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Research paper

Outcome of depressive mood disorder among adolescent outpatients in an eight-year follow-up

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ABSTRACT

Objectives: This study investigated the eight-year course and outcomes of depressive mood disorders and the key outcome predictors among adolescent outpatients.
Methods: Depressive adolescent outpatients ($N = 148$) in a naturalistic clinical setting were assessed at baseline, six months, 12 months and eight years using diagnostic and self-report instruments. Baseline predictors covered selected sociodemographic, clinical and treatment-related characteristics. The outcomes were time to recovery, recurrence, time spent being ill and longitudinal latent profiles of depressive symptoms.
Results: The recovery rate from any depressive mood disorder was 73% at two years, 91% at five years and 94% by the end of the eight-year follow-up. Two thirds (67%) of the subjects presented at least one recurrence and 57% of them were depressed for 25% or more of the follow-up period. At the eight-year follow-up, 36% had a mood disorder, 48% suffered from anxiety and 26% had a personality disorder. Less severe depression at baseline predicted a shorter time to recovery, whereas recurrence was predicted by a younger age. A latent profile with initially moderate-level depressive symptoms but a poor distal outcome was associated with being female and borderline personality disorder.
Limitations: The female preponderance in the sample warrants caution when interpreting sex differences in the findings.
Conclusions: Although the depression outcome for some adolescents making the transition to young adulthood is promising, many of them experience long, even chronic episodes, and recurrences are common. Personality-disorder characteristics appeared to be significant outcome predictors in this adolescent population.

1. Introduction

Mood disorders are common among adolescents: one in ten has suffered from such a disorder during the previous 12 months and life-time-prevalence estimates vary between 14 and 18% (Merikangas et al., 2010; Copeland et al., 2011; Kessler et al., 2012; Ormel et al., 2014). Mood disorders are also persistent, mostly in the form of recurrence, and it is common for childhood- and adolescent-onset disorders to recur in adulthood (Kessler et al., 2001; Ormel et al., 2014; Johnson et al., 2018). Although anxiety disorders are more prevalent among adolescents, a larger proportion of mood disorders are considered severe (Kessler et al., 2012; Ormel et al., 2014). They have various effects on young people's lives, including problems in peer and family relations, school performance, and physical functioning (Jaycox et al., 2009; Copeland et al., 2015), and may thus interfere with adolescent's successful transition to adulthood.

The course of adolescent depression varies considerably: for some it is chronic with poor outcomes, whereas for others it is more episodic (Pettit et al., 2009). It has been reported in clinical samples that approximately 90% of depressive episodes have remitted within two years of onset (Birmaher et al., 1996; Zalsman et al., 2006). In a more recent study Melvin et al. (2013) reported recovery rates of 82 and 87% two and four years after study entry, respectively, whereas Curry et al. (2011) found that 96% of their patients recovered within five years. Depression becomes more chronic in between six and 10% of adolescents (Birmaher et al., 1996). Birmaher et al. (2000) found in a two-year longitudinal study that 21% of adolescent outpatients receiving short-term psychotherapy experienced depression during at

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least 80% of the follow-up period. Recurrence rates of up to 40% at two years and 70% at five years have been reported in cases of adolescent depression (Birmaher et al., 1996). More recent clinical studies report recurrence rates of 47% in five years (Curry et al., 2011) and 52% over a mean five-year period (Melvin et al., 2013).

Various predictors of the course and outcomes of severe adolescent depression have been reported. It has been shown in naturalistic clinical populations that longer episode duration is associated with being female, a younger lifetime age at onset, an earlier psychiatric history, episode duration before treatment, level of impairment, and parental psychiatric history (Birmaher et al., 2004; Dunn and Goodyer, 2006; Karlsson et al., 2008). Reported predictors of recurrent episodes include being female, high levels of self-reported depressive symptoms, comorbidity, an older age at the onset of the index episode, parental psychiatric history and personality disorders (Birmaher et al., 2004; Dunn and Goodyer, 2006; Karlsson et al., 2008). Results of treatment studies indicate that a poor outcome in terms of higher depression severity at follow-up is associated with high baseline severity, comorbidity, functional impairment, personality features such as feelings of hopelessness and lower expectations of treatment benefits, an older age, suicidal ideation and self-injurious behavior, and family conflict (Curry et al., 2006; Asarnow et al., 2009). A good response to initial treatment has been found to predict recovery (Kennard et al., 2009; Curry et al., 2011), and self-reported depressive symptoms and anxiety disorder to associate with failure to achieve full remission (Melvin et al., 2013). Predictors of recurrence in these studies included being female, anxiety disorder, non-response to initial short-term treatment, and more severe depressive symptoms (Curry et al., 2011; Melvin et al., 2013).

