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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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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% CI1.05-11.3, 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

5. The clinical records are routine clinical data not primarily collected for research therefore rely on clinician documentation.

Introduction

Patients diagnosed with eating disorders (EDs), including anorexia nervosa (AN), bulimia nervosa (BN) and eating disorder not otherwise specified (EDNOS)[1] 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 within one year prior to the attempt (11, 12). Lifetime suicidal ideation is also associated with attempted suicide (up to 30%); those with a plan have an increased risk of completed suicide (up to 55%) and the majority of attempts occur within the first year of the onset of suicidal ideation (13). Therefore, identifying patients who report either lifetime suicidal ideation and self-harm is an important clinical marker for those at risk of later suicide.

Previous studies have demonstrated the association between suicidality, self-harm and EDs (14-17). Our previous study focusing on suicide attempts, demonstrated the cumulative 10-year incidence of suicide attempts in a population of patients with EDs as 6.8% (17). Rates of self-harm have been reported as high as 42% for AN, up to 55% for bulimia nervosa BN (18) and 26% for EDNOS (19). A recent meta-

[1] 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.

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

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

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

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

The aim of this study was to evaluate two NLP approaches that identify both self-harm and suicidality in the clinical records for a cohort of ED patients. To achieve this, we compared the performance of the NLP tools against a gold-standard set of manually annotated documents, using previously defined coding rules. We then used the tools to identify positive mentions of either self-harm or suicidality on a patient level, to evaluate the incidence of self-harm and

suicidality in patients diagnosed with eating disorders over a 12-year period.

Methods

Study Design and Setting

This study is a retrospective cohort study using data obtained from South London and Maudsley National Health Service Foundation trust (SLaM). This is a mental health service serving an estimated population of 2 million residents of southeast London. Patients come from the London boroughs of Croydon, Southwark, Lambeth, Lewisham, Bromley, Bexley and Greenwich. SLaM has had fully electronic records since 2006 and the National Institute for Health Research funded Biomedical Research Centre supports the infrastructure for rendering its anonymised records available for research.

Inclusion criteria and exposures

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

Primary outcomes

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

Workflow for validating the NLP tools

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

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

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

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

Testing the Algorithms

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

Figure 1: Workflow for validation of both NLP tools

Covariates

The year and month of birth, gender, ethnicity, deprivation score and marital status were retrieved from the CRIS database. Age in years was calculated from the individual's first eating disorder diagnosis in the observation window or from January 2007 if the diagnosis preceded the observation period.

Patient and Public involvement

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

Statistical analysis

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

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%)
TOTAL n= 7423 (11 missing detailed diagnosis)	**2553**	**1572**	**3298**

Self-harm and Suicidality amongst patients

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 of 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 suicidality	**Relevant documents for suicidality**	**Non-suicidal documents**	**Positive for self-harm**	**Relevant documents for self-harm**	**Negative for self-harm**
Precision	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 (%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%)
30-39	675 (14.7%)	722 (15.2%)
40-49	310 (6.75%)	168 (6.75%)
50+	187 (4.1%)	134 (5.38%)

TOTAL	**4591**	**4520**

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% CI1.10-1.78; 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**
Age (years)	26.0 (11.0)	4591	0.98 (0.97-0.98)	<0.001
Gender Female	6635 (91.5%)	4252 (58.6%)	ref	
Male	613 (8.5%)	334 (4.6%)	0.67 (0.58-0.79)	<0.001
Marital Status				
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
Ethnicity				
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
Deprivation Score				

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
Primary ED diagnosis				
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
All substance misuse				
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
Depression				
No	2532 (95.1%)	3777 (82.3%)	ref	
Yes	130 (4.89%)	814 (17.7%)	4.20 (3.46-5.01)	<0.001
Anxiety disorders				
No	2642 (99.3%)	4503 (98.1%)	ref	
Yes	20 (<1%)	88 (1.92%)	2.58 (1.58-4.21)	<0.001
Borderline Personality Disorder				
No	2656 (99.8%)	4090 (89.1%)	ref	
Yes	6 (<1%)	501 (10.9%)	54.2 (24.2-121.4)	<0.001
Other Personality Disorder				
No	2649 (99.5%)	3939 (85.8%)	ref	
Yes	13 (<1%)	652 (14.2%)	33.7 (19.4-58.5)	<0.001
Bipolar Disorder				
No	2648 (99.5%)	4370 (95.2%)	ref	
Yes	14 (<1%)	221 (4.81%)	9.57 (5.57-15.4)	<0.001

