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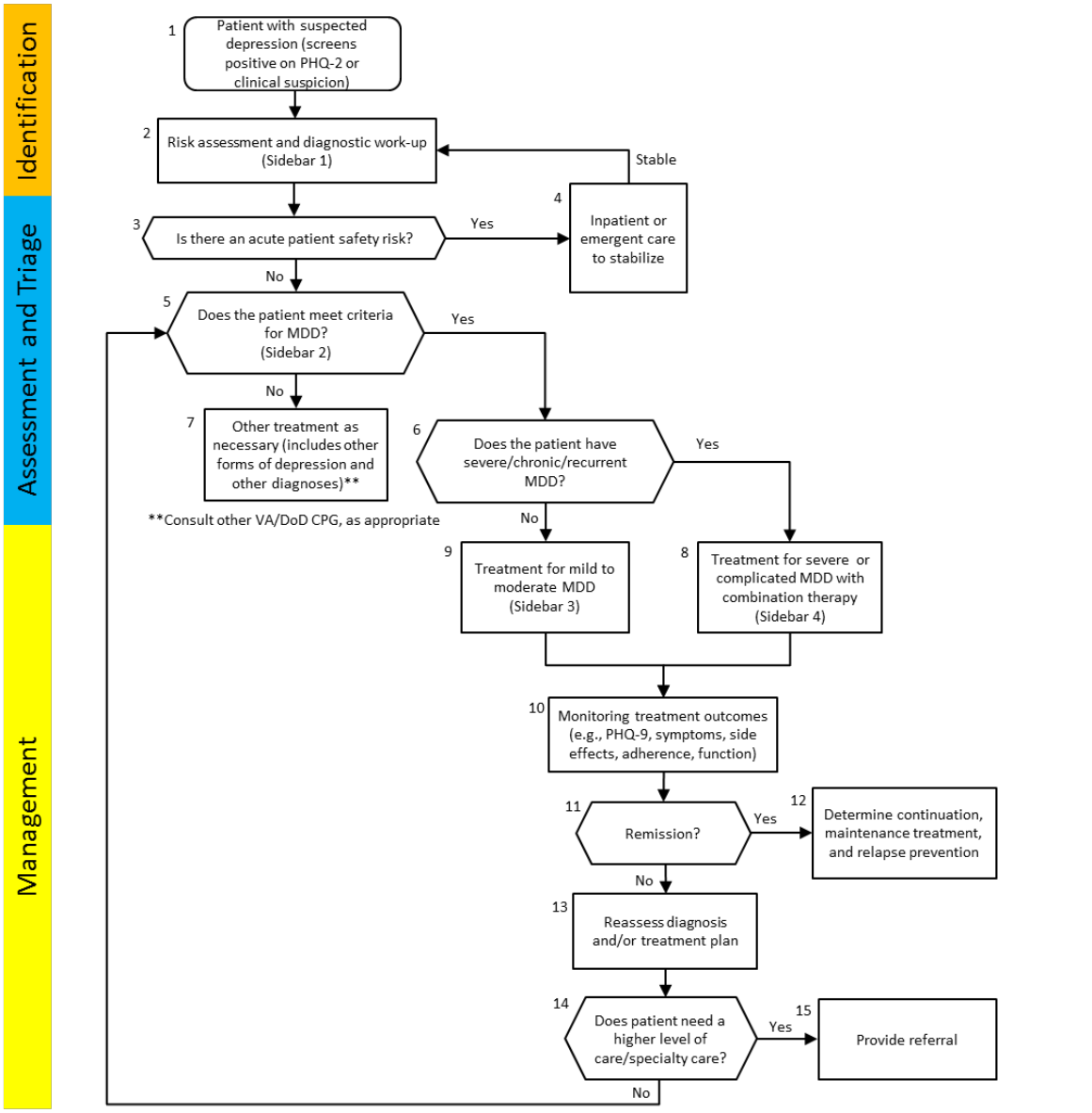
Algorithm



