
<b>Other Personality Disorder</b>				

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No	2649 (99.5%)	3939 (85.8%)	ref	
Yes	13 (<1%)	652 (14.2%)	33.7 (19.4-58.5)	<0.001
<b>Bipolar Disorder</b>				
No	2648 (99.5%)	4370 (95.2%)	ref	
Yes	14 (<1%)	221 (4.81%)	9.57 (5.57-15.4)	<0.001

293

294 **Suicidality reported amongst patients with eating disorders**

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296 Patients who reported suicidality were more likely to be younger (OR = 0.98, 95% CI 0.97-  
 297 0.99; p<0.001), of white ethnicity (OR=1.59, 95% CI 1.23-2.10; p<0.001), less likely to be  
 298 married or with a partner (OR=0.76, 95% CI 0.65-0.90; p=0.001 and have a diagnosis of AN  
 299 (OR=8.20, 95% CI 2.17-30.1; p=0.002). They were also more likely to have a comorbid  
 300 diagnosis, in particular BPD (OR = 26.2, 14.4-47.7; p<0.001), bipolar disorder (OR = 9.31,  
 301 95% CI 5.31-16.3; P<0.001) and alcohol misuse (OR = 6.59, 95% CI 3.56-12.2; p<0.001), as  
 302 seen in Table 5.

303

304 **Table 5: Univariable logistic regression to determine the effect of demographics,**  
 305 **primary ED diagnosis, and psychiatric comorbidities on risk of suicidality**

306

Variables	Number (%) Age=Mean +/- SD	Suicidality n (% of group)	Unadjusted Odds Ratio	P value
<b>Age (years)</b>	26.1 (11.0)		0.98 (0.97-0.99)	<0.001
<b>Gender %</b>	6635	4364 (65.8%)	ref	
Female	(91.5%)			
Male	613 (8.5%)	395 (64.4%)	0.94 (0.79-1.12)	
<b>Marital Status</b>				
Single	5081 (70.1%)	3476 (72.3%)	ref	
Married/partner	724 (9.98%)	451 (9.47%)	0.76 (0.65 -0.90)	P=0.001
Separate/divorced/widow	200 (2.76%)	131 (2.75%)	0.88 (0.65-1.18)	P=0.39
Not known	1248 (17.7%)	706 (14.8%)	n/a	n/a
<b>Ethnicity</b>				
White	6,008 (84.5%)	3907 (84.3%)	1.59 (1.23-2.10)	<0.001
Black	344 (4.84%)	255 (5.5%)	1.03 (0.77-1.37)	0.84
South Asian	219 (3.1%)	145 (3.13%)	0.97 (0.79-1.20)	0.80
Mixed and other	428 (6.0%)	276 (5.95%)	0.76 (0.49-1.17)	0.21
Unknown	115 (1.6%)	52 (1.12%)	n/a	n/a
<b>Deprivation Score</b>				

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Group 1	2001 (26.9%)	1300 (27.3%)	ref	
Group 2	2897 (39.0%)	1829 (38.9%)	0.93 (0.83-1.06)	0.27
Group 3	2514 (33.8%)	1623 (34.1%)	0.98 (0.86-1.11)	0.75
Not known	22 (<1%)	12 (<1%)	0.76 (0.31-1.87)	0.54
<b>Presence of eating Disorder</b>				
AN	2553 (34.4%)	1909 (75.5%)	8.20 (2.17-30.1)	0.002
BN	1572 (21.2%)	1005 (67.7%)	4.49 (1.48-21.2)	0.01
EDNOS	3298 (44.4%)	1847 (57.2%)	3.57 (0.94-13.47)	0.06
unknown	11 (<1%)	3 (<1%)	n/a	n/a
<b>All substance misuse</b>				
None	2472 (99.3%)	4570 (95.9%)	ref	
Alcohol	11 (<1%)	134 (2.81%)	6.59 (3.56-12.2)	<0.001
Substance misuse	6 (<1%)	60 (1.26%)	5.41 (2.33-12.5)	<0.001
<b>Depression</b>				
No	2383 (95.7%)	3926 (82.4%)	ref	
Yes	106 (4.26%)	838 (17.6%)	4.80 (3.90-5.91)	<0.001
<b>Borderline Personality Disorder</b>				
No	2478 (99.6%)	4268 (89.6%)	ref	
Yes	11 (<1%)	496 (10.4%)	26.2 (14.4-47.7)	<0.001
<b>Bipolar Disorder</b>				
No	2476 (99.5%)	4542 (95.3%)	ref	
Yes	13 (<1%)	222 (4.67%)	9.31 (5.31-16.3)	<0.001
<b>Anxiety</b>				
No	2476 (99.5%)	4669 (98.0%)	ref	
Yes	13 (<1%)	95 (2.0%)	3.88 (2.17-6.93)	<0.001
<b>Other Personality Disorder</b>				
No	2472 (99.3%)	4116 (86.4%)	ref	
Yes	17 (<1%)	648 (13.6%)	22.9 (14.1 -37.1)	<0.001

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### Multivariable analysis of the effect of comorbid psychiatric diagnoses on self-harm and suicidality

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When adjusting for demographics and the primary ED diagnosis, depression, bipolar disorder, other PD, substance misuse and alcohol use disorder remained significantly associated with suicidal behaviour. However, after adjusting for the demographics BPD remained only associated with self-harm (OR 2.84, 0.84-9.68,  $p=0.09$ ) and not with suicidality (OR =1.52, 0.51-4.50,  $p=0.45$ ). Anxiety disorders remained associated with suicidality (OR =1.93, 95% CI 1.01-3.69,  $p=0.05$ ) but not self-harm (OR =1.47, 95% CI 0.81-2.65,  $p=0.20$ ) as shown in Table 6 (i) and (ii).

**Table 6 (i) Multivariable logistic regression examining the association between psychiatric comorbidities and self-harm;** adjusted for demographics & ED diagnosis

Comorbid diagnosis	Adjusted Odds Ratio (95% CI)	P Value
Borderline Personality Disorder	2.84 (0.84-9.64)	0.09
Anxiety disorders	1.47 (0.81-2.65)	0.20
Depression	3.38 (2.72-4.21)	<0.001
Bipolar disorder	5.49 (2.97-10.2)	<0.001
Other PD	13.3 (5.72-30.8)	<0.001
Alcohol	5.26 (2.67-10.3)	<0.001
Substance misuse	4.35 (1.65-11.5)	0.003

**Table 6 (ii) Multivariable logistic regression examining the association between psychiatric comorbidities and suicidality;** adjusted for demographics & ED diagnosis

Comorbid diagnosis	Adjusted Odds Ratio (95% CI)	P Value
Borderline Personality Disorder	1.52 (0.51-4.50)	0.45
Anxiety disorders	1.93 (1.01-3.69)	0.05
Depression	3.62 (2.87-4.57)	<0.001
Bipolar disorder	5.07 (2.69-9.56)	<0.001
Other PD	11.6 (4.94-26.5)	<0.001

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Alcohol use disorder	5.75 (2.73-12.1)	<0.001
Substance misuse	2.84 (1.16-6.98)	0.02

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## Discussion

### Accuracy of the NLP output

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### Discussion of clinical findings

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3 365 aimed at supporting those diagnosed with BPD and self-harm have been shown to be  
4 366 effective at also supporting patients with a diagnosis of ED (46, 47).

5 367 Similarly, those with a diagnosis of alcohol or substance misuse had an elevated odds  
6 368 of reporting self-harm and suicidality. Substance and alcohol misuse are associated with  
7 369 impulsivity; impulsivity is associated with behaviours such as bingeing and purging and  
8 370 suicidal behaviour (48-50) which has been shown to increase risk of completed suicide (51,  
9 371 52). Bipolar Disorder was also significantly associated with a five-fold increase in odds of  
10 372 suicidal behaviour when adjusted for demographics and the primary ED diagnosis. This is  
11 373 consistent with previous studies demonstrating an increased risk of hospitalised suicide  
12 374 attempts in ED patients with bipolar disorder compared to those without (17).

