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## The association between depressive symptoms and CBT receipt within a psychosis sample.

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### Abstract

**Objectives:** To examine whether depressive symptoms predict receipt of cognitive behavioural therapy (CBTp) in individuals with psychosis.

**Design:** Retrospective cross-sectional analysis of electronic health records (EHRs) of a clinical cohort.

**Setting:** A secondary NHS mental health care service serving four boroughs of south London, UK.

**Participants:** 20,078 patients diagnosed with an ICD-10 code between F20-29 extracted from an EHR database.

**Primary and secondary outcome measures:** Primary: Whether recorded depressive symptoms predicted CBTp session receipt, defined as at least one session of CBT for psychosis (CBTp) identified from structured EHR fields supplemented by a natural language processing algorithm. Secondary: Whether age, gender, ethnicity, psychotic symptoms (negative, manic and disorganisation symptoms), a comorbid diagnosis of depression, anxiety or bipolar disorder, general CBT receipt prior to the primary psychosis diagnosis date, or type of psychosis diagnosis predicted CBTp receipt.

**Results:** Of patients with a psychotic disorder, 8.2% received CBTp. Individuals with at least one depressive symptom recorded and 12 out of 15 of the individual depressive symptoms independently predicted CBTp receipt. Female gender, White ethnicity and presence of a comorbid affective disorder or primary schizoaffective diagnosis were independently positively associated with CBTp receipt within the whole sample and the top 25% of mentioned depressive symptoms.

**Conclusions:** Individuals with a psychotic disorder who had recorded depressive symptoms were significantly more likely to receive CBTp sessions, aligning with CBTp guidelines of managing depressive symptoms related to a psychotic experience. However, overall receipt of CBTp needs to increase before targeted approaches can be undertaken.

### Strengths and limitations of the study

- To our knowledge, this is the first electronic health record (EHR) study to measure how clinical symptomatology predicts CBTp receipt, providing insight on a large sample into whether individuals who may be more in need of CBTp are more likely to have a session
- We replicate previous findings of inequalities in gender and ethnicity in real-world CBTp treatment receipt in a large heterogeneous sample.
- The natural language processing approach allows automated processing of EHR text at scale and can evaluate larger samples than manually conducted case note audits; this could therefore be used more routinely to monitor CBTp receipt.

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- This study was limited to a single service provider; however, the results identified themes consistent with previous CBTp provision research in other services.
- Analysing EHRs in this way can identify CBTp receipt but is less suited to investigate whether CBTp is offered or not, or to quantify the quality or focus of the sessions.

For peer review only

## Introduction

There are a variety of cognitive and emotional processes involved in the development of psychotic symptoms,<sup>1</sup> with intense distress emerging early on in the course of the disorder. Content of positive symptoms often mirrors the content of depressive thinking processes,<sup>2</sup> suggesting therapeutic need for individuals experiencing additional depressive symptoms. Specific depressive symptoms that often accompany psychotic disorders are hopelessness, social avoidance and problems in forming relationships.<sup>3</sup> Around 50% of patients with psychosis report having experienced suicidal ideation at least once,<sup>4</sup> and around 40% of individuals with schizophrenia report clinical levels of depression and low self-esteem.<sup>5</sup> Importantly, individuals report these emotional difficulties and resulting social exclusion to be more debilitating than their psychotic symptoms.<sup>6</sup> Consequentially, individuals' negative appraisal of their psychotic experiences may lead to loss of social goals and increased shame, predicting later hopelessness and post-psychotic depression.<sup>7</sup> This comorbid depression increases the likelihood of having a lower quality of life, function, motivation, poorer social relationships, lower medication adherence and relapse to mental health services.<sup>8,9</sup> Therefore, treatment should focus on the psychotic symptoms and the broader distress they produce, building self-esteem, confidence and a sense of self control and purpose.<sup>10</sup>

It is increasingly recognised that medication alone is inadequate for tackling psychosis symptoms.<sup>11</sup> In the UK, the National Institute of Clinical Excellence<sup>12</sup> has recommended that cognitive behavioural therapy for psychosis (CBTp) be offered universally to individuals with psychosis. Based on the stress-vulnerability model,<sup>13</sup> CBTp focuses on distress reduction through targeting negative beliefs and improving self-esteem.<sup>14</sup> Sessions often focus on goal setting and emotional issues such as rebuilding one's self, positivity and acceptance.<sup>10</sup> While CBTp reductions in depressive symptoms are promising, specifically with long term reductions in suicidal behaviour,<sup>15</sup> service provision of this intervention still falls far short of the universal access recommended.<sup>11</sup>

Considering the impact of targeting these symptoms in CBTp sessions, it is important to monitor receipt of CBTp within psychosis samples. While CBTp provision shows moderate yearly increases (12.8% in 2013 to 14.8% in 2014), the treatment is still only available to a small proportion of individuals,<sup>11</sup> short of NICE universal access recommendations.<sup>12</sup> Previous studies investigating CBTp receipt have conducted time-consuming audits on limited sample sizes; these can be affected by under-reporting. On the other hand, the UK's National Mental Health Minimum Data Set report does not require CBT interventions to be recorded in a given individual's record. Natural language processing techniques (NLP)<sup>16</sup> offer the opportunity to extract this information from free text in electronic health records (EHRs) across large numbers of patients with psychosis, and a recent study developed and applied NLP in this respect, finding higher levels of receipt than reported in previous audit, supported by the high positive predictive value and sensitivity of the technique (95% and 96% respectively).<sup>11</sup>

We investigated whether depressive symptoms predict CBTp receipt in people with psychosis by applying these previously data extraction techniques to secondary mental health care EHRs for a large South London catchment population. Secondary predictors of receipt were type of psychosis diagnosis (schizophrenia, schizoaffective disorder or other schizophrenia spectrum disorder), psychotic symptoms (negative, manic or disorganisation), general CBT receipt prior to psychosis diagnosis, comorbid depression, anxiety or bipolar diagnosis and socio-demographic factors (ethnicity, gender and age).

## Methods

For this study, we extracted data on individuals with a diagnosis of a recognised schizophrenia spectrum diagnosis from the case registry of the South London and Maudsley NHS Foundation Trust (SLaM). This is a large secondary care mental healthcare provider, serving around 1.3 million residents in Croydon, Lambeth, Lewisham and Southwark. EHRs have been used for all SLaM services since 2006, with the Clinical Record Interactive Search system (CRIS) being established in 2008 to facilitate the retrieval of de-identified data from these records of patients previously or currently receiving mental healthcare from SLaM.<sup>17</sup> The source EHR contains unstructured free text fields from correspondence, personal histories, mental health examinations and management plans, as well as structured fields for coding demographic information, like age and ethnicity. Implementing data from all these fields reduces selection bias of utilising only specific sources of information from the EHR. Consequently, a large programme of work has developed a range of NLP algorithms over the last decade, whose detailed descriptions and performance data are contained in an open-access catalogue.<sup>18</sup> CRIS has approval as a data resource for secondary analysis (Oxford Research Ethics Committee C, reference 18/SC/0372), and a service user-led committee considers all proposed research before access to CRIS data is granted.

We extracted data for all individuals receiving SLaM care between January 2007 and June 2020 with a primary diagnosis of an ICD-10-defined schizophrenia spectrum disorder (F20-F29) and above the age of 18 at the time their original referral was accepted. The index date for covariate definitions was the date of the first diagnosis within this grouping. Individuals may have been active within the service before their index date, allowing us to extract data on prior CBT receipt. The sample was restricted to those with data on all variables.

Ethnicity, age at referral and gender were also extracted. Ethnicity was categorised into six groups for analysis: 'White British' (British), 'White other' (Irish or any other white background), 'Black' (Caribbean, African or any other black background), 'Asian' (Indian, Bangladeshi, Pakistani, Chinese or any there Asian background), 'Other/mixed' (white and Asian, white and black Caribbean, white and black African, any other ethnic group) and 'Not stated'.

Diagnosis was categorised into three subgroups of schizophrenia (ICD-10 codes F20.0–F20.9), schizoaffective disorder (F25.0–F25.9) and other schizophrenia spectrum disorder (F21, F22.0–F22.9, F23.0–F23.9, F24, F28 and F29). Within the data collection period, secondary diagnosis of depression (ICD-10: F32 or F33), anxiety (ICD-10: F40 or F41), or bipolar disorder (ICD-10: F31) were also extracted from structured field data.

NLP algorithms for each specific symptom were used to identify recorded depressive and psychotic symptoms within participants. Symptoms were categorised as depressive, positive, negative, manic or disorganisation. These symptoms had been categorised *a priori* by developers of the original independent symptom NLP algorithms. As symptoms could be labelled in more than one category during analysis, multicollinearity tests using the R function `vif()` within the [car package] were undertaken to avoid issues with overlapping predictor variables. Positive symptoms were excluded from the regression analysis due to multicollinearity affecting results, all other variables were included due to their VIF values being well below five. The overall symptom list and subsequent recoding can be found in Table 1. Presence of at least one mention of any symptom in the five categories was computed as a binary variable (0/1). This was prioritised over calculating the frequency of mentions, as the number of symptoms in each of the categories was unevenly distributed (e.g. 15 depressive symptoms vs. 6 manic symptoms).

## Patient and public involvement

The Clinical Record Interactive system as a data resource was developed and is run with extensive patient involvement. However, this particular analysis did not involve patients in its design or implementation.

Table 1  
*Classification of symptom predictors*

Symptom	Symptom label
Aggression	Positive
Agitation	Positive
Anergia	Depressive /Negative
Anhedonia	Depressive/Negative
Apathy	Depressive/Negative
Arousal	Manic
Blunted affect	Depressive/Negative
Circumstantiality	Disorganisation
Delusions	Positive
Derailment	Disorganisation
Disturbed sleep	Depressive/Manic
Elation	Manic
Emotional Withdrawal	Negative
Flight of ideas	Disorganisation
Formal thought disorder	Disorganisation
Grandiosity	Manic
Guilt	Depressive
Hallucinations (auditory)	Positive
Helplessness	Depressive
Hopelessness	Depressive
Hostility	Positive
Insomnia	Depressive/Manic
Irritability	Manic
Paranoia	Positive
Persecutory ideation	Positive
Poor appetite	Depressive
Poor concentration	Depressive
Poor motivation	Depressive
Poverty of speech	Negative
Poverty of thought	Negative
Social withdrawal	Negative
Suicidal ideation	Depressive
Tangentiality	Disorganisation
Tearfulness	Depressive
Thought block	Disorganisation
Worthlessness	Depressive

The date of the first and last general CBT session before the index date was extracted. This was coded as a binary variable, with individuals in the 'Prior CBT' receipt group having at least one session date mention prior to their index date. This was included as a predictor to adjust for previous experience of the specific CBT intervention. Mentions were extracted using the same NLP tool as the CBTp outcome measure mentioned subsequently.



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3 The primary outcome was CBTp receipt, identified using a combination of structured fields and NLP.<sup>16</sup> The NLP  
4 algorithms for general CBT has high PPV and sensitivity,<sup>11</sup> consistent with other NLP algorithms such as  
5 medication dose and diagnosis.<sup>19</sup> The date of the first CBTp session on or after the index date was extracted  
6 and computed as a binary variable, so that individuals in the 'CBTp receipt' group had at least one CBTp  
7 session mention after the index date.  
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### 9 10 **Statistical analysis**

11 To avoid overfitting, we followed the 'one in ten' rule, whereby one predictor can be measured for every 10  
12 events. As the data included 1647 CBTp events, our study was able to include all 12 predictors within the same  
13 regression model.  
14

15 All statistical analyses were conducted using R (version 1.3.9). Descriptive statistics for demographic and  
16 clinical variables are reported as frequencies for categorical variables and means and standard deviations for  
17 the continuous variable (age at referral). Chi square tests were also calculated for categorical variables, and t-  
18 test for age to measure between-group differences in those with/without CBT receipt.  
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21 Binary logistic regression was used to examine the association between depressive symptoms and receipt of at  
22 least one CBT session in the whole sample. For this, three regression models were analysed. Model 1 was an  
23 unadjusted model with only depressive symptoms as the predictor variable. Due to significant provision  
24 differences seen in previous CBTp studies,<sup>11</sup> model 2 (partially adjusted model), adjusted for sociodemographic  
25 variables (age at referral, ethnicity, gender), primary diagnosis group and presence of a comorbid diagnosis  
26 (anxiety, depression and bipolar disorder). Model 3 (fully adjusted model) also adjusted for prior CBT receipt  
27 before the index date (first psychosis diagnosis date) and psychotic symptoms mention (manic, negative and  
28 disorganisation symptoms). Positive psychotic symptoms were not included in these models, as individuals all  
29 had at least one mention within their case notes.  
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33 As the primary aim of the study was to investigate depressive symptoms as a predictor of CBTp receipt, we  
34 also split the depressive symptoms category into the 15 specific depressive symptoms applications. Model 4  
35 was an unadjusted model with the 15 symptoms as predictor variables. Model 5 was a fully adjusted model  
36 that adjusted for all the variables in Model 3. We also conducted a sensitivity analysis to investigate how  
37 results were affected by overlap of negative or depressive symptom annotations, by removing negative  
38 symptoms as a predictor from the logistic regression model.  
39

40  
41 Lastly, to compare differences in the general sample with those with the top 25% quantity for depressive  
42 symptoms, we conducted two further regression models. Model 6 partially adjusted for socio-demographic  
43 factors, diagnostic group and comorbid diagnosis and Model 7 fully adjusted for prior CBT, negative and  
44 disorganisation symptoms additionally. This group all had at least one manic and psychotic symptom, so these  
45 variables were not included in the model.  
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## 48 **Results**

### 49 50 **Participants**

51 The cohort comprised 20,078 individuals with the inclusion diagnoses, 1647 (8.2%) of whom received at least  
52 one session of CBTp after their first diagnosis date. The mean age of the cohort was 42.4 years (SD=16.5).  
53 Distribution frequencies for all categorical variables can be found in Table 2. Chi-square test results  
54 represented in this table compared those with or without CBTp receipt. All mentioned variables showed  
55 significant between-group differences at  $p < .001$  apart from gender ( $X^2=2.75$ ,  $p=.097$ ). Additionally, the Welch  
56 two sample t-test found significant between-group differences in age ( $t=15.34$ ,  $p < .01$ ). Where those who had  
57 received CBTp had a lower mean age ( $M=33.12$   $SD= 11.5$ ) compared to those who did not ( $M=35.88$ ,  
58  $SD=13.08$ ). The significant results confirmed the need for further analysis through the regression models.  
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**Table 2***Distribution frequencies on baseline demographics and diagnoses split by CBTp receipt and primary diagnosis group.*

	<b>No CBTp delivery (n = 18431)</b>	<b>CBTp delivery (n=1647)</b>	<b>Chi square tests (<math>\chi^2</math>)</b>
<b>Ethnicity</b>			$\chi^2=100.57^{***}$
White British	<b>30%</b> (5516/18431)	<b>32.8%</b> (540/1647)	
White Other	<b>10.4%</b> (1908/18431)	<b>8.5%</b> (140/1647)	
Black	<b>36.5%</b> (6719/18431)	<b>41.7%</b> (687/1647)	
Asian	<b>6.5%</b> (1193/18431)	<b>5.2%</b> (86/1647)	
Other/Mixed	<b>9.8%</b> (1808/18431)	<b>10.5%</b> (173/1647)	
Not stated	<b>7.0%</b> (1287/18431)	<b>1.3%</b> (21/1647)	
<b>Gender</b>			$\chi^2= 2.75$
Female	<b>41.4%</b> (7636/18431)	<b>43.5%</b> (717/1647)	
Male	<b>58.6%</b> (10795/18431)	<b>56.5%</b> (930/1647)	
Bipolar diagnosis	<b>4.4%</b> (810/18431)	<b>9.0%</b> (149/1647)	$\chi^2=71.94^{***}$
<b>No biop diagnosis</b>	<b>95.6%</b> (17621/18431)	<b>91.0%</b> (1498/1647)	
Depression diagnosis	<b>7.4%</b> (1373/18431)	<b>14.0%</b> (230/1647)	$\chi^2=87.36^{***}$
<b>f32 no diagnosis</b>	<b>92.6%</b> (17058/18431)	<b>86.0%</b> (1417/1647)	
Anxiety diagnosis	<b>2.4%</b> (441/18431)	<b>7.0%</b> (115/1647)	$\chi^2=118.28^{***}$
<b>f40/41 no diagnosis</b>	<b>97.6%</b> (17990/18431)	<b>93.0%</b> (1532/1647)	
<b>Prior CBT</b>	<b>3.1%</b> (573/18431)	<b>14.4%</b> (237/1647)	$\chi^2=497^{***}$
<b>No prior cbt</b>	<b>96.9%</b> (17858/18431)	<b>85.6%</b> (1410/1647)	

\*\*\*p&lt;.001

Positive psychotic symptoms were excluded from chi square and regression analysis, as all patients had at least one positive psychotic symptom.

### General depressive symptom regression analysis

Results from the unadjusted (model 1), partially adjusted (model 2) and fully adjusted regression (model 3) are displayed in Table 3. Regression model 1 found that general mention of at least one of 15 potential depressive symptoms significantly predicted CBTp receipt. Regarding model 2 and 3, individuals with at least one depressive, negative or disorganisation symptom mention, being of female gender, white ethnicity, prior CBT receipt and presence of a comorbid affective disorder independently positively associated with CBTp receipt.

Table 3

Unadjusted, partially and fully adjusted logistic regression models for CBTp receipt (Regression model 1,2 and 3).