Adolescent depression is common and impairing. As adolescence is a critical period for attaining key developmental milestones, suffering from a mood disorder during this period might put the successful transition to adulthood at risk. Yet there are only few longitudinal studies on adolescent depression that cover this transitional stage and there is need for more knowledge about the course and outcome of depressive mood disorders during this period. Especially, little is known whether there are different types longitudinal courses of depression from adolescence to adulthood and whether the predictors of these longitudinal course patterns are different from each other. The present paper addresses these knowledge gaps, with the following specific aims:

1) To describe the course and outcome of depressive mood disorder among adolescent outpatients in an eight-year follow-up in a naturalistic clinical setting.
2) To assess baseline sociodemographic, clinical and treatment-related characteristics as predictors of the outcome of depressive mood disorder.

The outcome measures included time to recovery and the number of recurrent episodes. In addition, an outcome measure of total time being ill (due to a mood disorder) during the follow-up was used to assess the total burden of the disorder for the individual, in other words irrespective of whether due to one long index episode or several shorter ones (or both). Finally, in addition to the diagnosis-based outcomes, latent profiles of depressive-symptom scores were analyzed to capture change patterns of depressive symptoms during the follow-up.

2. Methods

This study is part of the Adolescent Depression Study, a longitudinal naturalistic clinical research and development project focusing on depressive mood disorders in adolescence. More detailed descriptions of the participants, procedures and assessments are available elsewhere (Karlsson et al., 2006; Tuisku et al., 2014).

2.1. Subjects

The participants were recruited from outpatient clinics in Peijas Medical Health Care District (PMCD) in Southern Finland, between 1 February 1998 and 31 December 2001. Consecutive adolescents aged 13–19 years were screened for depressive disorders by means of Beck's Depression Inventory (BDI) (Beck et al., 1961) and the General Health Questionnaire-36 (GHQ) (Goldberg, 1972). The screen positives (BDI ≥ 10 and GHQ ≥ 5) who were willing to participate were interviewed using the Schedule for Affective Disorders and Schizophrenia for school-aged children – Present and Life-time (K-SADS-PL) (Kaufman et al., 1997), a semi-structured interview to assess DSM-IV Axis I disorders. The diagnostic interviews were conducted by trained researchers who were also experienced clinicians. The 218 adolescents diagnosed with a current depressive mood disorder formed the original adolescent outpatient study population. Written informed consent was obtained, also from their legal guardians for those aged under 18. The study protocol was accepted by the Ethics Committees of Helsinki University Central Hospital and the Department of Adolescent Psychiatry of the PMCD.

Following the baseline evaluation, the participants were re-evaluated at six-month, 12-month and eight-year follow-up assessments based on structured diagnostic interviews and self-report scales. The median time interval between baseline and the eight-year follow-up evaluation was 8.2 (interquartile range, 1.4) years. Only the 148 subjects who participated in the eight-year follow-up were included in the present study. Of those, 126 also participated in the six-month and 137 in the 12-month follow-up assessments.

All the outpatients received “treatment as usual” of a clinically defined duration in an adolescent psychiatric setting within Finnish secondary healthcare. When the participants turned 20 years of age they could contact adult psychiatric services if needed.

2.2. Measures

Diagnostic interviews were conducted with K-SADS-PL instrument at baseline and six-month and 12-month follow-ups, whereas the SCID-I interview (First et al., 1996) was used at the eight-year follow-up. Personality disorders were assessed at baseline and follow-ups with the Structured Clinical Interview and Screen for DSM-IV Axis II disorders (SCID-II) (First et al., 1997).

Following the diagnostic interviews, diagnoses of major depressive disorder (MDD), dysthymia and bipolar disorder were based on the DSM-IV classification (American Psychiatric Association, 1994). The category of minor depression comprised subjects with a DSM-IV diagnosis of depression not otherwise specified, and adjustment disorder with depressed mood (Karlsson et al., 2006).

The time of onset and the duration were recorded for each depressive episode (including the first life-time episode). MDD was defined as in remission if no symptoms or only one (no depressed or irritable mood or anhedonia) were identified for between two weeks and two months. Recovery was defined as two months of sustained remission (Frank et al., 1991; Emslie et al., 1997). Recurrence was defined as a new depressive episode emerging after the commencement of recovery. The interviewers used probing questions and other means (including graphical representations of depression history) to achieve as accurate a picture as possible of the timing of the episodes, and they coded the diagnoses for each year of the follow-up on a modified version of the coding sheet used in the LIFE interview (Keller et al., 1987).

Comorbid diagnostic categories identified from the interview data included anxiety, substance use, disruptive behavior (comprising conduct disorder, oppositional defiant disorder and ADHD) and eating disorders. A three-category variable (none, borderline and other) was construed for personality disorders. Psychosocial functioning (Global Assessment of Functioning, GAF) was rated according to the DSM-IV Axis V definitions: the GAF score for current status was used in the

analyses.

Severity of depression was measured on the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960), a widely used clinician-rated 21-item scale assessing symptoms of depression. The rating was done by the interviewers as part of the diagnostic interview.

Information on any parental history of psychiatric treatment (yes/no) was obtained from the adolescent and his/her parent based on questions relating to parental use of psychiatric services as well as on clinical records.

