Modelling Effect: How Treatment Intensity and Duration Impact Depression Recurrence

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Abstract

Background

Optimizing depression treatment intensity and duration is crucial, given an overburdened mental healthcare system. However, decision-making is challenged by heterogeneous treatment effects. We aimed to investigate these effects, accounting for confounders and population heterogeneity, in a real-world dataset from specialized mental healthcare.

Method

The study included 36,946 participants from mental healthcare providers in the Northern Netherlands. We measured the effects of treatment duration and intensity on time to depression recurrence, using monthly costs as a proxy for treatment intensity. An accelerated failure time model was used, adjusting for confounding via entropy weighting. Non-linear effects were examined using restricted cubic splines to identify turning points, after which linear analyses were stratified. Population heterogeneity was explored through K-means clustering analyses, followed by cluster-specific analyses.

Results

In the high-intensity group (above €360/month), a €1000 /month increase in treatment intensity may reduce time to recurrence by 16% (acceleration factor [AF] 0.84, 95% CI 0.77–0.92). Conversely, the same increase in the low-intensity group might prolong recurrence-free time by 9.6-fold (AF 9.6, 95% CI 2.18–42.31). Extending treatment duration by six months may reduce time to recurrence by 7% (AF 0.93, 95% CI 0.89–0.97) in the long-duration group, with no significant effect in the short-duration group. Five clusters emerged, three of which comprised only women, with AFs of 0.67, 0.80 and 0.81, respectively, under high treatment intensity.

Conclusions

Increasing treatment intensity appears worthwhile only in the low-intensity group, though residual confounding remains possible.

Keywords: treatment intensity; real-world data; depression recurrence; individualized treatment.

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Background

Major depressive disorder (MDD) impacts over 300 million people globally[1], increasing the risk of suicide [2, 3] and overall mortality [4], and impairing occupational performance and overall quality of life [5], thereby imposing a high burden on society and healthcare systems [6]. MDD is highly recurrent, with a 60% recurrence rate within five years, 67% within ten years, and 85% within fifteen years [7]. Taken together, these characteristics illustrate the impressive burden of MDD on the mental healthcare system, which is often challenged by insufficient funding and staff. Developing a better understanding of the factors that impact recurrence and finding strategies to reduce this recurrence rate is crucial.

Several risk factors for the recurrence of MDD have been identified, with the baseline severity of an index episode providing the most evidence [8-14]. The severity of the index episode not only predicts recurrence but is also associated with treatment duration [10, 15, 16]. In addition, the chance of having an MDD recurrence is associated with the number of previous episodes [17]. The presence of comorbid psychiatric disorders [7, 9, 10, 18, 19] as well as residual symptoms after treatment [7, 20] also increases the likelihood of recurrence. Ongoing research is exploring other potential factors, such as neurocognitive function [21], cognitive bias [22], and time to clinical response [23]. Evidence regarding the influence of family history, social support, low socioeconomic status and stressful life events is still limited due to methodological constraints [7, 24].

The roles of treatment intensity and duration during the index episode in recurrence have scarcely been studied. Existing evidence [25] reported that longer illness duration before treatment initiation correlates with a higher probability of depressive episodes recurring. Additionally, research has explored how the recurrence rate is affected by the length of maintenance treatment. These studies suggest that while maintenance treatment can reduce the recurrence rate in the short term, extended maintenance treatment may not offer significant long-term benefits [26, 27]. However, these studies did not specifically investigate how the duration and intensity of treatment during the index episode might also influence time to recurrence. One study suggests that a shorter treatment duration of the index episode might lead to a higher risk of relapse and recurrence, but this finding was confounded by the number of previous episodes [28].

Furthermore, heterogeneity among MDD patients complicates treatment [29]. Understanding this heterogeneity, by identifying more homogeneous groups within the depressed patient population is essential, as different subgroups may have varied treatment needs. These subgroups may respond differently to treatments and show varying recurrence patterns [23]. The

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differences among these groups will help shed light on the underlying causes of disparity in treatment outcomes and recurrence rates. Group classifications are typically based on variables such as gender, age, diagnoses, severity of the disorder, the presence of comorbid conditions, and history of suicide attempts [30].

