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RESEARCH ARTICLE

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Depression subtypes and their response to cognitive behavioral therapy: A latent transition analysis

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Abstract

Background: Depression is a heterogeneous condition, with multiple possible symptom-profiles leading to the same diagnosis. Descriptive depression subtypes based on observation and theory have so far proven to have limited clinical utility.
Aim: To identify depression subtypes and to examine their time-course and prognosis using data-driven methods.
Methods: Latent transition analysis was applied to a large ($N = 8380$) multi-service sample of depressed patients treated with cognitive behavioral therapy (CBT) in outpatient clinics. Patients were classed into initial latent states based on their responses to the Patient Health Questionnaire-9 of depression symptoms, and transition probabilities to other states during treatment were quantified. Qualitatively similar states were clustered into overarching depression subtypes and we statistically compared indices of treatment engagement and outcomes between subtypes using post hoc analyses.
Results: Fourteen latent states were clustered into five depression subtypes: mild (2.7%), severe (9.8%), cognitive-affective (23.7%), somatic (21.4%), and typical (42.4%). These subtypes had high temporal stability, and the most common transitions during treatment were from severe toward milder states within the same subtype. Differential response to treatment was evident, with the highest improvement rate (63.6%) observed in the cognitive-affective subtype.
Conclusion: Replicated evidence indicates that depression subtypes are temporally stable and associated with differential response to CBT.

KEYWORDS
CBT, depression, latent profile analysis, psychotherapy

1 | INTRODUCTION

Depression, a highly common mental health problem that affects approximately 264 million people worldwide (James et al., 2018), is characterized by a wide range of symptoms, including cognitive (e.g., repetitive negative thoughts, suicidal ideas), affective (e.g., anhedonia, avolition) and somatic (e.g., problems with sleep, psychomotor disturbances) indicators. Despite a range of recommended, evidence-based treatment options including pharmacotherapy and various forms of psychotherapy (National Institute for Health and Care Excellence, 2009), only half of patients recover (Holtzheimer & Nemeroff, 2006; Khan et al., 2012). This evidence suggests that currently available treatments are only moderately effective. However, an alternative argument is that depression is a highly heterogeneous condition (Goldberg, 2011)—potentially characterized by various subtypes—and clinical outcomes could be improved if treatment was based on more precise assessments of each individual's symptom profile (Fried, 2017).

It is widely acknowledged that current diagnostic systems often fail to capture the underlying heterogeneity within a particular diagnostic label (Cuthbert & Insel, 2013). This is a particular issue for depression, where—in theory—over 100 different combinations of symptoms can result in the same unitary diagnosis of depression (Zimmerman et al., 2015). Research investigating the effectiveness of different treatments for different depression subtypes has offered mixed results, limiting the use of classification systems for determining the most appropriate treatment for a particular patient (Arnow et al., 2015; Uher et al., 2011). In particular, subtyping concepts that are derived from clinical observation and theory often have little empirical support or prognostic utility (Haslam & Beck, 1994).

In recent years, data-driven approaches, such as latent class analysis (LCA) that aim to define depression subtypes based on itemized scores in standardized questionnaires, without imposing any theoretical constructs on the statistical model a priori (e.g., Putnam et al., 2015; Ulbricht et al., 2015, 2018) have provided valuable insights into different symptom profiles. However, LCA has been limited to rigid clustering of patients into static classes, providing no indication of their temporal stability, or how different subtypes may respond to treatment. Latent transition analysis (LTA) is an extension of LCA which uses longitudinal data to explore transitions between classes over time (Ni et al., 2017; Ulbricht et al., 2016). This technique is better suited to examine how patients with different depression subtypes respond to treatment, which is potentially informative for personalized treatment planning.

In a recent demonstration, Catarino et al. (2020) applied LTA in a large (N = 9,891) sample of patients who accessed internet-enabled cognitive behavioral therapy (CBT) for depression. The results classed patients into seven distinctive depressive states, loading preferentially on cognitive/affective versus somatic symptoms. Transition probability analysis revealed that patients starting in cognitive/affective states typically do not transition to somatic states, and vice-versa. Although the distinction between cognitive/affective and somatic symptoms in depression is well supported by the literature (Barton et al., 2017; Carragher et al., 2009; Lee et al., 2012, 2014), this was the first study exploring how patients in these two distinct states respond to a highly standardized evidence-based psychological treatment. Importantly, Catarino et al. (2020) showed that patients who are classified into somatic states were less likely to improve, and more likely to be female, suffering from a long-term physical illness, and taking antidepressants (Catarino et al., 2020). Notwithstanding its clinically informative results, this study was based on a sample of patients who opted-in to receive CBT via text messages. It is unclear if patients who find this treatment modality acceptable may be systematically different to typical clinical samples who receive more traditional in-person therapy in healthcare settings. Thus, the generalizability of these findings to typical clinical samples is unknown.