Sidebar 1 - Risk Assessment and Work-up

a. Consider administration of PHQ-9
b. Evaluate for (1) suicidal and homicidal ideation, (2) history of suicide attempts, (3) presence of psychotic features
c. Rule out causes of secondary MDD (e.g., hypothyroidism, B-12 deficiency, syphilis, chronic disease)

Sidebar 3 – Considerations in Treatment of Mild/Moderate MDD

For example:

a. Select monotherapy or combination therapy: pharmacotherapy/psychotherapy
b. Treatment for special populations (e.g., treatment of co-occurring conditions, pregnant patients, geriatric patients)
c. Patient preferences (treatment refusers)
d. Consider referral

Sidebar 2 – DSM-5 Criteria

Criterion A: Five or more of the following symptoms present during the same 2-week period; at least one of the symptoms is either (1) depressed mood or (2) loss of interest/pleasure:

a. Depressed mood most of the day, nearly every day
b. Markedly diminished interest or pleasure in almost all activities most of the day, nearly every day
c. Significant weight loss when not dieting or weight gain
d. Insomnia or hypersomnia nearly every day
e. Psychomotor agitation or retardation nearly every day
f. Fatigue or loss of energy every day
g. Feelings of worthlessness or excessive inappropriate guilt
h. Diminished ability to think, concentrate, or indecisiveness, nearly every day
i. Recurrent thought of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

Criterion B: The symptoms cause significant distress or functional impairment
Criterion C: The episode is not attributable to the physiological effects of a substance or another medical condition

Sidebar 4 – Considerations in Treatment of Severe MDD

For example:

a. Recommend referral to specialty level care
b. Select combination therapy: pharmacotherapy/ psychotherapy
c. Treatment for special populations (e.g., treatment of co-occurring conditions, pregnant patients, geriatric patients)
d. Patient preferences (treatment refusers)

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Table 1: Patient Health Questionnaire-2 (PHQ-2) [1]

Question Number	Over the past two weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1	Little interest or pleasure in doing things	0	1	2	3
2	Feeling down, depressed, or hopeless	0	1	2	3
For office coding: Total Score = _____+_____					

Table 2: PHQ-2 Score Interpretation [1]

PHQ-2 Score	Probability of MDD (%)	Probability of any depressive disorder (%)
1	15.4	36.9
2	21.1	48.3
3	38.4	75.0
4	45.5	81.2
5	56.4	84.6
6	78.6	92.9

Table 3: Diagnostic Criteria for Major Depressive Episode based on DSM-5 [2]

Criterion A	Five or more of the following symptoms present during the same two-week period; at least one of the symptoms is either (1) depressed mood or (2) loss of interest/ pleasure: a. Depressed mood most of the day, nearly every day b. Markedly diminished interest or pleasure in almost all activities most of the day, nearly every day c. Significant weight loss when not dieting or weight gain d. Insomnia or hypersomnia nearly every day e. Psychomotor agitation or retardation nearly every day f. Fatigue or loss of energy every day g. Feelings of worthlessness or excessive inappropriate guilt h. Diminished ability to think, concentrate, or indecisiveness, nearly every day i. Recurrent thought of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide
Criterion B	The symptoms cause significant distress or functional impairment.
Criterion C	The episode is not attributable to the physiological effects of a substance or another medical condition

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Table 4: Nine Symptom Checklist (PHQ-9)

	Over the last 2 weeks, how often have you been bothered by any of the following?	Not at all	Several days	More than half the days	Nearly every day
a	Little interest or pleasure in doing things?	0	1	2	3
b	Feeling down, depressed, or hopeless?	0	1	2	3
c	Trouble falling or staying asleep, or sleeping too much?	0	1	2	3
d	Feeling tired or having little energy?	0	1	2	3
e	Poor appetite or overeating?	0	1	2	3
f	Feeling bad about yourself—or that you are a failure or have let yourself or your family down?	0	1	2	3
g	Trouble concentrating on things, such as reading the newspaper or watching television?	0	1	2	3
h	Moving or speaking so slowly that other people could have noticed? Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual?	0	1	2	3
i	Thoughts that you would be better off dead or of hurting yourself in some way?	0	1	2	3
For office coding: Total Score =_____+_____+_____+_____					

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

PHQ-9 Scoring Instructions:

Count the number (#) of boxes checked in a column. Multiply that number by the value indicated below, then add the subtotal to produce a total score. The possible range is 0-27. Use the table below to interpret the PHQ-9 score.

