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## Staging of Major Depressive Disorder

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## ADDENDUM TO CHAPTER 6

### Preliminary results of analyses applied to the data reported in chapter 6.

I report here preliminary results of analyses applied to the data reported in chapter 6. These analyses will in the future be published in a separate paper on predictors of the course of depression, but as they are relevant for my thesis I would like to report them here briefly. In chapter 6 we showed that the majority of patients have a severely disabling and chronic disorder, when taking a *long, broad* perspective on the course of depression (6-year follow-up, including MDD, dysthymia, (hypo)mania symptoms, anxiety disorders). We wondered what baseline socio-demographics, clinical characteristics (e.g. age at MDD onset, severity of symptoms), and psychological characteristics (e.g. presence of recent life-events, personality characteristic measures like neuroticism) would predict which patients would experience chronic-episodes over follow-up (see addendum Table 1 for the extensive list of predictors examined). Moreover, we wondered whether predictors are better in predicting a shorter than a longer follow-up, and whether predictors differ if we take only MDD diagnoses or also comorbid diagnoses into account. We thus examined predictors for the *short, narrow* perspective (2-year, including MDD only), two *middle* perspectives (2-year, including MDD, dysthymia, (hypo)mania, anxiety disorders; 6-year including MDD only), and the *long, broad* perspective (6-year, including MDD, dysthymia, (hypo)mania, anxiety disorders).

Using a multivariate binary logistic regression with backward LR stepwise procedure, we examined which demographics, clinical or psychological characteristics at baseline predicted who would experience a chronic course trajectories (recurrent with chronic episodes trajectory and consistently chronic trajectory), with non-chronic course-trajectories (recurrent without chronic episodes trajectory + recovery trajectory) being the reference category. To obtain an overall indication of the ability to discriminate between chronic and non-chronic-trajectories, the area under the Receiver Operating Characteristic (ROC) curve was calculated based on the final multivariate models. ROCs between 0.7-0.8 are generally considered as acceptable and between 0.8-0.9 as excellent.<sup>1</sup>

We found similar predictors of a chronic course for all four perspectives: older age, younger age at onset, high depressive symptom severity, and presence of dysthymia. A unique predictor for a chronic course, when the perspective is based on MDD diagnosis only (regardless of 2 or 6-year follow-up), was: longer duration of depressive symptoms prior to baseline. Unique predictors for a chronic course, when the perspective is based on affective- and anxiety diagnoses (regardless of 2 or 6-year follow-up) were: longer duration of avoidance symptoms prior to baseline and the presence of social phobia. No unique predictor for a chronic course was found for the 2-year vs. 6-year perspective (regardless of the MDD only or affective-anxiety inclusion). Finally, there were some predictors of a chronic course that were unique for a certain perspective, those can be found in addendum Table 1.

No differences were found in the ability of the characteristics to predict who will have a chronic episode over a *short, narrow vs. middle, vs. a long, broad* follow-up, which is reflected in the similar C-statistics found for all four perspectives.

Addendum Table 1. Baseline determinants predicting chronicity over 2-year (n=903) and 6-year (n=712) follow-up in multivariate models									
		2-year chronicity of MDD (Figure 1A)		2-year chronicity of affective & anxiety disorder (Figure 1G)		6-year chronicity of MDD (Figure 1C)		6-year chronicity of affective & anxiety disorders (Figure 1I)	
		backward LR <sup>2</sup>		backward LR <sup>2</sup>		backward LR <sup>2</sup>		backward LR <sup>2</sup>	
		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
<b>Sociodemographics</b>									
Age (per 10 year increase)		1.40 (1.18-1.66)	<.001	1.34 (1.15-1.56)	<.001	1.37 (1.16-1.62)	<.001	1.39 (1.18-1.65)	<.001
Sex [male = reference]									
Education (per 1year increase)									
<b>Clinical characteristics</b>									
Age at MDD onset (per 10 yr)		0.76 (0.65-0.89)	.001	0.78 (0.68-0.90)	.001	0.82 (0.70-0.96)	.015	0.81 (0.69-0.96)	.014
Recurrent episodes [1st episode=ref]				0.65 (0.47-0.91)	.011				
Family history of depression [no=ref]									
Severity of symptoms (per SD increase)	depressive (IDS) avoidance (FEAR)	1.76 (1.46-2.12)	<.001	1.65 (1.40-1.95)	<.001	1.72 (1.43-2.08)	<.001	1.71 (1.40-2.08)	<.001
	manic (MDQ)							1.16 (0.98-1.37)	.096
Duration in 4 yr prior to baseline (per 1yr increase)	Depressive	1.06 (1.00-1.13)	.068			1.11 (1.04-1.19)	.002	1.12 (1.06-1.19)	<.001
	Anxiety symptoms							1.10 (1.03-1.17)	.004
	Avoidance			1.10 (1.05-1.15)	<.001				
Treatment [no treatment=ref]	Only AD	0.92 (0.56-1.50)	.723					0.97 (0.61-1.55)	.912
	Only Psychological	1.54 (0.93-2.56)	.094					1.08 (0.67-1.74)	.749
	AD & Psychological	1.52 (0.96-2.40)	.073					1.92 (1.21-3.04)	.006
Comorbidity current [no=ref]	Dysthymia	2.06 (1.35-3.14)	.001	1.92 (1.33-2.78)	<.001	1.85 (1.19-2.86)	.006	1.73 (1.11-2.71)	.016
	GAD								
	Social Phobia			1.83 (1.33-2.53)	<.001			1.51 (1.01-2.24)	.038
	Panic disorder Agoraphobia								
<b>Psychosocial characteristics</b>									
Personality (per SD increase)	Neuroticism								
	Extraversion								
	Openness								
	Agreeableness								
Childhood trauma Index	Conscientiousness								
	Number of negative life-events	1.15 (0.99-1.32)	.061						
<b>Area under the curve (ROC curve) (area &amp; 95% CI)</b>		<b>0.76</b> (0.72-0.79)	<.001	<b>0.76</b> (0.73-0.79)	<.001	<b>0.74</b> (0.70-0.78)	<.001	<b>0.79</b> (0.75-0.82)	<.001

#### Addendum Table 1: preliminary results.

\* Figure 1A, 1C, 1G, and 1I can be found in chapter 6 (page 146) of this thesis.

Abbreviations: AD=antidepressant; FQ=fear questionnaire, GAD=generalized anxiety disorder; IDS=Inventory of Depressive Symptomatology; LR=Likelihood Ratio; MDQ=Mood Disorder Questionnaire; SD=Standard Deviation.

#### Addendum reference

- Hosmer DW, Hosmer T, Le Cessie S, Lemeshow S. A comparison of goodness-of-fit tests for the logisitc regression model. *Stat Med* 1997; 16: 965–980.