200121 Ikäihmisten mielialaoireet – masennus ja kaksisuuntainen mielialahäiriö

Yl Juha Kemppinen

200121 Ikäihmisten mielialaoireet – masennus ja kaksisuuntainen mielialahäiriö

- Agenda:

1) Mikä on masennus? Eroaako ikäihmisen masennus muista?
2) Ikäihmisen masennuksen seulonta ja diagnosointi
3) Ikäihmisen masennuksen hoito
4) Mikä on kaksisuuntainen mielialahäiriö? Eroaako se nuorempien bipolaaritaudista?
5) Ikäihmisen kaksisuuntaisen häiriön seulonta ja diagnosointi
6) Ikäihmisen kaksisuuntaisen mielialahäiriön hoito

200121 Ikäihmisten masennus

- Depressiodiagnoosia ei tehdä, jos kyseessä on **lähiomaisen kuolemaan** liittyvä **normaali surureaktio**. Raja surureaktion ja depression välillä on kuitenkin joskus häilyvä.
  - Surevan **tunteet liittyvät** menetettyä läheistä koskeviin **muistoihin**, kun taas depressiossa potilaan **kuva itsestään on negatiivinen** ja masennuksen oireet ovat yleistyneet monille elämänalueille.
  - Itsetuhoajatukset, selvät psykoottiset tai psykomotoriset oireet, vaikea oirekuva tai masennusoireyhtymän jatkuminen **kuukausien ajan** eivät enää liity tavalliseen surureaktioon [3]ja ovat siten aihe depressiodiagnoosin tekoon ja depression hoitoon.


TÄMÄ ON "MASENNUS-ASENTONI"
KUN ON MASENTUNUT, NIIN OIKEA ASENTO MERKITSEE HYVIN PALJON...
10-13
PAHINTA ON SUORISTAA SELKÄNSÄ JA NOSTAA PÄÄNSÄ PYSTYYN, KOSKA SILLOIN ALKAA TUNTEA OLONSA PAREMMAKSI...
JOS HALUAA SAADA MASENNUKSESTAAN ILOA, ON SEISTAVÄ JUURI NÄIN...

Masennuksen erotusdiagnostiikka

- Surureaktio (reaktiivinen, normaali; ei yli 2kk)
- Dystymia, krooninen masentuneisuus
- Kaksisuuntainen mielialahäiriö, bipolaaritauti I ja II → akuutti hoito psykiatrian erikoislääkäri
- Ruumiillinen sairaus (1.depressio, >50v aina ensin !; epätavallinen oirekuva, ei hyödy depression hoidosta)
- Lääkehoito
- Päihteet (alkoholiriippuvuus 10-30 % depressiopotilas)
- Persoonallisuus(häiriö): 50 % hoitoon hakeutuvista; erityisesti estynyt, epävakaa (10-15% depressiopt) ja vaativa (mitä vaikeampi, sitä suurempi kliininen merkitys) – vaativa, estynyt ja riippuvainen masennuksen kroonistumisen riski !

Masennus on mielen ja kehon sairaus

Mielialaoireet

- Masentunut mieliala
- Mielihyvän menetys, aloitekyvyttömyys
- Syyllisyyden ja arvottomuuden tunteet
- Itsemurha-ajatukset

Kognitiiviset oireet

- Muistihäiriöt
- Keskittymisvaikeudet
- Ajattelun hidastuminen (takkuaminen)

Ahdistuneisuusoireet

- Erilaisia ahdistuneisuusoireita, jollain jopa paniikkikohtauksia

Fyysiset oireet

- Ruokahalun muutokset
- Unihäiriöt
- Energiakato, väsymys
- Psykomotoriset muutokset (hidastuminen / kiihtyneisyys)
- Päänsärky
- Muut kivut ja säryt

Iäkkäiden depression hoito

- Vanhuusiässä ilmenevien depressioiden diagnostiikka, arviointi ja hoito ovat yleensä ainakin alle 75-vuotiailla samankaltaisia kuin nuoremmissa ikäryhmissä.
- Iäkkäillä depression seulonnassa voidaan käyttää GDS-15- tai GDS-30-asteikkoa (geriatrinen depressioasteikko, Geriatric Depression Scale) **5**.
- Jos ensimmäinen depressiojakso tulee vanhuusiässä, on erityisen tarkkaan arvioitava somaattisen sairauden mahdollisuus etiologisena tai myötävaikuttavana tekijänä.
- Tutkimuksia yli 75-vuotiaiden depression hoidosta on edelleen varsin vähän. Suosituksen ohjeita voidaan kuitenkin soveltaa myös heidän hoidossaan, kunhan otetaan huomioon, että ikääntymisen myötä psykiatrisen ja somaattisen hoidon yhdistämisen tarve lisääntyy.
- Ikääntymisen myötä psykoterapiassa korostuvat supportiiviset elementit. Myös lääkkeiden haitta- ja yhteisvaikutusten merkitys korostuu ja iänmukaiseen annokseen on kiinnitettävä erityistä huomiota. Masennuslääkeannokset ovat 65–75-vuotiailla samansuuruisia tai vain vähän pienempiä kuin keski-ikäisillä, kun taas yli 75-vuotiailla käytettävien annosten koko on ½–⅓ keski-ikäisillä käytettävistä annoksista.

Iäkkäiden depression hoito

- Ikääntyneiden lieviä ja keskivaikeita depressioita voidaan hoitaa psykoterapian avulla **A**.
- Eniten on tutkittu kognitiivis-behavioraalista psykoterapiaa. Sekä yksilö- että ryhmähoidoista on näyttöä, ja niiden saatavuutta tulisi lisätä. Ryhmämuotoisesta muisteluterapiasta on ilmeisesti myös hyötyä iäkkäiden masennuksen hoidossa **B**. Psykoterapiamenetelmiä esitellään taulukossa **6**.
- Depressiolääkkeet ovat tehokkaita myös iäkkäiden masennuksen hoidossa, eikä lääkeaineryhmien välillä ole kliinisesti merkittäviä tehoeroja **B**.
- Iäkkäiden depressiossa ylläpitolääkitys on ilmeisesti hyödyllistä **B**. Sitä harkittaessa on kuitenkin otettava huomioon lisääntyvän lääkekuorman mukanaan tuomat ongelmat.
- Vaikka trisykliset masennuslääkkeet ovat tehokkaita, niitä ei potentiaalisten verenkiertoelimistöön kohdistuvien haittavaikutustensa vuoksi yleensä suositella yli 75-vuotiaiden hoitoon. Jos iäkkäälle potilaalle suunnitellaan trisyklisen lääkkeen käytön aloittamista, kannattaa tarkistaa, ettei hänellä ole sydämen johtumishäiriötä, ja valita mahdollisimman vähän antikolinergisia ja muita haittavaikutuksia aiheuttava valmiste, esimerkiksi nortriptyliini.
- Sähköhoito on todettu tehokkaaksi ja turvalliseksi myös yli 75-vuotiaiden depressiossa **A**

läkkäiden depression hoito

Hoitomuoto ja kuvaus	Tyypillinen kesto ja tiheys	Näytön aste	
		Akuutti vaihe	
Kognitiivis-behavioraalinen			
Tavoitteina depressiota aiheuttavien ja ylläpitävien asenne- ja käyttäytymismallien muuttuminen ja ongelmanratkaisukeinojen lisääntyminen	Lyhyt: 10–20 käyntiä, 1 käynti viikossa	A	-
	Pitkäkestoinen: 40–80 käyntiä, 1–2 käyntiä viikossa	B	
Interpersoonallinen			
Tavoitteena depressiota aiheuttavien ja ylläpitävien ihmissuhdeongelmien, rooliristiriitojen tai menetysten fokusoitu käsittely	Lyhyt: 12–16 käyntiä, 1 käynti viikossa	A	
Psykodynaaminen			
Tavoitteina depressiolle altistavien kehityksellisten ongelmien selvittely ja minuuden vahvistuminen	Lyhyt: 16–25 käyntiä, 1 käynti viikossa	A	-
	Pitkäkestoinen: 80–240 käyntiä, 1–3 käyntiä viikossa	B	
Muisteluterapia			
Tavoitteena depression helpottuminen oman elämän mielekkyyden tavoittamisen ja kokemusten jakamisen myötä	Lyhyt: yleensä 8 viikoittaista ryhmäistuntoa tai joustavasti yksilöllisesti toteutettuna		

Maurer D et al 2018

TABLE 1

Risk Factors for Depression

Internal factors

Female sex
History of anxiety
Low self-esteem
Neuroticism*

External factors

Conduct disorder
Substance use

Adverse life events

Childhood sexual abuse
Chronic medical conditions
Disturbed family environment
History of divorce
Lifetime trauma
Low educational status
Low social support
Parental loss

*—A dimension of temperament marked by elevated stress reactivity resulting in frequent negative emotions.[9]

Information from references 7 through 9.

Spoelgoef G et al 2011

Table 5. Risk Factors for Suicide

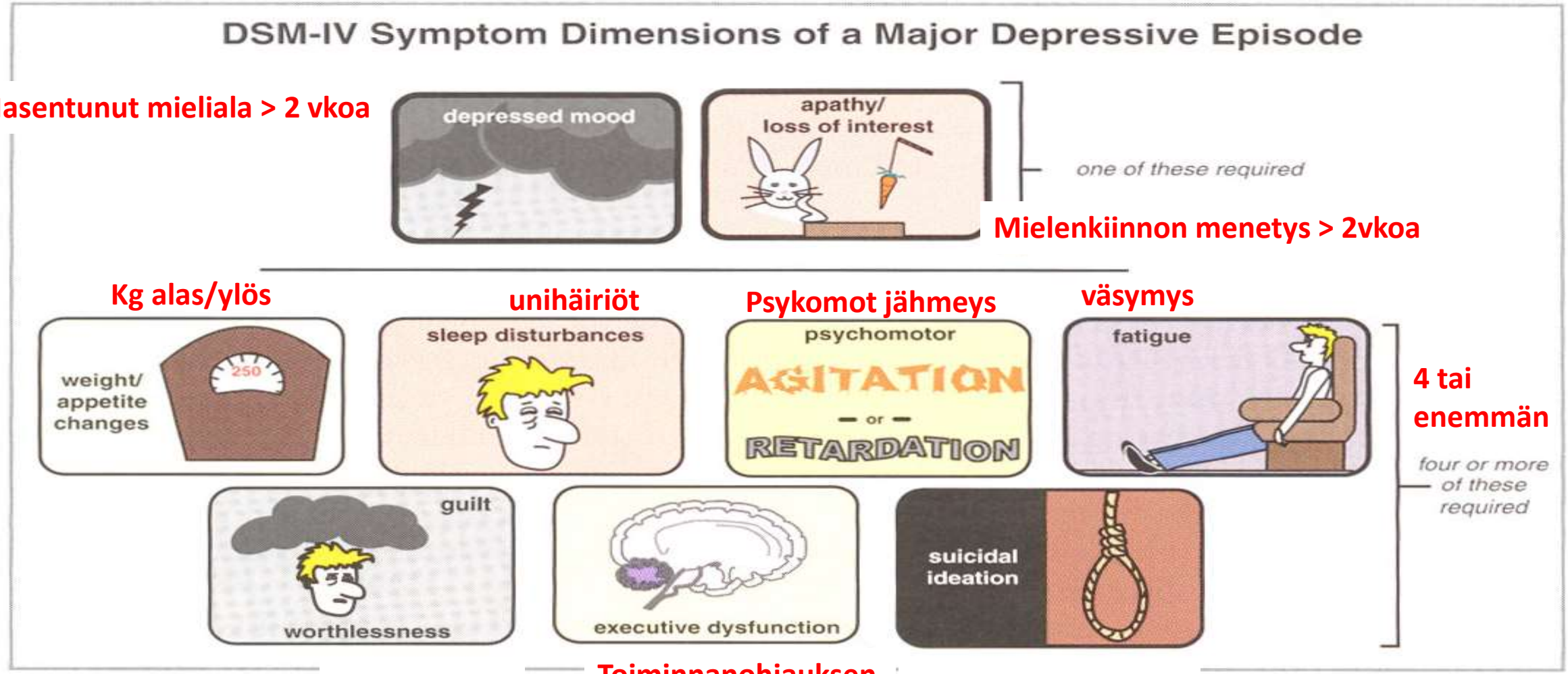
Bereavement
Depression
Living alone, social isolation
Male sex
Poor health status, development of disability
Poor sleep quality
Substance abuse (e.g., alcohol, sedatives, pain medications)
White race

Information from reference 20.

1) Mikä on masennus? Eroaako ikäihmisen masennus muista?

Yl juha kemppinen

Masennuksen oireet - vakavan masennuksen kriteerit



Masentunut mieliala > 2 vkoa

Mielenkiinnon menetys > 2vkoa

Kg alas/ylös

unihäiriöt

Psykomot jähmeys

väsymys

4 tai enemmän

Arvottomuus

Toiminnanohjauksen ongelmat

Itsemurha-ajatukset

FIGURE 11-44 DSM- f de atistical Manual of Mental *Disorders*, fourth edition (DSM-IV), a majo onsists of either depressed mood or loss of interest and at least four of the following: weight/appetite changes, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue, feelings of guilt or worthlessness, executive dysfunction, and suicidal ideation.

Masennustila on oireyhtymä

S. Stahl, 2004

TABLE 5. Major Depression

Tunne Feeling	Ajattelu Thinking	Käyttäytyminen Behavior	Interpersonal relations and role functioning
"Down," "blue," "sad," "dead" Often irritable	Diminished ability to concentrate, make decisions, solve problems Helpless/hopeless/ worthless mind-set Guilty feelings Thoughts of death and dying, self-harm May have delusions in severe cases Preoccupation with past In some older clients, serious confusion Greater impairment in visual–motor modalities	Apathetic and slowed pace, decreased level of activity May have decreased eating and sleeping, occasionally increased eating and sleeping May be agitated In some adolescents, acting out	Withdrawn, isolated Decreased functioning and activity

Masennus ja aivojen toimintahäiriöt

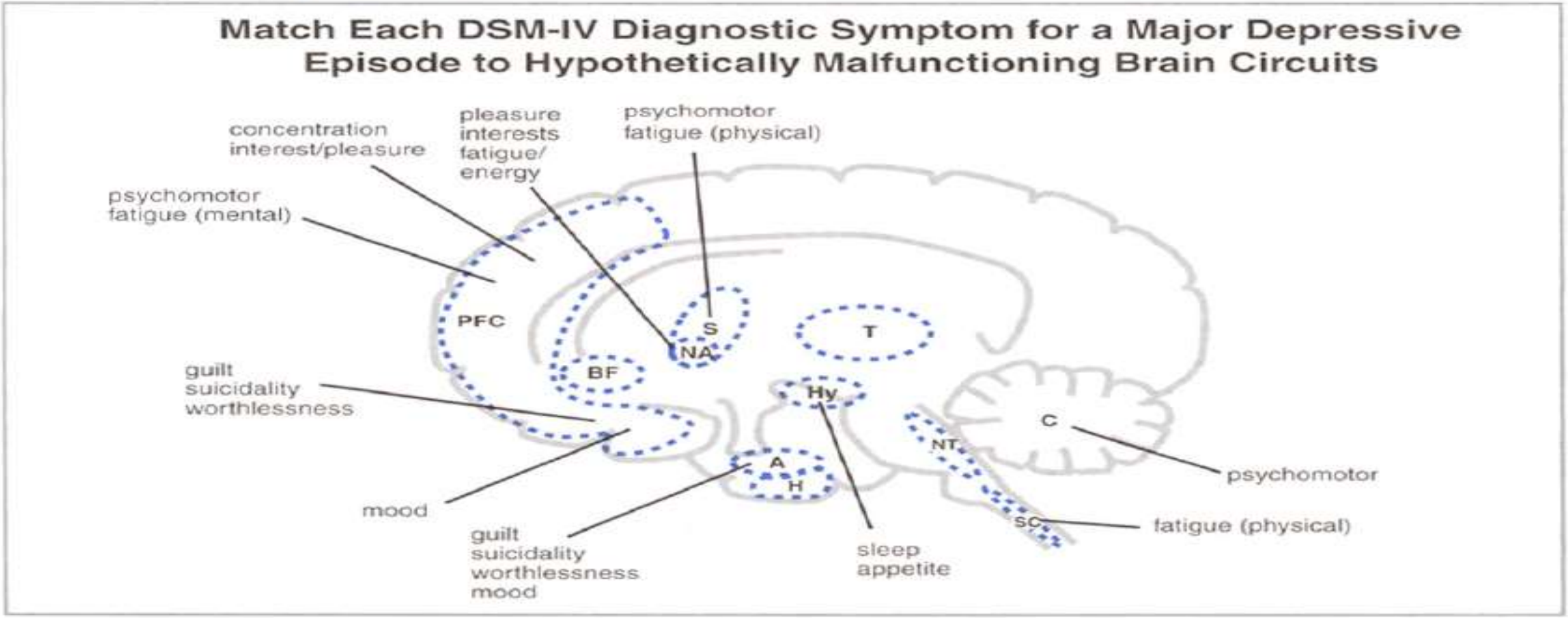


FIGURE 11-45 Matching depression symptoms to circuits. Alterations in neuronal activity and in the efficiency of information processing within each of the eleven brain regions shown here can lead to symptoms of a major depressive episode. Functionality in each brain region is hypothetically associated with a different constellation of symptoms. PFC, prefrontal cortex; BF, basal forebrain; S, striatum; NA, nucleus accumbens; T, thalamus; HY, hypothalamus; A, amygdala; H, hippocampus; NT, brainstem neurotransmitter centers; SC, spinal cord; C, cerebellum.

S. Stahl, 2004

TAULUKKO 1. ICD-10:n mukaiset masennustilan (F32) oirekriteerit, joita sovelletaan oirekuvan osalta myös toistuvassa masennuksessa (F33). Kriteerejä on hieman lyhennetty ja muokattu selkeyden vuoksi.

Oirekriteerit	Oirekuva
A. Masennusjakso on kestänyt vähintään kahden viikon ajan	**Kliinisesti merkittävää oireilua, eikä johdu som eikä päihteet**
B. Todetaan vähintään kaksi seuraavista oireista **Väh kaksi oiretta 1-3:**	1. Masentunut mieliala suurimman osan aikaa 2. Kiinnostuksen tai mielihyvän menettäminen asioihin, jotka ovat tavallisesti kiinnostaneet tai tuottaneet mielihyvää 3. Vähentyneet voimavarat tai poikkeuksellinen väsymys
C. Todetaan jokin tai jotkin seuraavista oireista niin, että oireita on yhteensä (B ja C yhteenlaskettuina) vähintään neljä **Väh neljä oiretta 1-10:** **Lievä = 4-5 oiretta** **Keskivaikea = 6-7 oiretta** **Vaikea = 8-10 oiretta** **Psykoottinen masennus = harhaluuloja ja - elämyksiä**	4. Itseluottamuksen tai omanarvontunnon väheneminen 5. Perusteettomat tai kohtuuttomat itsesyytökset 6. Toistuvat kuolemaan tai itsemurhaan liittyvät ajatukset tai itsetuhoinen käyttäytyminen 7. Subjektiivinen tai havaittu keskittymisvaikeus, joka voi ilmetä myös päättämättömyytenä tai jahkailuna 8. Psykomotorinen muutos (kiihtymys tai hidastuneisuus), joka voi olla subjektiivinen tai havaittu 9. Unihäiriöt 10. Ruokahalun lisääntyminen tai väheneminen, johon liittyy painon muutos

Lievässä masennustilassa oireita on 4–5, keskivaikeassa 6–7 ja vaikeassa 8–10 ja kaikki kohdasta B. Psykoottisessa esiintyy myös harhaluuloja tai -elämyksiä.

Taulukko 1. ICD-10:n mukaiset hypomanian, manian, masennusjakson ja sekamuotoisen jakson diagnostiset kriteerit hieman lyhennettyinä ja muokattuna selkeyden vuoksi. KH-suositus 2008

Häiriö	Diagnostiset kriteerit
Masennusjakso	**A. Masennusjakso on kestänyt vähintään kahden viikon ajan.**
	B. Todetaan vähintään kaksi seuraavista oireista:
	1.masentunut mieliala suurimman osan aikaa **2.kiinnostuksen tai mielihyvän menettäminen asioihin, jotka ovat tavallisesti kiinnostaneet tai tuottaneet mielihyvää** **3.vähentyneet voimavarat tai poikkeuksellinen väsymys**
	C. Todetaan jokin tai jotkin seuraavista oireista niin, että oireita on yhteensä (B ja C yhteenlaskettuina) vähintään neljä:
	4. itseluottamuksen tai omanarvontunnon väheneminen **5. perusteettomat tai kohtuuttomat itsesyytökset** **6. toistuvat kuolemaan tai itsemurhaan liittyvät ajatukset tai itsetuhoinen käyttäytyminen** **7. subjektiivinen tai havaittu keskittymisvaikeus, joka voi ilmetä myös päättämättömyytenä tai jahkailuna** **8. psykomotorinen muutos (kiihtymys tai hidastuneisuus), joka voi olla subjektiivinen tai havaittu** **9. unihäiriöt** **10. ruokahalun lisääntyminen tai väheneminen, johon liittyy painon muutos**
	Lievässä masennustilassa oireita on 4–5, keskivaikeassa 6–7 ja vaikeassa 8–10 ja kaikki kohdasta B.
Sekamuotoinen jakso	**Hypomaaniset, maaniset ja masennusoireet esiintyvät samanaikaisesti tai hyvin tiheästi vaihdellen. Aiemmin on ollut ainakin yksi mielialahäiriön jakso, ja ajankohtaisen jakson aikana sekä maanisia että masennusoireita on esiintynyt suurimman osan aikaa vähintään kahden viikon ajan.**

Somaattisesti sairaan potilaan tapauksessa ei aina ole helppoa erottaa somaattisen sairauden ja depression oireita toisistaan.

- Depression affektiiviset ja kognitiiviset oireet:
  - masentunut mieliala,
  - mielihyvän menetys,
  - huonontunut itsetunto,
  - keskittymisvaikeudet,
  - toivottomuus,
  - itsetuhoajatukset,
  - psykoottiset oireet

johtuvat harvemmin suoraan somaattisesta sairaudesta kuin

- Depression vegetatiiviset oireet :
  - **väsymys,**
  - **psykomotorinen hidastuneisuus,**
  - **ruokahaluttomuus,**
  - **laihtuminen**

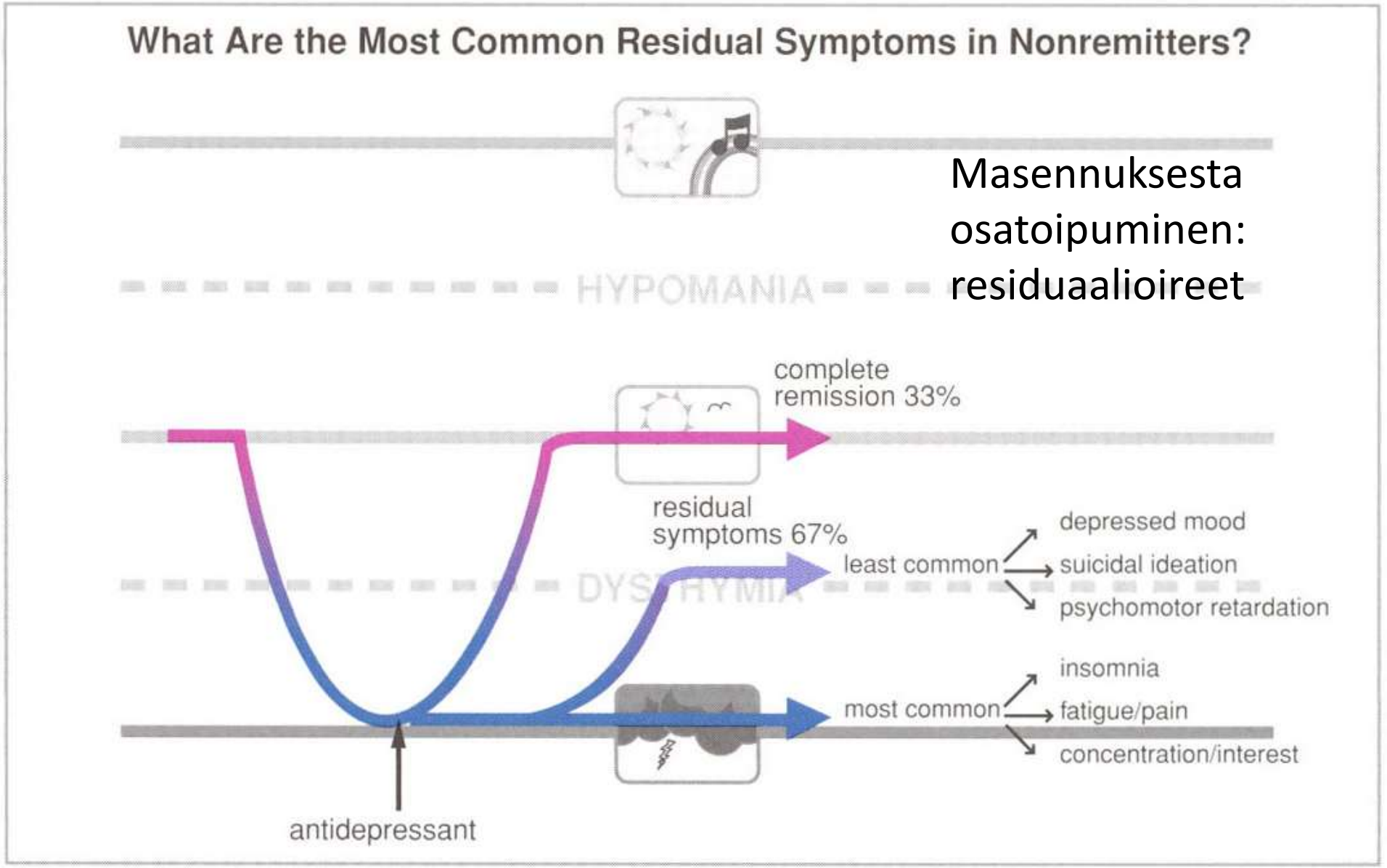


FIGURE 12-9 Common residual symptoms. In patients who do not achieve remission, the most common residual symptoms are insomnia, fatigue, painful physical complaints, problems concentrating, and lack of interest. The least common residual symptoms are depressed mood, suicidal ideation, and psychomotor retardation.

Table 143: Comparison of symptoms of depression in ICD–10 and DSM–IV

ICD–10	DSM–IV major/minor depressive disorder
Depressed mood*	Depressed mood by self-report or observation made by others*
Loss of interest*	Loss of interest or pleasure*
Reduction in energy*	Fatigue/loss of energy
Loss of confidence or self-esteem	Worthlessness/excessive or inappropriate guilt
Unreasonable feelings of self-reproach or inappropriate guilt	
Recurrent thoughts of death or suicide	Recurrent thoughts of death, suicidal thoughts or actual suicide attempts
Diminished ability to think/ concentrate or indecisiveness	Diminished ability to think/concentrate or indecisiveness
Change in psychomotor activity with agitation or retardation	Psychomotor agitation or retardation
Sleep disturbance	Insomnia/hypersomnia
Change in appetite with weight change	Significant appetite and/or weight loss

*Core symptoms.

A. 1 >5/2wk	Depressed mood most of the day, nearly every day, as indicated either by subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful)
2	Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated either by subjective account or observation made by others)
3	Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day
4	Insomnia or hypersomnia nearly every day
5	Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
6	Fatigue or loss of energy nearly every day
7	Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
8	Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
9	Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or specific plan for committing suicide
10	B. The symptoms do not meet criteria for a mixed episode. C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. D. The symptoms are not due to the direct physiological effects of a substance (e.g. a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism). E. The symptoms are not better accounted for by bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

Table 10.2 Comparison of predominant features in early-onset vs. late-onset depression [6, 25]

Early-onset depression	Late-onset depression
More family history of depression	More structural brain changes and cardiovascular risk factors
More depressive thoughts (suicidal thoughts, thoughts of worthlessness)	More anhedonia, apathy
Express depressive symptoms	Less expressed depressed mood but more somatic complaints
At risk for suicide	High risk for suicide
Mild cognitive impairments	More cognitive impairments
More substance misuse comorbidity	More medical comorbidity

Hategan A et al, Geriatric Psychiatry, 2018

Table 10.3 Suicide risk factors during a major depressive episode [9]

Suicide risk factors	Presence of suicidal or homicidal ideation, intent, or plans
	Male sex
	Age > 65 years
	Access to means for suicide (e.g., guns, knives)
	Previous suicide attempt or self-harm
	Family history of suicide attempt
	History of legal problems
	Stressful life events (e.g., loss of loved one, loss of independence)
	Presence of psychotic symptoms (especially command hallucinations)
	Presence of severe anxiety symptoms
	Presence of alcohol or other substance use
	Comorbid personality disorders
	Chronic systemic medical illness (including chronic pain and cancer)

Hategan A et al, Geriatric Psychiatry, 2018

Table 3. Potential Causes of Depressive Symptoms

Causes	*Examples*
Medication class or system	
Anticholinergics	Oxybutynin (Ditropan), cimetidine (Tagamet), antihistamines
Cardiac	Clonidine (Catapres), digoxin, hydralazine
Central nervous system	Levodopa, phenytoin (Dilantin), haloperidol
Hormones	Glucocorticoids, oral contraceptives, anabolic steroids
Sedatives	Benzodiazepines, ethanol, sleep aids
Illness	
Cancer	Pancreas, lung, colon
Endocrine	Hypothyroidism, hypercortisolism, Addison disease
Hematologic	Vitamin B_{12} deficiency, iron deficiency, leukemia
Infection	Syphilis, human immunodeficiency virus, pneumonia
Metabolic	Hypercalcemia, hyperkalemia, hypokalemia, porphyria
Neurologic	Alzheimer disease, stroke, intracranial mass
Impairments	
Hearing loss[9]	—
Pain[10]	Osteoarthritis, neuralgia
Substance abuse	Alcohol, opioids, benzodiazepines

Information from references 9 and 10.

Widera E et al, 2012

Table 1. Distinguishing Characteristics of Grief and Depression in Terminally Ill Patients

Characteristic	*Normal grief*	*Depression*
Nature of response	Adaptive	Maladaptive
Focus of distress	Distress is in response to a particular loss and does not affect all aspects of life	Distress is pervasive and affects all aspects of life
Symptom fluctuations	Comes in waves but generally improves with time	Constant
Mood	Sadness and dysphoria	Protracted and constant depression or flat affect
Interests/ capacity for pleasure	Interests and capacity for pleasure intact, although engagement in activities may be diminished because of functional decline	Anhedonia with markedly diminished interest or pleasure in all activities
Hope	Episodic and focal loss of hope; hopes may change over time, giving persons positive orientation toward the future	Hopelessness is persistent and pervasive
Self-worth	Maintained self-worth, although feelings of helplessness are common	Worthlessness with feeling that one's life has no value
Guilt	Regrets and guilt over specific events	Excessive feelings of guilt
Suicidal ideation	Passive and fleeting desire for hastened death	Preoccupation with a desire to die

Information from references 17 and 28.

Spoelgoef G et al 2011

Table 4. Drugs That May Cause Serotonin Syndrome

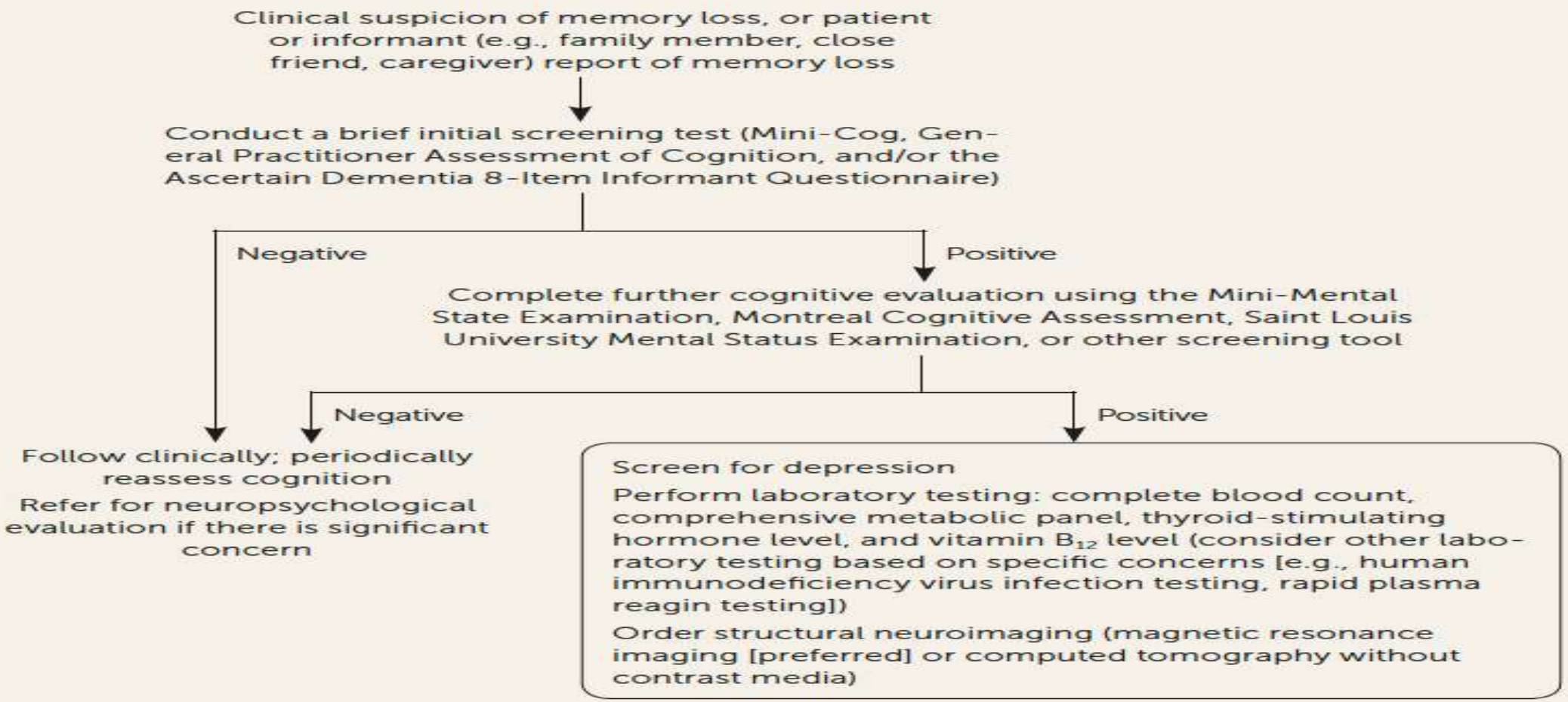
Category	*Examples*
Amphetamines	Methylphenidate (Ritalin)
Analgesics	Meperidine (Demerol), tramadol (Ultram)
Antispasmodics	Cyclobenzaprine (Flexeril)
Cough and cold	Dextromethorphan
Herbals	St. John's wort *(Hypericum perforatum)*
Migraine (triptans)	Sumatriptan (Imitrex)
Monoamine oxidase inhibitors	Phenelzine (Nardil)
Selective serotonin reuptake inhibitors	Sertraline (Zoloft)
Serotonin-norepinephrine reuptake inhibitors	Venlafaxine (Effexor), duloxetine (Cymbalta)
Other serotonergic medications	Lithium, trazodone

NOTE: *The risk of serotonin syndrome increases when agents are used in combination.*

Information from reference 12.

Falk N et al, 2018

FIGURE 1



Algorithm for the evaluation of suspected dementia.

