Research Article

LATENT CLASSES OF NONRESPONDERS, RAPID RESPONDERS, AND GRADUAL RESPONDERS IN DEPRESSED OUTPATIENTS RECEIVING ANTIDEPRESSANT MEDICATION AND PSYCHOTHERAPY

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Background: *We used growth mixture modeling (GMM) to identify subsets of patients with qualitatively distinct symptom trajectories resulting from treatment. Existing studies have focused on 12-week antidepressant trials. We used data from a concurrent antidepressant and psychotherapy trial over a 6-month period.* **Method:** *Eight hundred twenty-one patients were randomized to receive either fluoxetine or tianepine and received cognitive-behavioral therapy, supportive therapy, or psychodynamic therapy. Patients completed the Montgomery–Åsberg depression rating scale (MADRS) at the 0, 1, 3, and 6-month periods. Patients also completed measures of dysfunctional attitudes, functioning, and personality. GMM was conducted using MADRS scores and the number of growth classes to be retained was based on the Bayesian information criterion.* **Results:** *Criteria supported the presence of four distinct latent growth classes representing gradual responders of high severity (42% of sample), gradual responders of moderate severity (31%), nonresponders (15%), and rapid responders (11%). Initial severity, greater use of emotional coping strategies, less use of avoidance coping strategies, introversion, and less emotional stability predicted nonresponder status. Growth classes were not associated with different treatments or with proportion of dropouts.* **Conclusions:** *The longer time period used in this study highlights potential overestimates of nonresponders in previous research and the need for continued assessments. Our findings demonstrate distinct growth trajectories that are independent of treatment modality and generalizable to most psychotherapy patients. The correlates of class membership provide directions for future studies, which can refine methods to predict likely nonresponders as*

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INTRODUCTION

The designation treatment responder is the prevailing term for a patient who has benefited substantially from treatment. This classification is common in clinical settings as it can inform whether treatment should be terminated, continued, or modified. It is similarly common in research settings, wherein the proportion of treatment responders is used as an index of efficacy. Definitions of treatment response vary, but typically involve a relative reduction in symptoms (e.g. 50% reduction) and/or a reduction in symptoms below an absolute threshold of severity (e.g. scoring under eight on the Hamilton Depression Rating Scale).[1] Existing research suggests that responses to depression treatments vary markedly across individuals. For example, as many as 50% of patients receiving antidepressants can be classified as nonresponders.[2–4] Moreover, a minority of patients (15%) may be rapid-responders, benefiting substantially from only 2 weeks of antidepressants.[3, 5] Similar rates of nonresponders and rapid responders appear in psychotherapy research.[6–8]

The ability to classify patients as likely responders or nonresponders would be remarkably useful to clinical research and practice and would represent a crucial step toward effective personalized medicine. For example, rapid responders could be offered abbreviated therapy, gradual responders could be offered usual treatment, and nonresponders could be offered enhanced treatment. Similarly, researchers could explore the efficacy of aggressive treatments in expected nonresponders and of relatively cost-effective treatments in expected rapid responders. A great deal of research has thus focused on discovering predictors of nonresponse in depression treatments, such as biomarkers,[9] initial severity,[10] dysfunctional attitudes,[11] cooccurrence of other mental disorders,[12] and personality traits[13]; however, the utility of classifying nonresponders is only proportional to the validity of how a nonresponder is defined.

A contemporary method of statistical modeling, known as growth mixture modeling (GMM), can shed light on the latent nature of treatment responses. GMM identifies whether there are subsets of individuals whose growth trajectories are qualitatively dissimilar from that of others. For example, GMM can test whether data are best conceptualized as including one growth trajectory (e.g. most patients experience gradual improvement) or as encapsulating unobserved subpopulations with distinct growth trajectories. Use of GMM can thus evade the traditional and relatively arbitrary definitions of nonresponse (e.g. 50% reduction is a response but not 49%),

thereby increasing the validity of classification and of predictors of class membership. A total of five studies have applied GMM in antidepressant trials,[5, 14–16] with one of these studies also including psychotherapy as a concurrent treatment with medication.[17] All five studies supported the presence of distinct latent growth classes. Three out of the five studies supported the presence of distinct nonresponder and responder classes, one demonstrated responder and rapid responder classes, while results of the fifth study (including psychotherapy) supported three classes of varying severity, but with similar slopes of change.