Not at all (#) _____ x 0 = _____
Several days (#) _____ x 1 = _____
More than half the days (#) _____ x 2 = _____
Nearly every day (#) _____ x 3 = _____
Total score: _____

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Table 5: Summary of Evidence-based Elements of the Collaborative Care Model for MDD* [3-9]

Essential	Optimal	Equivocal	Not Recommended
Interdisciplinary, team approach to brief, problem-focused care	Access to evidence-based psychosocial services (e.g., behavioral activation, motivational interviewing, problem solving therapy, brief CBT)	Requiring or focusing on direct hand-offs from the primary care provider to the team	Consultation-liaison or co-located care without systematic follow-up
Structured protocols, including screening, case identification, and longitudinal measurement	Availability to provide crisis intervention	Acceptance of stable patients from specialty care	Assessment and triage (i.e., walk-in) model (no follow up)
Systematic follow-up (registries, measure-guided treatment)	Facilitated self-management		
Patient education and activation including adherence monitoring	A program that offers additional behavioral health services including brief alcohol interventions	Use of a prescribing provider (psychiatrists, certified registered nurse practitioner [CRNP]) for psychotropic medications (separate from supervision)	
Supervision by psychiatrist/prescriber	Open accessibility to primary care providers and patients		
Data-driven quality improvement	Referral management for more severe symptoms		

* Work Group's synthesis of collaborative care model for MDD based on literature available through January 2015.

Abbreviations: CBT: Cognitive Behavioral Therapy, CRNP: Certified Registered Nurse Practitioner

Table 6: Classification of MDD Symptoms Severity and Risk Modifiers

Severity Level	PHQ-9 Total Score	Number of Symptoms According to DSM-5	Functional Impairment
Mild	10-14	2	Mild
Moderate	15-19	3	Moderate
Severe	≥20	4 or 5	Severe
Modifiers			
Complications	Co-occurring PTSD, SUD, psychosis, suicide risk, mania, significant social stressors, war-related conditions, significant anxiety		
Chronicity	More than two years of symptoms despite treatment		
Treatment-Resistant Depression	At least two adequate treatment trials and lack of full response to each [10]		

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Table 7: Antidepressant Dosing[1] and Monitoring [11]

Class	Agent	Initial Dose	Titration Schedule[2]	Max. Dose/day	Initial Dose or Guidance: Special Populations			
					Geriatric	Renal	Hepatic	Pregnancy FDA Cat.
SSRIs	Citalopram	20 mg once a day	20 mg weekly	40 mg; 20 mg geriatric	10-20 mg once a day	Avoid: CrCl <20 ml/min	↓ dose	C
	Escitalopram	10 mg once a day	10 mg weekly	20 mg	5-10 mg once a day	Avoid: CrCl <20 ml/min	10 mg once a day	C
	Fluoxetine	20 mg once a day	20 mg every 2 weeks	80 mg	10 mg once a day	↓ dose and/or ↓ frequency	↓ dose 50%	C
	Fluoxetine weekly	90 mg once a week	N/A	90 mg	90 mg once a week	No change	Avoid	C
	Paroxetine	20 mg once a day	20 mg weekly	50 mg	10 mg once a day	10 mg once a day	10 mg once a day	D
	Paroxetine CR	25 mg once a day	12.5 mg weekly	62.5 mg; 50 mg geriatric	12.5 mg; once a day	12.5 mg once a day	12.5 mg once a day	D
	Sertraline	50 mg once a day	50 mg weekly	200 mg	25 mg once a day	25 mg once a day	↓ dose	C
	Vilazodone	10 mg once a day	10 mg weekly	20-40 mg	5 mg	No change	No change	C

[1] All dose oral except selegiline patch
[2] Recommended minimum time between dose increases

