090525 Masennuksen hoitoa - MTTP:n kehittämispäivä

Yl juha kemppinen

090525 Masennuksen hoitoa

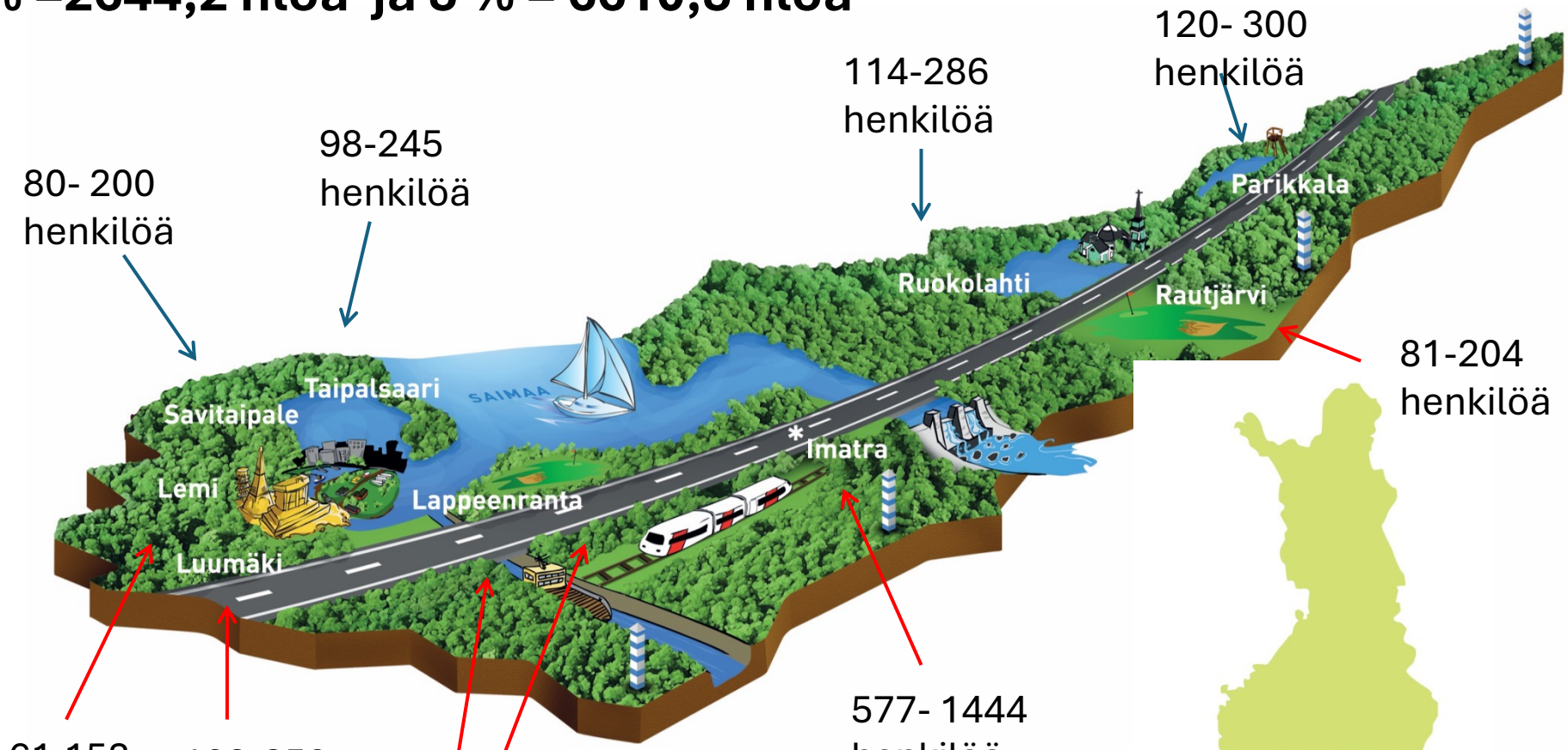
1. Mitä on masennus?
2. Masennuksen hoidon vaiheet
3. Masennuksen hoitoskeema
4. Masennuksen lääkehoito
5. Masennuksen psykoedukaatio
6. Masennuksen hoidon optimointi
7. Masennuksen hoidon räätälöinti
8. Masennuksen psykoterapiat
9. Lopuksi

1. Mitä on masennus?

Yl juha kemppinen

Ekhva kartalla – noin 130 000 ihmistä- Depression pisteprevalenssi 2-5 %

Ekhva 2 % =2644,2 hlöä ja 5 % = 6610,5 hlöä



Etäisyyksiä Lappeenrannasta:
Helsinkiin 220 km
Pietariin 230 km
Venäjän rajalle 35 km

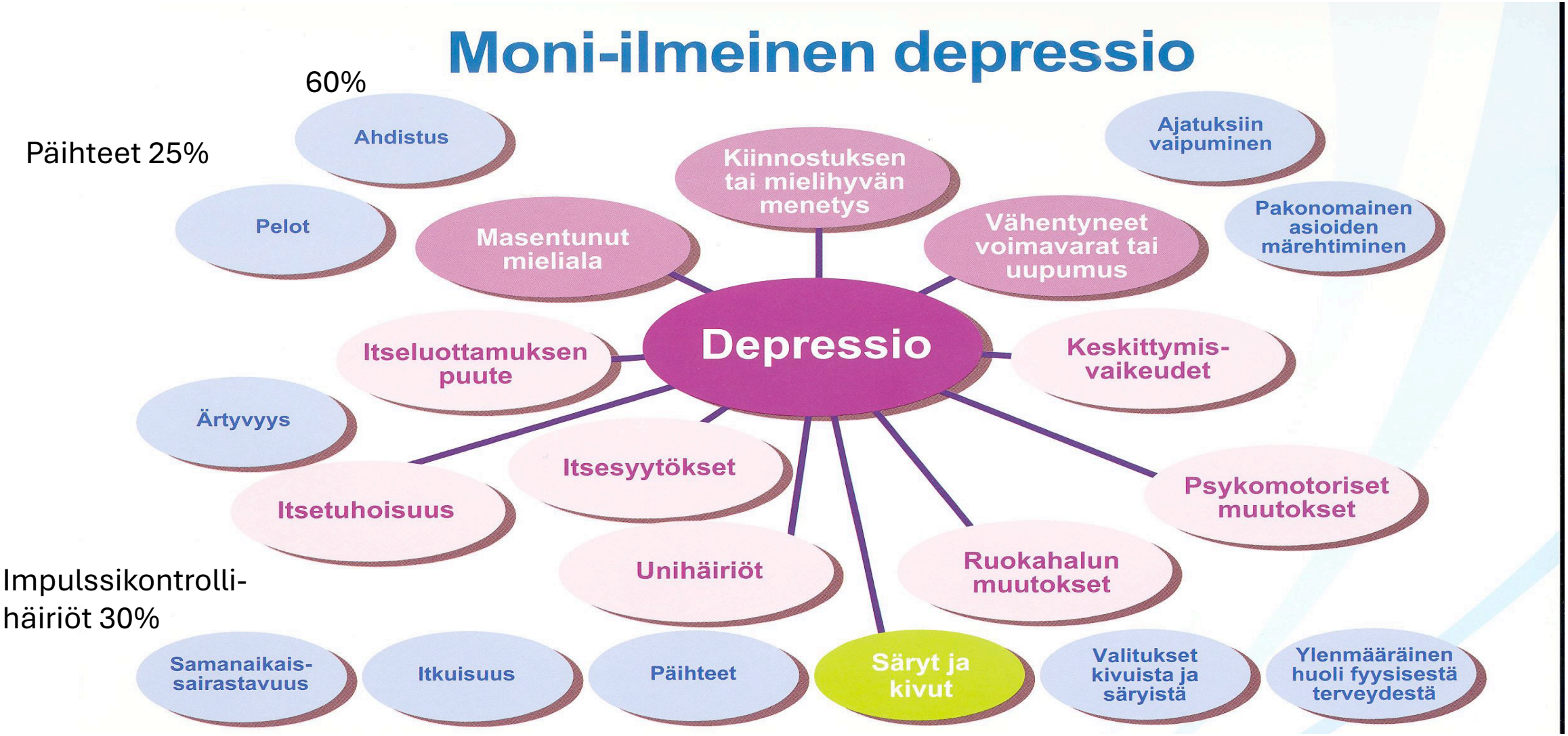
Keskeinen sanoma

- Depressiosta kärsii vuoden aikana noin 5–7 % suomalaisista.
- Depressioiden tunnistaminen ja erotusdiagnostiikka ovat tärkeitä.
- Hoidon suunnittelussa keskeisiä kysymyksiä ovat
  - depression vaikeusasteen arviointi
  - ensimmäistä kertaa elämässä esiintyvän masennustilan (F32) ja toistuvan depression (F33) välinen erottelu
  - monihäiriöisyyden, itsemurhavaaran ja toimintakyvyn arviointi.
- Yksilöllisessä hoitosuunnitelmassa sovitetaan yhteen potilaan tarpeet, käytettävissä olevat vaikuttavaksi osoitetut hoitomuodot sekä mahdolliset muut tukitoimet.
- Depression akuuttihoidossa keskeisimpiä spesifisiä hoitomuotoja ovat
  - vaikuttaviksi osoitetut psykoterapiat
  - masennuslääkkeet.
- Lievissä ja keskivaikeissa depressioissa nämä hoidot ovat yhtä tehokkaita ja niitä voidaan käyttää vaihtoehtoisesti tai yhtäaikaisesti. Yhtäaikainen käyttö on yleensä tehokkainta.

- Vaikeissa ja psykoottisissa depressioissa on aina syytä käyttää depressiolääkehoitoa, psykoottisissa yhdessä psykoosilääkkeen kanssa. Psykoottisessa depressiossa sähköhoito on tehokkain hoitomuoto.
- Spesifisten hoitomuotojen ohella elämäntilanteen tutkiminen ja psykososiaalisen tuen tarjoaminen kuuluvat hoidon keskeisiin tehtäviin.
- Depressiosta toipumisen jälkeen potilaan hoitoa ja seurantaa on depression suuren uusiutumisvaaran vuoksi jatkettava noin puolen vuoden ajan.
- Potilaille, joille on ilmaantunut jo elämänsä kolmas depressiojakso, on suositeltavaa jatkaa tehokkaaksi osoittautunutta masennuslääkehoitoa pitkäaikaisena ylläpitohoitona, jotta uusien sairausjaksojen puhkeaminen estyisi.
- Perusterveydenhuollossa hoito kannattaa toteuttaa depression hoidon yhteistoimintamallilla tai vastaavalla tavalla, jossa toteutuvat
  - yleislääkärin, depressiohoitajan ja psykiatrin yhteistyö
  - hoidon suunnitelmallisuus
  - potilaan seuranta, opastus ja psykososiaalinen tuki.
- Perusterveydenhuollossa tarvitaan psykiatrisia konsultaatioita tukemaan diagnostiikkaa ja hoitoa koskevaa päätöksentekoa.
- Työterveyshuollolla on keskeinen rooli työssäkäyvän depressiopotilaan työkyvyn ylläpitämisessä ja työhön paluun tukemisessa.

- Psykiatrisessa erikoissairaanhoidossa on syytä hoitaa potilaat, jotka kärsivät
  - vaikeasta tai psykoottisesta depressiosta
  - vakavasti monihäiriöisestä depressiosta
  - tavanomaiseen hoitoon huonosti vastanneesta depressiosta tai
  - vakavaa itsetuhoisuutta aiheuttavasta depressiosta.

Masennus on moni-ilmeinen oireyhtymä



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

TABLE 5. Major Depression

Keskittymisongelmat, päätöksenteon ja ongelmien ratkaisun vaikeus

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

Avuttomuus, toivottomuus, Arvottomuus

Syyllisyyden tunteet

Kuoleman ajattelu, Itsensä vahingoittaminen

Harhaluuloja?

Menneisyyden kaivelu

Sekavuus

Näkö- ja liikkumisongelmat

Vetäytyy, eristäytyy

Toimintakyky laskee

Aktiviteetti vähenee

Apaattinen, hidastunut, aktiviteetit vähenevät

Syöminen ja uni vähenee tai lisääntyy

Levottomuus ja rauhattomuus lisääntyy

Äkseeraus lisääntyy

Morrison, 1995

Diagnostiset kriteerit:

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025

DSM-5-TR diagnostic criteria for a major depressive episode

A. Five (or more) of the following symptoms have been present during the same two-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 (eg, feels sad, empty, hopeless) or observations made by others (eg, 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 (eg, 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 their 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 direct physiological effects of a substance or to another medical condition.