Despite advances in this field, there exist two salient areas in need of research. First, existing studies have included trials of only 12 weeks. The limited time frames of existing studies may obfuscate important features of growth trajectories. For example, nonresponders may reach standards of response during typical administrations of antidepressants (which go beyond 12 weeks), or some responders at 12 weeks may lose their gains and become nonresponders in the longer term. Second, there is a lack of research exploring growth trajectories in psychotherapy patients. The single study that has explored this matter,[17] while informative, does not generalize well to most settings. The study included only patients with chronic depression lasting over 2 years, made use of a patented and specialized form of psychotherapy (cognitive behavioral analysis system of psychotherapy, not to be confused with cognitive behavioral therapy), and included growth slopes fixed between sessions, precluding conclusions regarding when change occurred.

The current study was designed to address these gaps in existing research. We explored latent growth classes in individuals receiving antidepressants and participating in common forms of psychotherapy over 6 months. Based on previous research, we expected to identify three distinct classes, namely nonresponders, gradual responders, and rapid-responders. We also replicated our analyses using data up to only 12 weeks to compare our findings to previous research and to determine the impact of including data over a period of 6 months. Furthermore, we explored whether preexisting factors (e.g. personality dimensions) predicted class membership. These analyses were deemed exploratory and were not associated with a priori hypotheses.

METHODS

PATIENTS AND TREATMENT

Outpatients were recruited from psychiatric centers in 25 regions near Paris to participate in a multicenter randomized

double-blind study exploring the efficacy of two medications (flu-oxetine [20 mg/day] and tianepine [50 mg/day]) and three forms of psychotherapy (cognitive-behavioral therapy, supportive therapy, and psychodynamic therapy). Eight hundred twenty-one individuals participated and were eligible by presenting with moderate or severe major depressive disorder based on criteria of the diagnostic and statistical manual of mental disorders (DSM-IV)[18] and scores of 20 or higher on the Montgomery–Åsberg depression rating scale (MADRS).[19] Exclusion criteria included present or past psychosis, resistance to two previous pharmacological interventions, hospitalization for electroconvulsive therapy, or a history of drug or alcohol abuse. Patients were also excluded if they were previously treated with an antidepressant in the 15 days before participating, had undergone one of the three methods of psychotherapy in the previous year, or had failed a previous trial of either study medication. Inclusion and exclusion criteria were established by unstructured interviews and chart reviews conducted by the psychiatrists providing treatment. The majority (68.2%) of patients were women and ages ranged from 18 to 66 (mean = 39.74, SD = 10.61).

Four hundred twenty-four patients were randomized to receiving fluoxetine and 397 were randomized to receiving tianepine. Psychotherapy modalities were not randomized; rather, a patient's psychotherapy condition was based on the orientation of the psychiatrist performing the psychotherapy. Two hundred thirty-three (28.4%), 326 (39.6%), and 262 (31.9%) participants received psychotherapy from psychiatrists describing their orientation as cognitive-behavioral, supportive, and psychodynamic, respectively. Four patients (<1%) dropped out within one month, 86 (10%) patients dropped out within 3 months, and 136 (17%) patients dropped out within 6 months. Proportion of dropouts was not associated with type of medication (χ^2 = .80, df = 1, P > .30) or mode of psychotherapy (χ^2 = .24, df = 1, P > .80). The study procedures were approved on ethical grounds by the Institutional Review Board of l'Institut de Recherches Internationales Servier and by the Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale and complied with the Declaration of Helsinki and the Good Clinical Practice Guidelines.

MEASURES

The MADRS[19] was used to assess depression symptoms and to estimate latent growth classes. The MADRS is a 10-item clinician-rated instrument and a score of 10 (inclusive) has been demonstrated as the optimal cut-off for nonresponder status in depression trials.[20] Clinician-rated MADRS scores have been demonstrated as correlating very highly (>.80) with self-report MADRS scores.[21] MADRS scores exhibited good to excellent internal consistency at all time points (αs = .76, .87, .89, and .91).