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Class	Agent	Initial Dose	Titration Schedule[2]	Max. Dose/day	Initial Dose or Guidance: Special Populations			
					Geriatric	Renal	Hepatic	Pregnancy FDA Cat.
SNRIs	Duloxetine	20-30 mg twice a day	20-30 mg weekly	60 mg	20 mg once or twice a day	Avoid if CrCl <30 ml/min	Avoid	C
	Venlafaxine IR	37.5 mg twice a day	75 mg weekly	225-375 mg	25mg once or twice a day	↓dose based on CrCl	↓ dose 50%	C
	Venlafaxine XR	75 mg once a day	75 mg weekly	225 mg	37.5-75 mg once a day	↓dose based on CrCl	↓ dose 50%	C
	Levomilnacipran	20 mg once a day	20-40 mg every 2 days	120 mg	Refer to adult dosing, Consider CrCl	Max doses less if CrCl <60ml/min	No change	C
	Desvenlafaxine	50 mg once a day	Unnecessary	100 mg; no benefit at doses >50 mg per day	Consider CrCl	CrCl <30 ml/min, 25mg once daily	No change	C
5-HT3 receptor antagonist	Vortioxetine	10 mg once a day	10 mg once daily	5-20mg	5-20 mg once a day	No change	Severe: not recommended	C
NDRIs	Bupropion IR	100 mg twice a day	100 mg weekly	450 mg	37.5mg twice a day	Has not been studied	Severe: 75 mg/day	C
	Bupropion SR	150 mg once a day	150 mg weekly	200 mg twice daily	100 mg once a day		100 mg once a day or 150 mg every other day; Mod to severe: use with extreme caution	C
	Bupropion XR	150 mg once a day	150 mg weekly	450 mg	150 mg once a day			C

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Class	Agent	Initial Dose	Titration Schedule[2]	Max. Dose/day	Initial Dose or Guidance: Special Populations			
					Geriatric	Renal	Hepatic	Pregnancy FDA Cat.
5-HT2 receptor antagonist	Trazodone	50 mg three times a day	50 mg weekly	600 mg	25-50 mg at bedtime	Has not been studied	Unknown	C
	Nefazodone	100 mg twice a day	100 mg weekly	600 mg	50 mg twice a day	No change	Avoid	C
Noradrenergic antagonist	Mirtazapine	15 mg daily at bedtime	15 mg weekly	45 mg	7.5 mg at bedtime	Caution in renal impairment	Cl ↓ 30%	C
TCAs	Amitriptyline	25-50 mg daily single dose at bedtime or in divided doses	Weekly	300 mg	10–25 mg at bedtime	No change	Lower dose and slower titration recommended	C
	Imipramine	25 mg 1- 4 times a day	Weekly	300 mg	10-25 mg at bedtime	No change		Unclassified
	Nortriptyline	25 mg 3-4 times a day	Weekly	150 mg	30-50 mg/day	No change		Unclassified
	Desipramine	25-50 mg once daily or in divided doses	Weekly	300 mg; 150 mg geriatric	10-25 mg once a day	No change		Unclassified
	Doxepin	25-50 mg daily at bedtime or twice a day	Weekly	300 mg	Low dose, once daily	No change		C

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Class	Agent	Initial Dose	Titration Schedule[2]	Max. Dose/day	Initial Dose or Guidance: Special Populations			
					Geriatric	Renal	Hepatic	Pregnancy FDA Cat.
MAOIs	Isocarboxazid	10 mg twice a day	10 mg/day every 2-4 days to 40 mg/day. After first week, may increase by up to 20 mg/week to a maximum of 60 mg/day.	60 mg	10 mg twice a day	Avoid in any renal impairment. Contraindicated in severe	Contraindicated in patients with a history of liver disease or abnormal LFTs	C
	Phenelzine	15 mg 3 times a day	Increase rapidly, based on patient tolerance, to 60-90 mg/day	90 mg; 60 mg geriatric	7.5 mg once a day	Avoid if severe	Avoid	Undetermined
	Selegiline patch	6 mg/24 hours	3 mg/24 hours every 2 weeks	12 mg/24 hours	6 mg/24 hours	Use in patients with a CrCl <15 ml/min has not been studied	Mild to mod: no adjustment; Severe: not studied	C
	Tranylcypromine	10 mg twice a day	10 mg weekly	60 mg	10 mg twice a day	No change	Avoid	C

