



Supplementary Material

Article Title: A New Empirical Definition of Major Depressive Episode Recovery and Its Positive Impact on Future Course of Illness

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DOI Number: 10.4088/JCP.15m09918

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Supplementary eTable 1
Classification of Depressive Symptom Severity Levels
Based on Weekly Psychiatric Status Ratings (PSRs) across All Depressive Conditions^{a,b}

Depressive Symptom Severity Level	Major Depression (6-Point PSR Scale) ^c	Minor Depression (3-Point PSR Scale) ^d	DSM-III Depressive Conditions ^a (3-Point PSR Scale) ^d
1. Asymptomatic – No depressive symptoms of the episode; return to usual self	1	1	1
2. Subsyndromal (SSD) level - Depressive symptoms below the MinD/Dysthymia level	1 1 2	1 2 1 or 2	2 or 3 (Any) ^e (Any)
3. Depressive symptoms at the MinD/Dysthymia level	1 2 3 4	3 3 (Any) (Any)	(Any) (Any) (Any) (Any)
4. Depressive symptoms at the MDE level	5 6	(Any) (Any)	(Any) (Any)

Footnotes for Supplementary eTable 1:

- a. Weekly symptom severity level is assigned based on each week's ratings on all depressive conditions, regardless of whether the patient was in a Research Diagnostic Criteria (RDC) episode at that time. Rated affective conditions include RDC major depressive episode (MDE); RDC minor or intermittent depressive episode, long-term (dysthymic) or short-term (MinD); and DSM-III Atypical Depression (code 296.82) and Adjustment Disorder with Depressed Mood (code 309.00). Weekly depressive symptom severity levels 1-4 are mutually exclusive.
- b. Read across the table for combinations of PSR values that result in classifying a particular week at a given symptom depressive severity level. For example, a patient would be classified at the minor depression/dysthymia level for a given week if they were rated as PSR 3 or 4 on the 6-point major depression scale, or PSR 3 on the 3-point minor depression/dysthymia scale with a PSR 1 or 2 on the 6-point major depression scale.
- c. 6-Point Weekly Psychiatric Status Rating Scale values: 1 = asymptomatic, returned to usual self; 2 = residual/mild affective symptoms of the episode; 3 = partial remission, moderate symptoms or impairment; 4 = marked/major symptoms or impairment; 5 = meets definite criteria without prominent psychotic symptoms or extreme impairment; 6 = meets definite criteria with prominent psychotic symptoms or extreme impairment.
- d. 3-Point weekly Psychiatric Status Rating Scale values: 1 = asymptomatic, returned to usual self; 2 = meets probable criteria (mild symptoms, below those for meeting definite criteria); 3 = meets definite criteria.
- e. "(Any)" indicates any PSR value of this affective condition qualifies for the given symptom severity level, in conjunction with the values shown for other depressive conditions. For example, a given week is classified at the MDE level based on a PSR value of 5 or 6 for MDE, regardless of PSR values on any other depressive condition.

Supplementary eTable 2
Psychosocial Functioning/Impairment Associated with
Asymptomatic Recovery vs. Residual Subsyndromal (SSD) Depressive Symptom Resolution of Index MDE