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
Age (years)	26.1 (11.0)		0.98 (0.97-0.99)	<0.001
Gender % Female	6635 (91.5%)	4364 (65.8%)	ref	
Male	613 (8.5%)	395 (64.4%)	0.94 (0.79-1.12)	
Marital Status				
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
Ethnicity				
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
Deprivation Score				
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
Presence of eating Disorder				
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
All substance misuse				
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
Depression				
No	2383 (95.7%)	3926 (82.4%)	ref	
Yes	106 (4.26%)	838 (17.6%)	4.80 (3.90-5.91)	<0.001
Borderline Personality Disorder				
No	2478 (99.6%)	4268 (89.6%)	ref	
Yes	11 (<1%)	496 (10.4%)	26.2 (14.4-47.7)	<0.001
Bipolar Disorder				
No	2476 (99.5%)	4542 (95.3%)	ref	
Yes	13 (<1%)	222 (4.67%)	9.31 (5.31-16.3)	<0.001
Anxiety				
No	2476 (99.5%)	4669 (98.0%)	ref	
Yes	13 (<1%)	95 (2.0%)	3.88 (2.17-6.93)	<0.001
Other Personality Disorder				
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

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.

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

Discussion of clinical findings

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

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

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

Relative to BN and other EDs, AN presented with the highest risk of suicidal behaviour, particularly suicidality. This is consistent with previous studies reporting a higher prevalence of suicide attempts and completed suicide in individuals with AN compared to those with BN or other EDs (5, 17, 23). However, it is important to consider the number of studies reporting suicidal behaviour most prevalent in BN (24, 48, 51). One explanation for the difference between our results and the above findings is that the current study used a diagnostic hierarchy of AN>BN>EDNOS to assign a primary ED diagnosis to patients; we know there is a well-established diagnostic crossover between EDs, with 50% of patients initially being diagnosed with AN being re-

diagnosed with BN or AN-binge purge subtype (52). Evidence also indicates that individuals experiencing diagnostic cross-over may be at particularly elevated risk of suicidality (53). Therefore, there could be a subtype of particular interest; future investigations should focus on diagnostic flux and whether the suicidal behaviour risk correlates to fluctuating ED symptoms (26).

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

Strengths and limitations

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

The main limitation of this study is that the tools were not able to consider the timing of reported suicidality or self-harm relative to the ED diagnosis. Therefore, it is possible the reported suicidal behaviour was prior to ED diagnosis; an improvement of the NLP tool would be to include temporality to understand specific time periods of risk for self-harm or reported suicidality. Another consideration is that due to changing diagnostic codes between the follow up period of 2007-2020 and the introduction of the ICD-11 codes of binge eating disorder, we had to include all EDs aside from AN and BN into one heterogenous group of diagnoses 'Other EDs'. This was needed to ensure consistency over the time period and to avoid the problem of small group sizes in the

regression analysis. Finally, given that EHRs include routine clinical data not primarily collected for research purposes, the study relies on clinician documentation which could include non-grammatical errors, jargon and idiosyncratic abbreviations; all of these could increase the chance of NLP misclassification (35). However, this was mitigated by using all documents available for each patient. Therefore, there were multiple opportunities to capture suicidality information to compensate for lack of sensitivity of the tool.