The following secondary measures were included to characterize the latent growth classes. The single-item clinician-rated global assessment of functioning (GAF)[18] and clinical global impression (CGI)[22] scales were included to assess pretreatment functioning and severity. The dysfunctional attitude scale (DAS),[23] which includes 40 items, was included to assess the severity of preexisting cognitive distortions based on Beck's cognitive model of depression. The coping inventory for stressful situations (CISS)[24] was included to assess preferred coping styles of patients. The CISS includes 61 items describing how individuals react toward difficult situations and assesses proclivities toward task-oriented (e.g. focusing on the problem), emotion-oriented (e.g. feeling angry), and avoidance-oriented coping strategies (e.g. being with others). Higher scores reflect a greater tendency to use a particular coping strategy. Patients also completed the Système de Description en Cinq dimensions (D5D),[25] which includes 55 items assessing dimensions of the five factor personality model, namely openness to experiences, conscientiousness, introversion, agreeableness, and emotional stability (neuroticism). Higher scores on subscales reflect greater levels of the personality traits. Item-level scores were not available for the secondary measures.

ANALYSES

GMM was conducted using Latent Gold 4.5.[1] MADRS scores at month 0, month 1, month 3, and month 6, were used to estimate latent growth classes. Six models were tested, reflecting models with one to six latent growth classes. Model selection was based on the Bayesian information criterion (BIC) and the consistent Akaike information criterion (CAIC).[26, 27] The model with the lowest BIC and CAIC values was retained. BIC values would be given priority in case of a discrepancy between the indices.[26] Modalities of therapy and medication types were not specified in the models. This allowed the potential growth classes to vary freely across treatment groups and identification of whether treatment groups are associated with different growth classes. The six models were tested twice, once without covariates, and a second time with demographic covariates. Demographic covariates included age, sex, education level, marital status, and employment status. Individual heterogeneity within the classes was captured by estimating random effects.

A chi-square test examined whether individuals within different treatment groups exhibited varying odds of belonging to different growth classes. A series of one-way analyses of variance tested whether patients in different growth classes scored differently on variables at intake. Post-hoc analyses (Tukey) tested for differences between pairs of classes. Two chi-square tests examined whether individuals in different growth classes had varying odds of presenting with a cooccurring Axis I disorder or personality disorder. Multinomial logistic regressions were also conducted to determine whether intake variables predict growth classes. Three regressions were conducted using thematically similar predictors. The first regression included MADRS, CGI, GAF, and DAS scores, the second included the three CISS scales, and the third included the five D5D scales.

Lastly, our GMM analyses were repeated using data up to only the 12-week time point. These analyses would allow us to determine how use of a longer 6-month time period influences the estimation of latent growth classes, their relative proportions, and the nature of their growth trajectories.

RESULTS

IDENTIFYING LATENT GROWTH CLASSES

BIC and CAIC values for tested models supported the presence of four latent classes based on the GMM using covariates (Table 1). The classes represented 42, 31, 16, and 11% of the sample. The growth trajectories are displayed in Fig. 1. Patients in the first and largest class experienced on average a 70% reduction in symptoms during treatment. Patients in this class presented with an average MADRS score of 32.12 (SD = 5.06) at intake and approximately 40% of patients scored over 10 on the MADRS at 6 months. For the purposes of this report, this class is characterized as "gradual responders (severe)." Patients in the second class experienced on average an 80% reduction in symptoms during treatment. Patients in this class presented with an average

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[1]The term latent class growth modeling is preferred by the creators of the Latent Gold software; however, "latent class model" and "mixture model" are synonymous. We use the term GMM to be consistent with existing research in this area.

TABLE 1. Model selection criteria for models with different number of latent growth classes

	Selection criteria		Proportion of patients with each class					
Without covariates	BIC	CAIC	1	2	3	4	5	6
1 class	20,580	20,585	100%					
2 classes	19,826	19,837	54%	46%				
3 classes	19,620	19,637	42%	29%	29%			
4 classes	19,527	19,550	44%	30%	16%	11%		
5 classes	19,467	19,496	29%	26%	16%	15%	13%	
6 classes	19,442	19,477	22%	22%	19%	18%	15%	4%
With covariates	BIC	CAIC						
1 class	19,816	19,821	100%					
2 classes	19,178	19,204	53%	47%				
3 classes	19,062	19,109	43%	29%	28%			
4 classes	**19,041**	**19,109**	42%	30%	16%	11%		
5 classes	19,074	19,163	31%	24%	18%	16%	12%	
6 classes	19,155	19,265	27%	21%	18%	17%	10%	8%