		Unadjusted	Partially adjusted	Fully adjusted
	N(%)	OR(95%CI)	OR(95%CI)	OR(95%CI)
<b>Depressive symptoms</b>				
1+ depressive symptom mention	18286(91.1)	44.13(17-118)***	30.7(11.51-82.30)***	7.37(2.66-20.42)***
<b>Bipolar diagnosis</b>				
Has f31 diagnosis	959(4.80)		1.72(1.43-2.09)***	1.38(1.13-1.68)***
<b>Depression diagnosis</b>				
Has f32 diagnosis	603(80)		1.67(1.43-1.96)***	1.39(1.18-1.63)**
<b>Anxiety diagnosis</b>				
Has f40/41 diagnosis	556(2.80)		2.43(1.95-3.03)***	2.07(1.65-2.61)***
<b>Age</b>	N/A		0.034(0.03-0.04)***	0.028(0.024-0.03)***
<b>Gender</b>				
Male			Reference category	
Female	8353(41.60)		1.22(1.10-1.36)***	1.23(1.10-1.38)***
<b>Ethnic group</b>				
White British	6056(30.10)		Reference category	
White Other	2048(10.20)		0.67(0.55-0.81)***	0.69(0.57-0.85)***
Black	7406(36.90)		0.85(0.75-0.96)*	0.79(0.7-0.90)*
Asian	1279(6.40)		0.61(0.48-0.78)***	0.60(0.47-0.77)***
Other/Mixed	1981(9.90)		0.81(0.67-0.97)*	0.83(0.7-1.01)*
Not Stated	1308(6.50)		0.17(0.11-0.27)***	0.22(0.14-0.34)***
<b>Primary diagnosis</b>				
Schizophrenia	9845(49.00)		Reference category	
Schizoaffective disorder	2142(10.70)		1.04(0.88-1.24)	1.01(0.85-0.21)
Other schizophrenia spectrum	8091(40.30)		0.9(0.81-1.02)	0.98(0.87-1.01)
<b>Negative symptoms</b>				
1+ Negative symptom mention	13169(65.60)			2.12(1.80-2.50)***
<b>Manic symptoms</b>				
1+ Manic symptom mention	17945(89.40)			3.46(1.95-6.15)***
<b>Disorganisation symptoms</b>				
1+ Disorganisation symptom mention	11513(57.30)			1.36(1.20-1.55)***
<b>CBT prior</b>				
1+ prior CBT session				3.65(3.08-4.32)***

\*p<.05, \*\*p<.01, \*\*\*p<.001

**Unadjusted (model 1):** depressive symptom as a predictor with no adjusted covariates

**Partially adjusted (model 2):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis, depressive symptoms.

**Fully adjusted (model 3):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis, depressive symptoms, prior CBT, negative symptoms, disorganisation symptoms, manic symptoms.

### Regression analysis with individual depressive symptoms

Results from the unadjusted (model 4) and fully adjusted (model 5) regression analyses for each of the 15 individual depressive symptoms are displayed in Table 4. Each symptom refers to presence of at least one mention in the patients notes. While all variables were significant in the unadjusted model at  $p < .001$ , the fully adjusted model reduced the significance of suicide ideation ( $p < .01$ ) and disturbed sleep ( $p < .01$ ), with anhedonia, anergia, apathy, and blunted affect becoming non-significant ( $p > 0.05$ ).

Table 4

*Unadjusted and fully adjusted logistic regression models for CBTp receipt with individual depressive symptoms as covariates (Regression model 4 and 5).*

		Unadjusted	Fully adjusted
	N(%)	OR(95%CI)	OR(95%CI)
Hopelessness	7345(36.60)	4.81(4.3-5.40)***	1.45(1.26-1.66)
Helplessness	3124(15.60)	4.03(3.62-4.50)***	1.55(1.37-1.76)***
Suicide ideation	9451(47.10)	4.11(3.66-4.63)***	1.25(1.09-1.44)**
Poor appetite	8044(40.10)	3.31(2.97-3.68)***	1.28(1.13-1.45)***
Poor motivation	8630(43.00)	4.34(3.87-4.86)***	1.43(1.24-1.64)***
Insomnia	6870(34.20)	3.74(3.35-4.15)***	1.4(1.24-1.58)***
Disturbed sleep	16667(83.00)	15.3(10.16-22.8)***	2.76(1.5-5.08)**
Poor concentration	12289(61.20)	8.16(6.81-9.77)***	2.33(1.9-2.85)***
Anhedonia	4047(20.20)	2.9(2.61-3.22)***	0.97(0.85-1.10)
Anergia	873(43.50)	2.63(2.20-3.15)***	0.98(0.80-1.20)
Apathy	4149(20.70)	2.21(1.98-2.46)***	0.93(0.82-1.05)
Guilt	8178(40.70)	4.6(4.1-5.15)***	1.49(1.30-1.70)***
Tearfulness	10951(54.50)	3.87(3.41-4.39)***	1.22(1.05-1.42)**
Blunted affect	6889(34.30)	2.66(2.41-2.95)***	0.91(0.80-1.03)
Worthlessness	2921(14.50)	3.94(3.53-4.40)***	1.37(1.21-1.56)***

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

### Sensitivity analysis

The non-significant results of certain depressive symptoms (anhedonia and anergia) may have been due to their inclusion within the negative symptom category, causing over-adjustment of the model. To test this, sensitivity analysis was conducted, where the fully adjusted regression (model 3) did not include negative symptoms as a covariate. While all significant variables remained significant, non-significant results for anhedonia and apathy were still found. Therefore, we report the fully adjusted model with negative symptoms as a variable for both grouped and individual depressive symptom associations.

### Depressive symptom regression analysis within the top 25% number of depressive symptoms.

This sample comprised individuals with the top 25% number of depressive symptoms (5018 patients), defined to reflect those who might reasonably expect to receive CBT. The sample characteristics and regression analysis can be seen in Table 5. Results from the partially adjusted (model 6) and fully adjusted regression (model 7) are displayed in Table 5. Regression model 6 found that general mention of at least one of 15 potential depressive symptoms significantly predicted CBTp receipt. Regarding table 3, we found that individuals with at least one depressive, negative or disorganisation symptom mention, being of female

gender, white ethnicity, prior CBT receipt and presence of a comorbid affective disorder were positively associated with CBTp receipt.

Table 5

*Partially and fully adjusted logistic regression models for CBTp receipt with individual depressive symptoms as covariates within top 25% quantity of depressive symptoms (Regression model 6 and 7).*

		Partially adjusted	Fully adjusted
	N(%)	OR(95%CI)	OR(95%CI)
<b>Bipolar diagnosis</b>			
Has f31 diagnosis	541(10.78)	1.21(0.97-1.51)*	1.16(0.92-1.46)
<b>Depression diagnosis</b>			
Has f32 diagnosis	885(17.63)	1.11(0.93-1.35)	1.08(0.90-1.30)
<b>Anxiety diagnosis</b>			
Has f40/41 diagnosis	270(5.38)	1.70(1.29-2.24)****	1.61(1.21-2.13)***
<b>Age</b>			
M= 36.24(18-93)		0.98(0.97-0.99)****	0.98(0.97-0.99)****
<b>Gender</b>			
Male	2058(41.01)	Reference category	
Female	2960(58.99)	0.82(0.71-0.95)***	0.85(0.73-0.98)**
<b>Ethnic group</b>			
White British	1485(29.59)	Reference category	
White Other	433(8.63)	0.81(0.62-1.06)	0.80(0.61-1.05)
Black	2262(45.08)	0.73(0.62-0.86)****	0.74(0.63-0.87)****
Asian	328(6.53)	0.59(0.43-0.82)***	0.60(0.43-0.83)***
Other/Mixed	467(9.31)	0.93(0.72-1.19)	0.92(0.72-1.19)
Not Stated	43(0.86)	0.24(0.07-0.79)**	0.26(0.80-0.86)**
<b>Primary diagnosis</b>			
Schizophrenia	2219(44.22)	Reference category	
Schizoaffective disorder	740(14.72)	1.05(1.84-1.30)	1.00(0.80-1.25)
Other schizophrenia spectrum	2059(41.03)	1.02(0.87-1.19)	1.05(0.89-1.23)
<b>Negative symptoms</b>			
1+ Negative symptom mention	3744(74.61)		0.41(0.24-0.70)***
<b>Disorganisation symptoms</b>			
1+ Disorganisation symptom mention	3209(63.94)		1.19(0.97-1.46)*
<b>CBT prior</b>			
1+ prior CBT session	360(7.17)		2.45(1.98-3.04)****

\*p<.05, \*\*p<.01, \*\*\*p<.001, \*\*\*\*p<.000

**Partially adjusted (model ):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis.

**Fully adjusted (model ):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis, prior CBT, negative symptoms, disorganisation symptoms.

## Discussion

We believe that this is the first study to examine the relationship between clinical symptomatology and CBTp receipt within a sample of people with psychosis in a naturalistic community setting. In general, only 8.2% of individuals received CBTp, despite 91% having at least one depressive symptom recorded. Individuals with at least one depressive symptom mention were 7.37 times more likely to have at least one CBTp session in the fully adjusted model (table 3), suggesting that the minority who don't present with any depressive symptoms are very unlikely to receive CBTp. This could possibly be due to clinicians tending to cite a depressive symptom when referring an individual with psychosis to psychotherapy. In the sample of those with the highest number of depressive symptoms (top 25%), relationships between CBTp receipt and comorbid anxiety diagnosis, age, gender, ethnicity, prior CBT, negative and disorganised psychotic symptoms remained (effect size ranging from 0.26-2.45).

Overall there was therefore a low prevalence of CBTp receipt within those with one depressive symptom. The depressive symptom which was the strongest predictor of this intervention in fully adjusted models was disturbed sleep. There is a known high prevalence of sleeping problems in this population,<sup>20,21</sup> described by some researchers as

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2  
3 an 'intrinsic feature of schizophrenia,<sup>22</sup> known to reduce quality of life, decreasing coping and exacerbate positive  
4 symptoms.<sup>23</sup> Furthering this, the recommended first line of treatment for sleep problems in this sample is CBT.<sup>24</sup> Poor  
5 concentration was the next strongest depressive symptom predictor in the fully-adjusted model, supporting previous  
6 research of its association with psychosis vulnerability.<sup>25</sup> The significance of helplessness, guilt and hopelessness  
7 mirrors CBTp research that found significant post-treatment reduction in hopelessness, self-depreciation and guilt using  
8 the Calgary Depression Rating Scale for Schizophrenia.<sup>26</sup> Other significant depressive symptoms associated with low  
9 self-esteem and negative self-evaluation and emotions have been found to significantly affect the development and  
10 severity of positive symptoms.<sup>27</sup> This may be because positive symptoms develop as a psychological defence against  
11 low self-esteem<sup>28</sup> and depression-induced guilt.<sup>29</sup> Therefore, it can be said that the significance of each of the  
12 depressive symptoms is often linked to psychotic symptoms and CBTp effectiveness. However, general results suggest  
13 that receipt of this intervention requires an increase for all of this population before individuals with these specific  
14 symptoms could be targeted.

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17 Regarding negative symptoms, the contrasting results suggest multiple theories that require specific testing. Further  
18 testing was not conducted in the current study due to the primary aim focusing on depressive symptoms. However,  
19 from our results on specific depressive symptoms in table 4, symptoms that overlapped with negative symptoms  
20 (anhedonia, anergia, apathy and blunted affect) were not associated with CBTp receipt. This raises concerns, suggesting  
21 that individuals with these specific negative/depressive symptoms are no more likely to receive CBTp than someone  
22 without these symptoms. Possibly, this is due to clinicians not tending to refer these individuals because they don't  
23 believe intervention would be effective. This is in line with a CBTp review of randomised control trials, finding non-  
24 significant reductions of negative symptoms,<sup>30</sup> perhaps due to the narrowing of treatments to specifically target  
25 positive symptoms.<sup>31</sup> However, further work should be undertaken to verify that individuals are not being denied a  
26 potentially beneficial intervention because of their symptom profile.

27  
28 Prior CBT receipt, comorbid disorder presence and specific psychotic symptoms (manic, disorganised and negative) also  
29 emerged as independent predictors of CBTp receipt for the general sample and within those with the top 25%  
30 depressive symptom numbers. Within table 3, individuals who had any recorded CBT receipt prior to the index date  
31 were nearly four times more likely to have recorded CBTp receipt later on. Also, patients with an additional comorbid  
32 disorder were 1.38-2.07 times more likely to have received CBTp compared to those with just a psychosis diagnosis.  
33 Within table 5, individuals with prior CBT were 2.45 times more likely to receive CBTp, those with anxiety were 1.61  
34 times more likely and those with disorganised or negative symptoms were more 1.19 and 0.41 times more likely  
35 respectively. After general CBTp receipt has increased, there could be a method to focus more on patients with  
36 different types of psychotic symptoms and comorbid affective diagnosis. Furthering this, future research could  
37 investigate whether those who have had prior general CBT would benefit from CBTp, or whether those who have not  
38 had any experience developing cognitive behaviour skills in therapy should be targeted.

39  
40 Crucially, there were also significant differences in CBTp receipt between different ethnic and gender groups. Male  
41 patients were 1.23 times less likely in the general sample and 0.85 times less likely in the top 25% of depressive  
42 symptoms to have recorded CBTp receipt. Black, Asian, Other and Mixed ethnic groups were between 0.60 to 0.70  
43 times as likely to have a documented CBTp session compared to individuals of white ethnicity within both the general  
44 and top 25% depressive symptoms samples. Inequitable access to CBTp has been identified in previous CBTp research  
45 within a psychosis sample drawn from the same data resource in 2017, finding female patients to be more likely to  
46 have received CBTp and individuals of White ethnicity to have a significantly higher likelihood of CBT receipt than Black  
47 or other ethnicity groups.<sup>11</sup> This also supports results from a recent CBTp study focusing specifically on ethnic group  
48 differences in CBTp provision within SLAM, who found that in comparison to White British individuals, those from Black  
49 ethnic groups with psychosis or bipolar disorder were significantly less likely to have a documented CBTp session.<sup>33</sup>  
50 Inequality in CBTp receipt may be due to ethnic variations in CBTp engagement. Some of these barriers within certain  
51 communities may be increased stigma, fear of clinicians by service-users or service users by clinicians, institutional  
52 racism within mental health services, or non-culturally appropriate therapy.<sup>33</sup> As differences in documented CBTp  
53 receipt between ethnic groups have now been documented by three different papers in this service, it is imperative  
54 that further work is conducted to increase provision of CBTp within groups less likely to receive treatment. This may  
55 include targeted outreach programs and culturally adapting interventions<sup>34</sup> within these minority groups.

56  
57 The present study has a number of strengths and limitations. Generally, focusing on patients with more  
58 diverse functioning, comorbidity and symptom severity levels helps research identify a larger number of  
59 predictors of clinical outcomes. This can be seen through our results, where negative, manic and  
60



1  
2  
3 disorganisation symptoms significantly predicted CBTp receipt, as well as recent heterogenous research,<sup>31</sup>  
4 that was the first to identify depression as a significant predictor of positive symptom improvement post-  
5 CBTp. This highlights the importance of focusing on a clinically heterogeneous sample to realistically determine  
6 significant predictors of CBTp receipt. Secondly, using an NLP approach automates the measurement of what  
7 would otherwise require manually conducted audits on records and case notes, increasing the number of  
8 cases that can be investigated and providing a method that could be used more routinely to monitor CBT  
9 receipt. The large sample size enabled us to identify clinical differences in the real-life administration of CBTp  
10 within a psychosis cohort, and we were able to adjust for multiple clinical variables and comorbidity diagnoses  
11 to provide a more realistic understanding of the depressive symptom-CBTp receipt relationship. This time  
12 frame was broad to allow the inclusion of as many active patients receiving CBTp as possible, additionally  
13 circumventing monthly/seasonal variation of CBTp receipt.  
14

15 One limitation of the study was the omission of strict time periods for the mention of clinical symptoms prior  
16 to CBTp administration. Unfortunately, using this approach would have involved implementing time periods on  
17 all of the other clinical symptoms and variables, which would have been difficult considering the number of  
18 variables that would need to be controlled. In addition, the NLP symptom algorithms do not currently  
19 distinguish between past or present symptoms. Therefore, symptom mentions documented after the CBTp  
20 receipt date could refer to mentions of symptoms occurring prior to CBTp receipt, reducing the effectiveness  
21 of using time periods. Additionally, a follow-up time period after the index date was not established, meaning  
22 that participants included in the cohort at a later date may have been less likely to have had a CBTp session,  
23 due to their limited time period within the service.  
24

25 While our use of additional querying of text fields allowed us to identify a significantly larger number of CBTp  
26 episodes than using structured data alone, we were not able to quantify the gap between CBTp referral and  
27 CBTp receipt. This is because the CBTp NLP algorithm detects CBTp receipt rather than CBTp being offered,  
28 due to the wide range of subtle wording used for the latter more complex entity. Therefore, the results  
29 combine effects on the likelihood of CBTp being offered, with those on session receipt following an offer.  
30 While this may have affected our results, previous service audits have suggested that the severity and  
31 occurrence of depressive symptoms significantly decreases CBT receipt.<sup>34</sup> Therefore, if only receipt was  
32 directly measured, we would expect to see similar results.  
33

### 34 **Future directions**

35  
36 Initiatives such as the Improving Access to Psychological Therapies programme for serious mental illness, early  
37 intervention access and projects to decrease waiting times for referral have been developed to target this  
38 clinical population. However, access still falls short of recommendations and is inequitable for specific  
39 psychotic diagnoses, age and ethnicity.<sup>11</sup> Therefore, given the effect of CBTp on depressive symptoms, perhaps  
40 its more pragmatic to focus on patients with additional depressive symptoms. Monitoring CBTp receipt over  
41 time could decipher whether these initiatives are effective at increasing general access for those with  
42 psychosis, and specific access for different sociodemographic groups and those with additional depressive  
43 symptoms (who may benefit the most).  
44

45  
46 The significant secondary clinical and sociodemographic variables require further analysis in order to fully  
47 understand the services' provision. This could involve attention given to the independent psychotic symptoms  
48 within the negative, manic and disorganisation categories in a similar manner to the specific depressive  
49 symptom regression models analysed. Further research could also explore why the presence of co-morbid  
50 anxiety and bipolar disorder in this sample predicted CBTp receipt. Additionally, the results suggest a need to  
51 reflect on the steps taken since the previous service study,<sup>33</sup> regarding inequality in CBTp receipt among  
52 gender and ethnic groups, due to the consistent significant results seen. Regarding the use of EHR data, future  
53 work could involve developing a separate NLP algorithm to ascertain the offering of CBTp or provide another  
54 structured field for clinicians to complete for this. However, additional text fields seem an unlikely approach,  
55 as clinicians prioritise text field data for communication about CBTp sessions for themselves and their  
56 colleagues rather than to collect structure data for the sake of research. Therefore, as previously suggested,<sup>11</sup>  
57 it is important to accept the mixed structured-text field approach that will remain in healthcare record data  
58 and perhaps our time is best spent in improving NLP algorithms to detect the subtleties of intervention and  
59 clinical outcome data. However, the implications of our results and their consistency three years after the first  
60

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3 CBTp service paper suggest the need to use this or future algorithms for service monitoring independent of  
4 these improvements.  
5  
6

### 7 **Acknowledgments**

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9 thank Jessica Irving for her assistance in the statistical analysis and general manuscript.  
10  
11

### 12 **Contributorship statement**

13 Ava Mason planned the protocol, analysed the data and wrote the manuscript. Dr Rob Stewart provided  
14 access to the data, looked over edits and revisions on the manuscript. The data from this paper was accessed  
15 through the assistance of Megan Pritchard and Jyoti Sanyal. The applications used to obtain data specific to  
16 CBTp were developed by Craig Colling and David Chandran. Jessica Irving assisted in statistical analysis.  
17  
18

### 19 **Competing interests**

20  
21 The authors report no conflict of interest with respect to the findings described in this manuscript. RS declares  
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23  
24

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### 44 **Data Sharing Statement**

45 Due to the terms of Ethics and Information Governance approvals and clinical source of the data, CRIS datasets  
46 must remain within the South London and Maudsley NHS Foundation Trust (SLaM) firewall. All data used from  
47 this study can be made accessible on request from [cris.administrator@slam.nhs.uk](mailto:cris.administrator@slam.nhs.uk), subject to the setting up of  
48 an appropriate research passport or SLaM honorary contract.  
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### 51 **Transparency declaration**

52  
53 The lead author AM affirms that the manuscript is an honest, accurate, and transparent account of the study  
54 being reported; that no important aspects of the study have been omitted; and that any discrepancies from  
55 the study as planned (and, if relevant, registered) have been explained.  
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# Reporting checklist for cross sectional study.