13 375 Relative to BN and other EDs, AN presented with the highest risk of suicidal  
14 376 behaviour, particularly suicidality. This is consistent with previous studies reporting a higher  
15 377 prevalence of suicide attempts and completed suicide in individuals with AN compared to  
16 378 those with BN or other EDs (5, 17, 23). However, it is important to consider the number of  
17 379 studies reporting suicidal behaviour most prevalent in BN (24, 50, 53). One explanation for  
18 380 the difference between our results and the above findings is that the current study used a  
19 381 diagnostic hierarchy of AN>BN>EDNOS to assign a primary ED diagnosis to patients; we  
20 382 know there is a well-established diagnostic crossover between EDs, with 50% of patients  
21 383 initially being diagnosed with AN being re-diagnosed with BN or AN-binge purge subtype  
22 384 (54). Evidence also indicates that individuals experiencing diagnostic cross-over may be at  
23 385 particularly elevated risk of suicidality (55). Therefore, there could be a subtype of particular  
24 386 interest; future investigations should focus on diagnostic flux and whether the suicidal  
25 387 behaviour risk correlates to fluctuating ED symptoms (26).

26 388 This study highlights the importance of further understanding the shared mechanisms  
27 389 for suicidal behaviour and ED diagnosis. There are various explanations that have been  
28 390 hypothesised for the high risk of self-harm and suicidality; some studies have suggested there  
29 391 are shared genetic factors predisposing to both conditions (56, 57). Others suggest that  
30 392 emotional dysregulation is associated with EDs and others demonstrate that adjusting for  
31 393 comorbid psychiatric disorders weakens any association (22, 56, 57). Increased pain tolerance  
32 394 and fearlessness for death are other hypotheses for the increased risk amongst patients  
33 395 diagnosed with EDs (58). The interpersonal theory of suicide describes that a higher lethality  
34 396 attempt requires both a desire for death and capability for suicide; capability of suicide has  
35 397 been theorised as developing after gradual chronic exposure to painful ED behaviours and  
36 398 habituation to fear and pain (59, 60). Therefore, extreme restrictive eating may differentiate  
37 399 AN from other EDs, increasing the capability of both self-harm and suicidality (60).

### 400 401 **Strengths and limitations**

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403 The main strengths of this study are the size of the cohort (>7400), the longitudinal  
404 study design and long period of time for follow up (12.5 years), facilitated by the use of the

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4 405 CRIS database. There is currently a limited body of research on correlates and risk factors for  
5 406 suicidal behaviour amongst ED patients and previous studies have small numbers and a high  
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7 407 usage of cross-sectional studies as well as studies at risk of reporting bias (26). The NLP  
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9 408 approach used to extract clinician documentation of self-harm and suicidality from narrative  
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11 409 text in EHRs reduces the risk of reporting bias and allows access to detailed clinical  
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13 410 information that would not be available from EHR structured fields (30, 35).

14 411 The main limitation of this study is that the tools were not able to consider the timing  
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16 412 of reported suicidality or self-harm relative to the ED diagnosis. Therefore, it is possible the  
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18 413 reported suicidal behaviour was prior to ED diagnosis; an improvement of the NLP tool  
19  
20 414 would be to include temporality to understand specific time periods of risk for self-harm or  
21  
22 415 reported suicidality. Another consideration is that due to changing diagnostic codes between  
23  
24 416 the follow up period of 2007-2020 and the introduction of the ICD-11 codes of binge eating  
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26 417 disorder, we had to include all EDs aside from AN and BN into one heterogenous group of  
27  
28 418 diagnoses 'Other EDs'. This was needed to ensure consistency over the time period and to  
29  
30 419 avoid the problem of small group sizes in the regression analysis. Furthermore, given that  
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32 420 EHRs include routine clinical data not primarily collected for research purposes, the study  
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34 421 relies on clinician documentation which could include non-grammatical errors, jargon and  
35  
36 422 idiosyncratic abbreviations; all of these could increase the chance of NLP misclassification  
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38 423 (35). However, this was mitigated by using all documents available for each patient.

39 424 Therefore, there were multiple opportunities to capture suicidality information to compensate  
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41 425 for lack of sensitivity of the tool. Finally, the data relies on recording of suicidality and self-  
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43 426 harm following a clinical encounter. This is likely to result in some heterogeneity at a  
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45 427 document level, as some healthcare professionals may be more likely to discuss or record  
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47 428 self-harm or suicidal thoughts depending on their level of experience, clinical background or  
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49 429 their prior knowledge of the patient. However as there only needed to be one positive  
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51 430 mention of self-harm or one positive mention of suicidality, at a patient level, the threshold  
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53 431 was low for detection of either outcome.

54 432

### 55 433 **Clinical and research implications**

56 434 This study highlights the importance of risk assessment screening in all patients  
57  
58 435 diagnosed with EDs, with a particular emphasis on those diagnosed with AN and ED patients  
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60 436 with comorbid psychiatric diagnoses. This study also highlights the potential use of EHR  
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62 437 databases to further suicidality and self-harm research by utilising NLP techniques. These  
63  
64 438 tools could potentially have use with further development in risk prediction within ED

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439 services; their use along clinician reported decisions could help predict future suicidal  
440 behaviour in ED patients (13, 30).

441

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443 CC was supported by an NIHR Academic Clinical Fellowship training post and with support  
444 from the Biomedical Research Centre at the IoPPN.

445 **Competing interests:** nil

446 **Data Availability:** The data is made available under specific governance requirements:  
447 researchers need to have a contract with the South London and Maudsley NHS Trust, which  
448 can be applied for relevant research studies. Each research project is reviewed by a service-  
449 user led oversight committee of the National Institute of Health Research Biomedical  
450 Research Centre. On request, and after appropriate arrangements, the data and modelling  
451 employed in this study can be viewed within the secure system firewall

452 **Contribution:** Author's contribution: CC led the project, conducted the data analysis and  
453 wrote the final manuscript; RD supported with the title, analysis and final manuscript. US  
454 contributed with the final manuscript and topic expertise. AB, SV and HS conducted data  
455 extraction and analysis. AS and KV conducted data analysis and support with final  
456 manuscript.