Masennuksen seulat: MDQ (bipolaaritaudin seulonta)

(Saman ajanjakson aikana, ei elämän aikana)

Päivämäärä ___ ___ / ___ ___ / 20___

Nimi_____

Henkilötunnus_____--_____

Mieialahäiriökysely MDQ

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

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 kilsivät 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 yllaolevista, tapahtuiko useampi näistä asioista saman ajanjakson aikana? *Olkaa hyvä ja vastatkaa joko kyllä tai ei.*

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

	Kyllä	Ei
	☐	☐
	☐	☐
	☐	☐
	☐	☐
	☐	☐
	☐	☐
	☐	☐
	☐	☐
	☐	☐
	☐	☐
	☐	☐
	☐	☐
	☐	☐
	☐	☐

1 Ei ongelmia
2 Vähäisiä
3 Kohtalaisia
4 Vakavia

Seula +: ei dg!

- **7/13 oiretta**
- **Kohtalaisia tai vakavia**

Psykiatriset masennusdiagnoosit: uni- vai bipolar?

Addressing Clinical Diagnostic Challenges in Bipolar Disorders

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.

Nukkuu
Syö
Hidas
mm. hylätty
Patologinen syyllisyys
Mielialan vaihtelu

Unettomuus
Ei maistu ruoka
Levoton, rauhaton

Ruumiillisia valituksia

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

Psykiatriset masennusdiagnoosit: uni- vai bipolar?

Mielialalääkkeiden ja placebon teho

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

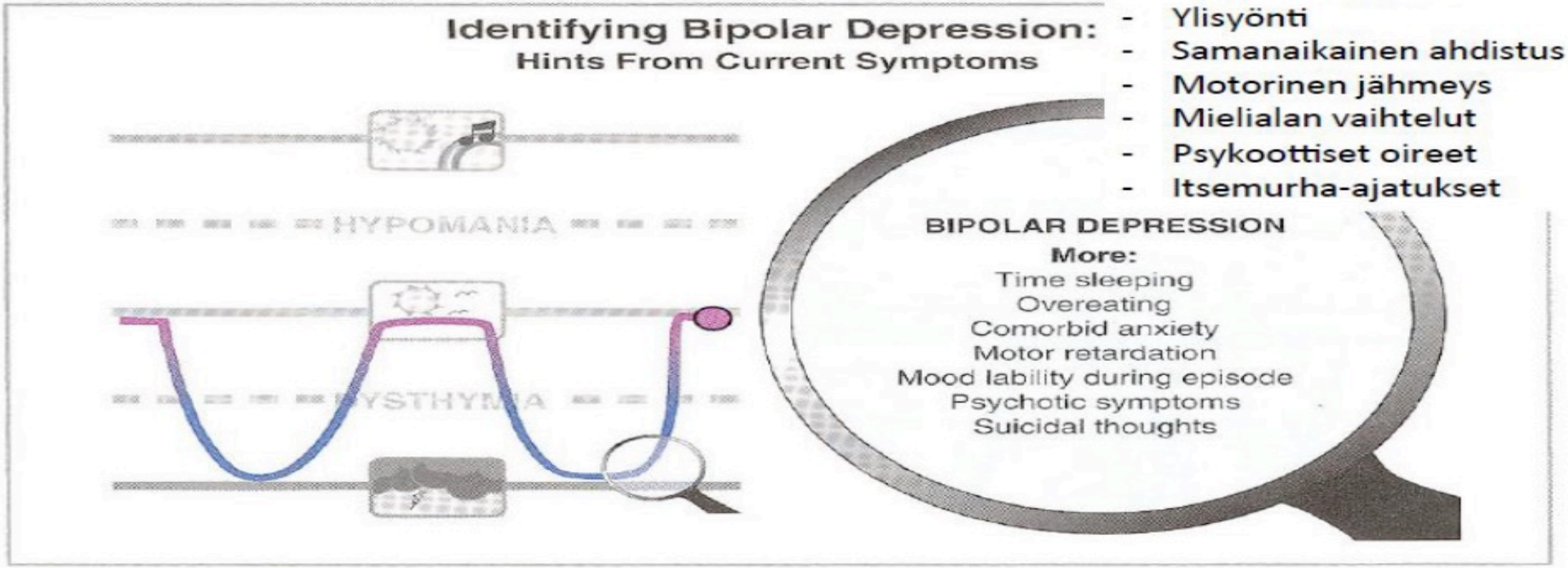


FIGURE 11-25 Bipolar depression symptoms. Although all symptoms of a major depressive episode can occur in either unipolar or bipolar depression, some symptoms may present more often in bipolar versus unipolar depression, providing hints if not diagnostic certainty that the patient has a bipolar spectrum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

S. Stahl, 2004

Diagnostiset kriteerit:

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025

NOTE: Responses to a significant loss (eg, 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 judgement 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 or 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.
Specify:
With anxious distress
With mixed features
With melancholic features
With atypical features
With psychotic features
With catatonia
With peripartum onset
With seasonal pattern

Epätyypillinen masennus

Reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, (Copyright © 2013). American Psychiatric Association. All Rights Reserved. Note: These diagnostic criteria remain unchanged in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision, American Psychiatric Association 2022.

Epätyypillinen masennus:

Tolmunen T Epätyypillinen masennustila - vakavan masennuksen salakavala muoto
Lääketieteellinen Aikakauskirja Duodecim 2002;118(9):889-895

Taulukko A. DSM-IV:n kriteerit depression epätyypillisille piirteille.

A. Mielialan reaktiivisuus (esim. jokin positiivinen tapahtuma tai sellaisen mahdollisuus parantaa mielialaa)

B. Vähintään kaksi seuraavista piirteistä: (1) merkittävä painon nousu tai ruokahalun lisääntyminen (2) liikaunisuus (3) lyijymäinen halvaus (lyijynraskauden tuntemukset käsissä tai jaloissa) (4) pitkään ilmennyt taipumus tuntea itsensä hylätyksi ihmissuhteissa (ei rajoitu mielialahäiriöjaksoihin), mistä aiheutuu merkittävää sosiaalista tai ammatillista haittaa

C. Melankolisten tai katatonisten piirteiden kriteerit eivät täyty saman jakson aikana

Taulukko B. DSM-IV:n kriteerit depression melankolisille piirteille.

A. Toinen seuraavista piirteistä ilmenee nykyisen jakson vakavimmassa vaiheessa: (1) mielihyvän menettäminen kaikissa tai lähes kaikissa toiminnoissa (2) reagointi miellyttäviin asioihin puuttuu (iloisilla tapahtumilla ei ole juuri vaikutusta mielialaan edes tilapäisesti.

B. Vähintään kolme seuraavista: (1) masentuneisuuden erityislaatu (erilainen, kuin esim. läheisen ihmisen kuoleman jälkeen) (2) masennus on säännöllisesti pahempi aamuisin (3) herääminen varhain (vähintään 2 tuntia ennen normaalia aikaa) (4) merkittävä psykomotorinen hitaus tai levottomuus (5) merkittävä painon lasku tai anoreksia (6) liiallinen tai suhteeton syyllisyydentunne

Aiemmin on käytetty rinnakkain nimityksiä "ahdistunut depressio" ja epätyypillinen masennustila. Nykyään ahdistuneella depressiolla tarkoitetaan kirjallisuudessa yleensä depressiota, johon liittyy ahdistuneisuutta, foobisuutta tai paniikkioireistoa. Ahdistunut depressio ja epätyypillinen masennustila reagoivat molemmat hyvin MAO:n estäjiin ja serotoniinilääkkeisiin (SSRI). Ilmeisesti ne ovat osittain päällekkäisiä diagnooseja (Sotsky ja Simmens 1999).

Erilaisia masennusmuotoja

Table 4. *DSM-5* Episode Specifiers and Other Clinical Dimensions Associated with MDE.

Subtype/ Dimension	*DSM-5* Specifier	Key Features
Melancholic depression	With melancholic features	Nonreactive mood, anhedonia, weight loss, guilt, psychomotor retardation or agitation, morning worsening of mood, early morning awakening, excessive or inappropriate guilt
Atypical depression	With atypical features	Reactive mood, oversleeping, overeating, leaden paralysis, interpersonal rejection sensitivity
Psychotic (delusional) depression	With psychotic features	Hallucinations or delusions
Catatonic depression	With catatonic features	Catalepsy (waxy flexibility), catatonic excitement, negativism or mutism, mannerisms or stereotypes, echolalia or echopraxia (uncommon in clinical practice)
Anxious depression	With anxious distress	Feeling keyed up or tense, restless, worried, something awful may happen, or afraid of losing control
Mixed states	With mixed features	Elevated mood, inflated self-esteem or grandiosity, more talkative, racing thoughts, increased energy and activity, decreased need for sleep, risky and impulsive activities
Seasonal affective disorder	Seasonal pattern	Regular onset and remission of depressive episodes during a particular season (usually fall/winter onset)
Postpartum and antepartum depression	With peripartum onset	Onset of depressive episode during pregnancy or within 4 weeks postpartum
Cognitive dysfunction	NA	Disturbances in attention, memory, processing speed, executive functioning and emotional processing
Sleep disturbance	NA	Insomnia or hypersomnia; circadian rhythm disturbance
Somatic symptoms	NA	Headaches, body aches, fatigue, anergia

DSM-5, *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*; MDE, major depressive episode; NA, not applicable.

Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder

Mania dg-kriteerit:

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025

DSM-5-TR diagnostic criteria for manic episode

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least one week and present most of the day, nearly every day (or any duration if hospitalization is necessary).

B. During the period of mood disturbance and increased energy or activity, three (or more) of the following symptoms (four if the mood is only irritable) are present to a significant degree and represent a noticeable change from usual behavior:

1. Inflated self-esteem or grandiosity.
2. Decreased need for sleep (eg, feels rested after only three hours of sleep).
3. More talkative than usual or pressure to keep talking.
4. Flight of ideas or subjective experience that thoughts are racing.
5. Distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.
6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation (ie, purposeless non-goal-directed activity).
7. Excessive involvement in activities that have a high potential for painful consequences (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

C. The mood disturbance is sufficiently severe to cause marked impairment in social or occupational functioning or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

D. The episode is not attributable to the physiological effects of a substance (eg, a drug of abuse, a medication, other treatment) or to another medical condition.

NOTE: A full manic episode that emerges during antidepressant treatment (eg, medication, electroconvulsive therapy) but persists at a fully syndromal level beyond the physiological effect of that treatment is sufficient evidence for a manic episode and, therefore, a bipolar I diagnosis.

NOTE: Criteria A through D constitute a manic episode. At least one lifetime manic episode is required for the diagnosis of bipolar I disorder.

Hypomania dg-kriteerit:

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025

DSM-5-TR diagnostic criteria for hypomanic episode

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least four consecutive days and present most of the day, nearly every day.

B. During the period of mood disturbance and increased energy and activity, three (or more) of the following symptoms (four if the mood is only irritable) have persisted, represent a noticeable change from usual behavior, and have been present to a significant degree:

1. Inflated self-esteem or grandiosity.
2. Decreased need for sleep (eg, feels rested after only three hours of sleep).
3. More talkative than usual or pressure to keep talking.
4. Flight of ideas or subjective experience that thoughts are racing.
5. Distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.
6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation.
7. Excessive involvement in activities that have a high potential for painful consequences (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the individual when not symptomatic.

D. The disturbance in mood and the change in functioning are observable by others.

E. The episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalization. If there are psychotic features, the episode is, by definition, manic.

F. The episode is not attributable to the physiological effects of a substance (eg, a drug of abuse, a medication, or other treatment).

NOTE: A full hypomanic episode that emerges during antidepressant treatment (eg, medication, electroconvulsive therapy) but persists at a fully syndromal level beyond the physiological effect of that treatment is sufficient evidence for a hypomanic episode diagnosis. However, caution is indicated so that one or two symptoms (particularly increased irritability, edginess, or agitation following antidepressant use) are not taken as sufficient for a diagnosis of a hypomanic episode, nor necessarily indicative of a bipolar diathesis.

NOTE: Criteria A through F constitute a hypomanic episode. Hypomanic episodes are common in bipolar I disorder but are not required for the diagnosis of bipolar I disorder.