Clinical and research implications

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

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

Ethical Approval and Data Availability

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

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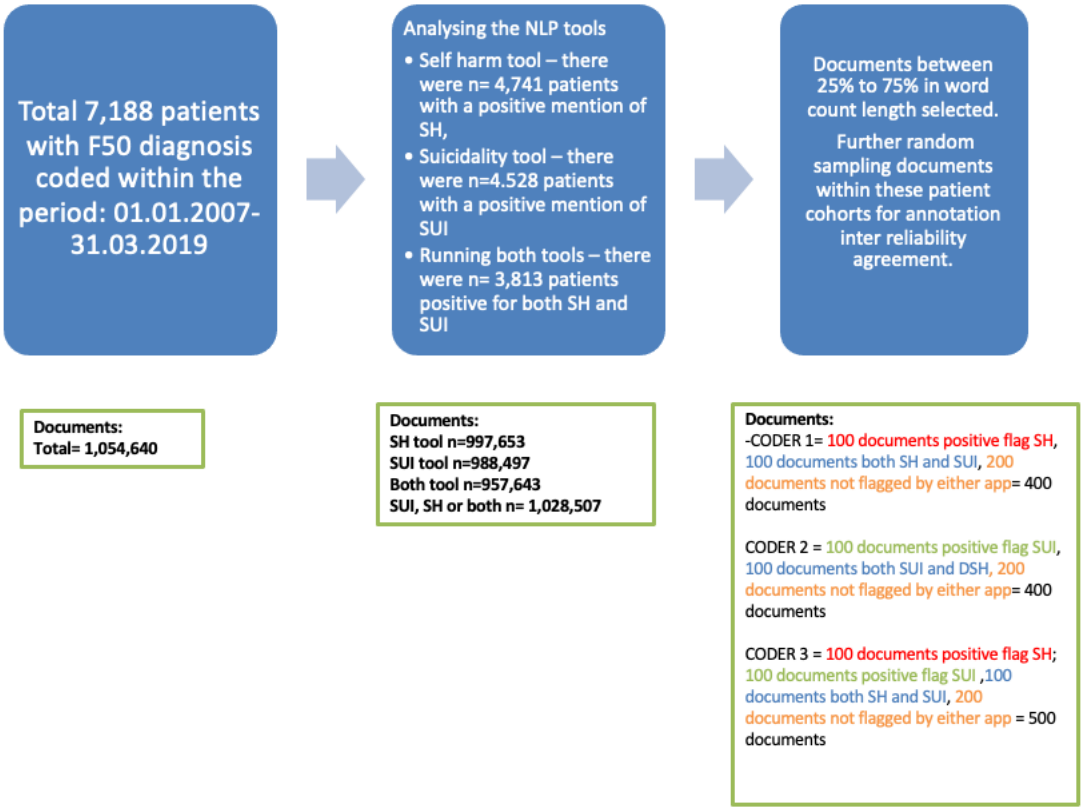
Supplementary File Figure 1

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
Title and abstract	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
Introduction			
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
Methods			
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
Results			
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

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 (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-8
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
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
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

*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.

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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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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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Key words: self-harm, suicidality, eating disorders, electronic health records, natural language processing

Word count: 3827

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

Charlotte Cliffe, Aida Seyedsalehi, Katerina Vardavoulia, Andre Bittar, Sumithra Velupillai, Ulrike Schmidt, Rina Dutta

Abstract

Objectives: The objective of this study was to determine risk factors for those diagnosed with eating disorders who report self-harm and suicidality.

Design & Setting: This study was a retrospective cohort study within a secondary mental health service, South London & Maudsley NHS Trust. **Participants**: All diagnosed with an F50 diagnosis of eating disorder from 01/2009-09/2019 were included. **Intervention and measures**: Electronic health records (EHRs) for these patients were extracted and two natural language processing tools were used to determine documentation of self-harm and 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 0.96 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% CI1.05-11.3, 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.

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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)[1] 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

[1] 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.

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

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

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

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

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

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

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

Methods

Study Design and Setting

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

Patient and public involvement

No patient involved.

Inclusion criteria and exposures

The analysed cohort was extracted via the Clinical Record Interactive Search (CRIS) system (37) and comprised of individuals who received an International Classification of Diseases, 10th Revision (ICD-10) (38) diagnosis of an ED (F50.0-F50.9) within the 12-year observation period of 1 January 2007 to 31 September 2019. These patients were identified using two data sources available within the EHRs. First, structured information on diagnosis

from drop down fields in the source record. Second, structured variables which are routinely extracted from open text fields using a bespoke algorithm generated by the Generalised Architecture for Text Engineering (GATE) software (39). The comorbidity exposures of interest were diagnoses of substance misuse (F10-F19), bipolar disorder (F31), anxiety disorders, depression (F32 and F33) and personality disorder (F60) determined by structured information on the EHRs in the drop-down fields in the source record.

Primary outcomes

The outcomes of interest were a patient reporting at least one positive mention of self-harm or one positive mention of suicidality. Information on these outcomes was extracted using NLP applications that have been previously developed and used within similar datasets (31, 34, 35). The first application used rule-based linguistic processing to identify positive mentions of self-harm (SH) in clinical texts, this included historic and current episodes, but did not include self-harm ideation. The second application, also rule-based and using lexical resource, included suicidal ideation (SUI) of both a passive and active nature; both of these were recorded as a binary outcome. A detailed description of the development of both NLP tools used to identify mentions of self-harm and suicidality are described in previous studies (35, 36).