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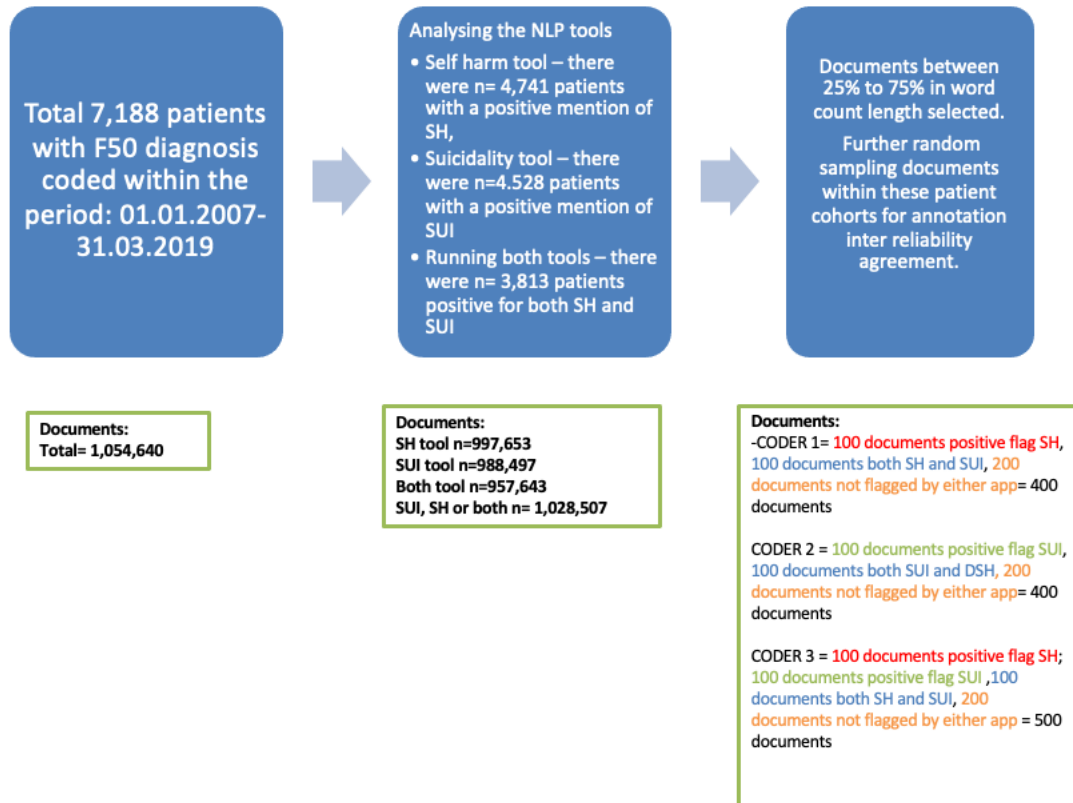
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Supplementary File Figure 1

**Figure 1: Workflow for validation of both NLP tools**



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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	2
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3
Bias	9	Describe any efforts to address potential sources of bias	4
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	5
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	5-6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	5-6
Outcome data	15*	Report numbers of outcome events or summary measures over time	7

1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5-7
2			(b) Report category boundaries when continuous variables were categorized	
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
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9	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5-7
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11	<b>Discussion</b>			
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13	Key results	18	Summarise key results with reference to study objectives	7-8
14	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8
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16	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
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19	Generalisability	21	Discuss the generalisability (external validity) of the study results	8
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21	<b>Other information</b>			
22	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	9
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\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

# BMJ Open

## Using natural language processing to extract self-harm and suicidality data from a clinical sample of patients with eating disorders: a retrospective cohort study

Journal:	<i>BMJ Open</i>
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<b>Primary Subject Heading</b>:	Mental health
Secondary Subject Heading:	Health informatics
Keywords:	Eating disorders < PSYCHIATRY, Suicide & self-harm < PSYCHIATRY, BIOTECHNOLOGY & BIOINFORMATICS, EPIDEMIOLOGY

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9 **Using natural language processing to extract self-harm and**  
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19 Charlotte Cliffe<sup>1</sup>, Aida Seyedsalehi<sup>1</sup>, Katerina Vardavoulia<sup>1</sup>, Andre Bittar<sup>1</sup>, Sumithra  
20 Velupillai<sup>1</sup>, Hitesh Shetty<sup>1</sup>, Ulrike Schmidt<sup>1</sup>, Rina Dutta<sup>1</sup>  
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**Key words:** self-harm, suicidality, eating disorders, electronic health records, natural  
language processing

**Word count:** 3612



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9 6 Charlotte Cliffe, Aida Seyedsalehi, Katerina Vardavoulia, Andre Bittar, Sumithra Velupillai,  
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11 7 Ulrike Schmidt, Rina Dutta

12 8 **Abstract**  
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16 10 **Objectives:** The objective of this study was to determine risk factors for those diagnosed with  
17 11 eating disorders who report self-harm and suicidality.

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19 12 **Design & Setting:** This study was a retrospective cohort study within a secondary mental  
20 13 health service, South London & Maudsley NHS Trust. **Participants:** All diagnosed with an  
21 14 F50 diagnosis of eating disorder from 01/2009-09/2019 were included. **Intervention and**  
22 15 **measures:** Electronic health records (EHRs) for these patients were extracted and two natural  
23 16 language processing tools were used to determine documentation of self-harm and suicidality  
24 17 in their clinical notes. These tools were validated manually for attribute agreement scores  
25 18 within this study.

26 19 **Results:** The attribute agreements for precision of positive mentions of self-harm were 0.96  
27 20 and for suicidality were 0.80; this demonstrates a 'near perfect' and 'strong' agreement and  
28 21 highlights the reliability of the tools in identifying the EHRs reporting self-harm or  
29 22 suicidality. There were 7434 patients with EHRs available and diagnosed with eating  
30 23 disorders included in the study from the dates 01/2007 to 09/2019. Of these, 4591(61.8%)  
31 24 had a mention of self-harm within their records and 4764 (64.0%) had a mention of  
32 25 suicidality; 3899 (52.4%) had mentions of both. Patients reporting either self-harm or  
33 26 suicidality were more likely to have a diagnosis of anorexia nervosa (self-harm, AN  
34 27 OR=3.44, 95% CI1.05-11.3, p=0.04; suicidality, AN OR=8.20, 95% CI 2.17-30.1; p=0.002).  
35 28 They were also more likely to have a diagnosis of borderline personality disorder (p<0.001),  
36 29 bipolar disorder (p<0.001) or substance misuse disorder (p<0.001).

37 30 **Conclusion:** A high percentage of patients (>60%) diagnosed with eating disorders report  
38 31 either self-harm or suicidal thoughts. Relative to other eating disorders, those diagnosed with  
39 32 anorexia nervosa were more likely to report either self-harm or suicidal thoughts. Psychiatric  
40 33 comorbidity, in particular borderline personality disorder and substance misuse were also  
41 34 associated with an increase risk in self-harm and suicidality. Therefore, risk assessment  
42 35 amongst patients diagnosed with eating disorders is crucial.  
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## Article Summary: Strengths and Limitations of this study

1. The size of the cohort is over 7400 patients
2. Long period of follow up (12.5 years)
3. Limited number of study designs (most cross sectional) reporting on suicidal behaviour amongst those with EDs
4. The tools used to detect self-harm and suicidality are not able to consider the temporality in relation to the ED diagnosis; therefore, the suicidal behaviour could have been detected prior to diagnosis
5. The clinical records are routine clinical data not primarily collected for research therefore rely on clinician documentation.

Word count: 3827

## Introduction

Patients diagnosed with eating disorders (EDs), including anorexia nervosa (AN), bulimia nervosa (BN) and eating disorder not otherwise specified (EDNOS)<sup>1</sup> are at a greater risk of mortality compared to the general population (1, 2). A major contribution to this increased mortality rate is the higher risk of completed suicide in patients with EDs (3). Individuals with a lifetime diagnosis of AN and BN are 18 and 7 times more likely to die from suicide compared to age-matched general population controls, respectively (4, 5). Those with a diagnosis of EDNOS are 4 times more likely to complete suicide (6). Therefore, given the elevated risk of suicide amongst patients diagnosed with EDs, it is of utmost importance that factors associated with this risk are determined (7).

Self-harm and suicidal ideation are both strong predictors of subsequent suicide (8). Self-harm can be defined as ‘self-injurious behaviour characterised by deliberate harm to the body in the absence of an intent to die’ (9) and suicidal ideation can be defined as ‘thoughts about killing oneself, which may or may not include a plan’ (10). It has been determined that a common antecedent for completed suicide in the general population, is previous self harm, with up to 60% of people who complete suicide having previously self-harmed, the majority

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<sup>1</sup> The DSM-V now refers to ‘Otherwise specified feeding or eating disorder’ (OFSED); but the studies and data included in this paper used the DSM-IV equivalent term of EDNOS.

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4 70 within one year prior to the attempt (11, 12). Lifetime suicidal ideation is also associated with  
5 71 attempted suicide (up to 30%); those with a plan have an increased risk of completed suicide  
6 72 (up to 55%) and the majority of attempts occur within the first year of the onset of suicidal  
7 73 ideation (13). Therefore, identifying patients who report either lifetime suicidal ideation and  
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9 74 self-harm is an important clinical marker for those at risk of later suicide.