Depression toimintakyvyn mittari

Taulukko 8. SOFAS-asteikko

Koodi[1]	Merkitys
91–100	Erinomainen toimintakyky useilla elämänalueilla
81–90	Hyvä toimintakyky kaikilla elämänalueilla; henkilö ammatillisesti ja sosiaalisesti tehokas
71–80	Vain vähäistä heikentymistä sosiaalisessa, ammatillisessa tai opiskelun edellyttämässä toimintakyvyssä (esim. harvinainen ihmissuhderistiriita tai tilapäinen jälkeen jääminen koulutyössä)
61–70	Lieviä vaikeuksia sosiaalisessa, ammatillisessa tai opiskelun edellyttämässä toimintakyvyssä mutta yleisesti hyvä toimintakyky ja joitakin mielekkäitä ihmissuhteita
51–60	Kohtalaisia vaikeuksia sosiaalisessa, ammatillisessa tai opiskelun edellyttämässä toimintakyvyssä (esim. vain vähän ystäviä tai ristiriitoja ikä- tai työtovereiden kanssa)
41–50	Vakavaa heikentymistä sosiaalisessa, ammatillisessa tai opiskelun edellyttämässä toimintakyvyssä (esim. ystävien puuttuminen tai kyvyttömyys säilyttää työpaikkaa)
31–40	Merkittävää heikentymistä useilla elämänalueilla, kuten työssä, koulussa tai perhesuhteissa (esim. masentunut mies, joka välttelee ystäviään, laiminlyö perhettään eikä pysty työhön, tai lapsi, joka pahoinpitelee usein nuorempiaan, on uhmakas kotona eikä menesty koulussa)
21–30	Toimintakyvyttömyys lähes kaikilla elämänalueilla (esim. pysytteleminen vuoteessa koko päivän, työttömyys ja kodittomuus)
11–20	Ajoittainen henkilökohtaisen hygienian vähimmäistason laiminlyöminen, kyvyttömyys toimia itsenäisti
1–10	Jatkuva henkilökohtaisen hygienian vähimmäistason laiminlyöminen; kyvyttömyys toimia vahingoittamatta itseään tai muita tai ilman huomattavaa ulkopuolista tukea (esim. hoitoa tai valvontaa)
0	Riittämättömät tiedot

[1] Käytä mahdollisuuksien mukaan tarkkoja lukuja, esimerkiksi 45, 68 tai 72. Tarkastele sosiaalista ja ammatillista toimintakykyä jatkumolla erinomaisesta toimintakyvystä huomattavasti heikentyneeseen toimintakykyyn. Ota huomioon toimintakyvyn heikentymät, jotka johtuvat fyysisistä tai henkisistä rajoitteista. Vain suoraan henkisistä tai fyysisistä terveysongelmista johtuvat rajoitteet tulee ottaa huomioon. Mahdollisuuksien puutteen ja muiden ympäristöseikkojen aiheuttamia rajoituksia ei oteta huomioon.

Koodi[1]	Merkitys
91–100	Erinomainen toimintakyky useilla elämänalueilla
81–90	Hyvä toimintakyky kaikilla elämänalueilla; henkilö ammatillisesti ja sosiaalisesti tehokas
71–80	Vain vähäistä heikentymistä sosiaalisessa, ammatillisessa tai opiskelun edellyttämässä toimintakyvyssä (esim. harvinainen ihmissuhderistiriita tai tilapäinen jälkeen jääminen koulutyössä)
61–70	Lieviä vaikeuksia sosiaalisessa, ammatillisessa tai opiskelun edellyttämässä toimintakyvyssä mutta yleisesti hyvä toimintakyky ja joitakin mielekkäitä ihmissuhteita
51–60	Kohtalaisia vaikeuksia sosiaalisessa, ammatillisessa tai opiskelun edellyttämässä toimintakyvyssä (esim. vain vähän ystäviä tai ristiriitoja ikä- tai työtovereiden kanssa)

Taulukko 8. SOFAS-asteikko

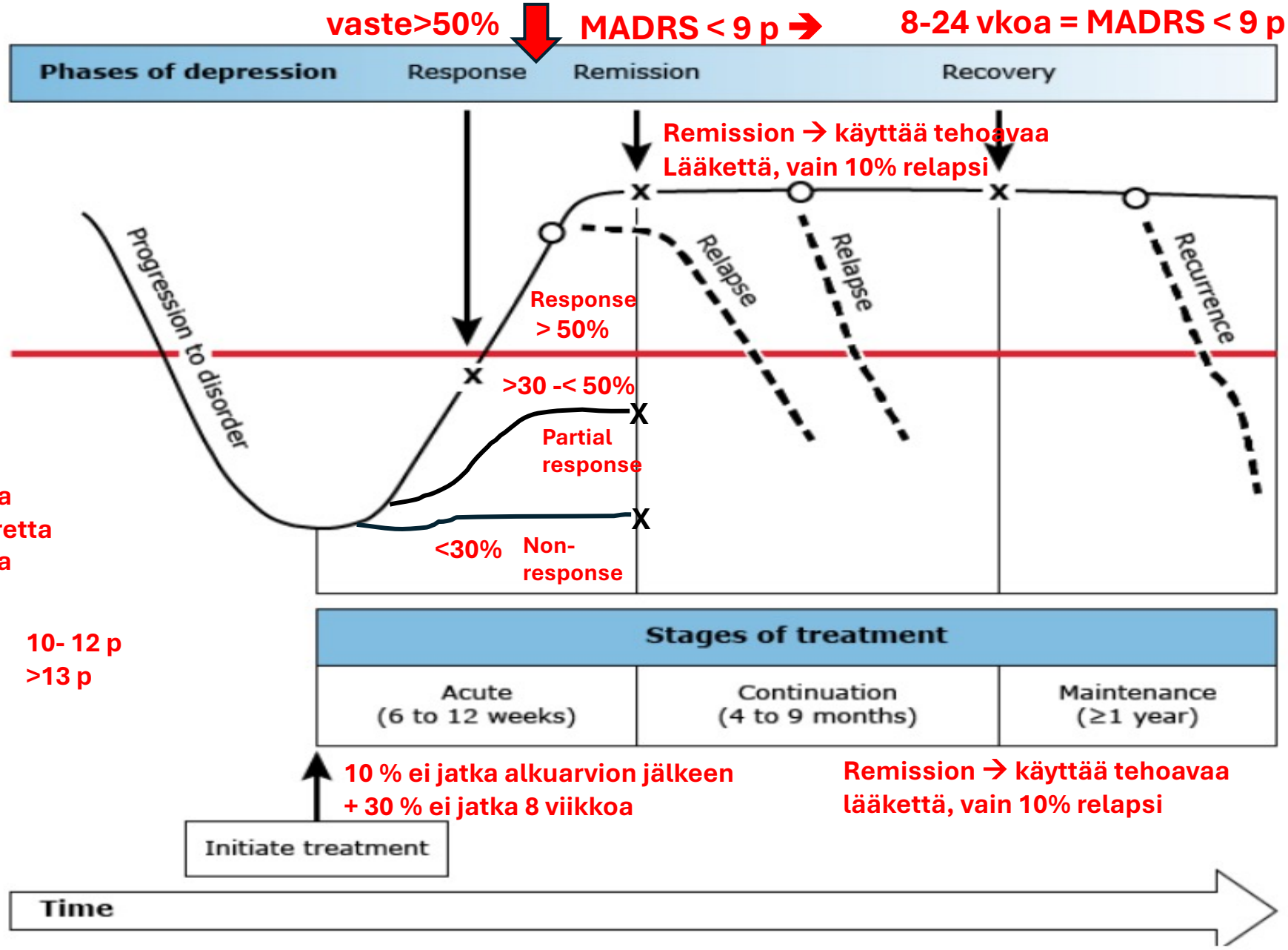
Koodi[1]	Merkitys
31–40	Merkittävää heikentymistä useilla elämänalueilla, kuten työssä, koulussa tai perhesuhteissa (esim. masentunut mies, joka välttelee ystäviään, laiminlyö perhettään eikä pysty työhön, tai lapsi, joka pahoinpitelee usein nuorempiaan, on uhmakas kotona eikä menesty koulussa)
21–30	Toimintakyvyttömyys lähes kaikilla elämänalueilla (esim. pysytteleminen vuoteessa koko päivän, työttömyys ja kodittomuus)
11–20	Ajoittainen henkilökohtaisen hygienian vähimmäistason laiminlyöminen, kyvyttömyys toimia itsenäisti
1–10	Jatkuva henkilökohtaisen hygienian vähimmäistason laiminlyöminen; kyvyttömyys toimia vahingoittamatta itseään tai muita tai ilman huomattavaa ulkopuolista tukea (esim. hoitoa tai valvontaa)
0	Riittämättömät tiedot

[1] Käytä mahdollisuuksien mukaan tarkkoja lukuja, esimerkiksi 45, 68 tai 72. Tarkastele sosiaalista ja ammatillista toimintakykyä jatkumolla erinomaisesta toimintakyvystä huomattavasti heikentyneeseen toimintakykyyn. Ota huomioon toimintakyvyn heikentymät, jotka johtuvat fyysisistä tai henkisistä rajoitteista. Vain suoraan henkisistä tai fyysisistä terveysongelmista johtuvat rajoitteet tulee ottaa huomioon. Mahdollisuuksien puutteen ja muiden ympäristöseikkojen aiheuttamia rajoituksia ei oteta huomioon.

2. Masennuksen hoidon vaiheet

Yl juha kemppinen

vaste>50% MADRS < 9 p → 8-24 vkoa = MADRS < 9 p



PHQ-9:
Lievä 5-9 p + >5 oiretta
Keskivaikea 10-19 p + >5 oiretta
Vaikea >20 p+ >5 oiretta

EPDS:
Lievä 10- 12 p
Vaikea >13 p

GDS-15:
Lievä <10 p
Keskivaikea 11-20 p
Vaikea 21-30 p

MADRS:
Normaali 0-7 p
Oireita 8-14 p
Lievä 15-24 p
Keskivaikea 25-30 p
Vaikea 31-43 p
Erittäin v >44p

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025

- **Phases of depression** – Trials of interventions to treat depression often use specific depression rating scales to rate symptom severity and describe clinical outcomes. The following commonly used terms delineate phases of treatment (figure 1) [7]. Although these definitions are useful for conceptualizing the illness course of depression and evaluating treatment interventions, they are not standardized. In clinical practice, the terms "relapse" and "recurrence" are often used interchangeably, as are "remission" and "recovery."

  - **Response** – Response is the reduction of depression symptoms by a clinically meaningful, specified amount. Response is usually defined as an improvement in symptom score of ≥50 percent that is still above the threshold for remission [8,9].

    - **Partial response** – Partial response is defined as an improvement in symptom score of >30 but <50 percent. However, definitions used in individual studies differ [8,9].

    - **Nonresponse (no meaningful benefit)** – A nonresponse to depression treatment is usually defined as a change in symptom score of ≤30 percent.

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025

- **Remission** – Remission is the stable reduction of symptoms below the threshold (or specific cut-off) for diagnosis. Studies using the nine-item Patient Health Questionnaire (PHQ-9) often define remission as a score of <5 (table 3). The Montgomery-Asberg Depression Rating Scale (figure 2A-C) often defines remission as a score <9.

- **Recovery** – Recovery occurs when symptom remission has been sustained for 8 to 24 weeks [10-14].

- **Relapse** – Relapse is the return of depressive symptoms prior to the time of recovery.

- **Recurrence** – Recurrence is the onset of a new episode of major depression after recovery from a prior episode.

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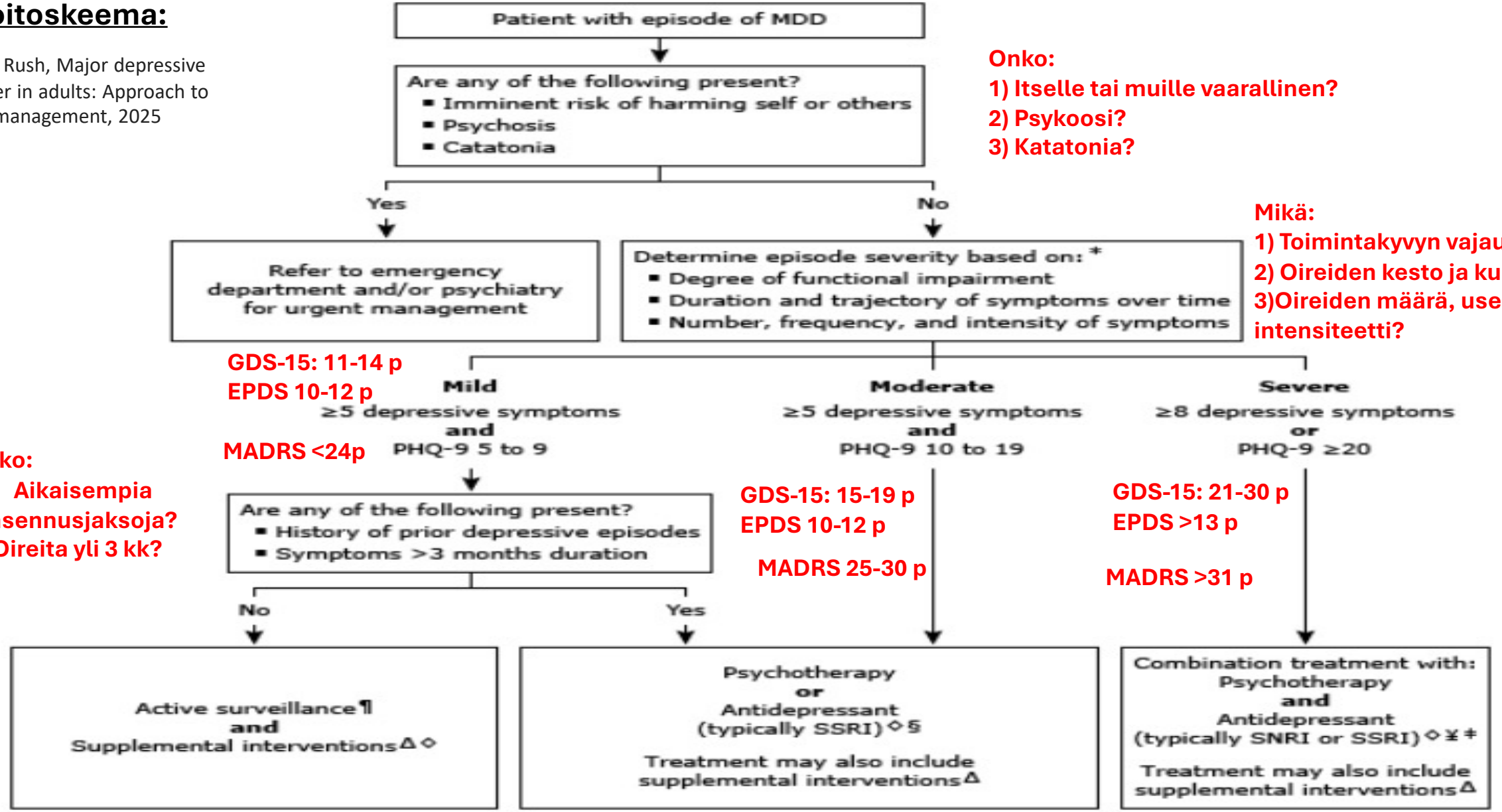
3. Masennuksen hoitoskeema

Yl juha kemppinen

Hoitoskeema:

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025



Onko:
1) Itselle tai muille vaarallinen?
2) Psykoosi?
3) Katatonia?