Notes: BIC, Bayesian information criterion; CAIC, consistent Akaike information criterion; lowest values indicate best fit and are in bold.
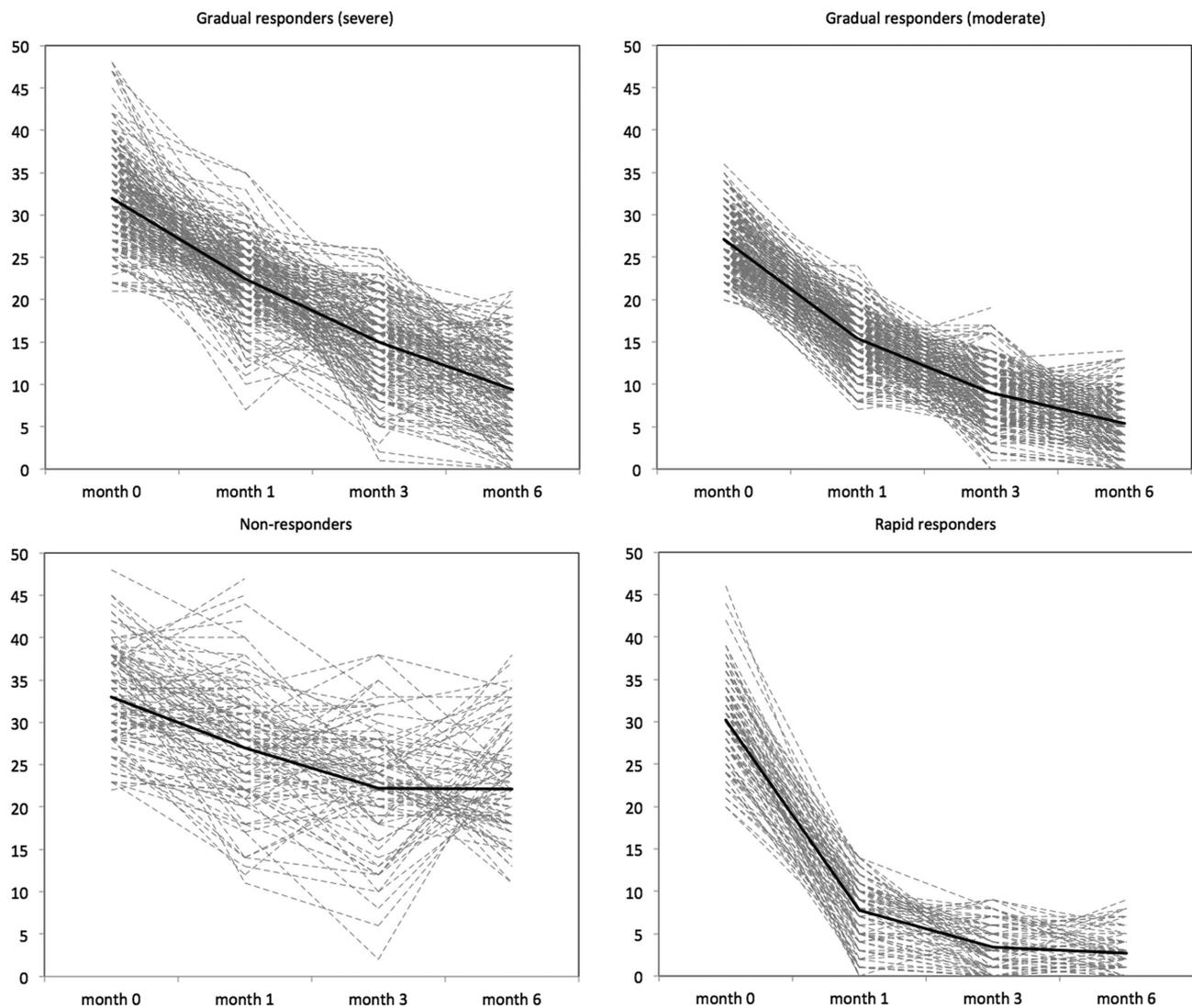
Figure 1. Symptom trajectories of individual patients within each of the growth classes. Bolded lines represent the mean growth trajectory for that class. Y-Axis values represent total Montgomery–Åsberg depression rating scale scores.