The present study aimed to address a gap in knowledge concerning the generalizability and clinical utility of depression subtyping based on LTA methods. To this end, we applied the methods used by Catarino et al. (2020) in a large multi-service sample of depressed patients accessing routinely-delivered CBT in community (outpatient) settings.

2 | METHODS

2.1 | Design and ethical approval

This naturalistic, retrospective, observational cohort study analyzed practice-based data collected between 2014 and 2017 across eight National Health Service (NHS) trusts in England.[1] Ethical approval for the analysis of this data set was granted by the London City & East NHS Research Ethics Committee (06/01/2016, Ref:15/LO/2200).

2.2 | Data sources and sample selection

All participating NHS Trusts offered psychological care as part of the Improving Access to Psychological Therapies (IAPT) program. IAPT services deliver evidence-based psychological interventions for common mental health disorders within a stepped-care model (Clark, 2011). In this system, most patients are initially referred for brief (≤8 sessions), low-intensity guided self-help interventions. Those who remain symptomatic, or who initially present with more severe and complicated problems, are referred for high intensity psychotherapies (up to 20 sessions), including CBT, person-centered experiential counseling or interpersonal psychotherapy as recommended by clinical guidelines (National Institute for Health and Care Excellence, 2011). IAPT interventions are highly standardized, protocol-driven, and delivered by practitioners qualified to a postgraduate level under regular supervision (National Collaborating Center for Mental Health, 2018).

Fully anonymised clinical records were obtained for a sample of 44,593 patients across all participating services, who were referred for and attended at least one session of CBT. To maximize comparability with prior research applying LTA, the sample was based on a subset of cases that met the following criteria: (a) patients presented with depression/affective disorder as their primary problem according to clinical records; (b) accessed face-to-face high intensity CBT in an outpatient clinic setting; (c) had at least one depression measure available; and (d) had sessional depression measures from no more than 10 sessions in total, to ensure the computational demand was manageable (70% of the sample had ≤10 measures). In this way, the only methodological difference between this study and

[1]South West Yorkshire Partnership NHS Foundation Trust, North East London NHS Foundation Trust, Whittington Health NHS Trust, Barnet Enfield and Haringey Mental Health Trust, Pennine Care NHS Foundation Trust, Cheshire and Wirral Partnership NHS Foundation Trust, Cambridgeshire and Peterborough NHS Foundation Trust, Humber NHS Foundation Trust.

TABLE 1 Sample characteristics ($N = 8380$)

Characteristics	Descriptive statistics
Age (mean, *SD*)	39.09 (13.94)
Gender (% male)	35.0
Ethnicity (% White British)	76.8
Employment status (% unemployed)	31.8
Medication (% prescribed pharmacotherapy)	52.0
Self-reported LTC (% with LTC)	29.0
Baseline PHQ-9 score (mean, *SD*)	15.81 (6.27)
Baseline GAD-7 score (mean, *SD*)	13.34 (5.40)
Baseline WSAS score (mean, *SD*)	20.85 (9.85)

Abbreviations: GAD-7, Generalized Anxiety Disorder-7; LTC, long-term health condition or illness; PHQ-9, Patient Health Questionnaire-9; WSAS, Work and Social Adjustment Scale.

Catarino et al. (2020), was that the present sample received traditional in-person CBT rather than internet-enabled CBT. The selected study sample consisted of 8380 patients (see Table 1 for sample characteristics). Study flowchart with reasons for exclusion is reported in the Supplemental Material.

2.3 | Measures

Patients accessing IAPT services complete standardized questionnaires at the start of each session, as part of routine outcome monitoring. The Patient Health Questionnaire-9 (PHQ-9) is a nine-item questionnaire assessing symptoms of major depression, including affective (items 1, 2), cognitive (items 6, 7, 9) and somatic domains (items 3, 4, 5, 8). Each item is rated on a 0–3 scale (0 = "not at all," 3 = "nearly every day"), with a total score between 0 and 27 (Kroenke et al., 2001). A cut-off point of ≥10 has been recommended to detect clinically significant depression symptoms (Kroenke et al., 2001). The GAD-7 is a seven-item questionnaire assessing symptoms of generalized anxiety. Each item is also rated from 0 to 3, producing a total score between 0 and 21 (Spitzer et al., 2006). A cut-off point of ≥8 has been recommended to identify clinically significant anxiety symptoms (Kroenke et al., 2007).

Additional anonymized demographic and clinical data included age, gender, ethnicity, employment status, medication status, presence of a long-term physical condition, and baseline impaired functioning severity measured using the Work and Social Adjustment Scale (WSAS; Mundt et al., 2002).