Workflow for validating the NLP tools

Figure 1 shows the workflow for validating the NLP tools to determine the primary outcomes. All F50 diagnoses between 1st Jan 2007 and 31st March 2019 were included in the validation; this period of time was 6 months shorter than the final analysis due to the lag time between the validation and final statistical analysis. In total, 7,188 patients met the inclusion criteria, of which 6,972 had at least one EHR document available. Overall, 1,054,640 documents were available for these patients. For all 6,972 patients, the NLP tools were used to search for mentions of both suicidality and self-harm. In total, 5,456 patients had positive mentions of either SH or SUI, 4741 had any mention of SH, 4528 had any mention of SUI, and 3813 patients had both SH and SUI mentioned. Manual annotations were compared to the NLP tool annotations and attribute agreements were calculated (40).

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

within the 1st and 3rd quartiles, to eliminate outliers with very few documents or with excessive documentation. This resulted in 2923 patients in total with positive mentions of either SH or SUI (**135,317** documents), 2431 patients with a positive mention of SH (**114,962 documents),** 2294 patients with a positive mention of SUI (**110,399 documents)**, and 1802 patients with a positive mention of both SH and SUI (**90,044 documents)**. Each patient had a minimum of 17 documents and maximum of 99 documents.

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

For the suicidality documents, two coders (CC and AS) independently labelled each document as suicidal, non-suicidal or uncertain. Inter-rater agreement was measured using Cohen's Kappa and the F1 statistic on a document level to determine interrater reliability (40). Any discrepancies were discussed and clarified to develop a 'gold standard' set of documents. The same principle was applied to mentions of self-harm within the documents, determined by two coders (CC, AV). Any mention of self-harm within the document was coded as positive, negative and whether relevant or non-relevant, for example a positive code refers to the note referring to an act of self-harm by the individual, negative refers to a denial or negated act of self-harm. If the mention was about a friend or family member that was not relevant to the patient non-relevant was coded. (see Figure 1).

Testing the Algorithms

The performance of each NLP tool was tested by comparing the output of the application against the 'gold standard' set of manual annotations and calculating precision (positive predictive value; PPV) and recall (sensitivity) statistics. Good inter-rater agreement between the NLP output and gold-standard was indicated by a Cohen's kappa of 0.80 for identifying both suicidality and self-harm. Scores > 0.80 demonstrate a 'strong' level of agreement and reliable data, scores > 0.90 are 'almost perfect' agreement and scores > 0.60 were considered 'moderate' in agreement (40).

Figure 1: Workflow for validation of both NLP tools

Covariates

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

Statistical analysis

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

Ethical Approval

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

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Results

Descriptive Statistics

Table 1 summarises the different types of ED diagnosis by age. The mean age was 26.0 (SD 11; range 10-90)

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%)
TOTAL n= 7423 (11 missing detailed diagnosis)	**2553**	**1572**	**3298**

Self-harm and Suicidality amongst patients

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 of 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.

	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

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

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

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% CI1.10-1.78; 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**
Age (years)	26.0 (11.0)	4591	0.98 (0.97-0.98)	<0.001
Gender Female	6635 (91.5%)	4252 (58.6%)	ref	
Male	613 (8.5%)	334 (4.6%)	0.67 (0.58-0.79)	<0.001
Marital Status				
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
Ethnicity				

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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
Deprivation Score				
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
Primary ED diagnosis				
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
All substance misuse				
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
Depression				
No	2532 (95.1%)	3777 (82.3%)	ref	
Yes	130 (4.89%)	814 (17.7%)	4.20 (3.46-5.01)	<0.001
Anxiety disorders				
No	2642 (99.3%)	4503 (98.1%)	ref	
Yes	20 (<1%)	88 (1.92%)	2.58 (1.58-4.21)	<0.001
Borderline Personality Disorder				
No	2656 (99.8%)	4090 (89.1%)	ref	
Yes	6 (<1%)	501 (10.9%)	54.2 (24.2-121.4)	<0.001
Other Personality Disorder				

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

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**
Age (years)	26.1 (11.0)		0.98 (0.97-0.99)	<0.001
Gender % Female	6635 (91.5%)	4364 (65.8%)	ref	
Male	613 (8.5%)	395 (64.4%)	0.94 (0.79-1.12)	
Marital Status				
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
Ethnicity				
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
Deprivation Score				