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Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

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			Page Number
<b>Title and abstract</b>			
Title	<a href="#">#1a</a>	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	<a href="#">#1b</a>	Provide in the abstract an informative and balanced summary of what was done and what was found	1
<b>Introduction</b>			
Background / rationale	<a href="#">#2</a>	Explain the scientific background and rationale for the investigation being reported	1,3
Objectives	<a href="#">#3</a>	State specific objectives, including any prespecified hypotheses	3
<b>Methods</b>			
Study design	<a href="#">#4</a>	Present key elements of study design early in the paper	4
Setting	<a href="#">#5</a>	Describe the setting, locations, and relevant dates, including periods of	4

		recruitment, exposure, follow-up, and data collection	
1			
2	Eligibility criteria	<a href="#">#6a</a> Give the eligibility criteria, and the sources and methods of selection of participants.	4
3			
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6		<a href="#">#7</a> Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	1,4-6,
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10	Data sources /	<a href="#">#8</a> 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. Give information separately for for exposed and unexposed groups if applicable.	4-6
11	measurement		
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17	Bias	<a href="#">#9</a> Describe any efforts to address potential sources of bias	4
18			
19	Study size	<a href="#">#10</a> Explain how the study size was arrived at	4
20			
21	Quantitative	<a href="#">#11</a> Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	4-6
22	variables		
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25	Statistical	<a href="#">#12a</a> Describe all statistical methods, including those used to control for confounding	6
26	methods		
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29	Statistical	<a href="#">#12b</a> Describe any methods used to examine subgroups and interactions	6
30	methods		
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33	Statistical	<a href="#">#12c</a> Explain how missing data were addressed	4
34	methods		
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37	Statistical	<a href="#">#12d</a> If applicable, describe analytical methods taking account of sampling strategy	6
38	methods		
39			
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41	Statistical	<a href="#">#12e</a> Describe any sensitivity analyses	6
42	methods		
43			
44	<b>Results</b>		
45			
46	Participants	<a href="#">#13a</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. Give information separately for for exposed and unexposed groups if applicable.	1,6
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55	Participants	<a href="#">#13b</a> Give reasons for non-participation at each stage	6
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57	Participants	<a href="#">#13c</a> Consider use of a flow diagram	N/A
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1	Descriptive data	<a href="#">#14a</a>	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	6,7
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6	Descriptive data	<a href="#">#14b</a>	Indicate number of participants with missing data for each variable of interest	4
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10	Outcome data	<a href="#">#15</a>	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	8
11				
12				
13				
14	Main results	<a href="#">#16a</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	8-10
15				
16				
17				
18				
19	Main results	<a href="#">#16b</a>	Report category boundaries when continuous variables were categorized	8-10
20				
21	Main results	<a href="#">#16c</a>	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
22				
23				
24				
25	Other analyses	<a href="#">#17</a>	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	10
26				
27				
28				
29	<b>Discussion</b>			
30				
31	Key results	<a href="#">#18</a>	Summarise key results with reference to study objectives	10-11
32				
33				
34	Limitations	<a href="#">#19</a>	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	12
35				
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38				
39	Interpretation	<a href="#">#20</a>	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	10-12
40				
41				
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43				
44	Generalisability	<a href="#">#21</a>	Discuss the generalisability (external validity) of the study results	12
45				
46				
47	<b>Other</b>			
48	<b>Information</b>			
49				
50				
51	Funding	<a href="#">#22</a>	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	2
52				
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# BMJ Open

## The association between depressive symptoms and Cognitive Behavioural Therapy receipt within a psychosis sample: A cross-sectional study.

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## The association between depressive symptoms and Cognitive Behavioural Therapy receipt within a psychosis sample: A cross-sectional study.

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### Abstract

**Objectives:** To examine whether depressive symptoms predict receipt of cognitive behavioural therapy (CBTp) in individuals with psychosis.

**Design:** Retrospective cross-sectional analysis of electronic health records (EHRs) of a clinical cohort.

**Setting:** A secondary NHS mental health care service serving four boroughs of south London, UK.

**Participants:** 20,078 patients diagnosed with an ICD-10 code between F20-29 extracted from an EHR database.

**Primary and secondary outcome measures:** Primary: Whether recorded depressive symptoms predicted recorded CBTp session receipt (at least one session) identified from structured EHR fields supplemented by a natural language processing algorithm. Secondary: Whether age, gender, ethnicity, symptom profiles (positive, negative, manic and disorganisation symptoms), a comorbid diagnosis of depression, anxiety or bipolar disorder, prior CBT receipt, or type of psychosis diagnosis predicted recorded CBTp receipt.

**Results:** Of patients with a psychotic disorder, only 8.2% were recorded as receiving CBTp. At least one depressive symptom recorded, depression symptom severity and 12 out of 15 of the individual depressive symptoms independently predicted CBTp receipt. Female gender, White ethnicity and presence of a comorbid affective disorder or primary schizoaffective diagnosis were independently positively associated with CBTp receipt within the whole sample and the top 25% of mentioned depressive symptoms.

**Conclusions:** Individuals with a psychotic disorder who had recorded depressive symptoms were significantly more likely to have recorded receipt of CBTp sessions, aligning with CBTp guidelines of managing depressive symptoms related to a psychotic experience. However, overall recorded receipt of CBTp is low, unequal between demographic groups, and needs to be increased.

### Strengths and limitations of the study

- To our knowledge, this is the first electronic health record (EHR) study to measure how clinical symptomatology predicts recorded CBTp receipt, providing insight on a large sample into whether individuals who may be more in need of CBTp are more likely to have a session
- We replicate previous findings of inequalities in gender and ethnicity in real-world CBTp treatment receipt in a large heterogeneous sample.
- The natural language processing approach allows automated processing of EHR text at scale and can evaluate larger samples than manually conducted case note audits; this could therefore be used more routinely to monitor CBTp receipt.



- This study was limited to a single service provider; however, the results identified themes consistent with previous CBTp provision research in other services.
- Analysing EHRs in this way can identify CBTp receipt but is less suited to investigate whether CBTp is offered or not, or to quantify the quality or focus of the sessions. Furthering this, it cannot be used to examine CBTp completion rates and effectiveness.

### **Conflict of Interest**

The authors report no conflict of interest with respect to the findings described in this manuscript. RS declares research support received in the last 36 months from Janssen, GSK and Takeda.

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The lead author AM affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

### **Patient and public involvement**

The Clinical Record Interactive system as a data resource was developed and is run with extensive patient involvement. However, this particular analysis did not involve patients in its design or implementation.

### **Ethics statement**

The CRIS data platform has received research ethics approval as an anonymised data resource for secondary analysis (Oxford Research Ethics Committee C, reference 18/SC/0372)

## Introduction

There are a variety of cognitive and emotional processes involved in the development of psychotic symptoms,<sup>1</sup> with intense distress emerging early on in the course of the disorder. Content of positive symptoms often mirrors the content of depressive thinking processes,<sup>2</sup> suggesting therapeutic need for individuals experiencing additional depressive symptoms. Specific depressive symptoms that often accompany psychotic disorders are hopelessness, social avoidance and problems in forming relationships.<sup>3</sup> Around 50% of patients with psychosis report having experienced suicidal ideation at least once,<sup>4</sup> and around 40% of individuals with schizophrenia report clinical levels of depression and low self-esteem.<sup>5</sup> Importantly, individuals report these emotional difficulties and resulting social exclusion to be more debilitating than their psychotic symptoms.<sup>6</sup> Consequentially, individuals' negative appraisal of their psychotic experiences may lead to loss of social goals and increased shame, predicting later hopelessness and post-psychotic depression.<sup>7</sup> This comorbid depression increases the likelihood of having a lower quality of life, function, motivation, poorer social relationships, lower medication adherence and psychotic relapse (significant increase in psychotic symptoms).<sup>8,9,10</sup> Therefore, treatment should focus on the psychotic symptoms and the broader distress they produce, building self-esteem, confidence and a sense of self control and purpose.<sup>11</sup> Additionally, focusing on mood symptoms such as self-esteem and pessimism can help differentiate depressive symptoms from negative psychotic symptoms, that often show significant clinical overlap.<sup>5</sup>

It is increasingly recognised that medication alone is inadequate for tackling psychosis symptoms.<sup>12</sup> In the UK, the National Institute of Clinical Excellence<sup>13</sup> has recommended that cognitive behavioural therapy for psychosis (CBTp) be offered universally to individuals with psychosis. Based on the stress-vulnerability model,<sup>14</sup> CBTp focuses on distress reduction related to hallucinations and delusions, through targeting negative beliefs and improving self-esteem.<sup>10, 15</sup> Sessions often focus on goal setting and emotional issues such as rebuilding one's self, positivity and acceptance.<sup>11</sup> While studies examining characteristics of CBTp show strong evidence that CBTp improves depressive symptoms in the context of psychosis, specifically with long term reductions in suicidal behaviour,<sup>10, 15, 16</sup> service provision of this intervention still falls far short of the universal access recommended.<sup>12</sup>

Considering the impact of targeting these symptoms in CBTp sessions, it is important to monitor receipt of CBTp within psychosis samples. While CBTp provision shows moderate yearly increases (12.8% in 2013 to 14.8% in 2014), the treatment is still only available to a small proportion of individuals,<sup>12</sup> short of NICE universal access recommendations.<sup>13</sup> Previous studies investigating CBTp receipt have conducted time-consuming audits on limited sample sizes; these can be affected by under-reporting. On the other hand, the UK's National Mental Health Minimum Data Set report does not require CBT interventions to be recorded in a given individual's record. Natural language processing techniques (NLP)<sup>17</sup> offer the opportunity to extract this information from free text in electronic health records (EHRs) across large numbers of patients with psychosis, and a recent study developed and applied NLP in this respect, finding higher levels of receipt than reported in previous audit, supported by the high positive predictive value and sensitivity of the technique (95% and 96% respectively).<sup>12</sup>

While studies have examined general CBTp receipt within patients with psychosis, no study has examined a link between depressive symptoms and CBTp receipt.<sup>12</sup> Therefore, we investigated whether depressive symptoms predict CBTp receipt in people with psychosis by applying these previously data extraction techniques to secondary mental health care EHRs for a large South London catchment population. Secondary predictors of receipt were type of psychosis diagnosis (schizophrenia, schizoaffective disorder, or other schizophrenia spectrum disorder), symptom profiles (negative, manic or disorganisation), general CBT receipt prior to psychosis diagnosis, comorbid depression, anxiety or bipolar diagnosis and socio-demographic factors (ethnicity, gender and age).

## Methods

For this study, we extracted data on individuals with a diagnosis of a recognised schizophrenia spectrum diagnosis from the case registry of the South London and Maudsley NHS Foundation Trust (SLaM). This is a large secondary care mental healthcare provider, serving around 1.3 million residents in Croydon, Lambeth, Lewisham, and Southwark. SLaM care covers all specialist mental health care, including early intervention services, liaison and crisis teams and community and inpatient services. EHRs have been used for all SLaM services since 2006, with the Clinical Record Interactive Search system (CRIS) being established in 2008 to facilitate the retrieval of de-identified data from these records of patients previously or currently receiving mental healthcare from SLaM.<sup>18</sup> The source EHR contains unstructured free text fields from correspondence, personal histories, mental health examinations and management plans, as well as structured fields for coding demographic information, like age and ethnicity. Implementing data from all these fields reduces selection bias of utilising only specific sources of information from the EHR. Consequently, a large programme of work has developed a range of NLP algorithms over the last decade, whose detailed descriptions and performance data are contained in an open-access catalogue.<sup>19</sup> CRIS has approval as a data resource for secondary analysis (Oxford Research Ethics Committee C, reference 18/SC/0372), and a service user-led committee considers all proposed research before access to CRIS data is granted.

We extracted data for all individuals receiving SLaM care between January 2007 and June 2020 with a primary diagnosis of an ICD-10-defined schizophrenia spectrum disorder (F20-F29) and above the age of 18 at the time their original referral was accepted. The index date for covariate definitions was the date of the first diagnosis within this grouping. Individuals may have been active within the service before their index date, allowing us to extract data on prior CBT receipt. The sample was restricted to those with data on all variables.

Ethnicity, age at referral and gender were also extracted. Ethnicity was categorised into six groups for analysis: 'White British' (British), 'White other' (Irish or any other white background), 'Black' (Caribbean, African or any other black background), 'Asian' (Indian, Bangladeshi, Pakistani, Chinese or any other Asian background), 'Other/mixed' (white and Asian, white and black Caribbean, white and black African, any other ethnic group) and 'Not stated'.

Diagnosis was categorised into three subgroups of schizophrenia (ICD-10 codes F20.0–F20.9), schizoaffective disorder (F25.0–F25.9) and other schizophrenia spectrum disorder (F21, F22.0–F22.9, F23.0–F23.9, F24, F28 and F29). Within the data collection period, secondary diagnosis of depression (ICD-10: F32 or F33), anxiety (ICD-10: F40 or F41), or bipolar disorder (ICD-10: F31) were also extracted from structured field data.

NLP algorithms for each specific symptom were used to identify recorded symptom profiles within participants. Symptoms were categorised as depressive, positive, negative, manic or disorganisation. These symptoms had been categorised *a priori* by developers of the original independent symptom NLP algorithms. As symptoms could be labelled in more than one category during analysis, multicollinearity tests using the R function `vif()` within the [car package] were undertaken to avoid issues with overlapping predictor variables. All variables were included due to their VIF values being below five. However, positive symptoms were excluded from regression models using categorical symptom variables (having at least one mention within the EHR), as this factor variable only had one level, due to all participants having at least one positive symptom. The overall symptom list and subsequent recoding can be found in Table 1. Presence of at least one mention of any symptom in the five categories was computed as a binary variable (0/1).

Table 1  
*Classification of symptom predictors*

Symptom	Symptom label
Aggression	Positive
Agitation	Positive
Anergia	Depressive /Negative
Anhedonia	Depressive/Negative
Apathy	Depressive/Negative
Arousal	Manic
Blunted affect	Depressive/Negative
Circumstantiality	Disorganisation
Delusions	Positive
Derailment	Disorganisation
Disturbed sleep	Depressive/Manic
Elation	Manic
Emotional Withdrawal	Negative
Flight of ideas	Disorganisation
Formal thought disorder	Disorganisation
Grandiosity	Manic
Guilt	Depressive
Hallucinations (auditory)	Positive
Helplessness	Depressive
Hopelessness	Depressive
Hostility	Positive
Insomnia	Depressive/Manic
Irritability	Manic
Paranoia	Positive
Persecutory ideation	Positive
Poor appetite	Depressive
Poor concentration	Depressive
Poor motivation	Depressive
Poverty of speech	Negative
Poverty of thought	Negative
Social withdrawal	Negative
Suicidal ideation	Depressive
Tangentiality	Disorganisation
Tearfulness	Depressive
Thought block	Disorganisation
Worthlessness	Depressive

The date of the first and last general CBT session before the index date was extracted. This was coded as a binary variable, with individuals in the 'Prior CBT' receipt group having at least one session date mention prior to their index date. This was included as a predictor to adjust for previous experience of the specific CBT intervention. Mentions were extracted using the same NLP tool as the CBTp outcome measure mentioned subsequently.