TABLE 2. ANOVA results and differences between growth classes on intake variables

	(1) Gradual	(2) Nonresponders	(3) Rapid	F	2 vs. 1 (*d*)	3 vs. 1 (*d*)	2 vs. 3 (*d*)
Intake MADRS	29.91 (5.14)	33.21 (5.55)	30.44 (5.33)	18.86**	.62	—	.51
Intake CGI	4.87 (.59)	5.08 (.58)	4.94 (.58)	6.05**	.36	—	—
Intake GAF	53.76 (9.54)	50.22 (8.34)	56.06 (8.35)	9.87**	−.40	—	−.70
Dysfunctional attitudes	164.37 (34.25)	175.04 (37.17)	154.76 (33.99)	7.73**	.30	—	.57
Emotional coping	55.42 (10.18)	57.61 (10.39)	51.07 (12.39)	8.40**	—	−.39	.57
Task coping	49.11 (11.36)	48.24 (14.25)	54.29 (10.67)	7.01**	—	.47	−.49
Avoidance coping	42.32 (11.33)	39.23 (12.10)	45.84 (13.18)	6.75**	−.26	.29	−.52
Introversion	43.76 (9.48)	47.65 (9.51)	42.74 (8.81)	8.30**	.41	—	.54
Agreeableness	45.38 (8.17)	45.4 (8.43)	48.26 (7.28)	4.53*	—	.37	−.36
Conscientiousness	47.76 (9.89)	47.26 (10.00)	48.41 (8.51)	0.31	—	—	—
Emotional stability	29.39 (8.64)	27.18 (9.54)	32.22 (9.24)	7.29**	—	.32	−.54
Openness to experiences	41.64 (8.93)	38.87 (11.24)	44.21 (9.04)	7.46**	−.27	—	−.53

Notes: **P < .01; *P < .05; cells with a hyphen indicate group differences that did not reach statistical significance in the post hoc test (*P* > .05); standard deviations in parentheses; *d*–Cohen's *d*; MADRS, Montgomery–Åsberg depression rating scale; CGI, clinical global impression; GAF, global assessment of functioning.

MADRS score of 26.97 ($SD = 3.51$) at intake and approximately 5% of patients scored over 10 on the MADRS at 6 months. This class is characterized as "gradual responders (moderate)." Patients in the third class experienced on average a 33% reduction in symptoms during treatment. Patients in this class presented with an average MADRS score of 33.21 ($SD = 5.51$) at intake and 100% of patients in this class scored over 10 on the MADRS at 6 months. Patients within this class shared markedly different growth trajectories and, generally speaking, did not fare well in treatment. This class is characterized as "nonresponders." Patients in the fourth class experienced on average an 88% reduction in symptoms during treatment. Of note, patients in this class experienced on average a 75% reduction in symptoms by the first month. Patients in this class presented with an average MADRS score of 30.44 ($SD = 5.30$) at intake and 0% of patients in this class scored over 10 on the MADRS at 6 months. This class is characterized as "rapid responders."

Model fit criteria best supported the presence of four latent growth classes, but the gradual responders (severe) and gradual responders (moderate) classes shared similar growth trajectories and differed mostly in overall severity (see Fig. 1).[2] Given our focus on preexisting factors predicting treatment trajectories, rather than initial severity, the two gradual responder groups were combined for subsequent analyses. This allowed more interpretable and parsimonious conclusions and conforms with recommendations in interpreting latent classes.[28, 29]

PREEXISTING DIFFERENCES BETWEEN CLASSES AND PREDICTING CLASS MEMBERSHIP

The one-way analyses of variance identified group differences on most intake indices, including intake de-

pression symptoms, clinical global impression scores, global assessment of functioning ratings, dysfunctional attitudes, emotion-oriented coping, task-oriented coping, avoidance-oriented coping, introversion, agreeableness, emotional stability, and openness to experiences. Means on these scores and results of the post-hoc tests are included in Table 2.

The predictors of group membership included in the multinomial logistic regressions are included in Table 3. Intake depression scores predicted nonresponder status relative to gradual responder status and global assessment of functioning ratings and dysfunctional attitudes predicted nonresponder relative to rapid-responder status. Greater emotional coping tendencies predicted nonresponder status relative to both gradual and rapid responder status and lower avoidance coping predicted nonresponder status relative to both gradual and rapid responder status. Greater introversion and lower emotional stability both predicted nonresponder status relative to gradual and rapid responder statuses.