Treatment-related information on adolescent outpatients was obtained from the patient records of outpatient clinics and inpatient wards. Intensity of treatment contact/days was calculated by summing up all outpatient contacts and hospital days and dividing by the length of the whole treatment period (from baseline to the last contact). Thus the measure captures the frequency of days the patient had treatment contacts, while no weighting of hospital days vs. outpatient visits was used. There were 25 adolescents with inpatient (in addition to outpatient) treatment and 123 subjects with only outpatient contacts. Information on the use of antidepressant medication (yes/no) was based on the diagnostic interview and patient records. Treatment-related factors covered the first follow-up year from the baseline.

2.3. Outcome measures

The length of the index episode and time to recovery from baseline in weeks were calculated. Of these, time to recovery from baseline was used in the outcome analyses. The number of recurrent mood disorder episodes was recoded in a dichotomized variable (yes/no), and categories of “2 or more” and “3 or more” recurrent episodes were formed and used in additional analyses. The total amount of time spent being ill due to a depressive mood disorder (“time spent depressed”) during the eight-year follow-up was calculated by summing up the lengths of all episodes (in weeks). A dichotomized measure of suffering from mood disorder for 25% or more of the eight-year follow-up time, i.e. more than two years on average, was constructed for the outcome analyses. The 25% / two-year cut-off was considered appropriate as it is in accordance with the minimum total length in the definition of persistent depression (American Psychiatric Association, 2013).

2.4. Attrition

Those lost to attrition between baseline and the eight-year follow-up (n = 70, 32.1%) did not differ from those who remained (n = 148) in terms of sex (χ^2 = 0.19, df = 1, p = 0.665), age (F = 0.96, p = 0.329) or baseline clinical characteristics including depressive disorder diagnosis (χ^2 = 0.33, df = 3, p = 0.954), comorbid anxiety (χ^2 = 0.85, df = 1, p = 0.357), a disruptive (χ^2 = 0.20, df = 1, p = 0.652) or eating disorder (χ^2 = 0.00, df = 1, p = 0.975), the presence of a personality disorder (χ^2 = 0.59, df = 1, p = 0.441), severity of depressive symptoms/HDRS (F = 0.30, p = 0.584) or global functioning/GAF (F = 0.54, p = 0.462). Comorbid substance use disorder was more common among those lost to attrition (24.3% vs. 12.8%; χ^2 = 4.52, df = 1, p = 0.034).

2.5. Statistical analyses

IBM SPSS Statistics 24 and Mplus 7.1 software (Muthén and Muthén, 1998-2012) were used for the analyses.

Time to recovery was analyzed by means of Cox proportional hazards regression, whereas binary logistic regression models were used with regard to recurrent episodes and being ill for 25% or more of the follow-up time. The first analyses included one predictor variable at a time in the model (univariate). The variables with a p-value < 0.10 were then included in the multivariate analysis, conducted using backward stepwise selection method.

The HDRS scores obtained from the psychiatric interviews were subjected to latent profile analysis (LPA) (Gibson, 1959) to enable exploration of the different longitudinal profiles or change patterns of depressive symptoms in the data. LPA is a finite mixture model that can be used to identify homogenous unobserved groups or profiles based on observed variables. The statistical criteria used to determine the best solution (number of profiles) were the Bayesian Information Criteria (BIC) and the Bootstrapped Likelihood Ratio Test (BLRT) (Nylund et al., 2007). Emphasis was also placed on having large-enough group sizes and a clinically relevant interpretation. Once the best solution had been determined, the cases were assigned to the latent profile groups according to their most likely group membership. Logistic regression analyses were then conducted to assess whether the baseline characteristics predicted profile membership.

P-values < 0.05 were considered statistically significant in the analyses, and 95% confidence intervals (CI) were calculated for odds ratios (OR) and Hazards Ratios (HR).

Table 1
Characteristics of the study population (N = 148) and outcomes of mood disorder during the follow-up.

Characteristics	% (N)	
	Baseline	8-year follow-up
Age, mean (SD)	16.5 (1.6)	24.5 (2.0)
Females	82.4 (122)	
Affective disorders		
None	0.0 (0)	64.2 (95)
MDD	79.7 (118)	22.3 (33)
Dysthymia	5.4 (8)	2.0 (3)
Minor depression	8.1 (12)	5.4 (8)
Bipolar disorder	6.8 (10)	6.1 (9)
Comorbidity		
Anxiety disorder	59.5 (88)	48.0 (71)
Substance use disorder	12.8 (19)	9.5 (14)
Disruptive disorder	9.5 (14)	1.4 (2)
Eating disorder	10.1 (15)	6.8 (10)
Personality disorders		
No personality disorder	55.6 (80)	74.0 (108)
Borderline personality disorder	11.8 (17)	5.5 (8)
Other personality disorder	32.6 (47)	20.5 (30)
HDRS, mean (SD)	15.3 (6.8)	5.9 (6.5)
GAF, mean (SD)	52.1 (10.4)	64.2 (15.0)
Age at onset of 1st life time episode, mean (SD)	13.3 (2.6)	
Parental history of psychiatric treatment	44.3 (62)	
Treatment characteristics during the 1st follow-up year		
Treatment contacts/days per month, mean (SD)	4.0 (4.8)	
Use of antidepressant medication	52.7 (78)	