1  
2  
3 The primary outcome was recorded CBTp receipt, identified using a combination of structured fields and  
4 NLP.<sup>17</sup> The NLP algorithms for general CBT has high PPV and sensitivity,<sup>12</sup> consistent with other NLP algorithms  
5 such as medication dose and diagnosis.<sup>20</sup> The date of the first CBTp session on or after the index date was  
6 extracted and computed as a binary variable, so that individuals in the 'CBTp receipt' group had at least one  
7 CBTp session mention after the index date.  
8

### 9 10 **Statistical analysis**

11 To avoid overfitting, we followed the 'one in ten' rule, whereby one predictor can be measured for every 10  
12 events. As the data included 1647 recorded CBTp events, our study was able to include all 12 predictors within  
13 the same regression model.  
14

15 All statistical analyses were conducted using R (version 1.3.9). Descriptive statistics for demographic and  
16 clinical variables are reported as frequencies for categorical variables and means and standard deviations for  
17 the continuous variable (age at referral). Chi square tests were also calculated for categorical variables, and t-  
18 test for age to measure between-group differences in those with/without CBT receipt. Descriptive statistics  
19 were also provided for yearly CBT prior to index date and recorded CBTp receipt post index date within the  
20 data extraction time period (2007-2020).  
21  
22

23  
24 Binary logistic regression was used to examine the association between depressive symptoms and recorded  
25 receipt of at least one CBT session in the whole sample. For this, three regression models were analysed.  
26 Model 1 was an unadjusted model with only depressive symptoms as the predictor variable. Due to significant  
27 provision differences seen in previous CBTp studies,<sup>12</sup> model 2 (partially adjusted model), adjusted for  
28 sociodemographic variables (age at referral, ethnicity, gender), primary diagnosis group and presence of a  
29 comorbid diagnosis (anxiety, depression, and bipolar disorder). Model 3 (fully adjusted model) also adjusted  
30 for prior CBT receipt before the index date (first psychosis diagnosis date) and symptoms mention (manic,  
31 negative and disorganisation symptoms). Positive psychotic symptoms were not included in these models, as  
32 individuals all had at least one mention within their case notes.  
33  
34

35  
36 As the primary aim of the study was to investigate depressive symptoms as a predictor of recorded CBTp  
37 receipt, we also split the depressive symptoms category into the 15 specific depressive symptoms applications  
38 within the whole sample. Model 4 was an unadjusted model with the 15 symptoms as predictor variables.  
39 Model 5 was a fully adjusted model that adjusted for all the variables in Model 3. We also conducted a  
40 sensitivity analysis to investigate how results were affected by overlap of negative or depressive symptom  
41 annotations, by removing negative symptoms as a predictor from the logistic regression model.  
42  
43

44 As well as investigating individual depressive symptoms as predictors of recorded CBTp receipt, we also  
45 investigated depression severity predicted CBTp receipt. These logistic regression models involved converting  
46 depressive, disorganised, manic, positive, and negative symptoms into continuous variables, whereby severity  
47 reflected the number of different individual symptoms mentioned within each symptom construct. This  
48 allowed for positive symptoms to also be included within regression models. Model 6 was an unadjusted  
49 model, with depressive symptom severity as a predictor of CBTp receipt. Model 7 and model 8 were partially  
50 and fully adjusted models, controlling for the same variables as model 2 and 3, except categorising symptoms  
51 as the continuous rather than categorical variable.  
52  
53

54 Lastly, to compare differences in the general sample with those with the top 25% quantity for depressive  
55 symptoms, we conducted two further regression models. This subsample analysis was conducted to examine  
56 predictors of CBTp receipt where a clear clinical indication was present, supplementing the overall findings.  
57 Model 9 partially adjusted for socio-demographic factors, diagnostic group and comorbid diagnosis and Model  
58 Model 10 fully adjusted for prior CBT, negative and disorganisation symptoms additionally. This group all had at least  
59 one manic and psychotic symptom, so these variables were not included in the model.  
60

**Table 2**

*Distribution frequencies on baseline demographics and diagnoses split by recorded CBTp receipt and primary diagnosis group.*

	No CBTp recorded (n = 18431)	Recorded CBTp (n=1647)	Chi square tests ( $\chi^2$ )
<b>Ethnicity</b>			$\chi^2=100.57^{***}$
White British	30% (5516/18431)	32.8% (540/1647)	
White Other	10.4% (1908/18431)	8.5% (140/1647)	
Black	36.5% (6719/18431)	41.7% (687/1647)	
Asian	6.5% (1193/18431)	5.2% (86/1647)	
Other/Mixed	9.8% (1808/18431)	10.5% (173/1647)	
Not stated	7.0% (1287/18431)	1.3% (21/1647)	
<b>Gender</b>			$\chi^2= 2.75$
Female	41.4% (7636/18431)	43.5% (717/1647)	
Male	58.6% (10795/18431)	56.5% (930/1647)	
Bipolar diagnosis	4.4% (810/18431)	9.0% (149/1647)	$\chi^2=71.94^{***}$
<b>No diagnosis</b>	95.6% (17621/18431)	91.0% (1498/1647)	
Depression diagnosis	7.4% (1373/18431)	14.0% (230/1647)	$\chi^2=87.36^{***}$
<b>No diagnosis</b>	92.6% (17058/18431)	86.0% (1417/1647)	
Anxiety diagnosis	2.4% (441/18431)	7.0% (115/1647)	$\chi^2=118.28^{***}$
<b>No diagnosis</b>	97.6% (17990/18431)	93.0% (1532/1647)	
<b>Prior CBT</b>	3.1% (573/18431)	14.4% (237/1647)	$\chi^2=497^{***}$
<b>No prior CBT</b>	96.9% (17858/18431)	85.6% (1410/1647)	

\*\*\* $p<.001$

## Results

### Participants

The cohort comprised 20,078 individuals with the inclusion diagnoses, 1647 (8.2%) of whom received at least one recorded session of CBTp after their first diagnosis date. The mean age of the cohort was 42.4 years (SD=16.5). Distribution frequencies for all categorical variables can be found in Table 2. Chi-square test results represented in this table compared those with or without CBTp receipt. All mentioned variables showed significant between-group differences at  $p<.001$  apart from gender (No CBTp group females=41.4%, CBTp delivery group females= 43.5%;  $\chi^2=2.75$ ,  $p=.097$ ). These significant variables include depression diagnosis ( $\chi^2=87.36$ ), bipolar diagnosis ( $\chi^2=71.94$ ), anxiety diagnosis ( $\chi^2=118.28$ ) and prior CBT receipt ( $\chi^2=497$ ). Additionally, the Welch two sample t-test found significant between-group differences in age ( $t=15.34$ ,  $p<.01$ ). Where those who had received CBTp had a lower mean age ( $M=33.12$  SD= 11.5) compared to those who did not ( $M=35.88$ , SD=13.08). The significant results confirmed the need for further analysis through the regression models. Positive psychotic symptoms were excluded from chi square and regression analysis, as all patients had at least one positive psychotic symptom.

### CBT receipt.

The descriptive results shown suggest that there is a low prevalence of both prior CBT and recorded CBTp post diagnosis across the years (Table 3, supplementary figure). The decrease in recorded receipt in 2020 can be explained by COVID-19, while 2019 receipt is comparable to previous years.

Table 3

*Distribution frequencies on recorded CBT receipt (prior to diagnosis) and recorded CBTp receipt (post diagnosis) per year of data extraction.*

Year	CBT prior	CBT post	All CBT
2007	130	81	211
2008	89	146	235
2009	59	111	170
2010	48	107	155
2011	37	105	142
2012	39	96	135
2013	32	128	160
2014	25	143	168
2015	24	150	174
2016	29	115	144
2017	16	127	143
2018	16	114	130
2019	15	153	168
2020	2	71	73
Total	561	1647	2208

#### **General depressive symptom mention regression analysis**

Results from the unadjusted (model 1), partially adjusted (model 2) and fully adjusted regression (model 3) are displayed in Table 4. Regression model 1 found that general mention of at least one of 15 potential depressive symptoms significantly predicted recorded CBTp receipt. Regarding model 2 and 3, individuals with at least one depressive, negative or disorganisation symptom mention, being of female gender, white ethnicity, prior CBT receipt and presence of a comorbid affective disorder independently positively associated with recorded CBTp receipt.



Table 4

Unadjusted, partially and fully adjusted logistic regression models for recorded CBTp receipt (Regression model 1, 2 and 3) with categorical symptom measures.

		Unadjusted	Partially adjusted	Fully adjusted
	N(%)	OR(95%CI)	OR(95%CI)	OR(95%CI)
<b>Depressive symptoms</b>				
1+ depressive symptom mention	18286(91.1)	3.78(2.94-4.96)***	3.42 (2.58-4.60)***	2.00(1.10-3.20)***
<b>Bipolar diagnosis</b>				
Has f31 diagnosis	959(4.80)		0.52(0.33-0.71)***	0.32(0.12-0.52)***
<b>Depression diagnosis</b>				
Has f32 diagnosis	603(80)		0.52(0.36-0.67)***	0.33(0.16-0.49)**
<b>Anxiety diagnosis</b>				
Has f40/41 diagnosis	556(2.80)		0.89(0.66-1.11)***	0.73(0.49-0.97)***
<b>Age</b>	N/A		-0.03(-0.04- -0.03)***	-0.03(-0.03- -0.02)***
<b>Gender</b>				
Male			Reference category	
Female	8353(41.60)		0.20(0.09-0.31)***	0.20 (0.10-0.32)***
<b>Ethnic group</b>				
White British	6056(30.10)		Reference category	
White Other	2048(10.20)		-0.40(-0.60 - -0.21)***	-0.37(-0.57- -0.17)***
Black	7406(36.90)		-0.16(-0.28- -0.04)**	-0.24 (-0.36- -0.11)***
Asian	1279(6.40)		-0.49(-0.74- -0.26)***	-0.50 (-0.75- -0.27)***
Other/Mixed	1981(9.90)		-0.21(-0.40- -0.02)**	-0.18(-0.37- -0.01)*
Not Stated	1308(6.50)		-1.75(2.23- -1.22)***	-1.52(-2.00- -1.10)***
<b>Primary diagnosis</b>				
Schizophrenia	9845(49.00)		Reference category	
Schizoaffective disorder	2142(10.70)		0.04(-0.13-0.21)	0.01(-0.17-0.19)
Other schizophrenia spectrum	8091(40.30)		-0.10(-0.22-0.01)*	-0.02(-0.14 -0.10)
<b>Negative symptoms</b>				
1+ Negative symptom mention	13169(65.60)			0.75(0.59-0.92)***
<b>Manic symptoms</b>				
1+ Manic symptom mention	17945(89.40)			1.24(0.70-1.87)***
<b>Disorganisation symptoms</b>				
1+ Disorganisation symptom mention	11513(57.30)			0.31(0.18-0.44)***
<b>CBT prior</b>				
1+ prior CBT session				1.29(1.12-1.46)***

\*p<.05, \*\*p<.01, \*\*\*p<.001

**Unadjusted (model 1):** depressive symptom as a predictor with no adjusted covariates

**Partially adjusted (model 2):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis

**Fully adjusted (model 3):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis, depressive symptoms, prior CBT, negative symptoms, disorganisation symptoms, manic symptoms.



### Regression analysis with individual depressive symptoms

Results from the unadjusted (model 4) and fully adjusted (model 5) regression analyses for each of the 15 individual depressive symptoms are displayed in Table 5 (N=20,078). Each symptom refers to presence of at least one mention in the patients notes compared to no mention. While all variables were significant in the unadjusted model at  $p < .001$ , the fully adjusted model reduced the significance of suicide ideation ( $p < .01$ ) and disturbed sleep ( $p < .01$ ), with anhedonia, anergia, apathy, and blunted affect becoming non-significant ( $p > 0.05$ ).

Table 5

*Unadjusted and fully adjusted logistic regression models for recorded CBTp receipt with individual depressive symptoms as covariates (Regression model 4 and 5) for the overall sample.*

		Unadjusted	Fully adjusted
	N(%)	OR(95%CI)	OR(95%CI)
Hopelessness	7345(36.60)	4.81(4.3-5.40)***	1.45(1.26-1.66)
Helplessness	3124(15.60)	4.03(3.62-4.50)***	1.55(1.37-1.76)***
Suicide ideation	9451(47.10)	4.11(3.66-4.63)***	1.25(1.09-1.44)**
Poor appetite	8044(40.10)	3.31(2.97-3.68)***	1.28(1.13-1.45)***
Poor motivation	8630(43.00)	4.34(3.87-4.86)***	1.43(1.24-1.64)***
Insomnia	6870(34.20)	3.74(3.35-4.15)***	1.4(1.24-1.58)***
Disturbed sleep	16667(83.00)	15.3(10.16-22.8)***	2.76(1.5-5.08)**
Poor concentration	12289(61.20)	8.16(6.81-9.77)***	2.33(1.9-2.85)***
Anhedonia	4047(20.20)	2.9(2.61-3.22)***	0.97(0.85-1.10)
Anergia	873(43.50)	2.63(2.20-3.15)***	0.98(0.80-1.20)
Apathy	4149(20.70)	2.21(1.98-2.46)***	0.93(0.82-1.05)
Guilt	8178(40.70)	4.6(4.1-5.15)***	1.49(1.30-1.70)***
Tearfulness	10951(54.50)	3.87(3.41-4.39)***	1.22(1.05-1.42)**
Blunted affect	6889(34.30)	2.66(2.41-2.95)***	0.91(0.80-1.03)
Worthlessness	2921(14.50)	3.94(3.53-4.40)***	1.37(1.21-1.56)***

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

### Sensitivity analysis

The non-significant results of certain depressive symptoms (anhedonia and anergia) may have been due to their inclusion within the negative symptom category, causing over-adjustment of the model. To test this, sensitivity analysis was conducted, where the fully adjusted regression (model 3) did not include negative symptoms as a covariate. While all significant variables remained significant, non-significant results for anhedonia and apathy were also still found. Therefore, we report the fully adjusted model with negative symptoms as a variable for both grouped and individual depressive symptom associations.

### General depressive symptom severity regression analysis

Results from the unadjusted (model 6), partially adjusted (model 7) and fully adjusted regression (model 8) are displayed in Table 6. Regression model 6 found that depression symptom severity significantly predicted CBTp receipt. Regarding model 7 and 8, depression symptom severity, positive symptom severity, anxiety diagnosis, and being of older age or being of white ethnicity independently positive predicted CBTp receipt. Within model 7., being female also positively increased likelihood of CBTp receipt. Within model 8, negative symptom severity and prior CBT significantly predicted CBTp receipt additionally.

Table 6

Unadjusted, partially and fully adjusted logistic regression models for recorded CBTp receipt (Regression model 1, 2 and 3) with continuous symptom measures.

		Unadjusted	Partially adjusted	Fully adjusted
	N(%)	OR(95%CI)	OR(95%CI)	OR(95%CI)
<b>Depressive symptoms</b>				
Severity	18286(91.1)	0.29(1.31-1.35)***	0.27(1.20-1.44)***	0.23(0.13-0.33)***
<b>Positive symptoms</b>				
Severity	20078(100)		-0.18(0.75-0.92)***	-0.21(-0.31- -0.09)***
<b>Bipolar diagnosis</b>				
Has f31 diagnosis	959(4.80)		0.21(0.94-1.63)	0.15(-0.13-0.43)
<b>Depression diagnosis</b>				
Has f32 diagnosis	603(80)		-0.09(0.72-1.15)	-0.09(-0.33-0.15)
<b>Anxiety diagnosis</b>				
Has f40/41 diagnosis	556(2.80)		0.49(1.15-2.29)***	0.46(0.11-0.80)***
<b>Age</b>	N/A		-0.02(0.97-0.99)***	-0.02(-0.03- -0.01)***
<b>Gender</b>				
Male			Reference category	
Female	8353(41.60)		0.17(0.97-1.44)*	0.17(-0.03-0.36)
<b>Ethnic group</b>				
White British	6056(30.10)		Reference category	
White Other	2048(10.20)		-0.41(0.45-0.96)**	-0.44(-0.93- -0.07)***
Black	7406(36.90)		-0.25(0.63-0.97)**	-0.29(-0.51- -0.07)**
Asian	1279(6.40)		-0.66(0.32-0.80)***	-0.67(-1.13 - -0.23)***
Other/Mixed	1981(9.90)		-0.14(0.62-1.22)	-0.16(-0.50-0.18)
Not Stated	1308(6.50)		-0.92(0.02-2.42)	-0.79(-3.74-1.01)
<b>Primary diagnosis</b>				
Schizophrenia	9845(49.00)		Reference category	
Schizoaffective disorder	2142(10.70)		-0.08(0.69-1.21)	-0.11(-0.40-0.18)
Other schizophrenia spectrum	8091(40.30)		0.02(0.82-1.26)	-0.06(-0.15-0.28)
<b>Negative symptoms</b>				
Severity	13169(65.60)			0.06(-0.01-0.123)*
<b>Manic symptoms</b>				
Severity	17945(89.40)			-0.01(-0.13-0.12)
<b>Disorganisation symptoms</b>				
Severity	11513(57.30)			0.10(-0.05-0.25)
<b>CBT prior</b>				
1+ prior CBT session	1647(8.20)			0.62(0.34-0.89)***

\*p<.05, \*\*p<.01, \*\*\*p<.001

**Unadjusted (model 1):** depressive symptom severity as a predictor with no adjusted covariates

**Partially adjusted (model 2):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis, positive symptom severity

**Fully adjusted (model 3):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis, positive symptom severity, prior CBT, negative symptom severity, disorganisation

symptom severity and manic symptom severity.

### Depressive symptom regression analysis within the top 25% number of depressive symptoms.

This sample comprised individuals with the top 25% number of depressive symptoms (5018 patients), defined to reflect a sub-group who might reasonably expect to receive CBT on this basis. The sample characteristics and regression analysis can be seen in Table 7. Results from the partially adjusted (model 9) and fully adjusted regression (model 10) are displayed in Table 7. Table 4 found that general mention of at least one of 15 potential depressive symptoms significantly predicted CBTp receipt. Regarding model 9, we found that individuals with at least one depressive, negative or disorganisation symptom mention, being of female gender, white ethnicity, prior CBT receipt and presence of comorbid bipolar disorder were positively associated with recorded CBTp receipt.