Falk N et al, 2018

TABLE 1

Diagnostic Criteria for Neurocognitive Disorders

Major neurocognitive disorder	Minor neurocognitive disorder
Significant cognitive decline in at least one cognitive domain as seen in *both* of the following:	Modest cognitive decline in at least one cognitive domain as seen in *both* of the following:
• Concerns expressed by the patient or reliable informant or as seen by the clinician	• Concerns expressed by the patient or reliable informant or as seen by the clinician
• Objective neurocognitive testing/ assessments	• Objective neurocognitive testing/ assessments
Interference with instrumental activities of daily living	Does not interfere with instrumental activities of daily living, but they require additional time and effort
Cannot occur exclusively during bouts of delirium	
Cannot be explained by another mental disorder	
Specify one or more causal subtypes	
• Alzheimer disease	• Lewy body dementia
• Frontotemporal lobar degeneration	• Parkinson disease
• Human immunodeficiency virus infection	• Prion disease
• Huntington disease	• Substance/medication use
	• Traumatic brain injury
	• Vascular disease
	• Other medical condition
	• Multiple etiologies

Information from references 23 and 24.

Falk N et al, 2018

TABLE 2

Cognitive Domains Affected by Dementia and Associated Symptoms

Cognitive domain	Symptoms and observations
Complex attention	Normal, routine tasks take longer; difficulty in completing tasks when multiple stimuli are present; difficulty in maintaining information while completing task (e.g., completing mental math calculations, remembering a phone number to dial); work requires more overview/rechecking than before
Executive function	Difficulty in completing previously familiar multistep tasks, such as preparing a meal; no longer wanting to participate in activities of the home; difficulty in completing activities or tasks because of easy distractibility; social outings become more taxing and less enjoyable
Language	Difficulty finding the correct words; using general pronouns regularly instead of names; mispronunciation of words; problems with understanding verbal and written communication
Learning and memory	Forgetting to buy items or buying the same items multiple times at the store; repetition in conversations; difficulty in recalling recent events; relying on lists of tasks to complete; forgetting to pay bills
Perceptual-motor	Difficulty in using familiar technology, tools, or kitchen appliances; getting lost in familiar environments
Social cognition	Apathy, increase in inappropriate behaviors, loss of empathy, impaired judgment

Information from references 23 and 24.

Falk N et al, 2018

TABLE 3

Key Findings and Suggested Etiologies in Patients with Cognitive Impairment

Suggested etiology	Key findings on history and examination
Alzheimer disease	Insidious and gradual onset of memory and learning symptoms without evidence of plateaus; recall of recent events is most affected; cardiovascular disease risk factors; depression and apathy; sleep disturbances
Delirium	Recent hospitalization or acute illness, inattention, fluctuating behavior changes, altered level of consciousness
Frontotemporal dementia	Socially inappropriate behaviors; loss of empathy; changes in dress, eating habits, religious/political beliefs; development of compulsive behaviors; progressive aphasia
Human immunodeficiency virus infection	History of high-risk sexual behavior or drug use, apathy, poor attention and concentration, hyperreflexia, slow limb movements
Hypoperfusion from heart failure	Syncope, history of heart failure
Intracranial tumor	Seizures, neurologic deficits
Medication adverse effects	Use of anticholinergic drugs, benzodiazepines, opioids, or muscle relaxants
Neurocognitive disorder with Lewy body dementia	Daytime drowsiness, daytime naps lasting more than two hours, prolonged staring spells, disorganized speech, visual hallucinations, parkinsonian symptoms
Vascular dementia	History of symptoms beginning after cerebrovascular events
Other medical conditions	
Depression	Anhedonia, feelings of worthlessness, slowed speech, flat affect, sleep disturbance
Hypothyroidism	Fatigue, cold intolerance, constipation, weight gain, dry skin, prolonged deep tendon reflexes, myalgias
Neurosyphilis	History of high-risk sexual behavior or injection drug use, vision and hearing loss, decreased proprioception, stabbing extremity pains
Niacin/vitamin B_3 deficiency	History of bariatric surgery or malabsorption disorders, photosensitive rash, anxiety, insomnia, diarrhea, vomiting
Normal-pressure hydrocephalus	Urinary incontinence and broad-based, shuffling gait
Vitamin B_{12} deficiency	Ascending paresthesias, tongue soreness, limb weakness, weight loss
Wernicke-Korsakoff syndrome	History of alcoholism, nystagmus or extraocular muscle weakness, broad-based gait and stance

Adapted with permission from Simmons BB, Hartmann B, Dejoseph D. Evaluation of suspected dementia. Am Fam Physician. 2011;84(8):897, with additional information from references 23 through 27, 31, and 32.

Falk N et al, 2018

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	References
In patients with suspected dementia, the Mini-Cog, the General Practitioner Assessment of Cognition, or the Ascertain Dementia 8-Item Informant Questionnaire should be used to determine the need for further evaluation.	C	29, 33-37
Patients who screen positive for cognitive impairment on brief screening tests should be evaluated further to quantify the degree of impairment.	C	29
The standard laboratory evaluation for patients with cognitive impairment includes testing for anemia, hypothyroidism, vitamin B_{12} deficiency, diabetes mellitus, and liver and kidney disease.	C	29
Magnetic resonance imaging without contrast media is the preferred imaging test to exclude other intracranial abnormalities, such as stroke, subdural hematoma, normal-pressure hydrocephalus, or a treatable mass.	C	41, 42

A = consistent, good-quality patient-oriented evidence; **B** = inconsistent or limited-quality patient-oriented evidence; **C** = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.

Levenson J, 2017

Delirium, which is characterized by restlessness, incoherence, and other behavioral changes, is common in hospitalized patients with severe illness, particularly patients in intensive care units (Inouye and Young 2006).

Delirium has a hypoactive form that resembles depression, a hyperactive form associated with agitation and psychosis, or a mixed state of both.

About one-third of psychiatric consultation requests at hospitals are to help manage behavioral disturbances of delirium (Schellhorn et al. 2009).

Levenson J, 2017

The optimal management of delirium involves properly identifying and treating the underlying cause of the disorder along with a multimodal strategy to alleviate existing symptoms.

Common causes of delirium include infection, dehydration, or metabolic problems. In addition to addressing the underlying source of the delirium, patients can benefit from psychopharmacology, as well as environmental and behavioral interventions that stimulate and orient them to their surroundings.

Among potential medication choices, haloperidol remains the gold standard for the pharmacological treatment of delirium (American Psychiatric Association 1999). Some randomized clinical trials of delirium comparing haloperidol with the atypical antipsychotics risperidone and olanzapine generally have not found significant differences in safety and effectiveness (Han and Kim 2004, Yoon et al. 2013, Maneeton et al. 2013).

The advantage of treating patients with haloperidol is that this is the only recommended agent that can be given orally, intravenously, intramuscularly, and subcutaneously; this allows for the treatment of patients with delirium and a wide range of conditions.

In patients with preexisting QTc prolongation over 500 msec, alternatives to QTc-prolonging antipsychotics should be considered. Possible options for treating this patient population include aripiprazole, propofol, and dexmedetomidine

As noted above, anticholinergic toxicity is one of the critical mechanisms of delirium (Trzepacz 2000).

Anticholinergic delirium is commonly seen in patients with impaired acetylcholine neurotransmission due to Alzheimer's disease or neural damage resulting from head trauma, hypoxia, or stroke; it can also be caused by medications with antimuscarinic effects (for example, benztropine, scopolamine, diphenhydramine, and tricyclic antidepressants).

Along with supportive measures to keep patients alert and oriented, anticholinergic delirium is addressed by stopping any offending agents, and, if necessary, treatment with the reversible acetylcholinesterase inhibitor physostigmine (Moore et al. 2015).

G et al, 2020

Box 1. Suggested questions for clinicians to screen for cognitive impairment in mood disorders.

1. Do you find that you are slower in your thinking than you used to be?
2. Do you find that you are more distractible than you used to be?
3. Do you find that you cannot hold things in your mind, such as shopping lists and telephone numbers?
4. Do you find that it is more difficult to learn new things?
5. Do you find that you forget people's names or other things that you used to remember?
6. Do you find that it is difficult to plan and carry out activities that have a number of steps?
7. Do you find that you are able to concentrate when reading a book or newspaper, but have to keep re-reading a paragraph?

2) Ikäihmisen masennuksen seulonta ja diagnosointi

Yl juha kemppinen

- Two questions

1) does the patient suffer from depressed mood?
2) is there diminished interest or pleasure?

- have a high sensitivity (about 95%), but unfortunately a low specificity (57%), for diagnosing MDD.

- Onko sinulla mieliala yli puolet päivästä masentunut?
- Tunnetko vähemmän mielihyvää tai mielenkiintoa harrastuksiisi kuin ennen?

9-1 Unipolar Depressive Disorders: Common Psychological and Cognitive Symptoms

- Depressed mood
- Lack of interest or motivation
- Inability to enjoy things
- Lack of pleasure (anhedonia)
- Apathy
- Irritability
- Anxiety or nervousness
- Excessive worrying
- Reduced concentration or attention
- Memory difficulties
- Indecisiveness
- Reduced libido
- Hypersensitivity to rejection or criticism
- Reward dependency
- Perfectionism
- Obsessiveness
- Ruminations
- Excessive guilt
- Pessimism
- Hopelessness
- Feelings of helplessness
- Cognitive distortions [e.g., ‘‘I am unlovable’’]
- Preoccupation with oneself
- Hypochondriacal concerns
- Low or reduced self-esteem
- Feelings of worthlessness
- Thoughts of death or suicide
- Thoughts of hurting other people

massachusetts general hospital handbook of general hospital psychiatry, 2010

9-2 Unipolar Depressive Disorders: Common Behavioral Symptoms

- Crying spells
- Interpersonal friction or confrontation
- Anger attacks or outbursts
- Avoidance of anxiety-provoking situations
- Social withdrawal
- Avoidance of emotional and sexual intimacy
- Reduced leisure-time activities
- Development of rituals or compulsions
- Compulsive eating
- Compulsive use of the Internet or video games
- Workaholic behaviors
- Substance use or abuse
- Intensification of personality traits or pathologic behaviors
- Excessive reliance or dependence on others
- Excessive self-sacrifice or victimization
- Reduced productivity
- Self-cutting or mutilation
- Suicide attempts or gestures
- Violent or assaultive behaviors

massachusetts general hospital handbook of general hospital psychiatry, 2010

9-3 Unipolar Depressive Disorders: Common Physical and Somatic Symptoms

- Fatigue
- Leaden feelings in arms or legs
- Difficulty falling asleep (early insomnia)
- Difficulty staying asleep (middle insomnia)
- Waking up early in the morning (late insomnia)
- Sleeping too much (hypersomnia)
- Frequent naps
- Decreased appetite
- Weight loss
- Increased appetite
- Weight gain
- Sexual arousal difficulties
- Erectile dysfunction
- Delayed orgasm or inability to achieve orgasm
- Pains and aches
- Back pain
- Musculoskeletal complaints
- Chest pain
- Headaches
- Muscle tension
- Gastrointestinal upset
- Heart palpitations
- Burning or tingling sensations
- Paresthesias

massachusetts general hospital handbook of general hospital psychiatry, 2010

MADRS
Montgomery – Åsberg: Depression Rating Scale

NIMI | SYNT.AIKA | PÄIVÄYS

1. ALENTUNUT MIELIALA (huomioitu)

Tarkoittaa emotionaalisen perusvireen alentumista (erotukseksi tilanteesta johtuvista tunnetiloista). Käsittää synkkyyden, raskasmielisyyden ja alakuloisuuden, mitkä käyvät ilmi ilmeistä, asennoista ja liikehdinnästä.

Arviointi perustuu siihen kuinka ilmeinen alakuloisuus ym. on sekä siihen kuinka helposti potilas on johdateltavissa muihin asioihin.

Kohonnut mieliala luokitellaan nollaksi.

- 0 Neutraali mieliala.
- 1
- 2 Näyttää koko ajan alakuloiselta, mutta voi tilapäisesti tulla valoisammalle tuulelle.
- 3
- 4 Näyttää alakuloiselta ja onnettomalta puheenaiheesta riippumatta.
- 5
- 6 Ilmaisee läpikotaista, äärimmäistä synkkyyttä, raskasmielisyyttä tai epätoivoista onnettomuuden tunnetta.

pisteet 0 – 6 ☐

2. ALAKULOISUUS

Tarkoittaa masennuksen tunnetta huolimatta siitä näkyykö se päällepäin vai ei. Käsittää murheellisuuden, onnettomuuden, raskasmielisyyden, toivottomuuden ja avuttomuuden tunteet.

Arviointi perustuu tunteen voimakkuuteen ja kestoon sekä siihen kuinka paljon ulkoiset tekijät vaikuttavat mielentilaan.

Kohonnut mieliala luokitellaan nollaksi.

- 0 Neutraali mielentila. Voi tuntea sekä tilapäistä hilpeyttä että apeutta olosuhteiden mukaan, ilman painoa kumpaankaan suuntaan.
- 1
- 2 Enimmäkseen alakuloinen, mutta valoisampiakin hetkiä on välillä.
- 3
- 4 Jatkuvasti alakuloinen ja synkkämielinen. Ulkoiset olosuhteet vaikuttavat hyvin vähän mielentilaan.
- 5
- 6 Jatkuva, erittäin syvä masennus.

pisteet 0 – 6 ☐

3. AHDISTUKSEN TUNTEET

Tarkoittaa epämääräistä, psyykkisen pahanolon tunnetta, epämiellyttävää sisäistä jännitystä, ahdistusta, kauhua tai sisäistä levottomuutta, joka voi kehittyä paniikiksi.

Arviointi perustuu tunteen voimakkuuteen ja kestoon sekä avun tarpeen suuruuteen.

Pidettävä erillään alakuloisuudesta sekä huolestuneisuudesta.

- 0 Enimmäkseen rauhallinen.
- 1
- 2 Tilapäisiä epämiellyttävän psyykkisen jännityksen tunteita.
- 3
- 4 Jatkuva sisäisen levottomuuden tunne, joka toisinaan kehittyy paniikiksi, joka vain vaivoin on hillittävissä.
- 5
- 6 Pitkäaikaisia paniikinomaisia ahdistuskohtauksia. Vallitseva kauhuntunne tai ahdistava kuolemanpelko, jota (potilas) ei yksin pysty hallitsemaan.

pisteet 0 – 6 ☐

4. VÄHENTYNYT YÖUNI

Tarkoittaa lyhentynyttä tai liiaksi keventynyttä unta tavallisiin nukkumatapoihin verrattuna. Lisääntynyt uni luokitellaan nollaksi.

Arviointi perustuu siihen kuinka ilmeinen alakuloisuus ym. on sekä siihen kuinka helposti potilas on johdateltavissa muihin asioihin.

- 0 Nukkuu tavalliseen tapaan.
- 1
- 2 Kohtuullisia vaikeuksia päästä uneen, tai lyhyempi, pinnallisempi tai rauhattomampi uni kuin tavallisesti.
- 3
- 4 Lyhentynyt nukkuma-aika (vähintään kaksi tuntia vähemmän kuin tavallisesti). Herää usein yön aikana myös ilman ulkoisia häiriöitä.
- 5
- 6 Nukkuu öisin vähemmän kuin kaksi – kolme tuntia kaikkiaan.

pisteet 0 – 6 ☐

5. VÄHENTYNYT RUOKAHALU

Tarkoittaa sitä, että ruokahalu tuntuu huonommalta kuin tavallisesti.

- 0 Normaali tai lisääntynyt ruokahalu.
- 1
- 2 Huono ruokahalu.
- 3
- 4 Ruokahalu puuttuu melkein kokonaan, ruoka ei maistu: täytyy pakottaa itsensä syömään.
- 5
- 6 Ei syö mitään, jollei joku maanittele. Kieltäytyy kokonaan syömästä.

pisteet 0 – 6 ☐

MADRS
Montgomery – Åsberg: Depression Rating Scale

6. KESKITTYMISVAIKEUDET

Tarkoittaa vaikeuksia koota ajatuksensa ja keskittyä. Arviointi perustuu voimakkuuteen, taajuuteen sekä siihen missä määrin eri toiminnat vaikeutuvat.

Pidettävä erillään muistihäiriöistä ja häiriöistä ajatuksen juoksussa.

- 0 Ei keskittymisvaikeuksia.
- 1
- 2 Tilapäisiä vaikeuksia pitää ajatukset koossa esim. lukiessa tai televisiota katsellessa.
- 3
- 4 Selviä keskittymisvaikeuksia, jotka vaikeuttavat lukemista tai keskustelua.
- 5
- 6 Jatkuvia invalidisoivia keskittymisvaikeuksia.

pisteet 0 – 6 ☐

7. ALOITEKYVYTTÖMYYS

Tarkoittaa omakohtaista tunnetta aloitekyvyttömyydestä sekä siitä, että on voitettava vastus ennen kuin voi ryhtyä toimiin.

Pidettävä erillään päättämättömyydestä ja väsymisestä.

- 0 Ei minkäänlaisia vaikeuksia käydä uusiin toimiin käsiksi.
- 1
- 2 Lieviä alkuvaikeuksia.
- 3
- 4 Vaikea ryhtyä yksinkertaisiinkin rutiinitehtäviin, nämä vaativat suuria ponnistuksia.
- 5
- 6 Kyvytön ryhtymään yksinkertaisiimpiinkin puuhiin. Ei pysty aloittamaan mitään toimintaa omin neuvoin.

pisteet 0 – 6 ☐

8. VÄHENTYNYT KYKY KOKEA TUNNE-ELÄMYKSIÄ

Tarkoittaa vähentynyttä kiinnostusta ulkomaailmaa tai tavallisesti huvia ja iloa tuottavia toimintoja kohtaan. Subjektiivinen kyvyttömyys tunnereaktioihin lähiympäristön ihmisiä ja tapahtumia kohtaan.

- 0 Normaalisti kiinnostunut ulkomaailmasta ja toisista ihmisistä.
- 1
- 2 Vaikea tuntea huvia siitä mikä tavallisesti kiinnostaa. Vähentynyt kyky suuttua tai ärsyyntyä.
- 3
- 4 Mielenkiinto ulkomaailmaa kohtaan puuttuu. Ystävät ja tuttavat tuntuvat samantekeviltä.
- 5
- 6 Täysin kyvytön tuntemaan adekvaattia surua tai vihaa. Täydellinen tai tuskallinen välinpitämättömyyden tunne ja kyvyttömyys tuntea mitään edes läheisimpiä ihmisiä kohtaan.

pisteet 0 – 6 ☐

9. DEPRESSIIVINEN AJATUSTEN SISÄLTÖ

Tarkoittaa kaikenlaisia itsesyytöksiä, kuvitelmia synnistä ja syyllisyydestä, alemmuudesta ja taloudellisesta perikadosta.

- 0 Ei pessimistisiä ajatuksia.
- 1
- 2 Lyhytaikaisia itsesyytöksiä ja alemmuudentunteita silloin tällöin.
- 3
- 4 Jatkuvia itsesyytöksiä. Selkeitä, mutta ei kohtuuttomia mietteitä synnistä tai syyllisyydestä. Selvästi ilmaistu pessimistinen näkemys tulevaisuudesta.
- 5
- 6 Absurdeja kuvitelmia taloudellisesta perikadosta ja anteeksiantamattomista synneistä. Absurdeja itsesyytöksiä.

pisteet 0 – 6 ☐

10. ELÄMÄÄN KYLLÄSTYNEISYYS JA ITSEMURHA-AJATUKSIA

Tarkoittaa elämään kyllästymistä, kuolemantoivomuksia, itsemurha-ajatuksia sekä itsemurhavalmisteluja. Mahdolliset itsemurhayritykset eivät sinänsä vaikuta luokitukseen.

- 0 Tavanomainen elämänhalu. Ei itsemurha-ajatuksia.
- 1
- 2 Elämään kyllästynyt, mutta ei ollenkaan tai vain epämääräisiä toiveita kuolla.
- 3
- 4 Itsemurha-ajatuksia esiintyy, ja itsemurha on ajateltavissa oleva ratkaisu, mutta ilman selkeitä itsemurha-aikeita.
- 5
- 6 Selvästi ilmaistuja aikeita tehdä itsemurha tilaisuuden tullen. Aktiivisia itsemurhavalmisteluja.

pisteet 0 – 6 ☐

MUISTIINPANOJA

0-7 p = ei oireita
8-14 p = masennusoireita
15-24 p = lievä masennus
25-30 p = keskivaikea
31-43 p= vaikea
>44 p = erittäin vaikea

– Lievään masennustilaan liittyy subjektiivista kärsimystä mutta toimintakyky on yleensä säilynyt, keskivaikea masennustila huonontaa yleensä selvästi toimintakykyä, ja vaikeasta masennustilasta kärsivä tarvitsee usein apua päivittäisissä toimissaan.
– Psykoottisessa masennustilassa esiintyy masennusoireiden lisäksi harhaluuloja tai hallusinaatioita.

Taulukko 3. Esimerkki Montgomery–Åsbergin arviointiasteikosta

1. Alentunut mieliala → Huomioitu alakuloisuus
2. Alakuloisuus → Ilmoitettu alakuloisuus
3. Ahdistuksentunteet
4. Vähentynyt yöuni
5. Vähentynyt ruokahalu
6. Keskittymisvaikeudet
7. Aloitekyvyttömyys
8. Vähentynyt kyky kokea tunne-elämyksiä
9. Depressiivinen ajatusten sisältö → Pessimistiset ajatukset
10. Elämään kyllästyneisyys ja itsemurha-ajatuksia → Itsemurha-ajatukset

MADRS-tulkinta :

MADRS-asteikon tulkintaohje:

Pisteet Tulkinta

0- 7 pistettä = ei masennusta

8- 14 pistettä = masennusoireita

15-24 pistettä = lievä masennustila

25- 30 pistettä = keskivaikea masennustila

31-43 pistettä = vaikea-asteinen masennustila

- **44 pistettä = erittäin vaikea-asteinen masennustila**

Psykiatrisk Forskningsenhed
Hillerød Sygehus

Depression demarkaatiolinja

Major (ICD-10) Depression Inventory

Alle olevat kysymykset koskevat vointiasi viimeisten 2 viikon aikana.

	Miten suuren osan ajasta ...	Koko ajan	Suurimman osan ajasta	Vähän yli puolet ajasta	Vähän alle puolet ajasta	Jonkin aikaa	Ei minkään ajankohtana
1	Oletko tuntenut itseesi masentuneeksi, surulliseksi?	☐	☐	☐	☐	☐	☐
2	Oletko menettänyt kiinnostukseesi päivittäisiin askareisiisi?	☐	☐	☐	☐	☐	☐
3	Oletko kärsinyt voimien ja energian puutteesta?	☐	☐	☐	☐	☐	☐
4	Onko itseluottamuksesi ollut heikompi?	☐	☐	☐	☐	☐	☐
5	Onko sinulla ollut huono omatunto tai syyllisyydentunteita?	☐	☐	☐	☐	☐	☐
6	Onko sinusta tuntunut, että elämä ei ole elämisen arvoista?	☐	☐	☐	☐	☐	☐
7	Onko sinulla ollut keskittymisvaikeuksia esim. lehteä lukiessa tai TV: tä katsellessa?	☐	☐	☐	☐	☐	☐
8a	Oletko tuntenut itseesi hyvin levottomaksi?	☐	☐	☐	☐	☐	☐
8b	Oletko tuntenut itseesi vaiteliaammaksi?	☐	☐	☐	☐	☐	☐
9	Onko sinulla ollut vaikeuksia saada unta yöllä?	☐	☐	☐	☐	☐	☐
10a	Onko ruokahalusi ollut vähentynyt?	☐	☐	☐	☐	☐	☐
10b	Onko ruokahalusi lisääntynyt?	☐	☐	☐	☐	☐	☐

Olsen LR, et al, Prevalence of major depression and stress indicators in the Danish general population, Acta Psychiatr Scand 2004: 109: 96–103.

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	Miten suuren osan ajasta ...	Koko ajan	Suurimman osan ajasta	Vähän yli puolet ajasta	Vähän alle puolet ajasta	Jonkin aikaa	Ei minkään ajankohtana
1	Oletko tuntenut itseesi masentuneeksi, surulliseksi?	☐	☐	☐			
2	Oletko menettänyt kiinnostukseesi päivittäisiin askareisiisi?	☐	☐	☐			
3	Oletko kärsinyt voimien ja energian puutteesta?	☐	☐	☐			
4	Onko itseluottamuksesi ollut heikompi?	☐	☐	☐	☐	☐	☐
5	Onko sinull… syyllisyyden						
6	Onko sinust… ole elämisen						
7	Onko sinull… keskittymisv… lukiessa tai						
8a	Oletko tunte… levottomaks…						
8b	Oletko tunte… vaiteliaamm…						
9	Onko sinulla ollut vaikeuksia saada unta yöllä?	☐	☐	☐	☐	☐	☐
10a	Onko ruokahalusi ollut vähentynyt?	☐	☐	☐	☐	☐	☐
10b	Onko ruokahalusi lisääntynyt?	☐	☐	☐	☐	☐	☐

Vähintään kahdessa pitää olla 4-5 tai kyse ei ole depressiosta

Depression vaikeusaste.

- **Kysymyksistä 1 – 10 valitse kaikki, joissa vähintään 3 pistettä (=yli puolet ajasta).**
- **Vähintään 4 oiretta = lievä masennus.**
- **Vähintään 6 oiretta = keskivaikea masennus.**
- **Vähintään 8 oiretta ja kysymyksistä 1-3 mukana kaikki 3 = vaikea masennus.**

Olsen LR, et al, Prevalence of major depression and stress indicators in the Danish general population, Acta Psychiatr Scand 2004: 109: 96–103.

Depression diagnoosi MDI-kyselylomakkeen avulla 5 minuutissa.

1. Potilas täyttää vastaanotolla MDI-kyselylomakkeen. (2 min.)
2. Pisteytä lomake potilaan läsnä ollessa. (30 sek.)

- Jokaisesta kysymyksestä pisteet 5 – 4 – 3 – 2 – 1 -0.
- Kysymyksissä 8 ja 10 on a- ja b-kohdat. Huomioi pisteitä laskiessa vain korkeamman pistemäärän vaihtoehto.
- Laske pisteet yhteen.

3. Tulkitse vastaukset. (2 min.)

1.

Diagnoosi perustuu kahden viikon aikana olleisiin oireisiin.

2.

Kysymykset 1-3 ratkaisevat, onko kyse depressiosta.

- Vähintään kahdessa tulee olla 4 tai 5 pistettä.
- Jos ehto ei täyty, on kyse jostakin muusta, kuin depressiosta. ***Syy tulee selvittää!***
- Selvitä aluksi, onko kyse korjaantumassa olevasta depressiosta.

3.

Depression vaikeusaste.

- Kysymyksistä 1 – 10 valitse kaikki, joissa vähintään 3 pistettä (=yli puolet ajasta).
- Vähintään 4 oiretta = lievä masennus.
- Vähintään 6 oiretta = keskivaikea masennus.
- Vähintään 8 oiretta ja kysymyksistä 1-3 mukana kaikki 3 = vaikea masennus.

Kokonaispistemäärä

- Maksimi 50 pistettä.
- Kuvaa depression vaikeusastetta silloin, kun kyse on depressiosta.
- On hyvä hoitovasteen mittari!
- Pelkästään pistemäärän perusteella ei saa tehdä depression diagnoosia!

Muista!

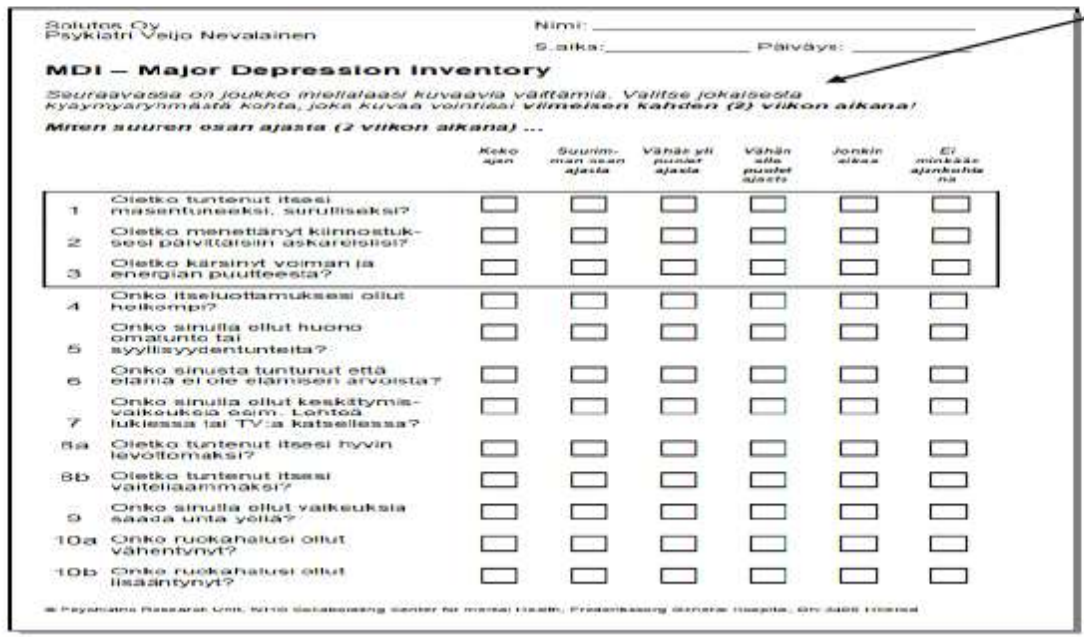
MDI on erinomainen apu depression tunnistamisessa, hoitovasteen seurannassa ja kaikkien tarpeellisten kysymysten muistamisessa.

Yksin sen perusteella ei kuitenkaan saa tehdä diagnoosia.

Myös muut, kuin oirekriteerit tulee huomioida.

Depression diagnoosi MDI-kyselylomakkeen avulla 5 minuutissa.

1. Potilas täyttää vastaanotolla MDI-kyselylomakkeen. (2 min.)
2. Pisteytä lomake potilaan läsnä ollessa. (30 sek.)
   - Jokaisesta kysymyksestä pisteet 5 – 4 – 3 – 2 – 1 -0.
   - Kysymyksissä 8 ja 10 on a- ja b-kohdat. Huomioi pisteitä laskiessa vain korkeamman pistemäärän vaihtoehto.
   - Laske pisteet yhteen.
3. Tulkitse vastaukset. (2 min.)



Solutos Oy
Psykiatri Veijo Nevalainen

Nimi: _____
S.aika: _____ Päiväys: _____

MDI – Major Depression Inventory

*Seuraavassa on joukko mielialaasi kuvaavia väittämiä. Valitse jokaisesta kyäymyaryhmästä kohta, joka kuvaa voinniaai **viimeisen kahden (2) viikon aikana!***

Miten suuren osan ajasta (2 viikon aikana) ...

		Koko ajan	Suurimman osan ajasta	Vähän yli puolet ajasta	Vähän alle puolet ajasta	Jonkin aikaa	Ei minkään ajankohdan aikana
1	Oletko tuntenut itsesi masentuneeksi, surulliseksi?	☐	☐	☐	☐	☐	☐
2	Oletko menettänyt kiinnostuksesi päivittäisiin askareisiisi?	☐	☐	☐	☐	☐	☐
3	Oletko kärsinyt voiman ja energian puutteesta?	☐	☐	☐	☐	☐	☐
4	Onko itseluottamuksesi ollut heikompi?	☐	☐	☐	☐	☐	☐
5	Onko sinulla ollut huono omatunto tai syyllisyydentunteita?	☐	☐	☐	☐	☐	☐
6	Onko sinusta tuntunut että elämä ei ole elämisen arvoista?	☐	☐	☐	☐	☐	☐
7	Onko sinulla ollut keskittymisvaikeuksia esim. Lehteä lukiessa tai TV:a katsellessa?	☐	☐	☐	☐	☐	☐
8a	Oletko tuntenut itsesi hyvin levolliomaksi?	☐	☐	☐	☐	☐	☐
8b	Oletko tuntenut itsesi vaitellaammaksi?	☐	☐	☐	☐	☐	☐
9	Onko sinulla ollut vaikeuksia saada unta yöllä?	☐	☐	☐	☐	☐	☐
10a	Onko ruokahalusi ollut vähentynyt?	☐	☐	☐	☐	☐	☐
10b	Onko ruokahalusi ollut lisääntynyt?	☐	☐	☐	☐	☐	☐

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Kokonaispistemäärä
- Maksimi 50 pistettä.
- Kuvaa depression vaikeusastetta silloin, kun kyse on depressiosta.
- On hyvä hoitovasteen mittari!
- Pelkästään pistemäärän perusteella ei saa tehdä depression diagnoosia!

1.
Diagnoosi perustuu kahden viikon aikana olleisiin oireisiin.

2.
Kysymykset 1-3 ratkaisevat, onko kyse depressiosta.
- Vähintään kahdessa tulee olla 4 tai 5 pistettä.
- Jos ehto ei täyty, on kyse jostakin muusta, kuin depressiosta. ***Syy tule selvittää!***
- Selvitä aluksi, onko kyse korjaantumassa olevasta depressiosta.

3.
Depression vaikeusaste.
- Kysymyksistä 1 – 10 valitse kaikki, joissa vähintään 3 pistettä (=yli puolet ajasta).
- Vähintään 4 oiretta = lievä masennus.
- Vähintään 6 oiretta = keskivaikea masennus.
- Vähintään 8 oiretta ja kysymyksistä 1-3 mukana kaikki 3 = vaikea masennus.

Muista!
MDI on erinomainen apu depression tunnistamisessa, hoitovasteen seurannassa ja kaikkien tarpeellisten kysymysten muistamisessa. Yksin sen perusteella ei kuitenkaan saa tehdä diagnoosia. Myös muut, kuin oirekriteerit tulee huomioida.

Solutos/ Veijo Nevalainen

Aina kun tehdään MDI tai MADRS, pitää tehdä MDQ
(Saman ajanjakson aikana, ei elämän aikana)

Bipolaariseula

Nimi_____

Päivämäärä ____ ____ /____ ____ / 20____

Henkilötunnus_____--_____

Mielialahäiriökysely MDQ

Hirschfeld et al,Am J Psych 2000;157:1873-5, suom. E.I & JoBS-työryhmä

MDQ+: >7 kyllä vastausta

1. Onko Teillä koskaan ollut sellaista ajanjaksoa jolloin ette oikein ollut oma itsenne ja ...

a) tunsitte olonne niin hyväksi tai niin kiihtyneeksi, että muidenkaan mielestä ette ollut oma itsenne, tai olitte niin kiihtynyt, että jouduitte vaikeuksiin?.....

b) olitte niin ärtyisä, että huusitte ihmisille, tai aloitte väittelyjä tai riitoja?.....

c) itseluottamuksenne oli paljon tavallista parempi?.....

d) nukuitte paljon tavallista vähemmän, ettekä tuntenut tarvitsevanne enempää unta?.....

e) olitte paljon puheliaampi tai puhuitte tavallista nopeammin?.....

f) ajatukset kilisivät mielessänne, tai ette saanut kiihtynyttä ajatustoimintaanne rauhoittumaan?.....

g) ulkoiset tapahtumat veivät huomiotanne niin paljon, ettette kyennyt keskittymään tai pysymään kärryillä?.....

h) olitte paljon tavallista energisempi?.....

i) olitte paljon aktiivisempi tai teitte useampia asioita kuin tavallisesti?

j) olitte paljon tavallista sosiaalisempi tai ulospäinsuuntautuneempi, esimerkiksi soittelitte ystäville keskellä yötä?.....

k) olitte paljon tavallista kiinnostuneempi seksistä?.....

l) teitte asioita joita yleensä ette tee tai joita muut ihmiset saattoivat pitää liioiteltuina, hölmöinä tai vaarallisina?.....

m) rahan tuhlaaminen aiheutti Teille tai läheisillenne vaikeuksia?.....