Preventing recurrence of depressive episodes is a central aim of treatment [31]. It is relevant to explore how the intensity and duration of treatment correlate with the time until a depressive episode recurs, both in the whole cohort and within specific subgroups. Such analysis can provide insights for customizing treatment effectively. Insufficient treatment duration or inadequate intensity may fall short of preventing recurrence [28]. Conversely, excessively prolonged treatment duration may not offer additional benefits in preventing recurrence and may potentially strain healthcare resources, leading to increased waiting times for new clients [32].

Our study aimed to analyze how treatment intensity and duration affect time to recurrence using real-world data, adjusting for potential confounders. We also aimed to use cluster analysis to identify subgroups and examine how the effects varied among these groups.

Methods

Study Setting and Data Source

This study used an administrative database containing individual-level data of specialist mental healthcare clients in the northern Netherlands, covering January 2004 to February 2020. Data include demographic and clinical variables, and the results of Routine Outcome Monitoring (ROM) questionnaires filled out by clients, primary diagnostic categories according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) [33], and detailed mental health service utilization.

Participants

The sample included 36,946 clients diagnosed with unipolar depression at the initial assessment. Clients treated for under 30 days or those without pre-treatment ROM scores within ±30 days of initiation were excluded. To ensure a minimum two-year follow-up period for each patient, only those clients whose treatment ended before December 2017 were included. The study was based on pseudonymized administrative healthcare data for which no ethical approval was needed.

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Outcome

The main outcome was time to recurrence of depression, defined as the initiation of a new treatment episode following a 6-month service-free period. This definition has been validated in previous studies using the same Dutch mental health dataset [34, 35]. For clients with multiple episodes, the second-to-last was the index episode; single episodes without recurrence served as the index.

Exposures

Treatment duration, measured in months, was determined by calculating the interval between two dates: the start of the index episode, which is the first face-to-face diagnostic contact of the clients with the clinician, and the date of the last in-person treatment session [36]. Treatment intensity was quantified as the total cost of treatment divided by its overall duration in the index episode. To calculate costs, the service durations of various healthcare professionals were multiplied by their respective unit costs, price year 2019 [37]. These unit costs, based on professional salary levels, were derived from the Dutch costing manual for health economic evaluations [38] and were hence fixed over patients and providers, as the corresponding unit prices detailed in Table S1. Detailed information on service types, contact times, and associated costs is provided in Supplementary Table S2.

Covariates and Measurements

Six covariates adjusted for confounding and cluster classification: baseline severity of the index episode (measured by the Outcome Questionnaire-45, where lower scores indicate better functioning), comorbidity, the number of previous treatment episodes, antidepressant use during the index episode (yes/no), age, and gender. Comorbidity was grouped into three categories: only personality disorders, only other psychiatric conditions (e.g., anxiety, sleep disorders, ADHD), or both, due to the low prevalence of non-personality psychiatric conditions.

Statistical Analysis

We employed the entropy weighting method, assigning weights to covariates based on their importance and variability, to adjust for confounding factors affecting the relationship between treatment intensity, duration, and recurrence [39]. Next, the generalized gamma distribution was selected for modeling time to recurrence based on the Akaike Information Criterion (Table S3) and validated using a 75%-25% training-validation split (Figures S2 and S3). Restricted cubic splines were used to capture

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non-linear exposure relationships, as this approach flexibly identifies dose, response patterns without arbitrary categorization while mitigating overfitting, and also have been applied in the field of depression care before, though during a different treatment phase [40]. Knots were placed at the 25th, 50th, and 75th percentiles, consistent with established practice [40, 41]. Numerical differentiation identified turning points. To facilitate interpretation, we divided the entire population into two groups based on this turning point and applied the model with linear spline to these groups. Specifically, clients with treatment intensity below the turning point were placed in the low-intensity group, while those above were assigned to the high-intensity group. Similarly, treatment durations shorter than the turning point were categorized as the short-duration group, whereas durations exceeding this point were considered the long-duration group. The analysis finally employed a weighted generalized gamma accelerated failure time (AFT) model with entropy weights. As the proportional hazard assumption had been violated, we chose the AFT model to examine the effects of treatment intensity and duration on the time to recurrence[42]. In the AFT model, an acceleration factor (AF) exceeding one signifies an extended time to recurrence, whereas an AF below one indicates a reduced time to recurrence.