Table 7

*Partially and fully adjusted logistic regression models for CBTp receipt with individual depressive symptoms as covariates within top 25% quantity of depressive symptoms (Regression model 9 and 10).*

	N(%)	Partially adjusted OR(95%CI)	Fully adjusted OR(95%CI)
<b>Bipolar diagnosis</b>			
Has f31 diagnosis	541(10.78)	0.19(-0.03-0.41)*	0.15(-0.08-0.38)
<b>Depression diagnosis</b>			
Has f32 diagnosis	885(17.63)	0.11(-0.08-0.30)	0.08(-0.90-1.30)
<b>Anxiety diagnosis</b>			
Has f40/41 diagnosis	270(5.38)	0.53 (0.25-0.80)***	0.47(0.19-0.75)***
<b>Age</b>			
M= 36.24(18-93)		-0.02(-0.02- -0.01)***	-0.02(-0.03- -0.01)***
<b>Gender</b>			
Male	2059(41.01)	Reference category	
Female	2960(58.99)	0.20 (0.05-0.34)***	0.17(0.02-0.32)**
<b>Ethnic group</b>			
White British	1486(29.59)	Reference category	
White Other	433(8.63)	-0.21(-0.48-0.05)	-0.22(0.50-0.05)
Black	2262(45.08)	-0.32(-0.49- -0.16)***	-0.31(0.47- -0.14)***
Asian	328(6.53)	-0.53(0.86- -0.21)***	-0.52(0.85- -0.20)***
Other/Mixed	467(9.31)	-0.08(-0.34-0.17)	-0.08(0.34-0.17)
Not Stated	43(0.86)	-1.42 (-2.85 -0.40)**	-1.34(-2.8 - -0.31)**
<b>Primary diagnosis</b>			
Schizophrenia	2219(44.22)	Reference category	
Schizoaffective disorder	740(14.72)	0.04(-0.18-0.26)	0.003(-0.22-0.22)
Other schizophrenia spectrum	2060(41.03)	0.02(-0.14 -0.17)	0.05(-0.11-0.21)
<b>Negative symptoms</b>			
1+ Negative symptom mention	4956(98.7)		-0.88(1.41- -0.33)***
<b>Disorganisation symptoms</b>			
1+ Disorganisation symptom mention	4199(83.66)		1.18(-0.02-0.38)*
<b>CBT prior</b>			
1+ prior CBT session	436(8.7)		-0.90(0.68-1.11)***

\*p<.05, \*\*p<.01, \*\*\*p<.001,

**Partially adjusted (model 9):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis.

**Fully adjusted (model 10):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis, prior CBT, negative symptoms, disorganisation symptoms

### Discussion

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4 We believe that this is the first study to examine the relationship between clinical symptomatology and CBTp receipt  
5 within a sample of people with psychosis in a naturalistic community setting. In general, only 8.2% of individuals were  
6 ascertained as having received CBTp within the 13-year timeframe of the study, showing the low prevalence of  
7 recorded receipt despite current clinical guidelines. This finding shows a lower overall level of recorded CBTp provision  
8 compared to previous studies in 2013 (12.8%) and 2014 (14.8%)<sup>12</sup>. This requires further examination, considering the  
9 importance of CBTp mentioned within NICE universal access recommendations.<sup>13</sup> Additionally, the significant decrease  
10 of CBTp receipt in 2020 can be explained by the COVID pandemic and therefore, it is important to consider how we can  
11 improve receipt despite this.  
12

13 In the analysed sample, 91% of patients had at least one recorded depressive symptom mention, and these individuals  
14 were 2 times more likely to have at least one recorded CBTp session in the fully adjusted model (table 4), suggesting  
15 that the minority who don't present with any depressive symptoms are very unlikely to receive CBTp. This could  
16 possibly be due to clinicians tending to cite a depressive symptom when referring an individual with psychosis to  
17 psychotherapy. Additionally, the severity of depressive symptoms, as well as having at least one recorded mention  
18 significantly increased likelihood of having at least one recorded CBTp session. In the sample of those with the highest  
19 number of depressive symptoms (top 25%), relationships between recorded CBTp receipt and comorbid anxiety  
20 diagnosis, age, gender, ethnicity, prior CBT, negative and disorganised psychotic symptoms remained. This suggests the  
21 importance of these predictors in a reasonable sample of patients with higher clinical need for CBTp receipt.  
22

23 Considering individual depressive symptom, the symptom which was the strongest predictor of this  
24 intervention in fully adjusted models was disturbed sleep. There is a known high prevalence of sleeping  
25 problems in this population,<sup>21,22</sup> described by some researchers as an 'intrinsic feature of schizophrenia,<sup>23</sup>  
26 known to reduce quality of life, decreasing coping and exacerbate positive symptoms.<sup>24</sup> The significant  
27 association between insomnia and psychotic-like symptoms, such as paranoia, has also been seen in non-  
28 clinical populations.<sup>25</sup> Further to this, the recommended first line of treatment for sleep problems in this  
29 clinical population is CBT.<sup>26</sup> Poor concentration was the next strongest depressive symptom predictor in the  
30 fully-adjusted model, possibly reflecting previous findings of its association with psychosis vulnerability.<sup>27</sup> The  
31 significance of helplessness, guilt and hopelessness is relevant to previous CBTp research that found significant  
32 post-treatment reduction in hopelessness, self-depreciation and guilt using the Calgary Depression Rating  
33 Scale for Schizophrenia.<sup>28</sup> Other significant depressive symptoms associated with low self-esteem and negative  
34 self-evaluation and emotions have been found to significantly affect the development and severity of positive  
35 symptoms.<sup>29</sup> This may be because positive symptoms develop as a psychological defence against low self-  
36 esteem<sup>30</sup> and depression-induced guilt.<sup>31</sup> Therefore, it could be suggested that the significance of each of the  
37 depressive symptoms is often linked to psychotic symptoms and CBTp effectiveness. However, while there is  
38 evidence of the clinical impact of depressive symptoms in schizophrenia, the associations with choice of  
39 therapy must be viewed as exploratory and in need of independent replication. While a possibility may be that  
40 clinicians are assuming that certain depressive symptoms are likely to be more responsive to CBTp than others,  
41 there may be other unknown reasons for therapy choice that requires further investigation. General results  
42 suggest that receipt of this intervention requires an increase for all of this clinical population before individuals  
43 with specific symptoms can be targeted.  
44  
45

46 Regarding negative symptoms, the non-significant associations between specific negative symptoms (that overlapped  
47 with depressive symptoms) and CBTp receipt requires further evaluation and confirmation. This was not conducted in  
48 the current study due to the primary aim focusing on depressive symptoms. However, from our results on specific  
49 depressive symptoms in table 5, symptoms that overlapped with negative symptoms (anhedonia, anergia, apathy and  
50 blunted affect) were not associated with CBTp receipt. Additionally, negative symptoms were associated with a  
51 significantly decreased likelihood of recorded CBTp receipt within the group with highest numbers of depressive  
52 symptoms mentioned. Overall, this raises concerns that individuals with these specific negative/depressive symptoms  
53 are no more likely and perhaps less likely to receive CBTp than someone without these symptoms. Possibly, this is due  
54 to clinicians not referring these individuals because they don't believe intervention will be effective. This is in line with a  
55 CBTp review of randomised control trials, finding non-significant reductions of negative symptoms,<sup>32</sup> perhaps due to  
56 the narrowing of treatments to specifically target positive symptoms.<sup>33</sup> However, further work should be undertaken to  
57 verify that individuals are not being denied a potentially beneficial intervention because of their symptom profile.  
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3 Prior CBT receipt, comorbid disorder presence and specific symptoms (manic, disorganised, and negative) also emerged  
4 as independent predictors of CBTP receipt for the general sample and within those with the top 25% depressive  
5 symptom numbers. Within table 4, individuals who had any recorded CBT receipt prior to the index date were 1.29  
6 times more likely to have recorded CBTP receipt later on. Also, patients with an additional comorbid disorder were  
7 0.32-0.73 times more likely to have received CBTP compared to those with just a psychosis diagnosis. However, in the  
8 top 25% of individuals within table 7, individuals with prior CBT were 0.40 times less likely to receive CBTP. This finding  
9 requires further research to understand the effects of prior CBT and negative symptoms on CBTP receipt within  
10 different psychosis subsamples. Additionally, those with anxiety were 0.47 times more likely to receive CBTP and those  
11 with disorganised symptoms were 1.18 times more likely respectively. After general CBTP receipt has increased, there  
12 could be a method to focus more on patients with different types of psychotic symptoms and comorbid affective  
13 diagnosis. Furthering this, future research could investigate whether those who have had prior general CBT would  
14 benefit from CBTP, or whether those who have not had any experience developing cognitive behaviour skills in therapy  
15 should be targeted.<sup>33</sup>

16  
17 Crucially, there were also significant differences in recorded CBTP receipt between different ethnic and gender groups.  
18 Male patients were 0.20 times as likely in the general sample and top 25% of depressive symptoms to have recorded  
19 CBTP receipt. Black, Asian, Other and Mixed ethnic groups were between 0.21 to 0.49 times as likely to have a  
20 documented CBTP session compared to individuals of white ethnicity within both the general and top 25% depressive  
21 symptoms samples. Inequitable access to CBTP has been identified in previous CBTP research within a psychosis sample  
22 drawn from the same data resource in 2017, finding female patients to be more likely to have received CBTP and  
23 individuals of White ethnicity to have a significantly higher likelihood of CBT receipt than Black or other ethnicity  
24 groups.<sup>12</sup> This also supports results from a recent CBTP study focusing specifically on ethnic group differences in CBTP  
25 provision within SLAM, who found that in comparison to White British individuals, those from Black ethnic groups with  
26 psychosis or bipolar disorder were significantly less likely to have a documented CBTP session. This is especially  
27 important when considering the high prevalence of psychosis within UK Black and minority ethnic group populations.<sup>34</sup>  
28 Inequality in CBTP receipt may be due to ethnic variations in CBTP engagement. Some of these barriers within certain  
29 communities may be increased stigma, fear of clinicians by service-users or service users by clinicians, institutional  
30 racism within mental health services, or non-culturally appropriate therapy.<sup>35</sup> As differences in documented CBTP  
31 receipt between ethnic groups have now been documented by three different papers in this service, it is imperative  
32 that further work is conducted to increase provision of CBTP within groups less likely to receive treatment. This may  
33 include targeted outreach programs and culturally adapting interventions<sup>35</sup> within these minority groups.

34  
35 The present study has a number of strengths and limitations. Generally, focusing on patients with more  
36 diverse functioning, comorbidity and symptom severity levels helps research identify a larger number of  
37 predictors of clinical outcomes. This can be seen through our results, where negative, manic and  
38 disorganisation symptoms significantly predicted recorded CBTP receipt, as well as recent research,<sup>33</sup> that was  
39 the first to identify depression as a significant predictor of positive symptom improvement post-CBTP. This  
40 highlights the importance of focusing on a clinically heterogeneous sample to realistically determine significant  
41 predictors of CBTP receipt. Secondly, using an NLP approach automates the measurement of what would  
42 otherwise require manually conducted audits on records and case notes, increasing the number of cases that  
43 can be investigated and providing a method that could be used more routinely to monitor CBT receipt. The  
44 large sample size enabled us to identify potential clinical differences in the real-life administration of CBTP  
45 within a psychosis cohort, and we were able to adjust for multiple clinical variables and comorbidity diagnoses  
46 to provide a more realistic understanding of the depressive symptom-CBTP receipt relationship. This time  
47 frame was broad to allow the inclusion of as many active patients receiving CBTP as possible, additionally  
48 circumventing monthly/seasonal variation of CBTP receipt.

49  
50 One limitation of the study was the omission of strict time periods for the mention of clinical symptoms prior  
51 to CBTP administration. Unfortunately, using this approach would have involved implementing time periods on  
52 all of the other clinical symptoms and variables, which would have been difficult considering the number of  
53 variables that would need to be controlled. In addition, the NLP symptom algorithms do not currently  
54 distinguish between past or present symptoms. Therefore, symptom mentions documented after the CBTP  
55 receipt date could refer to mentions of symptoms occurring prior to CBTP receipt, reducing the effectiveness  
56 of using time periods. A follow-up time period after the index date was also not established, meaning that  
57 participants included in the cohort at a later date may have been less likely to have had a CBTP session, due to  
58 their limited time period within the service. Additionally, we did not have data regarding which type of service  
59 was providing CBTP for each patient (for example, early intervention services compared to other community  
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3 services). Future studies should examine whether CBTp receipt differs depending on the service, especially  
4 considering how effective CBTp provision may be in those at ultra-high risk.  
5

6 While our use of additional querying of text fields allowed us to identify a significantly larger number of CBTp  
7 episodes than using structured data alone, we were not able to quantify the gap between CBTp referral and  
8 CBTp receipt. This is because the CBTp NLP algorithm detects CBTp receipt rather than CBTp being offered,  
9 due to the wide range of subtle wording used for the latter more complex entity. The results combine effects  
10 on the likelihood of CBTp being offered, with those on session receipt following an offer. While this may have  
11 affected our results, previous service audits have suggested that the severity and occurrence of depressive  
12 symptoms significantly decreases CBT receipt.<sup>36</sup> Therefore, if only receipt was directly measured, we would  
13 expect to see similar results. It is also important to consider that we are only ascertaining recorded CBTp  
14 receipt, which may result in failing to pick up all CBTp receipt instances. Considering that previous research  
15 describing the app development suggests high precision and recall performance of CBTp instances (PPV= 96%,  
16 sensitivity= 96%),<sup>12</sup> it could be suggested that low prevalence within the results is due to lack of recording  
17 within the clinical health records, rather than lack of app identification. Therefore, stricter regulations are  
18 required for CBTp to be reported within clinical health records. Additionally, completion rates and  
19 effectiveness of the CBTp was not measured, meaning we were unable to quantify the quality or focus of the  
20 sessions. Lastly, analysis was limited to patients above 18 years old, reducing the generalisability of results to  
21 those who develop a schizophrenia-spectrum disorder after this age. However, the outcome of interest was  
22 CBTp receipt within a relatively homogenous service structure of working age services, rather than young  
23 people treated within Child and Adolescent services. Future studies should examine whether CBTp receipt  
24 differs in these services.  
25

#### 26 **Future directions**

27 Initiatives such as the Improving Access to Psychological Therapies programme for serious mental illness, early  
28 intervention access and projects to decrease waiting times for referral have been developed to target this  
29 clinical population. However, access still falls short of recommendations and is inequitable for specific  
30 psychotic diagnoses, age, and ethnicity.<sup>12</sup> Therefore, given the effect of CBTp on depressive symptoms<sup>37</sup>,  
31 perhaps its more pragmatic to focus on patients with additional depressive symptoms. Monitoring CBTp  
32 receipt over time could decipher whether these initiatives are effective at increasing general access for those  
33 with psychosis, and specific access for different sociodemographic groups and those with additional depressive  
34 symptoms (who may benefit the most).  
35  
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37  
38 The significant secondary clinical and sociodemographic variables require further analysis in order to fully  
39 understand the services' provision. This could involve attention given to the independent symptoms within the  
40 negative, manic and disorganisation categories in a similar manner to the specific depressive symptom  
41 regression models analysed. Further research could also explore why the presence of co-morbid anxiety and  
42 bipolar disorder in this sample predicted CBTp receipt. Additionally, the results suggest a need to reflect on the  
43 steps taken since the previous service study,<sup>35</sup> regarding inequality in CBTp receipt among gender and ethnic  
44 groups, due to the consistent significant results seen. Regarding the use of EHR data, future work could involve  
45 developing a separate NLP algorithm to ascertain the offering of CBTp or provide another structured field for  
46 clinicians to complete for this. However, clinicians prioritise text field data for communication about CBTp  
47 sessions for themselves and their colleagues rather than to collect structure data for the sake of research.  
48 Therefore, as previously suggested,<sup>12</sup> it is important to accept the mixed structured-text field approach that  
49 will remain in healthcare record data and perhaps our time is best spent in improving NLP algorithms to detect  
50 the subtleties of intervention and clinical outcome data. However, the implications of our results and their  
51 consistency three years after the first CBTp service paper suggest the need to use this or future algorithms for  
52 service monitoring independent of these improvements.  
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### Author statement

Ava Mason planned the protocol, analysed the data and wrote the manuscript. Dr Rob Stewart provided access to the data, looked over edits and revisions on the manuscript. The data from this paper was accessed through the assistance of Megan Pritchard and Jyoti Sanyal. The applications used to obtain data specific to CBTp were developed by Craig Colling and David Chandran. Jessica Irving assisted in statistical analysis.

### Data Sharing Statement

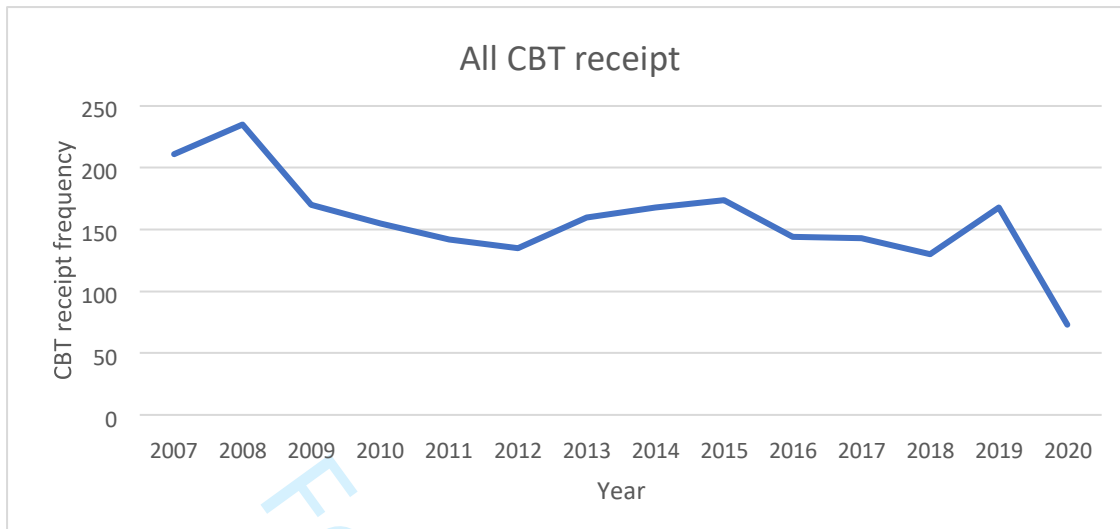
Due to the terms of Ethics and Information Governance approvals and clinical source of the data, CRIS datasets must remain within the South London and Maudsley NHS Foundation Trust (SLaM) firewall. All data used from this study can be made accessible on request from [cris.administrator@slam.nhs.uk](mailto:cris.administrator@slam.nhs.uk), subject to the setting up of an appropriate research passport or SLaM honorary contract.