2. Mikäli vastasitte KYLLÄ useampaan kuin yhteen kohtaan ylläolevista, tapahtuiko useampi näistä asioista saman ajanjakson aikana? *Olkaa hyvä ja vastatkaa joko kyllä tai ei.*

3. Kuinka paljon ongelmia ylläolevat asiat aiheuttivat Teille – esimerkiksi ongelmia liittyen perheeseen, rahaan tai virkavaltaan, työkyvyttömyyttä, tai sanaharkkoja ja riitoja? *Olkaa hyvä ja rengastakaa vain yksi vaihtoehto.*

Kyllä	Ei
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
X	☐

1 Ei ongelmia
2 Vähäisiä
3 Kohtalaisia
4 Vakavia

MDQ (Mood Disorders Questionnaire)

- **MDQ:n tulkinta**

  Seula on positiivinen, jos
  - kohdassa 1. on 7 kyllä-vastausta ja
  - kohdassa 2. kyllä-vastaus ja
  - kohdassa 3. vastauksena 3 tai 4

- Tarvitsee psykiatrian erikoislääkärin tutkimukset

200121 Ikäihmisten masennus

Geriatrinen depressioasteikko (GDS)

https://www.kaypahoito.fi/xmedia/hoi/hoi50044o.pdf

Nimi: _____ ***Syntymäaika:*** _____

Pvm: _____ ***Arvioitsija:*** _____

Pisteet yhteensä: _____

Nämä kysymykset koskevat jokapäiväistä mielialaa, asenteita ja tunteita. Haluaisin tietää, miltä Teistä on tuntunut viimeksi kuluneen viikon aikana, tämä päivä mukaan lukien. Luen kysymykset Teille ja toivon Teidän vastaavan niihin joko "kyllä" tai "ei".

		KYLLÄ	EI
1.	Oletteko pohjimmiltanne tyytyväinen elämäänne?	0	1
2.	Oletteko joutunut luopumaan monista kiinnostavista asioista ja harrastuksista?	1	0
3.	Tuntuuko elämänne tyhjältä?	1	0
4.	Tunnetteko olonne usein ikävystyneeksi?	1	0
5.	Oletteko toiveikas tulevaisuuden suhteen?	0	1
6.	Vaivaavatko Teitä ajatukset, jotka pyörivät jatkuvasti mielessänne?	1	0
7.	Oletteko enimmäkseen hyvällä tuulella?	0	1
8.	Pelkäättekö, että jotain pahaa tulee tapahtumaan Teille?	1	0
9.	Oletteko useimmiten onnellinen?	0	1
10.	Tunnetteko itsenne usein avuttomaksi?	1	0

200121 Ikäihmisten masennus

https://www.kaypahoito.fi/xmedia/hoi/hoi50044o.pdf

11. Oletteko usein levoton ja hermostunut?	1	0
12. Oletteko mielummin kotona sen sijaan, että lähtisitte ulos?	1	0
13. Oletteko usein huolissanne tulevaisuudesta?	1	0
14. Onko Teillä mielestänne enemmän muistivaikeuksia kuin muilla?	1	0
15. Onko Teistä hyvä, että olette yhä elossa?	0	1
16. Tuntuuko Teistä usein synkältä ja alakuloiselta?	1	0
17. Tunnetteko olonne arvottomaksi?	1	0
18. Kannatteko paljon huolta menneestä?	1	0
19. Onko elämänne mielestänne innostavaa?	0	1
20. Onko Teidän vaikea aloittaa uusia asioita?	1	0

200121 Ikäihmisten masennus

https://www.kaypahoito.fi/xmedia/hoi/hoi50044o.pdf

21. Tunnetteko itsenne tarmokkaaksi?	0	1
22. Tuntuuko elämäntilanteenne toivottomalta?	1	0
23. Tuntuuko Teistä, että muiden asiat ovat paremmin kuin Teidän?	1	0
24. Saavatko pienet asiat Teidät usein pois tolaltanne?	1	0
25. Itkettääkö Teitä usein?	1	0
26. Onko Teillä keskittymisvaikeuksia?	1	0
27. Onko mielestänne mukavaa nousta aamuisin?	0	1
28. Vältteletteköö toisten ihmisten tapaamista?	1	0
29. Onko Teidän helppo tehdä päätöksiä?	0	1
30. Kykenettekö ajattelemaan yhtä selkeästi kuin ennen?	0	1

Summapisteet:

0–10 normaali, 11–20 lievä depressio ja 21–30 keskivaikea tai vaikea depressio.

Geriatric depression screening scale

- Geriatrinen depressioasteikko (GDS) kehitettiin iäkkäiden henkilöiden masennuksen arviointia varten. Kehitystyössä painotettiin asteikon täyttämisen helppoutta. Lisäksi pyrittiin välttämään vanhuksilla yleisesti esiintyvien somaattisten oireiden mukaan ottamista kysymysvalikomaan. Alkuperäisestä 30 kysymystä (kyllä/ei) käsittävästä asteikosta on myöhemmin kehitetty 15, 10 ja 4 kysymyksestä koostuvat suppeammat arviointiasteikot.
- GDS on itsearviointiasteikko, mutta toinen henkilö voi täyttää asteikon luettuaan kysymykset ääneen tutkittavalle. Masennusoireita arvioidaan viimeksi kuluneen viikon ajalta. GDS soveltuu parhaiten depression seulontamittariksi vanhuksilla. Summapistemäärä 0–10 on normaali, 11–20 viittaa lievään depressioon ja 21–30 keskivaikeaan tai vaikeaan depressioon.
- Kysymysten esittämiseen kuluu n. 15 minuuttia. Tutkittavalle kannattaa ennen kyselyn aloittamista lyhyesti esitellä asteikon merkitys ja oikea vastaamistapa, esimerkiksi: ”Kysyn nyt teiltä kysymyksiä, joiden avulla haluan selvitellä tämänhetkistä mielialaanne. Toivoisin, että vastaisitte kaikkiin kysymyksiin hyvin lyhyesti, mieluiten ”kyllä” tai ”ei”. Se voi olla välillä vaikeata, mutta vastatkaa sen mukaan mikä mielestänne on lähinnä totuutta. Jotkut kysymykset herättävät uusia kysymyksiä tai tarvetta käydä kysymystä perusteellisemmin lävitse, mutta niihin kohtiin voimme palata myöhemmin, kun olemme koko kyselyn suorittaneet”.
- Tulostettava pdf-versio «GDS30.pdf»*1*. Lomakkeen voi myös ladata ja tallentaa omalle koneelleen, minkä jälkeen sen voi avata ja täyttää erillisessä Adobe Acrobat Reader -sovelluksessa. Tällöin on käytössä myös laskenta-automatiikka. Toiminto vaatii uusimman Reader-version käyttöä. Sen voit tarvittaessa ladata Adoben sivustolta, jonne pääset tästä linkistä «https://get.adobe.com/reader/»*1*.
- Käynnistä https://www.kaypahoito.fi/pgr00024

Maurer D et al 2018

TABLE 4

Five-Item Geriatric Depression Scale

Choose the best answer for how you have felt over the past week:

Are you basically satisfied with your life?	Yes/**No**
Do you often get bored?	**Yes**/No
Do you often feel helpless?	**Yes**/No
Do you prefer to stay at home rather than going out and doing new things?	**Yes**/No
Do you feel pretty worthless the way you are now?	**Yes**/No

Scoring: Bolded answers receive 1 point. A score of 2 or more is considered a positive result.

Adapted with permission from Maurer DM. Screening for depression [published correction appears in Am Fam Physician. *2013;87(7):464].* Am Fam Physician. *2012;85(2):142.*

Maurer D et al 2018

TABLE 5

15-Item Geriatric Depression Scale

Choose the best answer for how you have felt over the past week:

Are you basically satisfied with your life?	Yes/**No**
Have you dropped many of your activities and interests?	**Yes**/No
Do you feel that your life is empty?	**Yes**/No
Do you often get bored?	**Yes**/No
Are you in good spirits most of the time?	Yes/**No**
Are you afraid that something bad is going to happen to you?	**Yes**/No
Do you feel happy most of the time?	Yes/**No**
Do you often feel helpless?	**Yes**/No
Do you prefer to stay at home, rather than going out and doing new things?	**Yes**/No
Do you feel you have more problems with memory than most?	**Yes**/No
Do you think it is wonderful to be alive now?	Yes/**No**
Do you feel pretty worthless the way you are now?	**Yes**/No
Do you feel full of energy?	Yes/**No**
Do you feel that your situation is hopeless?	**Yes**/No
Do you think that most people are better off than you are?	**Yes**/No

Scoring: Bolded answers receive 1 point. A score of more than 5 suggests depression that should be further evaluated clinically.

Adapted with permission from Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. In: Brink TL, ed. Clinical Gerontology: A Guide to Assessment and Intervention. New York, NY: Haworth Press; 1986.

Spoelgoef G et al 2011

Table 2. Geriatric Depression Scale (10-Item Shortened Form)

Question	*Response*
1. Are you basically satisfied with your life?*	Yes/NO
2. Do you feel that your life is empty?*	YES/No
3. Are you afraid that something bad is going to happen to you?*	YES/No
4. Do you feel happy most of the time?*	Yes/NO
5. Have you dropped many of your activities and interests?	YES/No
6. Do you often feel helpless?	YES/No
7. Do you feel that you have more problems with memory than most?	YES/No
8. Do you feel full of energy?	Yes/NO
9. Do you feel that your situation is hopeless?	YES/No
10. Do you think that most people are better off than you are?	YES/No

NOTE: *One point is scored for each response in capital letters. A score of 3 or greater may indicate depression.*

**—The first four questions are sometimes used as a four-item version of the scale, with one or more abnormal responses possibly indicating depression.*

Adapted with permission from D'ath P, et al. Screening, detection and management of depression in elderly primary care attenders. I: The acceptability and performance of the 15 item Geriatric Depression Scale (GDS15) and the development of short versions. Fam Pract. *1994;11(3):264.*

Malhi G et al, 2020

Table 5. Clinical assessment of circadian function.

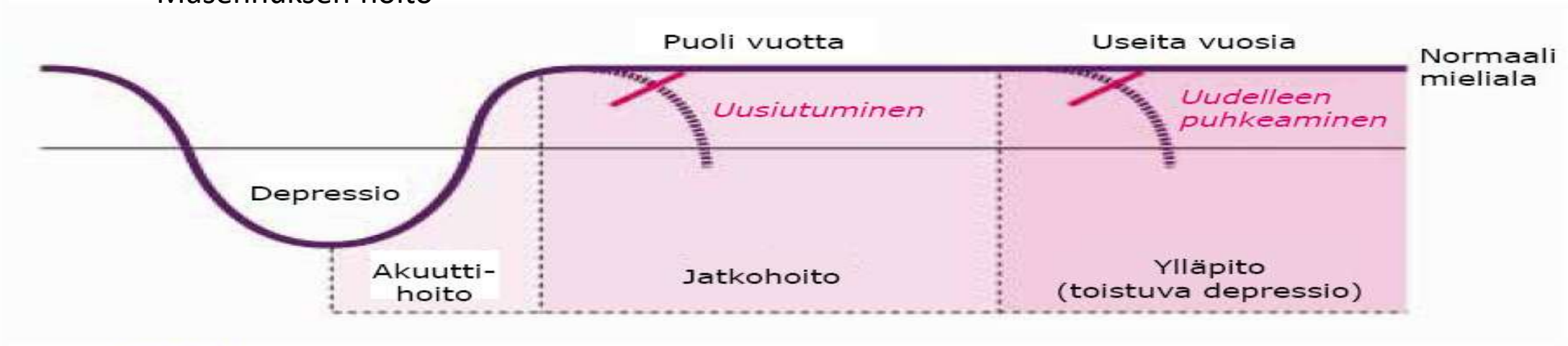
Construct	Measurement instrument/technology	Clinical application
Chronotype	Morningness-eveningness questionnaire (MEQ) (Horne and Östberg, 1976)	1. Completing the MEQ (understood as relating to individual differences in circadian phase) is a useful way to introduce circadian function to mood disorder patients. 2. Marked eveningness (common in BD and psychopathology generally) may explain sleep onset insomnia and difficulties with full-time work.
Social rhythm stability	Social rhythm metric (SRM) Ashman et al., 1999)	The SRM is a diary measure, assessing the regularity of key daily behaviours (particularly waketime and bedtime) across 7 days. Social rhythmicity ('routine' is a more meaningful term for many patients) is a key therapeutic target in IPSRT, and its measurement provides useful psychoeducation about how lifestyle might impact circadian vulnerability to mood disorder.
24-hour activity/ rest cycle	Actigraphy, or commercial activity monitors	Objective measurement of the 24-hour rest-activity cycle encourages patients to attend to this level of their motivational functioning and may identify important discrepancies with self-report about lifestyle and sleep/wake rhythms.

BD: bipolar disorder; IPSRT: interpersonal and social rhythm therapy.

3) Ikäihmisen masennuksen hoito

Yl juha kemppinen

Masennuksen hoito



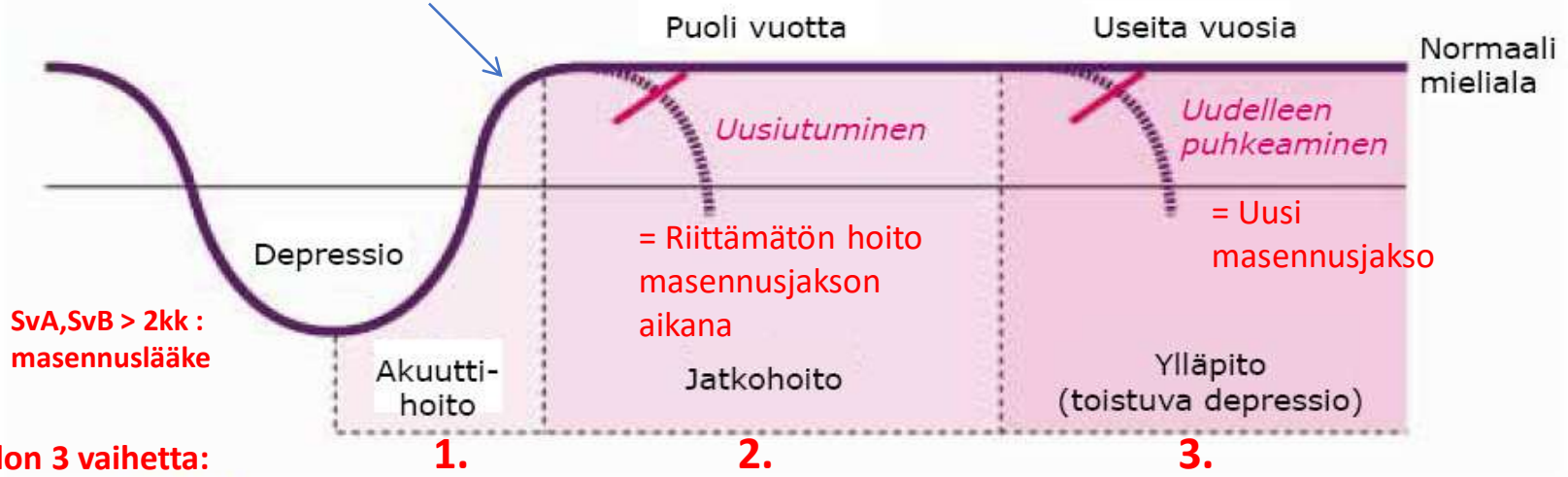
KUVA 1. Depression hoidon vaiheet.

- *Hoidon suunnittelu ja seuranta*
- Hoidon lähtökohta on depression diagnosointi.
- – Depression hoito jaetaan kolmeen vaiheeseen,
- 1. **akuuttivaihe**,
  - tavoitteena oireettomuus, kestää tämän tavoitteen saavuttamiseen asti
- 2. **jatkohoito**, tavoitteena estää oireiden palaaminen (uusiutuminen, relapsi) ja
- 3. **ylläpitohoito**, tavoitteena ehkäistä uuden sairausjakson puhkeaminen.

Depression Käypä Hoito-suositus 2010

- 40-50% oireiden häviäminen 6-8 viikkoa
- yli 30 % ei reagoi masennuslääkitykselle 8-12 vkon aikana
- yli 50% ei saavuta taudin remissiota = jää oireita

Akuuttihoidon varsinaisena tavoitteena on täydellinen tai lähes täydellinen oireettomuus



SvA,SvB > 2kk : masennuslääke

Hoidon 3 vaihetta:

KUVA 1. Depression hoidon vaiheet.

+ 6 kk masennuslääke

+ 6 kk seuranta

+ harhaluulot ja/tai hallusinaatiot

TAULUKKO 2. Depression vaikeusaste ja akuuttivaiheen hoitomuodot.

Hoitomuoto	Lievä	Keskivaikea	Vaikea	Psykoottinen
Psykoterapia	+	+	(+)	–
Masennuslääkkeet	+	+	+	+
Psykoosilääkkeet (masennuslääkkeen ohella)	–	–	–	+
Sähköhoito (ECT)	–	–	+	+

MADRS **15-24 pistettä** **25-30 p** **31-43 p** **” > 44 p ”**

➔ Työ- ja toimintakyky alenee

Psykoterapeuttinen hoito

- **Psykoterapian tavoitteet**
- Depressioiden hoidossa psykoterapioiden tavoitteena on saada potilas toipumaan ja hänen toimintakykynsä paranemaan vaikuttamalla
  - masennusta ylläpitäviin mielikuviin
  - ajattelumalleihin
  - tunne-elämään
  - minäkäsitykseen
  - toimintatapoihin.
- Psykoterapiat perustuvat teoreettisiin malleihin ja tutkimustietoon mielenterveyden ja käyttäytymisen ongelmista, normaalista ja häiriintyneestä psyykkisestä kehityksestä ja psykoterapian muutosprosesseista ja soveltavat niistä johdettuja kliinisiä käytäntöjä.

https://www.kaypahoito.fi/hoi50023#readmore

Masennuksen hoito - Psykoterapia

- – Lievien ja keskivaikeiden depressioiden akuuttivaiheen hoidossa voidaan käyttää joko yksin tai yhdessä lääkehoidon kanssa jotain seuraavista tähän mennessä vaikuttavaksi osoitetuista lyhytkestoisten terapioiden muodoista
  - kognitiivista psykoterapiaa [146–151] A
  - interpersonaalista terapiaa [146–151] A
  - psykodynaamista psykoterapiaa [144, 152–155] B.
- Lähinnä lievien masennustilojen hoidossa, kun kyse ei ole moniongelmaisista potilaista, voidaan käyttää myös
  - ongelmanratkaisuterapiaa [156] A
  - ratkaisu- ja voimavarakeskeistä terapiaa (155] C.
- Kognitiivisten, interpersonaalisten, psykodynaamisten ja ongelmanratkaisuterapioiden välillä ei ilmeisesti ole kliinisesti merkittäviä vaikuttavuuseroja [150].

Ihmisen käyttäytymisen muutoksessa vaikuttavat :

<u>Epäspesifit muuttujat</u> :

1. Tuliko minulle tunne ymmärretyksi tulemisesta ?

2. Kunnioitettiinko minun avunpyyntöä ja tavoitteitani terapiaistunnossa tai kuntoutustapahtumassa?

3. Oliko minuun kohdistunut mielenkiinto aitoa ja autenttista?

4. Synnyttikö terapiaistunto tai kuntoutus-tapahtuma minussa toivoa muutoksesta ja sen mahdollisuudesta?

5. Tarjosiko terapiaistunto/kuntoutus-tapahtuma vaihtoehtoisen selityksen (toteutettavissa minun resursseillani) ongelmilleni?

Depression Käypä Hoito-suositus 2010 : Depression psykoterapiat

TAULUKKO 2. Depression vaikeusaste ja akuuttivaiheen hoitomuodot.

Hoitomuoto	Lievä	Keskivaikea	Vaikea	Psykoottinen
Psykoterapia	+	+	(+)	–
Masennuslääkkeet	+	+	+	+
Psykoosilääkkeet (masennuslääkkeen ohella)	–	–	–	+
Sähköhoito (ECT)	–	–	+	+

TAULUKKO 4. Keskeiset psykoterapiamuodot depression hoidossa.

Hoitomuoto ja kuvaus	Tyypillinen kesto ja tiheys	Näytön aste		
		Akuutti vaihe	Ylläpito- ja jatkohoito-vaihe	Krooninen ja komplisoitu-nut masennus
Kognitiivinen Tavoitteena depressiota aiheuttavien ja ylläpitävien asenne- ja käyttäytymismallien muuttuminen ja ongelmanratkaisukeinojen lisääntyminen	Lyhyt: 10–20 käyntiä, yksi kerta viikossa	[146–151] A	–	–
	Lyhyt: 8–16 käyntiä (uusiutumisen estoterapia ja tietoisuustaitoihin perustuva MBCT)	–	[166–172] A	–
	Lyhyt/keskipitkä: 12–40 käyntiä (CBASP)	–	–	[173–176] B
	Pitkäkestoinen: 40–80 käyntiä, 1–2 käyntiä viikossa	D	D	C
Interpersonaalinen Tavoitteena depressiota aiheuttavien ja ylläpitävien ihmissuhdeongelmien, rooliristiriitojen tai menetysten fokusoitu käsittely	Lyhyt: 12–16 käyntiä, yksi käynti viikossa	[146–151] A	[166–172] A	–
Psykodynaaminen Tavoitteena depressiolle altistavien kehityksellisten ongelmien selvittely ja minuuden vahvistuminen	Lyhyt: 16–25 käyntiä, yksi käynti viikossa	[177–179] B	–	–
	Pitkäkestoinen: 80–240 käyntiä, 1–3 käyntiä viikossa	[155, 180] B	D	[155, 180] B

Hoitomuoto ja kuvaus	Tyypillinen kesto ja tiheys	Näytön aste		
		Akuutti vaihe	**Ylläpito- ja jatkohoitovaihe**	**Krooninen ja komplisoitunut masennus**
Kognitiivis-behavioraalinen				
Tavoitteina depressiota aiheuttavien ja ylläpitävien ajatus- ja toimintamallien muuttuminen ja ongelmanratkaisukeinoj en lisääntyminen	Lyhyt: 10–20 käyntiä, 1 käynti viikossa	A, A	-	-
	Lyhyt: 8–16 käyntiä (uusiutumisen estoterapia ja tietoisuustaitoihin perustuva MBCT)	-	A	-
	Lyhyt/keskipitkä: 12–40 käyntiä (CBASP)	-	-	B
	Pitkäkestoinen: 40–80 käyntiä, 1–2 käyntiä viikossa			B

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Hoitomuoto ja kuvaus	Tyypillinen kesto ja tiheys	Näytön aste		
		Akuutti vaihe	**Ylläpito- ja jatkohoitovaihe**	**Krooninen ja komplisoitunut masennus**
Käyttäytymisen aktivointi				
Tavoitteina depressiota aiheuttavien ja ylläpitävien käyttäytymismallien muuttuminen ja ongelmanratkaisukeinoj en lisääntyminen	Lyhyt: 10–20 käyntiä	A	-	-
Interpersoonallinen				
Tavoitteena depressiota aiheuttavien ja ylläpitävien ihmissuhdeongelmien, rooliristiriitojen tai menetysten fokusoitu käsittely	Lyhyt: 12–16 käyntiä, 1 käynti viikossa	A	A	-

https://www.kaypahoito.fi/hoi50023#readmore

Hoitomuoto ja kuvaus	Tyypillinen kesto ja tiheys	Näytön aste		
		Akuutti vaihe	**Ylläpito- ja jatkohoitovaihe**	**Krooninen ja komplisoitunut masennus**
Psykodynaaminen				
Tavoitteina depressiolle altistavien kehityksellisten ongelmien selvittely ja minuuden vahvistuminen	Lyhyt: 16–25 käyntiä, 1 käynti viikossa	A	-	-
	Pitkäkestoinen: 80–240 käyntiä, 1–3 käyntiä viikossa	B		B

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Depression hoito: lääke

Masennuslääkeryhmät

Esimerkkejä lääkeaineryhmittäin:

SSRI-lääkkeet
- essitalopraami
- fluoksetiini
- fluvoksamiini
- paroksetiini
- sertraliini
- sitalopraami

SNRI-lääkkeet
- duloksetiini
- milnasipraani
- venlafaksiini

Trisykliset
- amitriptyliini

Muut
- mirtatsapiini
- moklobemidi
- reboksetiini

- Voxra
- Valdoxan
- Brintellix

Suomessa vuonna 2020 käytössä olevat masennuslääkkeet ja niiden annokset aikuispotilaille

Geneerinen nimi	Aloitusannos (mg/vrk)	Hoitoannos (mg/vrk)	Tavallisia haittavaikutuksia
Selektiiviset serotoniinin takaisinoton estäjät (SSRI)			Ryhmälle luonteenomaisia mm. pahoinvointi, suolisto-oireet ja seksuaalitoimintojen häiriöt
Essitalopraami Cipralex	10	10–20	
Fluoksetiini Seronil	20	20–80	
Fluvoksamiini Fevarin	50	100–300	
Paroksetiini	20	20–50	
Sertraliini Zoloft	50	50–200	
Sitalopraami- Cipramil	20	20–40	

https://www.kaypahoito.fi/hoi50023#readmore

Suomessa vuonna 2020 käytössä olevat masennuslääkkeet ja niiden annokset aikuispotilaille

Geneerinen nimi		Aloitusannos (mg/vrk)	Hoitoannos (mg/vrk)	Tavallisia haittavaikutuksia
Muut depressiolääkkeet				
valdoxan				
Agomelatiini		25	25–50	Päänsärky, huimaus
Bupropioni	Voxra	150	150–300	Päänsärky, unettomuus, pahoinvointi
Duloksetiini		60	60–120	Pahoinvointi, suun kuivuminen, päänsärky, uneliaisuus
Mianseriini	Tolvon	30	30–90	Väsymys, huimaus
Milnasipraani	Ixel	50	50–100	Pahoinvointi, sydämentykytys, virtsaamisongelmat
Mirtatsapiini	Remeron	15–30	30–60	Väsymys, painon nousu
Moklobemidi	Aurorix	300	300–900	Unettomuus, huimaus
Reboksetiini		8	8–10	Ahdistuneisuus, yliaktivoituminen
Tratsodoni	Azona	50–100	150–500	Väsymys, huimaus, rytmihäiriöt
Venlafaksiini		75	75–375	Kuten SSRI-lääkkeillä
Vortioksetiini	Brintellix	10	5–20	Pahoinvointi

https://www.kaypahoito.fi/hoi50023#readmore

Suomessa vuonna 2020 käytössä olevat masennuslääkkeet ja niiden annokset aikuispotilaille

Geneerinen nimi	Aloitusannos (mg/vrk)	Hoitoannos (mg/vrk)	Tavallisia haittavaikutuksia
Trisykliset depressiolääkkeet[1)]			Ryhmälle luonteenomaisia muun muassa antikolinergiset ja alfa1-salpauksen haittavaikutukset
Amitriptyliini Triptyl	25–50	75–300	
Doksepiini Doxal	25–50	75–300	
Klomipramiini Anafranil	25–50	75–300	
Nortriptyliini Noritren	25–50	50–200	
Trimipramiini Surmontil	25–50	75–300	

[1)] Käyttö depressioon edellyttää pitoisuusmittauksia.

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- **Seurannan aikana arvioidaan saavutettua lääkevastetta. Ellei viitettä alkavasta hoitovasteesta ilmene 4 viikon kuluessa (oirepistemäärän < 20 %:n pieneneminen), on jo yleensä syytä vaihtaa toiseen masennuslääkkeeseen.**

- **Vastetta on syytä arvioida kriittisesti, kun täyttä hoitoannosta on käytetty 6–12 viikon ajan.**

- **Seuranta-ajan jatkaminen 8–12 viikkoon voi olla aiheellista, jos ensimmäisten 6–8 viikon aikana on jo ilmennyt osittainen hoitovaste (oirepistemäärän 20–50 %:n pieneneminen).**

- **Ellei selvää hoitovastetta (oirepistemäärän > 50 %:n pieneneminen) saavuteta, on tehoton lääke syytä vaihtaa toiseen 12. viikkoon mennessä**

https://www.kaypahoito.fi/hoi50023#readmore

Muut biologiset hoidot

- **Sähköhoito**
- Sähköhoitoa annetaan yleensä psykiatrisen sairaalahoidon yhteydessä, joskin myös polikliininen sähköhoito on mahdollista. Ennen hoitoa potilas nukutetaan laskimoanestesian avulla **8**.
- Sähköhoito on tehokkain hoitomuoto oirekuvaltaan vaikeassa tai psykoottisessa depressiossa **A**.
- Sitä tulee harkita erityisesti silloin, jos
  - lääkehoito ei ole tehonnut tai
  - muutoin tarvitaan nopeatehoista hoitoa esimerkiksi itsemurhavaaran vuoksi.
- Sähköhoitoa voidaan harkitusti käyttää myös keskivaikean, usealle lääkehoitoyritykselle resistentin depression hoidossa **C**.
- Masennuslääkehoitoa on sähköhoidon jälkeen syytä jatkaa tavanomaiseen tapaan akuuttivaiheen jälkeisissä jatkohoito- ja ylläpitovaiheissa.
- Sähköhoitoa voidaan käyttää harvajaksoisena ylläpitohoitona tilanteissa, joissa vaikean tai psykoottisen depression lääkkeellinen ylläpitohoito ei ole tehonnut **A**.

https://www.kaypahoito.fi/hoi50023#readmore

Muut biologiset hoidot

- **Kaamosmasennuksen kirkasvalohoito**
- Joillakuilla depressiopotilailla masennusjaksoja esiintyy toistuvasti ja lähes yksinomaan vain pimeän talvikauden aikana niin sanottuna kaamosmasennuksena, joka on vuodenaikamasennuksen (Seasonal Affective Disorder, SAD) alamuoto. Kirkasvalohoito tehoaa kaamosmasennukseen hyvin **A**. Hoitoa annetaan siihen tarkoitetulla laitteella aamuisin (2 500–10 000 luksin valoteholla) yleensä 30–60 minuutin ajan
  - ensimmäisten parin viikon aikana yleensä päivittäin
  - myöhemmin joko kuureina tai jatkuvasti
  - ainakin viidesti viikossa talvikauden ajan.
- Kaamosmasennusta on mahdollista hoitaa myös serotoniinin takaisinottoa estävillä masennuslääkkeillä **C**.
- Kirkasvalohoidosta saattaa olla hyötyä depression hoitovaihtoehtona muulloinkin kuin kaamosmasennuksessa, mutta tällaisen hoidon rooli on toistaiseksi epäselvä **C**.

https://www.kaypahoito.fi/hoi50023#readmore

Muut biologiset hoidot

- **Transkraniaalinen magneettistimulaatiohoito**
- Aivojen transkraniaalinen magneettistimulaatio (TMS) on turvallinen ja vähän haittavaikutuksia aiheuttava depression hoitomuoto, jonka teho akuuttihoidossa vastaa masennuslääkehoidon tehoa. Sen keskeiset rajoitukset liittyvät toimenpiteen saatavuuteen ja laitekustannuksiin **A**.
- TMS-hoitoa voidaan kohdentaa erityyppisenä eri aivoalueille. Paras näyttö vaikuttavuudesta on nykyisin suuritaajuuksisesta stimulaatiosta vasemmanpuoleiselle DLPFC (dorsolateraalinen prefrontaalikorteksi) -alueelle.
- TMS tehoaa myös lääkeresistenttiin depressioon **A**.
- **Tasavirtastimulaatio**
- Aivojen tasavirtastimulaatio (transcranial direct current stimulation, tDCS) on uusi aivojen stimulaatiohoito, jotka toteutetaan yleensä päähän laitettava elektrodimyssyn avulla. Hoitoa annetaan yleensä 20–30 minuuttia kerrallaan, tavallisesti viidesti viikossa noin kolmen viikon ajan, minkä jälkeen hoitoa voidaan jatkaa kertaviikkoisena. Hoidon teho on korkeintaan masennuslääkehoidon veroinen **B**. Se on yleensä hyvin siedetty, ja sen keskeisin haittavaikutus on päänahan ihoärsytys.

https://www.kaypahoito.fi/hoi50023#readmore

Muut biologiset hoidot

- **Invasiiviset neuromodulaatiohoidot**
- Neuromodulaatioon perustuvia hoitomuotoja, joiden asemaa muulle hoidolle resistentissä depressiossa punnitaan, ovat
  - vagaalinen hermostimulaatio (Vagal Nerve Stimulation, VNS) **C**
  - syvä aivostimulaatio (Deep Brain Stimulation, DBS) **C**

https://www.kaypahoito.fi/hoi50023#readmore

Table 10.5 Treatment recommendations for antidepressants in acute treatment of major depressive disorder in the general population [29, 30]

	CANMAT guidelines	APA guidelines
First-line options	Bupropion SR or XL, citalopram, desvenlafaxine, duloxetine, escitalopram, fluoxetine, fluvoxamine, mirtazapine, paroxetine, sertraline, venlafaxine, vortioxetine, agomelatine*, mianserin*, milnacipran*	Bupropion, citalopram, desvenlafaxine, duloxetine, escitalopram, fluoxetine, fluvoxamine, mirtazapine, paroxetine, sertraline, venlafaxine
Alternative options	Amitriptyline, clomipramine, moclobemide, phenelzine, quetiapine/quetiapine XR, reboxetine*, tranylcypromine, trazodone, vilazodone, levomilnacipran*, selegiline transdermal*	Amitriptyline, desipramine, doxepin, imipramine, isocarboxazid, nortriptyline, phenelzine, tranylcypromine, trimipramine, selegiline transdermal*

*Not available in Canada

Hategan A et al, Geriatric Psychiatry, 2018

Widera E et al, 2012

Table 2. Selected Antidepressant Medications Commonly Used in Patients with Advanced Illness

*Medication**	*Starting dosage (per day)†*	*Usual dosage (per day)*	*Onset of action*	*Clinical considerations*	*Cost of generic (brand)‡*
Amitriptyline§	10 to 25 mg	25 to 100 mg	4 to 8 weeks	Anticholinergic effects common (sedation, delirium, urinary retention, orthostatic hypotension); may lower seizure threshold[17] Useful agent for neuropathy[17]	$12
Bupropion (Wellbutrin)§	100 to 200 mg	200 to 450 mg	4 to 8 weeks	Lowers seizure threshold; may cause insomnia, nausea, and dry mouth Minimal sexual adverse effects	$30 ($108)
Citalopram (Celexa)§‖	10 mg	20 to 40 mg	4 to 8 weeks	Causes dose-dependent QT interval prolongation Maximum dosage of 20 mg per day recommended in older patients	$17 ($120)
Desipramine (Norpramin)	10 to 25 mg	25 to 100 mg	4 to 8 weeks	Fewer anticholinergic adverse effects than amitriptyline[17]	$33 ($41)
Duloxetine (Cymbalta)	30 to 60 mg	60 mg	4 to 8 weeks	Noradrenergic activity may cause dry mouth, excessive sweating, and constipation May help with neuropathic pain	NA ($182)
Escitalopram (Lexapro)‖	5 to 10 mg	10 to 20 mg	4 to 8 weeks	Causes dose-dependent QT interval prolongation	NA ($120)
Fluoxetine (Prozac)§‖	5 to 10 mg	20 to 40 mg	4 to 8 weeks	Fluoxetine associated with weight loss, others associated with weight gain Fluoxetine and paroxetine have high potential for drug-drug interactions caused by potent CYP2D6 inhibition[17]	$15 ($214) for 10 mg

Widera E et al, 2012

Table 2. Selected Antidepressant Medications Commonly Used in Patients with Advanced Illness

*Medication**	*Starting dosage (per day)†*	*Usual dosage (per day)*	*Onset of action*	*Clinical considerations*	*Cost of generic (brand)‡*
Methylphenidate (Ritalin)	2.5 to 5 mg	10 to 20 mg	1 to 3 days	Dose in the morning and at noon to avoid insomnia[17] Well tolerated in most patients, with most having good response at lower doses[17] May also help with fatigue, opioid-induced sedation, and appetite[17]	$45 ($65) for 5 mg
Mirtazapine (Remeron)§	7.5 to 15 mg	15 to 45 mg	4 to 8 weeks	Administer at bedtime because of sedative effects May increase appetite Antinausea effects have been reported	$50 ($135) for 30 mg
Nortriptyline (Pamelor)§	10 to 25 mg	25 to 100 mg	4 to 8 weeks	Fewer anticholinergic adverse effects than amitriptyline[17]	$18 ($696)
Paroxetine (Paxil)§‖	10 mg	20 to 40 mg	4 to 8 weeks	Fluoxetine and paroxetine have high potential for drug-drug interactions due to potent CYP2D6 inhibition[17] Withdrawal toxicity more likely to occur with paroxetine	$30 ($117)
Sertraline (Zoloft)§‖	12.5 to 25 mg	50 to 200 mg	4 to 8 weeks	—	$20 ($138)

CYP2D6 = cytochrome P450 2D6; NA = not available.