2.3.1 | Outcomes of interest

To allow comparison with the study by Catarino et al. (2020), treatment outcomes were assessed according to the same criteria for treatment engagement and reliable change. An additional dropout outcome was also assessed in the current study. Patients were deemed treatment engagers if they attended two or more treatment sessions. Consistent with outcome definitions used routinely by IAPT services to examine reliable change (National Collaborating Center for Mental Health, 2018), reliable improvement was present when at least one of the two primary outcome measures showed a statistically reliable reduction in scores (≥6 points on the PHQ-9 and/or ≥4 points on the GAD-7), in the absence of a reliable increase in the other measure (Gyani et al., 2013). Reliable deterioration was recorded when at least one of the measures showed a reliable increase in scores (≥6 points on the PHQ-9 and/or ≥4 points on the GAD-7). Finally, patients were classed by therapists as having dropped out if they unilaterally discontinued treatment and had an unplanned ending to their episode of care.

2.4 | Statistical analysis

2.4.1 | Latent Markov modeling procedure

Analyses were conducted in R (version 3.6.1) using the package LMest (Bartolucci et al., 2017). Following the procedure reported in Catarino et al. (2020), a Hidden Markov Model (HMM) was applied to the longitudinal item-level PHQ-9 data from the entire sample ($N = 8380$) to estimate latent depressive subtypes and the corresponding state-to-state transition probabilities. Unlike Catarino et al. (2020), we decided to interpret the model that had best empirical support (smallest Bayesian Information Criterion value), rather than to identify a reduced state model that aimed to balance fit and interpretability. This was to ensure complete objectivity in model selection and to explore differences and/or similarities between states and transitions with greater granularity. After determining the optimal model, global decoding was performed to approximate a depressive state for each patient at every time point. Transition probabilities were extracted and plotted to explore between-state transitions in response to treatment.

2.4.2 | Post-hoc analyses of state groupings

Qualitatively similar states were grouped into a smaller set of overarching depression subtypes. Patients' starting states were compared using post-hoc analyses in relation to treatment engagement, duration and posttreatment clinical outcomes. These analyses were based on chi-square (for binary outcomes) and analysis of variance (for continuous outcomes). In addition, we applied logistic regressions to investigate which clinical and demographic features were associated with patients' starting states. In the interest of parsimony and statistical power, post hoc comparisons were performed between the three subtypes that encompassed most of the sample (>85%).

3 | RESULTS

3.1 | Optimal depressive states model

The HMM analysis produced an optimal model with 14 separate depressive states, each exhibiting different symptom-profiles and levels of severity. Figure 1 displays the overall mean score and a plot of the corresponding intensity of each PHQ-9 item for all 14 states. State 1 displayed a profile of minimal symptoms with very low severity. States 2, 4, 6, and 10 showed similar symptom-profiles at differing overall severities, with peak intensity on PHQ-9 items 3, 4, and 5, representing somatic symptoms. We therefore considered these to belong to an overarching somatic depression subtype. States 3, 5, and 11 also displayed similar symptom-profiles with different levels of severity, but with patterns of peak intensity on items 1, 2, and 6, representing cognitive-affective symptoms. We considered these to belong to an overarching cognitive-affective depression subtype. States 7, 8, 9, 12 and 13 all showed relatively even intensity across most items (1–8) for different levels of severity; we considered these to belong to an overarching typical depression subtype. However, there was a further distinction between the symptom-profiles of states 8 and 13 and states 9 and 12, with the latter two states showing greater intensity on the suicidal risk item (item 9). We therefore draw a further distinction between low-risk typical (8, 13) and high-risk typical (9, 12) subtypes (7 being a typical state with moderate-risk). Finally, state 14 displayed a *severe* depressive state with high severity across all items. Overall, the majority (87.5%) of patients' starting states were classified into three broad subtypes (cognitive-affective, 23.7%; somatic, 21.4%; and typical, 42.4%).

Inspection of probable states over time was achieved through the visualization of within and between-state transitions. First, Figure 2 presents stacked area plots for each starting state, showing the probable states those patients will be in at each subsequent treatment session. Across each figure, it is evident that most patients remain in their starting state over time, and relatively small proportions of patients transitioned into different states over the course of therapy.