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12 75 Previous studies have demonstrated the association between suicidality, self-harm and  
13 76 EDs (14-17). Our previous study focusing on suicide attempts, demonstrated the cumulative  
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15 77 10-year incidence of suicide attempts in a population of patients with EDs as 6.8% (17).  
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17 78 Rates of self-harm have been reported as high as 42% for AN, up to 55% for bulimia nervosa  
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19 79 BN (18) and 26% for EDNOS (19). A recent meta-analysis summarised that 22% of patients  
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21 80 with AN and 33% of patients with BN reported lifetime self-harm (20).

22 81 Studies have reported mixed findings in terms of suicide attempts across ED  
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24 82 diagnostic categories (21-24), with many showing no difference in suicide attempts between  
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26 83 ED subtypes, some demonstrated higher rates of suicide attempts and self-harm in AN  
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28 84 compared to BN (17, 23, 25, 26) and others reported more frequent suicide attempts and  
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30 85 ideation in BN compared to AN (24, 27). Furthermore, binge eating disorder (BED), a  
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32 86 relatively new diagnostic category, has also been associated with increased suicidality (22).  
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34 87 In other studies, it appears that binge eating and purging are particularly associated with  
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36 88 increased risks of attempted suicide, due to their association with impulsivity (26, 28). Some  
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38 89 of these heterogenous findings have been attributed to differences in patient settings  
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40 90 (outpatient or inpatient) (21), diagnostic subtyping (e.g. restricting vs binge-purging AN) (28)  
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42 91 or the methods used for determining suicide attempts (26).

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44 92 Some studies have focused on risk factors for developing suicidal behaviour amongst  
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46 93 those with EDs. A number of risk factors have been identified, such as younger age of ED  
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48 94 onset, specific personality traits, comorbid disorders, negative life events and substance  
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50 95 misuse (17, 26, 29). However, there are limitations with a number of past studies in terms of  
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52 96 low numbers of suicidal behaviour within the study population, resulting in low power (5).  
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54 97 One possibility to improve this problem is to use longitudinal psychiatric case records, such  
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56 98 as electronic health records (EHRs). This captures a large enough population manifesting  
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58 99 suicidal behaviour, to ensure sufficient power (30).

59 100 The increasing use of EHRs in hospital care systems, alongside the growth of health  
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101 informatics allows us to develop computational tools that can analyse these large clinical  
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103 datasets (31). Natural language processing (NLP) tools allow us to determine information  
about symptomatology from information written in free-text EHRs (32). Previous research

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4 104 has shown that using NLP applications increases the positive predictive value of detecting  
5 105 patient-level suicidality (33). This is of particular use for suicidal behaviour, as both positive  
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7 106 and negated mentions of suicidality and self-harm are routinely reported within free text  
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9 107 during psychiatric assessments and follow-up (31, 34, 35).

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11 108 The aim of this study was to evaluate two NLP tools, one that identifies mentions of  
12 109 self-harm (36), and the other that identifies suicidality (35) for a cohort of ED patients. To  
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14 110 achieve this, we compared the performance of the NLP tools against a gold-standard set of  
15 111 manually annotated documents, using previously defined coding rules. We then used the tools  
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17 112 to identify positive mentions of either self-harm or suicidality on a patient level, to evaluate  
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19 113 the incidence of self-harm and suicidality in patients diagnosed with eating disorders over a  
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21 114 12-year period.

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## 23 116 **Methods**

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### 25 118 **Study Design and Setting**

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28 119 This study is a retrospective cohort study using data obtained from South London and  
29 120 Maudsley National Health Service Foundation trust (SLaM). This is a mental health service  
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31 121 serving an estimated population of 2 million residents of southeast London. Patients come  
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33 122 from the London boroughs of Croydon, Southwark, Lambeth, Lewisham, Bromley, Bexley  
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35 123 and Greenwich. SLaM has had fully electronic records since 2006 and the National Institute  
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37 124 for Health Research funded Biomedical Research Centre supports the infrastructure for  
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39 125 rendering its anonymised records available for research. We analysed the data as ‘event  
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41 126 notes’ in the electronic health records (EHRs), irrespective whether they were created during  
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43 127 an inpatient stay, during follow-up or a telephone appointment.

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### 45 129 **Patient and public involvement**

46 130 No patient involved.

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### 48 132 **Inclusion criteria and exposures**

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51 133 The analysed cohort was extracted via the Clinical Record Interactive Search (CRIS)  
52 134 system (37) and comprised of individuals who received an International Classification of  
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54 135 Diseases, 10<sup>th</sup> Revision (ICD-10) (38) diagnosis of an ED (F50.0-F50.9) within the 12-year  
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56 136 observation period of 1 January 2007 to 31 September 2019. These patients were identified  
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58 137 using two data sources available within the EHRs. First, structured information on diagnosis  
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4 138 from drop down fields in the source record. Second, structured variables which are routinely  
5 139 extracted from open text fields using a bespoke algorithm generated by the Generalised  
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7 140 Architecture for Text Engineering (GATE) software (39). The comorbidity exposures of  
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9 141 interest were diagnoses of substance misuse (F10-F19), bipolar disorder (F31), anxiety  
10 142 disorders, depression (F32 and F33) and personality disorder (F60) determined by structured  
11 143 information on the EHRs in the drop-down fields in the source record.  
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### 17 146 **Primary outcomes**

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19 147 The outcomes of interest were a patient reporting at least one positive mention of self-  
20 148 harm or one positive mention of suicidality. Information on these outcomes was extracted  
21 149 using NLP applications that have been previously developed and used within similar datasets  
22 150 (31, 34, 35). The first application used rule-based linguistic processing to identify positive  
23 151 mentions of self-harm (SH) in clinical texts, this included historic and current episodes, but  
24 152 did not include self-harm ideation. The second application, also rule-based and using lexical  
25 153 resources, included suicidal ideation (SUI) of both a passive and active nature; both of these  
26 154 were recorded as a binary outcome. A detailed description of the development and evaluation  
27 155 of both NLP tools used to identify mentions of self-harm and suicidality are described in  
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29 153 previous studies (35, 36, 40).  
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### 40 160 **Workflow for validating the NLP tools**

41 161 **Figure 1** shows the workflow for validating the NLP tools to determine the primary  
42 162 outcomes. All F50 diagnoses between 1<sup>st</sup> Jan 2007 and 31<sup>st</sup> March 2019 were included in the  
43 163 validation; this period of time was 6 months shorter than the final analysis due to the lag time  
44 164 between the validation and final statistical analysis. In total, 7,188 patients met the inclusion  
45 165 criteria, of which 6,972 had at least one EHR document available. Overall, **1,054,640**  
46 166 documents were available for these patients. For all 6,972 patients, the NLP tools were used  
47 167 to search for mentions of both suicidality and self-harm. In total, 5,456 patients had positive  
48 168 mentions of either SH or SUI, 4741 had any mention of SH, 4528 had any mention of SUI,  
49 169 and 3813 patients had both SH and SUI mentioned. Manual annotations were compared to  
50 170 the NLP tool annotations and attribute agreements were calculated (41).  
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58 171 From these patients, a sample of documents was randomly extracted. This was  
59 172 achieved by firstly restricting the patients to those who had a number of EHR documents

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4 173 within the 1<sup>st</sup> and 3<sup>rd</sup> quartiles, to eliminate outliers with very few documents or with  
5 174 excessive documentation. This resulted in 2923 patients in total with positive mentions of  
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7 175 either SH or SUI (135,317 documents), 2431 patients with a positive mention of SH (114,962  
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9 176 documents), 2294 patients with a positive mention of SUI (110,399 documents), and 1802  
10 177 patients with a positive mention of both SH and SUI (90,044 documents). Each patient had a  
11  
12 178 minimum of 17 documents and maximum of 99 documents.