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
Presence of eating Disorder				
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
All substance misuse				
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
Depression				
No	2383 (95.7%)	3926 (82.4%)	ref	
Yes	106 (4.26%)	838 (17.6%)	4.80 (3.90-5.91)	<0.001
Borderline Personality Disorder				
No	2478 (99.6%)	4268 (89.6%)	ref	
Yes	11 (<1%)	496 (10.4%)	26.2 (14.4-47.7)	<0.001
Bipolar Disorder				
No	2476 (99.5%)	4542 (95.3%)	ref	
Yes	13 (<1%)	222 (4.67%)	9.31 (5.31-16.3)	<0.001
Anxiety				
No	2476 (99.5%)	4669 (98.0%)	ref	
Yes	13 (<1%)	95 (2.0%)	3.88 (2.17-6.93)	<0.001
Other Personality Disorder				
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

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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

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 (40) 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. This is likely due to errors in the linguistic pre-processing needed to identify negation. As we are relying on at least one positive mention to ascertain those with any past or current history of suicidal behaviour, this is unlikely to significantly impact the validity of the results.

Discussion of clinical findings

This study highlights the high lifetime prevalence (>60%) of both self-harm and suicidality reported amongst those diagnosed with eating disorders in both inpatient and outpatient settings. One explanation for the high rates of suicidal behaviour is that patients with EDs are at an increased risk of psychiatric comorbidities (1, 2), particularly mood disorders, substance misuse and personality disorders (29, 41). It is well documented that patients with comorbidities are more likely to self-harm and attempt suicide (42, 43). However, studies have demonstrated that even when adjusted for comorbid disorders, the risk of suicidal behaviour remains higher in patients with EDs than in the general population and comorbid disorders just elevate that risk further (17, 41, 44).

In our study, psychiatric comorbidity was associated with increased suicidal behaviour. In particular, BPD was associated with highly elevated odds of self-harm and suicidality, prior to adjustment. When adjusted, BPD increased the odds of self-harm, but interestingly not suicidality; although this adjusted association could reflect a lack of statistical power, as the cell size was small and CIs wide. This is consistent with previous studies as BPD presents with emotional dysregulation and impulsivity; associated with self-harm and ED symptoms such as bingeing or purging (18, 45). Furthermore, psychotherapies

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

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

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

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

Strengths and limitations

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

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

The main limitation of this study is that the tools were not able to consider the timing of reported suicidality or self-harm relative to the ED diagnosis. Therefore, it is possible the reported suicidal behaviour was prior to ED diagnosis; an improvement of the NLP tool would be to include temporality to understand specific time periods of risk for self-harm or reported suicidality. Another consideration is that due to changing diagnostic codes between the follow up period of 2007-2020 and the introduction of the ICD-11 codes of binge eating disorder, we had to include all EDs aside from AN and BN into one heterogenous group of diagnoses 'Other EDs'. This was needed to ensure consistency over the time period and to avoid the problem of small group sizes in the regression analysis. Furthermore, given that EHRs include routine clinical data not primarily collected for research purposes, the study relies on clinician documentation which could include non-grammatical errors, jargon and idiosyncratic abbreviations; all of these could increase the chance of NLP misclassification (35). However, this was mitigated by using all documents available for each patient. Therefore, there were multiple opportunities to capture suicidality information to compensate for lack of sensitivity of the tool. Finally, the data relies on recording of suicidality and self-harm following a clinical encounter. This is likely to result in some heterogeneity at a document level, as some healthcare professionals may be more likely to discuss or record self-harm or suicidal thoughts depending on their level of experience, clinical background or their prior knowledge of the patient. However as there only needed to be one positive mention of self-harm or one positive mention of suicidality, at a patient level, the threshold was low for detection of either outcome.