Outcome measures of the 8-year follow-up	
Length of index episode, median (Q1, Q3), weeks	110.8 (56.6, 209.8)
Time to recovery from baseline, median (Q1, Q3), weeks	57.3 (28.0, 113.3)
Number of recurrent episodes,% (N)	
None, index episode only	33.1 (49)
Ongoing index episode / no recovery	*6.1 (9)*
One recurrent episode	29.7 (44)
Two recurrent episodes	25.0 (37)
Three or more recurrent episodes	12.2 (18)
Total time spent ill, median (Q1, Q3), weeks	125.6 (70.6, 250.8)
Time spent ill 25% or more of the follow-up time,% (N)	57.4 (85)

HDRS = Hamilton Depression Rating Scale; GAF = Global Assessment of Functioning.

3. Results

Table 1 presents the descriptive statistics of the study variables. A clear majority of the participants were females, and major depressive disorder (MDD) was the most common mood disorder diagnosis. There were 53 (35.8%) cases with a mood disorder diagnosis at the eight-year follow-up, and anxiety disorders were even more common (48.0%).

Personality disorders were present in 44.4% of the cases at baseline and 26.0% at the eight-year follow-up: of these, 26.6 and 21.1% presented borderline personality disorders at baseline and the eight-year follow-up, respectively. All in all, over two thirds (68.2%) of the participants had at least one psychiatric diagnosis at the eight-year follow-up. Antidepressant medication was prescribed to 52.7% of the adolescent outpatients during the first year of the follow-up.

Median time to recovery after entering the study was 57.3 weeks (Table 1). The recovery rate was 93.9%, although nine subjects had a chronic index episode lasting the whole eight-year study period. The recovery rates calculated for the two- and five-year time points were 72.8 and 90.5%, respectively. The majority (66.9%) had at least one recurrent episode (Table 1). Suffering from a mood disorder for 25% or more of the follow-up time (i.e. at least two years on average) was observed among 85 (57.4%) of the cases.

3.1. Predictors of time to recovery

Of the baseline clinical characteristics, minor depression (compared to MDD), a lower HDRS score, a higher GAF score and a higher age at the onset of the first lifetime mood disorder episode predicted a more rapid recovery from the index episode (Table 2). Fig. 1 depicts the cumulative survival function by the mood disorder diagnosis category. A higher frequency of treatment contacts/days during the first year of follow-up as well as the use of antidepressant medication predicted slower recovery (Table 2). Minor depression (HR = 2.64, 95% CI: 1.35–5.17, $p = 0.005$), GAF (HR = 1.03, 95% CI: 1.02–1.05, $p < 0.001$), frequency of treatment contacts/days (HR = 0.80, 95% CI: 0.66–0.95, $p = 0.013$) and the use of antidepressant medication (HR = 0.62, 95% CI: 0.43–0.88, $p = 0.008$) remained significant in the multivariate analyses. Neither HDRS nor age at the onset of the first mood disorder episode remained significant in the multivariate Cox regression analysis.

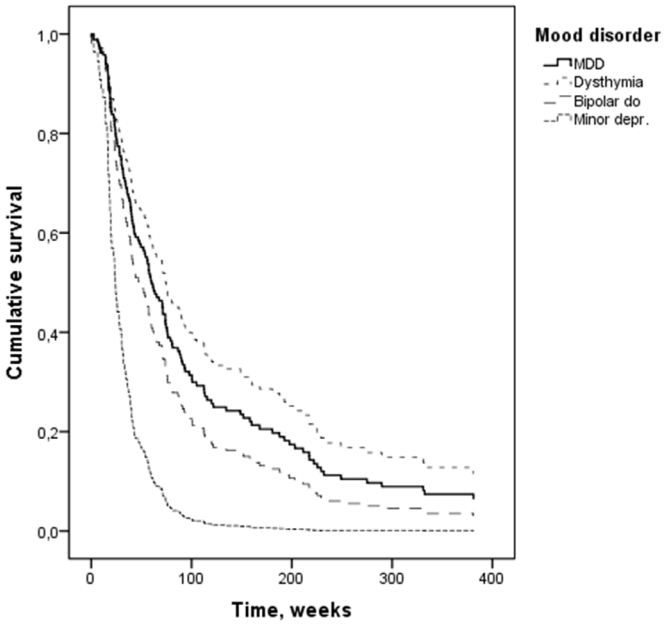

Fig. 1. Time to recovery from index mood disorder episode, from baseline: survival function for mood disorder diagnoses.

3.2. Predictors of recurrent episodes

A younger age was associated with a higher and dysthymia (compared to MDD) with a lower risk of recurrence, although the association was only marginally significant in the latter case (Table 2). Further analyses were conducted for two or more (vs. none) and three or more (vs. none) recurrent episodes: again, the younger age of the respondent was the only significant predictor, being associated with a higher risk of recurrence (results not shown). A younger age remained significant in the multivariate analyses (OR = 0.76; 95% CI: 0.60–0.97; $p = 0.026$),

Table 2
Baseline predictors of time to recovery, any recurrent episode and time spent ill over 25% of the follow-up time: estimates from Cox proportional hazards and logistic regression models.