Psychosocial Functioning/Impairment Variables ^a	Asymptomatic Recovery (N=197)		Residual Symptom (SSD) Resolution (N=125)		Significance		
	Mean (sd)	N	Mean (sd)	N	t	df	P
Adolescent Friendship Patterns ^a	2.90 (0.87)	197	3.20 (0.91)	124	-2.94	319	0.004
Worst Level of Overall Functional Impairment in Intake Episode (due to Psychopathology) ^b	3.44 (1.20)	197	3.81 (1.08)	125	-2.78	320	0.006
<u>Best Level in 5 Years Prior to Intake:^c</u>							
Work ^d	1.58 (0.88)	175	2.04 (1.24)	103	-3.27	276	0.001
Household Duties ^d	1.67 (0.75)	180	1.90 (0.80)	120	-2.57	298	0.011
Relationship with Spouse/Partner ^e	1.96 (1.02)	139	2.12 (1.04)	80	-1.12	217	0.264
Relationship with Children ^e	1.72 (0.74)	119	2.04 (0.87)	74	-2.72	191	0.007
Relationship with Friends ^e	1.91 (0.85)	196	2.15 (0.94)	125	-2.40	319	0.017
Enjoyment of Recreation/Hobbies ^e	1.84 (0.87)	196	2.07 (0.91)	125	-2.28	319	0.023
Subjective Satisfaction/Contentment ^e	1.99 (0.89)	196	2.26 (0.88)	125	-2.62	319	0.009
Overall Rating of Social Adjustment ^d	2.16 (0.91)	196	2.52 (0.87)	125	-3.55	319	<0.001
<u>Mean Level during Long-Term Follow-Up, after Start of First Well Interval:^f</u>							
Work ^d	1.96 (0.86)	161	2.82 (1.33)	96	-5.69	142.98*	<0.001
Household Duties ^d	2.08 (0.57)	173	2.33 (0.58)	105	-3.60	276	<0.001
Relationship with Spouse/Partner ^e	2.06 (0.84)	127	2.20 (0.83)	65	-1.10	190	0.272
Relationship with Children ^e	1.89 (0.65)	127	2.27 (0.85)	75	-3.31	125.5*	0.001
Relationship with Friends ^e	2.24 (0.83)	176	2.68 (0.83)	107	-4.38	281	<0.001
Involvement in Recreation/Hobbies ^e	2.12 (0.75)	176	2.64 (0.75)	107	-5.64	281	<0.001
Subjective Satisfaction/Contentment ^e	2.31 (0.71)	175	2.89 (0.69)	107	-6.70	281	<0.001
Overall Rating of Social Adjustment ^d	2.34 (0.78)	176	2.94 (0.77)	107	-6.30	281	<0.001
Mean Level during Long-Term Follow-Up ^g	N (%)		N (%)		χ^2	df	P
Very Good or Good	114 (64.8)		33 (30.8)				
Fair	49 (27.8)		49 (45.8)		33.60	2	<0.001
Poor or Very Poor	13 (7.4)		25 (23.4)				

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Footnotes for Supplementary eTable 2:

- a. From Schedule of Affective Disorders and Schizophrenia (SADS) item 539 at intake, with rating values 1='superior'; 2='very good'; 3='good'; 4='fair'; 5='poor'; 6='grossly inadequate'.
- b. From SADS item 465 at intake, with rating values 1='none'; 2='minor'; 3='significant effects'; 4='important modifications'; 5='major modifications'; 6='major disruption'.
- c. From LIFE Base interviews, with ratings as indicated per item.
- d. Rating values 1='no impairment – high level of function'; 2='no impairment – satisfactory level of function'; 3='mild impairment – mild difficulty in carrying out these activities'; 4='moderate impairment – considerable difficulty in carrying out these activities'; 5='severe impairment – virtually unable to carry out these activities' (or not doing so at all due to psychopathology).
- e. Rating values = 'very good'; 2='good'; 3='fair'; 4='poor'; 5='very poor'.
- f. Psychosocial assessments of worst level of function were made for each month during follow-up years 3-5, and for the last month (only) of follow-up years 6 to 31, using variants of the original LIFE interviews. Mean per-subject level of impairment was calculated based on monthly ratings after the start of asymptomatic recovery or SSD resolution of the index MDE.
- g. Based on mean per-person rating across rated months during long-term follow-up, where mean ≤ 2.50 ='very good or good'; mean >2.50 and ≤ 3.50 ='fair'; and mean >3.50 ='poor or very poor'.

Supplementary eTable 3 (Page 1 of 3)
Median Time (Weeks) to First Depressive Relapse/Recurrence
Based on Each of 18 Clinical Variables, within Groups Defined by
Asymptomatic Recovery vs. Residual Subsyndromal (SSD) Depressive Symptom Resolution
from Index MDE^a