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14 179 A randomised sample of 500 documents was taken for manual review: 100 with a  
15 180 positive mention of suicidality only, 100 with a positive mention of self-harm only, 100 with  
16 181 a mention of both self-harm and suicidality and 200 with no mention of either. Three manual  
17 182 coders, including one clinically trained psychiatrist (CC, AS, AV), were assigned either  
18 183 suicidality (AS, 400 documents), self-harm (AV, 400 documents) or both (CC, 500  
19 184 documents) for review. The sets were independently classified with 300 of them crossing  
20 185 over and classified by all three authors.

21 186 For the suicidality documents, two coders (CC and AS) independently labelled each  
22 187 document as suicidal, non-suicidal or uncertain. Inter-rater agreement was measured using  
23 188 Cohen's Kappa and the F1 statistic on a document level to determine interrater reliability  
24 189 (41). Any discrepancies were discussed and clarified to develop a 'gold standard' set of  
25 190 documents. The same principle was applied to mentions of self-harm within the documents,  
26 191 determined by two coders (CC, AV). Any mention of self-harm within the document was  
27 192 coded as positive, negative and whether relevant or non-relevant, for example a positive code  
28 193 refers to the note referring to an act of self-harm by the individual, negative refers to a denial  
29 194 or negated act of self-harm. If the mention was about a friend or family member that was not  
30 195 relevant to the patient non-relevant was coded. (see Figure 1).

### 31 196 32 197 **Testing the Algorithms**

33 198 The performance of each NLP tool was tested by comparing the output of the  
34 199 application against the 'gold standard' set of manual annotations and calculating precision  
35 200 (positive predictive value; PPV) and recall (sensitivity) statistics. Good inter-rater agreement  
36 201 between the NLP output and gold-standard was indicated by a Cohen's kappa of 0.80 for  
37 202 identifying both suicidality and self-harm. Scores > 0.80 demonstrate a 'strong' level of  
38 203 agreement and reliable data, scores > 0.90 are 'almost perfect' agreement and scores > 0.60  
39 204 were considered 'moderate' in agreement (41).

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## 207 **Figure 1: Workflow for validation of both NLP tools**

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### 211 **Covariates**

212 The year and month of birth, gender, ethnicity, deprivation score and marital status were  
213 retrieved from the CRIS database. Age in years was calculated from the individual's first  
214 eating disorder diagnosis in the observation window or from January 2007 if the diagnosis  
215 preceded the observation period. We used the 'multiple deprivation score' which is a small-  
216 area-level measure of socioeconomic status, based on the individual's address closest to the  
217 diagnosis of the eating disorder in the observation window, covering seven components:  
218 employment, income, education, health, barriers to housing and services, crime and the living  
219 environment with specific weightings. The index of multiple deprivation is a well-established  
220 measure that has been widely used as a regional indicator for socioeconomic status in  
221 previous studies; the scores are transformed into percentiles (1-100) with higher scores  
222 indicating greater deprivation. The deprivation score was grouped into tertiles (33<sup>rd</sup>  
223 percentiles) and converted into a categorical variable. Previous studies have used this method  
224 of categorical definition using the same data source (2).

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### 226 **Statistical analysis**

227 Analysis was completed using Stata software. All patients were eligible for analysis.  
228 Descriptive statistics were used to characterise the patients. Logistic regression was used to  
229 calculate odd ratios with 95% confidence intervals with self-harm or suicidality as the  
230 'outcome' and the comorbid psychiatric diagnoses as exposure. ED diagnoses were  
231 categorised into AN (both restricting and purging types), BN, and all other F50 diagnoses.  
232 For those with multiple diagnoses, a diagnostic hierarchy of AN>BN>other was used. The  
233 observation period started from the first date of diagnosis or 1 Jan 2007 if the diagnosis was  
234 made prior to this date and the ended on the 31 September 2019. Univariate logistic  
235 regression was used to estimate the effect of the primary ED diagnosis, demographic  
236 characteristics and psychiatric comorbidities on each of the outcomes of interest (SH and  
237 SUI). Next, multivariable analyses were performed to calculate the adjusted odds ratio (OR)  
238 and 95% confidence interval (CI) for each comorbid psychiatric diagnosis, whilst controlling  
239 for demographics and the ED diagnosis. the effect of the psychiatric comorbidities and  
240 demographics.

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4 242 **Ethical Approval**

5 243 The CRIS database has received ethical approval for secondary analysis: Oxford REC  
6 244 C, reference 18/SC/0372.  
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13 249 **Results**

14 250  
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16 251 **Descriptive Statistics**

17 252 Table 1 summarises the different types of ED diagnosis by age. The mean age was  
18 253 26.0 (SD 11; range 10-90)  
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23 255 **Table 1: Summary of all diagnoses by age group** (11 patients had no detailed information  
24 256 about the diagnosis other than 'F50')  
25  
26 257

Age group Years, (n)% total	AN	BN	EDNOS
<10 (39) <1%	4 (<1%)	0	35 (1.1%)
10-19 (2572) 34.6%	1250 (49.0%)	320 (20.4 %)	1002 (30.4%)
20-29 (2720) 36.6%	807 (31.6%)	714 (45.4 %)	1199 (36.4%)
30-39 (1233) 16.6%	276 (10.8%)	354 (22.5 %)	603 (18.3%)
40-49 (527) 7.10%	118 (4.62%)	122 (7.76 %)	287 (8.70%)
50+ (332) 4.47%	98 (3.84%)	62 (3.94 %)	172 (5.22%)
<b>TOTAL</b> n= 7423 (11 missing detailed diagnosis)	<b>2553</b>	<b>1572</b>	<b>3298</b>

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264 **Self-harm and Suicidality amongst patients**

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The attribute agreements for the final corpus of documents on self-harm and suicidality are displayed below in Table 2. The three attributes include ‘positive’ ie there is a mention of either self-harm or suicidality, ‘negative or non’ ie there is a denial of self-harm or suicidality and ‘relevant’ i.e. the mention is relevant to the patient and not a family member or friend. A summary of those reporting self-harm or suicidality by age are displayed in Table 3.

**Table 2 ; Attribute agreements:** attribute agreements reflect the comparison of the NLP tool output to the gold standard set of manually annotated documents. Annotations are document-level for suicidality and mention-level for self-harm. The results from the study that developed and evaluated the suicidality tool reported 0.58-0.72 precision, 0.70-0.87 for recall and 0.69-0.75 F1-score (35) and the results from the study that developed and evaluated the self-harm tool reported 0.88-0.96 precision, 0.88-0.96 recall and 0.88-0.96 F1 score (40).

	Positive document for suicidality	Non-relevant document for suicidality	Non-suicidal documents	Positive mention of self-harm	Relevant mention of self-harm	Negative mention of self-harm
Precision	0.80	0.98	0.58	0.96	0.89	0.59
Recall	0.82	0.92	0.87	0.91	0.72	0.79
F1-score	0.81	0.95	0.70	0.94 (	0.80	0.68
Number of documents / mentions	114	106	55	528	385	86

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**Table 3: Self harm and suicidality reported amongst patients by age**

Age group, years	Self- harm present during follow up period, n (%)	Suicidality present, n (%)
<10	16 (<1%)	15 (<1%)
10-19	1914 (41.7%)	1928 (40.5%)
20-29	1489 (32.4%)	1553 (32.6%)
30-39	675 (14.7%)	722 (15.2%)
40-49	310 (6.75%)	168 (6.75%)
50+	187 (4.1%)	134 (5.38%)
<b>TOTAL</b>	<b>4591</b>	<b>4520</b>

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**Self-harm-reported amongst patients with eating disorders**

Patients who reported self-harm (past or present) were more likely to be younger in age (OR = 0.98, 95% CI 0.97-0.98; P<0.001), less likely to be female (OR = 0.67, 95% CI 0.58-0.79; P<0.001) more likely to be of white ethnicity (OR = 1.40, 95% CI 1.10-1.78; p=0.006), and more likely to have a diagnosis of AN (OR = 3.44, 95% CI 1.05-11.3; p=0.04). They were also more likely to have a comorbid diagnosis; in particular a diagnosis of borderline personality disorder (BPD; OR = 54.2, 95% CI 24.2-121.4; p<0.001), bipolar disorder (OR = 9.57, 95% CI 5.57-15.4; p<0.001) and substance misuse (OR =7.22 , 95% CI 2.94- 18.3; p<0.001); as displayed in Table 4.