Mikä:
1) Toimintakyvyn vajaus?
2) Oireiden kesto ja kulku??
3)Oireiden määrä, useus ja intensiteetti?

GDS-15: 11-14 p
EPDS 10-12 p
MADRS <24p

Onko:
1) Aikaisempia masennusjaksoja?
2) Oireita yli 3 kk?

GDS-15: 15-19 p
EPDS 10-12 p
MADRS 25-30 p

GDS-15: 21-30 p
EPDS >13 p
MADRS >31 p

Seuraa aktiivisesti ja tarvittaessa lisäinterventio

Psykoterapia ja/tai lääkitys sekä tarvittaessa lisäinterventio

Psykoterapia ja lääkitys sekä tarvittaessa lisäinterventio

Hoitoskeema: (jatkuu)

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025

This algorithm outlines an approach to the initial management of MDD. It should be used in conjunction with UpToDate content on the diagnosis and initial management of MDD.

When assessing the level of depression severity to determine treatment selection, clinicians should consider degree of functional impairment and the duration, trajectory, and intensity of symptoms as well as the number of depressive symptoms and/or PHQ-9 score.

For details on depressive symptoms, use of the PHQ-9, and how to determine symptom severity, please refer to related UpToDate content.

MDD: major depressive disorder; PHQ-9: 9-item Patient Health Questionnaire; SNRI: serotonin-norepinephrine reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor.

* The number and frequency of symptoms is a starting point for assessing episode severity. The level of functional impairment and symptom duration and trajectory may further modulate the assessment of severity.

¶ Patients who opt for active surveillance require close follow-up (eg, 2 to 4 weeks) to monitor for symptom progression.

Δ "Supplemental interventions" refer to interventions that can be added as adjuncts to active surveillance, antidepressants, psychotherapy, or combination treatment. These include exercise (recommended for all patients), internet-based psychotherapy, self-help interventions (support groups, smartphone applications), mind-body interventions (yoga, tai chi), and bright light therapy.

◇ At a given level of symptom severity, the following factors influence the selection of a treatment regimen: patient preferences, prior treatment experiences, history of prior episodes of depression, ability to engage in multiple treatments simultaneously (ie, when considering combination treatment or supplemental interventions), and availability and affordability of psychotherapy.

§ SSRIs, such as escitalopram or sertraline, are generally preferred medications for treating mild to moderate MDD. Refer to UpToDate topics on initial treatment with antidepressants for MDD in adults.

¥ To improve treatment feasibility and adherence, combination treatment can be administered sequentially (ie, start treatment 1, then start treatment 2 within 8 weeks). Refer to UpToDate topics on initial treatment with antidepressants for MDD in adults.

‡ We suggest SNRIs, such as venlafaxine or duloxetine, because some data suggest their superiority for treating severe MDD. SSRIs are reasonable alternatives. Refer to UpToDate topics on initial treatment with antidepressants for MDD in adults.

Hoitoskeema:

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025

Severity of depression

The severity of depression is determined by a combination of symptom number, frequency, severity, and duration and the degree of functional impairment.

Severity

Mild

Individuals with mild major depression have ≥5 symptoms of depression **and** a PHQ-9 score of 5 to 9. They generally do not have:

- Marked distress or significant functional impairment
- Frequent suicidal or homicidal ideation or plans
- Psychotic features (eg, delusions or hallucinations)
- Catatonic features (eg, immobility, mutism, excessive purposeless motor activity)
- Significant aggressiveness

Moderate

Individuals with moderate major depression have ≥5 symptoms of depression **and** a PHQ-9 score of 10 to 19. They may have suicidal or homicidal ideation and plans. They generally do not have:

- Psychotic features (eg, delusions or hallucinations)
- Catatonic features (eg, immobility, mutism, excessive purposeless motor activity)
- Marked distress or functional impairment

Severe

Individuals with severe major depression have ≥7 symptoms of depression **or** a PHQ-9 score of ≥20 **or** any of the following:

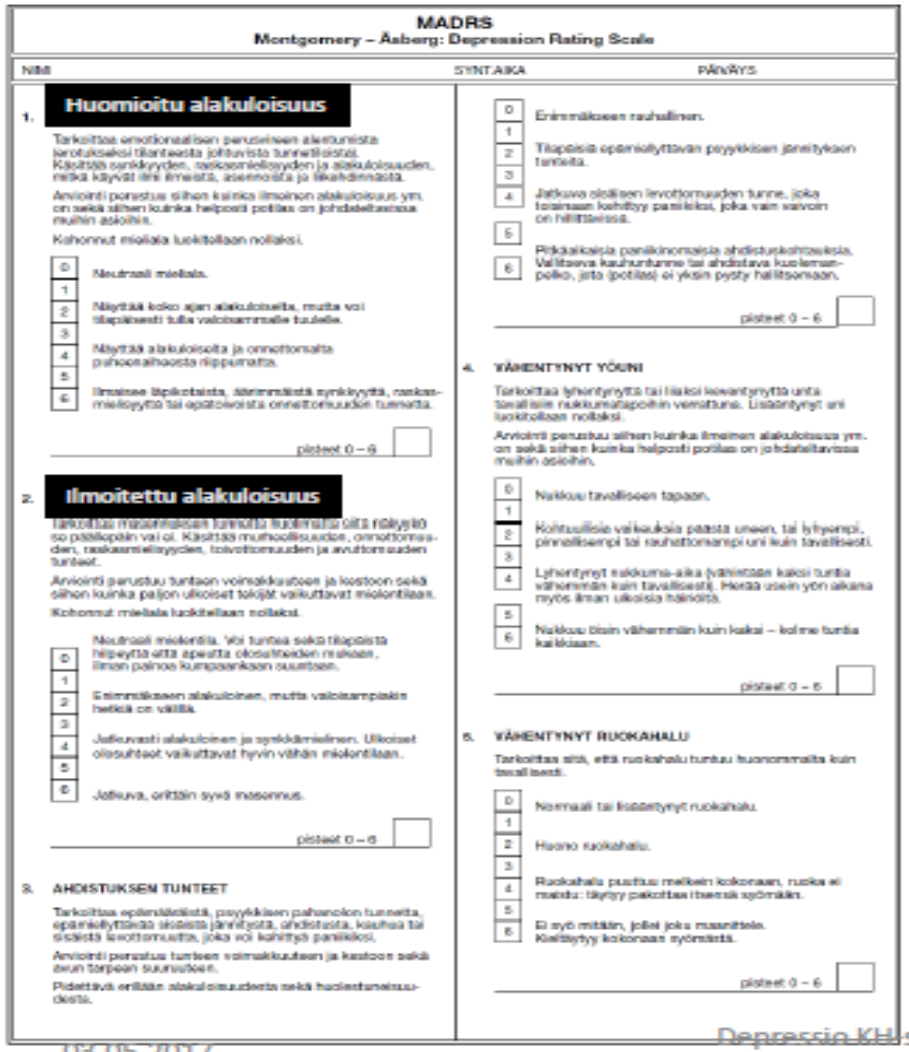
- Psychotic features (eg, delusions or hallucinations)
- Catatonic features (eg, immobility, mutism, excessive purposeless motor activity)
- Marked distress or functional impairment
- Very likely to have suicidal or homicidal ideation and behavior (ie, a specific plan and intent to act upon it)

Symptoms of major depression

Masennuksen seulat: MADRS

MADRS

Muut:
- MDI



MADRS
Montgomery – Åsberg: Depression Rating Scale

NIMI SYNT.AIKA PÄIVÄYS

1. **Huomioitu alakuloisuus**

Tarkoittaa emotionaalisen perusteinen alentunista tarotuksekst tilanteesta johtuvista tunnetiloista. Käsittää synkkyyden, raskasmielisyyden ja alakuloisuuden, mitkä käyvät ilmi ilmeistä, asennoista ja liikehdinnästä.

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

Kohonnut mielialla luokitellaan nollaksi.

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

pisteet 0 – 6

2. **Ilmoitettu alakuloisuus**

Tarkoittaa masennuksen tunnetta itsestään siitä näkyykö se päälleopäin vai ei. Käsittää muhoollisuuden, onnettomuuden, raskasmielisyyden, toivottomuuden ja avuttomuuden tunteet.

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

Kohonnut mielala luokitellaan nollaksi.

0 Neutraali mielentila. Voi tuntea sekä tilapäistä helpeyttä että apeutta olosuhteiden mukaan, ilman painoa kumpaankaan suuntaan.
1
2 Ensimmäisen 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 epämiellistä, psyykkisen pahoinolon 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 huolentuneisuudesta.

0 Enimmäkseen rauhallinen.
1
2 Tilapäisiä epämiellyttävän psyykkisen jännityksen tunteita.
3
4 Jatkuva sisäisen levottomuuden tunne, joka toisinaan kehittyy paniikiksi, jolka vain vaivoin on hillittävissä.
5
6 Pitkaaikaisia paniikinomaisia ahdistuskohtauksia. Valitsevia 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 yrn. on sekä siihen kuinka helposti potilas on johdateltavissa muihin asioihin.

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

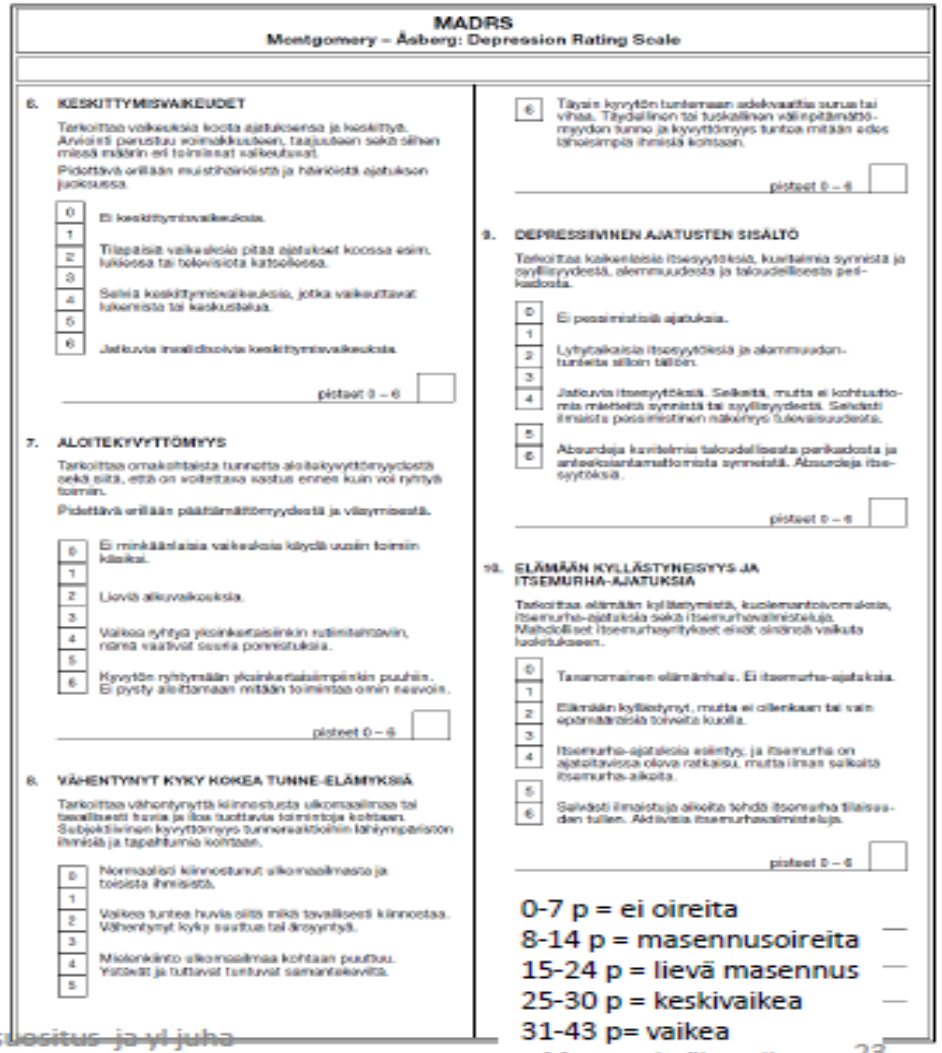
pisteet 0 – 6

5. **VÄHENTYNYT RUOKAHALU**

Tarkoittaa sitä, että ruokahalu tuntuu huonommalta kuin tavallisesti.