**—Drugs listed in alphabetical order.*

†—Lower starting dosage recommended in most patients with advanced or terminal illnesses.

‡—Estimated retail price of one month's treatment of the lowest amount of the starting dosage of each drug (e.g., $20 for the 12.5-mg dose of sertraline). For drugs that have a designated dose listed with the price, prices are for the commercially available product closest to the lower starting dosage. Information obtained at http://www.drugstore.com (accessed February 2, 2012).

§—May be available at discounted prices at one or more national retail chains; only the 75-mg dose of bupropion is on the discount list.

‖—Common adverse effects include nausea, diarrhea, insomnia, restlessness; these often attenuate with time.

Information from reference 17.

MacQueen G et al, 2016

Table 5. Current Evidence for Treatment of Perimenopausal Depression.

Recommendation	Treatment	Level of Evidence
First line	Desvenlafaxine	Level 1
	CBT	Level 2
Second line	Transdermal estradiol[a]	Level 2
	Citalopram, duloxetine, escitalopram, mirtazapine, quetiapine XR, venlafaxine XR	Level 3
	Omega-3 fatty acids, fluoxetine, nortriptyline, paroxetine, sertraline	Level 4
Third line	Mindfulness-based CBT, supportive psychotherapy	Level 4

CBT, cognitive-behavioural therapy.
[a]Women with an intact uterus should also be prescribed concomitant progesterone.

Spoelgoef G et al 2011

Table 6. Medications for Geriatric Depression

Medication	*Initial dosage*	*Maximal dosage*	*Risk of drug interaction*	*Adverse effects**
Selective serotonin reuptake inhibitors				
Citalopram (Celexa)	10 to 20 mg once per morning	40 mg once per day	Low	Hyponatremia, GI symptoms, sexual dysfunction, weight gain, extrapyramidal symptoms
Escitalopram (Lexapro)	10 mg once per day	20 mg once per day	Low	GI symptoms, sexual dysfunction, weight gain
Fluoxetine (Prozac)	10 to 20 mg once per day	40 mg once per day	High	Insomnia, GI symptoms, sexual dysfunction, weight gain
Paroxetine (Paxil)†	10 mg once per day	40 mg once per day	Moderate	GI symptoms, sedation, weight gain, withdrawal symptoms
Sertraline (Zoloft)	25 to 50 mg once per day	200 mg once per day	Low	Sexual dysfunction, weight gain
Serotonin-norepinephrine reuptake inhibitors				
Duloxetine (Cymbalta)	20 mg once or twice per day	60 mg once per day or 30 mg twice per day	Low	GI symptoms, xerostomia, urinary hesitancy
Venlafaxine (Effexor)†	25 to 50 mg twice per day	75 to 225 mg total twice per day	High	GI symptoms, headaches, hyponatremia, withdrawal symptoms, hypertension, extrapyramidal symptoms
Other serotonergic agents				
Bupropion (Wellbutrin)†	37.5 to 50 mg twice per day	75 to 150 mg twice per day	Moderate	GI symptoms, sexual dysfunction, seizures, psychosis
Mirtazapine (Remeron)	7.5 to 15 mg at bedtime	45 mg once per day	Low	Sedation, sexual dysfunction, weight gain
Tricyclic agents				
Desipramine (Norpramin)	10 to 25 mg once at bedtime	50 to 150 mg once per day	High	Hypotension, sedation, GI symptoms, weight gain
Nortriptyline (Pamelor)	10 to 25 mg once at bedtime	75 to 150 mg once per day	High	Hypotension, sedation, weight gain

GI = gastrointestinal.

**—Adverse effects are similar within each class; more prominent symptoms listed for individual agents.*

†—These agents are available in extended-release formulations at different dosages.

Adapted with permission from Pollock BG, Semla TP, Forsyth CE. Psychoactive drug therapy. In: Halter JB, et al., eds. Hazzard's Geriatric Medicine and Gerontology. *6th ed. New York, NY: McGraw-Hill Medical; 2009:769.*

Mitä potilaalle tulee kertoa psyykenlääkkeestä?

1. Lääkkeen nimi (kauppanimi ja kemiallinen nimi)
2. Lääkkeen käyttötarkoitus (sairaustilan hoito, oireen lievittäminen ja lääkkeen ottamisen tärkeys)
3. Miten lääkkeen hoitovaikutus ilmenee ja mitä tehdä jos lääke ei tunnu auttavan
4. Koska ja kuinka lääke tulee ottaa – vuorokauden aika, ennen vai jälkeen aterioiden)
5. Mitä tulee tehdä, jos annos jää ottamatta
6. Kuinka kauan lääkettä on tarkoitus käyttää

Jenkins SC et al: A Pocket Reference to Psychiatrists.3.p., American Psychiatric Press, Washington DC,2001

Mitä potilaalle tulee kertoa psyykenlääkkeestä?

7. Potilaan kannalta tärkeät mahdolliset haittavaikutukset sekä kuinka niihin tulee suhtautua
8. Lääkkeen mahdolliset vaikutukset autolla ajoon, työhön tms. – ja mitä varotoimenpiteitä tulee tämän vuoksi tehdä.
9. Interaktiot alkoholin ja muiden lääkkeiden kanssa.
10. Lääkkeen käytön aiheuttamat kulut.
11. Vastaavien muiden lääkkeiden annossuhteet.
12. Koska lääkkeen vaikutus alkaa ilmetä.
13. Mitä laboratoriotutkimuksia tarvitaan.
14. Mitä muita hoito- tai lääkevaihtoehtoja on, jos tämä lääke ei lievitä oireita.

Jenkins SC et al: A Pocket Reference to Psychiatrists.3.p., American Psychiatric Press, Washington DC,2001

Masennuslääkkeiden tehossa ei ole eroja, sivuvaikutuksissa on

TAULUKKO 3. Suomessa vuonna 2009 käytössä olevat depressiolääkkeet ja niiden annokset aikuispotilaille.

Geneerinen nimi	Aloitusannos (mg/vrk)	Hoitoannos (mg/vrk)	Tavallisia haittavaikutuksia
Trisykliset depressiolääkkeet			Ryhmälle luonteenomaisia muun muassa antikolinergiset ja alfa$_1$-salpauksen haittavaikutukset
Amitriptyliini	25–50	75–300	
Doksepiini	25–50	75–300	
Klomipramiini	25–50	75–300	
Nortriptyliini	25–50	50–200	
Trimipramiini	25–50	75–300	
Selektiiviset serotoniinin takaisinoton estäjät (SSRI)			Ryhmälle luonteenomaisia muun muassa pahoinvointi, suolisto-oireet ja seksuaalitoimintojen häiriöt
Essitalopraami	10	10–20	
Fluoksetiini	20	20–80	
Fluvoksamiini	50	100–300	
Paroksetiini	20	20–50	
Sertraliini	50	50–200	
Sitalopraami	20	20–60	
Muut depressiolääkkeet			
Agomelatiini	25	25–50	Päänsärky, huimaus
Duloksetiini	60	60–120	Pahoinvointi, suun kuivuminen, päänsärky, uneliaisuus
Mirtatsapiini	15–30	30–60	Väsymys, painon nousu
Moklobemidi	300	300–900	Unettomuus, huimaus
Venlafaksiini	75	75–375	Kuten SSRI:t
Tratsodoni	50–100	150–500	Väsymys, huimaus, rytmihäiriöt

Markkinoilla oleva reboksetiini ei, depressioindikaatiosta huolimatta, todennäköisesti ole tehokas masennuslääke.

http://www.kaypahoito.fi/web/kh/suositukset/naytaartikkeli/tunnus/hoi50023

TABLE 3. Half-lives of Antidepressants[a]

Antidepressant	Half-life range (hr)	Average half-life (hr)	Steady state (days)
Tertiary amines			
Amitriptyline	10–50	24	4–10
Clomipramine	19–37	32	7–14
Doxepin	8–36	8	2–8
Trimipramine	7–30	9	2–6
Imipramine	6–24	16	2–5
Secondary amines			
Desipramine	12–76	22	2–11
Nortriptyline	15–93	24	4–19
Protriptyline	54–198	126	10
Dibenzoxazepine			
Amoxapine	—	8	2–7
SSRIs			
Fluoxetine	24–216	72	28–35
Fluvoxamine	—	20	7
Paroxetine	7–37	20[b]	7–14
Sertraline	26	26	7–12
Others			
Venlafaxine	4	4	16
Nefazodone	2–4	—[c]	—
Trazodone	4–9	5	3–7
Maprotiline	27–58	51	6–10
Buproprion	8–24	14	2–5
Nomifensine	2–10	—	2–5
Mirtazapine	20–40	22	5

[a]Refs. 13–15, 21, and 22.
[b]Highly variable.
[c]Dose dependent.

5 x T ½ = tasainen pitoisuus veressä
Ja poistuminen elimistöstä

Serotoniinireseptorit ja niiden tavallisin sivuvaikutus

Table 98–5 Common Reported Side Effects of Antidepressant Medications

SSRI	SNRI	Mirtazepine	Nefazodone	Bupropion	MAOI	TCA
Headache	SSRI side effects	Increased appetite	Sedation	Numbness	Hypertension	Dry mouth
Nausea	Dry mouth	Weight gain	Liver failure	Dizziness	Initial anxiety	Blurred vision
Decreased motivation	Constipation	Sedation	Fatigue	Spaciness	Weight gain	Constipation
Insomnia	Agitation	Fatigue	Ataxia	Seizures (in high doses)	Insomnia	Weight gain
Fatigue	Diaphoresis		Dry mouth	Ataxia	Dry mouth	Fatigue
Ejaculatory dysfunction	Increased blood pressure		Constipation		Blurred vision	Sedation
Anorgasmia	Weight gain?				Ejaculatory dysfunction	Insomnia
Decreased libido					Anorgasmia	Hypersomnia
Weight gain?					Constipation	Ejaculatory dysfunction
					Dizziness	Initial jitteriness/ anxiety

Tasman et al, 2011

Mielialalääkkeiden ja placebon teho: sivuvaikutuksia

TABLE 11. Selected Side Effects of SSRIs[a,b]

Side effect	Fluoxetine	Sertraline	Paroxetine	Fluvoxamine	Venlafaxine
Nausea	+++	++++	++++	+++++++	+++++++
Nervousness	+++	+	+	++	+++
Anorexia	++	−	+	+	++
Insomnia	++	++	++	+++	++
Drowsiness	+	++	++++	+++	+++
Tremor	+	++	++	+	+
Fatigue	+	+	+++	++	+
Dry mouth	+	++	+	+	+++
Dizziness	+	+	++	++	+++
Sweating	+	++	++	+	++
Diarrhea	+	++	+	+	−
Constipation	−	−	+	+/−	++
Sexual dysfunction	+	+++	+++	++	++++

[a]Refs 15 and 157.

[b]Each + represents about a 4% incidence of the side effect after adjusting for placebo effect; a − represents a decreased incidence of the side effect relative to that reported for placebo.

Table 25–14
Pharmacokinetic Profiles of the Selective Serotonin Reuptake Inhibitors

Drug	Time to Peak Plasma Concentration	Half-Life	Half-Life Metabolite	Time to Steady State (days)	Plasma Protein Binding (percentage)
Citalopram (Celexa)	4 hr	35 hr	3 hr	7	80
Escitalopram (Lexapro)	5 hr	27–32 hr	—	7	56
Fluoxetine (Prozac)	6–8 hr	4–6 days	4–16 days	28–35	95
Fluvoxamine (Luvox)	3–8 hr	15 hr	—	5–7	80
Paroxetine (Paxil)	5–6 hr	21 hr	—	5–10	95
Paroxetine CR (Paxil CR)	6–10 hr	15–20 hr	—	< 14	95
Sertraline (Zoloft)	4.5–8.5 hr	26 hr	62–104 hr	7	95

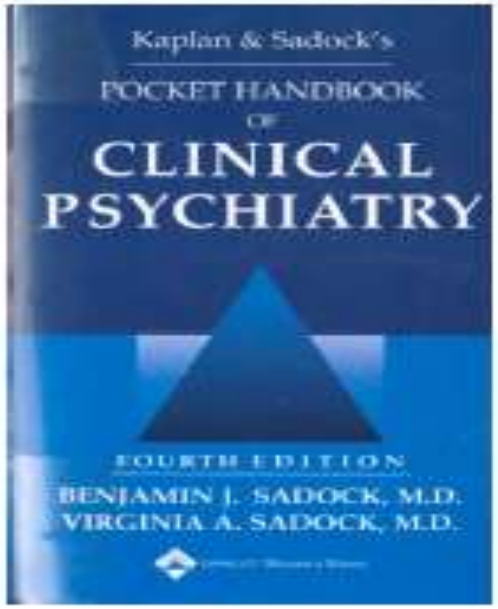


Table 25–17
Non-SSRI Antidepressants

Drugs	Time to Peak Plasma Concentration (hr)	Half-Life (hr)	Starting Dose (mg)	Maintenance Dose (mg)	High Dose (mg)
Venlafaxine	2.5	9	75	225	300–375
Venlafaxine XR	5	11	37.5–75	150	225
Bupropion	2	8	100	300	450
Bupropion SR	3	12	150	300	400
Bupropion XL	5	35	150	300	>300
Mirtazapine	2	20–40	15	45	60
Duloxetine	6	12	30–40	60	>60
Nefazodone	1	4–8	100–200	300–600	>600

Table 25–19
Available Preparations and Typical Dosages of MAOIs

Generic Name	Trade Name	Preparations	Usual Daily Dosage (mg)	Usual Maximum Daily Dosage (mg)
Isocarboxazid[a]	Marplan	10-mg tablets	20–40	60
Moclobemide[b]	Manerix	100- 150-mg tablets	300–600	600
Phenelzine	Nardil	15-mg tablets	30–60	90
Selegiline	Eldepryl, Atapryl	5-mg capsules; 5-mg tablets	10	30
Tranylcypromine	Parnate	10-mg tablets	20–60	60

[a] Available directly from the manufacturer.
[b] Not available in the United States.

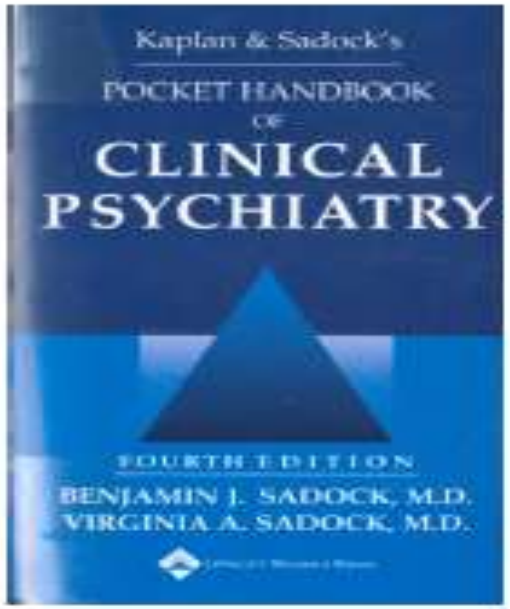


Table 25–18
Clinical Information for the Tricyclic and Tetracyclic Drugs

Generic Name	Trade Name	Usual Adult Dosage Range (mg/day)[a]
Imipramine	Tofranil	150–300[b]
Desipramine	Norpramin	150–300[b]
Trimipramine	Surmontil	150–200
Amitriptyline	Elavil	150–300[b]
Nortriptyline	Pamelor, Aventyl	50–150
Protriptyline	Vivactil	15–60
Amoxapine	Asendin	150–400
Doxepin	Adapin, Sinequan	150–300[b]
Maprotiline	Ludiomil	150–225
Clomipramine	Anafranil	150–250

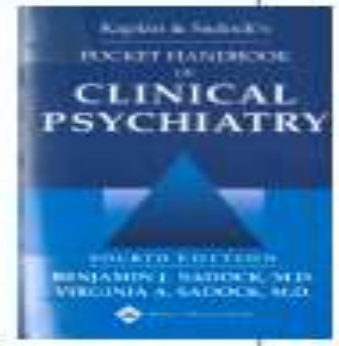
[a] Exact range may vary among laboratories.
[b] Includes parent compound and desmethyl metabolite.

Tolvon

Table 25–16
Interactions of Drugs With the SSRs

SSRI	Other Drugs	Effect	Clinical Importance
Fluoxetine	Desipramine	Inhibits metabolism	Possible
	Carbamazepine	Inhibits metabolism	Possible
	Diazepam	Inhibits metabolism	Not important
	Haloperidol	Inhibits metabolism	Possible
	Warfarin	No interaction	
	Tolbutamide	No interaction	
Fluvoxamine	Antipyrine	Inhibits metabolism	Not important
	Propranolol	Inhibits metabolism	Unlikely
	Tricyclics	Inhibits metabolism	Unlikely
	Warfarin	Inhibits metabolism	Possible
	Atenolol	No interaction	
	Digoxin	No interaction	
Paroxetine	Phenytoin	AUC increases by 12%	Possible
	Procyclidine	AUC increases by 39%	Possible
	Cimetidine	Paroxetine AUC increases by 50%	Possible
	Antipyrine	No interaction	
	Digoxin	No interaction	
	Propranolol	No interaction	
	Tranylcypromine	No interaction	Caution with combined treatment
Sertraline	Warfarin	No interaction	Not important
	Antipyrine	Increased clearance	
	Diazepam	Clearance decreased by 13%	Not important
	Tolbutamide	Clearance decreased by 16%	Not important
	Digoxin	No interaction	
	Lithium	No pharmacokinetic interaction	Caution with combined treatment
	Desipramine	No interaction	
	Atenolol	No pharmacokinetic interaction	
Citalopram	Cimetidine	Citalopram AUC increases	
	Metoprolol	May double blood concentration	

[a]Adapted from Warrington SJ: Clinical implications of the pharmacology of serotonin reuptake inhibitors. *Int Clin Psychopharmacol* 1987; 7(Suppl 2):13, with permission.
AUC, area under curve.



Serotoniinireseptorit ja niiden vaikutus

Table 98–4 The Proposed Function of Different 5-HT Receptors

1A	Anxiety Depression Sexual behavior Appetite Aggression Pain Emesis ? obsessions Vasoconstriction
1D	Migraine Appetite Depression
2A	Vasoconstriction Migraine Anxiety
2B	Depression Sleep Hallucination Suicide
2C	Appetite Anxiety Depression Learning Psychosis
3	Emesis Anxiety Psychosis Migraine Reward
4	Muscle contraction, gut and heart Learning Cognition Anxiety Sleep Emesis
5	Unknown
6	OCD?
7	Circadian rhythms

Source: Dubovsky SL, and Thomas M (1995) Serotonergic mechanisms and current and future psychiatric practice. J Clin Psychiatr 56(2), 38–48.

Tasman et al, 2011

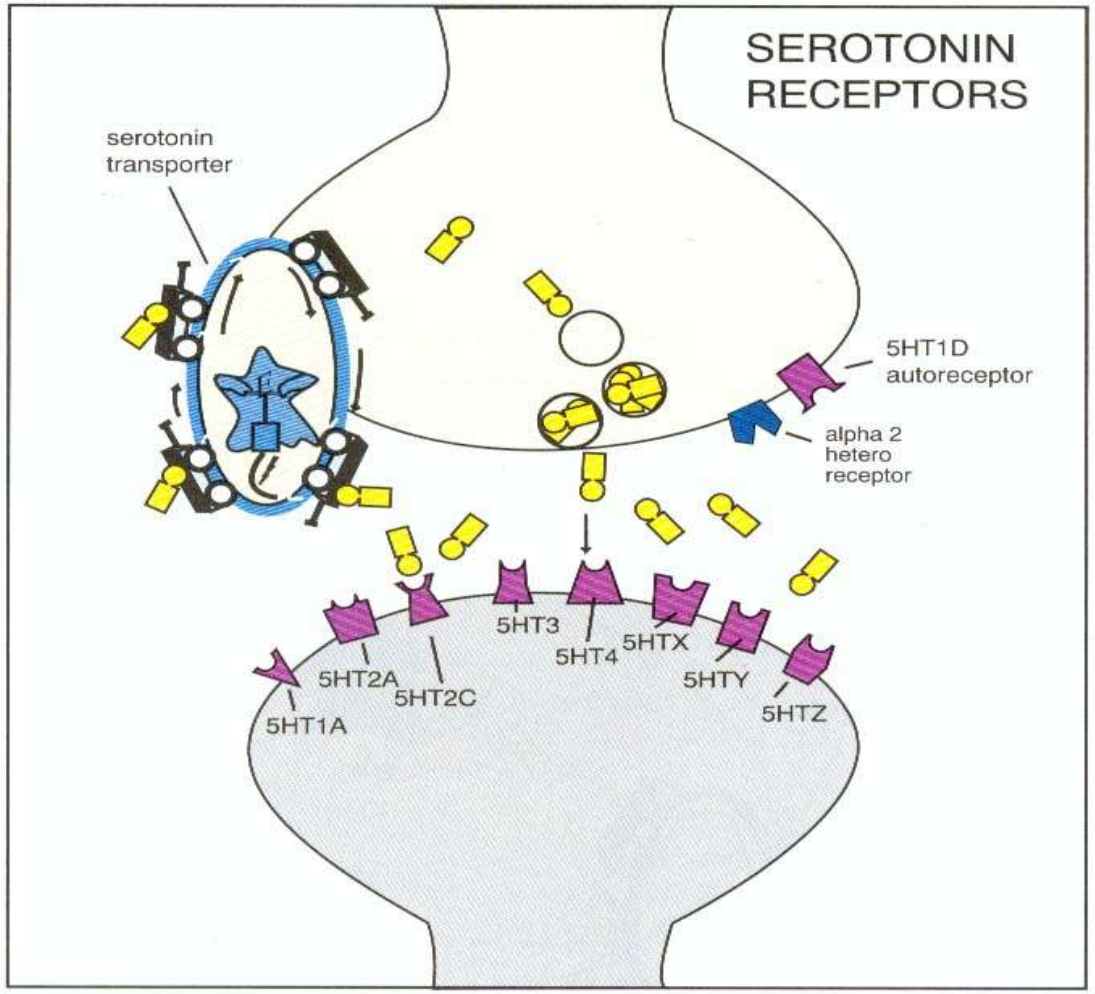


FIGURE 5–36. **Receptor subtyping for the serotonergic neuron** has proceeded at a very rapid pace, with at least four major categories of 5HT receptors, each further subtyped depending on pharmacological or molecular properties. In addition to the serotonin transporter, there is a key presynaptic serotonin receptor (the 5HT1D receptor) and another key presynaptic receptor, the alpha 2 noradrenergic heteroreceptor. This organization allows serotonin release to be controlled not only by serotonin but also by norepinephrine, even though the serotonin neuron does not itself release norepinephrine. Several postsynaptic serotonin receptors (5HT1A, 5HT1D, 5HT2A, 5HT2C, 5HT3, 5HT4, and many others denoted by 5HT X, Y, and Z) are shown as well. They convey messages from the presynaptic serotonergic neuron to the target cell postsynaptically.

S.Stahl, 2000

Table 98–4 The Proposed Function of Different 5-HT Receptors

1A	Anxiety Depression Sexual behavior Appetite Aggression Pain Emesis ? obsessions Vasoconstriction
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Source: Dubovsky SL, and Thomas M (1995) Serotonergic mechanisms and current and future psychiatric practice. J Clin Psychiatr 56(2), 38–48.

Tasman et al, 2011

9-4 Relationship of Antidepressants to Neurotransmitter Receptors

Adapted from Richelson E: Pharmacology of antidepressants—characteristics of the ideal drug, *Mayo Clin Proc* 69:1069–1081, 1994.

Antidepressant	Effect on Biogenic Amine Uptake: Potency*		Selectivity for Blocking Uptake of 5-HT Over NE	Affinities† for Neurotransmitter Receptors							
				Histamine		Adrenergic		Serotonin		Muscarinic	Dopamine
	5-HT	NE		H_1	H_2	α_1	α_2	S_1	S_2	ACh	D-2
Doxepin	0.36	5.3	0.068	420	0.6	4.2	0.091	0.34	4.0	1.2	0.042
Amitriptyline	1.5	4.2	0.36	91	2.2	3.7	0.11	0.53	3.4	5.5	0.10
Imipramine	2.4	7.7	0.31	9.1	0.4	1.1	0.031	0.011	1.2	1.1	0.050
Clomipramine	18	3.6	5.2	3.2	—	2.6	0.031	0.014	3.7	2.7	0.53
Trimipramine	0.040	0.20	0.2	370	33.3	4.2	0.15	0.012	3.1	1.7	0.56
Protriptyline	0.36	100	0.0035	4	0.05	0.77	0.015	0.011	1.5	4.0	0.043
Nortriptyline	0.38	25	0.015	10	0.12	1.7	0.040	0.32	2.3	0.67	0.083
Desipramine	0.29	110	0.0026	0.91	0.08	0.77	0.014	0.010	0.36	0.50	0.030
Amoxapine	0.21	23	0.0094	4	—	2	0.038	0.46	170.0	0.10	0.62
Maprotiline	0.030	14	0.0022	50	—	1.1	0.011	0.0083	0.83	0.18	0.29
Trazodone	0.53	0.020	26	0.29	—	2.8	0.20	1.7	13.0	0.00031	0.026
Fluoxetine	8.3	0.36	23.0	0.016	—	0.017	0.008	0.0042	0.48	0.050	—
Bupropion	0.0064	0.043	0.15	0.015	—	0.022	0.0012	0.0059	0.0011	0.0021	0.00048

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9-4 Relationship of Antidepressants to Neurotransmitter Receptors
Adapted from Richelson E: Pharmacology of antidepressants—characteristics of the ideal drug, *Mayo Clin Proc* 69:1069–1081, 1994.

Antidepressant	Effect on Biogenic Amine Uptake: Potency*		Selectivity for Blocking Uptake of 5-HT Over NE	Affinities† for Neurotransmitter Receptors							
				Histamine		Adrenergic		Serotonin		Muscarinic	Dopamine
	5-HT	NE		H_1	H_2	α_1	α_2	S_1	S_2	ACh	D-2
Sertraline	29	0.45	64.0	0.0041	—	0.27	—	—	—	0.16	0.0093
Paroxetine	136.0	3	45.0	0.0045	—	0.029	—	—	—	0.93	0.0031
Fluvoxamine	14.0	0.2	71.0	—	—	—	—	—	—	—	—
Venlafaxine	2.6	0.48	5.4	0	—	0	—	—	—	0	0
Nefazodone	0.73	0.18	4.2	—	—	—	—	—	—	—	—
Mirtazapine	—	—	—	200.00	—	0.2	5	—	0.2	0.040	—
(Dextromphetamine)‡	2	—	—	—	—	—	—	—	—	—	—
(Diphenhydramine)‡	—	—	—	7.1	—	—	—	—	—	—	—
(Phentolamine)‡	—	—	—	—	—	6.7	—	—	—	—	—
(Yohimbine)‡	—	—	—	—	—	—	62	—	—	—	—
(Methysergide)‡	—	—	—	—	—	—	—	—	7.8	—	—
(Atropine)‡	—	—	—	—	—	—	—	—	—	42	—
(Haloperidol)‡	—	—	—	—	—	—	—	—	—	—	23

ACh, Acetylcholine; *HT*, serotonin; *NE*, norepinephrine.

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9-5 Characteristics of Antidepressant Drugs

	Elimination Half-Life (hr)	Sedative Potency	Anticholinergic Potency	Orthostatic Hypotension	Cardiac Arrhythmia Potential	Target Dosage (mg/day)	Dosage Range (mg/day)
Tricyclics							
Doxepin	17	High	Moderate	High	Yes	200	75-400
Amitriptyline	21	High	Highest	High	Yes	150	75-300
Imipramine	28	Moderate	Moderate	High	Yes	200	75-400
Trimipramine	13	High	Moderate	High	Yes	150	75-300
Clomipramine	23	High	High	High	Yes	150	75-300
Protriptyline	78	Low	High	Moderate	Yes	30	15-60
Nortriptyline	36	Moderate	Moderate	Moderate	Yes	100	40-150
Desipramine	21	Low	Moderate	Moderate	Yes	150	75-300

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9-5 Characteristics of Antidepressant Drugs

	Elimination Half-Life (hr)	Sedative Potency	Anticholinergic Potency	Orthostatic Hypotension	Cardiac Arrhythmia Potential	Target Dosage (mg/day)	Dosage Range (mg/day)
Others							
Citalopram	33	Low	Low	Low	Low	20	20-80
Escitalopram	22	Low	Low	Low	Low	10	10-20
Maprotiline	43	High	Moderate	Moderate	Yes	150	75-300
Trazodone	3.5	High	Lowest	Moderate	Yes	150	50-600
Fluoxetine	87	Low	Low	Lowest	Low	20	40-80
Sertraline	26	Low	Low	Lowest	Low	50	50-200
Paroxetine	21	Low	Low-Moderate	Lowest	Low	20	20-60
Fluvoxamine	19	Low	Low	Low	Low	200	50-300

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9-5 Characteristics of Antidepressant Drugs

	Elimination Half-Life (hr)	Sedative Potency	Anticholinergic Potency	Orthostatic Hypotension	Cardiac Arrhythmia Potential	Target Dosage (mg/day)	Dosage Range (mg/day)
Others							
Bupropion	15	Low	Low	Lowest	Low	200	75-300
Venlafaxine	3.6	Low	Low	Low	Low	300	75-375
Desvenlafaxine	10	Low	Low	Low	Low	50	50-400
Duloxetine	12	Low	Low	Low	Low	40	40-120
Nefazodone	3	Moderate	Low	Low	Low	300	300-600
Mirtazapine	30	High	Low	Low	Low	15	15-45
Selegiline (transdermal)	18	Low	Low	Moderate	Low	6	6-12
Monoamine oxidase inhibitors	—	Low	Low	High	Low	—	—

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Late-Life Depression, LDD (MacQueen G et al, 2016)

- Late-life depression (LLD) can be defined as MDD occurring in adults 60 years and older.
- When discussing LLD, it is important to differentiate early adult-onset depression recurring in late life from late-onset depression. Compared to patients with earlier onset of MDD,
- late-onset depression has a **worse prognosis**, a **more chronic course**, a higher **relapse rate**, and higher levels of **medical comorbidity**, **cognitive impairment**, and **mortality**.
- The vascular depression hypothesis posits that cerebrovascular disease predisposes, precipitates, or perpetuates some depressive syndromes in older age. This vascular burden affects **fronto-striatal circuitry**, resulting in depression and associated cognitive impairment, especially **executive dysfunction**.
- Evidence also suggests that late-onset depression or depressive symptoms may be a **prodrome for dementia**; hence, monitoring of cognition at initial assessment and over time is warranted.

Late-Life Depression (MacQueen G et al, 2016)

- What Is the Role of Nonpharmacological Treatments in LLD?
- Meta-analyses have demonstrated efficacy for psychological treatments of depression in older adults, **with even higher effect sizes** when minor depression and dysthymia were included.
- The authors suggested that supportive therapy best controlled for the nonspecific elements of psychotherapy and should be used as the control for future studies and that **problem-solving therapy (PST)** has the strongest evidence base using supportive therapy as a control.
- A recent meta-analysis assessed **the efficacy of PST** in MDD in older adults, demonstrating that PST significantly reduced depression rating scale scores and reduced disability. The authors also noted that PST is one of the few therapies studied in older people **with cognitive impairment and executive dysfunction.**

Late-Life Depression (MacQueen G et al, 2016)

- What Are the Principles of Pharmacological Treatment of LLD?
- The adage of ‘‘start low and go slow (and keep going)’’ is relevant in LLD.
- Divisions into young-old (<75 years) and old-old (75 years) can be helpful, with a greater degree of vigilance required in treating the old-old.
- Overall, there are pharmacokinetic changes with aging that may decrease the rate of absorption, modify bioavailability, increase half-life for lipid-soluble drugs, and increase relative concentration for water-soluble drugs and metabolites.

Late-Life Depression (MacQueen G et al, 2016)

- What Are the Principles of Pharmacological Treatment of LLD?
- As comorbid medical burden and polypharmacy expand, the risk for pharmacokinetic and pharmacodynamic drug interactions increases.
- In addition, rare antidepressant side effects in adults such as bone loss, serotonin syndrome, extrapyramidal side effects, and neuroleptic malignant syndrome are **more common** in the elderly.
- Particular attention should be paid to **falls, hyponatremia,and gastrointestinal bleeding**, which are associated with SSRIs in general and to QTc prolongation with citalopram.
- Standard principles of conservative prescribing should be applied to minimize adverse drug outcomes.
- Meta-analyses also suggest that **longer antidepressant treatment trials (10-12 weeks)** are required in LLD.

Late-Life Depression (MacQueen G et al, 2016)

- What Is the Pharmacological Approach to LLD?
- An inherent paradox in the treatment of LLD stems from the dissonance between routine clinical practice and RCT evidence.
- For example, while **citalopram and escitalopram** are generally considered by clinicians to be **first-line treatments for LLD** due to tolerability and fewer drug interactions,**none of the RCTs** involving these drugs demonstrated **superiority over placebo** in the elderly, with the exception of **citalopram** in a subset of **old-old (>75 years**) patients with **severe depression** (Hamilton Depression Rating Scale score > 24)

Late-Life Depression (MacQueen G et al, 2016)

- What Is the Pharmacological Approach to LLD?
- In fact, a meta-analysis of 7 studies demonstrated **no difference** between citalopram and other antidepressants for depression remission or trial withdrawal for adverse effects.
- In contrast, geriatric clinicians are reluctant to prescribe **paroxetine** due to anticholinergic effects and fluoxetine due to drug interactions, yet these same SSRIs have positive RCT evidence in the treatment of LLD.
- Thus, treatment recommendations for LLD have been evidence-informed, rather than evidence-based.

Late-Life Depression (MacQueen G et al, 2016)

- What Is the Pharmacological Approach to LLD?
- Overall, recent systematic reviews and meta-analyses support the efficacy of antidepressants in LLD, with **no difference between SSRI and SNRI classes**, and in adult-onset MDD where episodes recurred in LLD.
- A subsequent meta-analysis, in adult and geriatric populations, demonstrated that **antidepressants are efficacious for depression in adults 55. years of age.**
- However, drug-placebo differences for studies with an entry criterion of 65. years were modest and nonsignificant. Heterogeneity, small study number, physical comorbidity, and chronicity were all considered to affect the ability of a trial to separate drug from placebo effects.