Growth classes did not exhibit different proportions of individuals with a cooccurring Axis I disorder ($\chi^2 = 3.67$, $df = 2$, $P > .15$), but growth classes had different proportions of individuals with a personality disorder ($\chi^2 = 17.62$, $df = 2$, $P < .001$). Individuals from the nonresponder class had 43% greater risk of having a personality disorder compared to the gradual responder class (risk ratio = 1.43 [95% CI = 1.20–1.70]) and 84% greater risk compared to the rapid responder class (risk ratio = 1.84 [95% CI = 1.32–2.57]). The gradual and rapid-responder classes did not seem to differ in terms of proportion of individuals with a personality disorder (risk ratio = 1.29 [95% CI = 0.94–1.76]).

GROWTH CLASSES AND TREATMENT GROUPS AND PATIENT DROP OUTS

Treatment groups were not associated with membership in growth classes ($\chi^2 = 9.93$, $df = 10$, $P > .40$). Moreover, proportion of dropouts was not associated with latent growth classes ($\chi^2 = 4.04$, $df = 2$, $P > .10$).

[2]A repeated-measures analysis of variance supported differences in presenting severity (i.e., MADRS, CGI, and GAF scores) and also supported the relative parallelism (i.e., slope profiles) of the two gradual growth trajectories ($\eta_{g^2} < .01$).

TABLE 3. Independent predictors of class membership resulting from three multinomial logistic regressions

	Gradual responders			Rapid responders		
	B	*SE*	Wald	*B*	*SE*	Wald
1. Initial severity variables						
Intercept	4.21	1.51	7.77**	−0.25	1.94	0.02
Intake MADRS	−0.08	0.03	10.89**	−0.06	0.03	3.15†
Intake CGI	0.01	0.24	<0.01	0.39	0.32	1.48
Intake GAF	0.02	0.01	2.65	0.05	0.02	9.01**
Dysfunctional attitudes	−0.01	0.00	3.21†	−0.02	0.01	11.89**
2. Coping strategies						
Intercept	2.05	0.88	5.42*	−0.64	1.24	0.27
Emotional coping	−0.03	0.01	4.66*	−0.06	0.02	13.70**
Task coping	0.00	0.01	0.06	0.03	0.01	3.36†
Avoidance coping	0.03	0.01	7.66**	0.05	0.01	13.13**
3. Personality dimensions						
Intercept	2.55	1.03	6.08*	−1.97	1.44	1.87
Introversion	−0.05	0.02	10.15**	−0.06	0.02	7.98**
Agreeableness	−0.01	0.02	0.79	0.02	0.02	1.05
Conscientiousness	0.01	0.01	0.33	0.00	0.02	0.00
Emotional stability	0.04	0.01	8.51**	0.07	0.02	13.73**
Openness to experiences	0.01	0.01	0.74	0.03	0.02	2.28

Notes: The reference category is the nonresponder class; †$P < .10$, *$P < .05$, **$P < .01$; MADRS, Montgomery–Åsberg depression rating scale; CGI, clinical global impression; GAF, global assessment of functioning.

IDENTIFYING LATENT GROWTH CLASSES USING OUTCOMES UP TO 12 WEEKS

GMM using only three time points supported the presence of three latent growth classes (BIC for 1, 2, 3, and 4 classes = 15,267; 14,923; 14,911; 14,943, respectively). The classes represented 46, 41, and 13% of patients. The three classes differed from those observed using the four time points. The third and smallest class was similar to the rapid responder class resulting from the first analyses, with patients experiencing on average an 88% reduction in symptoms and 0% of patients reporting a score of 10 or higher on the MADRS at the third time point. In contrast, a nonresponder class was not present in the second GMM analyses. Instead, the two remaining classes can be described generally as gradual responders, but these gradual responders faired poorly compared to those identified in the previous analysis. The classes experienced 45 and 65% reductions in symptoms (compared to 70 and 80% for the gradual responders in the previous analysis) with 88 and 35% of patients scoring higher than 10 on the MADRS at the 3-month point (compared to 40 and 5% at the 6-month point). In essence, the nonresponders described when using the four time points were amalgamated into the two gradual responder classes obtained from using the shorter time period.

DISCUSSION

We examined growth trajectories in depressed individuals participating in 6 months of antidepressant treatment and psychotherapy. Our results add to existing studies supporting the presence of distinct trajectories of patient responses to depression treatments.[5, 14–17] We identified four latent growth classes that occurred naturally in our data. The first two classes included individuals who reported gradual changes in treatment, the third class included individuals who generally did not respond well to treatment, and the fourth class included individuals who responded very rapidly to treatment (i.e. within 4 weeks).