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

pisteet 0 – 6



MADRS
Montgomery – Åsberg: Depression Rating Scale

6. **KESKITTYMISVAIKEUDET**

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

Pidettävä erillään muistihäiriöistä ja häiriöistä ajatuksen jatkuvuudessa.

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 päähtämättömyydestä ja viivyttelystä.

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

pisteet 0 – 6

8. **VÄHENTYNYT KYKY KOKEA TUNNE-ELÄMYKSIÄ**

Tarkoittaa vähentynyttä kiinnostusta ulkomaailmaan tai tavallisesti tuota 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 saattaa tai ärsyyntyä.
3
4 Mielenkiinto ulkomaailmaa kohtaan puuttuu. Ystävät ja tuttavat tuntuvat samantekeviltä.
5
6 Täysin kyvytön tuntemaan edellvaalitia suruu 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 pet-kastoista.

0 Ei pessimistisiä ajatuksia.
1
2 Lyhytaikaisia itsesyytöksiä ja alemmuudon-tunteita silloin tällöin.
3
4 Jatkuvia itsesyytöksiä. Selkeitä, mutta ei kohtuuttomia mietteitä synnistä tai syyllisyydestä. Selvästi ilmaista 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 oinkeä 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 ajatuksissa olova ratkaisu, mutta ilman selkeitä itsemurha-aikoita.
5
6 Selvästi ilmaistuja aikoita tehdä itsemurha tilaisuuden tullen. Aktiivisia itsemurhavalmisteluja.

pisteet 0 – 6

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

Masennuksen seulat: MDQ (bipolaaritaudin seulonta)

(Saman ajanjakson aikana, ei elämän aikana)

Päivämäärä ___ ___ / ___ ___ / 20___

Nimi_____

Henkilötunnus_____--_____

Mieialahäiriökysely MDQ

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

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 kilsivät 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 yllaolevista, tapahtuiko useampi näistä asioista saman ajanjakson aikana? *Olkaa hyvä ja vastatkaa joko kyllä tai ei.*

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

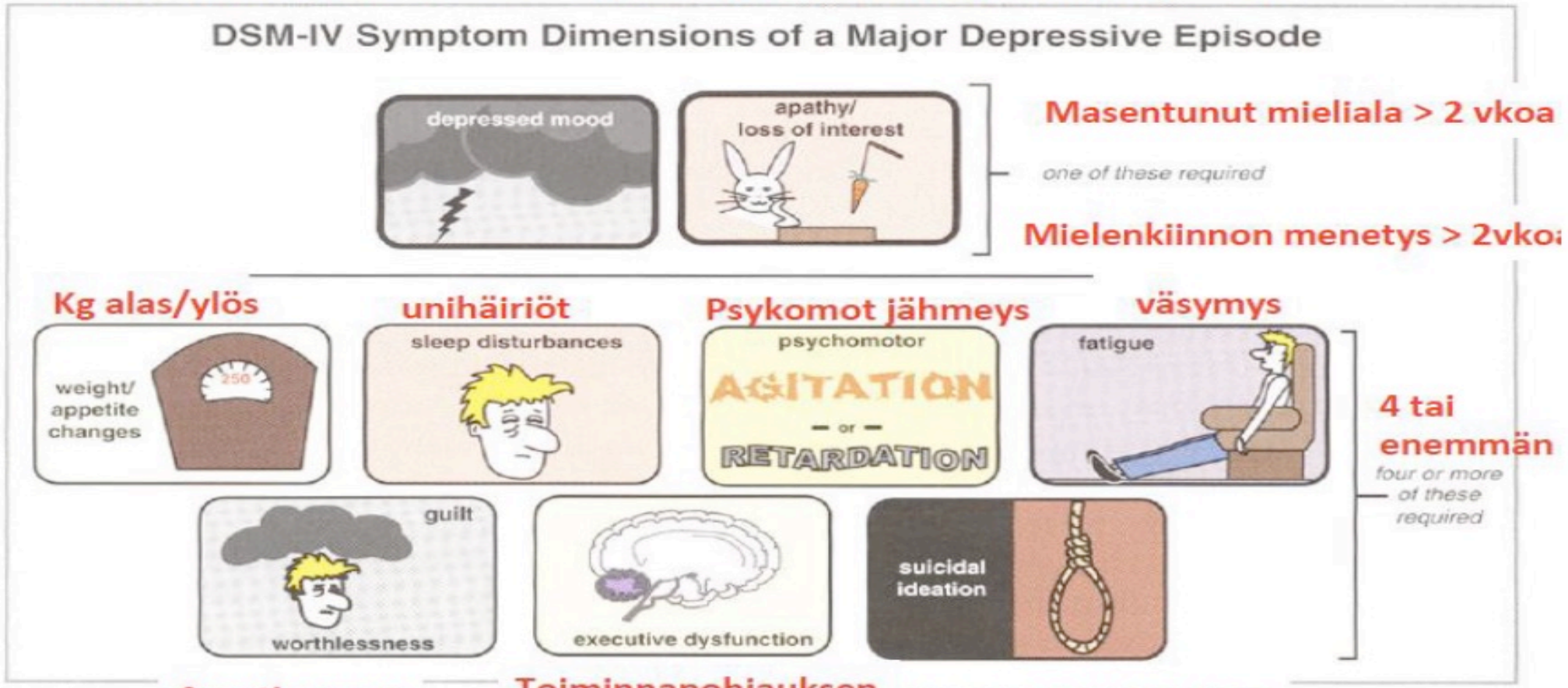
Kyllä	Ei
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐

1 Ei ongelmia
2 Vähäisiä
3 Kohtalaisia
4 Vakavia

Seula +: ei dg!

- **7/13 oiretta**
- **Kohtalaisia tai vakavia**

Masennuksen oireet - vakavan masennuksen kriteerit



Masentunut mieliala > 2 vkoa

Mielenkiinnon menetys > 2vko

Kg alas/ylös

unihäiriöt

Psykomot jähmeys

väsymys

4 tai enemmän

Arvottomuus

Toiminnanohjauksen ongelmat

Itsemurha-ajatukset

FIGURE 11 ...oms ... *Manual of Mental Disorders*, fourth edition (DSM-IV), a ... sists 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

4. Masennuksen lääkehoito

Yl juha kemppinen

Masennuksen hoito:

Hoidon tavoitteena on remissio, eli oireettomuus

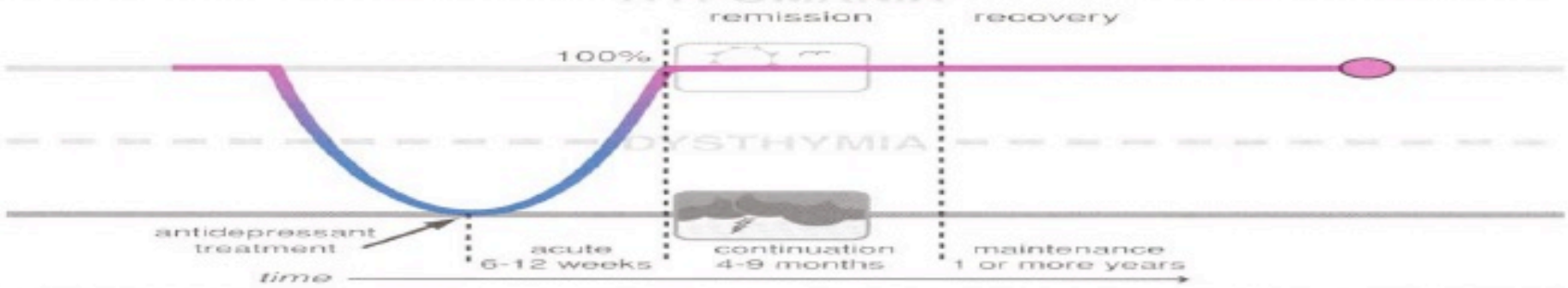


FIGURE 12-2 Remission. When treatment of depression results in removal of essentially all symptoms, it is called remission for the first several months and then recovery if it is sustained for longer than six to twelve months. Such patients are not just better — they are well. However, they are not cured, since depression can still recur. Remission and recovery are now the goals when treating patients with depression.

Jos oireitten väistyttyä jättää masennuslääkkeen pois, voi masennusoireet palata

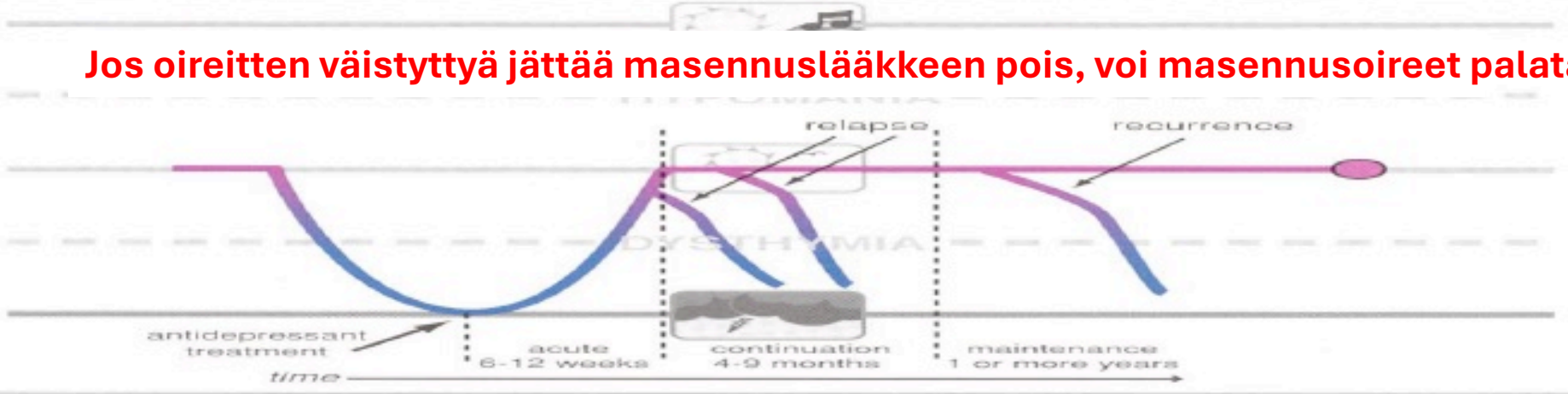
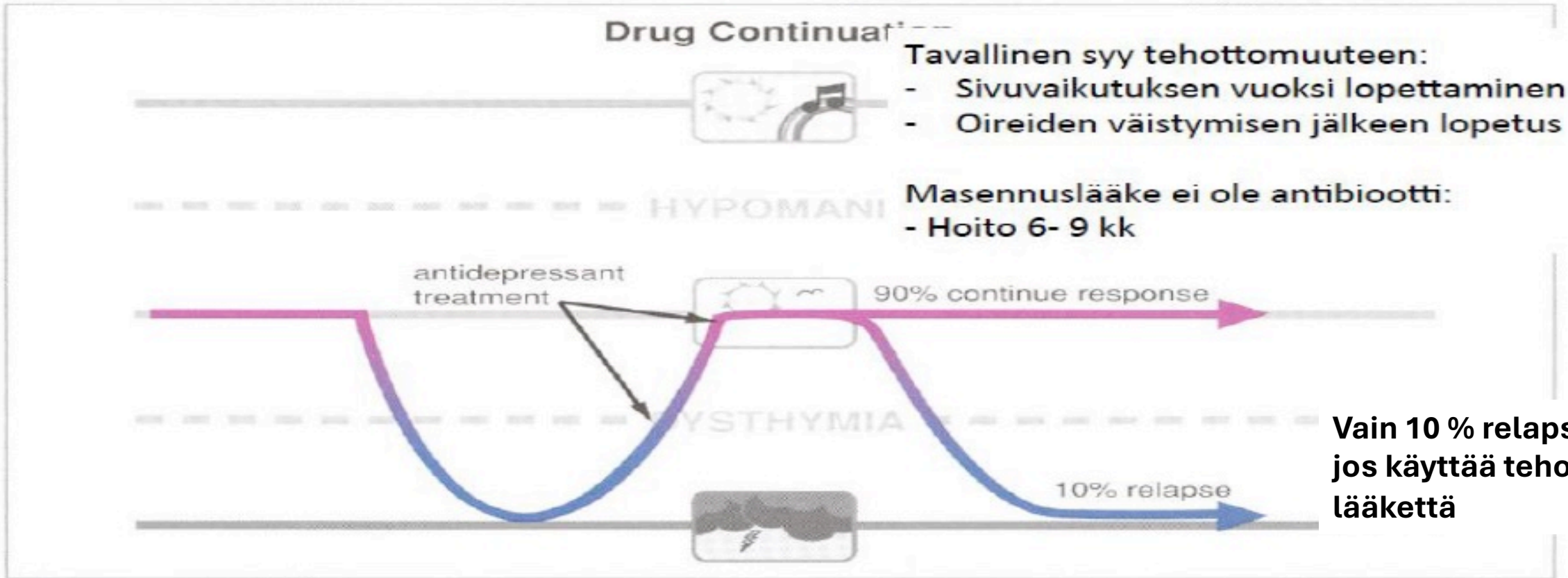


FIGURE 12-3 Relapse and recurrence. When depression returns before there is a full remission of symptoms or within the first several months following remission of symptoms, it is called a relapse. When depression returns after a patient has recovered, it is called a recurrence.