**Table 4: Univariable logistic regression to determine the effect of demographics, primary ED diagnosis, and psychiatric comorbidities on risk of self-harm**

Variables	Number (%) Age=Mean +/- SD	Self harm n (% of group)	Unadjusted Odds Ratio	P value
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<b>Age (years)</b>	26.0 (11.0)	4591	0.98 (0.97-0.98)	<0.001
<b>Gender</b>	6635	4252	ref	
Female	(91.5%)	(58.6%)		
Male	613 (8.5%)	334 (4.6%)	0.67 (0.58-0.79)	<0.001
<b>Marital Status</b>				
Single	5081 (70.1%)	3,341 (46.0%)	ref	
Married/partner	724 (9.98%)	429 (5.91%)	0.76 (0.65 -0.89)	P=0.001
Separate/divorced/widow	200 (2.76%)	122 (1.68%)	0.81 (0.61-1.1)	P=0.17
Not known	1248 (17.7%)	699 (9.64%)	n/a	n/a
<b>Ethnicity</b>				
White	6,008 (84.5%)	3752 (53.8%)	1.40 (1.10-1.78)	0.006
Black	344 (4.84%)	239 (3.50%)	1.26 (0.94-1.68)	0.12
South Asian	219 (3.1%)	149 (2.17%)	1.06 (0.86-.1.30)	0.59
Mixed and other	428 (6.0%)	273 (3.97%)	0.81 (0.53-1.25)	0.34
Unknown	115 (1.6%)	51 (<1%)	n/a	n/a
<b>Deprivation Score</b>				
Group 1	2001 (26.9%)	1240 (27.0%)	ref	
Group 2	2897 (39.0%)	1778 (38.7%)	0.88 (0.83-1.11)	0.83
Group 3	2514 (33.8%)	1559 (34.0%)	1.00 (0.88-1.13)	0.99
Not known	22 (<1%)	14 (<1%)	1.34 (0.52-3.51)	0.54
<b>Primary ED diagnosis</b>				
AN	2553 (34.4%)	1876 (40.9%)	3.44 (1.05-11.3)	0.04
BN	1572 (21.2%)	973 (21.2%)	2.28 (0.69-7.52)	0.17
EDNOS	3298 (44.4%)	1737 (37.8%)	1.40 (0.43-4.59)	0.55
Unknown/other?	181 (2%)	5 (<1%)	n/a	n/a
<b>All substance misuse</b>				
None	2644 (99.3%)	4398 (95.8%)	ref	
Alcohol	13 (<1%)	132 (2.89%)	6.10 (3.44-10.8)	<0.001
Substance misuse	5 (<1%)	61 (1.33%)	7.22 (2.94- 18.3)	<0.001
<b>Depression</b>				
No	2532 (95.1%)	3777 (82.3%)	ref	

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Yes	130 (4.89%)	814 (17.7%)	4.20 (3.46-5.01)	<0.001
<b>Anxiety disorders</b>				
No	2642 (99.3%)	4503 (98.1%)	ref	
Yes	20 (<1%)	88 (1.92%)	2.58 (1.58-4.21)	<0.001
<b>Borderline Personality Disorder</b>				
No	2656 (99.8%)	4090 (89.1%)	ref	
Yes	6 (<1%)	501 (10.9%)	54.2 (24.2-121.4)	<0.001
<b>Other Personality Disorder</b>				
No	2649 (99.5%)	3939 (85.8%)	ref	
Yes	13 (<1%)	652 (14.2%)	33.7 (19.4-58.5)	<0.001
<b>Bipolar Disorder</b>				
No	2648 (99.5%)	4370 (95.2%)	ref	
Yes	14 (<1%)	221 (4.81%)	9.57 (5.57-15.4)	<0.001

303

304 **Suicidality reported amongst patients with eating disorders**

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306 Patients who reported suicidality were more likely to be younger (OR = 0.98, 95% CI 0.97-  
 307 0.99; p<0.001), of white ethnicity (OR=1.59, 95% CI 1.23-2.10; p<0.001), less likely to be  
 308 married or with a partner (OR=0.76, 95% CI 0.65-0.90; p=0.001 and have a diagnosis of AN  
 309 (OR=8.20, 95% CI 2.17-30.1; p=0.002). They were also more likely to have a comorbid  
 310 diagnosis, in particular BPD (OR = 26.2, 14.4-47.7; p<0.001), bipolar disorder (OR = 9.31,  
 311 95% CI 5.31-16.3; P<0.001) and alcohol misuse (OR = 6.59, 95% CI 3.56-12.2; p<0.001), as  
 312 seen in Table 5.

313

314 **Table 5: Univariable logistic regression to determine the effect of demographics,**  
 315 **primary ED diagnosis, and psychiatric comorbidities on risk of suicidality**

316

Variables	Number (%) Age=Mean +/- SD	Suicidality n (% of group)	Unadjusted Odds Ratio	P value
<b>Age (years)</b>	26.1 (11.0)		0.98 (0.97-0.99)	<0.001
<b>Gender %</b>	6635	4364 (65.8%)	ref	
Female	(91.5%)			
Male	613 (8.5%)	395 (64.4%)	0.94 (0.79-1.12)	
<b>Marital Status</b>				

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Single	5081 (70.1%)	3476 (72.3%)	ref	
Married/partner	724 (9.98%)	451 (9.47%)	0.76 (0.65 -0.90)	P=0.001
Separate/divorced/widow	200 (2.76%)	131 (2.75%)	0.88 (0.65-1.18)	P=0.39
Not known	1248 (17.7%)	706 (14.8%)	n/a	n/a
<b>Ethnicity</b>				
White	6,008 (84.5%)	3907 (84.3%)	1.59 (1.23-2.10)	<0.001
Black	344 (4.84%)	255 (5.5%)	1.03 (0.77-1.37)	0.84
South Asian	219 (3.1%)	145 (3.13%)	0.97 (0.79-1.20)	0.80
Mixed and other	428 (6.0%)	276 (5.95%)	0.76 (0.49-1.17)	0.21
Unknown	115 (1.6%)	52 (1.12%)	n/a	n/a
<b>Deprivation Score</b>				
Group 1	2001 (26.9%)	1300 (27.3%)	ref	
Group 2	2897 (39.0%)	1829 (38.9%)	0.93 (0.83-1.06)	0.27
Group 3	2514 (33.8%)	1623 (34.1%)	0.98 (0.86-1.11)	0.75
Not known	22 (<1%)	12 (<1%)	0.76 (0.31-1.87)	0.54
<b>Presence of eating Disorder</b>				
AN	2553 (34.4%)	1909 (75.5%)	8.20 (2.17-30.1)	0.002
BN	1572 (21.2%)	1005 (67.7%)	4.49 (1.48-21.2)	0.01
EDNOS	3298 (44.4%)	1847 (57.2%)	3.57 (0.94-13.47)	0.06
unknown	11 (<1%)	3 (<1%)	n/a	n/a
<b>All substance misuse</b>				
None	2472 (99.3%)	4570 (95.9%)	ref	
Alcohol	11 (<1%)	134 (2.81%)	6.59 (3.56-12.2)	<0.001
Substance misuse	6 (<1%)	60 (1.26%)	5.41 (2.33-12.5)	<0.001
<b>Depression</b>				
No	2383 (95.7%)	3926 (82.4%)	ref	
Yes	106 (4.26%)	838 (17.6%)	4.80 (3.90-5.91)	<0.001
<b>Borderline Personality Disorder</b>				
No	2478 (99.6%)	4268 (89.6%)	ref	
Yes	11 (<1%)	496 (10.4%)	26.2 (14.4-47.7)	<0.001
<b>Bipolar Disorder</b>				
No	2476 (99.5%)	4542 (95.3%)	ref	
Yes	13 (<1%)	222 (4.67%)	9.31 (5.31-16.3)	<0.001
<b>Anxiety</b>				