Predictor variable[a]	Time to recovery		Any recurrent episode		Time spent ill over 25% of the follow-up time	
	HR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age	0.95 (0.86–1.05)	0.295	0.78 (0.62–0.98)	**0.031**	0.92 (0.75–1.13)	0.448
Female	1.06 (0.68–1.66)	0.787	1.97 (0.83–4.66)	0.124	1.19 (0.51–2.79)	0.684
Mood disorder		**0.002**		*0.085*		*0.086*
MDD (ref)	1.00		1.00		1.00	
Dysthymia	0.79 (0.37–1.70)	0.549	0.29 (0.07–1.23)	*0.097*	1.03 (0.23–4.51)	0.971
Bipolar disorder	1.28 (0.65–2.55)	0.477	0.48 (0.13–1.74)	0.261	0.41 (0.11–1.54)	0.186
Minor depression	3.20 (1.75–5.85)	**<0.001**	5.23 (0.65–41.96)	0.120	0.21 (0.05–0.80)	**0.022**
Comorbidity						
Anxiety disorder	0.96 (0.68–1.35)	0.881	0.79 (0.39–1.59)	0.507	1.33 (0.68–2.57)	0.405
Substance use disorder	0.90 (0.55–1.49)	0.691	0.83 (0.30–2.23)	0.711	1.02 (0.39–2.71)	0.965
Disruptive disorder	0.85 (0.48–1.50)	0.569	1.92 (0.51–7.21)	0.336	1.97 (0.59–6.59)	0.273
Eating disorder	0.79 (0.45–1.38)	0.406	0.72 (0.24–2.14)	0.551	1.55 (0.50–4.77)	0.448
Personality disorder		0.278		0.504		0.573
No personality disorder (ref)	1.00		1.00		1.00	
Borderline personality disorder	0.63 (0.36–1.12)	0.118	0.58 (0.20–1.70)	0.318	0.92 (0.32–2.63)	0.877
Other personality disorder	0.88 (0.60–1.27)	0.485	0.71 (0.33–1.53)	0.386	1.44 (0.69–3.03)	0.331
HDRS	0.97 (0.94–0.99)	**0.012**	1.00 (0.95–1.05)	0.879	1.07 (1.02–1.13)	**0.011**
GAF	1.04 (1.02–1.06)	**<0.001**	1.03 (0.99–1.06)	0.158	0.97 (0.94–1.00	**0.037**
Age at onset of 1st episode	1.08 (1.01–1.15)	**0.018**	0.95 (0.83–1.09)	0.459	0.87 (0.76–0.99)	**0.033**
Parental history of psychiatric treatment	0.97 (0.68–1.38)	0.871	0.99 (0.49–2.00)	0.967	1.14 (0.58–2.24)	0.704
Treatment characteristics during the 1st follow-up year						
Treatment contacts/days per month	0.96 (0.92–1.00)	**0.036**	0.98 (0.91–1.05)	0.471	1.07 (0.99–1.16)	0.108
Use of antidepressant medication	0.62 (0.45–0.87)	**0.006**	1.25 (0.63–2.48)	0.524	2.24 (1.15–4.36)	**0.017**

HDRS = Hamilton Depression Rating Scale; GAF = Global Assessment of Functioning.
[a] Univariate analyses, one predictor in the model at a time.

whereas dysthymia was marginally significant (OR = 0.23: 95% CI: 0.05–1.10; p = 0.065).

3.3. Predictors of time spent being ill

Minor depression was associated with a lower risk of suffering from a mood disorder for 25% or more of the follow-up time, whereas a lower GAF score, a younger age at the first lifetime episode, more severe depressive symptoms and the use of antidepressant medication predicted a higher risk (Table 2). Only younger age at the first mood disorder episode (OR = 0.87; 95% CI: 0.76–0.99; p = 0.038) and the use of antidepressant medication (OR = 2.34; 95% CI: 1.18–4.63; p = 0.015) remained significant in the multivariate models.

3.4. Longitudinal latent profiles of HDRS

Latent profiles were analyzed to examine longitudinal change patterns in the HDRS scores from baseline to the six-month, 12-month and eight-year follow-ups. Solutions with between two and five profiles were requested. Of these, the three-profile solution (BIC = 3647.2) outperformed the two-profile solution (BIC = 3668.8; BLRT: $p < 0.001$), whereas the four-profile solution (BIC = 3629.0) was better than the three-profile solution (BLRT: $p < 0.001$) based on statistical criteria. Requesting five profiles did not further improve the statistical outcome (BIC = 3637.9; BLRT: p = 0.082). Although the four-profile solution was statistically better than the three-profile solution, the smallest group was quite small (n = 12) in analytical terms. Given that the main difference between the two solutions concerned the group with a poor distal outcome in the latter (see Fig. 2), splitting it into two groups in the four-profile analysis with only slight and clinically irrelevant differences, the three-profile solution was chosen for the later analyses. Entropy of the three-profile solution was 0.792.