Figure 3 depicts the range of transition probabilities within and between-states during CBT, displaying the most likely between-state transitions. In general, the most probable between-state transitions were to a state of a similar symptom-profile but with lower symptom severity. Patients that started treatment in a cognitive-affective or somatic state tended to transition to another state within the same overreaching cluster (i.e., somatic to somatic). There were a small proportion of cross-state cognitive-affective to somatic transitions from state 11 to 10 and from state 5 to 4, but almost no prominent

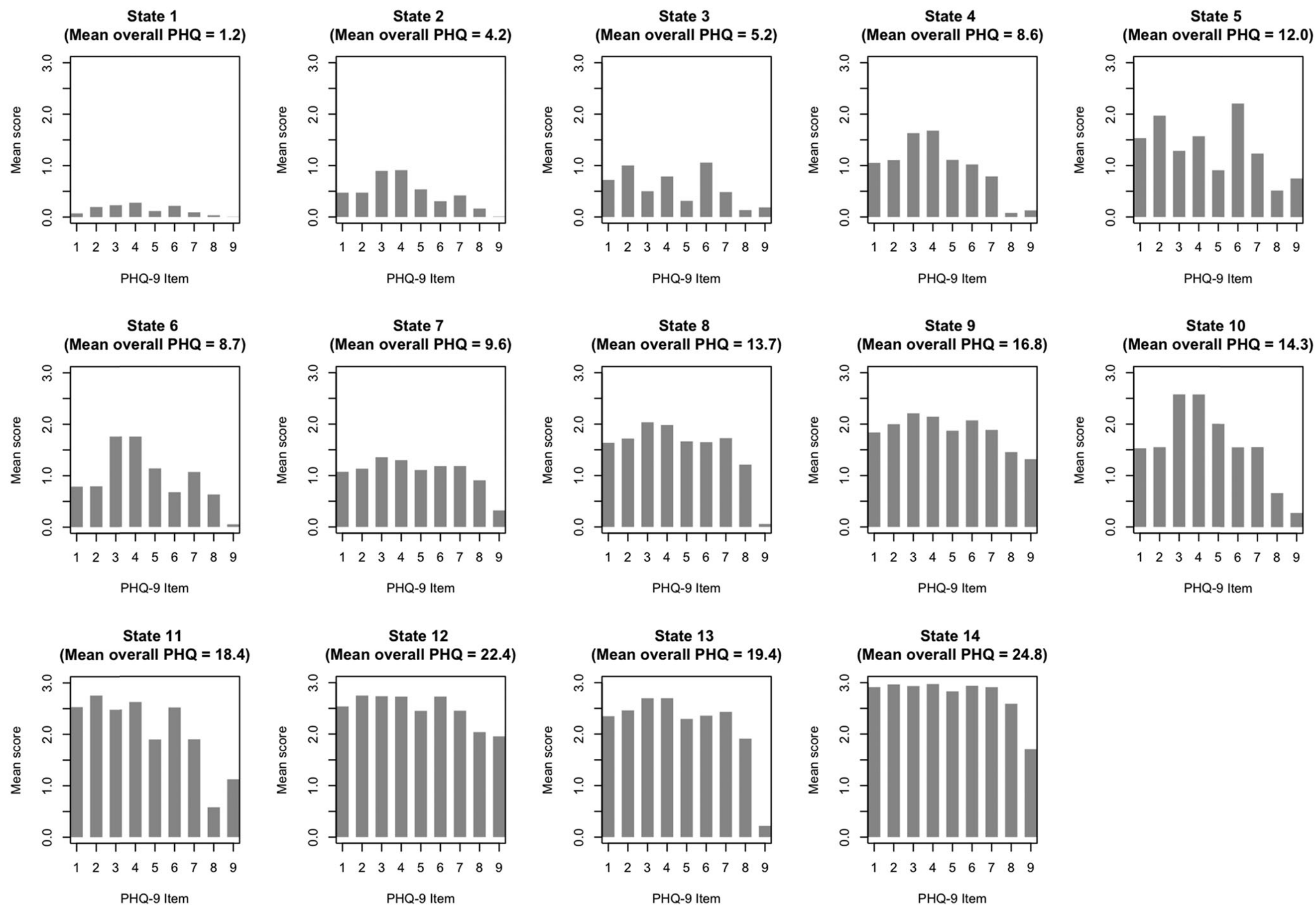

FIGURE 1 Depressive state profiles for the optimal 14-state model. PHQ-9, Patient Health Questionnaire-9