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No	2476 (99.5%)	4669 (98.0%)	ref	
Yes	13 (<1%)	95 (2.0%)	3.88 (2.17-6.93)	<0.001
<b>Other Personality Disorder</b>				
No	2472 (99.3%)	4116 (86.4%)	ref	
Yes	17 (<1%)	648 (13.6%)	22.9 (14.1 -37.1)	<0.001

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### 319 **Multivariable analysis of the effect of comorbid psychiatric diagnoses on self-harm and** 320 **suicidality**

321

322 When adjusting for demographics and the primary ED diagnosis, depression, bipolar  
323 disorder, other PD, substance misuse and alcohol use disorder remained significantly  
324 associated with suicidal behaviour. However, after adjusting for the demographics BPD  
325 remained only associated with self-harm (OR 2.84, 0.84-9.68, p=0.09) and not with  
326 suicidality (OR =1.52, 0.51-4.50, p=0.45). Anxiety disorders remained associated with  
327 suicidality (OR =1.93, 95% CI 1.01-3.69, p=0.05) but not self-harm (OR =1.47, 95% CI 0.81-  
328 2.65, p=0.20 as shown in Table 6 (i) and (ii)).

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### 331 **Table 6 (i) Multivariable logistic regression examining the association between psychiatric** 332 **comorbidities and self-harm;** adjusted for demographics & ED diagnosis

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Comorbid diagnosis	Adjusted Odds Ratio (95% CI)	P Value
Borderline Personality Disorder	2.84 (0.84-9.64)	0.09
Anxiety disorders	1.47 (0.81-2.65)	0.20
Depression	3.38 (2.72-4.21)	<0.001
Bipolar disorder	5.49 (2.97-10.2)	<0.001
Other PD	13.3 (5.72-30.8)	<0.001
Alcohol	5.26 (2.67-10.3)	<0.001
Substance misuse	4.35 (1.65-11.5)	0.003

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### 335 **Table 6 (ii) Multivariable logistic regression examining the association between psychiatric** 336 **comorbidities and suicidality;** adjusted for demographics & ED diagnosis

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Comorbid diagnosis	Adjusted Odds Ratio (95% CI)	P Value
Borderline Personality Disorder	1.52 (0.51-4.50)	0.45
Anxiety disorders	1.93 (1.01-3.69)	0.05
Depression	3.62 (2.87-4.57)	<0.001
Bipolar disorder	5.07 (2.69-9.56)	<0.001
Other PD	11.6 (4.94-26.5)	<0.001
Alcohol use disorder	5.75 (2.73-12.1)	<0.001
Substance misuse	2.84 (1.16-6.98)	0.02

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## Discussion

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### Accuracy of the NLP output

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4 364 patients with comorbidities are more likely to self-harm and attempt suicide (43, 44).  
5 365 However, studies have demonstrated that even when adjusted for comorbid disorders, the risk  
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7 366 of suicidal behaviour remains higher in patients with EDs than in the general population and  
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9 367 comorbid disorders just elevate that risk further (17, 42, 45).

10 368 In our study, psychiatric comorbidity was associated with increased suicidal  
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12 369 behaviour. In particular, BPD was associated with highly elevated odds of self-harm and  
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14 370 suicidality, prior to adjustment. When adjusted, BPD increased the odds of self-harm, but  
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16 371 interestingly not suicidality; although this adjusted association could reflect a lack of  
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18 372 statistical power, as the cell size was small and CIs wide. This is consistent with previous  
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20 373 studies as BPD presents with emotional dysregulation and impulsivity; associated with self-  
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22 374 harm and ED symptoms such as bingeing or purging (18, 46). Furthermore, psychotherapies  
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24 375 aimed at supporting those diagnosed with BPD and self-harm have been shown to be  
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26 376 effective at also supporting patients with a diagnosis of ED (47, 48).

27 377 Similarly, those with a diagnosis of alcohol or substance misuse had an elevated odds  
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29 378 of reporting self-harm and suicidality. Substance and alcohol misuse are associated with  
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31 379 impulsivity; impulsivity is associated with behaviours such as bingeing and purging and  
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33 380 suicidal behaviour (49-51) which has been shown to increase risk of completed suicide (52,  
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35 381 53). Bipolar Disorder was also significantly associated with a five-fold increase in odds of  
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37 382 suicidal behaviour when adjusted for demographics and the primary ED diagnosis. This is  
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39 383 consistent with previous studies demonstrating an increased risk of hospitalised suicide  
40  
41 384 attempts in ED patients with bipolar disorder compared to those without (17).

42 385 Relative to BN and other EDs, AN presented with the highest risk of suicidal  
43  
44 386 behaviour, particularly suicidality. This is consistent with previous studies reporting a higher  
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46 387 prevalence of suicide attempts and completed suicide in individuals with AN compared to  
47  
48 388 those with BN or other EDs (5, 17, 23). However, it is important to consider the number of  
49  
50 389 studies reporting suicidal behaviour most prevalent in BN (24, 51, 54). One explanation for  
51  
52 390 the difference between our results and the above findings is that the current study used a  
53  
54 391 diagnostic hierarchy of AN>BN>EDNOS to assign a primary ED diagnosis to patients; we  
55  
56 392 know there is a well-established diagnostic crossover between EDs, with 50% of patients  
57  
58 393 initially being diagnosed with AN being re-diagnosed with BN or AN-binge purge subtype  
59  
60 394 (55). Evidence also indicates that individuals experiencing diagnostic cross-over may be at  
61  
62 395 particularly elevated risk of suicidality (56). Therefore, there could be a subtype of particular  
63  
64 396 interest; future investigations should focus on diagnostic flux and whether the suicidal  
65  
66 397 behaviour risk correlates to fluctuating ED symptoms (26).

67 398 This study highlights the importance of further understanding the shared mechanisms  
68  
69 399 for suicidal behaviour and ED diagnosis. There are various explanations that have been  
70  
71 400 hypothesised for the high risk of self-harm and suicidality; some studies have suggested there  
72  
73 401 are shared genetic factors predisposing to both conditions (57, 58). Others suggest that  
74  
75 402 emotional dysregulation is associated with EDs and others demonstrate that adjusting for  
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77 403 comorbid psychiatric disorders weakens any association (22, 57, 58). Increased pain tolerance  
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79 404 and fearlessness for death are other hypotheses for the increased risk amongst patients

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4 405 diagnosed with EDs (59). The interpersonal theory of suicide describes that a higher lethality  
5 406 attempt requires both a desire for death and capability for suicide; capability of suicide has  
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7 407 been theorised as developing after gradual chronic exposure to painful ED behaviours and  
8  
9 408 habituation to fear and pain (60, 61). Therefore, extreme restrictive eating may differentiate  
10 409 AN from other EDs, increasing the capability of both self-harm and suicidality (61).