The largest profile started, on average, at a relatively mild level of depressive symptoms (HDRS < 14), improved rapidly and had a good outcome at the eight-year follow-up (Fig. 2). The second-largest profile started, on average, at a moderate level of symptoms, with some decrease initially, but then improvement stopped and the distal, eight-year outcome was poor. The third group had the most severe symptoms at baseline, but with a constant decrease it ended up with low levels of symptoms at the eight-year follow-up assessment.

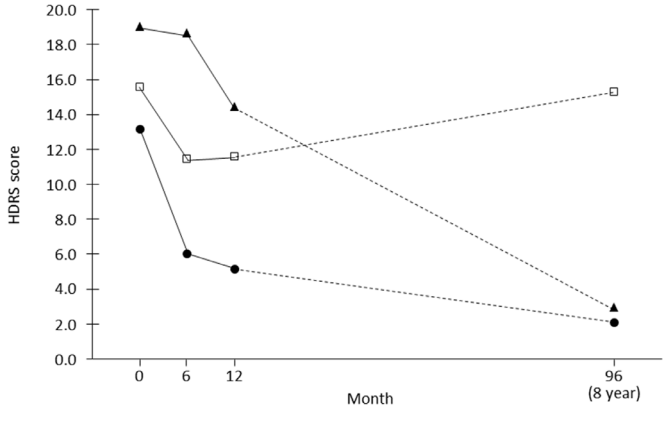

Fig. 2. Three-class solution of latent profiles of HDRS scores at baseline, 6 and 12 months, and at 8-year follow-up.

3.5. Predictors of latent HDRS profiles

As revealed in the univariate logistic regression analyses predicting profile memberships, being female, bipolar disorder (compared to MDD), comorbid anxiety, eating disorders and personality disorders (borderline disorder marginally) predicted membership of the "initially most severe, good distal outcome" profile, with the largest, initially mild profile as the reference group (Table 3). Also a lower GAF, a younger age at the onset of the first mood-disorder episode as well as treatment intensity and antidepressant medication predicted this profile membership. In the multivariate analyses, bipolar disorder, comorbid anxiety and eating disorders, lower global functioning and a younger age at the onset of mood disorder remained significant predictors of the "initially most severe, good distal outcome" profile.

Significant predictors in the univariate analyses of the "initially moderate, poor distal outcome" profile included being female, eating disorder, borderline personality disorder and marginally also a lower GAF (Table 3). Of these, being female and borderline personality disorder were also significant in the multivariate model.

Finally, the "initially moderate, poor distal outcome" profile was analyzed against the "initially most severe, good distal outcome" profile. There were only two marginally significant associations: personality disorder (other than borderline) was associated with a lower risk of belonging to the "initially moderate, poor distal outcome" profile (OR = 0.35; 95% CI: 0.12–1.01; p = 0.052), whereas a higher GAF predicted membership of this profile (OR = 1.05; 95% CI: 0.99–1.11; p = 0.080).

4. Discussion

This study examined the course and outcomes of depression among depressed adolescent outpatients in an eight-year follow-up. The median time to recovery in this clinical population was relatively long, over a year after entering the study. We also observed that the majority of the initially recovered subjects suffered from at least one recurrent episode during the follow-up. Furthermore, the estimated total amount of time lost to depressive mood disorders was high in that most of the subjects experienced at least two years of episodes in total. The majority of participants still had a current psychiatric diagnosis at the end of the follow-up, most commonly an anxiety disorder, and both affective and personality disorders continued to be common. These comorbidities suggest that continuity in psychopathology from adolescence to young adulthood is manifest in both its homotypic and heterotypic forms (Costello et al., 2011).

Our results on recovery rates are well in line with those given in other clinical studies. For example, Melvin et al. (2013) reported a recovery rate of 82% within two years and Curry et al. (2011) reported 96% within five years, corresponding with our respective results of 73 and 91%. Nine (6%) of our subjects had a chronic index episode lasting throughout the whole eight-year study period, whereas 66.9% had at least one recurrent episode. Similar findings have been reported in earlier studies. According to Birmaher et al. (1996), between six and 10% of adolescent depression becomes more chronic, whereas five-year recurrence rates have varied between 47 and 70% among adolescents participating in clinical studies (Birmaher et al., 1996; Curry et al., 2011; Melvin et al., 2013). A majority (57%) of subjects in our study suffered from mood disorder for 25% or more of the follow-up time, whereas Birmaher et al. (2000) reported that 21% of the adolescent outpatients in their two-year longitudinal study were depressed during at least 80% of the follow-up period. Although the figures are not fully comparable in the two studies, the measures of time spent being ill indicate that adolescent depression is a persistent and debilitating condition.

We found that a diagnosis of minor depression, less severe depressive symptoms and better baseline global functioning were associated with more rapid recovery from the index episode and a lower risk of

Table 3
Baseline predictors of longitudinal latent profiles of HDRS: estimates from logistic regression models.