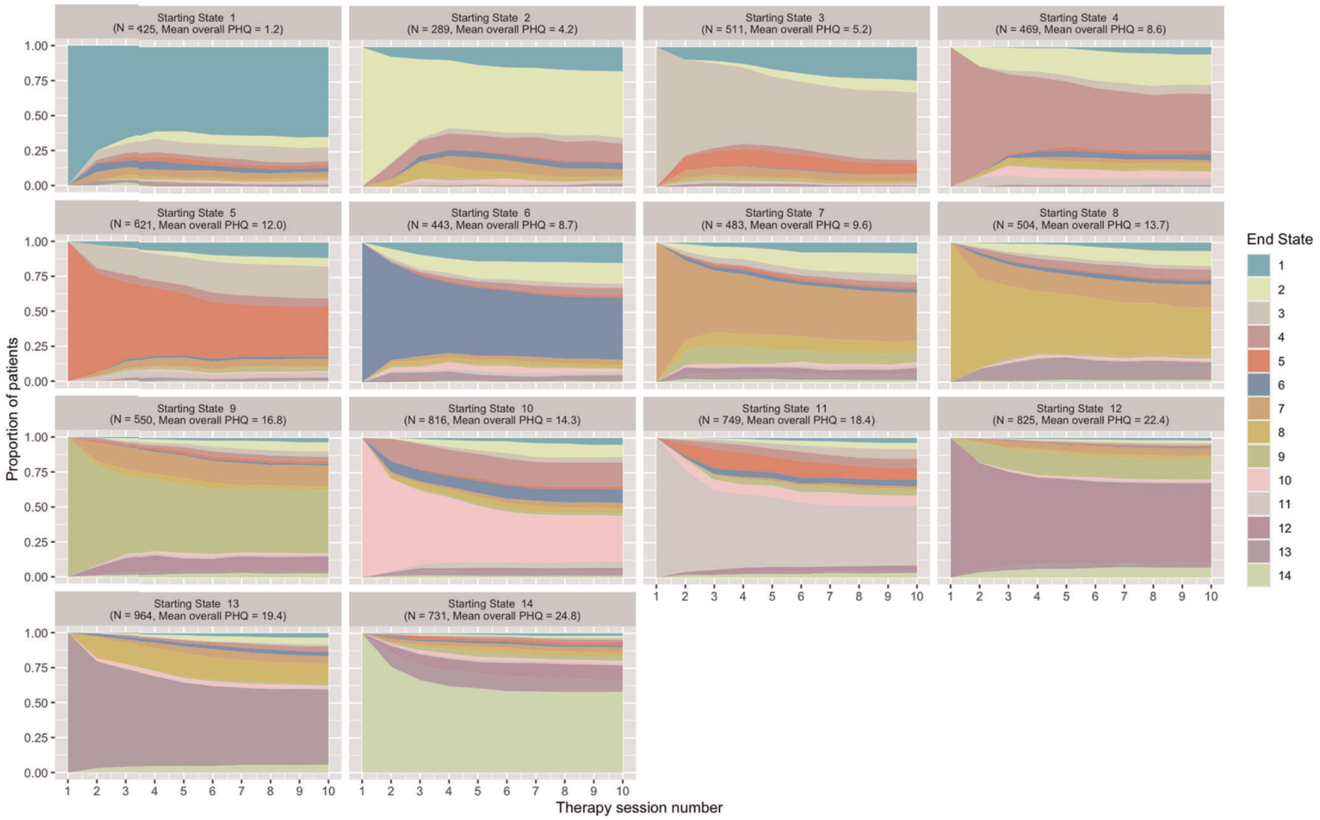

FIGURE 2 Depressive state transitions in response to cognitive behavioral treatment (CBT) based on the 14 starting states. PHQ-9, Patient Health Questionnaire-9

transitions in the opposite direction (i.e., from somatic to cognitive-affective).

The most severely depressed patients appeared to be most likely to transition into the two typical states, either low-risk typical (states 8 and 13) or high-risk typical (states 9 and 12). However, there were rarely any crossover transitions between these two states, with patients merging into state 7 when symptoms were at a subthreshold severity. Similar trends were seen within the small number of cases who experienced deterioration in their symptoms, with transitions to higher severity states within the same symptom cluster (e.g., state 3–5; state 8–13; state 9–12). Interestingly there were no prominent deterioration transitions within the somatic states.

3.2 | Relationship between clinical outcomes, demographics, and depressive states

3.2.1 | Comparing somatic, cognitive-affective, and typical depression subtypes

Significantly different patterns of engagement ($\chi^2 = 17.802$, $p < .001$) and number of sessions attended ($F(2,7328) = 6.093$, $p = .002$) were observed across subtypes. Patients starting treatment in typical states had significantly lower rates of engagement than cognitive-affective states and attended significantly fewer sessions ($p = .002$). Comparisons between typical and somatic states ($p = .729$) and cognitive-affective and somatic states ($p = .056$) were not significant. Of those who engaged in treatment ($n = 6364$), patients in somatic and typical states were found to have significantly lower rates of reliable improvement than those in cognitive-affective states, but did not differ from each other ($\chi^2 = 13.764$, $p = .001$). Rates of deterioration did not differ between the three depression subtypes ($\chi^2 = 1.121$, $p = .571$). Significantly more patients in the typical states dropped out of treatment compared to the cognitive-affective and somatic states ($\chi^2 = 15.047$, $p = .001$).