Clustering analysis was conducted to address population heterogeneity by identifying clusters. Models were also fitted by clusters to evaluate the clusters' effect of exposure on outcomes. We employed K-means with Gower distance [43] as a clustering technique. Clusters were classified based on five variables, as identified in existing literature: age [7], gender [23], prior treatment episodes (yes/no) [22, 44], comorbidities [7], and baseline severity [7]. The number of clusters was established by iteratively repeating clustering and then selecting optimal clusters based on the Silhouette Width and Within-Cluster Sum of Squares with 100 bootstraps [45].

Sensitivity Analysis

Given the potential selection bias due to the substantial exclusion of data in the main analysis, we employed an imputation approach for handling missing data, where each missing value was imputed using Bayesian linear regression [42], which generates plausible values by sampling from posterior predictive distributions based on observed covariates, thereby preserving both statistical relationships and appropriate uncertainty in the imputed values. Following the imputation process, we re-conducted the analysis on the larger dataset using the imputed data. Additionally, we tested the robustness of our spline models using alternative knot placements (3, 4, and 5 knots) following Harrell's recommendations [41].

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Results

A total of 36,946 clients were diagnosed with MDD between 2004 and 2020. Among them, 27,276 were excluded due to the absence of baseline severity of the index episode, resulting in 6,863 participants included in our study (see supplementary Figure S3). Included participants were significantly younger (average age 41 years) than those excluded (average age 48 years). Over a 10-year follow-up, the included group had a shorter time to recurrence (42.82 months) compared to the excluded group (50.39 months).

Table 1 Baseline Characteristics and Outcome in Included and Excluded Groups

Measures		Included group (N=6863)	Excluded group (N=27,276)	P-Value[1]
Age (mean (SD))		40.33(13.16)	46.80(19.25)	<0.001
Gender-female (%)		3935 (57.30)	16259 (59.60)	0.100
Number of Prior treatment episodes (%)	0	6317(92.04)	25205(92.40)	0.330
	>=1	546(7.960)	2071 (7.600)	
Comorbidities (%)	MDD only	3772 (55.00)	14044 (51.50)	0.090
	MDD and PD	1317 (19.20)	5906 (21.70)	
	MDD and other comorbidities	778 (11.30)	3036 (11.10)	
	MDD, PD and other comorbidities	996 (14.50)	4290 (15.70)	
Total OQ45 at baseline (mean (SD)		88.10(22.00)	NA	-
Time to recurrence (months)		42.82(31.85)	50.39(37.56)	<0.001

MDD: Major Depressive Disorder; PD: personality disorder. [1] statistical comparison between these two group clients were performed with a chi-square test for categorical, with a t-test for numerical variables.

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Figure S4 presents the correlation between six covariates and two exposures before and after entropy weighting. Before adjustment, the severity of the index episode, antidepressant use, and the presence of comorbidities were associated with both treatment duration and treatment intensity, while the number of previous treatment episodes and clients' age were only correlated with treatment intensity. These associations had modest effect sizes.

The linearity assessment revealed a non-linear relationship between exposures and recurrence (Figures S5 and S6). Within the entire cohort, the turning point for treatment intensity is €360/month (Table 2). For clients undergoing treatment above this threshold, referred to as the high-intensity group, the AFT model showed an acceleration factor of 0.841 (95% CI: 0.770–0.918). This indicates that each €1000/month increase in treatment intensity was associated with a 15.9% (95% CI: 8.2%–23.0%) shorter time to recurrence. Conversely, for clients with treatment intensities below this threshold, referred to as the low-intensity group, the AFT model showed a significantly higher acceleration factor of 9.599 (95% CI: 2.177–42.31), suggesting that each €1000/month increase in monthly treatment expenditure was associated with a 9.6-fold longer time to recurrence. Regarding treatment duration, the turning point within the whole cohort was 7.8 months. The long-duration group had an acceleration factor of 0.928 (95% CI: 0.886–0.973), indicating that a six-month extension in treatment duration was associated with a 7.2% (95% CI: 2.7%–11.4%) shorter time to recurrence. No significant association was observed for the short-duration group (Table 3)