Late-Life Depression (MacQueen G et al, 2016)

- What Is the Pharmacological Approach to LLD?
- A recent network meta-analysis, with **response as an outcome (>50% reduction in depression score** from baseline), demonstrated relative risks compared to placebo of greater than 1.2 for only 3 drugs: sertraline, paroxetine, and duloxetine.
- A meta-analysis of moderators of treatment response in LLD suggests **older adults with longer illness duration and moderate to severe depression** benefit from antidepressants compared to placebo, whereas **short illness duration does not show** antidepressant response.

Late-Life Depression (MacQueen G et al, 2016)

- What Is the Pharmacological Approach to LLD?
- Furthermore, **executive dysfunction**, especially in the subdomains of **planning and organization**, has been associated with **poor antidepressant treatment response** in LLD, which may be a factor in trial heterogeneity.
- One can speculate that **vascular depression**, associated with **executive dysfunction**, may be **more resistant to traditional pharmacotherapeutic approaches**, and may be related to depressive syndromes that are in fact **early manifestations of dementia**.
- These are important considerations when assessing lack of response to initial treatment approaches.

Late-Life Depression (MacQueen G et al, 2016)

- What Is the Pharmacological Approach to LLD?
- Among new antidepressants, **vortioxetine and agomelatine** have been evaluated in LLD.
- An RCT (N . 453) comparing **vortioxetine, duloxetine**, and placebo demonstrated significant reduction of depression scores with both comparators versus placebo in adults (aged 65. years) with depression. Additionally, both medications **improved verbal learning**, with **vortioxetine** demonstrating an additional improvement in **processing speed**.
- **Agomelatine** was associated with improved depressive symptoms and better treatment response than placebo but **did not separate from placebo for remission**.
- There is also evidence to support efficacy of continuation and maintenance treatment in LLD. A meta-analysis of 8 double-blind RCTs found antidepressants effective in preventing relapses and recurrences in the elderly, **with similar tolerability for TCAs and SSRIs**.

Late-Life Depression (MacQueen G et al, 2016)

- Is There a Role for **Atypical Antipsychotic** Medication in LLD?
- In a post-hoc analysis pooling clinical trial data of the 61- to 67-year age group, adjunctive aripiprazole and antidepressants showed **a large effect size of 0.8** compared to placebo; the most common side effects were **akathisia and dizziness**.
- A recent National Institute of Mental Health–funded RCT (N . 181) reported on **aripiprazole augmentation** (10- 15 mg) in older adults (aged 60. years) with late and early onset LLD who were **nonremitters to venlafaxine XR monotherapy**.
- For remission, **aripiprazole** was superior to placebo (40/91 [44%] vs. 25/90 [29%], respectively). The most common adverse events were **akathisia** (26%) and Parkinsonism
- (17%). Serious adverse events were reported in 4% of patients on aripiprazole and 2% on placebo, with 6% discontinuation on aripiprazole and 9% with placebo

Late-Life Depression (MacQueen G et al, 2016)

- Is There a Role for **Atypical Antipsychotic** Medication in LLD?
- When prescribed **for dementia**, antipsychotic medications are associated with **increased risk of all-cause mortality**, with greater risks for **typical than atypical antipsychotics**; the risk is less well elucidated in cognitively intact elderly populations.
- Antipsychotic medications may be considered in selected elderly individuals, recognizing that the risk profile in cognitively intact individuals has not been confirmed.

Late-Life Depression & medication (MacQueen G et al, 2016)

Table 6. Algorithmic Pharmacological Treatment of Late-Life Depression.

Recommendation	Treatment	Level of Evidence
First line	Duloxetine, mirtazapine, nortriptyline	Level 1
	Bupropion, citalopram/escitalopram, desvenlafaxine, duloxetine, sertraline, venlafaxine, vortioxetine	Level 2
Second line	Switch to	
	Nortriptyline	Level 1
	Moclobemide, phenelzine, quetiapine, trazodone	Level 2
	Bupropion	Level 3
	Combine with	
	Aripiprazole, lithium	Level 1
	Methylphenidate	Level 2
Third line	Switch to	
	Amitriptyline, imipramine	Level 2
	Combine SSRI or SNRI with	
	Bupropion, SSRI	Level 3

SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

Kovich H et al, 2015

Table 1. Adverse Effects Associated with Antidepressant Medications

Adverse effect	*Risk*	*Associated medication*	*Time to onset*	*Evidence*
Gastrointestinal bleeding	OR = 1.2 to 1.55[8-10]; risk is higher with concurrent use of antiplatelet or nonsteroidal anti-inflammatory drug[9]	SSRIs and serotonin-norepinephrine reuptake inhibitors associated with increased risk[9,10]; mixed findings for TCAs[8,10]	Anytime during treatment[9]	Meta-analyses[9,10] and cohort study[8]
Hepatotoxicity	0.5% to 3% will have asymptomatic mild elevation in transaminase levels[11]	Higher risk with TCAs and nefazodone; lower risk with SSRIs[11,12]	Within six months[11]	Literature review
Hyponatremia	0.5% to 12% in older adults[13,14]	OR = 3.3 (95% CI, 1.3 to 8.6) for SSRIs compared with other drug classes[15]	Within first month[16]	Case-control study
QT prolongation	Dose dependent (2012 boxed warning not to exceed doses of citalopram [Celexa] > 40 mg per day or > 20 mg per day in adults older than 60 years)[17]	Citalopram, escitalopram (Lexapro), and amitriptyline	Initiation (but typically dependent on the presence of coexisting risk factors)[18]	Cross-sectional retrospective studies
Sexual effects	Weighted mean incidence across observational studies = 40% (95% CI, 28.3 to 52.6)[19]	Decreased risk with bupropion (Wellbutrin); trend toward increased risk with escitalopram and paroxetine (Paxil)[19]	Within first week[20]	Meta-analysis
Suicidality	Age related; slightly increased risk (OR = 2.30; 95% CI, 1.04 to 5.09) for adults 18 to 24 years of age; neutral for adults 25 to 64 years of age; protective for adults 65 years and older (OR = 0.06; 95% CI, 0.01 to 0.58)[21]	Insufficient evidence to determine differences between second-generation antidepressants	Within one to two months of initiation or dose increase[22]	Meta-analysis

CI = confidence interval; OR = odds ratio; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant.

Information from references 8 through 22.

Kovich H et al, 2015

Table 2. Medications that May Contribute to Serotonin Syndrome

Class	*Drugs*
Amphetamines and derivatives	3,4-methylenedioxymethamphetamine ("Ecstasy")
	Dextroamphetamine
	Methamphetamine
Analgesics	Buprenorphine
	Cyclobenzaprine (Flexeril)
	Fentanyl
	Hydrocodone
	Meperidine (Demerol)
	Morphine
	Oxycodone
	Pentazocine (Talwin)
	Tramadol
Antidepressants/ mood stabilizers	Buspirone (Buspar)
	Lithium
	Monoamine oxidase inhibitors
	Olanzapine (Zyprexa)
	Selective serotonin reuptake inhibitors
	Serotonin 2A receptor blockers
	Serotonin-norepinephrine reuptake inhibitors
	St. John's wort
	Tricyclic antidepressants
Antiemetics	Droperidol
	Metoclopramide (Reglan)
	Ondansetron (Zofran)
Antimigraine drugs and antiepileptics	Carbamazepine (Tegretol)
	Ergot alkaloids
	Triptans
	Valproic acid (Depakene)
Other medications	Chlorpheniramine
	Cocaine
	Dextromethorphan
	Ginseng
	5-hydroxytryptophan
	Linezolid (Zyvox)
	L-tryptophan
	Nutmeg
	Reserpine
	Ritonavir (Norvir)
	Yohimbe

Adapted with permission from Ables AZ, Nagubilli R. Prevention, recognition, and management of serotonin syndrome. Am Fam Physician. 2010;81(9):1140, with additional information from reference 25.

Table 2. Medications that May Contribute to Serotonin Syndrome

Class	*Drugs*
Amphetamines and derivatives	3,4-methylenedioxymethamphetamine ("Ecstasy")
	Dextroamphetamine
	Methamphetamine
Analgesics	Buprenorphine
	Cyclobenzaprine (Flexeril)
	Fentanyl
	Hydrocodone
	Meperidine (Demerol)
	Morphine
	Oxycodone
	Pentazocine (Talwin)
	Tramadol
Antidepressants/ mood stabilizers	Buspirone (Buspar)
	Lithium
	Monoamine oxidase inhibitors
	Olanzapine (Zyprexa)
	Selective serotonin reuptake inhibitors
	Serotonin 2A receptor blockers
	Serotonin-norepinephrine reuptake inhibitors
	St. John's wort
	Tricyclic antidepressants

Kovich H et al, 2015

Table 2. Medications that May Contribute to Serotonin Syndrome

Class	*Drugs*
Antiemetics	Droperidol
	Metoclopramide (Reglan)
	Ondansetron (Zofran)
Antimigraine drugs and antiepileptics	Carbamazepine (Tegretol)
	Ergot alkaloids
	Triptans
	Valproic acid (Depakene)
Other medications	Chlorpheniramine
	Cocaine
	Dextromethorphan
	Ginseng
	5-hydroxytryptophan
	Linezolid (Zyvox)
	L-tryptophan
	Nutmeg
	Reserpine
	Ritonavir (Norvir)
	Yohimbe

Adapted with permission from Ables AZ, Nagubilli R. Prevention, recognition, and management of serotonin syndrome. Am Fam Physician. 2010;81(9):1140, with additional information from reference 25.

Kovich H et al, 2015

Table 3. Commonly Used Antidepressant Medications

Medication	*Dosage range per day (outpatient)*	*Cost**	*Decrease dose in renal/hepatic disease?*
Amitriptyline	25 to 300 mg	$5 to $12 (NA)	No/no
Bupropion SR (Wellbutrin SR)	100 to 400 mg	$14 to $33 ($150 to $575)	Yes/yes
Citalopram (Celexa)	20 to 40 mg	$4 ($185)	Consider/yes
Desipramine	100 to 300 mg	$55 to $155 (NA)	No/no
Duloxetine (Cymbalta)	40 to 120 mg	$65 ($400 to $450)	Yes/yes
Escitalopram (Lexapro)	10 to 20 mg	$10 ($210 to $220)	No/no
Fluoxetine (Prozac)	20 to 80 mg	$4 to $8 ($280 to $1,100)	No/yes
Milnacipran (Savella)	12.5 to 200 mg	NA ($115 to $220)	Yes/consider
Mirtazapine (Remeron)	15 to 45 mg	$5 to $20 ($160 to $170)	Consider/consider
Nortriptyline (Pamelor)	25 to 150 mg	$4 to $12 ($950 to $2,000)	No/yes
Paroxetine (Paxil)	20 to 50 mg	$4 to $20 ($160 to $700)	Yes/no
Sertraline (Zoloft)	50 to 200 mg	$7 to $10 ($200 to $400)	No/yes
Trazodone	50 to 400 mg	$4 to $10 (NA)	No/yes
Venlafaxine	37.5 to 225 mg	$14 to $30 (NA)	Yes/yes

NA = not available.

**—Estimated retail price for one month's treatment based on information obtained at http://www.goodrx.com (accessed March 30, 2015). Cost for generic listed first; brand name in parentheses.*

Table 9. Pharmacological treatment based on clinical profile.

Key/prominent symptom(s)	Preferred antidepressant
Anxiety	SNRIs SSRIs
Cognitive difficulties (learning, memory, decision-making)	Duloxetine Vortioxetine
Sleep disturbances (e.g. Insomnia)	Agomelatine Mirtazapine
Fatigue	Bupropion
Pain	Duloxetine TCAs
Melancholia (psychomotor slowing, diurnal mood variation)	TCAs
Psychotic symptoms (mood congruent delusions)	Antipsychotic medication in addition to antidepressants
Atypical symptoms (Increased sleep, increased appetite)	MAOIs

SNRI: serotonin and noradrenaline reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor; TCA: tricyclic antidepressants; MAOI: monoamine oxidase inhibitor.

Malhi G et al, 2020

Masennuslääkkeiden tehossa ei ole eroja, sivuvaikutuksissa on

TAULUKKO 3. Suomessa vuonna 2009 käytössä olevat depressiolääkkeet ja niiden annokset aikuispotilaille.

Geneerinen nimi	Aloitusannos (mg/vrk)	Hoitoannos (mg/vrk)	Tavallisia haittavaikutuksia
Trisykliset depressiolääkkeet			Ryhmälle luonteenomaisia muun muassa antikolinergiset ja alfa$_1$-salpauksen haittavaikutukset
Amitriptyliini	25–50	75–300	
Doksepiini	25–50	75–300	
Klomipramiini	25–50	75–300	
Nortriptyliini	25–50	50–200	
Trimipramiini	25–50	75–300	
Selektiiviset serotoniinin takaisinoton estäjät (SSRI)			Ryhmälle luonteenomaisia muun muassa pahoinvointi, suolisto-oireet ja seksuaalitoimintojen häiriöt
Essitalopraami	10	10–20	
Fluoksetiini	20	20–80	
Fluvoksamiini	50	100–300	
Paroksetiini	20	20–50	
Sertraliini	50	50–200	
Sitalopraami	20	20–60	
Muut depressiolääkkeet			
Agomelatiini	25	25–50	Päänsärky, huimaus
Duloksetiini	60	60–120	Pahoinvointi, suun kuivuminen, päänsärky, uneliaisuus
Mirtatsapiini	15–30	30–60	Väsymys, painon nousu
Moklobemidi	300	300–900	Unettomuus, huimaus
Venlafaksiini	75	75–375	Kuten SSRI:t
Tratsodoni	50–100	150–500	Väsymys, huimaus, rytmihäiriöt

Markkinoilla oleva reboksetiini ei, depressioindikaatiosta huolimatta, todennäköisesti ole tehokas masennuslääke.

http://www.kaypahoito.fi/web/kh/suositukset/naytaartikkeli/tunnus/hoi50023

TABLE 3. Half-lives of Antidepressants[a]

Antidepressant	Half-life range (hr)	Average half-life (hr)	Steady state (days)
Tertiary amines			
Amitriptyline	10–50	24	4–10
Clomipramine	19–37	32	7–14
Doxepin	8–36	8	2–8
Trimipramine	7–30	9	2–6
Imipramine	6–24	16	2–5
Secondary amines			
Desipramine	12–76	22	2–11
Nortriptyline	15–93	24	4–19
Protriptyline	54–198	126	10
Dibenzoxazepine			
Amoxapine	—	8	2–7
SSRIs			
Fluoxetine	24–216	72	28–35
Fluvoxamine	—	20	7
Paroxetine	7–37	20[b]	7–14
Sertraline	26	26	7–12
Others			
Venlafaxine	4	4	16
Nefazodone	2–4	—[c]	—
Trazodone	4–9	5	3–7
Maprotiline	27–58	51	6–10
Buproprion	8–24	14	2–5
Nomifensine	2–10	—	2–5
Mirtazapine	20–40	22	5

[a]Refs. 13–15, 21, and 22.
[b]Highly variable.
[c]Dose dependent.

5 x T ½ = tasainen pitoisuus veressä
Ja poistuminen elimistöstä

Mielialalääkkeiden ja placebon teho: ensilinjan lääkkeet ja muut linjat

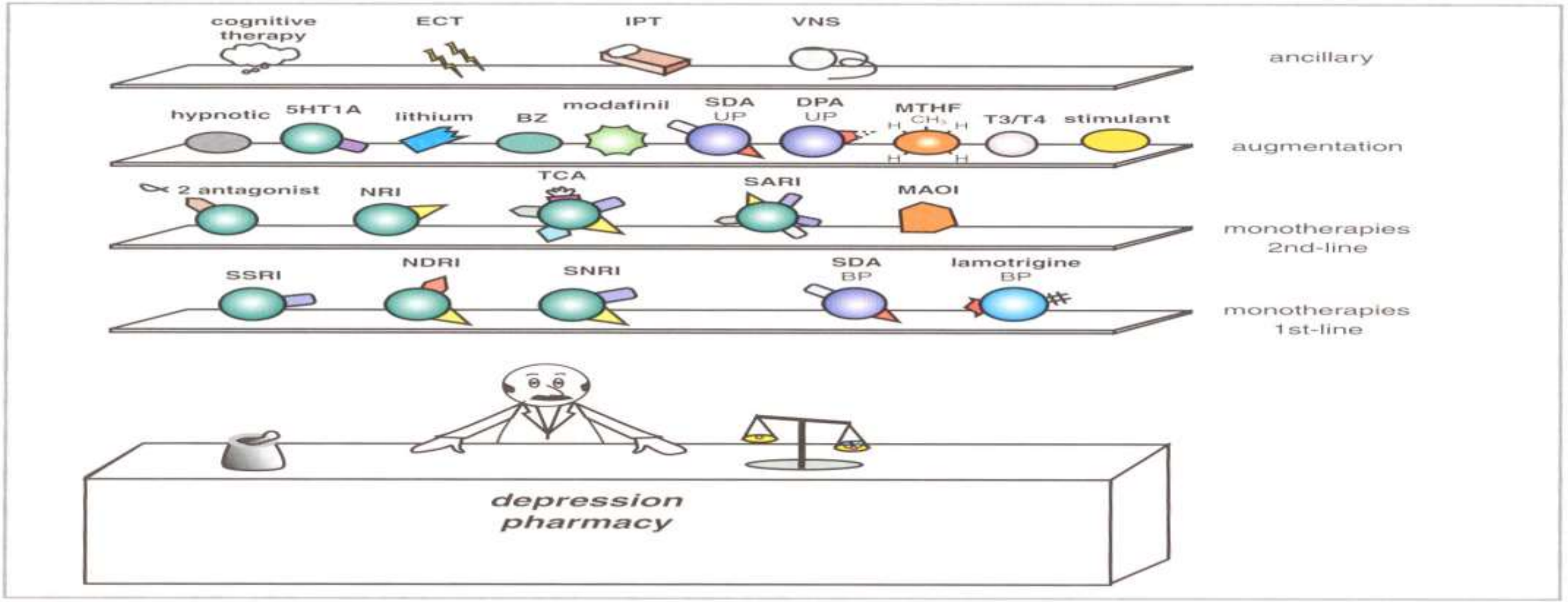

FIGURE 12-117 Depression pharmacy. First-line treatments for unipolar depression include serotonin selective reuptake inhibitors (SSRIs), norepinephrine and dopamine reuptake inhibitors (NDRIs), and serotonin norepinephrine reuptake inhibitors (SNRIs), while first-line treatments for bipolar depression include serotonin dopamine antagonists (SDAs) and lamotrigine. Second-line monotherapies include alpha 2 antagonists, selective norepinephrine reuptake inhibitors (NRIs), tricyclic antidepressants (TCAs), serotonin 2A antagonist/reuptake inhibitors (SARIs), and monoamine oxidase inhibitors (MAOIs). Potentially useful augmenting agents include hypnotics, serotonin 1A (5HT1A) agonists, lithium, benzodiazepines, modafinil, SDAs, dopamine partial agonists (DPAs), L-5-methyl-tetrahydrofolate (MTHF), thyroid hormone (T3/T4), and stimulants. Ancillary treatments to medications may include cognitive therapy, electroconvulsive therapy (ECT), interpersonal therapy (IPT), and vagus nerve stimulation (VNS).

S. Stahl, 2004

Mielialalääkkeiden ja placebon teho: sivuvaikutuksia

TABLE 11. Selected Side Effects of SSRIs[a,b]

Side effect	Fluoxetine	Sertraline	Paroxetine	Fluvoxamine	Venlafaxine
Nausea	+++	++++	++++	+++++++	+++++++
Nervousness	+++	+	+	++	+++
Anorexia	++	−	+	+	++
Insomnia	++	++	++	+++	++
Drowsiness	+	++	++++	+++	+++
Tremor	+	++	++	+	+
Fatigue	+	+	+++	++	+
Dry mouth	+	++	+	+	+++
Dizziness	+	+	++	++	+++
Sweating	+	++	++	+	++
Diarrhea	+	++	+	+	−
Constipation	−	−	+	+/−	++
Sexual dysfunction	+	+++	+++	++	++++

[a]Refs 15 and 157.

[b]Each + represents about a 4% incidence of the side effect after adjusting for placebo effect; a − represents a decreased incidence of the side effect relative to that reported for placebo.

Depression Käypä Hoito-suositus - päivitys 11.10.13

- **Masennuspotilaiden hoidon laatua** seurattaisiin **perusterveydenhuollossa** seuraavilla kriteereillä:

1. Vastaako diagnosoitujen masennuspotilaiden osuus kaikista hoidetuista epidemiologista kuvaa masennuksen todennäköisestä esiintyvyydestä väestössä?
2. Kuinka suuri osa depressiopotilaista on saanut masennuslääkettä?
3. Kuinka suurella osalla masennuspotilaista depressiolääkitys on jatkunut yhtäjaksoisesti vähintään puoli vuotta?
4. Kuinka suuri osa depressiopotilaista on saanut jotakin psykoterapeuttista tai muuta psykososiaalista hoitoa?

http://www.terveysportti.fi/xmedia/hoi/hoi50023.pdf

Depression Käypä Hoito-suositus - päivitys 11.10.13

- **Masennuspotilaiden hoidon laatua** seurattaisiin **perusterveydenhuollossa** seuraavilla kriteereillä: (jatkuu)

5. Kuinka suurella osalla depressiopotilaista hoitoon on liittynyt riittävä määrä seurantakäyntejä?
6. Kuinka suurella osalla depressiopotilaista on seurannassa käytetty hyväksi oiremittareita?
7. Kuinka suuri osa potilaista saavuttaa seurannassa täyden remission oiremittareilla arvioituna?

http://www.terveysportti.fi/xmedia/hoi/hoi50023.pdf

Psykiatrisessa erikoissairaanhoidossa noudatettaviksi työryhmä ehdottaa seuraavia laatukriteereitä:

1. Kuinka suuri osa depressiopotilaista on saanut masennuslääkettä?
2. Kuinka suurella osalla depressiopotilaista lääkehoito on jatkunut yhtäjaksoisesti vähintään puoli vuotta?
3. Kuinka suuri osa potilaista, jotka kärsivät toistuvasta masennuksesta, saa ylläpitohoitoa?
4. Kuinka suuri osa depressiopotilaista on saanut jotakin intensiivistä yksilöpsykoterapeuttista hoitoa?
5. Kuinka suurella osalla parisuhteessa elävistä potilaista hoitoon on liittynyt pari- tai perhetapaaminen?
6. Kuinka suurella osalla depressiopotilaista on seurannassa käytetty hyväksi oiremittareita?
7. Kuinka suuri osa potilaista saavuttaa seurannassa täyden remission oiremittareilla arvioituna?

http://www.kaypahoito.fi/web/kh/suositukset/naytaartikkeli/tunnus/hoi50023

Table 84: Efficacy (expressed as response rate) and acceptability (reflected in dropout rates) of antidepressants, expressed as odds ratios (OR) of fluoxetine versus each of the antidepressants assessed (taken from Cipriani *et al.*, 2009)

	Efficacy (response rate) OR (95% credible interval)	Acceptability (dropout rate) OR (95% credible interval)
Bupropion	0.93 (0.77–1.11)	1.12 (0.92–1.36)
Citalopram	0.91 (0.76–1.08)	1.11 (0.91–1.37)
Duloxetine	1.01 (0.81–1.27)	0.84 (0.64–1.10)
Escitalopram	0.76 (0.65–0.89)*	1.19 (0.99–1.44)
Fluvoxamine	1.02 (0.81–1.30)	0.82 (0.62–1.07)
Milnacipran	0.99 (0.74–1.31)	0.97 (0.69–1.32)
Mirtazapine	0.73 (0.60–0.88)*	0.97 (0.77–1.21)
Paroxetine	0.98 (0.86–1.12)	0.91 (0.79–1.05)
Reboxetine	1.48 (1.16–1.90)*	0.70 (0.53–0.92)*
Sertraline	0.80 (0.69–0.93)*	1.14 (0.96–1.36)
Venlafaxine	0.78 (0.68–0.90)*	0.94 (0.81–1.09)

Credible interval; *$p < 0.05$.
For efficacy, OR higher than 1 favours fluoxetine.
For acceptability, OR lower than 1 favours fluoxetine.

4) Mikä on kaksisuuntainen mielialahäiriö? Eroaako se nuorempien bipolaaritaudista?

Yl juha kemppinen

Reported Causes of Secondary Mania

Drugs	Alcohol intoxication, alprazolam, captopril, cimetidine, corticosteroids, cyclobenzaprine, cyproheptadine, disulfiram, felbamate, isoniazid, levodopa, l-glutamine, l-tryptophan, lysergic acid diethylamide, methylphenidate, metrizamide, metoclopramide, procainamide, procarbazine, propafenone, sympathomimetics, thyroxine, tolmetin, triazolam, yohimbine, zidovudine
Drug withdrawal	Clonidine, diltiazem, atenolol, isocarboxazid, propranolol
Metabolic	Hemodialysis, postoperative state, hyperthyroidism, vitamin B_{12}deficiency, Cushing's syndrome, cerebral hypoxia
Infection	Influenza, Q fever, post–St. Louis type A encephalitis, cryptococcosis, human immunodeficiency virus, neurosyphilis
Neoplasm	Meningiomas, gliomas, thalamic metastases, brainstem tumor
Epilepsy	Complex partial seizures with right temporal focus
Surgery	Right hemispherectomy
Cerebrovascular accident	Thalamic stroke
Other	Cerebellar atrophy, head trauma, multiple sclerosis, Wilson's disease

Mielialalääkkeiden ja placebon teho

BP depressio:
- Liikanukkuminen
- Ylisyönti
- Samanaikainen ahdistus
- Motorinen jähmeys
- Mielialan vaihtelut
- Psykoottiset oireet
- Itsemurha-ajatukset

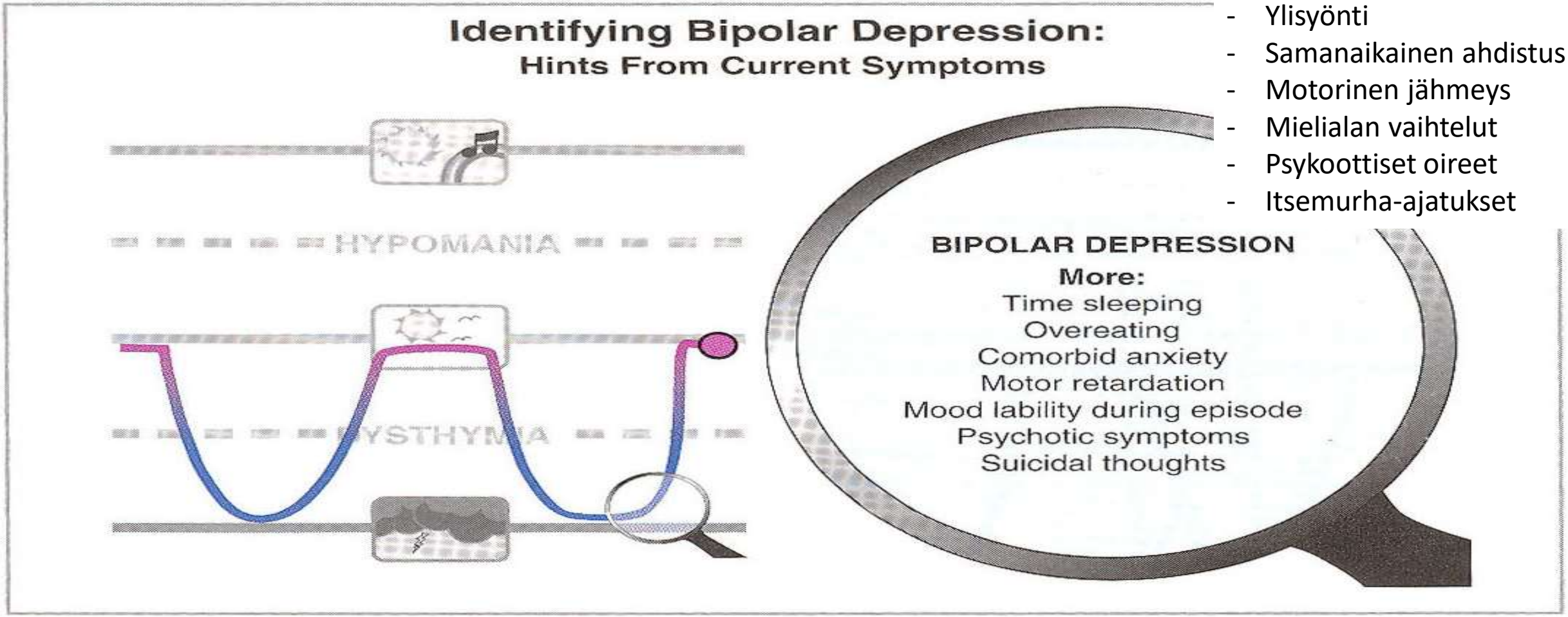

FIGURE 11-25 Bipolar depression symptoms. Although all symptoms of a major depressive episode can occur in either unipolar or bipolar depression, some symptoms may present more often in bipolar versus unipolar depression, providing hints if not diagnostic certainty that the patient has a bipolar spectrum disorder. These symptoms include increased time sleeping, overeating, comorbid anxiety, psychomotor retardation, mood lability during episodes, psychotic symptoms, and suicidal thoughts.

S. Stahl, 2004

Yksisuuntaisen ja Kaksisuuntaisen masennuksen erotusdiagnoosi

TABLE 3–3. Probabilistic approach to bipolar depression proposed by the Task Force on Diagnostic Guidelines of the International Society for Bipolar Disorders

Bipolar I depression more likely if ≥5:	Unipolar depression more likely if ≥4:
Symptomatology	
Hypersomnia	Insomnia
Hyperphagia	Decreased appetite
Psychomotor retardation	Psychomotor agitation
Other "atypical" symptoms	
Psychosis and/or pathological guilt	Somatic complaints
Mood lability or manic symptoms	
Course of illness	
Earlier onset (<25 years)	Later onset (>25 years)
Multiple depressions (≥5 episodes)	Long current depression (>6 months)
Family history	
Bipolar disorder	No bipolar disorder

Note. Confirmation of specific numbers requires further study.
Source. Adapted from Mitchell et al. 2008.

TA Ketter, ed, Handbook of Diagnosis and Treatment of Bipolar Diseases, 2010, American Psychiatric Association, Inc: Washington

Masennustilojen psykiatrinen erotusdiagnostiikka :

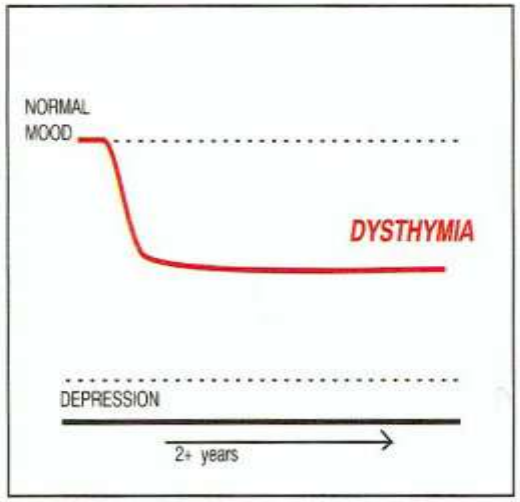

FIGURE 5–7. **Dysthymia** is a low-grade but very chronic form of depression, which lasts for more

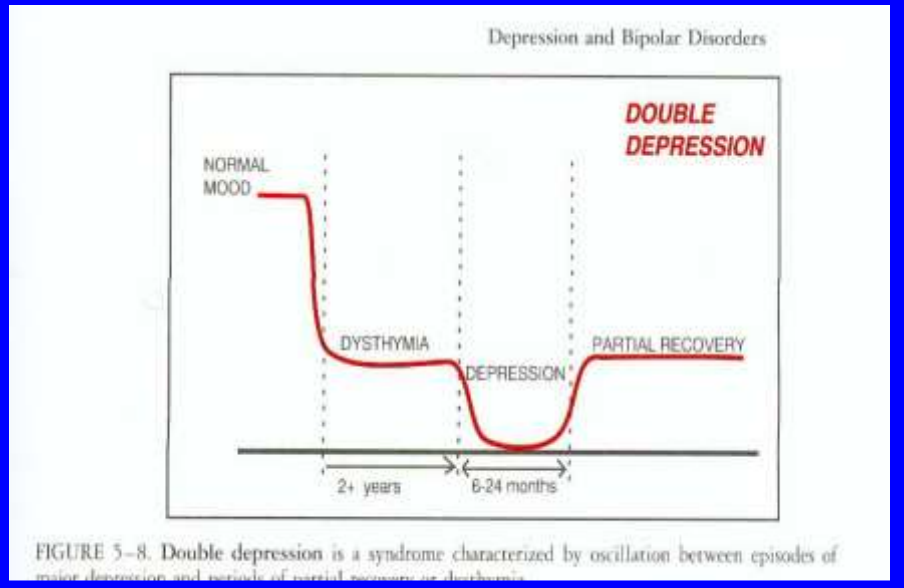

FIGURE 5–8. **Double depression** is a syndrome characterized by oscillation between episodes of

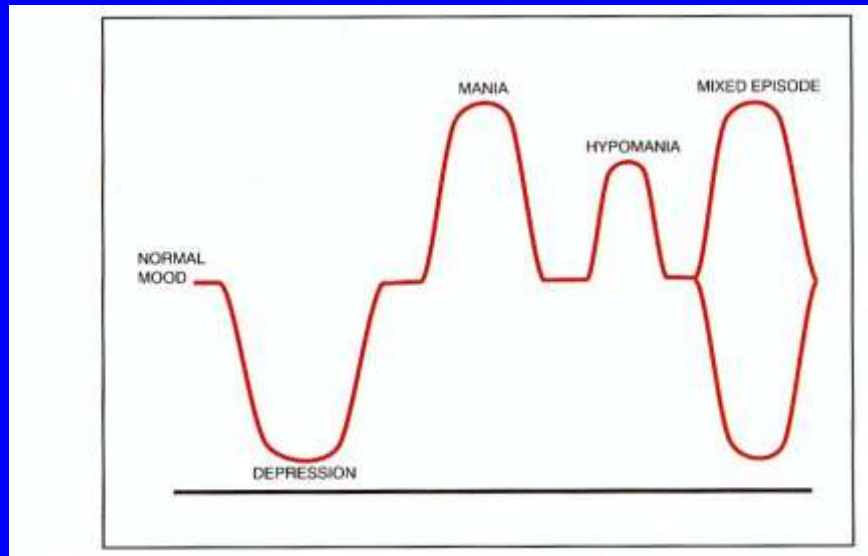

FIGURE 5–5. Bipolar disorder is characterized by various types of episodes of affective disorder, including **depression**, full **mania**, lesser degrees of mania called **hypomania**, and even **mixed episodes** in which mania and depression seem to coincide.

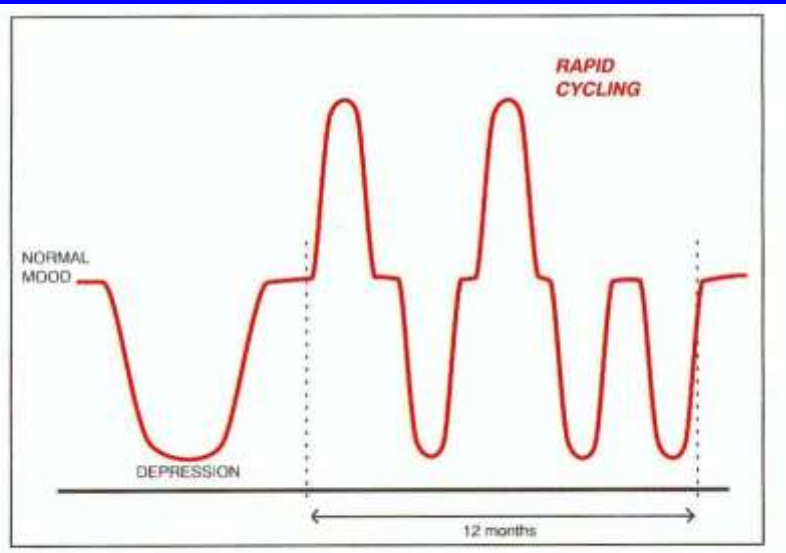

FIGURE 5–6. Bipolar disorder can become **rapid cycling**, with at least four switches into mania, hypomania, depression, or mixed episodes within a 12-month period. This is a particularly difficult form of bipolar disorder to treat.