11 410

### 12 411 **Strengths and limitations**

13 412

14 413 The main strengths of this study are the size of the cohort (>7400), the longitudinal  
15 414 study design and long period of time for follow up (12.5 years), facilitated by the use of the  
16 415 CRIS database. There is currently a limited body of research on correlates and risk factors for  
17 416 suicidal behaviour amongst ED patients and previous studies have small numbers and a high  
18 417 usage of cross-sectional studies as well as studies at risk of reporting bias (26). The NLP  
19 418 approach used to extract clinician documentation of self-harm and suicidality from narrative  
20 419 text in EHRs reduces the risk of reporting bias and allows access to detailed clinical  
21 420 information that would not be available from EHR structured fields (30, 35).

22 421 The main limitation of this study is that the tools were not able to consider the timing  
23 422 of reported suicidality or self-harm relative to the ED diagnosis. Therefore, it is possible the  
24 423 reported suicidal behaviour was prior to ED diagnosis; an improvement of the NLP tool  
25 424 would be to include temporality to understand specific time periods of risk for self-harm or  
26 425 reported suicidality. Another consideration is that due to changing diagnostic codes between  
27 426 the follow up period of 2007-2020 and the introduction of the ICD-11 codes of binge eating  
28 427 disorder, we had to include all EDs aside from AN and BN into one heterogenous group of  
29 428 diagnoses 'Other EDs'. This was needed to ensure consistency over the time period and to  
30 429 avoid the problem of small group sizes in the regression analysis. Furthermore, given that  
31 430 EHRs include routine clinical data not primarily collected for research purposes, the study  
32 431 relies on clinician documentation which could include non-grammatical errors, jargon and  
33 432 idiosyncratic abbreviations; all of these could increase the chance of NLP misclassification  
34 433 (35). However, this was mitigated by using all documents available for each patient.

35 434 Therefore, there were multiple opportunities to capture suicidality information to compensate  
36 435 for lack of sensitivity of the tool. Finally, the data relies on recording of suicidality and self-  
37 436 harm following a clinical encounter. This is likely to result in some heterogeneity at a  
38 437 document level, as some healthcare professionals may be more likely to discuss or record  
39 438 self-harm or suicidal thoughts depending on their level of experience, clinical background or

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4 439 their prior knowledge of the patient. However as there only needed to be one positive  
5 440 mention of self-harm or one positive mention of suicidality, at a patient level, the threshold  
6  
7 441 was low for detection of either outcome.  
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9 442

### 10 443 **Clinical and research implications**

11 444 This study highlights the importance of risk assessment screening in all patients  
12  
13 445 diagnosed with EDs, with a particular emphasis on those diagnosed with AN and ED patients  
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15 446 with comorbid psychiatric diagnoses. This study also highlights the potential use of EHR  
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17 447 databases to further suicidality and self-harm research by utilising NLP techniques. These  
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19 448 tools could potentially have use with further development in risk prediction within ED  
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21 449 services; their use along clinician reported decisions could help predict future suicidal  
22  
23 450 behaviour in ED patients (13, 30).  
24

25 451  
26 452 **Funding statement:** This research did not receive a specific grant, but the primary researcher  
27  
28 453 CC was supported by an NIHR Academic Clinical Fellowship training post and with support  
29  
30 454 from the Biomedical Research Centre at the IoPPN.

31 455 **Competing interests:** nil

32 456 **Data Availability:** The data is made available under specific governance requirements:  
33  
34 457 researchers need to have a contract with the South London and Maudsley NHS Trust, which  
35  
36 458 can be applied for relevant research studies. Each research project is reviewed by a service-  
37  
38 459 user led oversight committee of the National Institute of Health Research Biomedical  
39  
40 460 Research Centre. On request, and after appropriate arrangements, the data and modelling  
41  
42 461 employed in this study can be viewed within the secure system firewall

43 462 **Contribution:** Author's contribution: CC led the project, conducted the data analysis and  
44  
45 463 wrote the final manuscript; RD supported with the title, analysis and final manuscript. US  
46  
47 464 contributed with the final manuscript and topic expertise. AB, SV and HS conducted data  
48  
49 465 extraction and analysis. AS and KV conducted data analysis and support with final  
50  
51 466 manuscript.

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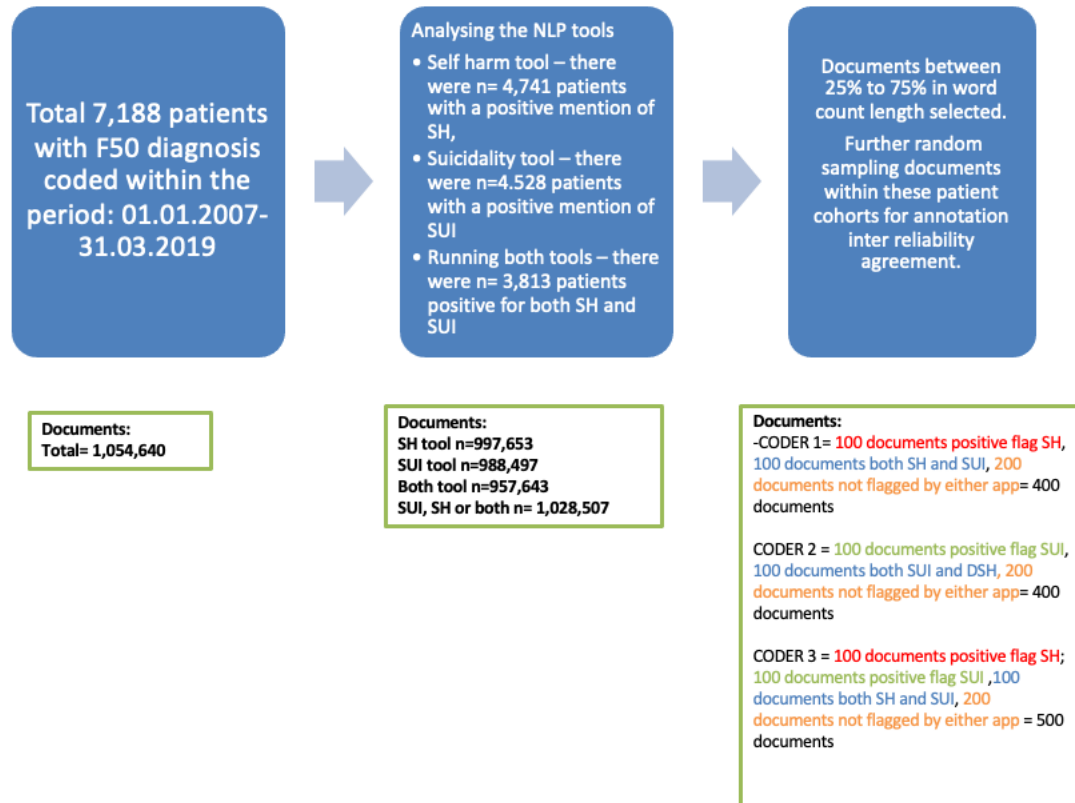
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## Supplementary File Figure 1

**Figure 1: Workflow for validation of both NLP tools**

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	2
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3
Bias	9	Describe any efforts to address potential sources of bias	4
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	5
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	5-6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	5-6
Outcome data	15*	Report numbers of outcome events or summary measures over time	7



1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5-7
2			(b) Report category boundaries when continuous variables were categorized	
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
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9	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5-7
10				
11	<b>Discussion</b>			
12				
13	Key results	18	Summarise key results with reference to study objectives	7-8
14	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8
15				
16	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
17				
18				
19	Generalisability	21	Discuss the generalisability (external validity) of the study results	8
20				
21	<b>Other information</b>			
22	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	9
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26 \*Give information separately for exposed and unexposed groups.

27  
28 **Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and  
29 published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely  
30 available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at  
31 <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is  
32 available at <http://www.strobe-statement.org>.  
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