Stahl, 2004

Mielialalääkkeiden ja placebon teho: lääkitys lopetetaan, kun oireet väistyvät



Tavallinen syy tehottomuuteen:
- Sivuvaikutuksen vuoksi lopettaminen
- Oireiden väistymisen jälkeen lopetus

Masennuslääke ei ole antibiootti:
- Hoito 6- 9 kk

Vain 10 % relapsi, jos käyttää tehoavaa lääkettä

FIGURE 12-6 Drug continuation. Depressed patients who have an initial treatment response to an antidepressant will relapse at a rate only of about 10% to 20% if their medication is continued for six months to a year following recovery.

S. Stahl, 2004

Stahl, 2008

What Proportion of Major Depressive Disorders Remit?

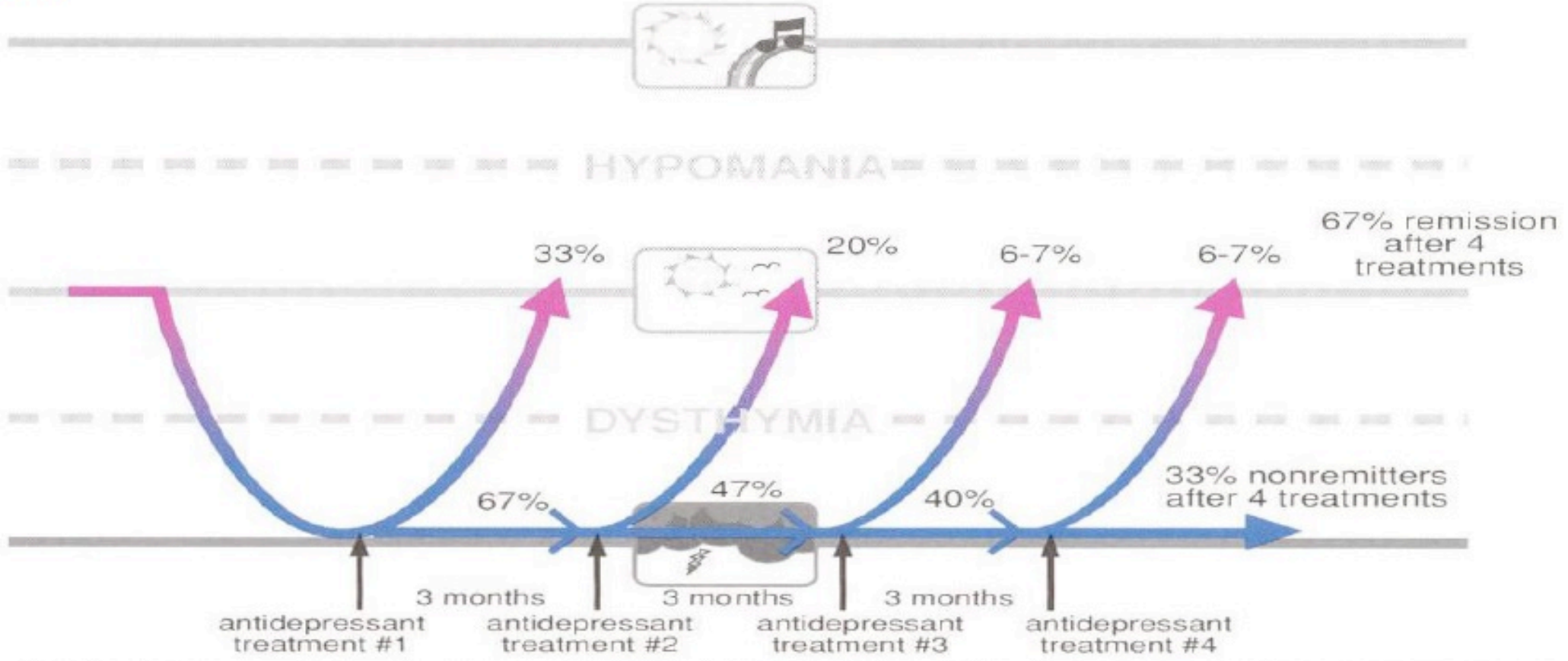


FIGURE 12-8 Remission rates in MDD. Approximately one-third of depressed patients will remit during treatment with any antidepressant initially. Unfortunately, for those who fail to remit, the likelihood of remission with another antidepressant monotherapy goes down with each successive trial. Thus, after a year of treatment with four sequential antidepressants taken for twelve weeks each, only two-thirds of patients will have achieved

Stahl, 2004

Mielialalääkkeiden ja placebon teho: oireista toipuminen

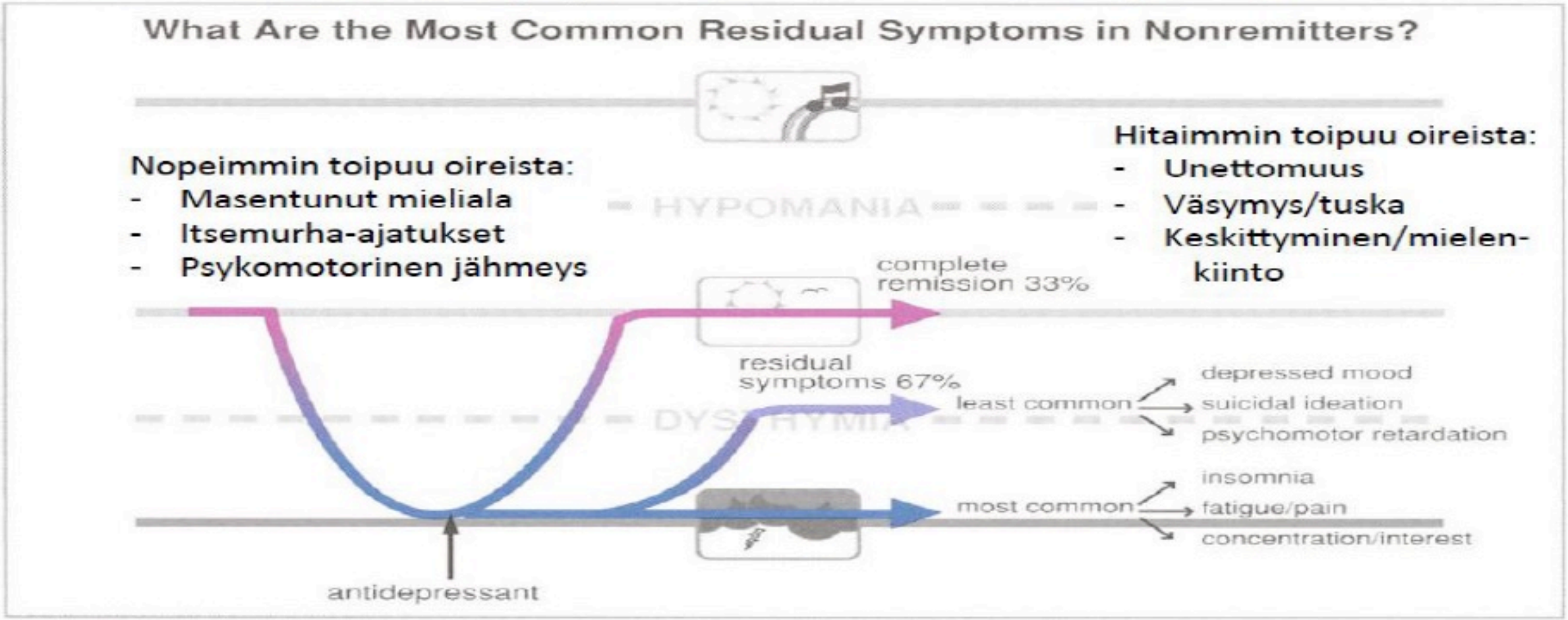
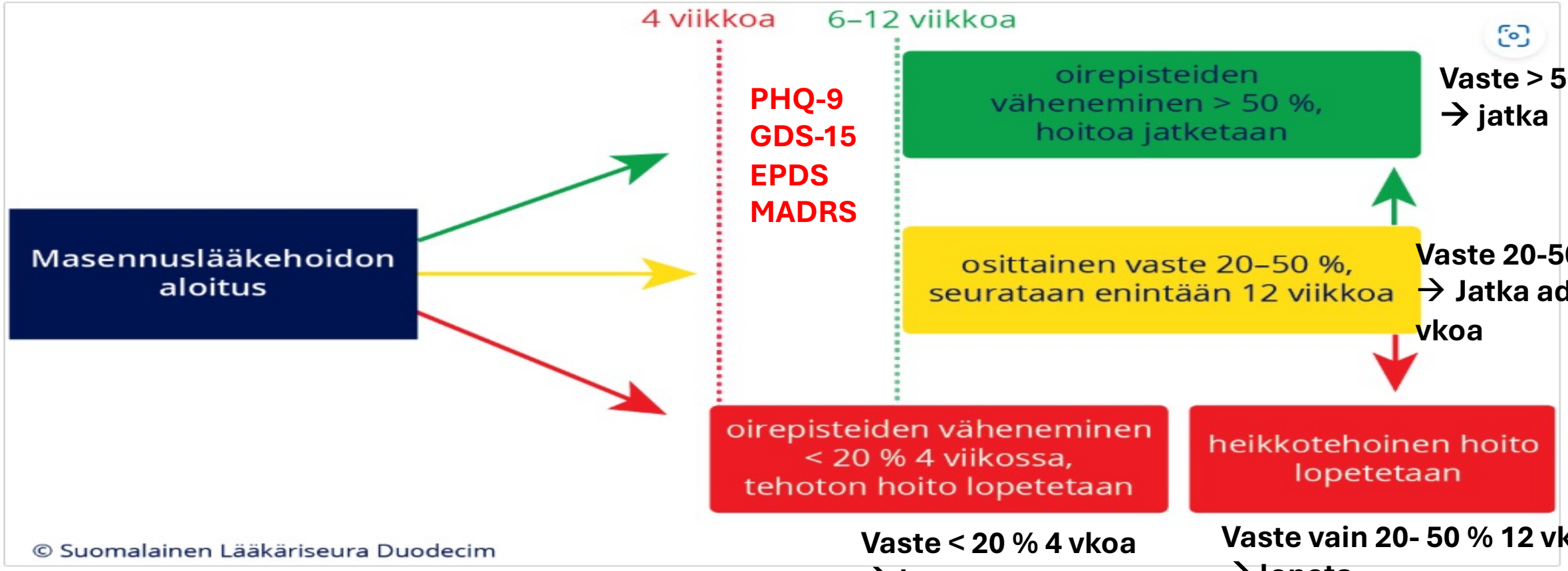


FIGURE 12-9 Common residual symptoms. In patients who do not achieve remission, the most common residual symptoms are insomnia, fatigue, painful physical complaints, problems concentrating, and lack of interest. The least common residual symptoms are depressed mood, suicidal ideation, and psychomotor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