Clinical and research implications

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

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

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Competing interests: nil

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

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

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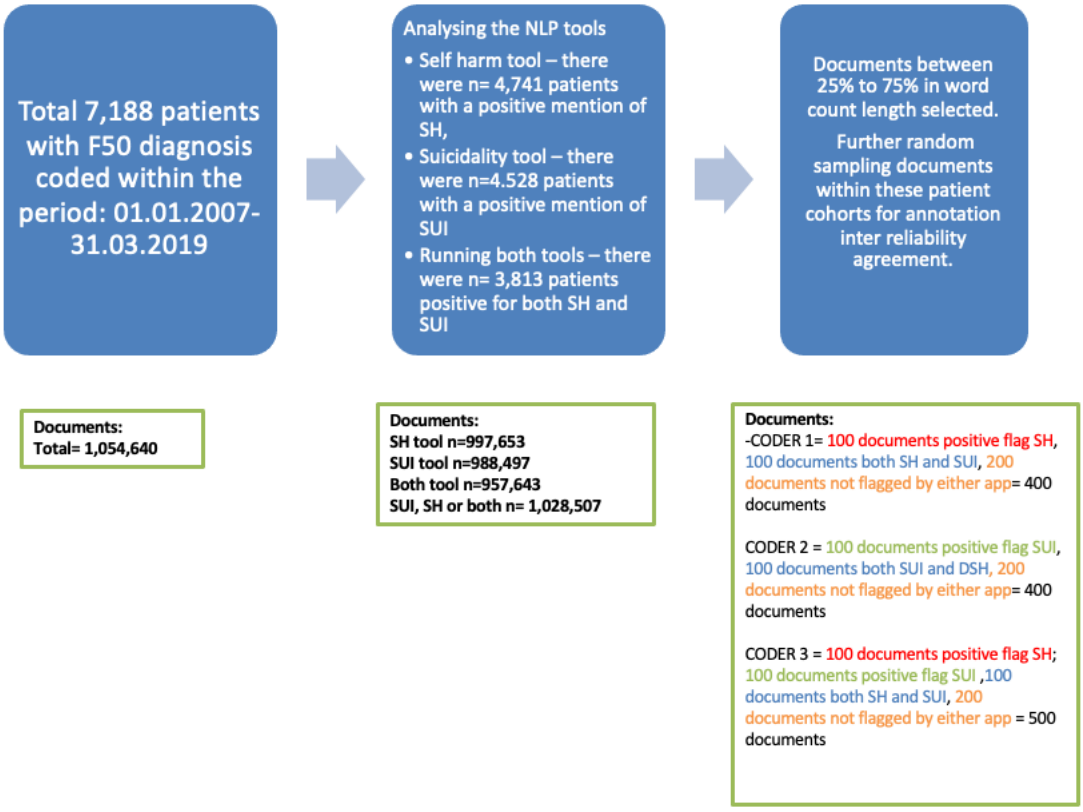
Supplementary File Figure 1

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
Title and abstract	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
Introduction			
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
Methods			
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
Results			
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

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 (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-8
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
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
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

*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.

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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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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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Key words: self-harm, suicidality, eating disorders, electronic health records, natural language processing

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

Charlotte Cliffe, Aida Seyedsalehi, Katerina Vardavoulia, Andre Bittar, Sumithra Velupillai, Ulrike Schmidt, Rina Dutta

Abstract

Objectives: The objective of this study was to determine risk factors for those diagnosed with eating disorders who report self-harm and suicidality.

Design & Setting: This study was a retrospective cohort study within a secondary mental health service, South London & Maudsley NHS Trust. **Participants**: All diagnosed with an F50 diagnosis of eating disorder from 01/2009-09/2019 were included. **Intervention and measures**: Electronic health records (EHRs) for these patients were extracted and two natural language processing tools were used to determine documentation of self-harm and 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 0.96 and for suicidality were 0.80; this demonstrates a 'near perfect' and 'strong' 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% CI1.05-11.3, 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
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)[1] 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

[1] 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.

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

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

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

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

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

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

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

Methods

Study Design and Setting

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

Patient and public involvement

No patient involved.

Inclusion criteria and exposures

The analysed cohort was extracted via the Clinical Record Interactive Search (CRIS) system (37) and comprised of individuals who received an International Classification of Diseases, 10th Revision (ICD-10) (38) diagnosis of an ED (F50.0-F50.9) within the 12-year observation period of 1 January 2007 to 31 September 2019. These patients were identified using two data sources available within the EHRs. First, structured information on diagnosis

from drop down fields in the source record. Second, structured variables which are routinely extracted from open text fields using a bespoke algorithm generated by the Generalised Architecture for Text Engineering (GATE) software (39). The comorbidity exposures of interest were diagnoses of substance misuse (F10-F19), bipolar disorder (F31), anxiety disorders, depression (F32 and F33) and personality disorder (F60) determined by structured information on the EHRs in the drop-down fields in the source record.

Primary outcomes

The outcomes of interest were a patient reporting at least one positive mention of self-harm or one positive mention of suicidality. Information on these outcomes was extracted using NLP applications that have been previously developed and used within similar datasets (31, 34, 35). The first application used rule-based linguistic processing to identify positive mentions of self-harm (SH) in clinical texts, this included historic and current episodes, but did not include self-harm ideation. The second application, also rule-based and using lexical resources, included suicidal ideation (SUI) of both a passive and active nature; both of these were recorded as a binary outcome. A detailed description of the development and evaluation of both NLP tools used to identify mentions of self-harm and suicidality are described in previous studies (35, 36, 40).