Cluster analysis identified five groups (Clusters 1-5). A graphical representation of this analysis is available in Supplementary Figure S7. Variations in the recurrence rates across these clusters are illustrated in Figure 1. Cluster 1 (female clients with depression only) had the lowest recurrence rate at 18%, while Cluster 5 (female clients with MDD, personality disorder, and comorbidities) had the highest at about 60%. Generalized gamma distribution parameters are reported in Table S4.

The AFT models showed that Clusters 1, 4, and 5 had similar patterns to the whole cohort in the high-intensity group (Figure 2), with higher treatment intensity associated with shorter time to recurrence. In contrast, the low-intensity group showed no significant associations. Clusters 2 and 3 showed no significant associations with recurrence time in either group. Cluster 4 had the highest turning point at €500/month.

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Regarding treatment duration, Cluster 1 displayed an AF of 0.868 (95% CI: 0.762–0.988), indicating that longer treatment duration was associated with shorter time to recurrence in the long-duration group. Cluster 5 showed an AF of 2.2 in the short-duration group, suggesting an association with longer time to recurrence. No significant associations with time to recurrence were observed in the other clusters. Cluster 5 had the largest turning point for treatment duration at 11.5 months.

Table 2 The Effect of Treatment Intensity in the complete Cohort and by Cluster

Clusters	Turning point(1000 € /month)	N (Low intensity)	Effect of intensity (1000 € /month 95% CI)	P-value	N (high intensity)	Effect of intensity (1000 € /month 95% CI)	P-value
Whole cohort	0.360	3972	9.599 (2.177–42.31)	<0.001	2891	0.841(0.770–0.918)	<0.001
Cluster 1	0.330	1296	15.20 (0.463–499.9)	0.127	1030	0.669(0.552–0.808)	<0.001
Cluster 2	0.450	582	5.190 (0.471–57.15)	0.179	316	1.031 (0.857–1.241)	0.741
Cluster 3	0.340	1106	19.39 (0.610–616.9)	0.092	821	0.848 (0.664–1.082)	0.186
Cluster 4	0.500	598	5.222 (0.375–72.76)	0.218	248	0.798 (0.638–0.996)	<0001
Cluster 5	0.260	260	8.923 (0.0457–174.4)	0.416	606	0.807 (0.689–0.946)	<0.001

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Table 3 The Effect of Treatment Duration in the complete Cohort and by Cluster

Clusters	Turning point(months)	N (Short duration group)	Effect of Duration (6 months 95% CI)	P-value	N (Long duration group)	Effect of Duration (6 months 95% CI)	P-value
Whole cohort	7.8	2508	1.062(0.649–1.737)	0.810	4355	0.928(0.886–0.973)	<0.001
Cluster 1	7.8	986	1.326(0.536–3.280)	0.540	1340	0.868(0.762–0.988)	<0.05
Cluster 2	7.6	270	0.539(0.136–2.135)	0.332	628	0.957(0.876–1.046)	0.379
Cluster 3	6.0	576	1.346(0.314–5.776)	0.689	1351	0.879(0.768–1.005)	0.059
Cluster 4	6.2	215	0.845(0.086–8.546)	0.268	631	1.090(0.963–1.233)	0.268
Cluster 5	11.5	271	2.211(1.237–3.954)	<0.00	595	0.951(0.876–1.032)	0.225

Results from the sensitivity analysis, conducted on an imputed dataset comprising 34,139 cases, aligned with the findings of the main analysis (Tables S5 and S6). The non-linear relationships for treatment intensity and duration are shown in Figures S7 and S8. Higher treatment intensity in the low-intensity group was associated with extended time to recurrence, while in the high-intensity group, it was associated with shorter time to recurrence. The turning point for treatment intensity in this larger dataset was €340/month for the whole cohort, aligning closely with €360/month from the main analysis.