S.Stahl,2003

5) Ikäihmisen kaksisuuntaisen häiriön seulonta ja diagnosointi

Yl juha kemppinen

Birrer et al 2004

TABLE 1
Geriatric Depression Scale

Are you basically satisfied with your life? (no)
Have you dropped many of your activities/interests? (yes)
Do you feel that your life is empty? (yes)
Do you often get bored? (yes)
Are you hopeful about the future? (no)
Are you bothered by thoughts that you just cannot get out of your head? (yes)
Are you in good spirits most of the time? (no)
Are you afraid something bad is going to happen to you? (yes)
Do you feel happy most of the time? (no)
Do you often feel helpless? (yes)
Do you often feel restless and fidgety? (yes)
Do you prefer to stay home at night, rather than go out and do new things? (yes)
Do you frequently worry about the future? (yes)
Do you feel that you have more problems with memory than most? (yes)
Do you think it is wonderful to be alive now? (no)
Do you often feel downhearted and blue? (yes)
Do you feel pretty worthless the way you are now? (yes)
Do you worry a lot about the past? (yes)
Do you find life very exciting? (no)
Is it hard for you to get started on new projects? (yes)
Do you feel full of energy? (no)
Do you feel that your situation is hopeless? (yes)
Do you think that most persons are better off than you are? (yes)
Do you frequently get upset over little things? (yes)
Do you frequently feel like crying? (yes)
Do you have trouble concentrating? (yes)
Do you enjoy getting up in the morning? (no)
Do you prefer to avoid social gatherings? (yes)
Is it easy for you to make decisions? (no)
Is your mind as clear as it used to be? (no)

NOTE: *The Geriatric Depression Scale screens for seven characteristics of depression in the elderly: somatic concern, lowered affect, cognitive impairment, feelings of discrimination, impaired motivation, lack of future orientation, and lack of self-esteem. The yes-or-no questionnaire is administered orally, and one point is scored for each answer in parentheses. A score of 10 or more indicates depression (84 percent sensitivity; 95 percent specificity). The sensitivity diminishes in patients with a score of less than 24 on the Mini-Mental State Examination.*

Reprinted with permission from Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey MB, et al. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1982-83;17:37-49.

Birrer et al 2004

TABLE 2
Medications That May Cause Depression

Cardiovascular drugs
Clonidine (Catapres)
Digitalis
Guanethidine (Ismelin)
Hydralazine (Apresoline)
Methyldopa (Aldomet)
Procainamide (Pronestyl)
Propranolol (Inderal)
Reserpine (Serpasil)
Thiazide diuretics

Chemotherapeutics
6-Azauridine
Asparaginase (Elspar)
Azathioprine (Imuran)
Bleomycin (Blenoxane)
Cisplatin (Platinol)
Cyclophosphamide (Cytoxan)
Doxorubicin (Adriamycin)
Mithramycin (Mithracin)
Vinblastine (Velban)
Vincristine

Antiparkinsonian drugs
Amantadine (Symmetrel)
Bromocriptine (Parlodel)
Levodopa (Larodopa)

Antipsychotic drugs
Fluphenazine (Prolixin)
Haloperidol (Haldol)

Sedatives and antianxiety drugs
Barbiturates
Benzodiazepines
Chloral hydrate
Ethanol

Anticonvulsants
Carbamazepine (Tegretol)
Ethosuximide (Zarontin)
Phenobarbital
Phenytoin (Dilantin)
Primidone (Mysoline)

Anti-inflammatory/ anti-infective agents
Ampicillin
Cycloserine (Seromycin)
Dapsone
Ethambutol (Myambutol)
Griseofulvin (Grisactin)
Isoniazid (INH)
Metoclopramide (Reglan)
Metronidazole (Flagyl)
Nalidixic acid (NegGram)
Nitrofurantoin (Furadantin)
Nonsteroidal anti-inflammatory agents
Penicillin G procaine
Streptomycin
Sulfonamides
Tetracycline

Stimulants
Amphetamines (withdrawal)
Caffeine
Cocaine (withdrawal)
Methylphenidate (Ritalin)

Hormones
Adrenocorticotropin
Anabolic steroids
Glucocorticoids
Oral contraceptives

Other drugs
Choline
Cimetidine (Tagamet)
Disulfiram (Antabuse)
Lecithin
Methysergide (Sansert)
Phenylephrine (Neo-Synephrine)
Physostigmine (Antilirium)
Ranitidine (Zantac)

Birrer et al 2004

TABLE 3
Physical Disorders Associated with Depression

- Addison's disease
- Acquired immunodeficiency syndrome
- Angina
- Cancer (particularly of the pancreas)
- Cerebral arteriosclerosis, cerebral infarction
- Cushing's disease
- Diabetes
- Electrolyte abnormalities (e.g., hypernatremia, hypercalcemia, hypokalemia, hyperkalemia)
- Folate and thiamine deficiencies
- Hepatitis
- Hypoglycemia
- Hypothyroidism, hyperthyroidism, hyperparathyroidism
- Influenza
- Intracranial tumors (malignant or benign)
- Multiple sclerosis
- Myocardial infarction
- Parkinson's disease
- Pernicious anemia
- Porphyria
- Renal disease
- Rheumatoid arthritis
- Senile dementia
- Syphilis
- Systemic lupus erythematosus
- Temporal arteritis
- Temporal lobe epilepsy
- Viral pneumonia

Birrer et al 2004

TABLE 4
Differentiating Dementia and Depression

Characteristic	*Dementia*	*Depression*
Onset	Insidious, indeterminate	Relatively rapid, associated with mood changes
Duration of symptoms	Usually long	Usually short
Orientation, mood, behavior, affect	Impaired, inconsistent, fluctuating	Intact, diurnal variation depressed/anxious, complaints worse than on testing
Cognitive impairment	Consistent; stable or worsening	Inconsistent, fluctuating
Neurologic defects	Often present (e.g., agnosia, dysphasia, apraxia)	Absent
Disabilities	Concealed by patient	Highlighted by patient
Depressive symptoms	Present	Present
Memory impairment	Doesn't remember recent events, often unaware of memory loss. Onset of memory loss occurs before mood change.	Concentration poor, patient complains of memory loss of recent and remote events, follows onset of depressed mood
Psychiatric history	None	Often, history of depression
Answers to questions	Near answers	"Don't know" answers
Performance	Tries hard but is unconcerned about losses	Does not try hard but is more distressed by losses
Associations	Unsociability, uncooperativeness, hostility, emotional instability, reduced alertness, confusion, disorientation	Appetite and sleep disturbances, suicidal thoughts

Birrer et al 2004

TABLE 5
Pharmacologic Agents Used to Treat Depression in Elderly Patients

Drug	*Dosage (mg per day)**	*Dosing*	*Cost (generic)†*	*Common side effects*	*Interactions*
Tricyclic antidepressants (tertiary)					
Amitriptyline (Elavil)‡	25 to 300	Single or divided	$16 ($11)	Anticholinergic effects, sedation, cardiac effects, orthostatic hypotension, weight gain, lower seizure threshold	Antiarrhythmics,§ MAOIs§
Imipramine (Tofranil)	25 to 300	Single or divided	48 (1 to 22)	Same as above	Antiarrhythmics,§ MAOIs§
Doxepin (Sinequan)‡	25 to 300	Single or divided	17 (12)	Same as above	Antiarrhythmics,§ MAOIs§
Trimipramine (Surmontil)	25 to 300	Single or divided	32	Same as above	Antiarrhythmics,§ MAOIs§
Clomipramine (Anafranil)	25 to 300	Single or divided	90 (25)	Same as above	Antiarrhythmics,§ MAOIs§
Tricyclic antidepressants (secondary)					
Nortriptyline (Pamelor)	25 to 250	Single or divided	102 (6 to 26)	Same as above	Antiarrhythmics,§ MAOIs§
Protriptyline (Vivactil)	15 to 60	Single or divided	85	Same as above	Antiarrhythmics,§ MAOIs§
Desipramine (Norpramin)	25 to 300	Single or divided	26 (8 to 15)	Same as above	Antiarrhythmics,§ MAOIs§
Amoxapine (Asendin)‡	50 to 600	Single or divided	(30 to 37)	Extrapyramidal movement disorders, male sexual dysfunction, endocrine dysfunction	MAOIs§
MAOIs					
Phenelzine (Nardil)	45 to 90	Divided	49	Orthostatic hypotension	MAOIs,§ meperidine (Demerol),§ vasoconstrictors,§ narcotics,§ decongestants§
Tranylcypromine (Parnate)	30 to 60	Divided	60	Orthostatic hypotension	MAOIs,§ meperidine,§ vasoconstrictors,§ narcotics,§ decongestants§
SSRI					

Birrer et al 2004

Pharmacologic Agents Used to Treat Depression in Elderly Patients

Drug	*Dosage (mg per day)**	*Dosing*	*Cost (generic)†*	*Common side effects*	*Interactions*
SSRIs					
Sertraline (Zoloft)	50 to 200	Single	72	GI symptoms, sexual dysfunction, weight gain, headache	MAOIs,§ tricyclic antidepressants, neuroleptics, antiarrhythmics§
Fluoxetine (Prozac)	20 to 80	Single or divided	100 (80)	GI symptoms, anxiety, insomnia, weight loss	MAOIs,§ tricyclic antidepressants, neuroleptics, antiarrhythmics§
Paroxetine (Paxil)	20 to 50	Single	85	GI symptoms, anxiety, insomnia, fatigue	MAOIs,§ tricyclic antidepressants, neuroleptics, antiarrhythmics§
Fluvoxamine (Luvox)	50 to 300	Single	(77 to 89)	GI symptoms, anxiety, insomnia	MAOIs,§ tricyclic antidepressants, neuroleptics, antiarrhythmics,§ antihistamines§
Citalopram (Celexa)	20 to 60	Single	72	GI symptoms, anxiety, somnolence, sexual dysfunction	MAOIs,§ tricyclic antidepressants, neuroleptics, antiarrhythmics,§ antihistamines§
Escitalopram (Lexapro)	10 to 20	Single	67	GI symptoms, anxiety, somnolence, sexual dysfunction	MAOIs,§ tricyclic antidepressants, neuroleptics, antiarrhythmics,§ antihistamines§
Other agents					
Maprotiline (Ludiomil)‡	50 to 225	Single or divided	(22)	Lower seizure threshold	MAOIs§
Bupropion (Wellbutrin)	100 to 450	Divided	42 (29)	Lower seizure threshold	MAOIs§
Trazodone (Desyrel)‡	50 to 600	Single or divided	65 (13)	Sedation, orthostatic hypotension, priapism	MAOIs§
Venlafaxine (Effexor)	75 to 375	Divided	51	Anxiety, sexual dysfunction, increased blood pressure, mild sedation, visual symptoms	MAOIs,§ SSRIs, antihistamines,§ benzodiazopines, neuroleptics
Nefazodone (Serzone)	200 to 600	Divided	36	Same as above	MAOIs,§ SSRIs, antihistamines,§ benzodiazopines, neuroleptics
Mirtazapine (Remeron)	15 to 45	Single	81 (72)	Sedation, increased appetite, constipation, asthenia	MAOIs,§ SSRIs, antihistamines,§ benzodiazopines, neuroleptics

MAOIs = monoamine oxidase inhibitors; SSRIs = selective serotonin reuptake inhibitors; GI = gastrointestinal.

**—Lower dosage recommended in elderly patients.*

†—Estimated cost to the pharmacist for a 30-day supply at the lowest recommended dosage based on average wholesale prices in Red book. Montvale, N.J.: Medical Economics Data, 2004. Cost to the patient will be higher, depending on prescription filling fee.

‡—Not recommended for use in elderly patients.

§—May cause potentially fatal interactions.

Birrer et al 2004

TABLE 6
Drug Monitoring and Contraindications

Medication	*Extra monitoring for side effects*	*Contraindications*
Atenolol (Tenormin)	MAOIs, tricyclic antidepressants, trazodone (Desyrel), venlafaxine (Effexor)	
Caffeine	Bupropion (Wellbutrin), fluvoxamine (Luvox), MAOIs, venlafaxine	
Captopril (Capoten)	MAOIs, tricyclic antidepressants, trazodone	
Codeine	Fluoxetine (Prozac), fluvoxamine, paroxetine (Paxil), tricyclic antidepressants, trazodone	MAOIs (hypertensive crisis)
Digoxin	Tricyclic antidepressants	
Nifedipine (Procardia)	MAOIs, nefazodone (Serzone), tricyclic antidepressants	
Phenytoin (Dilantin)	Fluoxetine, fluvoxamine, sertraline (Zoloft)	
Theophylline	Fluoxetine, fluvoxamine, MAOIs	
Tramadol (Ultram)	Citalopram (Celexa), fluoxetine, fluvoxamine, mirtazapine (Remeron), nefazodone, paroxetine, sertraline, tricyclic antidepressants, trazodone, venlafaxine	MAOIs (potentiate seizure risk)
Tricyclic antidepressants	Bupropion, citalopram, fluoxetine, fluvoxamine, mirtazapine, paroxetine, sertraline, trazodone, venlafaxine	MAOIs, tricyclic antidepressants (serotonin syndrome)
Warfarin (Coumadin)	Citalopram, fluoxetine, fluvoxamine, MAOIs, mirtazapine, paroxetine, sertraline, venlafaxine	

MAOIs = Monoamine oxidase inhibitors.

Information from reference 5.

Birrer et al 2004

TABLE 7

Indications for Psychiatric Referral in Elderly Patients with Depression

- Bipolar disorder
- Suicidal ideation
- Psychosis
- Unresponsive or intolerant to adequate trial of first-line treatment
- Diagnostically complex or uncertain
- Candidate for electroconvulsive therapy
- Severely ill
- Need for treatment beyond drug therapy
- Double depression (i.e., episodes of major depression superimposed on dysthymic disorder)

Taylor W et al, 2018

- Vascular depression is often characterized as a disorder of **executive dysfunction**, including **difficulty with task completion and decision making**, both of which may increase the likelihood of experiencing irritability and social withdrawal.
- Additional cognitive features of vascular depression include slowed speed of information processing and impairments in concentration and attention.
- It is not uncommon for these cognitive complaints, rather than depressive symptoms, to be the trigger for a clinical evaluation.
- The assessment for vascular depression ideally includes not only a review of vascular risk factors and history of vascular disease but also **evidence demonstrating subcortical white matter disease**. Such findings are observed on an MRI brain scan **as periventricular or deep whitematter hyperintensities.**

Taylor W et al, 2018

- Vascular depression is
- Despite the lack of clarity in general clinical practice regarding the relevance of white matter hyperintensities on MRI scans, numerous neuroimaging studies have demonstrated that a greater burden of **white matter hyperintensities** correlates with **poor treatment response** (9, 20).
- Consequently, the best approach for incorporating white matter hyperintensities into clinical decision making may be to consider the **presence of white matter hyperintensities** as **a risk factor** for symptoms of vascular depression as well as potentially a prognostic factor when evidence of particularly **severe white matter hyperintensities** is observed in the context of depression

Taylor W et al, 2018

- Vascular depression is
- TREATMENT ISSUES
- Management
- Vascular depression not only increases the likelihood of **poor response to antidepressant treatment** and **persistent depressive symptoms** but also may contribute to **poor self-management of medical comorbidities** and **greater impairments in daily function**.
- There may also be cumulative disability associated with **impaired sleep, chronic pain, and use of analgesic medications,** as well as complex conditions such as **peripheral neuropathy** and **impaired mobility,** all of which add to the likelihood of poor outcomes in vascular depression.

Taylor W et al, 2018

- Vascular depression is
- CLINICAL PEARLS
- • The presenting features of vascular depression may involve poor motivation and slowed information processing as opposed to traditional mood complaints.
- • Although there is not currently an indication to obtain neuroimaging, when records are available, the assessment includes reviewing MRI reports for findings of deep white matter and periventricular hyperintensities as well as subcortical gray matter lesions.
- • Treatment planning should recognize that there may be a modest response to antidepressants and that other treatments, such as problem-solving therapy, may offer additional benefit.
- • Sleep hygiene may be important, and the patient may benefit from treatment with low-dose melatonin if indicated.
- • Management should include active support for the patient to reduce obesity, hypertension, hyperlipidemia, and glucose intolerance and to engage in appropriate dietary and exercise strategies to reduce vascular risk.

Tatum P et al, 2018

TABLE 2

Assessment Considerations for Older Patients—Adjusted for Life Expectancy, Dementia, and End of Life

	≥ 10 years remaining life expectancy	5 to < 10 years remaining life expectancy	Moderate dementia	Near end of life
Healthy lifestyle counseling				
Smoking cessation	Every visit	Every visit	Discuss with caregiver	Not recommended
Alcohol misuse	Annually	Annually	Annually	Initially, then if symptomatic
Exercise	Annually	Annually	Consider annually	Consider
Sexual function	Annually	Annually	Consider annually	Not recommended
Driving assessment	Consider	Consider	Routinely	Consider
Geriatric health issues				
Depression screening	Annually			
Falls risk assessment	Annually			
Gait and balance screening	Annually			
Urinary incontinence screening	Annually			
Hearing impairment screening	Consider annually			Not recommended
Visual acuity testing	Consider annually			Not recommended
Cognitive impairment screening	If symptomatic			
Advance directives completion	Complete and update as needed			

Adapted with permission from American Geriatrics Society and Talebreaz S, ed. Geriatrics Evaluation and Management Tools. New York, NY: American Geriatrics Society; 2016. https://geriatricscareonline.org/ProductAbstract/geriatrics-evaluation-management-tools/B007#. Accessed March 27, 2018.

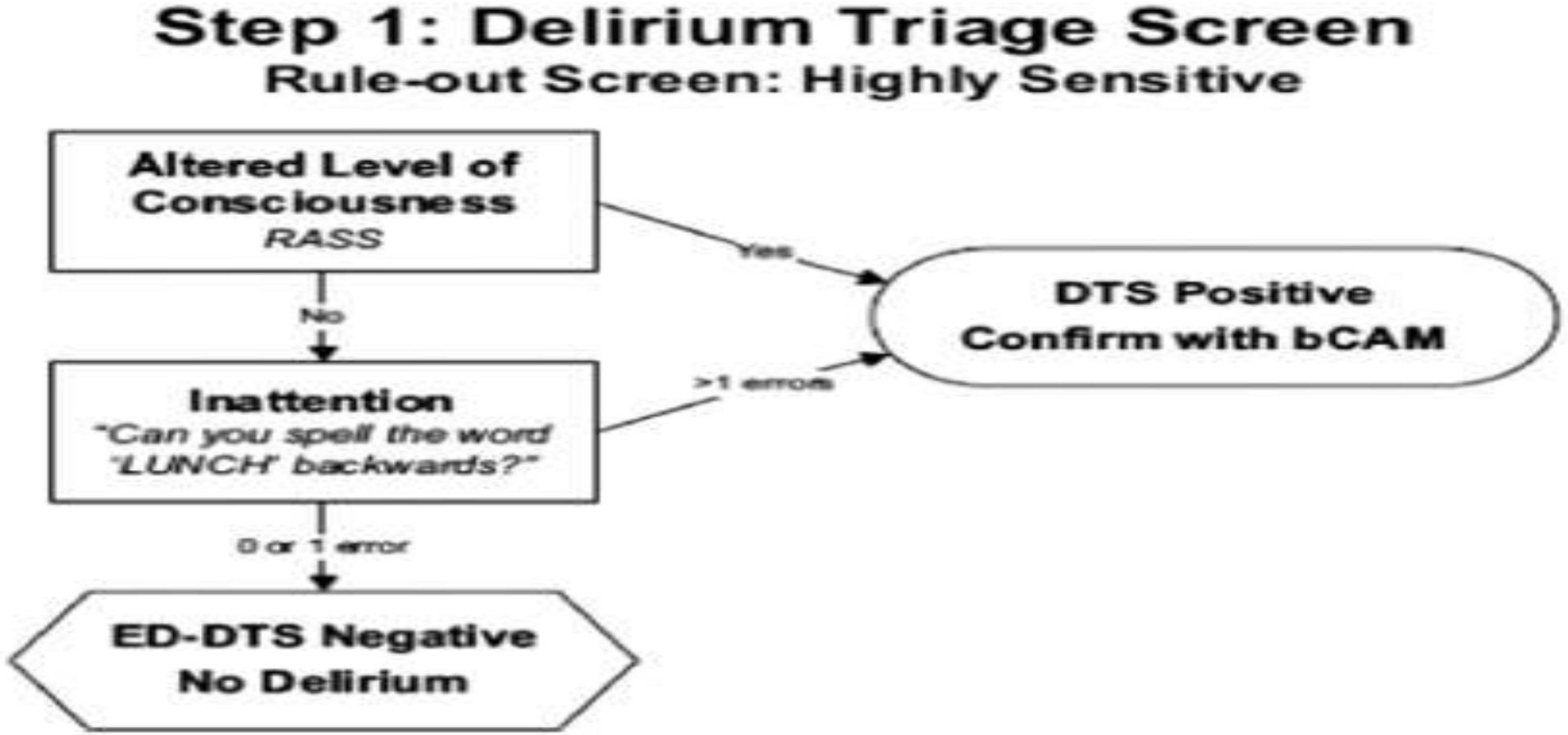

Figure 4. Delirium Screening Instruments. *RASS*, Richmond Agitation-Sedation Scale; *DTS*, Delirium Triage Screen; *bCAM*, Brief Confusion Assessment Method.

Volume 63, NO. 5 : May 2014 Annals of Emergency Medicine

Adapted from Katzman R, Brown T, Fuld P, et al. Validation of a short orientation-memory-concentration test of cognitive impairment. *Am J Psychiatry*. 1983;140(6):734-739.

Instructions to the patient: "Now I would like to ask you some questions to check your memory and concentration. Some of them may be easy and some of them may be hard."

	Correct	Incorrect
1) What year is it now? _____	(0)	(1)
2) What month is this? _____	(0)	(1)

Please repeat this name and address after me:
John Brown, 42 Market Street, Chicago
John Brown, 42 Market Street, Chicago
John Brown, 42 Market Street, Chicago

(underline words repeated correctly in each trial)
Trials to learning _____ (if unable to do in 3 trials = C)

3) Without looking at your watch or the clock, tell me what time it is.
(If response is vague, prompt for specific response

	Correct	Incorrect
(within 1-hour) _____ Actual time: _____	(0)	(1)

4) Count aloud backwards from 20 to 1 **0 1 2 Errors**

(mark correctly sequenced numerals)
If subject starts counting forward or forgets the task, repeat instructions and score one error.

20 19 18 17 16 15 14 13 12 11
10 9 8 7 6 5 4 3 2 1

5) Say the months of the year in reverse order.
If the tester needs to prompt with the last name of the month of the year, one error should be scored. (Mark correctly sequenced months.)

D N O S A JL JN MY AP MR F J **0 1 2 Errors**

6) Repeat the name and address you were asked to remember.

(John Brown, 42 Market Street, Chicago) **0 1 2 3 4 5 Errors**
_____, _____, ____, _____, _____

Scoring the Short Blessed Test

Item #	Errors (0-5)	Weighting Factor	Final Item Score
1		×4	
2		×3	
3		×3	
4		×2	
5		×2	
6		×2	
			Sum Total=_____ (Range 0-28)

0-4 Normal Cognition
5-9 Questionable Impairment
≥ 10 Impairment consistent with dementia

Figure 5. The Short Blessed Test (SBT) for ED Dementia Screening

Scoring the MMSE

Adapted from Folstein MF, Folstein SE, McHugh PR: “Mini-mental state”: a practical method for grading the cognitive state of patients for the clinician, *J Psychiatr Res* 12:189–198, 1975.

5 points	Orientation to state, country, town, hospital, floor
5 points	Orientation to year, season, month, day, date
3 points	Registration of three words
3 points	Recall of three words after 5 minutes
5 points	Serial 7s or spelling *world* backward
2 points	Naming two items
1 points	Understanding a sentence
1 points	Writing a sentence
1 points	Repeating “No *if’s*, *and’s*, or *but’s*”
3 points	Following a three-step command
1 points	Copying a design
30 points	Total

Life-Threatening Causes of Delirium, Recalled by the Mnemonic WWHHHHIMPS

Wernicke's encephalopathy
Withdrawal
Hypertensive crisis
Hypoperfusion/hypoxia of the brain
Hypoglycemia
Hyper/hypothermia
Intracranial process/infection
Metabolic/meningitis
Poisons
Status epilepticus

Serum and Urine Toxicology Screens

Substance	Serum Detection	Urine Detection
Alcohol	1–2 days	1 day
Amphetamine	Variable	1–2 days
Barbiturates	Variable	3 days to 3 weeks
Benzodiazepines	Variable	2–3 days
Cocaine	Hours to 1 day	2–3 days
Codeine, morphine, heroin	Variable	1–2 days
Delta-9-THC	N/A	~30 days, longer if chronic use
Methadone	15–29 hours	2–3 days
Phencyclidine	N/A	8 days
Propoxyphene	8–34 hours	1–2 days

N/A, Not applicable.

8-8 Cytochrome P450 Isoenzymes Active in Metabolizing Commonly Prescribed Psychotropic Medications

CYP1A2	CYP2C9	CYP2C19	CYP2D6	CYP3A3/4/5
Amitriptyline	Fluoxetine	Amitriptyline	Amitriptyline	Alprazolam
Clomipramine	Moclobemide	Citalopram	Amphetamines	Amitriptyline
Clozapine	Ramelteon	Clomipramine	Aripiprazole	Aripiprazole
Duloxetine	THC	Clozapine	Atomoxetine	Buspirone
Fluvoxamine		Diazepam	Clozapine	Carbamazepine
Haloperidol		Imipramine	Codeine	Clozapine
Imipramine		Moclobemide	Desipramine	Haloperidol
Methadone		Ramelteon	Dextromethorphan	Imipramine
Mirtazapine		Sertraline	Duloxetine	Lamotrigine
Olanzapine			Fluoxetine	Methadone
Ramelteon			Mianserin	Midazolam
Tacrine			Haloperidol	Nefazodone
			Hydrocodone	Oxcarbazepine
			Methadone	Pimozide
			m-CPP	Quetiapine
			Nortriptyline	Risperidone
			Olanzapine	Trazodone
			Oxycodone	Triazolam
			Paliperidone	Zaleplon
			Paroxetine	Zolpidem
			Phenothiazines	Ziprasidone
			Risperidone	
			Sertraline	
			Thioridazine	
			Tricyclics (TCAs)	
			Venlafaxine	

Cieri, F et al , te-Life Depression: Modifications of Brain Resting State Activity,2017

- **Late-life depression (LLD**) is a common emotional and mental disability in the elderly population characterized by the presence of **depressed mood**, the **loss of interest or pleasure** in daily activities, and **other depression symptoms.**

6) Ikäihmisen kaksisuuntaisen mielialahäiriön hoito

Yl juha kemppinen

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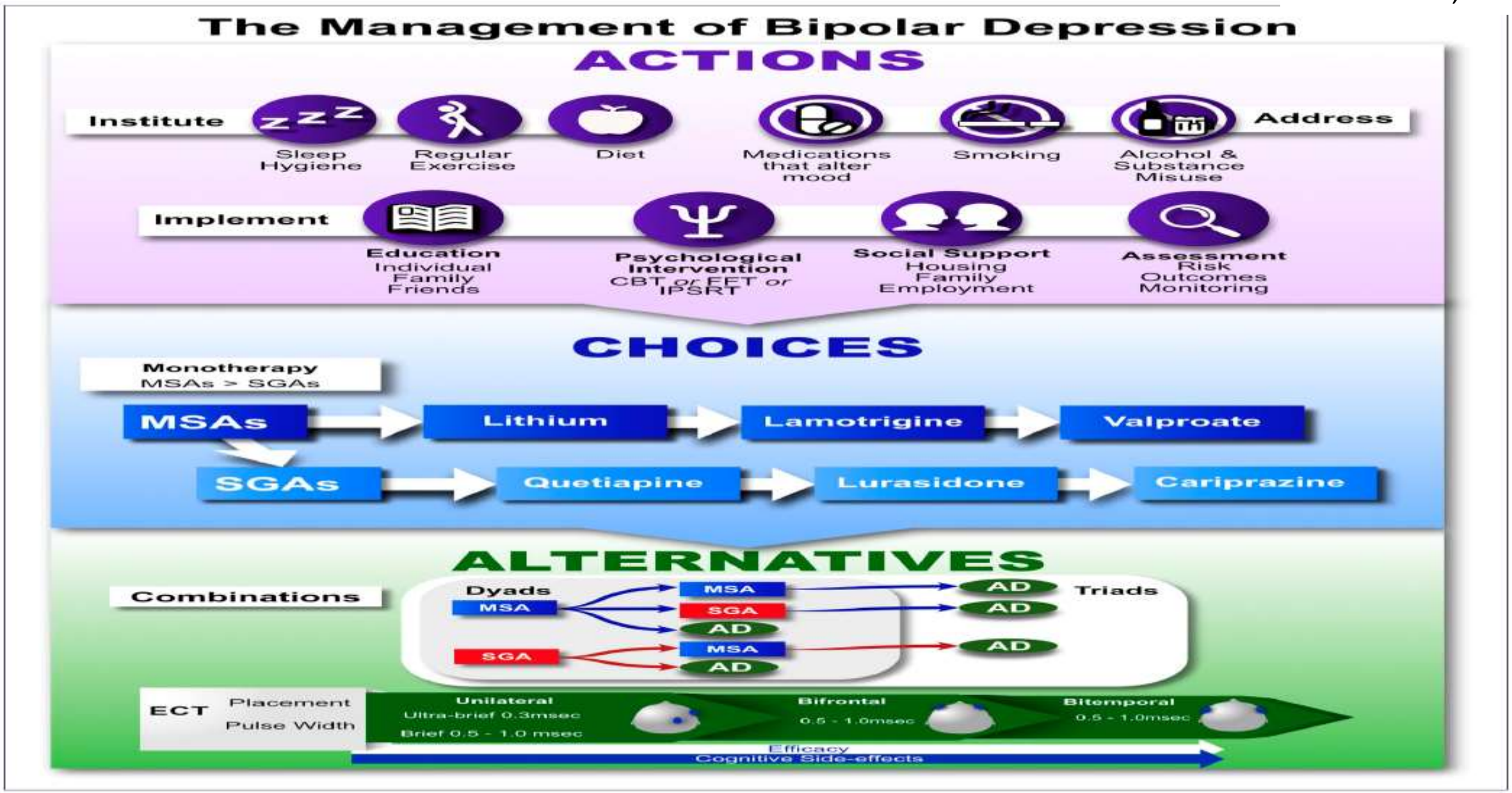

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Figure 28. The management of bipolar depression.

This schematic summarises the treatment recommendations for the management of bipolar depression. It begins with measures that are necessary and form a foundation for specific treatment strategies.

Actions

Management begins with *Actions* that *need* to be undertaken to facilitate functional recovery. These *Actions* have been categorised further into those that have to be *instituted* largely by the patient such as lifestyle changes, those that must be *addressed, often jointly with a specialist*, such as the cessation of smoking and substance misuse and those that must be *implemented* such as psychological interventions and psychoeducation – usually necessitating the involvement of a psychologist and other mental health care staff such as case managers and social workers. These three groups of *Actions* are considered *essential* for the management of major depression.

Choices

Building upon the foundation provided by the *Actions*, further pharmacological interventions – termed *Choices* can be considered should they be needed. The clinician can choose from the agents listed, which have been ranked giving mood-stabilising agents (MSAs) primacy over second generation antipsychotics (SGAs). This preference is based on both efficacy and tolerability. In the pharmacotherapy of bipolar depression, it is critical to bear in mind the long-term management of the disorder, and therefore, potential mood stabilising properties and long-term tolerability are important considerations. Within the various monotherapy *Choices*, mood-stabilising agents are also given preference because their blood levels can be carefully monitored.

Overall, lithium is the first *Choice* followed by lamotrigine and valproate and among the SGAs quetiapine is first *Choice* followed by lurasidone and cariprazine.

However, it is important to note these differences are subtle and in essence, any one of these *Choice* agents is suitable.

Alternatives

Once suitable *Choice* agents have been trialled, if a satisfactory response has still not been achieved, several management options are available to achieve a suitable response and full recovery. These *Alternatives* include combinations of mood-stabilising agents and SGAs and antidepressants, both as dyads and triads. Once again, preference should be given to fewer medications and therefore dyads are regarded as preferable to triads. MSAs are given preference and so combinations initially begin with these agents. Each of the three groups can be combined and so 5 options are possible (excluding dyads of two SGAs, and two ADs, and allowing for an MSA and SGA to be combined reciprocally).

Triads can then be formed by extending some of these dyad combinations by adding an AD where this has not already been prescribed. Note once again combinations of more than one SGA or AD are *not* advised.

Note: Among these *Alternatives*, the various combinations have a particular sequence and where possible, this should be adhered to. The MSAs and SGAs used in these combination dyads and triads should, in the first instance, include *Choice* agents. However, many other combinations can also be trialled if need be, and after appropriate pharmacotherapeutic strategies have been trialled, ECT, which is widely available and has a long-standing track record, may be considered. For ECT, the recommended placement and pulse width options have been outlined and the order in which these should be considered has been specified to minimise cognitive side effects.

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Table 15. Further options for the treatment of acute bipolar depression.

Monotherapy	1. Carbamazepine 2. Olanzapine
Adjunctive	1. Asenapine 2. Armodafinil 3. Levothyroxine

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Recommendation Box 5. Administration of antidepressants in bipolar disorder		Grade
General considerations		
5.1	The use of antidepressants in the treatment of bipolar disorder should be overseen by a psychiatrist where possible.	CBR
5.2	The clinical risks versus benefits of antidepressants in treating bipolar depression should be determined on an individual basis.	CBR
Treatment		
5.3	Adjunctive antidepressant therapy should be used cautiously in the treatment of bipolar depression when there is a history of antidepressant-induced mania, current or predominant mixed features, or a history of rapid cycling.	EBR III
5.4	Antidepressant monotherapy should be avoided in bipolar disorder	EBR III
Treatment emergent affective switch (TEAS)		
5.5	Upon commencing antidepressants, patients with bipolar disorder should be closely monitored for symptoms of mania, and if these emerge then antidepressant therapy should be discontinued. Psychoeducation should be provided so that patients, family and friends can identify early warning signs of mania and/or mixed symptoms.	CBR
5.6	Antidepressant therapy should be avoided in bipolar disorder patients with a history of rapid cycling and/or a high level of mood instability.	CBR
5.7	The prescription of antidepressants should consider any past history of a TEAS.	CBR

CBR: consensus-based recommendation; EBR: evidence-based recommendation.