Six demographic variables were significantly associated with starting treatment in a somatic state (relative to a cognitive-affective state) ($\chi^2 = 239.57$, $p < .001$, Nagelkerke $R^2 = 0.127$). Patients with somatic subtypes were more likely to be females from a white British background, with a long-term physical illness, additionally having pharmacotherapy, and who had lower baseline depression and anxiety severity (Table 2).

Analyses comparing patients entering treatment in typical states with differing risk profiles (low vs. high-risk) and for states with similar elevated risk scores, but differing state profiles (high-risk typical vs. high-risk cognitive-affective) are reported in the Supplemental Material and indicate that high-risk typical subtypes had lower dropout rates compared to low-risk typical and high-risk cognitive-affective subtypes.

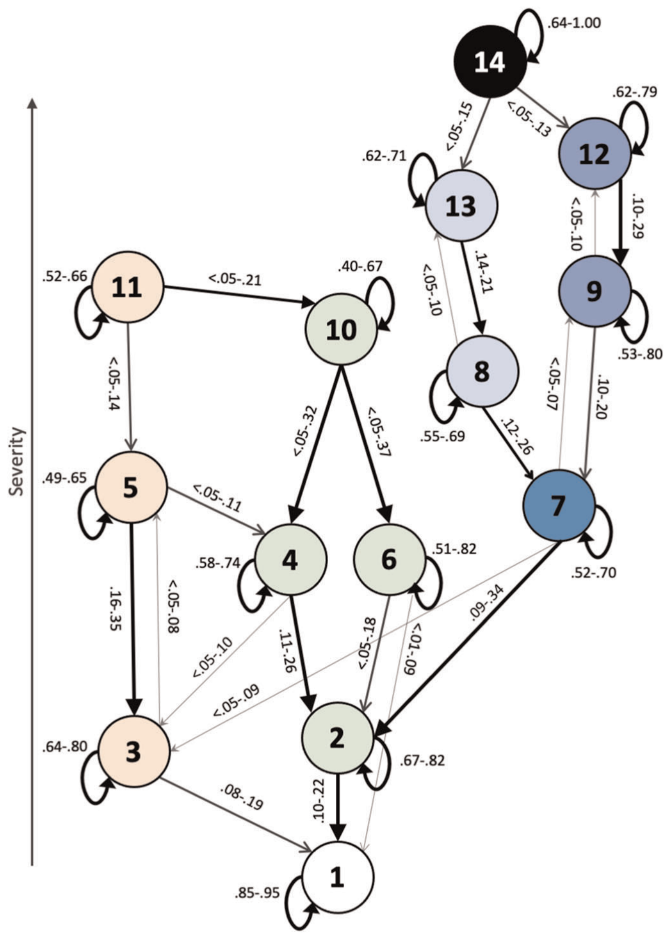

FIGURE 3 Within and between-state transition probabilities in response to CBT; the range of probabilities over the course of treatment are reported for each transition; *p* < .05 at more than half the time points are hidden; thickness of the arrow depicts the magnitude of the probability, with thicker arrows representing more likely transitions; states are color coded accordingly–green = somatic, pale orange = cognitive-affective, blue = typical, pale blue = typical with low-risk and dark blue = typical with high-risk. CBT, cognitive behavioral treatment

4 | DISCUSSION

4.1 | Summary of findings

This large (*N* = 8380) multi-service cohort study identified a total of 14 depressive states based on the combination of symptoms that patients endorsed on the PHQ-9 during the course of CBT. Grouping qualitatively similar states together resulted in an overarching framework of five broad depression subtypes: mild (2.7%), severe (9.8%), cognitive-affective (23.7%), somatic (21.4%), and typical (42.4%). These subtypes had high temporal stability, and the most common transitions during treatment were from severe toward milder states within the same overarching subtype. We also found that state transitions denoting a deterioration of symptom-severity occurred predominantly within the cognitive-affective and typical subtypes. Some cases transitioned to other subtypes, but the probability tended to be low (<20%).

Post-hoc comparisons of indicators of treatment engagement and outcomes revealed that these depression subtypes do not merely have descriptive value, but also have prognostic utility. As shown in Table 3, symptom-states characterized by moderate-to-severe levels of depression (8, 9, 10, 11) showed the highest rates of reliable improvement (>60%). States 1 and 2 had the lowest improvement rates (<31%), though these had the lowest baseline severity, so this is likely to be a floor effect (i.e., little room for improvement). Deterioration rates were generally low (<10%) across all states, with the highest probability (9.6%) observed for state 7 and the lowest (0.5%) for state 14—although a ceiling effect is likely for the latter. The four states with highest depression severity (11–14) also had the highest dropout rates (>35%). Comparisons between overarching depression subtypes revealed that patients with a cognitive-affective subtype were more likely to engage, attended more sessions, and attain reliable improvement compared to the typical and somatic subtypes. Patients with a typical subtype were more likely to drop out of treatment compared to those with cognitive-affective and somatic subtypes. Furthermore, cases in the high-risk typical subtype had lower dropout rates compared to the low-risk typical subtype and the cognitive-affective subtype cases with comparably acute suicidal risk.