The turning points of treatment intensity for each cluster ranged from €320/month to €390/month, with Cluster 5 having the highest at €390/month. As in the main analysis, longer treatment duration in the long-duration group was associated with shorter time to recurrence. In the sensitivity analysis, effects were significant across all clusters in the long-duration group, with Cluster 5 showing the largest turning point at 19.5 months. Effects in short-duration groups were not statistically significant. In sensitivity analyses examining knot placement, the non-linear relationship remained stable across all alternative knot placements tested as shown in Figure S9, with turning points ranging from €300-€340/month, closely approximating our main estimate of €360/month.

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Discussion

This study found that increasing treatment intensity may potentially extends the time to recurrence in the group receiving low treatment intensity, after adjusting for confounders. Conversely, for clients in the high-intensity group, an increase in treatment intensity appeared to shorten the time to recurrence. These results suggest a non-linear relationship between treatment intensity and recurrence, which was supported by the linearity check. Our analysis also showed that extended treatment duration reduced the time to recurrence in clients with longer treatment duration, while no significant effect of treatment duration was observed on the time to recurrence in the short-duration group.

To our knowledge, this was the first study to use extensive longitudinal data to explore the effects of treatment intensity and duration on recurrence, accounting for potential confounders, and hence comparisons with similar studies are challenging. Our research found no evidence of an association between extending treatment duration and time to recurrence in the short-duration group, defined as clients with treatment durations below 7.8 months. This finding remains robust even after adjusting for confounders, such as baseline symptom scores. Consistent findings were also observed in a larger, imputed dataset. Additionally, results indicate that for clients receiving treatment at an intensity below the average turning point of €360/month, higher treatment intensity was associated with longer time to recurrence. This observation could be interpreted as suggestive that low treatment intensity in this group may result in residual symptoms, which subsequently lead to rapid recurrence of depressive symptoms [20]. In the high-treatment intensity group, however, further increases in treatment intensity were associated with shorter time to recurrence. This could have at least two possible explanations: first, clients may develop a dependency on the treatment or therapist, leading to increased difficulty in discontinuing treatment, which in turn increases the likelihood of recurrence. Second, the presence of unaddressed confounding factors could also contribute to this outcome.

In the literature, a similar non-linear relationship was observed between the total number of treatment sessions and symptom improvement. Shorter treatments with fewer sessions typically lead to faster improvement, while longer durations result in slower gains. However, the optimal number of sessions, or ‘turning point’, varies across studies, with some suggesting eight sessions as the turning point, beyond which no additional benefit is observed [46-48]. Other studies recommend 10 to 16 sessions [49, 50], while one found the maximum benefit at 25 sessions, noting diminishing returns after that [51]. Despite variations in settings, populations, and outcome measures, these findings support our conclusion that extended treatment duration may not enhance treatment outcome [52].

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Our cluster analysis identified five groups with varying recurrence rates. Cluster 1 had the lowest recurrence rate, likely due to its composition of female clients with MDD, who tend to respond better to treatment [53]. In contrast, Cluster 5 had the highest recurrence rate. This can be ascribed to the complexity of the client profiles within this cluster, which includes individuals with MDD in combination with comorbid personality disorders and other psychiatric conditions, presenting a more challenging scenario to prevent or postpone recurrence [54]. This result is consistent with a previous study [10], indicating that clients with more comorbidities are more likely to experience a recurrence. Notably, our observations indicated a 30% recurrence rate in the entire cohort, lower than the rates reported in prior studies [7]. Two possible explanations for this difference might be: first, the minimum duration of our follow-up period is two years, which raises the possibility that some clients may not have experienced a relapse within this timeframe; second, our definition of recurrence is re-entering the healthcare service provider's system. However, a relapse can also occur during the treatment process and may thus not be identified in our data.