Overall, the majority of patients (approximately 85%) belonged to a class exhibiting a significant reduction in symptoms. In other words, the treatments were at least moderately effective for most patients, even if patients varied markedly in presenting severity. Generally speaking, the gradual change classes reported continued decreases in symptoms until the 6-month point. The continued change is exemplified in the gradual responders (severe) class, such that mean scores declined from 15 to 9 between the 3 and 6-month periods (Fig. 1). Moreover, the rapid responder class maintained its early gains throughout the entire treatment. These patterns subsequent to the 12-week point highlight the importance of longer term assessments in this field. Continued symptom decline suggests that shorter trials might greatly underestimate the proportion of responders in typical treatment settings, and that nonresponders may reach standards of response after continued treatment. Indeed, our analyses using only 12 weeks of data did not demonstrate an independent nonresponder class, but rather supported two gradual responder classes with relatively poor outcome. The longer time period allowed differentiation between individuals who meet a substantial level of nonresponse compared to those who

responded gradually and substantially over time. These results thus highlight the importance of using treatment periods more typical of real-world applications, particularly if using strict cut-off scores (e.g. scoring less than 10 on the MADRS).

Our findings support previous research demonstrating rapid responders to depression treatments.[6–8] Preliminary research suggested that sudden gains in depression treatments may represent a placebo effect,[30] but more recent analyses of medication and psychotherapy trials with placebo controls suggest that sudden gains are likely attributable to pharmacological and psychotherapeutic agents.[31,32] Additionally, our findings are the first to demonstrate that nonresponders and rapid responders in psychotherapy represent unique classes with change trajectories warranting distinction. We believe our findings generalize well to naturalistic psychotherapy treatments given that most clients are also prescribed antidepressants.[33,34] Growth class membership was not associated with type of medication or the psychotherapeutic orientation of the psychiatrists, suggesting that preexisting factors associated with nonresponder status may have played a larger role in observed treatment outcomes than the actual type of treatment.

Our findings suggest that nonresponders are associated with a constellation of preexisting factors. Initial severity, greater use of emotional coping strategies, less use of avoidance coping strategies, introversion, and less emotional stability predicted nonresponder status relative to gradual or rapid responder status. These associations were above and beyond other coping strategies and personality dimensions, underscoring the relative salience of these factors predicting nonresponse. Moreover, nonresponders were more likely to present with a co-occurring Axis II disorder. Our findings suggest that assessment of these variables could assist in predicting likely nonresponders, although future research is needed to identify other salient risk factors associated with nonresponse and how these can be modified to increase efficacy in this group.

Our study has several limitations. First, we included two types of antidepressants and three modalities of psychotherapy, which limits the specificity of our findings. The different types of treatments may include their own unique types growth trajectories, which are not explored in this study; however, since the treatment modalities were not associated with growth class membership, it seems unlikely that they would share markedly dissimilar growth classes. Relatedly, psychotherapies were not manualized or formally standardized that limits the applicability of these findings to standardized applications. Second, our use of four time points is a relatively coarse series of data points over 6 months. Studies exploring weekly depression scores over 6 months or more may unveil that certain growth classes are associated with significant between-session variability. Third, the dropping out of patients and the exclusion of patients could have conceivably influenced the results by preventing the discovery of latent growth classes unique to these subpopulations. Fourth, our use of unstructured interviews may have reduced the inter-rater reliability of the diagnoses. Fifth, the current study did not include a self-report inventory of symptoms, which could have offered an alternative perspective of symptom severity and thus strengthened our conclusions.

Our study supports that gradual responders, rapid responders, and nonresponders in depression treatments represent classes that share qualitatively different growth trajectories. Moreover, our study is the first to demonstrate qualitatively distinct growth trajectories in psychotherapy outcomes. Predicting what patients are likely to be nonresponders would be remarkably useful and we demonstrate that nonresponder status is associated with a constellation of preexisting personality features and coping tendencies. Future research is needed to identify what factors cause certain patients to experience minimal symptom reduction in treatment, and why others get better after only a few weeks. Lastly, our use of a longer time period relative to other studies in this area highlights potential overestimates of nonresponders in previous research. Indeed, our findings support the effectiveness of antidepressants and psychotherapy by suggesting that the vast majority of patients experience at least moderate improvement over 6 months of routine treatment.

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