Clinical Variable		Asymptomatic Recovery (N=197)		Residual Symptom(SSD) Resolution (N=125)	
1. Sex	Group [N] Mdn Wks. Well (95% CI) Signif.	Male [86] 192 (107-243)	Female [111] 108 (83-150) P=0.161	Male [43] 30 (20-42)	Female [82] 32 (24-8) P=0.962
2. Early Onset (Before Age 21)	Group [N] Mdn Wks. Well (95% CI) Signif.	Not Early [140] 149 (102-214)	Early [57] 108 (62-192) P=0.082	Not Early [77] 35 (29-43)	Early [48] 24 (18-32) P=0.004
3. Lifetime Number of Affective Episodes (Including Index MDE)	Group [N] Mdn Wks. Well (95% CI) Signif.	1-3 [155] 150 (111-227)	4 or More [42] 62 (36-107) P<0.0001	1-3 [84] 34 (25-42)	4 or More [41] 28 (19-36) P=0.422
4. Chronicity of Index Episode (Total Duration \geq 2 Years)	Group [N] Mdn Wks. Well (95% CI) Signif.	Not Chronic [127] 197 (131-269)	Chronic [70] 108 (59-209) P=0.244	Not Chronic [56] 34 (23-43)	Chronic [69] 30 (23-42) P=0.474
5. Severity of Index Episode (Global Assessment of Severity Score \leq 40 for Worst Period in Episode, Prior to Intake)	Group [N] Mdn Wks. Well (95% CI) Signif.	Not Severe [81] 131 (84-208)	Severe [116] 135 (93-219) P=0.987	Not Severe [44] 38 (25-46)	Severe [81] 30 (22-36) P=0.393
6. Comorbid Anxiety Disorder at Intake (Generalized Anxiety, Phobic, Panic, or Obsessive/ Compulsive Disorder)	Group [N] Mdn Wks. Well (95% CI) Signif.	No [177] 149 (108-208)	Yes [20] 69 (32-111) P=0.031	No [109] 33 (25-38)	Yes [16] 30 (14-65) P=0.869
7. Comorbid Anxiety Disorder during First Well Interval	Group [N] Mdn Wks. Well (95% CI) Signif.	No [163] 124 (92-197)	Yes [34] 149 (81-220) P=0.489	No [108] 32 (24-36)	Yes [17] 34 (16-68) P=0.341

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Clinical Variable		Asymptomatic Recovery (N=197)		Residual Symptom(SSD) Resolution (N=125)	
8. Any Substance Abuse (Alcohol or Drug Use) Disorder at Intake	Group [N] Mdn Wks. Well (95% CI) Signif.	No [157] 124 (84-184)	Yes [40] 201 (93-664) P=0.025	No [97] 33 (23-38)	Yes [28] 32 (22-68) P=0.293
9. Any Substance Abuse (Alcohol or Drug Use) Disorder during First Well Interval	Group [N] Mdn Wks. Well (95% CI) Signif.	No [171] 124 (92-184)	Yes [26] 220 (84-607) P=0.185	No [108] 31 (23-36)	Yes [17] 41 (19-227) P=0.266
10. Any Comorbid Miscellaneous Disorder at Intake (Representing Miscellaneous Psychopathology)	Group [N] Mdn Wks. Well (95% CI) Signif.	No [154] 131 (92-208)	Yes [43] 138 (62-259) P=0.996	No [79] 38 (30-43)	Yes [46] 23 (18-30) P=0.190
11. Any Comorbid Miscellaneous Disorder during First Well Interval	Group [N] Mdn Wks. Well (95% CI) Signif.	No [151] 131 (88-214)	Yes [46] 135 (91-201) P=0.787	No [87] 34 (25-39)	Yes [38] 28 (19-43) P=0.596
12. Very Good Work Role Function (No Impairment, High Level of Function) in Best Period during 5 Years Prior to Intake (from LIFE Base)	Group [N] Mdn Wks. Well (95% CI) Signif.	Yes [103] 150 (107-214)	No [72] 92 (66-197) P=0.275	Yes [41] 34 (23-43)	No [62] 32 (22-38) P=0.902
13. Very Good Household Function (No Imp., High Level Function) in Best Period during 5 Years Prior to Intake (from LIFE Base)	Group [N] Mdn Wks. Well (95% CI) Signif.	Yes [83] 135 (102-227)	No [97] 111 (83-201) P=0.699	Yes [36] 35 (23-43)	No [84] 30 (23-36) P=0.382
14. Very Good Social Relationships in Best Period during 5 Years Prior to Intake (from SADS Item 1242)	Group [N] Mdn Wks. Well (95% CI) Signif.	Yes [81] 151 (107-214)	No [115] 111 (81-197) P=0.587	Yes [32] 34 (21-50)	No [93] 32 (23-36) P=0.401
15. Very Good Involvement in Recreation/ Hobbies in Best Period during 5 Years Prior to Intake (from LIFE Base)	Group [N] Mdn Wks. Well (95% CI) Signif.	Yes [82] 151 (107-243)	No [114] 108 (83-167) P=0.447	Yes [38] 26 (18-36)	No [87] 34 (25-41) P=0.665