The cluster analysis revealed a non-linear relationship between exposures, treatment duration and intensity, and the time to recurrence. For these clusters consisting of female clients diagnosed with depression, with and without additional comorbidities, or with personality disorders and other comorbid conditions, increasing treatment intensity may be harmful. In the sensitivity analysis, treatment intensity significantly impacted outcomes in all clusters except Cluster 5, following the same trend as the whole cohort. Treatment duration significantly affected outcomes only in Cluster 1 in the main analysis, but extended across all clusters in the long-duration group during the sensitivity analysis, potentially due to the large imputed sample. Cluster 5 had the highest turning points for both treatment duration and intensity, likely due to the complex conditions of clients with multiple comorbidities.

Our results highlight the importance of estimating treatment intensity and duration to determine the optimal treatment strategies for individuals. Clinicians are advised to closely monitor clients, especially individuals diagnosed with depression, personality disorders, and other comorbidities. Although these clients require relatively longer treatment durations and slightly higher intensity to reach their turning point compared to other clusters, there is no evidence that increasing treatment intensity beyond this point prolongs the time to recurrence for this group. Such attention is essential, considering the limited benefits of excessive treatments and the common belief that more comorbidities need more extensive treatment [55]. Effective monitoring and appropriate treatment adjustment are key to enhancing client outcomes. This could also lead to more efficient resource allocation, allowing for shorter waiting times for new clients and improving the overall quality of care.

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Given the pandemic-related shifts in prevalence and service delivery, we next consider the applicability of our findings to current practice in the Netherlands. Our data extend only until February 2020 due to availability; thus, the cohort primarily reflects pre-pandemic care patterns. During the pandemic, depression prevalence fluctuated in line with public health restrictions, and services shifted from face-to-face to tele-mental care. Overall contact volumes were maintained in Dutch large providers [56] during pandemic, and tele-mental care has been shown to achieve outcomes comparable to those of in-person care [57]. Nowadays, a mix of in-person and tele-mental care is provided. We estimate the associations between treatment intensity and duration and time to recurrence adjusting for confounders, with intensity defined as unit costs multiplied by clinician time per month, rather than by the mode of delivery. The therapeutic mechanisms linking treatment intensity and duration to time to recurrence, such as skill acquisition, symptom monitoring, and therapeutic alliance, remain operative regardless of delivery modality [58]. On this basis, we expect the direction and overall pattern of the intensity/duration on recurrence to generalize to current practice, although the turning points of treatment intensity may have shifted after 2020, calling for external validation in post-2020 cohorts.

This study should be seen in light of several strengths and limitations. Firstly, our analyses were not specific to any single treatment modality, but rather included all treatments received, irrespective of treatment type. This reflects that the vast majority of Dutch patients (approximately 95%) receive multimodal care. Additional analyses conducted for the small subgroup of CBT-only patients yielded similar patterns, although these were not statistically significant due to the limited sample size (see Supplementary Figure S10 and Table S7). Secondly, a large number of clients were excluded due to the absence of their baseline severity scores, which are essential to adjust for confounding. Clients who were excluded were, on average, older, but did not differ in other available demographics. The correlation between baseline severity and treatment intensity and duration, as confirmed by the results of entropy balancing weights, aligns with previous research [10, 15]. The outcomes of our sensitivity analysis on the imputed dataset are consistent with our primary analysis, suggesting that the selection bias resulting from the absence of baseline severity scores may not have significantly impacted our findings. It is important to note that we only employed simple imputation to address missing data, as further steps such as confounder correction and cluster identification were also necessary before modeling effects.

Thirdly, the main analysis may not accurately pinpoint the turning point for each individual across the clusters, leading to relatively wide confidence intervals in the low-intensity group. This issue likely arises from the small sample sizes within each

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cluster. To address this concern, we conducted sensitivity analyses using a larger imputed dataset, which not only helped narrow the confidence intervals but also further confirmed the robustness of our model. However, this limitation highlights the need for further research employing more sophisticated methods to determine optimal treatment duration and intensity on an individual basis. Furthermore, residual confounding by baseline depression severity may exist despite OQ-45 adjustment. The low-intensity group could consist of a mix of mild cases, non-adherent patients, and fast responders. Future research should use comprehensive severity measures to separate true intensity effects from selection bias. Additional unmeasured confounders, including genetic factors and neurocognitive functioning, may also have influenced our results. Lastly, our recurrence definition, based on 6-month treatment gaps, may misclassify some dropouts or non-adherent patients as remitted, potentially biasing recurrence estimates in either direction.