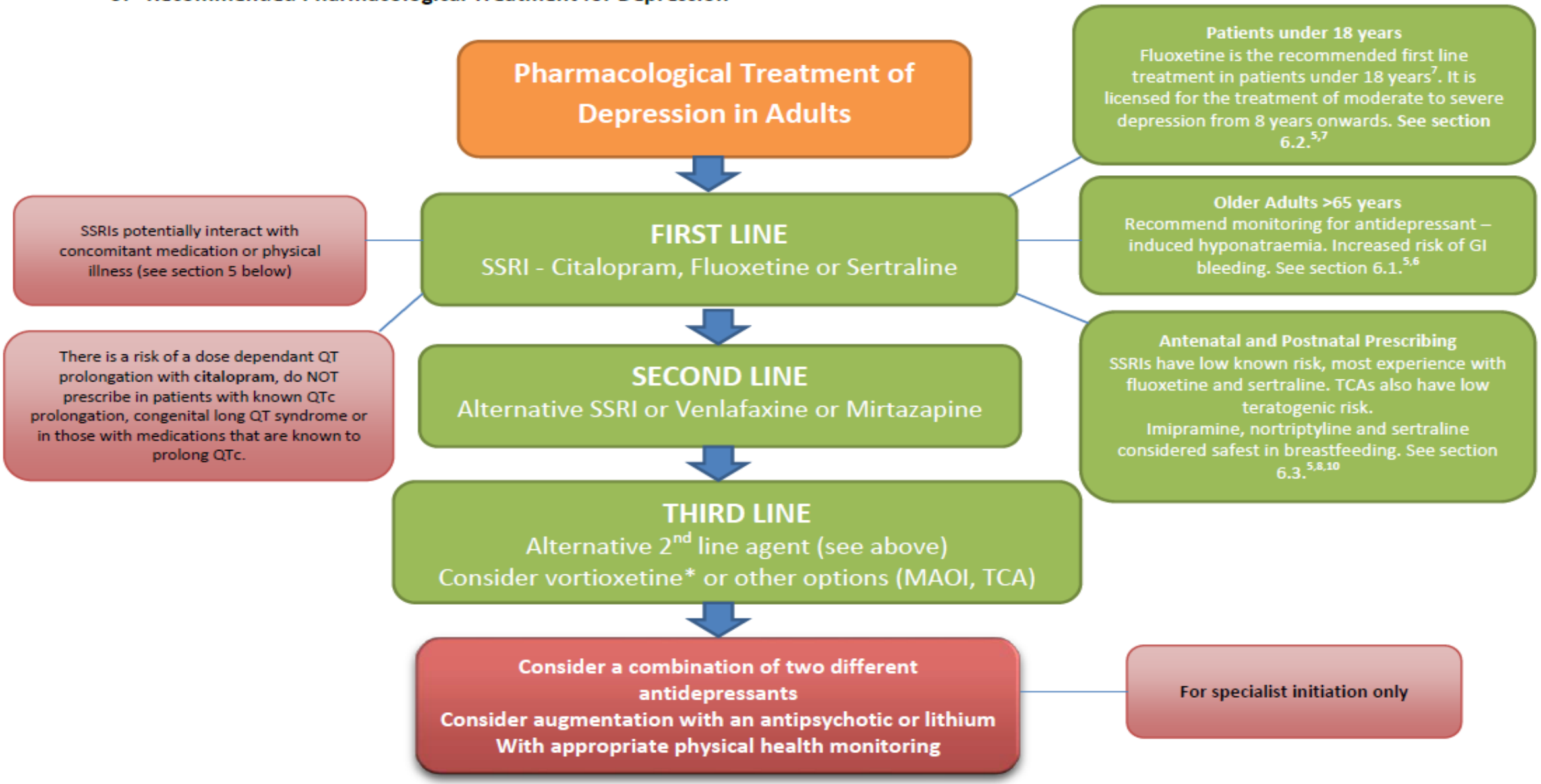
S. Stahl, 2004



Kuva 2. Akuuttivaiheen masennuslääkehoidon vasteen arviointi

Jos depression oirepisteet vähenevät alle 20 % 4 ensimmäisen hoitoviikon aikana, on tehoton hoito syytä lopettaa. Hoitovaste on usein aluksi vain osittainen (20–50 %), mutta kehittyy vähitellen tyydyttäväksi (yli 50 %). Mikäli asianmukaisesti annostellulla masennuslääkkeellä ei saavuteta yli 50 %:n hoitovastetta 6–12 viikon aikana, on yleensä syytä lopettaa heikkotehoinen hoito ja vaihtaa lääkettä. Jos lopetettava lääkehoito oli jo toinen hoitoyritys akuuttivaiheessa, toimitaan sen jälkeen lääkeresistentin depression ohjeiden mukaisesti.

3. Recommended Pharmacological Treatment for Depression



*Refer to prescribing notes, page 8

Taulukko 3. Suomessa vuonna 2024 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	Essitalopraami **t 1/2**/ **5x T1/2 h/ T1/2 pv**= 30 h /150 h / 6.25 vrk
Fluoksetiini	Seronil	20	20–80	Fluoksetiini 96-144 h /480 -720 h / 30 vrk
Fluvoksamiini	Fevarin	50	100–300	Fluvoksamiini 17-22 h/ 85-110 h/ 4.58 vrk
Paroksetiini	Seroxat	20	20–50	Paroksetiini 24 h /120 h / 5.00 vrk
Sertraliini	Zoloft	50	50–200	Sertraliini 22-36 h/ 110-180 h/ 7.50 vrk
Sitalopraami	Cipramil	20	20–40	Sitalopraami 36 h/ 180 h / 7.50 vrk

Taulukko 3. Suomessa vuonna 2024 käytössä olevat masennuslääkkeet ja niiden annokset aikuispotilaille

Geneerinen nimi		Aloitusannos (mg/vrk)	Hoitoannos (mg/vrk)	Tavallisia haittavaikutuksia
Muut depressiolääkkeet				**T1/2 h/ 5 x T1/2 h/ 5 x T1/2 vrk**
Agomelatiini	Valdoxan	25	25–50	Päänsärky, huimaus 1-2 h/ 5-10 h/ 0.42 vrk
Bupropioni	Voxra	150	150–300	Päänsärky, unettomuus, pahoinvointi 10-27 h /50-135 h/ 5.62 vrk
Duloksetiini	Cymbalta	60	60–120	Pahoinvointi, suun kuivuminen, päänsärky, uneliaisuus 8-17 h/ 40-85 h /3.54 vrk
Mianseriini	Tolvon	30	30–90	Väsymys, huimaus 6-39 h/ 30-195 h /8.13 vrk
Mirtatsapiini	Remeron	15–30	30–60	Väsymys, painon nousu 20-40 h/ 100 - 200 h/ 8.33 vrk
Moklobemidi	Aurorix	300	300–900	Unettomuus, huimaus 2-4 h/ 10-20h /0.83 vrk
Tratsodoni	Azona	50–100	150–500	Väsymys, huimaus, rytmihäiriöt 5-13 h/ 25-65 h/ 2.70 vrk
Venlafaksiini	Efexor	75	75–375	Kuten SSRI-lääkkeillä 4-7 h / 20-35 h /1.46 vrk
Vortioksetiini	Brintellix	10	5–20	Pahoinvointi 66 h/ 330 h /13.75 vrk

Taulukko 3. Suomessa vuonna 2024 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 alfa$_1$-salpauksen haittavaikutukset
Amitriptyliini	Elavil /Triptyl	25–50	75–300	
Klomipramiini	Anafranil	25–50	75–300	
Nortriptyliini	Noritren	25–50	50–200	

[1)] Käyttö depressioon edellyttää pitoisuusmittauksia.

T1/2 h/ 5 x T1/2 h/ 5 x T1/2 vrk

Amitriptyliini 9-25 h/ 45- 125 h / 5.21 vrk

Klomipramiini 12-36 h/ 60-180 h / 7.50 vrk

Nortriptyliini 36 h/ 180 h / 7.50 vrk

(Tr)Imipramiini	Surmontil	25-50	75- 150 mg	19 h / 95 h/ 3.96 vrk
Doksepiini (vanha)	Doxal	25-50	75 – 150 mg	33-80 h/165- 400 h/ 16.67 vrk
Doksepiini (uusi)	Doxal	3- 5	ad 10mg	6-24 h/ 30-120 h/ 5 vrk

Depression in adults: Antidepressant doses*

Drug	Usual total starting dose per day (mg)¶	Usual total maintenance dose per day (mg)¶	Extreme daily dose range (mg)¶
Selective serotonin reuptake inhibitors			
Citalopram	20	20 to 40Δ	10 to 40Δ
Escitalopram	10	10 to 20	5 to 30
Fluoxetine	20	20 to 60	10 to 80
Fluvoxamine	50	100 to 200	25 to 300
Fluvoxamine CR	100	100 to 200	100 to 300
Paroxetine	20	20 to 40	10 to 50
Paroxetine CR	25	25 to 50	12.5 to 62.5
Sertraline	50	50 to 200	25 to 300
Serotonin-norepinephrine reuptake inhibitors			
Desvenlafaxine	25 to 50	50 to 100	50 to 400◇
Duloxetine	30 to 60	60	30 to 120§
Levomilnacipran	20	40 to 80	20 to 120
Milnacipran	12.5	100 to 200	50 to 300
Venlafaxine	37.5 to 75	75 to 375	75 to 375
Venlafaxine XR	37.5 to 75	75 to 225	75 to 375

Depression in adults: Antidepressant doses*

Drug	Usual total starting dose per day (mg)¶	Usual total maintenance dose per day (mg)¶	Extreme daily dose range (mg)¶
Atypical agents			
Agomelatine¥ (not available in United States)	25	25 to 50	25 to 50
Bupropion	200	300 (maximum single dose 150 mg)	100 to 450
Bupropion SR 12 hour	150	300 (maximum single dose 200 mg)	150 to 400
Bupropion XL 24 hour	150	300	150 to 450 (United States) 150 to 300 (Europe)
Bupropion hydrobromide 24 hour	174	348	174 to 522
Mirtazapine	15	15 to 45	7.5 to 60
Serotonin modulators			
Nefazodone‡	200	300 to 600	50 to 600
Trazodone	100	200 to 400	100 to 600
Vilazodone	10	40	10 to 40
Vortioxetine	10	20	5 to 20

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Depression in adults: Antidepressant doses*

Drug	Usual total starting dose per day (mg)¶	Usual total maintenance dose per day (mg)¶	Extreme daily dose range (mg)¶
Tricyclics and tetracyclics†			
Amitriptyline	25	150 to 300	10 to 300
Ei Amoxapine	25	200 to 300	25 to 400
Clomipramine	25	100 to 250	25 to 300
Desipramine	25	150 to 300	25 to 300
Ei Doxepin	25	100 to 300	10 to 300
Imipramine	25	150 to 300	10 to 300
Maprotiline	25	100 to 225	25 to 225
Nortriptyline	25	50 to 150	10 to 200
Ei Protriptyline	10	15 to 60	5 to 60
Ei Trimipramine	25	150 to 300	25 to 300
Monoamine oxidase inhibitors†			
Ei Isocarboxazid	10	10 to 40	10 to 60
Ei Phenelzine	15	15 to 90	7.5 to 90
Selegiline transdermal	6 mg/24-hour patch	6 to 12 mg/24-hour patch	6 to 12 mg/24-hour patch
Ei Tranylcypromine	10	30 to 60	10 to 60

CR: controlled release; SR: sustained release; XL: extended release; XR: extended release.

* Total daily oral doses shown in table may need to be given as 2 or 3 equally divided doses per day, depending on specific antidepressant and other factors. For additional detail, refer to individual Lexidrug monographs included with UpToDate.

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Depression in adults: Antidepressant doses*

Drug	Usual total starting dose per day (mg)¶	Usual total maintenance dose per day (mg)¶	Extreme daily dose range (mg)¶

¶ Lower doses may be useful for initiating or maintaining patients who are older or medically compromised (eg, kidney or liver disease) or drug-sensitive patients, as well as patients with a low body mass index. High doses may be used for medications that are well tolerated but ineffective at lower doses. In patients with panic disorder, UpToDate contributors initiate treatment at one-half or less of the usual starting dose shown and titrate more gradually; refer to UpToDate topics on the management of panic disorder.

Δ Maximum recommended dose of citalopram is 20 mg for patients >60 years of age, with significant hepatic insufficiency, or taking interacting medications that can increase citalopram levels. For more information, refer to the UpToDate topic on unipolar depression in adults and selective serotonin reuptake inhibitors.

◇ Data regarding increased efficacy of doses >50 mg/day are limited; however, individual patients can benefit by titrating up to 100 mg/day.

§ Although duloxetine doses >60 mg/day did not confer additional benefit in clinical trials, individual patients may benefit from dose escalation up to a maximum of 120 mg/day.

¥ Agomelatine may be hepatotoxic and is contraindicated with any degree of liver impairment. Transaminase monitoring is required.

‡ Caution: Nefazodone can cause liver failure and has been withdrawn from the market in several countries. Refer to UpToDate topic on serotonin modulators pharmacology, administration, and side effects for additional information.

† Conservative starting doses shown in table are lower than starting doses shown in some other references. For additional information, refer to UpToDate topics on the treatment of depression with antidepressants as well as cyclic antidepressants and monoamine oxidase inhibitors for treatment of adults with depression.