Workflow for validating the NLP tools

Figure 1 shows the workflow for validating the NLP tools to determine the primary outcomes. All F50 diagnoses between 1st Jan 2007 and 31st March 2019 were included in the validation; this period of time was 6 months shorter than the final analysis due to the lag time between the validation and final statistical analysis. In total, 7,188 patients met the inclusion criteria, of which 6,972 had at least one EHR document available. Overall, **1,054,640** documents were available for these patients. For all 6,972 patients, the NLP tools were used to search for mentions of both suicidality and self-harm. In total, 5,456 patients had positive mentions of either SH or SUI, 4741 had any mention of SH, 4528 had any mention of SUI, and 3813 patients had both SH and SUI mentioned. Manual annotations were compared to the NLP tool annotations and attribute agreements were calculated (41).

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

within the 1st and 3rd quartiles, to eliminate outliers with very few documents or with excessive documentation. This resulted in 2923 patients in total with positive mentions of either SH or SUI (**135,317** documents), 2431 patients with a positive mention of SH (**114,962 documents),** 2294 patients with a positive mention of SUI (**110,399 documents)**, and 1802 patients with a positive mention of both SH and SUI (**90,044 documents)**. Each patient had a minimum of 17 documents and maximum of 99 documents.

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

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

Testing the Algorithms

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

Figure 1: Workflow for validation of both NLP tools

Covariates

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

Statistical analysis

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

Ethical Approval

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

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Results

Descriptive Statistics

Table 1 summarises the different types of ED diagnosis by age. The mean age was 26.0 (SD 11; range 10-90)

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%)
TOTAL n= 7423 (11 missing detailed diagnosis)	**2553**	**1572**	**3298**

Self-harm and Suicidality amongst patients

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 of 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

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

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

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% CI1.10-1.78; 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

Age (years)	26.0 (11.0)	4591	0.98 (0.97-0.98)	<0.001
Gender Female	6635 (91.5%)	4252 (58.6%)	ref	
Male	613 (8.5%)	334 (4.6%)	0.67 (0.58-0.79)	<0.001
Marital Status				
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
Ethnicity				
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
Deprivation Score				
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
Primary ED diagnosis				
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
All substance misuse				
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
Depression				
No	2532 (95.1%)	3777 (82.3%)	ref	

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

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**
Age (years)	26.1 (11.0)		0.98 (0.97-0.99)	<0.001
Gender % Female	6635 (91.5%)	4364 (65.8%)	ref	
Male	613 (8.5%)	395 (64.4%)	0.94 (0.79-1.12)	
Marital Status				

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
Ethnicity				
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
Deprivation Score				
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
Presence of eating Disorder				
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
All substance misuse				
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
Depression				
No	2383 (95.7%)	3926 (82.4%)	ref	
Yes	106 (4.26%)	838 (17.6%)	4.80 (3.90-5.91)	<0.001
Borderline Personality Disorder				
No	2478 (99.6%)	4268 (89.6%)	ref	
Yes	11 (<1%)	496 (10.4%)	26.2 (14.4-47.7)	<0.001
Bipolar Disorder				
No	2476 (99.5%)	4542 (95.3%)	ref	
Yes	13 (<1%)	222 (4.67%)	9.31 (5.31-16.3)	<0.001
Anxiety				

No	2476 (99.5%)	4669 (98.0%)	ref	
Yes	13 (<1%)	95 (2.0%)	3.88 (2.17-6.93)	<0.001
Other Personality Disorder				
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 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

[Type here]

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 (41) 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. This is likely due to errors in the linguistic pre-processing needed to identify negation. As we are relying on at least one positive mention to ascertain those with any past or current history of suicidal behaviour, this is unlikely to significantly impact the validity of the results.

Discussion of clinical findings

This study highlights the high lifetime prevalence (>60%) of both self-harm and suicidality reported amongst those diagnosed with eating disorders in both inpatient and outpatient settings. One explanation for the high rates of suicidal behaviour is that patients with EDs are at an increased risk of psychiatric comorbidities (1, 2), particularly mood disorders, substance misuse and personality disorders (29, 42). It is well documented that