Abbreviations: 5-HT = serotonin, BID = twice a day, CrCl = creatinine clearance, CR = controlled release, IR = immediate release, LFT = liver function test, MAOI = monoamine oxidase inhibitor, mg = milligram, min = minute, ml = milliliter, N/A= not applicable, NDRI= norepinephrine and dopamine reuptake inhibitor, QD = once a day, QHS = once before bedtime, QID = four times a day, QOD = every other day, SNRI = serotonin norepinephrine reuptake inhibitor, SR = sustained-release, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant, TDM = therapeutic drug monitoring, XR = extended-release

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Table 8: Antidepressant Adverse Event Profiles [11]

Drug Class or Drug	Amine Update		Anti-cholinergic Activity	Sedation (H1 activity)	Orthostatic Hypotension (alpha-1 act.)	Cardiac Conduction Effects	GI Effects	Weight Gain	Comments
	5HT	NE							
SSRIs	+++	0/+	0/++	0/ +	0	0/+	+++	0/+	▪ Sexual dysfunction common ▪ Citalopram and escitalopram dose-related conduction effects ▪ Paroxetine most anticholinergic; avoid in elderly ▪ Paroxetine and fluoxetine CYP2D6 and CYP2B6 inhibitors ▪ Vilazodone CYP2C8 2C1 and 2D6 inhibitor
SNRIs	++/+++	++/+++	0/+	0/+	0/++	0/+	++/+++	0/+	▪ Sexual dysfunction common ▪ Venlafaxine NE activity dose-related ▪ Desvenlafaxine active metabolite of venlafaxine
Bupropion	0/+	0/+	0	0	0	0	++	0	▪ Risk of seizures is dose-related; avoid if seizure history, bulimia or eating disorder ▪ CYP2D6 inhibitor
Trazodone Nefazodone	+++	0/+	0	+++	0	0/+	++	0/+	▪ Very sedating ▪ Nefazodone associated with a higher risk of hepatotoxicity ▪ Nefazodone CYP3A4 inhibitor
Mirtazapine	0/+	0/+	0	+++	0/+	0	0/+	+++	▪ Doses >15 mg less sedating ▪ May stimulate appetite
Vortoxetine	+++	++	0	0	0	0	+++	0	

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Drug Class or Drug	Amine Update		Anti-cholinergic Activity	Sedation (H1 activity)	Orthostatic Hypotension (alpha-1 act.)	Cardiac Conduction Effects	GI Effects	Weight Gain	Comments
	5HT	NE							
TCAs	+/+++	+/+++	+/+++	0/+++	+/+++	++/+++	0/+	0/++	▪ Desipramine and nortriptyline more tolerable; least sedating, anticholinergic and orthostatic hypotension ▪ Therapeutic blood concentrations established for desipramine, imipramine, and nortriptyline
MAOIs	0	0	0	0/+	0/+	0	0/+	0/+	▪ Requires a low tyramine diet except selegiline 6 mg/24 hours patch ▪ Contraindicated with sympathomimetics and other antidepressants ▪ Observe appropriate washout times when switching from or to another class of antidepressant

Key: +++ = strong effect, ++ = moderate effect, + = minimal effect, 0 = no effect

Abbreviations: MAOI = monoamine oxidase inhibitor, SNRI = serotonin norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant

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Table 9: Augmentation, Adjunct and Alternative Pharmacotherapy [11]