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Supplementary figure  
*Graph demonstrating the frequency of general CBT receipt (CBT receipt prior to diagnosis and recorded CBTp receipt post diagnosis) per year of extraction period.*

For peer review only



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Supplementary figure

*Graph demonstrating the frequency of general CBT receipt (CBT receipt prior to diagnosis and recorded CBTp receipt post diagnosis) per year of extraction period.*

# Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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		Reporting Item	Page Number
<b>Title and abstract</b>			
Title	<a href="#">#1a</a>	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	<a href="#">#1b</a>	Provide in the abstract an informative and balanced summary of what was done and what was found	1
<b>Introduction</b>			
Background / rationale	<a href="#">#2</a>	Explain the scientific background and rationale for the investigation being reported	1,3
Objectives	<a href="#">#3</a>	State specific objectives, including any prespecified hypotheses	3
<b>Methods</b>			
Study design	<a href="#">#4</a>	Present key elements of study design early in the paper	4

1	Setting	<a href="#">#5</a>	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
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4	Eligibility criteria	<a href="#">#6a</a>	Give the eligibility criteria, and the sources and methods of selection of participants.	4
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8		<a href="#">#7</a>	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	1,4-6,
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14	Data sources / measurement	<a href="#">#8</a>	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. Give information separately for for exposed and unexposed groups if applicable.	4-6
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21	Bias	<a href="#">#9</a>	Describe any efforts to address potential sources of bias	4
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23	Study size	<a href="#">#10</a>	Explain how the study size was arrived at	4
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25	Quantitative variables	<a href="#">#11</a>	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	4-6
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29	Statistical methods	<a href="#">#12a</a>	Describe all statistical methods, including those used to control for confounding	6
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33	Statistical methods	<a href="#">#12b</a>	Describe any methods used to examine subgroups and interactions	6
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37	Statistical methods	<a href="#">#12c</a>	Explain how missing data were addressed	4
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41	Statistical methods	<a href="#">#12d</a>	If applicable, describe analytical methods taking account of sampling strategy	6
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44	Statistical methods	<a href="#">#12e</a>	Describe any sensitivity analyses	6
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48	<b>Results</b>			
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51	Participants	<a href="#">#13a</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. Give information separately for for exposed and unexposed groups if applicable.	1,6
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1	Participants	<a href="#">#13b</a>	Give reasons for non-participation at each stage	6
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3	Participants	<a href="#">#13c</a>	Consider use of a flow diagram	N/A
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5	Descriptive data	<a href="#">#14a</a>	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	4-7
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12	Descriptive data	<a href="#">#14b</a>	Indicate number of participants with missing data for each variable of interest	4
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16	Outcome data	<a href="#">#15</a>	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	8
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21	Main results	<a href="#">#16a</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	7-12
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28	Main results	<a href="#">#16b</a>	Report category boundaries when continuous variables were categorized	7-12
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32	Main results	<a href="#">#16c</a>	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
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36	Other analyses	<a href="#">#17</a>	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	12
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40	<b>Discussion</b>			
41				
42	Key results	<a href="#">#18</a>	Summarise key results with reference to study objectives	13-15
43				
44	Limitations	<a href="#">#19</a>	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	14-15
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50	Interpretation	<a href="#">#20</a>	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13-15
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55	Generalisability	<a href="#">#21</a>	Discuss the generalisability (external validity) of the study results	13-15
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1 **Other**  
2 **Information**

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5 Funding [#22](#) Give the source of funding and the role of the funders for the present 2  
6 study and, if applicable, for the original study on which the present  
7 article is based  
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# BMJ Open

## The association between depressive symptoms and Cognitive Behavioural Therapy receipt within a psychosis sample: A cross-sectional study.

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## The association between depressive symptoms and Cognitive Behavioural Therapy receipt within a psychosis sample: A cross-sectional study.

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**Keywords:** CBTp, psychosis, cognitive behaviour therapy, depression, mental illness.

Abstract word count: 248

Main body word count: 2918

### Abstract

**Objectives:** To examine whether depressive symptoms predict receipt of cognitive behavioural therapy (CBTp) in individuals with psychosis.

**Design:** Retrospective cross-sectional analysis of electronic health records (EHRs) of a clinical cohort.

**Setting:** A secondary NHS mental health care service serving four boroughs of south London, UK.

**Participants:** 20,078 patients diagnosed with an ICD-10 code between F20-29 extracted from an EHR database.

**Primary and secondary outcome measures:** Primary: Whether recorded depressive symptoms predicted CBTp session receipt, defined as at least one session of CBT for psychosis (CBTp) identified from structured EHR fields supplemented by a natural language processing algorithm. Secondary: Whether age, gender, ethnicity, symptom profiles (positive, negative, manic and disorganisation symptoms), a comorbid diagnosis of depression, anxiety or bipolar disorder, general CBT receipt prior to the primary psychosis diagnosis date, or type of psychosis diagnosis predicted CBTp receipt.

**Results:** Of patients with a psychotic disorder, only 8.2% received CBTp. Individuals with at least one depressive symptom recorded, depression symptom severity and 12 out of 15 of the individual depressive symptoms independently predicted CBTp receipt. Female gender, White ethnicity and presence of a comorbid affective disorder or primary schizoaffective diagnosis were independently positively associated with CBTp receipt within the whole sample and the top 25% of mentioned depressive symptoms.

**Conclusions:** Individuals with a psychotic disorder who had recorded depressive symptoms were significantly more likely to receive CBTp sessions, aligning with CBTp guidelines of managing depressive symptoms related to a psychotic experience. However, overall receipt of CBTp is low and more common in certain demographic groups, and needs to be increased.

### Strengths and limitations of the study

- To our knowledge, this is the first electronic health record (EHR) study to measure how clinical symptomatology predicts CBTp receipt, providing insight on a large sample into whether individuals who may be more in need of CBTp are more likely to have a session
- We replicate previous findings of inequalities in gender and ethnicity in real-world CBTp treatment receipt in a large heterogeneous sample.

- The natural language processing approach allows automated processing of EHR text at scale and can evaluate larger samples than manually conducted case note audits; this could therefore be used more routinely to monitor CBTp receipt.
- This study was limited to a single service provider; however, the results identified themes consistent with previous CBTp provision research in other services.
- Analysing EHRs in this way can identify CBTp receipt but is less suited to investigate whether CBTp is offered or not, or to quantify the quality or focus of the sessions. Furthering this, it cannot be used to examine CBTp completion rates and effectiveness.

### **Conflict of Interest**

The authors report no conflict of interest with respect to the findings described in this manuscript. RS declares research support received in the last 36 months from Janssen, GSK and Takeda.

### **Financial Support**

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### **Transparency declaration**

The lead author AM affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

### **Patient and public involvement**

The Clinical Record Interactive system as a data resource was developed and is run with extensive patient involvement. However, this particular analysis did not involve patients in its design or implementation.

### **Ethics statement**

The CRIS data platform has received research ethics approval as an anonymised data resource for secondary analysis (Oxford Research Ethics Committee C, reference 18/SC/0372)

## Introduction

There are a variety of cognitive and emotional processes involved in the development of psychotic symptoms,<sup>1</sup> with intense distress emerging early on in the course of the disorder. Content of positive symptoms often mirrors the content of depressive thinking processes,<sup>2</sup> suggesting therapeutic need for individuals experiencing additional depressive symptoms. Specific depressive symptoms that often accompany psychotic disorders are hopelessness, social avoidance and problems in forming relationships.<sup>3</sup> Around 50% of patients with psychosis report having experienced suicidal ideation at least once,<sup>4</sup> and around 40% of individuals with schizophrenia report clinical levels of depression and low self-esteem.<sup>5</sup> Importantly, individuals report these emotional difficulties and resulting social exclusion to be more debilitating than their psychotic symptoms.<sup>6</sup> Consequentially, individuals' negative appraisal of their psychotic experiences may lead to loss of social goals and increased shame, predicting later hopelessness and post-psychotic depression.<sup>7</sup> This comorbid depression increases the likelihood of having a lower quality of life, function, motivation, poorer social relationships, lower medication adherence and psychotic relapse.<sup>8,9</sup> Therefore, treatment should focus on the psychotic symptoms and the broader distress they produce, building self-esteem, confidence and a sense of self control and purpose.<sup>10</sup> Additionally, focusing on mood symptoms such as self-esteem and pessimism can help differentiate depressive symptoms from negative psychotic symptoms, that often show significant clinical overlap.<sup>5</sup>

It is increasingly recognised that medication alone is inadequate for tackling psychosis symptoms.<sup>11</sup> In the UK, the National Institute of Clinical Excellence<sup>12</sup> has recommended that cognitive behavioural therapy for psychosis (CBTp) be offered universally to individuals with psychosis. Based on the stress-vulnerability model,<sup>13</sup> CBTp focuses on distress reduction related to hallucinations and delusions, through targeting negative beliefs and improving self-esteem.<sup>14</sup> Sessions often focus on goal setting and emotional issues such as rebuilding one's self, positivity and acceptance.<sup>11</sup> While studies examining characteristics of CBTp show strong evidence that CBTp improves depressive symptoms in the context of psychosis, specifically with long term reductions in suicidal behaviour,<sup>14,15</sup> service provision of this intervention still falls far short of the universal access recommended.<sup>11</sup>

Considering the impact of targeting these symptoms in CBTp sessions, it is important to monitor receipt of CBTp within psychosis samples. While CBTp provision shows moderate yearly increases (12.8% in 2013 to 14.8% in 2014), the treatment is still only available to a small proportion of individuals,<sup>11</sup> short of NICE universal access recommendations.<sup>12</sup> Previous studies investigating CBTp receipt have conducted time-consuming audits on limited sample sizes; these can be affected by under-reporting. On the other hand, the UK's National Mental Health Minimum Data Set report does not require CBT interventions to be recorded in a given individual's record. Natural language processing techniques (NLP)<sup>16</sup> offer the opportunity to extract this information from free text in electronic health records (EHRs) across large numbers of patients with psychosis, and a recent study developed and applied NLP in this respect, finding higher levels of receipt than reported in previous audit, supported by the high positive predictive value and sensitivity of the technique (95% and 96% respectively).<sup>11</sup>

While studies have examined general CBTp receipt within patients with psychosis, no study has examined a link between depressive symptoms and CBTp receipt.<sup>11</sup> Therefore, we investigated whether depressive symptoms predict CBTp receipt in people with psychosis by applying these previously data extraction techniques to secondary mental health care EHRs for a large South London catchment population. Secondary predictors of receipt were type of psychosis diagnosis (schizophrenia, schizoaffective disorder or other schizophrenia spectrum disorder), symptom profiles (negative, manic or disorganisation), general CBT receipt prior to psychosis diagnosis, comorbid depression, anxiety or bipolar diagnosis and socio-demographic factors (ethnicity, gender and age).

## Methods

For this study, we extracted data on individuals with a diagnosis of a recognised schizophrenia spectrum diagnosis from the case registry of the South London and Maudsley NHS Foundation Trust (SLaM). This is a large secondary care mental healthcare provider, serving around 1.3 million residents in Croydon, Lambeth, Lewisham and Southwark. SLaM care covers all specialist mental health care, including early intervention services, liaison and crisis teams and community and inpatient services. EHRs have been used for all SLaM services since 2006, with the Clinical Record Interactive Search system (CRIS) being established in 2008 to facilitate the retrieval of de-identified data from these records of patients previously or currently receiving mental healthcare from SLaM.<sup>17</sup> The source EHR contains unstructured free text fields from correspondence, personal histories, mental health examinations and management plans, as well as structured fields for coding demographic information, like age and ethnicity. Implementing data from all these fields reduces selection bias of utilising only specific sources of information from the EHR. Consequently, a large programme of work has developed a range of NLP algorithms over the last decade, whose detailed descriptions and performance data are contained in an open-access catalogue.<sup>18</sup> CRIS has approval as a data resource for secondary analysis (Oxford Research Ethics Committee C, reference 18/SC/0372), and a service user-led committee considers all proposed research before access to CRIS data is granted.

We extracted data for all individuals receiving SLaM care between January 2007 and June 2020 with a primary diagnosis of an ICD-10-defined schizophrenia spectrum disorder (F20-F29) and above the age of 18 at the time their original referral was accepted. The index date for covariate definitions was the date of the first diagnosis within this grouping. Individuals may have been active within the service before their index date, allowing us to extract data on prior CBT receipt. The sample was restricted to those with data on all variables.

Ethnicity, age at referral and gender were also extracted. Ethnicity was categorised into six groups for analysis: 'White British' (British), 'White other' (Irish or any other white background), 'Black' (Caribbean, African or any other black background), 'Asian' (Indian, Bangladeshi, Pakistani, Chinese or any other Asian background), 'Other/mixed' (white and Asian, white and black Caribbean, white and black African, any other ethnic group) and 'Not stated'.

Diagnosis was categorised into three subgroups of schizophrenia (ICD-10 codes F20.0–F20.9), schizoaffective disorder (F25.0–F25.9) and other schizophrenia spectrum disorder (F21, F22.0–F22.9, F23.0–F23.9, F24, F28 and F29). Within the data collection period, secondary diagnosis of depression (ICD-10: F32 or F33), anxiety (ICD-10: F40 or F41), or bipolar disorder (ICD-10: F31) were also extracted from structured field data.

NLP algorithms for each specific symptom were used to identify recorded symptom profiles within participants. Symptoms were categorised as depressive, positive, negative, manic or disorganisation. These symptoms had been categorised *a priori* by developers of the original independent symptom NLP algorithms. As symptoms could be labelled in more than one category during analysis, multicollinearity tests using the R function `vif()` within the [car package] were undertaken to avoid issues with overlapping predictor variables. All variables were included due to their VIF values being below five. However, positive symptoms were excluded from regression models using categorical symptom variables (having at least one mention within HER), as this factor variable only had one level, due to all participants having at least one positive symptom. The overall symptom list and subsequent recoding can be found in Table 1. Presence of at least one mention of any symptom in the five categories was computed as a binary variable (0/1).

Table 1  
*Classification of symptom predictors*

Symptom	Symptom label
Aggression	Positive
Agitation	Positive
Anergia	Depressive /Negative
Anhedonia	Depressive/Negative
Apathy	Depressive/Negative
Arousal	Manic
Blunted affect	Depressive/Negative
Circumstantiality	Disorganisation
Delusions	Positive
Derailment	Disorganisation
Disturbed sleep	Depressive/Manic
Elation	Manic
Emotional Withdrawal	Negative
Flight of ideas	Disorganisation
Formal thought disorder	Disorganisation
Grandiosity	Manic
Guilt	Depressive
Hallucinations (auditory)	Positive
Helplessness	Depressive
Hopelessness	Depressive
Hostility	Positive
Insomnia	Depressive/Manic
Irritability	Manic
Paranoia	Positive
Persecutory ideation	Positive
Poor appetite	Depressive
Poor concentration	Depressive
Poor motivation	Depressive
Poverty of speech	Negative
Poverty of thought	Negative
Social withdrawal	Negative
Suicidal ideation	Depressive
Tangentiality	Disorganisation
Tearfulness	Depressive
Thought block	Disorganisation
Worthlessness	Depressive

The date of the first and last general CBT session before the index date was extracted. This was coded as a binary variable, with individuals in the 'Prior CBT' receipt group having at least one session date mention prior to their index date. This was included as a predictor to adjust for previous experience of the specific CBT intervention. Mentions were extracted using the same NLP tool as the CBTp outcome measure mentioned subsequently.

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2  
3 The primary outcome was CBTp receipt, identified using a combination of structured fields and NLP.<sup>16</sup> The NLP  
4 algorithms for general CBT has high PPV and sensitivity,<sup>12</sup> consistent with other NLP algorithms such as  
5 medication dose and diagnosis.<sup>19</sup> The date of the first CBTp session on or after the index date was extracted  
6 and computed as a binary variable, so that individuals in the 'CBTp receipt' group had at least one CBTp  
7 session mention after the index date.  
8

### 9 10 **Statistical analysis**

11 To avoid overfitting, we followed the 'one in ten' rule, whereby one predictor can be measured for every 10  
12 events. As the data included 1647 CBTp events, our study was able to include all 12 predictors within the same  
13 regression model.  
14

15 All statistical analyses were conducted using R (version 1.3.9). Descriptive statistics for demographic and  
16 clinical variables are reported as frequencies for categorical variables and means and standard deviations for  
17 the continuous variable (age at referral). Chi square tests were also calculated for categorical variables, and t-  
18 test for age to measure between-group differences in those with/without CBT receipt. Descriptive statistics  
19 were also provided for yearly CBT prior to index date and CBTp receipt post index date within the data  
20 extraction time period (2007-2020).  
21  
22

23 Binary logistic regression was used to examine the association between depressive symptoms and receipt of at  
24 least one CBT session in the whole sample. For this, three regression models were analysed. Model 1 was an  
25 unadjusted model with only depressive symptoms as the predictor variable. Due to significant provision  
26 differences seen in previous CBTp studies,<sup>11</sup> model 2 (partially adjusted model), adjusted for sociodemographic  
27 variables (age at referral, ethnicity, gender), primary diagnosis group and presence of a comorbid diagnosis  
28 (anxiety, depression and bipolar disorder). Model 3 (fully adjusted model) also adjusted for prior CBT receipt  
29 before the index date (first psychosis diagnosis date) and symptoms mention (manic, negative and  
30 disorganisation symptoms). Positive psychotic symptoms were not included in these models, as individuals all  
31 had at least one mention within their case notes.  
32  
33

34 As the primary aim of the study was to investigate depressive symptoms as a predictor of CBTp receipt, we  
35 also split the depressive symptoms category into the 15 specific depressive symptoms applications within the  
36 whole sample. Model 4 was an unadjusted model with the 15 symptoms as predictor variables. Model 5 was a  
37 fully adjusted model that adjusted for all the variables in Model 3. We also conducted a sensitivity analysis to  
38 investigate how results were affected by overlap of negative or depressive symptom annotations, by removing  
39 negative symptoms as a predictor from the logistic regression model.  
40  
41  
42

43 Additionally to measuring whether individual depressive symptoms could predict CBTp receipt, we also also  
44 measured whether overall depression severity predicted CBTp receipt. These logistic regression models  
45 involved converting depressive, disorganised, manic, positive and negative symptoms into a continuous  
46 variable, whereby severity reflected the number of different individual symptoms mentioned within each  
47 symptom construct. This allowed for positive symptoms to also be included within regression models. Model 6  
48 was an unadjusted model, with depressive symptom severity as a predictor of CBTp receipt. Model 7 and  
49 model 8 were partially and fully adjusted models, controlling for the same variables as model 2 and 3, except  
50 categorising symptoms as the continuous rather than categorical variable.  
51  
52  
53

54 Lastly, to compare differences in the general sample with those with the top 25% quantity for depressive  
55 symptoms, we conducted two further regression models. This subsample analysis was conducted to examine  
56 predictors of CBTp receipt where a clear clinical indication was present, supplementing the overall findings.  
57 Model 9 partially adjusted for socio-demographic factors, diagnostic group and comorbid diagnosis and Model  
58 Model 10 fully adjusted for prior CBT, negative and disorganisation symptoms additionally. This group all had at least  
59 one manic and psychotic symptom, so these variables were not included in the model.  
60



**Table 2***Distribution frequencies on baseline demographics and diagnoses split by CBTp receipt and primary diagnosis group.*