Predictor variable[a]	Initially most severe, good distal outcome (N = 34)[b]						Initially moderate, poor distal outcome (N = 39)[b]					
	Univariate			Multivariate[a]			Univariate			Multivariate[a]		
	OR (95% CI)		p	OR (95% CI)		p	OR (95% CI)		p	OR (95% CI)		p
Age	0.97	(0.75–1.24)	0.800				1.06	(0.83–1.35)	0.644			
Female	4.02	(1.11–14.57)	**0.034**				7.19	(1.59–32.55)	**0.010**	7.43	(1.58–34.96)	**0.011**
Mood disorder			0.159			0.116			0.628			
MDD (ref)	1.00			1.00			1.00					
Dysthymia	0.91	(0.17–4.99)	0.911	0.34	(0.03–4.71)	0.424	0.36	(0.04–3.19)	0.357			
Bipolar disorder	6.81	(1.29–36.00)	**0.024**	12.84	(1.36–120.96)	**0.026**	1.79	(0.24–13.29)	0.570			
Minor depression	n/a			n/a			0.60	(0.15–2.36)	0.460			
Comorbidity												
Anxiety disorder	3.96	(1.54–10.21)	**0.004**	4.67	(1.45–15.04)	**0.010**	1.64	(0.75–3.61)	0.217			
Substance use disorder	0.41	(0.08–1.97)	0.263				1.42	(0.50–4.08)	0.513			
Disruptive disorder	1.30	(0.35–4.76)	0.697				0.81	(0.20–3.32)	0.769			
Eating disorder	5.14	(1.20–21.99)	**0.027**	28.71	(2.14–385.08)	**0.011**	4.36	(1.03–18.53)	**0.046**			
Personality disorder			**0.002**						**0.049**			**0.049**
No personality disorder (ref)	1.00						1.00			1.00		
Borderline personality disorder	4.08	(0.93–17.91)	*0.062*				4.30	(1.25–14.77)	**0.021**	3.95	(1.11–14.12)	**0.034**
Other personality disorder	5.40	(2.09–13.94)	**<0.001**				1.90	(0.77–4.70)	0.168	2.33	(0.88–6.13)	*0.087*
GAF	0.93	(0.89–0.97)	**0.001**	0.93	(0.88–0.99)	**0.026**	0.97	(0.93–1.00)	*0.067*			
Age at onset of 1st episode	0.82	(0.69–0.97)	**0.019**	0.78	(0.63–0.97)	**0.025**	0.95	(0.82–1.10)	0.504			
Parental history of psychiatric treatment	0.61	(0.25–1.47)	0.269				0.83	(0.37–1.84)	0.641			
Treatment characteristics during the 1st follow-up year												
Treatment contacts/days per month	1.10	(1.01–1.20)	**0.025**				1.03	(0.94–1.13)	0.496			
Use of antidepressant medication	3.94	(1.62–9.60)	**0.003**				1.84	(0.84–4.02)	0.128			

HDRS = Hamilton Depression Rating Scale; GAF = Global Assessment of Functioning.
[a] Including variables with $p < 0.10$ in univariate models; using backward selection method.
[b] HDRS profile of initially mild, rapid decrease, good distal outcome (N = 75) as a reference group.

being depressed over two years of the follow-up period. Milder and less debilitating depression has been shown to predict better outcomes in earlier follow-up studies on adolescent depression (Curry et al., 2006; Asarnow et al., 2009; Melvin et al., 2013). We also found that more frequent treatment appointments and the use of antidepressant medication were associated with slower recovery. Although this finding might, at first sight, seem counterintuitive, it probably merely indicates the proper use of treatment modalities: those with more severe conditions and relatively slower treatment response have been offered more intensive treatment and/or medication when appropriate (see also below). An earlier age at the onset of the first lifetime episode was a risk factor for taking longer to recover and being depressed for over 25% of the follow-up time. This accords with previous findings: Lewinsohn et al. (1994) reported that earlier depression among community adolescents (at or before the age of 15) was associated with longer episode duration, whereas Dunn and Goodyer (2006) found that early psychiatric episodes predicted a longer time before remission. A younger age among the adolescents was the only factor in the present study to predict recurring episodes. This was somewhat surprising, given findings from earlier research that an older age at the onset of index episodes (Birmaher et al., 2004), in addition to many other factors including being female, depression severity, comorbidity and personality disorder, predict recurrent episodes (Birmaher et al., 2004; Dunn and Goodyer, 2006; Karlsson et al., 2008).