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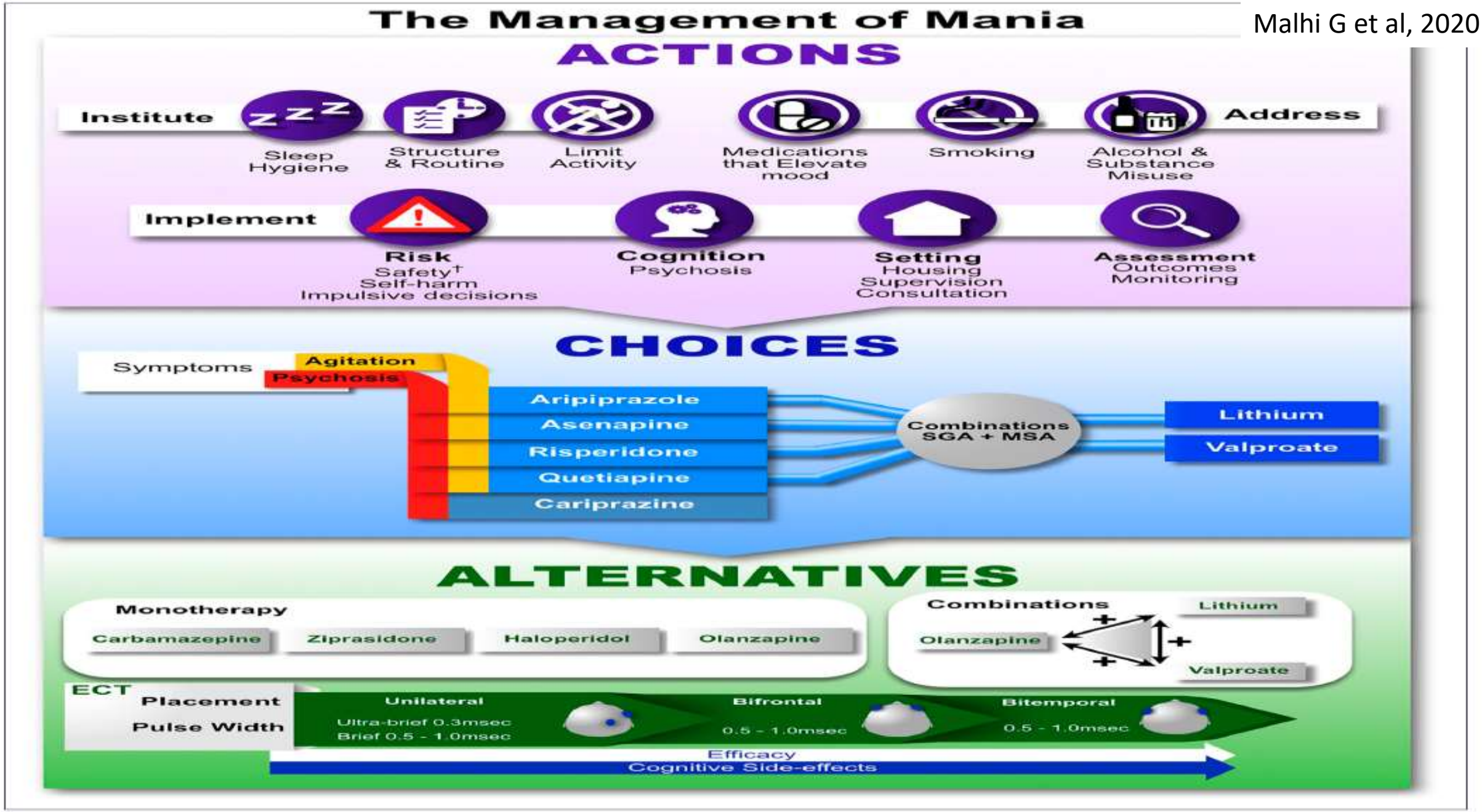

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Table 14. Pharmacotherapy for agitation.

Route of administration	Monotherapy
Oral	Asenapine[a]
	Risperidone[b]
	Quetiapine
	Haloperidol
Intramuscular	Aripiprazole
	Olanzapine[c]
	Haloperidol
	Combinations
	Haloperidol + Midazolam
	Haloperidol + Promethazine

[a]Sublingual.
[b]Also available as orally disintegrating formulation.
[c]Also available in wafer formulation.

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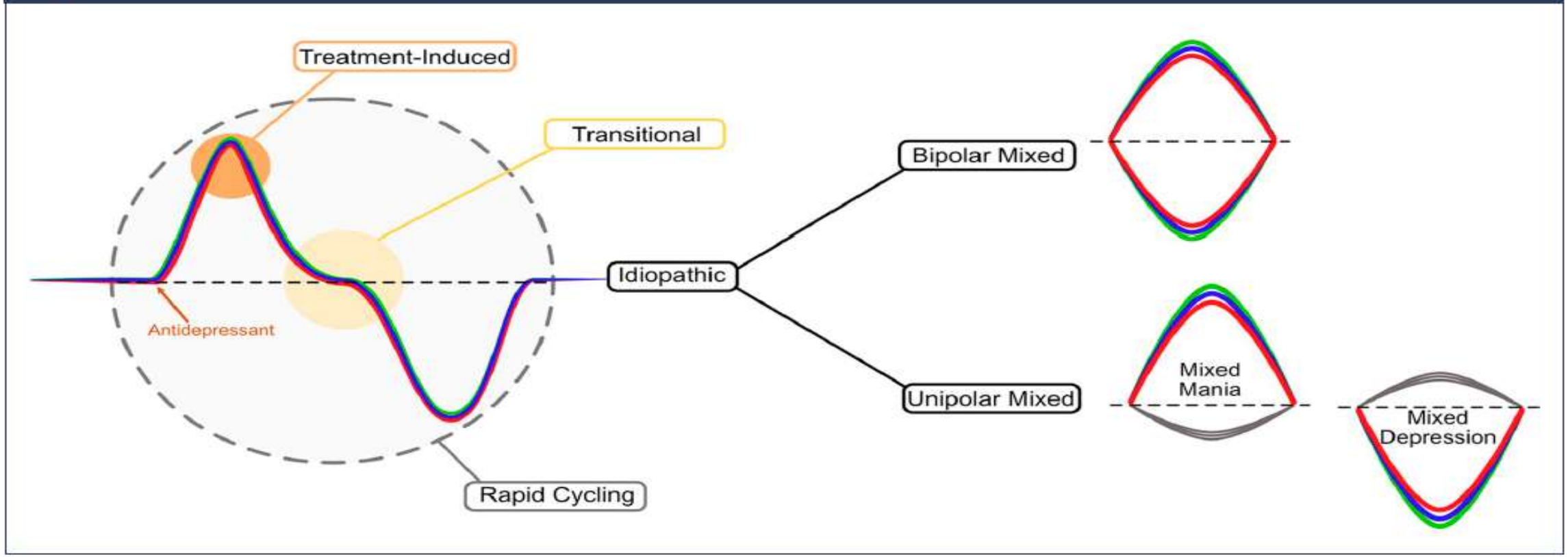
Figure 29. Overview of the management of mixed states.



The management of mixed states is complicated and therefore a structured approach is necessary. At the outset it is important to exclude alternative causes for a mixed state presentation (e.g. treatment-induced mixed state). Once it has been established that the mixed state is *idiopathic* then it is necessary to determine its composition with respect to the distribution of manic and depressed symptoms. An equal distribution of both depressed and manic symptoms is termed *bipolar mixed* but, when the distribution is skewed towards one pole, it is described as *unipolar mixed* and this can be further specified as either *mixed mania* or *mixed depression* (these approximate to DSM-5 mania and depression with mixed features, respectively). For the purposes of management, it is useful to identify these three subtypes as each requires slightly different treatment considerations (see Figure 30).

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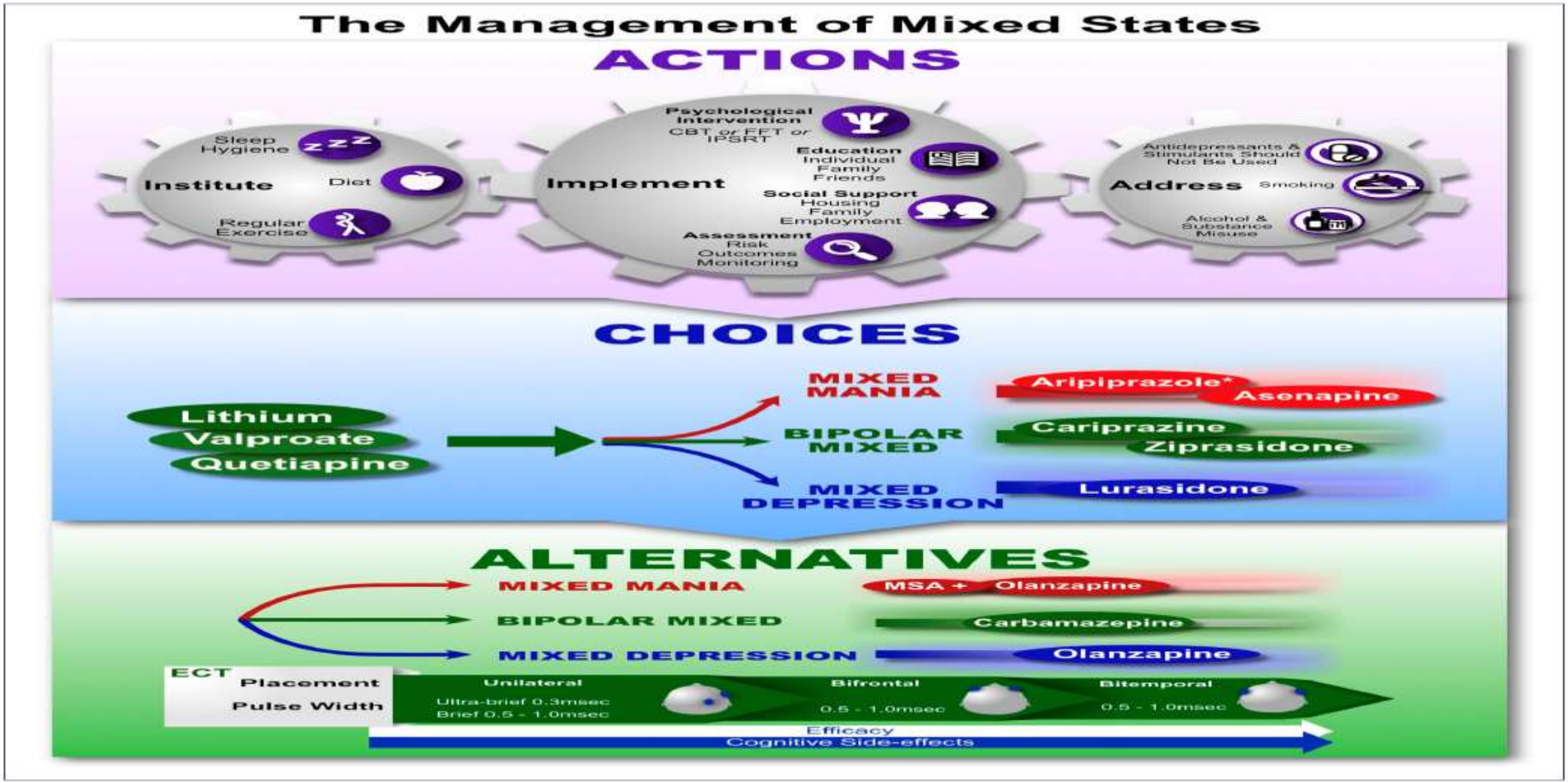

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Figure 30. The management of mixed states.

The management of mixed states is complicated because it encompasses elements of the treatment of mania, bipolar depression and mood stabilisation.

Actions

It is vital to have a firm foundation for the management of mixed states. It is therefore important to institute good habits involving sleep hygiene, regular exercise and a healthy diet. Excess alcohol, substance misuse, smoking, energy drinks and excessive caffeine need to be addressed but the most critical step is the cessation of medications that destabilise mood such as antidepressants and stimulants. Psychoeducation is especially important because of the complexity of the presentation and the challenges it poses for treatment. Risk assessment is also critical and where available psychological interventions should be initiated as soon as possible.

Choices

Agents that have equipotency across both mania and depression should be administered first to achieve mood stability and prevent the development of contrapolar symptoms. Therefore lithium, valproate and quetiapine monotherapy are *Choice* agents in this regard. Then if treating a *bipolar mixed* state these can be substituted if need be with cariprazine or ziprasidone monotherapy or combined, if monotherapy is unsuccessful. To treat *mixed mania*, aripiprazole or asenapine can be added to one of the mood-stabilising agents and similarly, lurasidone can be added to treat *mixed depression*.

Alternatives

If the suggested *Choice* agents are unsuccessful (as monotherapy or in combination) then further combinations of *Choice* agents can be trialled in the first instance. And depending upon the mixed state subtype, additional agents can be prescribed. For a bipolar mixed state, carbamazepine is a potential *Alternative* and, for mixed mania, olanzapine may be effective (in combination with a mood stabiliser). Olanzapine can also be prescribed to treat mixed depression. However, the side effect profile of olanzapine is of concern and long-term prescription should be avoided if at all possible.

Finally, it is important to note that ECT is a useful option for the management of mixed states as it has potent actions against both manic and depressed symptoms.

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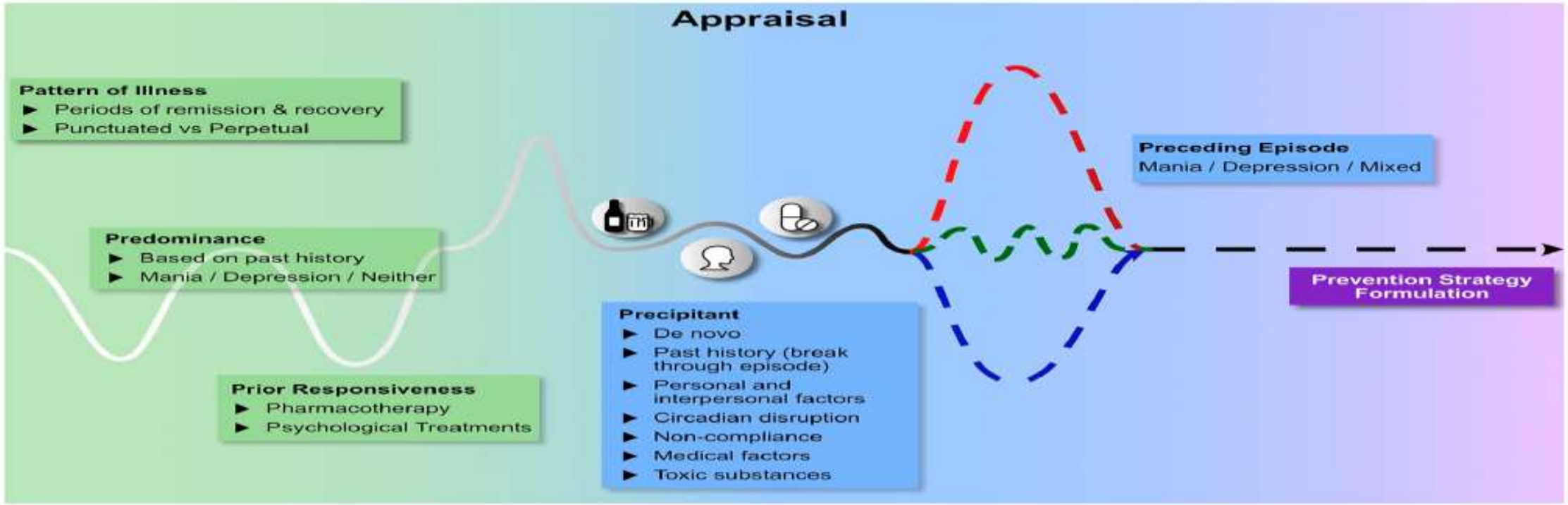
Figure 31. Appraisal for maintenance treatment in bipolar disorder.



The long-term management of bipolar disorder is arguably the most important and definitely the largest component of therapy in terms of time. It is therefore worthwhile investing significant effort into planning the long-term management of bipolar disorder, which includes maintenance and prophylaxis. Specific recommendations are provided in the management figure (Figure 32). However, prior to implementing the necessary treatments, it is important to formulate an appropriate prevention strategy. This requires appraisal and involves gaining an appreciation of the nature of the illness, and then on the basis of this, determining likely outcomes so as to anticipate these and prevent them. Appraisal involves mapping the pattern of the illness, its predominance in terms of symptoms, evaluating its prior responsiveness, then determining what has precipitated the recent episode – taking into consideration the nature of the preceding episode. By collating this information, it should be possible to prognosticate what is the likely pattern of illness in the future, and on this basis, plan a prevention strategy accordingly. For example, if the most recent episode is that of depression and the past pattern of illness has been that of repeated depressive episodes separated by relatively long periods of recovery (achieved with combinations of medications), it is likely that the same strategy will be necessary. Future prevention should therefore focus on ensuring there is sufficient prophylaxis against depression, especially as the patient recovers, and that the individual remains engaged with treatment. If tolerability issues or ongoing compromise because of medications is a significant concern, then medications should be selected accordingly to ensure the individual is able to continue with treatment long term and remain well. Understanding the nature of the illness, in particular its past history, is critical to understanding its future course and likely responsivity to treatment.

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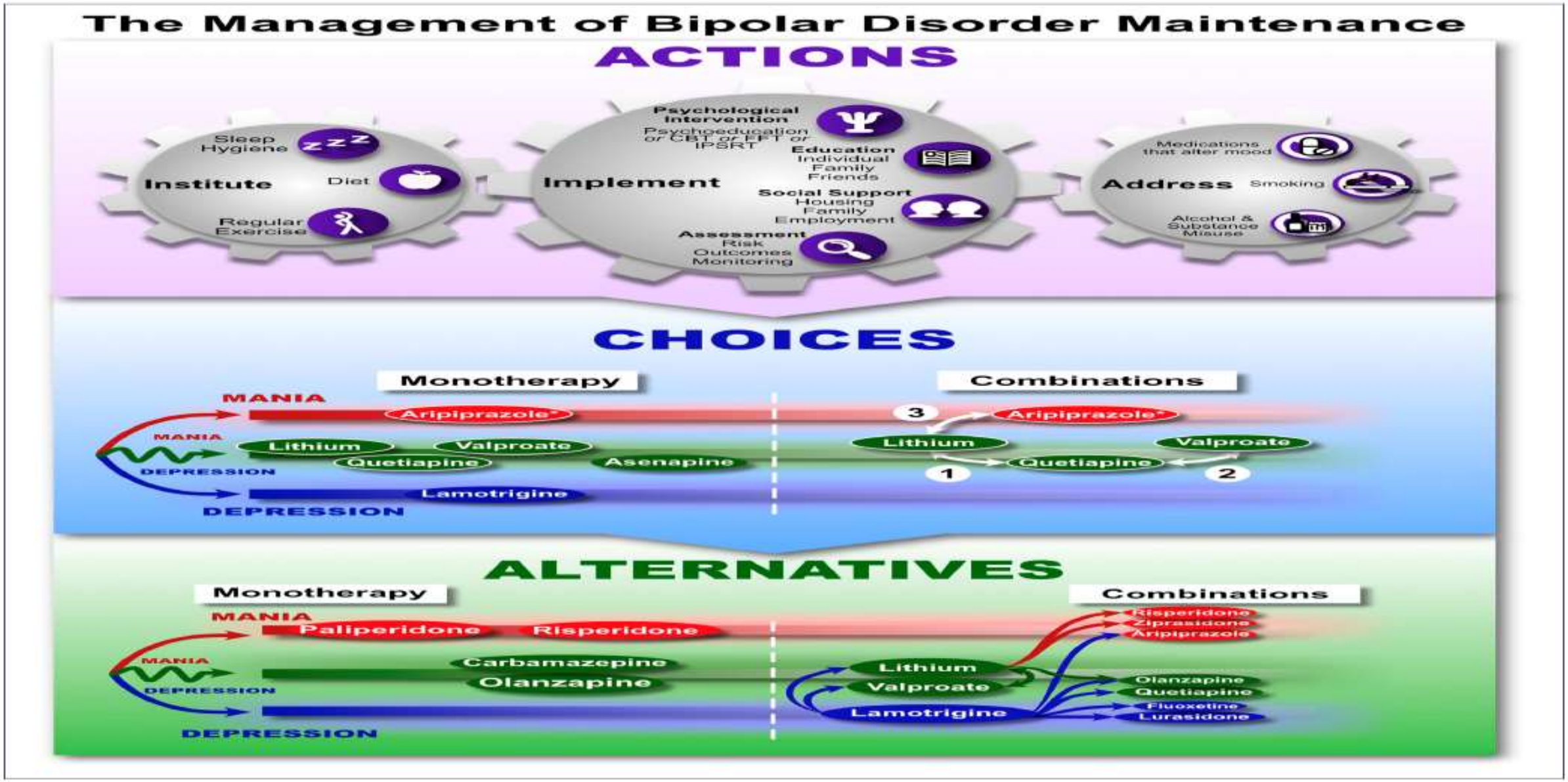

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Figure 32. The management of bipolar disorder – maintenance.

This schematic summarises the treatment recommendations for the maintenance management of bipolar disorder. It begins with measures that are necessary and form a foundation for specific treatment strategies.

Actions

Management begins with *Actions* that need to be undertaken to maintain functional recovery. These *Actions* are shown as parts of interconnected cogs emphasising the cyclical nature of bipolar disorder and the normal vicissitudes of mood and the need to maintain emotional regulation. The *Actions* have been categorised further into three broad types. Some *Actions* can be instituted largely by the patient such as lifestyle changes (e.g. regular exercise, diet and sleep hygiene). Others may involve referral to a specialist to address challenges such as cessation of smoking, alcohol and substance misuse and the withdrawal of medications that alter mood. Finally, *Actions* that ideally must be implemented include providing psychoeducation, organising social support (housing, relationship and employment issues), and commencement of an evidence-based psychological intervention (group Psychoeducation, CBT, IPSRT or FFT, see above). These three interdependent sets of *Actions* are considered essential for the successful long-term management of bipolar disorder.

Choices

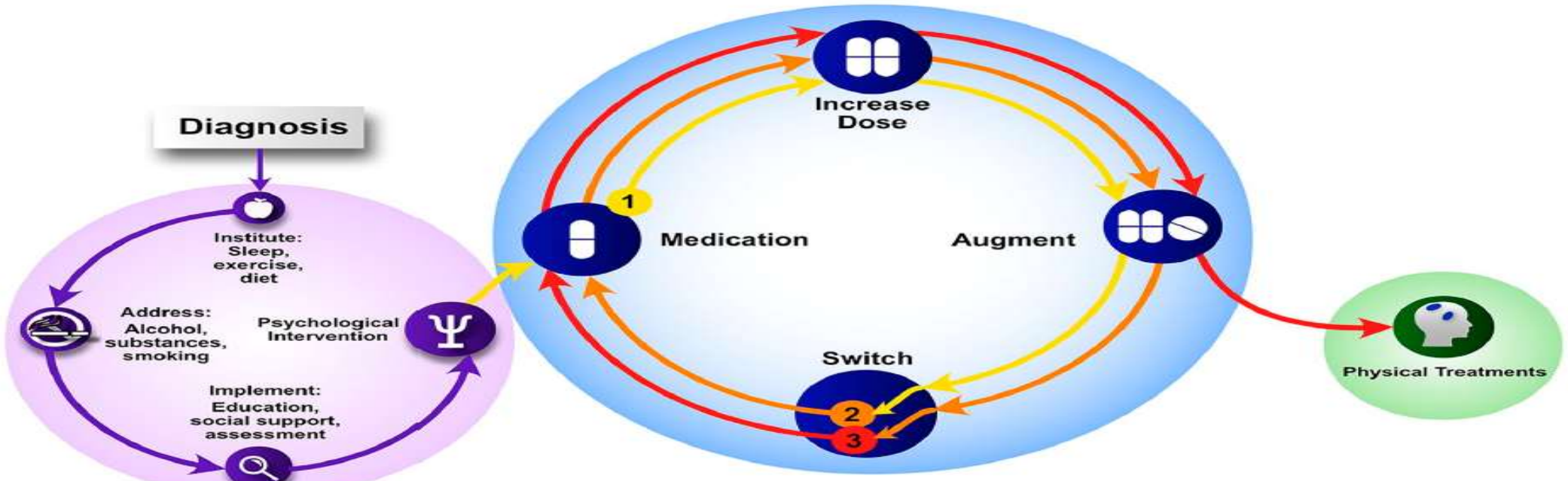
Actions, if implemented correctly, provide a solid foundation upon which to focus on the pharmacotherapy of bipolar disorder. It is important to note that psychological interventions implemented as part of *Actions* must be continued and that pharmacological *Choices* are to be considered in addition to ongoing psychological treatment. Selection among the various *Choices* provided is determined by a number of factors that have been summarised separately under *Appraisal* (see Figure 31). These considerations are critical when transitioning from acute treatment to maintenance and prophylaxis, and they will be key determinants of the selections made. In the schematic, monotherapy is once again preferable to combination strategies and medications are displayed reflecting their relative efficacies for mania, depression or both phases of the illness. The latter refers to agents that have near equal efficacy in maintaining mood stability and preventing future relapses for both mania and depression. These agents are therefore also suited to instances in which there are mixed states. Maintenance monotherapy places lithium in pole position followed by valproate, quetiapine and asenapine. The mood stabilisers are preferable because of their better long-term tolerability profile (note: asenapine is more complicated to administer than other agents). Where there is a preponderance of mania, aripiprazole is a suitable *Choice* and conversely where there is a preponderance of depression, lamotrigine may be a suitable option for monotherapy. However, in most cases, combinations will be required and the three combinations that are most efficacious are lithium + quetiapine, valproate + quetiapine, and lithium + aripiprazole (* it is important to note that aripiprazole can be administered also as a long acting depot).

Alternatives

Once suitable *Choice* agents have been trialled, a number of *Alternatives* can be considered as monotherapy or in combinations, to achieve optimal mood stability and prophylaxis. For instance, where both mania and depression are prevalent, carbamazepine and olanzapine are options and where mania is the main concern, paliperidone and risperidone are options. In addition to these monotherapy *Alternatives*, a number of combinations can be considered, the foundation of which involves lithium or valproate or lamotrigine. To these agents, medications with additional antimanic and antidepressant properties can be added, and where there is a *Choice*, lithium is to be preferred over valproate because of the additional risks associated with valproate prescription in young women. Please note, although olanzapine + fluoxetine does have evidence and has been marketed as a specific combination [OFC], the poor long-term tolerability of olanzapine is a serious concern.

Malhi G et al, 2020

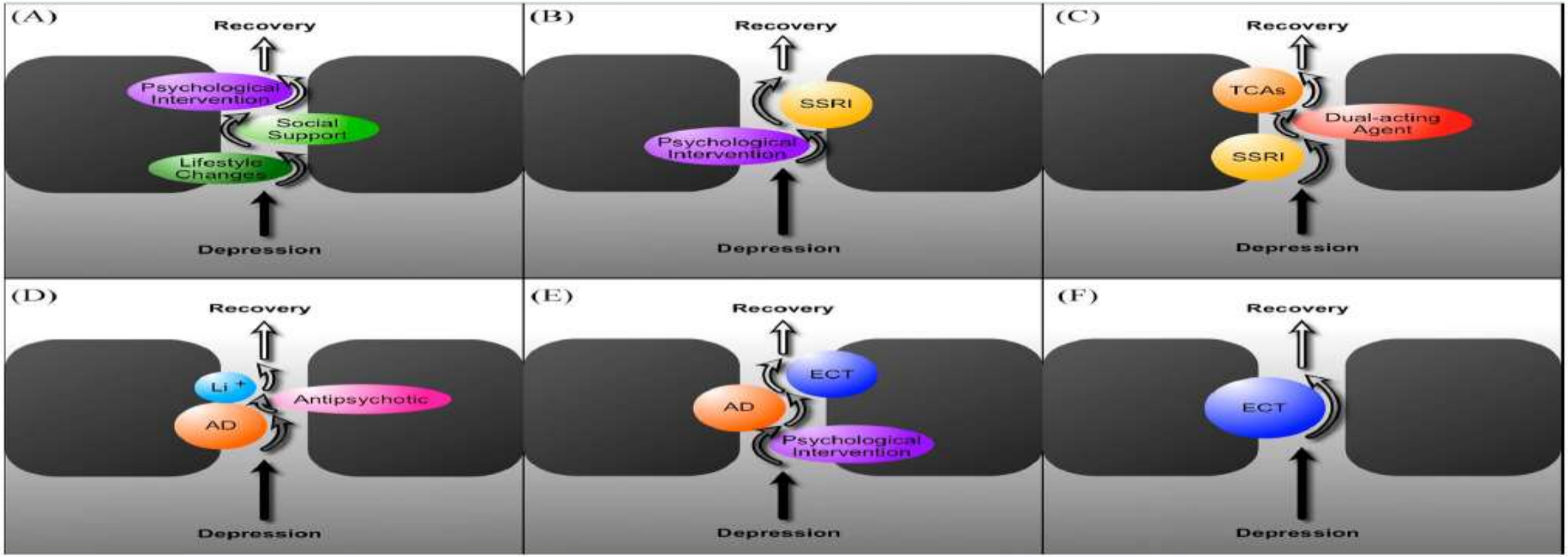
Figure 33. Strategies for channelling response.



In the management of depression, following diagnosis and the institution of appropriate *Actions*, treatment involves the implementation of psychological interventions (purple), which can if necessary be combined with medication. Pharmacotherapy (blue) involves the administration of *Choice* medications and following the administration of a suitable medication for an appropriate duration of time, an increase in dose may be trialled in order to achieve an optimal response. Subsequent to this any response that has occurred can be augmented – for example with the addition of lithium but if these strategies are unsuccessful the antidepressant medication can be switched (From 1 To 2) and the whole process can be repeated (2 to 3). Given the number of *Choice* antidepressants available for the management of depression, the prescription of a suitable medication (M), followed by an Increase in Dose (ID), its Augmentation (A) and finally a Switch (S) to another antidepressant should be trialled a minimum three times (repeating the cycle [MIDAS]) so as to experience the effects of antidepressants from at least three different classes, and many more times if considering *Alternatives*. However, at some time, to achieve a response it may be necessary to switch from pharmacotherapy to physical treatments (Green) and this may occur much earlier if there are specific indications that are particularly responsive to ECT such as psychotic symptoms and melancholia.

Malhi G et al, 2020

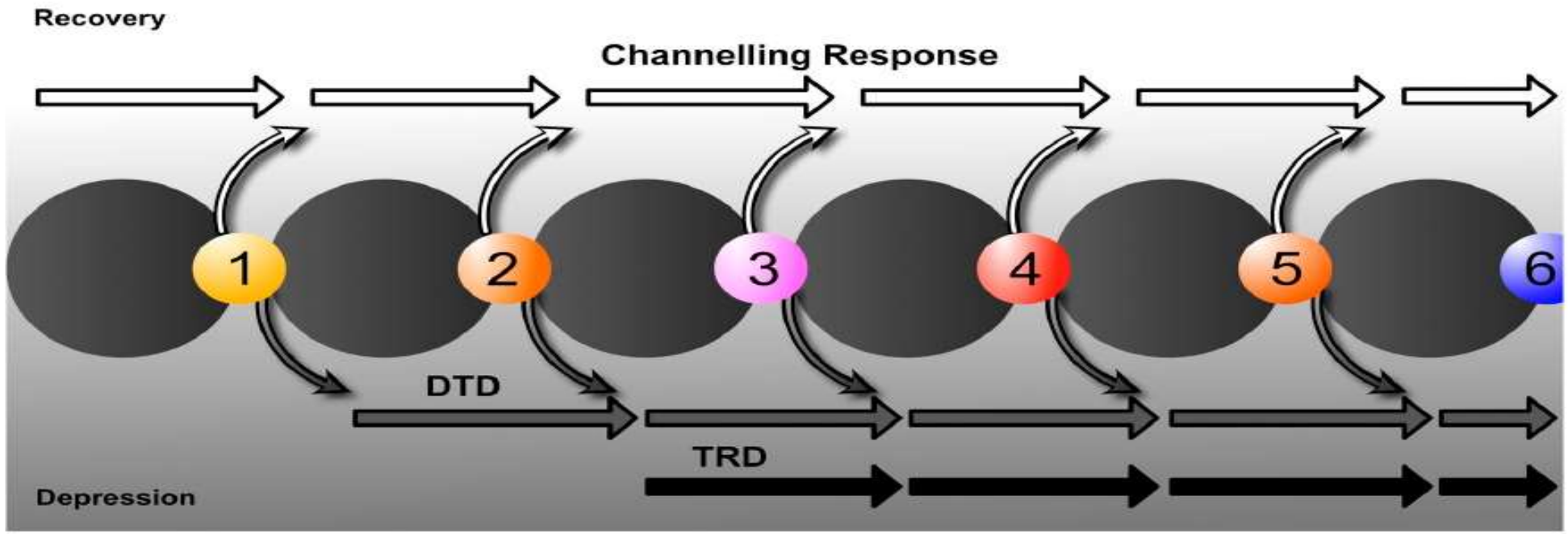
Figure 34. Modelling therapeutic channels of response.



This composite schematic illustrates by way of examples how different sequences of treatments (and their combinations) may be needed to transition from a depressed mood state to one of functional recovery. Various treatments work individually or in combination to facilitate or accelerate this transition, and their individual effects (responses) are depicted as arrows.
(A) Combination of lifestyle changes, social support and psychological interventions (such as CBT) to facilitate recovery from depression. (B) Combination of a psychological intervention and an SSRI to achieve recovery. (C) Sequencing of agents. First an SSRI may be prescribed, but this only achieves a partial response, and therefore it is switched to a dual-action agent and then further supplanted by a tricyclic (TCA) antidepressant. Ultimately, recovery is achieved, and this particular sequence may have been critical. (D) Use of lithium to augment the effects of an antidepressant (AD) in combination with an antipsychotic. The combination of an antidepressant and an antipsychotic produces a partial response, but recovery is only possible with the additional augmenting effect of lithium. (E) Pathway in which a combination of a psychological intervention and an antidepressant achieve a partial response and ECT is then administered to recover fully. Finally, (F) response for which only ECT will work and thus it is essential for the individual to recover.

Malhi G et al, 2020

Figure 35. Models of treatment: DTD, TRD and Channelling Response.



This schematic illustrates the channels of response that connect depression and recovery. Successive treatments (numbered 1-5) open channels that may lead to remission and recovery. The various models of treatment can be divided into those that focus on non-response and those that focus on responsivity. Difficult to treat depression (DTD) and treatment resistant depression (TRD are predicated on non-response. Both paradigms require a threshold, namely that of non-response, either of specific agents or a number of strategies. For DTD, the threshold is lower, and the depression is regarded as 'challenging' after the very first treatment failure. For TRD the focus is principally on pharmacotherapy, although some aspects of the definitions also include physical treatments and the threshold is usually 2 or more treatment failures.
In contrast, the channelling response paradigm (CRP) runs alongside the treatment of depression throughout and is a perspective that is adopted from the outset. Thus, the CRP has no threshold and there is no focus on treatment failures. Instead, the focus is on responsivity, and depression is conceptualised as an amalgam of responsivities to different types of treatment. Therefore, the CRP automatically instils a positive outlook whereas DTD and TRD are prone to generate a negative perspective.

Malhi G et al, 2020

Recommendation Box 6. The pharmacological management of poor response		Grade
Increasing dose		
6.1	If there is no improvement after 3 weeks of treatment using standard antidepressant doses it is reasonable to consider dose escalation	CBR
6.2	Dose escalation beyond recommended maximum doses should only be considered if the patient has had a partial response at a lower dose	CBR
6.3	Higher than recommended dose ranges should only be employed in specialist psychiatric settings where regular, careful and close monitoring is possible	CBR
6.4	When prescribing above the recommended maximum dose, the patient should be made aware a higher than usual dose is being used and a second opinion can be considered	CBR
Augmentation		
6.5	Lithium	EBR I
6.6	Second/third generation antipsychotics	CBR
Switching		
6.7	Switching to an antidepressant from a *different* class, improves the likelihood of response when switching for reasons of either non-response or intolerability	CBR
6.8	Switching *within* class is best reserved for when the first antidepressant has had to be ceased because of intolerable side effects	CBR

CBR: consensus-based recommendation.