	<b>No CBTp delivery (n = 18431)</b>	<b>CBTp delivery (n=1647)</b>	<b>Chi square tests (<math>\chi^2</math>)</b>
<b>Ethnicity</b>			$\chi^2=100.57^{***}$
White British	<b>30%</b> (5516/18431)	<b>32.8%</b> (540/1647)	
White Other	<b>10.4%</b> (1908/18431)	<b>8.5%</b> (140/1647)	
Black	<b>36.5%</b> (6719/18431)	<b>41.7%</b> (687/1647)	
Asian	<b>6.5%</b> (1193/18431)	<b>5.2%</b> (86/1647)	
Other/Mixed	<b>9.8%</b> (1808/18431)	<b>10.5%</b> (173/1647)	
Not stated	<b>7.0%</b> (1287/18431)	<b>1.3%</b> (21/1647)	
<b>Gender</b>			$\chi^2= 2.75$
Female	<b>41.4%</b> (7636/18431)	<b>43.5%</b> (717/1647)	
Male	<b>58.6%</b> (10795/18431)	<b>56.5%</b> (930/1647)	
Bipolar diagnosis	<b>4.4%</b> (810/18431)	<b>9.0%</b> (149/1647)	$\chi^2=71.94^{***}$
<b>No diagnosis</b>	<b>95.6%</b> (17621/18431)	<b>91.0%</b> (1498/1647)	
Depression diagnosis	<b>7.4%</b> (1373/18431)	<b>14.0%</b> (230/1647)	$\chi^2=87.36^{***}$
<b>No diagnosis</b>	<b>92.6%</b> (17058/18431)	<b>86.0%</b> (1417/1647)	
Anxiety diagnosis	<b>2.4%</b> (441/18431)	<b>7.0%</b> (115/1647)	$\chi^2=118.28^{***}$
<b>No diagnosis</b>	<b>97.6%</b> (17990/18431)	<b>93.0%</b> (1532/1647)	
<b>Prior CBT</b>	<b>3.1%</b> (573/18431)	<b>14.4%</b> (237/1647)	$\chi^2=497^{***}$
<b>No prior cbt</b>	<b>96.9%</b> (17858/18431)	<b>85.6%</b> (1410/1647)	

\*\*\*p&lt;.001

## Results

### Participants

The cohort comprised 20,078 individuals with the inclusion diagnoses, 1647 (8.2%) of whom received at least one session of CBTp after their first diagnosis date. The mean age of the cohort was 42.4 years (SD=16.5). Distribution frequencies for all categorical variables can be found in Table 2. Chi-square test results represented in this table compared those with or without CBTp receipt. All mentioned variables showed significant between-group differences at p<.001 apart from gender (No CBTp group females=41.4%, CBTp delivery group females= 43.5%;  $\chi^2=2.75$ , p=.097). These significant variables include depression diagnosis ( $\chi^2=87.36$ ), bipolar diagnosis ( $\chi^2=71.94$ ), anxiety diagnosis ( $\chi^2=118.28$ ) and prior CBT receipt ( $\chi^2=497$ ). Additionally, the Welch two sample t-test found significant between-group differences in age (t=15.34, p<.01). Where those who had received CBTp had a lower mean age (M=33.12 SD= 11.5) compared to those who did not (M=35.88, SD=13.08). The significant results confirmed the need for further analysis through the regression models. Positive psychotic symptoms were excluded from chi square and regression analysis, as all patients had at least one positive psychotic symptom.

### CBT receipt.

The descriptive results shown in table 3 and figure 1 (found in supplementary materials), suggest that there is a low prevalence of both prior CBT and CBTp post diagnosis across the years, with receipt reducing in recent years (2019-2020) compared to earlier years (2007) of the data extraction period.



Table 3

*Distribution frequencies on CBT receipt (prior to diagnosis) and CBTp receipt (post diagnosis) per year of data extraction.*

Year	CBT prior	CBT post	All CBT
2007	130	81	211
2008	89	146	235
2009	59	111	170
2010	48	107	155
2011	37	105	142
2012	39	96	135
2013	32	128	160
2014	25	143	168
2015	24	150	174
2016	29	115	144
2017	16	127	143
2018	16	114	130
2019	15	153	168
2020	2	71	73
Total	561	1647	2208

#### **General depressive symptom mention regression analysis**

Results from the unadjusted (model 1), partially adjusted (model 2) and fully adjusted regression (model 3) are displayed in Table 4. Regression model 1 found that general mention of at least one of 15 potential depressive symptoms significantly predicted CBTp receipt. Regarding model 2 and 3, individuals with at least one depressive, negative or disorganisation symptom mention, being of female gender, white ethnicity, prior CBT receipt and presence of a comorbid affective disorder independently positively associated with CBTp receipt.

Table 4

Unadjusted, partially and fully adjusted logistic regression models for CBTp receipt (Regression model 1,2 and 3) with categorical symptom measures.

		Unadjusted	Partially adjusted	Fully adjusted
	N(%)	OR(95%CI)	OR(95%CI)	OR(95%CI)
<b>Depressive symptoms</b>				
1+ depressive symptom mention	18286(91.1)	3.78(2.94-4.96)***	3.42 (2.58-4.60)***	2.00(1.10-3.20)***
<b>Bipolar diagnosis</b>				
Has f31 diagnosis	959(4.80)		0.52(0.33-0.71)***	0.32(0.12-0.52)***
<b>Depression diagnosis</b>				
Has f32 diagnosis	603(80)		0.52(0.36-0.67)***	0.33(0.16-0.49)**
<b>Anxiety diagnosis</b>				
Has f40/41 diagnosis	556(2.80)		0.89(0.66-1.11)***	0.73(0.49-0.97)***
Age	N/A		-0.03(-0.04- -0.03)***	-0.03(-0.03- -0.02)***
<b>Gender</b>				
Male			Reference category	
Female	8353(41.60)		0.20(0.09-0.31)***	0.20 (0.10-0.32)***
<b>Ethnic group</b>				
White British	6056(30.10)		Reference category	
White Other	2048(10.20)		-0.40(-0.60 - -0.21)***	-0.37(-0.57- -0.17)***
Black	7406(36.90)		-0.16(-0.28- -0.04)**	-0.24 (-0.36- -0.11)***
Asian	1279(6.40)		-0.49(-0.74- -0.26)***	-0.50 (-0.75- -0.27)***
Other/Mixed	1981(9.90)		-0.21(-0.40- -0.02)**	-0.18(-0.37- -0.01)*
Not Stated	1308(6.50)		-1.75(2.23- -1.22)***	-1.52(-2.00- -1.10)***
<b>Primary diagnosis</b>				
Schizophrenia	9845(49.00)		Reference category	
Schizoaffective disorder	2142(10.70)		0.04(-0.13-0.21)	0.01(-0.17-0.19)
Other schizophrenia spectrum	8091(40.30)		-0.10(-0.22-0.01)*	-0.02(-0.14 -0.10)
<b>Negative symptoms</b>				
1+ Negative symptom mention	13169(65.60)			0.75(0.59-0.92)***
<b>Manic symptoms</b>				
1+ Manic symptom mention	17945(89.40)			1.24(0.70-1.87)***
<b>Disorganisation symptoms</b>				
1+ Disorganisation symptom mention	11513(57.30)			0.31(0.18-0.44)***
<b>CBT prior</b>				
1+ prior CBT session				1.29(1.12-1.46)***

\*p<.05, \*\*p<.01, \*\*\*p<.001

**Unadjusted (model 1):** depressive symptom as a predictor with no adjusted covariates

**Partially adjusted (model 2):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis

**Fully adjusted (model 3):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis, depressive symptoms, prior CBT, negative symptoms, disorganisation symptoms, manic symptoms.

### Regression analysis with individual depressive symptoms

Results from the unadjusted (model 4) and fully adjusted (model 5) regression analyses for each of the 15 individual depressive symptoms are displayed in Table 5 (N=20078). Each symptom refers to presence of at least one mention in the patients notes compared to no mention. While all variables were significant in the unadjusted model at  $p < .001$ , the fully adjusted model reduced the significance of suicide ideation ( $p < .01$ ) and disturbed sleep ( $p < .01$ ), with anhedonia, anergia, apathy, and blunted affect becoming non-significant ( $p > 0.05$ ).

Table 5

*Unadjusted and fully adjusted logistic regression models for CBTp receipt with individual depressive symptoms as covariates (Regression model 4 and 5) for the overall sample.*

		Unadjusted	Fully adjusted
	N(%)	OR(95%CI)	OR(95%CI)
Hopelessness	7345(36.60)	4.81(4.3-5.40)***	1.45(1.26-1.66)
Helplessness	3124(15.60)	4.03(3.62-4.50)***	1.55(1.37-1.76)***
Suicide ideation	9451(47.10)	4.11(3.66-4.63)***	1.25(1.09-1.44)**
Poor appetite	8044(40.10)	3.31(2.97-3.68)***	1.28(1.13-1.45)***
Poor motivation	8630(43.00)	4.34(3.87-4.86)***	1.43(1.24-1.64)***
Insomnia	6870(34.20)	3.74(3.35-4.15)***	1.4(1.24-1.58)***
Disturbed sleep	16667(83.00)	15.3(10.16-22.8)***	2.76(1.5-5.08)**
Poor concentration	12289(61.20)	8.16(6.81-9.77)***	2.33(1.9-2.85)***
Anhedonia	4047(20.20)	2.9(2.61-3.22)***	0.97(0.85-1.10)
Anergia	873(43.50)	2.63(2.20-3.15)***	0.98(0.80-1.20)
Apathy	4149(20.70)	2.21(1.98-2.46)***	0.93(0.82-1.05)
Guilt	8178(40.70)	4.6(4.1-5.15)***	1.49(1.30-1.70)***
Tearfulness	10951(54.50)	3.87(3.41-4.39)***	1.22(1.05-1.42)**
Blunted affect	6889(34.30)	2.66(2.41-2.95)***	0.91(0.80-1.03)
Worthlessness	2921(14.50)	3.94(3.53-4.40)***	1.37(1.21-1.56)***

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

### Sensitivity analysis

The non-significant results of certain depressive symptoms (anhedonia and anergia) may have been due to their inclusion within the negative symptom category, causing over-adjustment of the model. To test this, sensitivity analysis was conducted, where the fully adjusted regression (model 3) did not include negative symptoms as a covariate. While all significant variables remained significant, non-significant results for anhedonia and apathy were still found. Therefore, we report the fully adjusted model with negative symptoms as a variable for both grouped and individual depressive symptom associations.

### General depressive symptom severity regression analysis

Results from the unadjusted (model 6), partially adjusted (model 7) and fully adjusted regression (model 8) are displayed in Table 6. Regression model 6 found that depression symptom severity significantly predicted CBTp receipt. Regarding model 7 and 8, depression symptom severity, positive symptom severity, anxiety diagnosis, and being of older age or being of white ethnicity independently positive predicted CBTp receipt. Within model 7., being female also positively increased likelihood of CBTp receipt. Within model 8, negative symptom severity and prior CBT significantly predicted CBTp receipt additionally.

Table 6

Unadjusted, partially and fully adjusted logistic regression models for CBTp receipt (Regression model 1,2 and 3) with continuous symptom measures.

		Unadjusted	Partially adjusted	Fully adjusted
	N(%)	OR(95%CI)	OR(95%CI)	OR(95%CI)
<b>Depressive symptoms</b>				
Severity	18286(91.1)	0.29(1.31-1.35)***	0.27(1.20-1.44)***	0.23(0.13-0.33)***
<b>Positive symptoms</b>				
Severity	20078(100)		-0.18(0.75-0.92)***	-0.21(-0.31- -0.09)***
<b>Bipolar diagnosis</b>				
Has f31 diagnosis	959(4.80)		0.21(0.94-1.63)	0.15(-0.13-0.43)
<b>Depression diagnosis</b>				
Has f32 diagnosis	603(80)		-0.09(0.72-1.15)	-0.09(-0.33-0.15)
<b>Anxiety diagnosis</b>				
Has f40/41 diagnosis	556(2.80)		0.49(1.15-2.29)***	0.46(0.11-0.80)***
Age	N/A		-0.02(0.97-0.99)***	-0.02(-0.03- -0.01)***
<b>Gender</b>				
Male			Reference category	
Female	8353(41.60)		0.17(0.97-1.44)*	0.17(-0.03-0.36)
<b>Ethnic group</b>				
White British	6056(30.10)		Reference category	
White Other	2048(10.20)		-0.41(0.45-0.96)**	-0.44(-0.93- -0.07)***
Black	7406(36.90)		-0.25(0.63-0.97)**	-0.29(-0.51- -0.07)**
Asian	1279(6.40)		-0.66(0.32-0.80)***	-0.67(-1.13 - -0.23)***
Other/Mixed	1981(9.90)		-0.14(0.62-1.22)	-0.16(-0.50-0.18)
Not Stated	1308(6.50)		-0.92(0.02-2.42)	-0.79(-3.74-1.01)
<b>Primary diagnosis</b>				
Schizophrenia	9845(49.00)		Reference category	
Schizoaffective disorder	2142(10.70)		-0.08(0.69-1.21)	-0.11(-0.40-0.18)
Other schizophrenia spectrum	8091(40.30)		0.02(0.82-1.26)	-0.06(-0.15-0.28)
<b>Negative symptoms</b>				
Severity	13169(65.60)			0.06(-0.01-0.123)*
<b>Manic symptoms</b>				
Severity	17945(89.40)			-0.01(-0.13-0.12)
<b>Disorganisation symptoms</b>				
Severity	11513(57.30)			0.10(-0.05-0.25)
<b>CBT prior</b>				
1+ prior CBT session	1647(8.20)			0.62(0.34-0.89)***

\*p<.05, \*\*p<.01, \*\*\*p<.001

**Unadjusted (model 1):** depressive symptom severity as a predictor with no adjusted covariates

**Partially adjusted (model 2):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis, positive symptom severity

**Fully adjusted (model 3):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis, positive symptom severity, prior CBT, negative symptom severity, disorganisation

symptom severity and manic symptom severity.

### Depressive symptom regression analysis within the top 25% number of depressive symptoms.

This sample comprised individuals with the top 25% number of depressive symptoms (5018 patients), defined to reflect those who might reasonably expect to receive CBT. The sample characteristics and regression analysis can be seen in Table 7. Results from the partially adjusted (model 9) and fully adjusted regression (model 10) are displayed in Table 7. Table 4 found that general mention of at least one of 15 potential depressive symptoms significantly predicted CBTp receipt. Regarding model 9, we found that individuals with at least one depressive, negative or disorganisation symptom mention, being of female gender, white ethnicity, prior CBT receipt and presence of comorbid bipolar disorder were positively associated with CBTp receipt.

Table 7

*Partially and fully adjusted logistic regression models for CBTp receipt with individual depressive symptoms as covariates within top 25% quantity of depressive symptoms (Regression model 9 and 10).*

	N(%)	Partially adjusted OR(95%CI)	Fully adjusted OR(95%CI)
<b>Bipolar diagnosis</b>			
Has f31 diagnosis	541(10.78)	0.19(-0.03-0.41)*	0.15(-0.08-0.38)
<b>Depression diagnosis</b>			
Has f32 diagnosis	885(17.63)	0.11(-0.08-0.30)	0.08(-0.90-1.30)
<b>Anxiety diagnosis</b>			
Has f40/41 diagnosis	270(5.38)	0.53 (0.25-0.80)***	0.47(0.19-0.75)***
<b>Age</b>			
M= 36.24(18-93)		-0.02(-0.02- -0.01)***	-0.02(-0.03- -0.01)***
<b>Gender</b>			
Male	2059(41.01)	Reference category	
Female	2960(58.99)	0.20 (0.05-0.34)***	0.17(0.02-0.32)**
<b>Ethnic group</b>			
White British	1486(29.59)	Reference category	
White Other	433(8.63)	-0.21(-0.48-0.05)	-0.22(0.50-0.05)
Black	2262(45.08)	-0.32(-0.49- -0.16)***	-0.31(0.47- -0.14)***
Asian	328(6.53)	-0.53(0.86- -0.21)***	-0.52(0.85- -0.20)***
Other/Mixed	467(9.31)	-0.08(-0.34-0.17)	-0.08(0.34-0.17)
Not Stated	43(0.86)	-1.42 (-2.85 -0.40)**	-1.34(-2.8 - -0.31)**
<b>Primary diagnosis</b>			
Schizophrenia	2219(44.22)	Reference category	
Schizoaffective disorder	740(14.72)	0.04(-0.18-0.26)	0.003(-0.22-0.22)
Other schizophrenia spectrum	2060(41.03)	0.02(-0.14 -0.17)	0.05(-0.11-0.21)
<b>Negative symptoms</b>			
1+ Negative symptom mention	4956(98.7)		-0.88(1.41- -0.33)***
<b>Disorganisation symptoms</b>			
1+ Disorganisation symptom mention	4199(83.66)		1.18(-0.02-0.38)*
<b>CBT prior</b>			
1+ prior CBT session	436(8.7)		-0.90(0.68-1.11)***

\*p<.05, \*\*p<.01, \*\*\*p<.001,

**Partially adjusted (model 9):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis.

**Fully adjusted (model 10):** results were adjusted for age, ethnicity, gender, diagnostic group, f31 diagnosis, f32 diagnosis, f40/41 diagnosis, prior CBT, negative symptoms, disorganisation symptoms

### Discussion

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4 We believe that this is the first study to examine the relationship between clinical symptomatology and CBTp receipt  
5 within a sample of people with psychosis in a naturalistic community setting. In general, only 8.2% of individuals  
6 received CBTp within the 13-year timeframe of the study, showing the low prevalence of receipt despite current clinical  
7 guidelines. This finding shows a reduction in CBTp provision compared to previous studies in 2013 (12.8%) and 2014  
8 (14.8%)<sup>11</sup>, which was further supported by the descriptive frequency results, showing a drop in both CBT and CBTp  
9 receipt in recent years. This requires further examination, as it is unclear why receipt is decreasing considering the  
10 importance of CBTp mentioned within NICE universal access recommendations.<sup>12</sup>  
11