TABLE 2 Logistic regression analyses examining the association between patient demographics and starting state for somatic versus cognitive-affective state comparisons

Predictor variable	Mean (*SD*)/prevalence		*b*	*SE*	Wald	*p*
(i) Cognitive (signal) versus somatic (reference)	Cognitive-affective	Somatic				
Baseline PHQ-9 score	13.97 (5.46)	11.35 (4.06)	0.92	0.01	60.78	<.001***
Baseline GAD-7 score	12.29 (4.93)	10.37 (4.93)	0.02	0.01	7.48	.006**
Baseline WSAS score	19.17 (9.17)	16.10 (8.21)	0.01	0.01	3.31	.069
Age (years)	38.43 (14.84)	38.14 (14.35)	0.01	0.00	3.45	.063
Gender (% male)	36.1	27.1	0.52	0.09	31.05	<.001***
Ethnicity (% White British)	79.4	83.7	−0.24	0.11	4.72	.030*
Employment (% unemployed)	26.8	20.8	0.12	0.10	1.48	.223
Medication (% prescribed pharmacotherapy)	43.6	45.9	−0.19	0.08	4.59	.032*
Self-report LTC (% with LTC)	28.8	33.2	−0.40	0.09	17.14	<.001***

Note: A positive relationship signifies that the variable is more likely to occur in patients entering treatment in a cognitive-affective state. Continuous variables were mean centered. Reference categories for categorical variables: gender "female," ethnicity "minority," employment "employed," medication "not prescribed pharmacotherapy," self-report LTC "no LTC."

Abbreviations: GAD-7, Generalized Anxiety Disorder-7; LTC, long-term health condition or illness; PHQ-9, Patient Health Questionnaire-9; WSAS, Work and Social Adjustment Scale.

$^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$.

4.2 | Wider empirical context

Previous empirical studies using the PHQ-9 have proposed that these symptoms load onto distinctive cognitive-affective and somatic factors, particularly in studies that included participants with co-morbid physical illnesses/chronic health problems (e.g., Chilcot et al., 2013; Doi et al., 2018; Krause et al., 2010). Approximately 29% of our sample reported comorbid long-term health problems, and this was one of the significant features that characterized the somatic depression subtype. However, studies specifically seeking to identify depressive subtypes using data-driven LCA have thus far yielded mixed and inconclusive results (see review by Ulbricht et al., 2018). Methodological advances, such as LTA have rarely been applied in the wider field of mental health (e.g., McElroy et al., 2017; Rodgers et al., 2014; Ulbricht et al., 2016), and less so in the specific field of CBT for depression. Like other studies (e.g., Rodgers et al., 2014) we found that gender played a role in determining class membership. In the present sample, females were more likely to have the somatic depression subtype whereas males were more likely to have the cognitive-affective subtype. Within the majority class of typical depression, males were more likely to have acute suicidal risk. Of those that exhibited high-levels of suicidal risk, females were more likely to have a cognitive-affective subtype whereas males were more likely to have a typical subtype.

To our knowledge, the study by Catarino et al. (2020) was the first application of LTA in a large clinical sample of depressed patients accessing internet-enabled CBT, albeit in an atypical format. Our findings show remarkable similarities. Catarino et al. (2020) also found distinctive states that clustered around three overarching subtypes characterized by cognitive-affective, somatic and "hybrid" (typical) depression symptoms. Those with the somatic subtype had lower indices of engagement and improvement, and were more likely to be females, with comorbid long-term health conditions who were taking prescribed pharmacotherapy. The temporal stability of these subtypes and their transition patterns were also highly similar. Most transitions occurred toward lower severity states within the same overarching subtype, and cross-class transitions from "hybrid" (typical) to somatic subtypes were more likely than transitions from "hybrid" to cognitive-affective subtypes. Taken together, our findings show strong evidence of replication and generalizability of these depression subtypes and their prognostic utility across different studies and different treatment samples receiving internet-enabled and more traditional (in-person) CBT.

4.3 | Strengths, limitations, and future directions

This study used a large and adequately powered sample, covering multiple regions of England, thus enhancing the external validity and generalizability of findings to a typical population of patients accessing CBT in routine care. Relative to other cluster methods, LTA is a state-of-the-art method that makes best use of time-series data simultaneously enabling the modeling of symptom-states, their temporal stability and transition probabilities to other states (Bartolucci et al., 2017). In addition, our sample selection, modeling strategy, outcome measures and outcome definitions were closely aligned to prior research (Catarino et al., 2020), thus enabling direct comparability.