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Clinical Variable		Asymptomatic Recovery (N=197)		Residual Symptom(SSD) Resolution (N=125)	
16. Very Good Subjective Contentment/Satisfaction with Life in Best Period during 5 Years Prior to Intake (from LIFE Base)	Group [N] Mdn Wks. Well (95% CI) Signif.	Yes [69] 149 (93-209)	No [127] 111 (84-201) P=0.977	Yes [25] 30 (20-36)	No [100] 34 (25-42) P=0.270
17. Very Good or Good Overall Social Adjustment in Best Period during 5 Years Prior to Intake (from LIFE Base)	Group [N] Mdn Wks. Well (95% CI) Signif.	Yes [127] 143 (100-209)	No [69] 111 (71-192) P=0.051	Yes [64] 36 (26-43)	No [61] 26 (21-34) P=0.299
18. Satisfied with Major Life Role Most of the Time Prior to Intake (from Personal Resources Inventory Item 255)	Group [N] Mdn Wks. Well (95% CI) Signif.	Yes [97] 149 (92-227)	No [97] 124 (81-192) P=0.156	Yes [48] 34 (22-38)	No [75] 31 (23-42) P=0.852

Footnote for Supplementary eTable 3:

- a. Survival analysis was run on the number of weeks from the start of asymptomatic or SSD resolution of the index MDE to the start week of the next depressive episode relapse/recurrence of any type (MDE or minor depression). Significance (P-value) for comparison *within* the asymptomatic or SSD recovery group is based on the Log Rank χ^2 statistic, comparing overall survival distributions of the 2 comparison groups across all of follow-up until censoring of data due to end of follow-up or a period of missing or "unreliable" weekly Psychiatric Status Rating (PSR) data.

Supplementary eTable 4
Within-Subject Outcomes for 68 CDS Participants
after Residual Subsyndromal (SSD) Depressive Symptom Resolution of Their Index MDE
vs. after Asymptomatic Recovery Later during Follow-Up

Survival Analysis of Time to First Depressive Episode (Major, Minor, or Dysthymic) Relapse/Recurrence (N=68)	Weeks to Next Depressive Episode Relapse/Recurrence			
		Post-SSD Index MDE Resolution	Post-Asymptomatic Later Recovery	Significance
	25% (95%CI) 50% (95%CI) 75% (95%CI)	17.5 (14-230) 33 (25-39) 55 (42-142)	42 (30-56) 102 (59-155) 241 (166-310)	P<0.001
	Probability of Relapse/Recurrence by This Time			
	6 Mos. 1 Year 2 Years 5 Years	0.401 0.751 0.851 1.000	0.105 0.329 0.512 0.780	P<0.001
Severity of Depressive Illness during the Interval (N=68)	Percentage of Weeks with Each of Four Levels of Depressive Illness Severity			
		Post-SSD Index MDE Resolution	Post-Asymptomatic Later Recovery	Significance
Asymptomatic (Returned to Usual Self)	Mean (sd)	2.3 (9.3)	62.6 (30.3)	P<0.001
Subsyndromal (SSD) Depressive Symptoms	Mean (sd)	68.1 (24.3)	10.7 (15.2)	P<0.001
Minor Depressive Episode (MinD) Threshold Symptoms	Mean (sd)	22.4 (18.1)	16.9 (19.5)	N.S.
Major Depressive Episode (MDE) Threshold Symptoms	Mean (sd)	7.2 (11.0)	9.9 (14.7)	N.S.
Global Rating of Psychosocial Impairment (N=38) ^a	Level of Psychosocial Impairment			
		Post-SSD Index MDE Resolution	Post-Asymptomatic Later Recovery	Significance
	Mean (sd)	2.98 (0.65)	2.60 (0.70)	P<0.001

Footnote for Supplementary eTable 4:

- a. 38 participants experienced both levels of recovery after 2 years of follow-up, when the wording for this rating was changed on versions of the LIFE interview used thereafter during follow-up. The rating is a summary judgment by the clinical rater of overall psychosocial functioning, on a scale where 1=very good; 2=good; 3=fair; 4=poor; 5=very poor.