Malhi G et al, 2020

Recommendation Box 9. Management of mood disorders with comorbid medical illnesses		Grade
9.1	First presentation mood disorders should undergo general medical evaluation with organic investigation as indicated.	EBR III
9.2	Lifestyle factors should be monitored, with ongoing education and encouragement especially important in this vulnerable group.	EBR II
9.3	Close monitoring of medications to mitigate risks of medication interactions, toxicity and problematic side effects (such as metabolic syndrome) is advised.	CBR

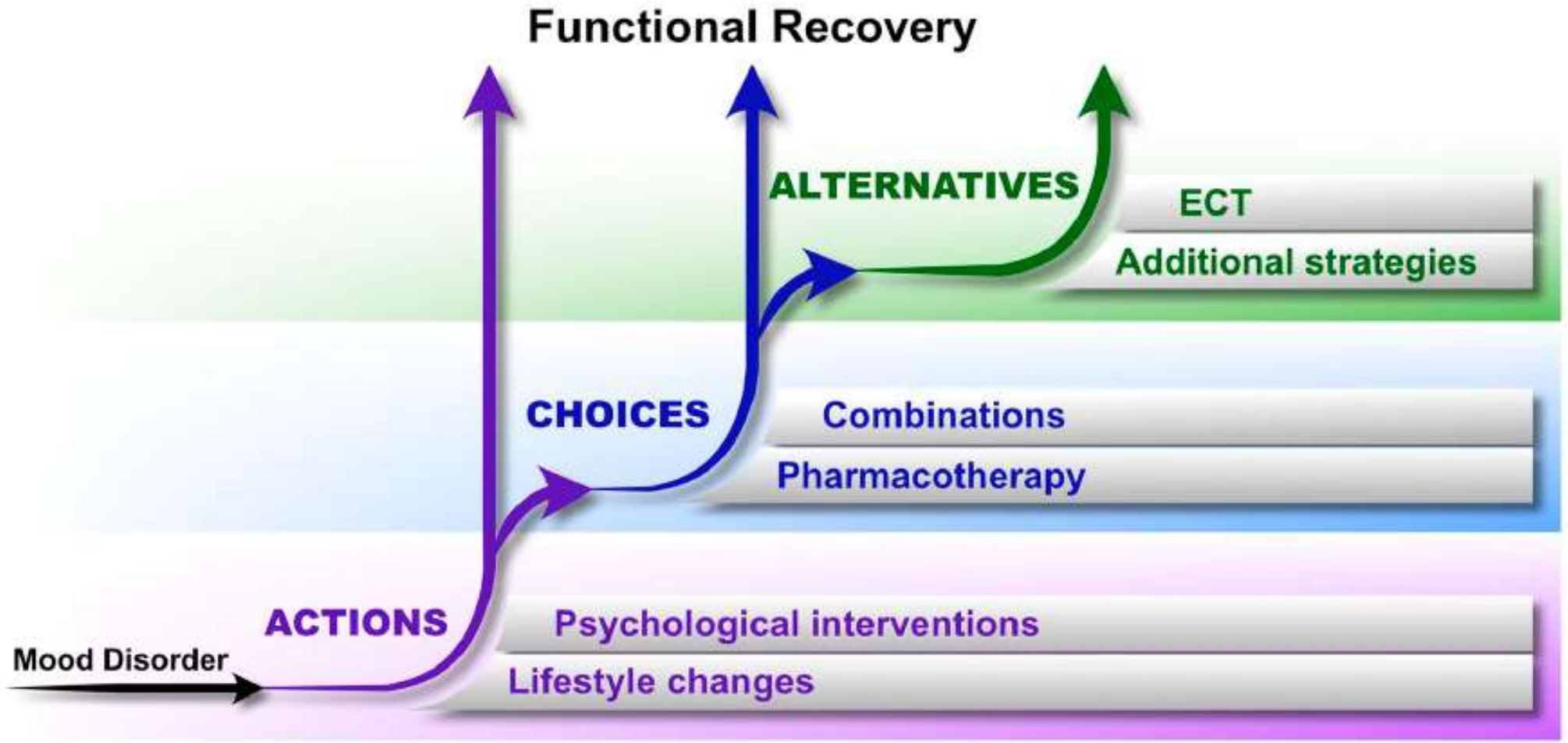
EBR: evidence-based recommendations; CBR: consensus-based recommendations.

Tausta-aineistoja

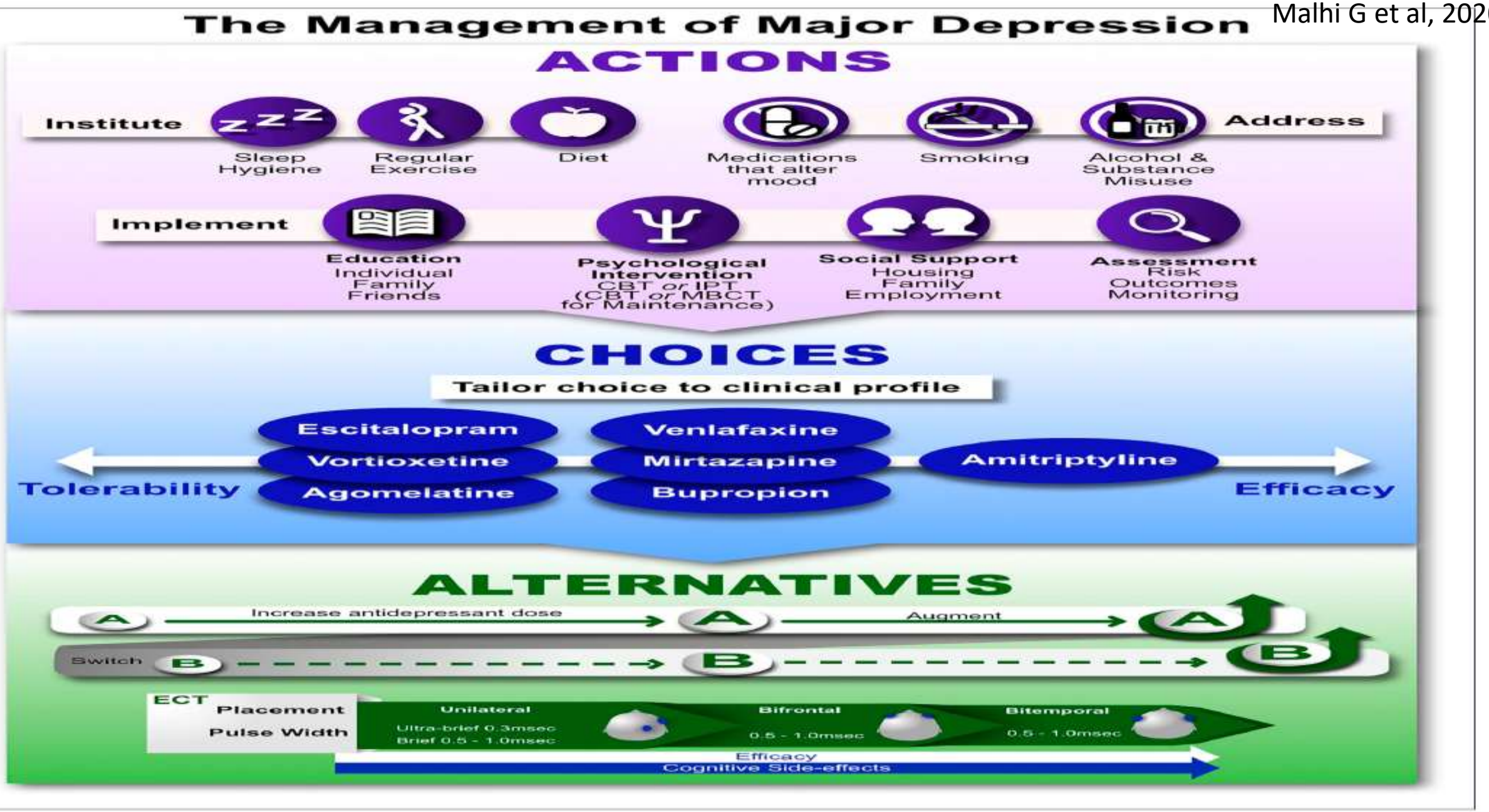
Yl juha kemppinen

Malhi G et al, 2020

Figure 18. Foundations of treatment.



Malhi G et al, 2020



Recommendation Box 2. Management of acute MDD		Grade
2.1	Clinicians should assist patients to overcome well-recognised barriers to accessing psychological interventions (e.g. via providing information about online psychological treatments, advice about local therapists, and the rationale for developing skills to prevent relapse).[a]	CBR
2.2	Psychological interventions should only be delivered by clinicians trained in the relevant evidence-based approach.	EBR I
2.3	One of the evidence-based psychological interventions should be offered as foundational care (Action) to all patients (the most extensive evidence is for CBT and IPT, but a range of interventions have strong evidentiary support).	EBR I
2.4	Combined psychological intervention and antidepressant medication is more effective than either type of intervention alone.	EBR I

MDD: major depressive disorder; CBR: consensus-based recommendation; EBR: evidence-based recommendation; CBT: cognitive behavioural therapy; IPT: interpersonal therapy.

[a]Two contextual factors regarding psychological treatments are important in the management of acute MDD: patients generally prefer psychological intervention over antidepressant medication; and psychological interventions are becoming more accessible due to increased numbers of trained clinicians, online self-management programs and telehealth platforms (see section 'Digital therapies' within section 6.1. 'Actions').

Australian & New Zealand Journal of Psychiatry, 55(1)

Malhi G et al , 2020

Recommendation Box 3. Long-term treatment of MDD		Grade
3.1	All patients with depression should receive psychoeducation regarding the lifetime risk of relapse.	CBR
3.2	Patients with depression should be monitored regularly beyond the acute phase of treatment to ensure complete remission of symptoms and full functional recovery.	CBR
3.3	CBT should be offered to prevent relapse of depression, and where available, MBCT should be offered to patients with recurrent depressive episodes.	EBR I
3.4	Once a satisfactory therapeutic response has been achieved, antidepressant dosage should remain the same during continuation and preventative phases of treatment.	EBR I
3.5	Maintenance antidepressant treatment should be continued for at least 6 months and a detailed review of ongoing pharmacotherapy should occur at 1 year.[a]	CBR

MDD: major depressive disorder; CBR: consensus-based recommendation; CBT: cognitive behavioural therapy; MBCT: mindfulness-based cognitive therapy; EBR: evidence-based recommendation.
Note: Treatments aiming to prevent relapse are more effective if full remission of the initial episode is achieved. The choice of antidepressant dose is also determined by additional factors such as prior illness severity and response to treatment, comorbid disorders and medication tolerance.
[a]This is particularly important if a recurrent pattern of illness has been established.

Malhi G et al , 2020

Table 13. Symptoms of discontinuation and withdrawal (adapted from Haddad and Anderson, 2007, and Jha et al., 2018).

General	Chills, malaise, flu-like symptoms, diaphoresis
Sensory	Paraesthesia, numbness, 'electric-shock-like' sensations, rushing noise 'in head', blurred vision, palinopsia
Disequilibrium	Light-headedness, dizziness, vertigo
General Somatic Symptoms	Lethargy, fatigue, headache, tremor, sweating, anorexia
Affective symptoms	Irritability, anxiety/agitation, low mood, tearfulness
Gastrointestinal symptoms	Nausea, vomiting, diarrhoea
Sleep disturbance	Insomnia, nightmares, excessive dreaming

Malhi G et al , 2020

Recommendation Box 4. Withdrawal of antidepressants		Grade
4.1	Inform patients when starting on an antidepressant that they may experience discontinuation and withdrawal symptoms and should not stop antidepressants abruptly and should discuss stopping their antidepressant with their treating physician	CBR
4.2	The dose of AD should be tapered down with the dose lowered generally in at least weekly steps, and the rate of stepping down the dose needs to be tailored to the individual patient	EBR IV
	(a) Initially, titrate down to the recommended minimum effective dose of the antidepressant	CBR
	(b) Once minimum effective dose is achieved, reduce the dose by no more than 50% weekly	CBR
4.3	For patients with one or more risk factors for withdrawal and discontinuation symptoms (treatment at higher than usual dose, long-term period on antidepressant, previous discontinuation and withdrawal symptoms or symptoms emerging with missed dose(s)), a slower taper is recommended.	EBR IV
	(a) Initially, drop to the recommended minimum effective dose of the antidepressant	EBR IV
	(b) Reduce the dose by small decrements (dependent on how the tablets can be cut up) every 2 weeks	EBR IV
4.4	For patients stopping their medication in order to switch to another antidepressant because of lack of efficacy or intolerable side-effects, a more rapid dose reduction can be used (over days) while the new antidepressant is introduced at a low dose and then the dose increased (provided there are no contraindications for this, such as switching to and from an MAOI).	CBR
	(a) Discontinuation/withdrawal symptoms from the first antidepressant (after careful review of the symptoms the patient reports) need to be distinguished from treatment emergent side-effects from the newly introduced antidepressant.	CBR

CBR: consensus-based recommendation; AD: antidepressants; EBR: evidence-based recommendation; MAOI: monoamine oxidase inhibitor.

Malhi G et al , 2020

Malhi G et al, 2020

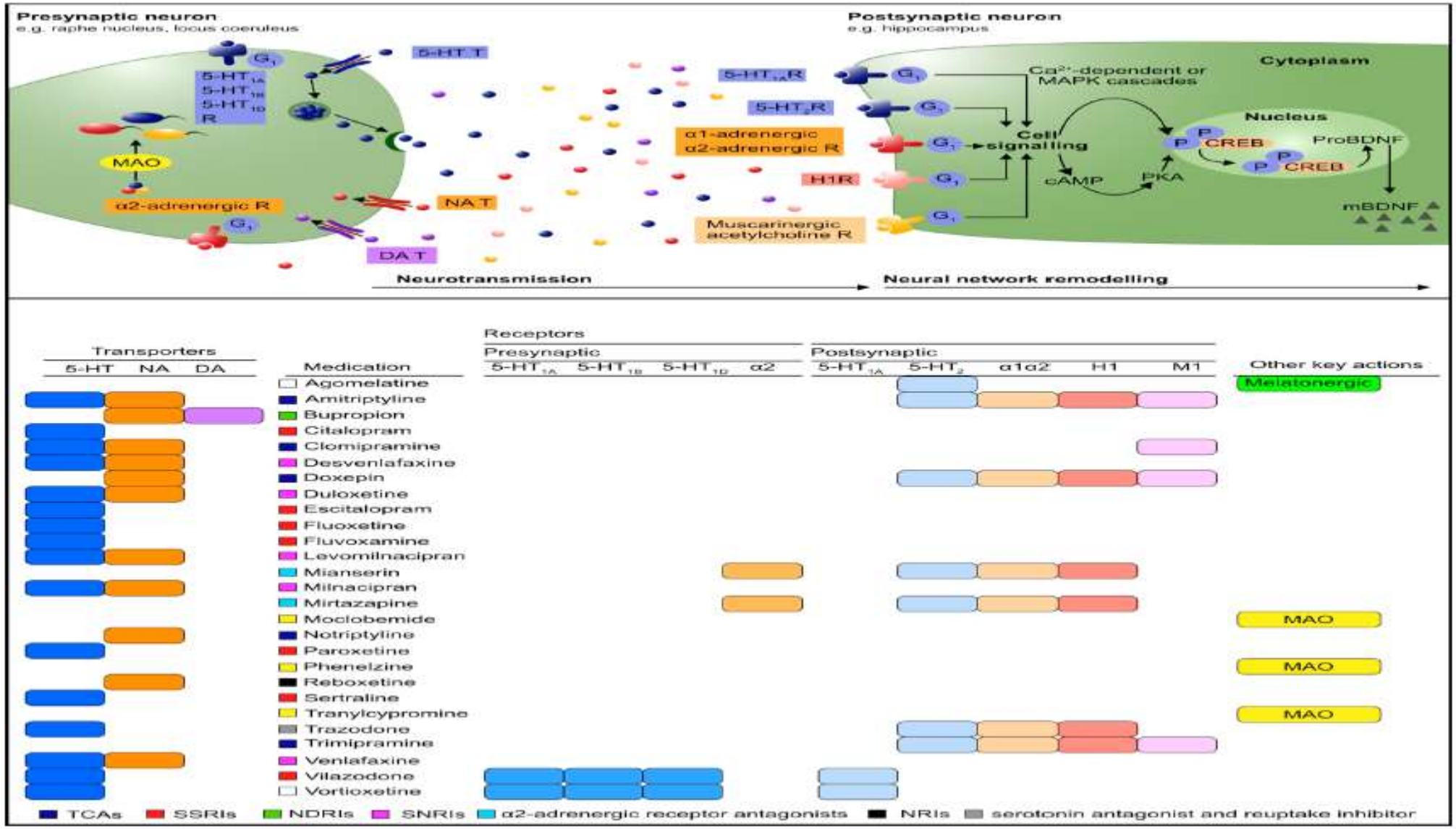
Table 10. Classes of antidepressants.

CLASS	ANTIDEPRESSANTS
Selective serotonin reuptake inhibitors (SSRIs)	Escitalopram, citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline
Serotonin-noradrenaline reuptake inhibitors (SNRIs)	Venlafaxine, duloxetine, desvenlafaxine, levomilnacipran, milnacipran
Selective noradrenergic reuptake inhibitors (NRIs)	Reboxetine, atomoxetine, teniloxazine
Noradrenaline-dopamine reuptake inhibitor (NDRI)	Bupropion[c]
Noradrenergic and specific serotonergic antagonist (NASSA)	Mirtazapine[c], mianserin[c]
Serotonin partial agonist and serotonin reuptake inhibitor (SPARI)	Vilazodone
Serotonin receptor antagonist and serotonin reuptake inhibitor (SARI)	Vortioxetine,[a] nefazodone, trazodone
Serotonin-noradrenaline reuptake inhibitor and serotonin receptor antagonist (SNRISA)	Amoxapine[c]
Noradrenaline reuptake inhibitor with serotonin receptor antagonism (NRISA)	Maprotiline[c]
Tricyclic antidepressants (TCAs)	Amitriptyline, clomipramine, dosulepin, doxepin, imipramine, nortriptyline
Monoamine oxidase inhibitor (MAOIs)	Moclobemide,[b] phenelzine, tranylcypromine
NMDA-glutaminergic receptor blockers	Esketamine, ketamine
Melatonergic agonist and selective serotonergic antagonism	Agomelatine
Atypical antipsychotics with potent $5HT_{2A/2C}$ receptor blockade	Aripiprazole, brexpiprazole, lurasidone, quetiapine, olanzapine, risperidone
Neurosteroid progesterone analogue and gamma aminobutyric acid (GABA) receptor modulator	Brexanolone

[a]Also referred to as a serotonin modulator.
[b]Reversible.
[c]Bupropion is unicyclic; mirtazapine, mianserin, maprotiline and amoxapine are tetracyclic.

Malhi G et al, 2020

Figure 22. Antidepressant mechanisms (adapted from Malhi and Mann, 2018).

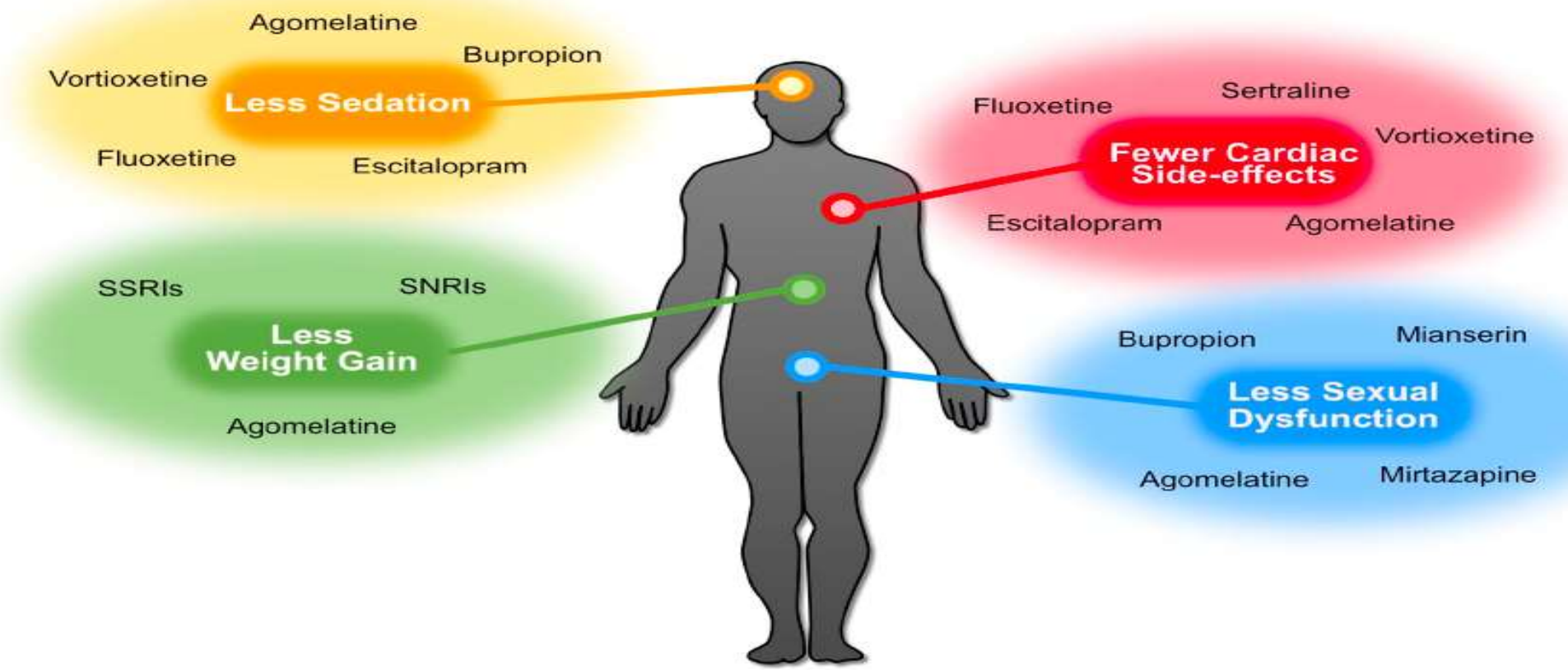


Malhi G et al, 2020

The key actions of all antidepressants involve presynaptic and postsynaptic receptors and neurotransmitter transporters within monoaminergic neurotransmitter systems (e.g. serotonin, noradrenaline and dopamine). Broadly speaking, antidepressants are thought to increase the concentration of monoamines within the synapse and thereby ultimately facilitate downstream neurotransmission. The precise mechanisms of action are complicated by the fact that pre- and post- synaptic receptors can have facilitatory and inhibitory actions and there is significant crosstalk between neurotransmitter systems. This is important to bear in mind since the 'site of action' refers principally to initial receptor/transporter binding and it is possible that in many instances, the downstream effects of many antidepressants converge. Figure 22 shows the detailed intracellular changes that are thought to occur upon signal transduction and secondary cell signalling within the postsynaptic neuron. This eventually leads to changes in transcription processes within the nucleus that are necessary to develop new enzymes and proteins. It is now thought that the antidepressant effect of most medications acting through these pathways eventuates because of remodelling of neural networks within key regions of the brain and that antidepressants facilitate this through neurogenesis. One region where this likely occurs within the brain is the hippocampus.
5-HT: serotonin; R: receptor; T: transporter; NA: noradrenaline; HI: histamine; DA: dopamine; MAO: monoamine oxidase; mBDNF: mature brain-derived neurotrophic factor; TCAs: tricyclic antidepressants; NDRIs: noradrenaline dopamine reuptake inhibitors; SSRIs: selective serotonin reuptake inhibitors; SNRIs: serotonin-noradrenaline reuptake inhibitors.

Figure 23. Antidepressant side effects.

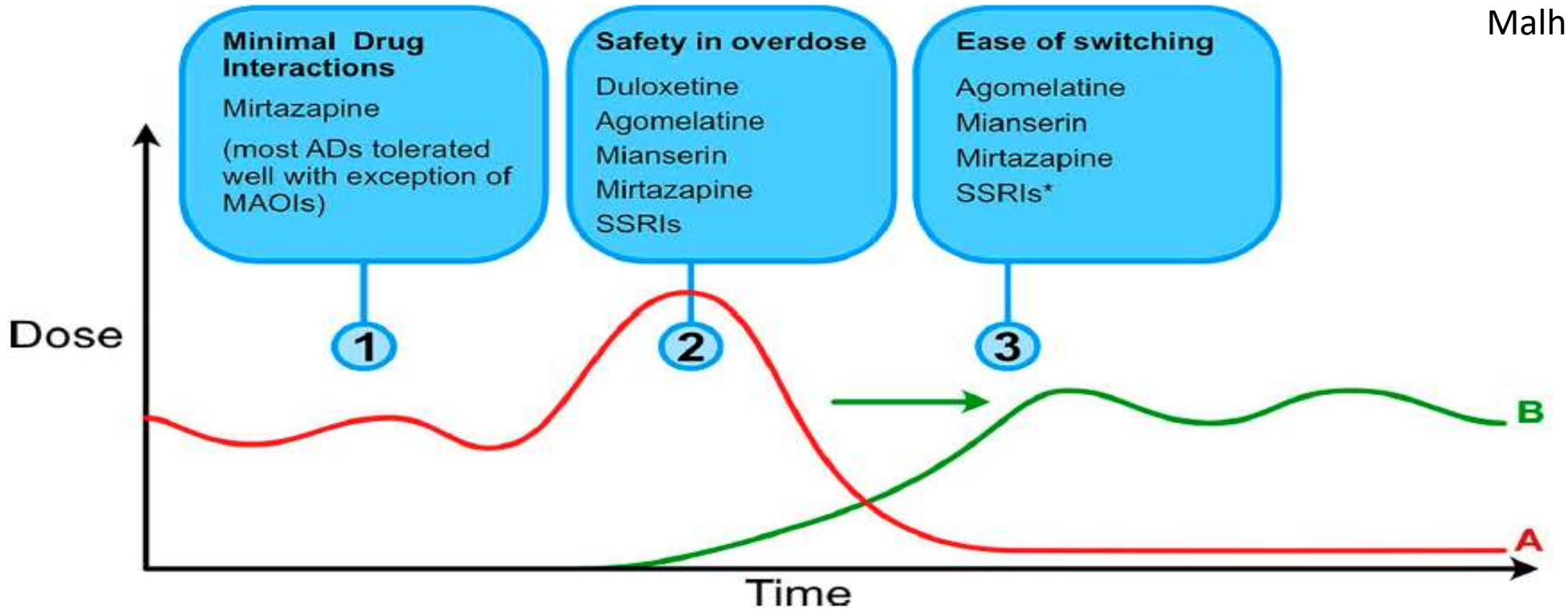
Malhi G et al, 2020



Treatment with antidepressant medication is potentially associated with many side effects. Fortunately, the majority of these are mild and transient, but in some instances, side effects can be severe and debilitating. In practice, the key problem with respect to poor antidepressant tolerability is that patients are unlikely to complete a course of antidepressant treatment if they are experiencing significant side effects. The figure shows four groups of common side effects that can limit the use of antidepressants and, alongside each side-effect, the antidepressants least likely to cause these problems are shown in no particular order. It is important to note that these side effects *can* occur with these agents, but are less likely to occur as compared to other antidepressants.

Figure 24. Properties of antidepressants.

Malhi G et al, 2020



The schematic shows a number of key issues that are important to consider to ensure safe prescribing and minimise important adverse effects. (1) Some patients may already be on medications or will require additional medications, and therefore drug interactions need to be taken into account, the agents listed (see 1) have minimal drug interactions. (2) Patients with depression have a risk of suicide, especially early in treatment. The antidepressants shown are relatively safer[a] if taken in overdose (see 2). (3) When initiating an antidepressant, it may be necessary to switch to a different agent (drug A to drug B) because the initial agent lacks efficacy. Therefore, choosing a medication that is easy to switch from is an important consideration.
*Note: paroxetine (a SSRI) has significant withdrawal symptoms and fluoxetine has a long half-life.
[a]Note: relatively safer in comparison to older antidepressants such as tricyclic antidepressants (TCAs).

Malhi G et al, 2020

Table 11. Supplements in depression.

Supplement	Comments	Level
Methylfolate	Methylfolate supplements are valuable in managing depression when specific polymorphisms of MTHFR gene are present.	II
Omega-3 fatty acids	EPA rich (>60%) omega-3 fatty acid supplements may be helpful in managing depression, but quality and EPA composition of supplements is an impediment.	II
Hypericum perforatum	*Hypericum perforatum* (St John's Wort) does appear to be helpful in some patients with depressive disorders but there are risks with some medication combinations; mania may be precipitated, and the dose is difficult to define. SSRI pharmaceutical agents are recommended instead.	III
S-adenosylmethionine	There is insufficient evidence to recommend the use of S-adenosylmethionine (SAM-e) in the management of depression.	IV
Cannabidiol	There is insufficient evidence to recommend the use of cannabinoids in the management of mood disorders.	IV

MTHFR: methylene tetrahydrofolate reductase gene; EPA: eicosapentaenoic acid; SSRI: selective serotonin reuptake inhibitor.

Malhi G et al, 2020

Table 12. Indications for ECT in mood disorders.

First-line treatment	*Severe melancholic depression*, especially when the patient may not want to eat or drink because of depression. *Imminent risk of suicide* *Severe levels of distress* *Psychotic depression* *Catatonia* *Previously responded to ECT* *Patient preference* (chooses to have ECT)
Second-line treatment	Patients who *fail to respond to one or more adequate courses of medication*, preferably including a TCA or MAOI if appropriate

ECT: electroconvulsive therapy; TCA: tricyclic antidepressants; MAOI: monoamine oxidase inhibitor.

Malhi G et al, 2020

Recommendation Box 1. Physical treatments		Grade
ECT		
1.1	ECT is a safe and effective treatment for more severe presentations of depression[a] and should be considered first-line for psychotic depression or when an immediate response is necessary.	EBR I
1.2	ECT should not be regarded as a treatment of last resort and its administration should be considered on the basis of individual patient and illness factors.	EBR IV
1.3	Before considering ECT as second line, patients should have failed to respond to adequate trials of psychological interventions and pharmacology *Choices* and *Alternatives* to treat depression.[b]	CBR
1.4	Ultra-brief and brief unilateral ECT are recommended because of reduced cognitive side-effects. Bilateral and bifrontal ECT may be used when unilateral ECT has failed or the depression is life-threatening.	EBR II
1.5	Following a successful course of ECT, maintenance treatment with an antidepressant +/− lithium should be continued for at least 12 – 24 months; medication may need to be combined with maintenance ECT, which should then be carefully monitored to avoid an unnecessarily prolonged course.	EBR II
Repetitive Transcranial Magnetic Stimulation (rTMS)		
1.6	Before considering rTMS, patients should have failed to respond to a reasonable number of adequate trials of pharmacotherapy and psychological treatment *Choices* and adequate trials of *Alternatives* to treat depression[b]	CBR
1.7	Given the modest response and remission rates and effect size of rTMS compared to sham, patient expectations of outcome should be discussed fully as part of the consenting process.	CBR
ECT versus rTMS for MDD		
1.8	For severe depression or psychotic depression, ECT is the preferred treatment	EBR I
1.9	There is insufficient evidence to recommend rTMS to patients who have failed to respond to ECT	CBR

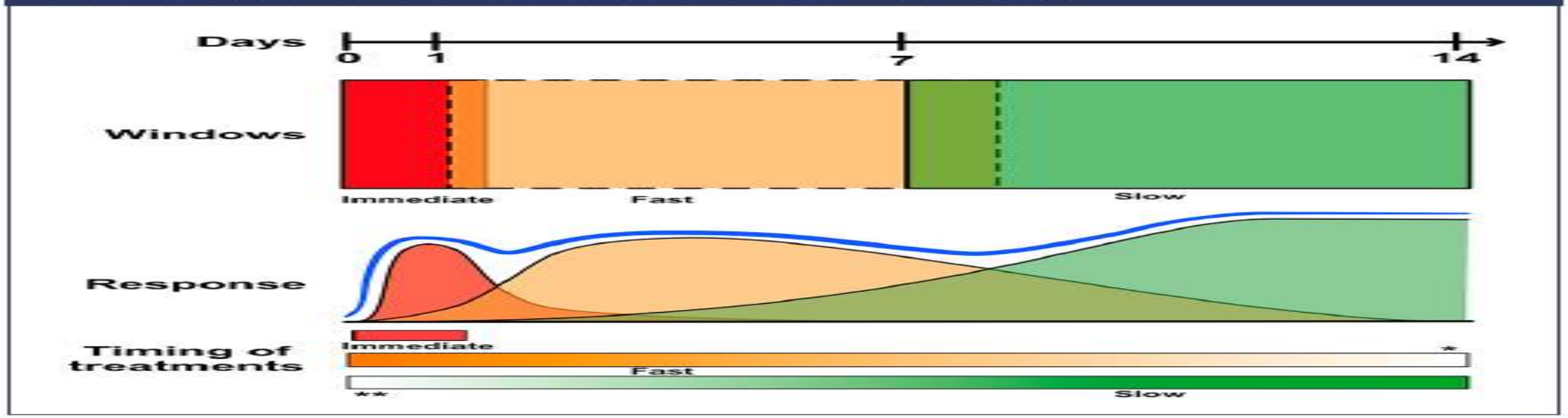
ECT: electroconvulsive therapy; EBR: evidence-based recommendations; CBR: consensus-based recommendations; MDD: major depressive disorder; SSRI: selective serotonin reuptake inhibitor; SNRI: serotonin and noradrenaline reuptake inhibitor; TCA: tricyclic antidepressants; MAOI: monoamine oxidase inhibitor.

[a]Includes major depressive episodes occurring in the context of bipolar disorder. MIDAS: medication, increase dose, augmentation, switch.

[b]Pharmacotherapy *Choices* should ideally include antidepressants from putatively different classes (e.g. SSRIs, SNRIs, TCAs and MAOIs) and, where appropriate, each antidepressant should be suitably optimised through use of therapeutic dosing (e.g. increasing dose) and augmentation. This sequence should be considered for every antidepressant trialled and typically several courses of antidepressants may be necessary to achieve full functional recovery (see section 9, 'Response to treatment').

Malhi G et al, 2020

Figure 25. Windows of antidepressant response paradigm (WARP) (adapted from Malhi et al., 2020c).



This schematic outlines the proposed windows of treatment response: immediate, fast and slow. Agents that produce an immediate response (red) are typically effective within a day or two of commencing treatment but may not have a sustained effect. Agents that produce a fast response (orange) relative to the effects of typical antidepressants provide a bridging response between the immediate and slow response windows. Typical antidepressants invoke a slow response (green), usually taking at least a week to bring about clinical improvement. However, this response is more sustained and more likely to lead to remission of depressive symptoms and functional recovery. By implementing treatments that can be utilised in all three response windows, an overall improvement in response can be achieved (yellow) that is sustained from the beginning of treatment through to when the antidepressant becomes effective. In order to achieve this comprehensive response, all three treatments can be instituted simultaneously. The immediate treatment is administered and concurrently the fast treatment is also commenced to maintain the response achieved during the immediate window, following this it is then gradually reduced (*). At the same time, the antidepressant is also administered from the beginning and is gradually titrated to a therapeutic dose (**) to ensure a sustained response.

Maurer D et al 2018

TABLE 6

DSM-5 Diagnostic Criteria for Major Depressive Disorder

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure. **Note:** Do not include symptoms that are clearly attributable to another medical condition.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (**Note:** In children and adolescents, can be irritable mood.)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (**Note:** In children, consider failure to make expected weight gain.)
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

Note: Criteria A–C represent a major depressive episode.

Note: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual's history and the cultural norms for the expression of distress in the context of loss.

D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

E. There has never been a manic episode or a hypomanic episode. **Note:** This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

DSM = Diagnostic and Statistical Manual of Mental Disorders.

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