Data supplement to Lamers et al. Six-year longitudinal course and outcomes of subtypes of depression. Br J Psychiatry doi: 10.1192/bjp.bp.114.153098

Table DS1 Participation rates at follow-up among groups* (N=1248)

	LCA-based depressive subtypes			Controls	p-value
	Severe melancholic	Severe atypical	Moderate		
N	308	167	173	600	
2-yr follow-up, N (%)	291 (94.5)	155 (92.8)	165 (95.4)	585 (97.5)	0.02[a,b]
4-yr follow-up, N (%)	260 (84.4)	147 (88.0)	158 (91.3)	556 (92.7)	0.001[a,,c]
6-yr follow-up, N (%)	236 (76.6)	132 (79.0)	151 (87.3)	531 (88.5)	<.0001[a,b,c,d]

*Sample (N=1248) consists of persons with a baseline assessment and at least 1 follow-up assessment

[a] C vs Mel p<.05

[b] C vs. Atyp p<.05

[c] Mod vs Mel p<.05

[d] Mod vs Atyp p<.05

Table DS2 Model coefficients psychiatric outcomes

Outcome	MDD[#]	ANX	Suicidal thoughts	QIDS	BAI	Whodas	MDQ
Model	GEE Binomial	GEE Binomial	GEE Binomial	Mixed Linear	Mixed Linear	Mixed Linear	GEE Poisson
Intercept	-0.37*	0.08	-2.43*	9.86*	12.45*	25.42*	1.64*
Group							
Moderate	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Severe Melancholic	0.90*	1.04*	2.10*	5.20*	10.19*	16.37*	0.15*
Severe Atypical	0.75*	0.92*	1.78*	5.24*	8.94*	13.72*	0.11
Time							
0	NA	Ref	Ref	Ref	Ref	Ref	Ref
2	Ref	-0.82*	-0.14	-3.09*	-3.56*	-7.97*	-0.27*
4	-0.24	-0.94*	0.24	-2.50*	-3.03*	-6.89*	-0.22*
6	-0.68*	-1.14*	0.14	-3.37*	-3.11*	-8.51*	-0.72*
Time*group							
2* Severe Melancholic	NA	0.08	-0.51	-1.32*	-2.50*	-2.20	-0.01
2* Severe Atypical	NA	-0.18	-0.87*	-1.86*	-2.92*	-2.83**	-0.02
4* Severe Melancholic	-0.33	-0.29	-0.97*	-2.51*	-3.82*	-5.39*	-0.02
4* Severe Atypical	-0.25	-0.45**	-1.35*	-2.61*	-4.43*	-3.97*	-0.01
6* Severe Melancholic	-0.06	-0.33	-0.95*	-2.04*	-4.08*	-4.46*	-0.06
6* Severe Atypical	0.11	-0.31	-0.79*	-1.87*	-3.24*	-2.94**	-0.15

Reference group=Moderate subtype, NA Not applicable

*p<0.05; **p<0.10; # MDD is modeled without baseline as inclusion of baseline leads to non-convergence of model due to no variance in MDD at baseline (all persons are depressed at baseline).

Table DS3. Model coefficients somatic outcomes

Outcome	BMI	Metabolic syndrome	Num Met Syn criteria
Model	Mixed Linear	GEE Binomial	GEE Poisson
Group	25.03*	-1.46*	0.35*
Control	Ref	Ref	Ref
Severe Melancholic	0.15	0.07	0.06
Severe Atypical	3.27*	0.68*	0.27*
Moderate	0.66	0.02	0.06
Time			
0	Ref	Ref	Ref
2	0.23*	0.11	0.02
4	0.55*	NA	NA
6	0.61*	0.26*	0.09*
Time*group			
2* Severe Melancholic	0438*	0.45*	0.13*
2* Severe Atypical	-0.04	0.12	0.06
2* Moderate	0.03	0.22	-0.02
4* Severe Melancholic	0.66*	NA	NA
4* Severe Atypical	0.07	NA	NA
4* Moderate	0.25	NA	NA
6* Severe Melancholic	0.75*	0.62*	0.17*
6* Severe Atypical	-0.15	0.13	0.06
6* Moderate	0.38**	0.40**	0.09

Reference group=control group
*p<0.05
NA Not applicable

Online supplement DS1

Rationale for using Latent modeling techniques for the identification of depressive subtypes

The high heterogeneity[55–58] of major depressive disorder could potentially imply heterogeneity in aetiology. The origin of existing DSM-specifiers mostly lies in observational research, but a reverse strategy – using symptoms as a starting point – can help to define more empirically based subtypes of depression.[31] Techniques such as latent class analysis (LCA) use such an approach and can evaluate clustering of an observed set of depressive symptoms.

Methods

For the current study we used subtypes derived from LCA. LCA is a data-driven techniques that assumes that an underlying latent categorical variable explains the associations between observed variables (here, depressive symptoms).[38]

We performed an LCA using data from the baseline measurement from the NESDA study.[31] The study sample included 818 persons with current (1 month) MDD (n=743) or minor depression (n=75). As input for the LCA models we used all DSM symptoms of major depressive disorder from the mood section of the Composite International Diagnostic Interview and specific atypical and melancholic

symptoms from the Inventory of Depressive Symptomatology (IDS). The best fitting model was a model with three classes (i.e. subtypes). Based on symptom probabilities, the subtypes were labelled as 'severe melancholic' (prevalence 46.3%) characterised mainly by decreased appetite and weight loss, but also had the highest probabilities on suicidal thought, psychomotor changes and lack of responsiveness, 'severe atypical' (24.6%) characterised mainly by overeating and weight gain, and with the highest probabilities of leaden paralysis and interpersonal sensitivity, and 'moderate' (29.1%) that was characterised by lower symptom probabilities and overall lower severity. Figure DS1 shows the symptom probabilities across classes.