Class	Agent	Initial Dose	Titration Schedule[3]	Max. Dose/day	Initial Dose or Guidance: Special Populations			
					Geriatric	Renal	Hepatic	Pregnancy FDA Cat.
SGAs	Aripiprazole	2-5 mg once a day	2-5 mg after ≥1 week	15 mg	2 mg once a day	No change	No change	C
	Olanzapine	2.5-5 mg once a day	2.5-5 mg weekly	20 mg	2.5 mg once a day	No change	No change	C
	Quetiapine	50 mg once a day for 1 day	100 mg daily as tolerated	300 mg	50 mg once a day	No change	Initial 25 or 50 mg once a day	C
	Risperidone	0.25-0.5 mg once a day	0.5 mg daily	3 mg	0.25 mg once a day	Adjust if CrCl <30 ml/min	Severe: Caution	C
	Ziprasidone	20 mg twice a day	20 mg twice a day every 2-4 days	160 mg	20 mg twice a day	No change	Caution	C
5-HT1A & -HT2 agonist	Buspirone	7.5 mg twice a day	7.5 mg twice a day weekly	60 mg	7.5 mg twice a day	Avoid if severe	Avoid if severe	B
Lithium	Lithium	300 mg 1-2 times a day	300 mg weekly	1200 mg	150mg once or twice a day	↓ dose 25% - 75%	No change	D
Thyroid hormone	Liothyronine	25 µg once a day	May be increased to 50 µg/day after ~1 week	50 µg	5 µg once a day; increase by 5 µg/day every 2 weeks	No change	No change	A
Herbal	St. John's wort	300 mg 2-3 times a day	Unknown	1200 mg	Unknown	Has not been studied	Has not been studied	Avoid

Abbreviations: 5-HT = serotonin, CrCl = creatinine clearance, mg = milligram, µg = microgram, SGA = Second Generation Antipsychotic

[3] Recommended minimum time between dose increases

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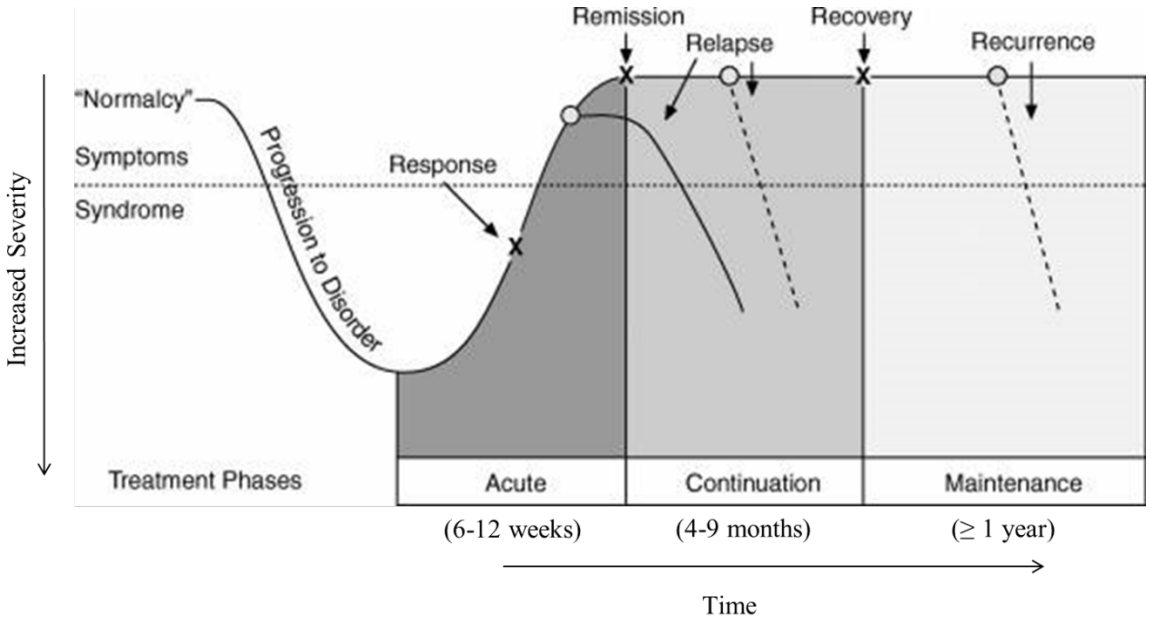
Figure 1: Distinguishing Relapse and Recurrence [12]



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