12 91% of patients had at least one recorded depressive symptom mention. Individuals with at least one depressive  
13 symptom mention were 2 times more likely to have at least one CBTp session in the fully adjusted model (table 4),  
14 suggesting that the minority who don't present with any depressive symptoms are very unlikely to receive CBTp. This  
15 could possibly be due to clinicians tending to cite a depressive symptom when referring an individual with psychosis to  
16 psychotherapy. Additionally, the severity of depressive symptoms, as well as having at least one recorded mention  
17 significantly increased likelihood of having at least one CBTp session. In the sample of those with the highest number of  
18 depressive symptoms (top 25%), relationships between CBTp receipt and comorbid anxiety diagnosis, age, gender,  
19 ethnicity, prior CBT, negative and disorganised psychotic symptoms remained (effect size ranging from 0.08-1.34). This  
20 suggests the importance of these predictors in a reasonable sample of patients with higher clinical need for CBTp  
21 receipt.  
22

23 Overall there was therefore a low prevalence of CBTp receipt within those with one depressive symptom. The  
24 depressive symptom which was the strongest predictor of this intervention in fully adjusted models was  
25 disturbed sleep. There is a known high prevalence of sleeping problems in this population,<sup>20,21</sup> described by  
26 some researchers as an 'intrinsic feature of schizophrenia,<sup>22</sup> known to reduce quality of life, decreasing coping  
27 and exacerbate positive symptoms.<sup>23</sup> *The significant association between insomnia and psychotic-like*  
28 *symptoms, such as paranoia, has also been seen in non-clinical populations.*<sup>24</sup> Furthering this, the  
29 recommended first line of treatment for sleep problems in this sample is CBT.<sup>25</sup> Poor concentration was the  
30 next strongest depressive symptom predictor in the fully-adjusted model, supporting previous research of its  
31 association with psychosis vulnerability.<sup>26</sup> The significance of helplessness, guilt and hopelessness mirrors CBTp  
32 research that found significant post-treatment reduction in hopelessness, self-depreciation and guilt using the  
33 Calgary Depression Rating Scale for Schizophrenia.<sup>27</sup> Other significant depressive symptoms associated with  
34 low self-esteem and negative self-evaluation and emotions have been found to significantly affect the  
35 development and severity of positive symptoms.<sup>28</sup> This may be because positive symptoms develop as a  
36 psychological defence against low self-esteem<sup>29</sup> and depression-induced guilt.<sup>30</sup> Therefore, it could be  
37 suggested that the significance of each of the depressive symptoms is often linked to psychotic symptoms and  
38 CBTp effectiveness. However, while there is evidence on the clinical impact of depressive symptoms in  
39 schizophrenia, the associations with choice of therapy must be viewed as exploratory and in need of  
40 independent replication. While a possibility may be that clinicians are assuming that certain depressive  
41 symptoms are likely to be more responsive to CBTp than others, there may be other unknown reasons for  
42 therapy choice that requires further investigation. General results suggest that receipt of this intervention  
43 requires an increase for all of this population before individuals with these specific symptoms could be  
44 targeted.  
45

46  
47 Regarding negative symptoms, the non-significant associations between specific negative symptoms (that overlapped  
48 with depressive symptoms) and CBTp receipt requires specific further testing. This was not conducted in the current  
49 study due to the primary aim focusing on depressive symptoms. However, from our results on specific depressive  
50 symptoms in table 5, symptoms that overlapped with negative symptoms (anhedonia, anergia, apathy and blunted  
51 affect) were not associated with CBTp receipt. Additionally, negative symptoms significantly decreased likelihood of  
52 CBTp receipt within the top 25% of individuals with a depressive symptom mention. Overall, this raises concerns that  
53 individuals with these specific negative/depressive symptoms are no more likely and perhaps less likely to receive CBTp  
54 than someone without these symptoms. Possibly, this is due to clinicians not tending to refer these individuals because  
55 they don't believe intervention would be effective. This is in line with a CBTp review of randomised control trials,  
56 finding non-significant reductions of negative symptoms,<sup>31</sup> perhaps due to the narrowing of treatments to specifically  
57 target positive symptoms.<sup>32</sup> However, further work should be undertaken to verify that individuals are not being  
58 denied a potentially beneficial intervention because of their symptom profile.  
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3 Prior CBT receipt, comorbid disorder presence and specific symptoms (manic, disorganised and negative) also emerged  
4 as independent predictors of CBTp receipt for the general sample and within those with the top 25% depressive  
5 symptom numbers. Within table 4, individuals who had any recorded CBT receipt prior to the index date were 1.29  
6 times more likely to have recorded CBTp receipt later on. Also, patients with an additional comorbid disorder were  
7 0.32-0.73 times more likely to have received CBTp compared to those with just a psychosis diagnosis. However, in the  
8 top 25% of individuals within table 7, individuals with prior CBT were 0.40 times less likely to receive CBTp. This finding  
9 requires further research to understand the effects of prior CBT and negative symptoms on CBTp receipt within  
10 different psychosis subsamples. Additionally, those with anxiety were 0.47 times more likely to receive CBTp and those  
11 with disorganised symptoms were 1.18 times more likely respectively. After general CBTp receipt has increased, there  
12 could be a method to focus more on patients with different types of psychotic symptoms and comorbid affective  
13 diagnosis. Furthering this, future research could investigate whether those who have had prior general CBT would  
14 benefit from CBTp, or whether those who have not had any experience developing cognitive behaviour skills in therapy  
15 should be targeted.<sup>33</sup>

16  
17 Crucially, there were also significant differences in CBTp receipt between different ethnic and gender groups. Male  
18 patients were 0.20 times less likely in the general sample and top 25% of depressive symptoms to have recorded CBTp  
19 receipt. Black, Asian, Other and Mixed ethnic groups were between 0.21 to 0.49 times less likely to have a documented  
20 CBTp session compared to individuals of white ethnicity within both the general and top 25% depressive symptoms  
21 samples. Inequitable access to CBTp has been identified in previous CBTp research within a psychosis sample drawn  
22 from the same data resource in 2017, finding female patients to be more likely to have received CBTp and individuals of  
23 White ethnicity to have a significantly higher likelihood of CBT receipt than Black or other ethnicity groups.<sup>11</sup> This also  
24 supports results from a recent CBTp study focusing specifically on ethnic group differences in CBTp provision within  
25 SLaM, who found that in comparison to White British individuals, those from Black ethnic groups with psychosis or  
26 bipolar disorder were significantly less likely to have a documented CBTp session. This is especially important when  
27 considering the high prevalence of psychosis within UK BAME populations.<sup>33</sup> Inequality in CBTp receipt may be due to  
28 ethnic variations in CBTp engagement. Some of these barriers within certain communities may be increased stigma,  
29 fear of clinicians by service-users or service users by clinicians, institutional racism within mental health services, or  
30 non-culturally appropriate therapy.<sup>34</sup> As differences in documented CBTp receipt between ethnic groups have now  
31 been documented by three different papers in this service, it is imperative that further work is conducted to increase  
32 provision of CBTp within groups less likely to receive treatment. This may include targeted outreach programs and  
33 culturally adapting interventions<sup>34</sup> within these minority groups.

34  
35 The present study has a number of strengths and limitations. Generally, focusing on patients with more  
36 diverse functioning, comorbidity and symptom severity levels helps research identify a larger number of  
37 predictors of clinical outcomes. This can be seen through our results, where negative, manic and  
38 disorganisation symptoms significantly predicted CBTp receipt, as well as recent heterogenous research,<sup>32</sup>  
39 that was the first to identify depression as a significant predictor of positive symptom improvement post-  
40 CBTp. This highlights the importance of focusing on a clinically heterogeneous sample to realistically determine  
41 significant predictors of CBTp receipt. Secondly, using an NLP approach automates the measurement of what  
42 would otherwise require manually conducted audits on records and case notes, increasing the number of  
43 cases that can be investigated and providing a method that could be used more routinely to monitor CBT  
44 receipt. The large sample size enabled us to identify clinical differences in the real-life administration of CBTp  
45 within a psychosis cohort, and we were able to adjust for multiple clinical variables and comorbidity diagnoses  
46 to provide a more realistic understanding of the depressive symptom-CBTp receipt relationship. This time  
47 frame was broad to allow the inclusion of as many active patients receiving CBTp as possible, additionally  
48 circumventing monthly/seasonal variation of CBTp receipt.

49  
50 One limitation of the study was the omission of strict time periods for the mention of clinical symptoms prior  
51 to CBTp administration. Unfortunately, using this approach would have involved implementing time periods on  
52 all of the other clinical symptoms and variables, which would have been difficult considering the number of  
53 variables that would need to be controlled. In addition, the NLP symptom algorithms do not currently  
54 distinguish between past or present symptoms. Therefore, symptom mentions documented after the CBTp  
55 receipt date could refer to mentions of symptoms occurring prior to CBTp receipt, reducing the effectiveness  
56 of using time periods. A follow-up time period after the index date was also not established, meaning that  
57 participants included in the cohort at a later date may have been less likely to have had a CBTp session, due to  
58 their limited time period within the service. Additionally, we did not have data regarding which type of service  
59 was providing CBTp for each patient (for example, early intervention services compared to other community  
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3 services). Future studies should examine whether CBTp receipt differs depending on the service, especially  
4 considering how effective CBTp provision may be in those at ultra-high risk.  
5

6 While our use of additional querying of text fields allowed us to identify a significantly larger number of CBTp  
7 episodes than using structured data alone, we were not able to quantify the gap between CBTp referral and  
8 CBTp receipt. This is because the CBTp NLP algorithm detects CBTp receipt rather than CBTp being offered,  
9 due to the wide range of subtle wording used for the latter more complex entity. The results combine effects  
10 on the likelihood of CBTp being offered, with those on session receipt following an offer. While this may have  
11 affected our results, previous service audits have suggested that the severity and occurrence of depressive  
12 symptoms significantly decreases CBT receipt.<sup>35</sup> Therefore, if only receipt was directly measured, we would  
13 expect to see similar results. Additionally, completion rates and effectiveness of the CBTp was not measured,  
14 meaning we were unable to quantify the quality or focus of the sessions. Lastly, analysis was limited to  
15 patients above 18 years old, reducing the generalisability of results to those who develop a schizophrenia-  
16 spectrum disorder after this age. However, the outcome of interest was CBTp receipt within a relatively  
17 homogenous service structure of working age services, rather than young people treated within Child and  
18 Adolescent services. Future studies should examine whether CBTp receipt differs in these services.  
19

### 20 **Future directions**

21  
22 Initiatives such as the Improving Access to Psychological Therapies programme for serious mental illness, early  
23 intervention access and projects to decrease waiting times for referral have been developed to target this  
24 clinical population. However, access still falls short of recommendations and is inequitable for specific  
25 psychotic diagnoses, age and ethnicity.<sup>11</sup> Therefore, given the effect of CBTp on depressive symptoms<sup>36</sup>,  
26 perhaps its more pragmatic to focus on patients with additional depressive symptoms. Monitoring CBTp  
27 receipt over time could decipher whether these initiatives are effective at increasing general access for those  
28 with psychosis, and specific access for different sociodemographic groups and those with additional depressive  
29 symptoms (who may benefit the most).  
30

31  
32 The significant secondary clinical and sociodemographic variables require further analysis in order to fully  
33 understand the services' provision. This could involve attention given to the independent symptoms within the  
34 negative, manic and disorganisation categories in a similar manner to the specific depressive symptom  
35 regression models analysed. Further research could also explore why the presence of co-morbid anxiety and  
36 bipolar disorder in this sample predicted CBTp receipt. Additionally, the results suggest a need to reflect on the  
37 steps taken since the previous service study,<sup>34</sup> regarding inequality in CBTp receipt among gender and ethnic  
38 groups, due to the consistent significant results seen. Regarding the use of EHR data, future work could involve  
39 developing a separate NLP algorithm to ascertain the offering of CBTp or provide another structured field for  
40 clinicians to complete for this. However, additional text fields seem an unlikely approach, as clinicians prioritise  
41 text field data for communication about CBTp sessions for themselves and their colleagues rather than to  
42 collect structure data for the sake of research. Therefore, as previously suggested,<sup>11</sup> it is important to accept  
43 the mixed structured-text field approach that will remain in healthcare record data and perhaps our time is  
44 best spent in improving NLP algorithms to detect the subtleties of intervention and clinical outcome data.  
45 However, the implications of our results and their consistency three years after the first CBTp service paper  
46 suggest the need to use this or future algorithms for service monitoring independent of these improvements.  
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### Author statement

Ava Mason planned the protocol, analysed the data and wrote the manuscript. Dr Rob Stewart provided access to the data, looked over edits and revisions on the manuscript. The data from this paper was accessed through the assistance of Megan Pritchard and Jyoti Sanyal. The applications used to obtain data specific to CBTp were developed by Craig Colling and David Chandran. Jessica Irving assisted in statistical analysis.

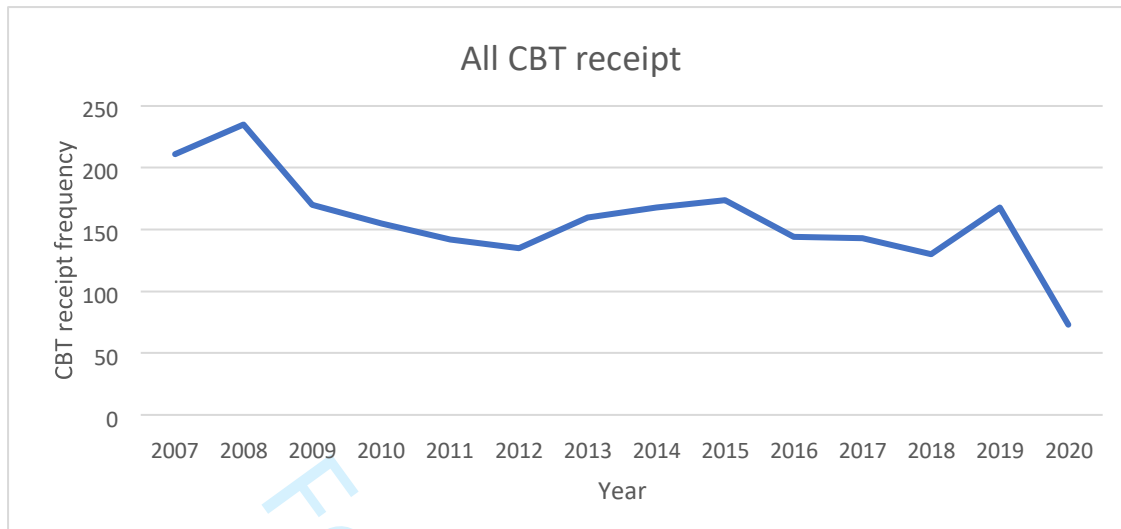
### Data Sharing Statement

Due to the terms of Ethics and Information Governance approvals and clinical source of the data, CRIS datasets must remain within the South London and Maudsley NHS Foundation Trust (SLaM) firewall. All data used from this study can be made accessible on request from [cris.administrator@slam.nhs.uk](mailto:cris.administrator@slam.nhs.uk), subject to the setting up of an appropriate research passport or SLaM honorary contract.

Figure 1: Graph demonstrating the frequency of general CBT receipt (CBT receipt prior to diagnosis and recorded CBTp receipt post diagnosis) per year of extraction period.

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Supplementary figure

*Graph demonstrating the frequency of general CBT receipt (CBT receipt prior to diagnosis and recorded CBTp receipt post diagnosis) per year of extraction period.*

# Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cross sectional reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
<b>Title and abstract</b>			
Title	<a href="#">#1a</a>	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	<a href="#">#1b</a>	Provide in the abstract an informative and balanced summary of what was done and what was found	1
<b>Introduction</b>			
Background / rationale	<a href="#">#2</a>	Explain the scientific background and rationale for the investigation being reported	1,3
Objectives	<a href="#">#3</a>	State specific objectives, including any prespecified hypotheses	3
<b>Methods</b>			
Study design	<a href="#">#4</a>	Present key elements of study design early in the paper	4



1	Setting	<a href="#">#5</a>	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
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4	Eligibility criteria	<a href="#">#6a</a>	Give the eligibility criteria, and the sources and methods of selection of participants.	4
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8		<a href="#">#7</a>	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	1,4-6,
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14	Data sources / measurement	<a href="#">#8</a>	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. Give information separately for for exposed and unexposed groups if applicable.	4-6
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21	Bias	<a href="#">#9</a>	Describe any efforts to address potential sources of bias	4
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23	Study size	<a href="#">#10</a>	Explain how the study size was arrived at	4
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25	Quantitative variables	<a href="#">#11</a>	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	4-6
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29	Statistical methods	<a href="#">#12a</a>	Describe all statistical methods, including those used to control for confounding	6
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33	Statistical methods	<a href="#">#12b</a>	Describe any methods used to examine subgroups and interactions	6
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37	Statistical methods	<a href="#">#12c</a>	Explain how missing data were addressed	4
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41	Statistical methods	<a href="#">#12d</a>	If applicable, describe analytical methods taking account of sampling strategy	6
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44	Statistical methods	<a href="#">#12e</a>	Describe any sensitivity analyses	6
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48	<b>Results</b>			
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51	Participants	<a href="#">#13a</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. Give information separately for for exposed and unexposed groups if applicable.	1,6
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1	Participants	<a href="#">#13b</a>	Give reasons for non-participation at each stage	6
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3	Participants	<a href="#">#13c</a>	Consider use of a flow diagram	N/A
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5	Descriptive data	<a href="#">#14a</a>	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	4-7
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12	Descriptive data	<a href="#">#14b</a>	Indicate number of participants with missing data for each variable of interest	4
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16	Outcome data	<a href="#">#15</a>	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	8
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21	Main results	<a href="#">#16a</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	7-12
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28	Main results	<a href="#">#16b</a>	Report category boundaries when continuous variables were categorized	7-12
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32	Main results	<a href="#">#16c</a>	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
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36	Other analyses	<a href="#">#17</a>	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	12
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40	<b>Discussion</b>			
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42	Key results	<a href="#">#18</a>	Summarise key results with reference to study objectives	13-15
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44	Limitations	<a href="#">#19</a>	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	14-15
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50	Interpretation	<a href="#">#20</a>	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13-15
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55	Generalisability	<a href="#">#21</a>	Discuss the generalisability (external validity) of the study results	13-15
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1 **Other**  
2 **Information**

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5 Funding [#22](#) Give the source of funding and the role of the funders for the present 2  
6 study and, if applicable, for the original study on which the present  
7 article is based  
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11 This checklist was completed on 11. March 2021 using <https://www.goodreports.org/>, a tool made by the  
12 [EQUATOR Network](#) in collaboration with [Penelope.ai](#)  
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