Strong points of our study include the unique dataset with a reasonably large sample size of nearly 7,000 individuals, with at least 2 years and up to 10 years of follow-up. This provides insights into long-term recurrence patterns in a real-world context. We observed that recurrence rates and the effects of treatment duration and intensity varied across different clusters after adjusting for confounding, enriching our understanding of the impact of treatment intensity and duration on the time to recurrence. It is noteworthy that, at least in the high-intensity group, further increasing the intensity or duration of treatment may not yield additional benefits and could even be harmful. This insight is helpful for decision-makers aiming to optimize treatment strategies in a cost-effective manner. Nonetheless, these results should be interpreted with caution due to the potential presence of other residual confounding factors. Finally, the generalized gamma distribution for time to recurrence offers relevant input for future studies that need detailed information about the time until depression re-occurs, such as in health economic decision models.

Conclusion

In conclusion, higher treatment intensity was associated with longer time to recurrence in the low-intensity treatment group, even after accounting for confounding factors, suggesting potential value in more intensive treatment. Conversely, in the high-intensity treatment group, greater treatment intensity was associated with significantly shorter time to recurrence, which could indicate that intensity increases beyond this threshold did not offer additional benefits. These observations highlight the importance of matching treatment intensity to suit the specific needs of each client. Moreover, cluster analyses showed variation in how treatment intensity affects time to recurrence across patient subgroups, suggesting that individualized treatment

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approaches warrant further investigation. These findings should be interpreted with caution, as this is an observational study. Despite our efforts to control for all potential confounders, some residual confounding may still be present.

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Conflicts of Interest

All authors have no conflicts of interest to declare.

Data availability statement

Data may be obtained from a third party and are not publicly available. The programming code will be made available upon reasonable request to the corresponding author.

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Figure 1: Cumulative Incidence of Recurrence across Five Clusters