TABLE 3 Treatment engagement and clinical outcomes by starting state (1–14) and overarching depression subtypes

Start state	*N*	Baseline PHQ-9 (*SD*)	Mean number of sessions (*SD*)	Treatment engagement (%)	Dropout rate (%)[a]	Improvement (%)[a]	Deterioration (%)[a]
1. Mild	229	1.50 (1.19)	3.33 (2.71)	60.7	19.4	28.3	3.6
2. Somatic	155	4.42 (1.41)	4.84 (3.04)	78.1	17.4	30.8	2.5
3. Cognitive-affective	377	5.47 (1.61)	5.21 (2.95)	83.8	18.0	55.4	3.8
4. Somatic	385	8.80 (1.70)	5.24 (2.94)	86.2	27.1	50.2	4.3
5. Cognitive-affective	687	12.16 (2.51)	5.67 (2.90)	90.2	24.8	70.0	3.8
6. Somatic	396	9.40 (2.89)	4.93 (2.89)	84.1	25.5	57.1	5.2
7. Typical (moderate-risk)	343	9.86 (1.65)	5.16 (2.83)	86.3	21.3	55.5	9.6
8. Typical (low-risk)	497	13.82 (1.71)	5.38 (2.82)	88.5	25.9	70.3	4.4
9. Typical (high-risk)	588	16.86 (2.00)	5.43 (2.94)	88.1	28.4	64.7	5.1
10. Somatic	858	14.56 (2.34)	5.40 (2.82)	90.4	28.4	64.8	2.7
11. Cognitive-affective	923	18.54 (2.70)	5.35 (2.82)	90.8	35.2	61.8	4.0
12. Typical (high-risk)	974	22.36 (1.79)	4.83 (3.01)	81.1	35.8	52.4	1.2
13. Typical (low-risk)	1148	19.39 (1.96)	5.17 (2.95)	85.7	36.4	59.1	1.7
14. Severe	820	24.53 (1.86)	4.72 (2.92)	81.1	36.5	47.6	0.5
Cognitive-affective (3, 5, & 11)	1987	13.83 (5.53)	5.43 (2.87)	89.3	28.5	63.6	3.9
Somatic (2, 4, 6 & 10)	1794	11.30 (4.07)	5.21 (2.88)	87.1	26.6	57.4	3.6
Typical (7, 8, 9, 12, & 13)	3550	18.10 (4.28)	5.14 (2.94)	85.3	31.9	58.2	3.2
Typical low-risk (8 & 13)	1645	17.70 (3.17)	5.23 (2.91)	86.6	36.7	54.9	2.2
Typical high-risk (9 & 12)	1562	20.30 (3.25)	5.05 (2.99)	83.7	32.9	57.2	2.7

Abbreviation: PHQ-9, Patient Health Questionnaire for major depressive disorder.
[a]Percentage within subset of treatment engagers.

Despite these strengths, these findings should be interpreted in light of some limitations. The depression subtypes identified in this study are inevitably constrained by the limited number and specific type of items contained in the PHQ-9. Other studies using LTA on different measures have reported different concepts and symptom-patterns, for example an atypical depression subtype associated with eating disorder and psychotic symptoms (e.g., Rodgers et al., 2014). Outcomes were defined using patient-reported symptom measures, and no formal diagnoses or observer-rated outcomes were available. Furthermore, outcomes could only be defined based on end-of-treatment measures, so the longer-term prognosis of patients with different subtypes remains unclear.

Despite these caveats, the replicated evidence from this and a previous study (Catarino et al., 2020) offer actionable clinical insights. The subtyping algorithm could be prospectively applied to routinely-collected depression scores from new patients starting treatment to classify them according to their latent depression profiles. Patients with depression subtypes that have higher chances of dropout and lower chances of symptomatic improvement could be identified as early as the first therapy session and prioritized for clinical supervision. In particular, patients with somatic depression, who have comorbid illnesses may benefit from integrated care from medical and psychological specialists (Naylor et al., 2016). The present evidence, however, is specific to CBT and the generalizability of these depression subtypes and treatment response patterns to other forms of psychological or pharmacological treatment is unknown. Replications of this method in clinical samples accessing different treatments could help to advance future insights for personalized treatment planning.

5 | CONCLUSION

Replicated evidence indicates that depression is a heterogeneous condition characterized by several subtypes which are stable over time, which are more likely to change in severity but less likely to transition into other subtypes, and which show differential treatment engagement and response patterns.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

In line with the requirements of the ethics review board for this study, requests for access to data are to be made in writing to the corresponding author.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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