To complement the diagnosis-based analysis we used longitudinal latent profiles of depressive symptoms to get a more comprehensive view of the course of adolescent depression. The profile analyses indicated that the majority of participants belonged to groups with a good eight-year outcome of depressive symptoms. As such, this finding could be considered good news. Whereas the largest group seemed to have mild to moderate symptoms at baseline, rapid improvement and a relatively short time to recovery, the other latent group with a good distal outcome was the one presenting the most severe depressive symptoms at baseline. Moreover, many of the baseline clinical characteristics, including comorbid anxiety and eating disorders, as well as functional impairment, predicted membership of this profile group, further indicating the severity of its clinical presentation. Perhaps the severity, along with slower recovery, had also instigated more intensive treatment in that more frequent appointments and the use of antidepressant medication were associated with this profile. This finding, again, indirectly implies that these treatment modalities had been in place, and possibly also contributed to the good distal outcome. These results are in line with the notion that the long-term outcome of depression cannot always be predicted by a short-term response (Curry et al., 2011), indicating that long follow-up periods are essential to achieve a fully comprehensive understanding of the phenomenon.

Our findings point to the existence of a relatively large subgroup of depressed adolescents whose depressive symptoms seem to endure or persist in the long run, although appearing to improve at first. There were no baseline characteristics that differentiated this profile from the profile with severe symptoms and a good long-term outcome, although the absence of significant findings might have been attributable to the small sizes of the groups and thus a loss of statistical power. Compared to the largest profile with milder symptoms, being female was the most prominent predictor of this profile of a poor distal outcome. This is in line with previous research indicating that being female is associated with a longer time to recovery and with recurrent episodes (Birmaher et al., 2004; Dunn and Goodyer, 2006). However, there are also findings suggesting that being male is a risk factor for a more chronic course of depression (Dunn and Goodyer, 2006; Melvin et al., 2013).

We have reported earlier that a poorer depression outcome at a one-year follow-up was associated with a personality-disorder diagnosis (Strandholm et al., 2014). The present paper extends this finding beyond adolescent years into early adulthood. By indicating the longitudinal latent depressive symptom profiles our analyses were able show that personality disorders were associated with both of the two more severe profiles. The role of personality disorders was not found in the more traditional analyses of time to recovery and recurrent episodes, indicating further that different types of analyses can shed light

on different aspects of the same data. Especially the role of borderline personality disorder was emphasized in that it was the only other (in addition to female sex) significant baseline predictor of the poor-outcome profile that prevailed in the multivariate analyses, while it was also associated (albeit only marginally significantly) with the other severe profile with good distal outcome. Previous research indicates that borderline personality disorder may disturb the key developmental processes of identity formation and may be associated with poor psychosocial functioning during adolescence (Pinto et al., 1996; Wright et al., 2016). These problems, in turn, might lead to continued or exacerbated mental health problems in the future (Boden et al., 2008). This suggests a possible mechanism through which a comorbid borderline personality disorder might delay recovery from depression. Indeed, reciprocal effects between borderline personality disorder and major depressive disorder, delaying each disorder's time to remission, have been reported among adults in a 10-year follow-up (Gunderson et al., 2014).

4.1. Methodological considerations

The eight-year long follow-up period covering the major transitional period from adolescence to young adulthood is one of the strengths of our study. The assessments were also comprehensive and based on well-established interview instruments, observer-rated and self-report scales in a sample of consecutively referred adolescent outpatients. The study population was relatively small, however, precluding some possibly relevant subgroup analyses. The clear female preponderance in our sample warrants caution in the interpretation of sex differences in our findings. As the follow-up data collection was conducted between 2007 and 2009, replicating our findings in a more recent sample would be advisable. Some of the measures used were relatively crude, e.g. the category of “other personality disorder” included all personality disorders other than borderline personality disorder and thus might not be as meaningful as the specific diagnostic categories.

The seven-year time interval between the last two follow-ups is longer than optimal for an accurate description of the course of a mood disorder. The type of interview method we used (e.g., using timeline and asking probing questions about key life events) has been used in previous studies (Dunn and Goodyer, 2006; Pettit et al., 2009; Melvin et al., 2013). Moreover, the relatively small differences in recovery and recurrence rates between our and other studies imply reasonably accurate recollection of past depression episodes. However, the long interval warrants caution in interpreting results relating to the number of episodes or amount of time being ill, for example. Similarly, the latent profiles of depressive symptoms are only indicative regarding the last time interval – they should be treated as patterns of states that were observed at the available measurement points, not as suggesting that depressive symptoms developed linearly between the assessments.

5. Conclusions

The outcome of adolescent depressive mood disorders in young adulthood seems promising in that almost all subjects recover at some point. For many, however, the episodes are long, even chronic, recurrences are common, and the proportion of illness time attributable to depression is considerable. Our analyses also identify a subgroup of cases for whom the distal outcome is poor, even if they seem to respond rather well in the first months after study entry. Comorbid diagnoses and heterotypic continuity of depression seem prevalent among depressed adolescent outpatients as they move into young adulthood.

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CRediT authorship contribution statement

Olli Kiviruusu: Formal analysis, Writing - original draft, Writing - review & editing. **Thea Strandholm:** Investigation, Writing - original draft, Writing - review & editing. **Linnea Karlsson:** Conceptualization, Investigation, Writing - review & editing. **Mauri Marttunen:** Conceptualization, Funding acquisition, Supervision, Writing - review & editing.

Declaration of Competing Interest

The authors declare no conflict of interest.

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Supplementary materials

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