Correlates of Subtypes

We previously reported on the characteristics of the subgroups,[31] showing that in a multivariable comparison of subtypes, atypical depressed persons were significantly more likely to be women than persons with melancholic depression. Those with severe atypical depression further had a higher BMI than those with moderate or severe melancholic subtypes. Persons with severe melancholic depression were more often smokers and had more childhood trauma than other subtypes . Besides a slightly younger age at onset, no differences in clinical characteristics were observed between the severe atypical and severe melancholic subtype, while the moderate subtype had a shorter duration of the depression and a lower percentage of family history of depression.

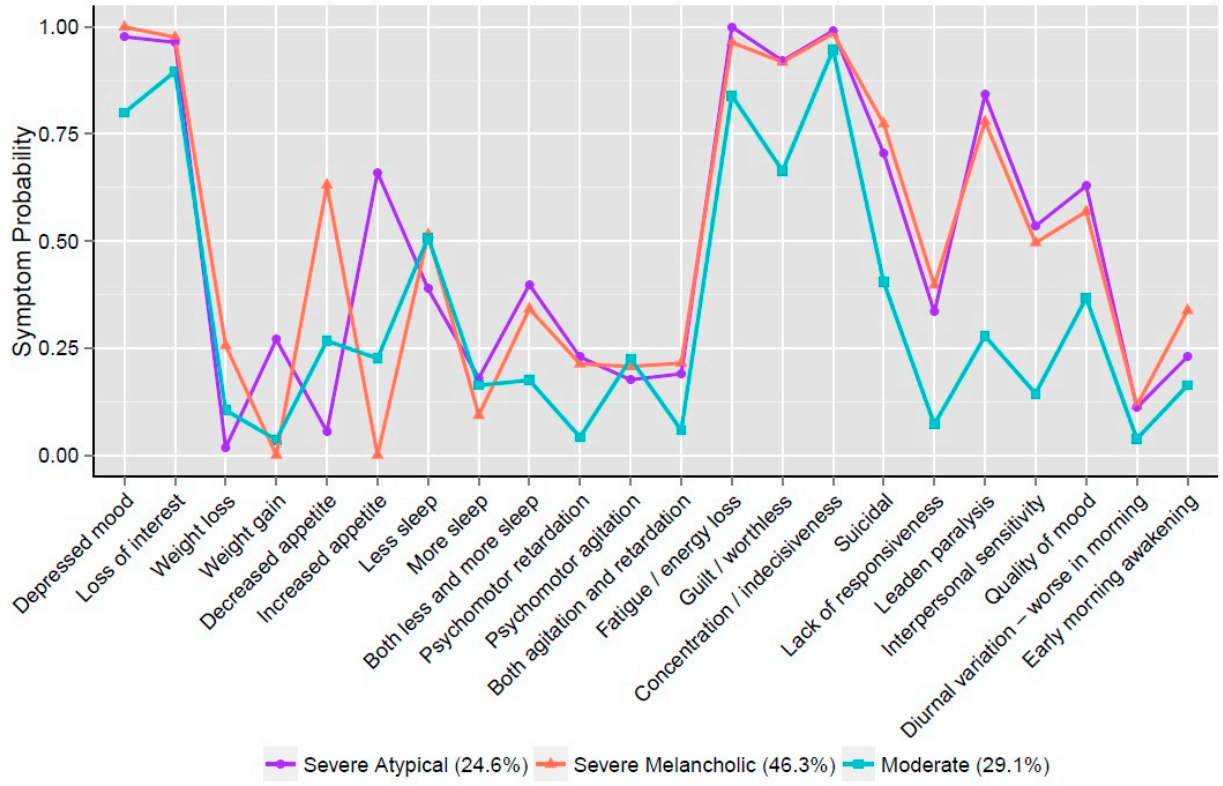

Figure DS1 Symptom profiles in the classes at baseline

(based on Table from Lamers et al. Identifying depressive subtypes in a large cohort study: results from the Netherlands Study of Depression and Anxiety (NESDA). *J Clin Psychiatry* 2010; **71**: 1582-1589.)[31]

Stability

Further evaluation of the stability of the subtypes, using baseline and 2-year follow-up data showed that 76% of the sample endorsed the same subtype at both measurements, indicating that this relatively stability of depressive subtypes.[32]

Additional references

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56 Joyce PR. Classification of mood disorders in DSM-V and DSM-VI. *Aust N Z J Psychiatry* 2008; **42**: 851-62.

57 Klein DN. Classification of depressive disorders in the DSM-V: proposal for a two-dimension system. *J Abnorm Psychol* 2008; **117**: 552-60.

58 Ostergaard SD, Jensen SO, Bech P. The heterogeneity of the depressive syndrome: when numbers get serious. *Acta Psychiatr Scand* 2011; **124**: 495-96.