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

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

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

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

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

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

Strengths and limitations

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

The main limitation of this study is that the tools were not able to consider the timing of reported suicidality or self-harm relative to the ED diagnosis. Therefore, it is possible the reported suicidal behaviour was prior to ED diagnosis; an improvement of the NLP tool would be to include temporality to understand specific time periods of risk for self-harm or reported suicidality. Another consideration is that due to changing diagnostic codes between the follow up period of 2007-2020 and the introduction of the ICD-11 codes of binge eating disorder, we had to include all EDs aside from AN and BN into one heterogenous group of diagnoses 'Other EDs'. This was needed to ensure consistency over the time period and to avoid the problem of small group sizes in the regression analysis. Furthermore, given that EHRs include routine clinical data not primarily collected for research purposes, the study relies on clinician documentation which could include non-grammatical errors, jargon and idiosyncratic abbreviations; all of these could increase the chance of NLP misclassification (35). However, this was mitigated by using all documents available for each patient. Therefore, there were multiple opportunities to capture suicidality information to compensate for lack of sensitivity of the tool. Finally, the data relies on recording of suicidality and self-harm following a clinical encounter. This is likely to result in some heterogeneity at a document level, as some healthcare professionals may be more likely to discuss or record self-harm or suicidal thoughts depending on their level of experience, clinical background or

their prior knowledge of the patient. However as there only needed to be one positive mention of self-harm or one positive mention of suicidality, at a patient level, the threshold was low for detection of either outcome.

Clinical and research implications

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

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Competing interests: nil

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

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

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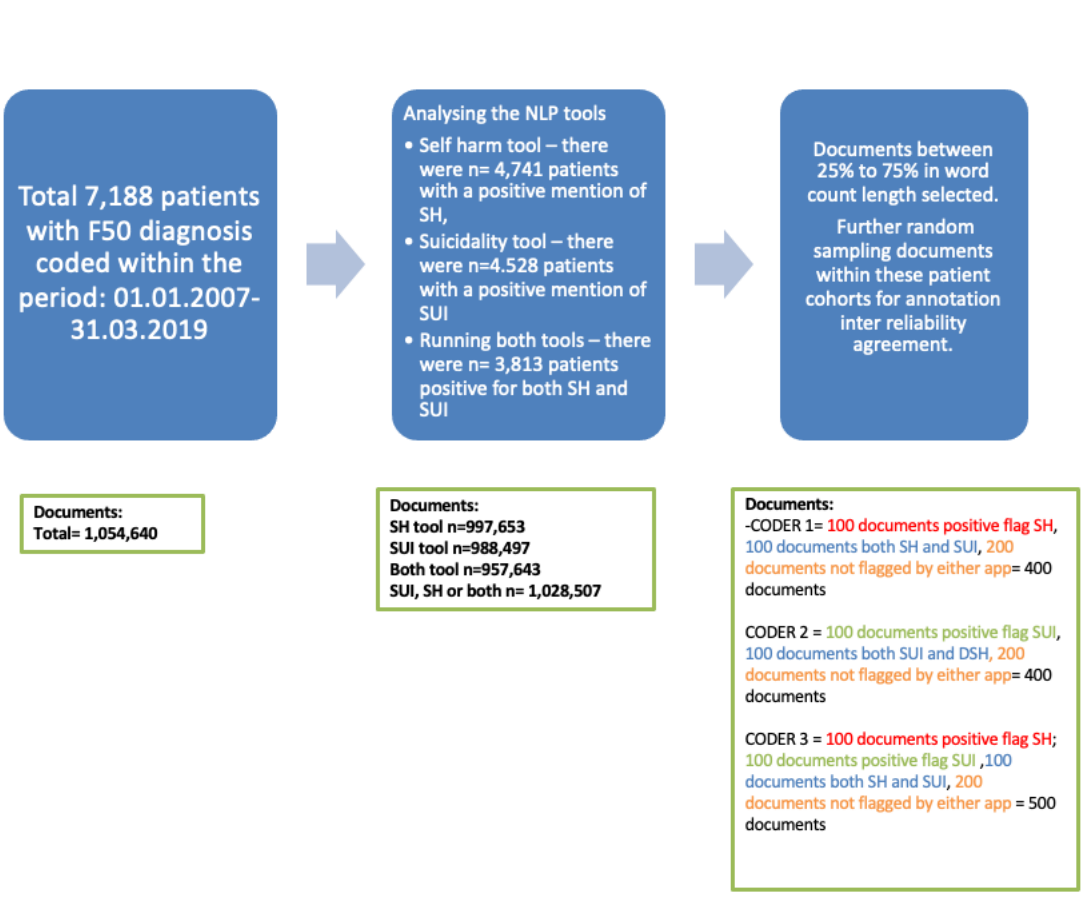
Supplementary File Figure 1

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
Title and abstract	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
Introduction			
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
Methods			
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
Results			
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

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 (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-8
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
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
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

*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.