MDD: Major Depressive Disorder; PD: personality disorder; CM: comorbidity

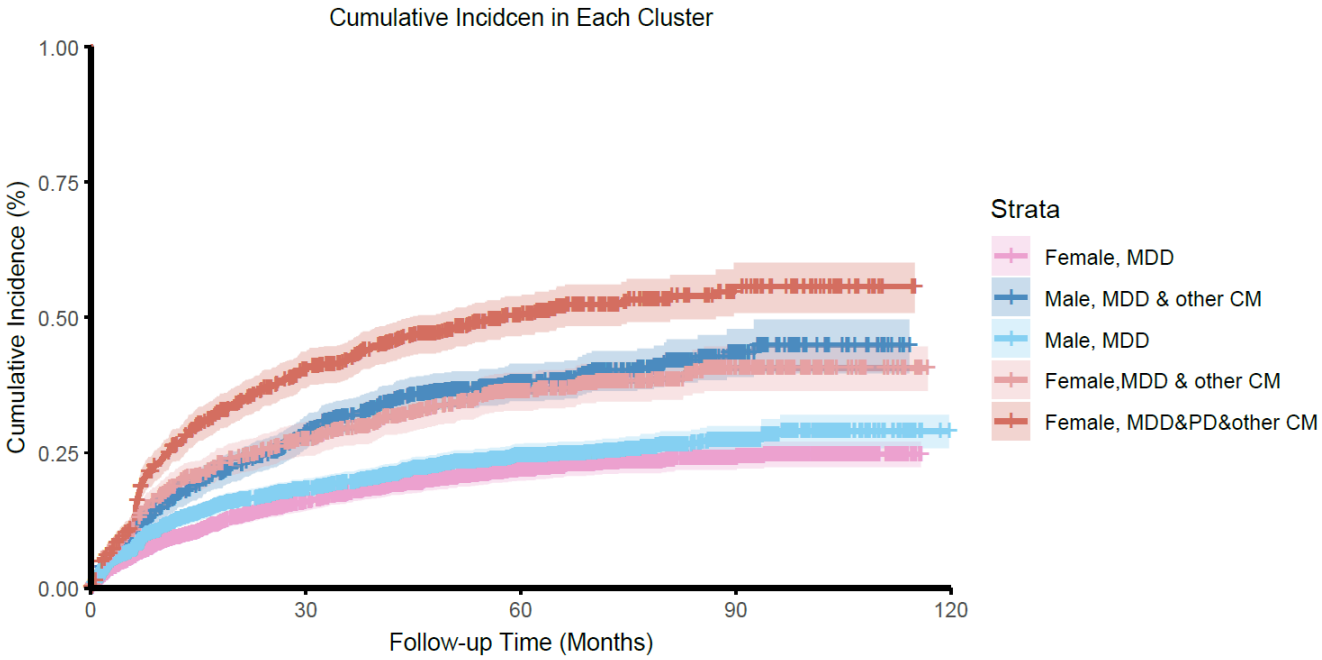

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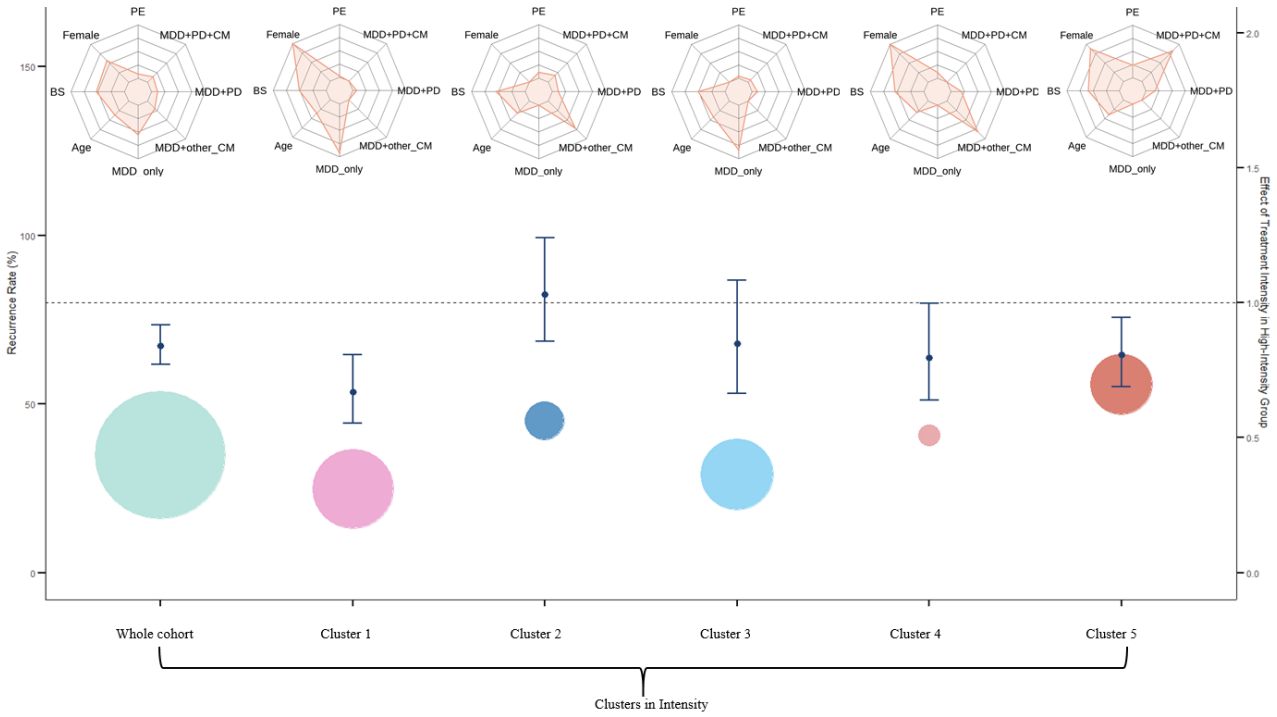
Figure 2 Clustering for Recurrence Rate and Effect Treatment Intensity in High-intensity Group

MDD: Major Depressive Disorder; PD: personality disorder; CM: comorbidity; PE: previous episode; BS: Baseline symptom score



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