Data from:

1. *The American Psychiatric Association Publishing Textbook of Psychopharmacology, 5th edition, Schatzberg AF, Nemeroff CB (Eds), American Psychiatric Association Publishing 2017.*
2. *Kennedy SH, Lam RW, McIntyre RS, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 3. Pharmacological Treatments. Can J Psychiatry 2016; 61:540.*
3. *Gartlehner G, Thaler K, Hill S, Hansen RA. How should primary care doctors select which antidepressants to administer? Curr Psychiatry Rep 2012; 14:360.*
4. *UpToDate Lexidrug. More information available at https://online.lexi.com/.*

Masennuksen hoito:

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)	**Cipramil**	4 hr	35 hr	3 hr	7	80
Escitalopram (Lexapro)	**Cipralex**	5 hr	27–32 hr	—	7	56
Fluoxetine (Prozac)	**Seronil**	6–8 hr	4–6 days	4–16 days	28–35	95
Fluvoxamine (Luvox)	**Fevarin**	3–8 hr	15 hr	—	5–7	80
Paroxetine (Paxil)	**Seroxat**	5–6 hr	21 hr	—	5–10	95
Paroxetine CR (Paxil CR)		6–10 hr	15–20 hr	—	< 14	95
Sertraline (Zoloft)	**Zoloft**	4.5–8.5 hr	26 hr	62–104 hr	7	95

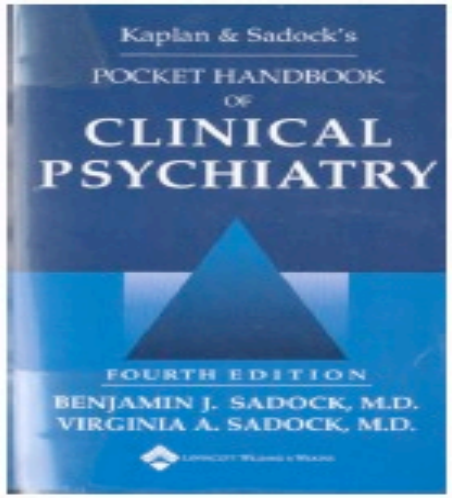


Table 25–17
Non-SSRI Antidepressants

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

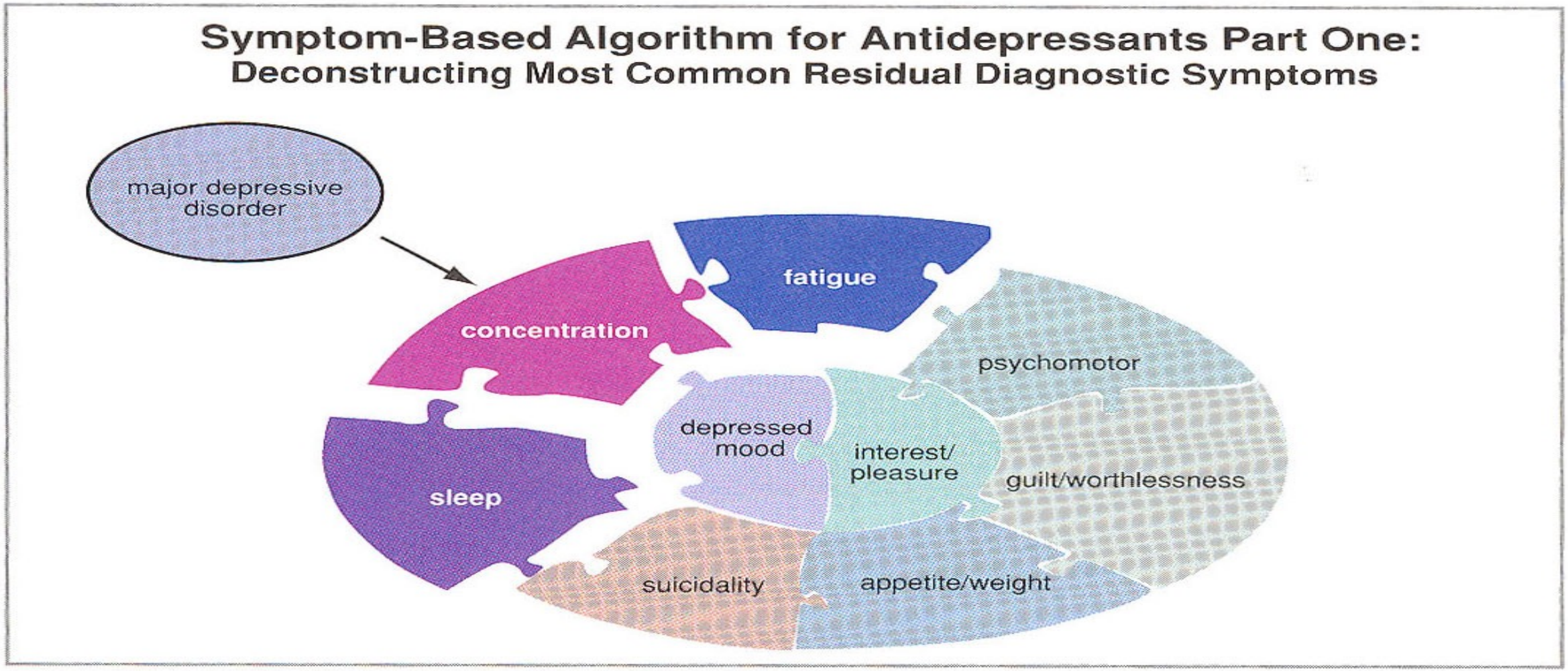


FIGURE 12-121 Symptom-based algorithm for antidepressants, part 1. Shown here is the diagnosis of major depressive disorder deconstructed into its symptoms [as defined by the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV)]. Of these, sleep disturbances, problems concentrating, and fatigue are the most common residual symptoms.

Stahl, 2008

Symptom Based Algorithm for Antidepressants Part Two:
Match Most Common Residual Symptoms to Hypothetically Malfunctioning Brain Circuits

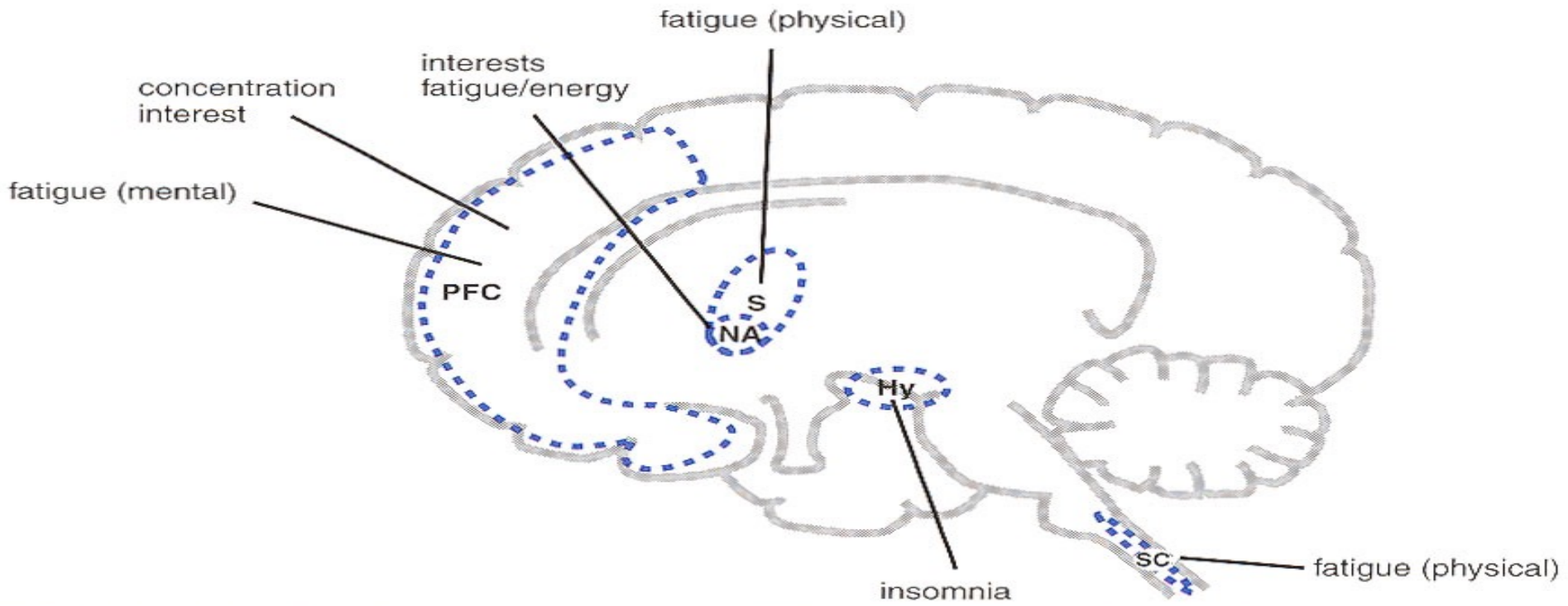


FIGURE 12-122 Symptom-based algorithm for antidepressants, part 2. In this figure the most common residual symptoms of major depression are linked to hypothetically malfunctioning brain circuits. Insomnia may be linked to the hypothalamus, problems concentrating to the dorsolateral prefrontal cortex (PFC), reduced interest to the PFC and nucleus accumbens (NA), and fatigue to the PFC, striatum (S), NA, and spinal cord (SC).

Stahl, 2008

Symptom-Based Algorithm for Antidepressants Part Three: Target Regulatory Neurotransmitters With Selected Pharmacological Mechanisms

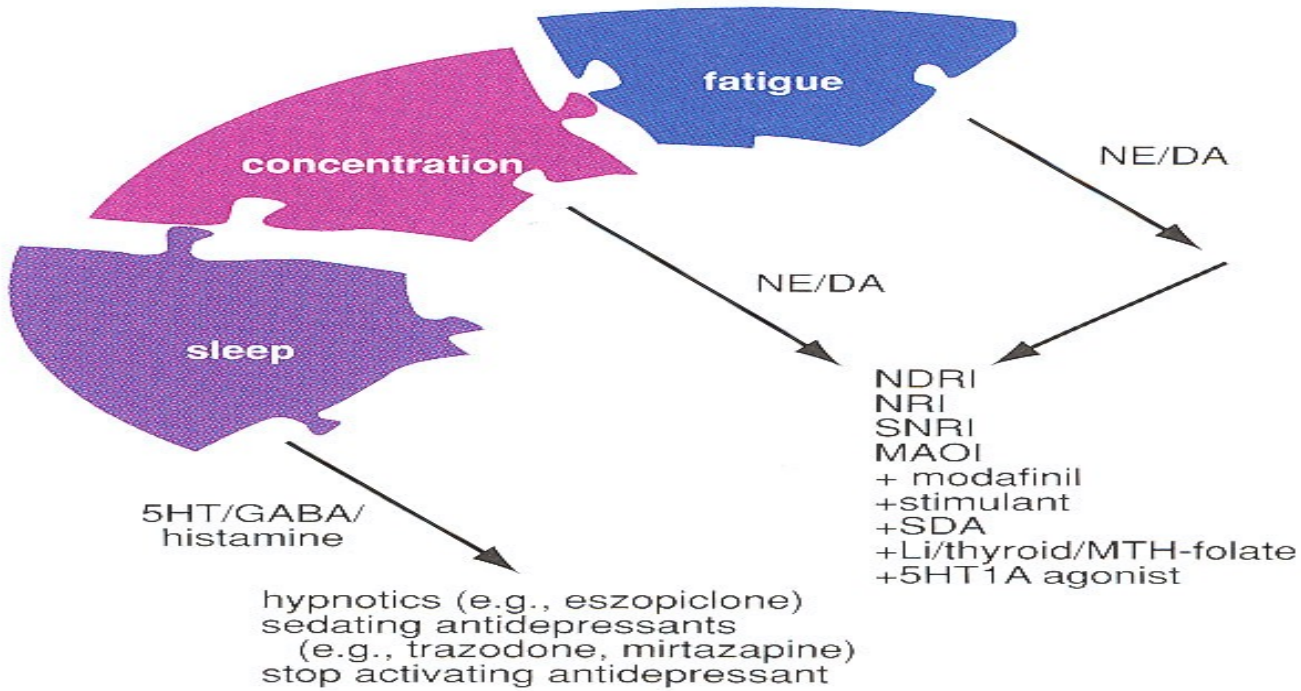


FIGURE 12-123 Symptom-based algorithm for antidepressants, part 3. Residual symptoms of depression can be linked to the neurotransmitters that regulate them and then, in turn, to pharmacological mechanisms. Fatigue and concentration are regulated in large part by norepinephrine (NE) and dopamine (DA), which are affected by many antidepressants, including norepinephrine dopamine reuptake inhibitors (NDRIs), selective norepinephrine reuptake inhibitors (NRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), and monoamine oxidase inhibitors (MAOIs). Augmenting agents that affect NE and/or DA include modafinil, stimulants, serotonin dopamine antagonists (SDAs), lithium, thyroid hormone, L-5-methyl-tetrahydrofolate (MTHF), and serotonin (5HT) 1A agonists. Sleep disturbance is regulated by 5HT, gamma-aminobutyric acid (GABA), and histamine and can be treated with sedative hypnotics, sedating antidepressants such as trazodone or mirtazapine, or by discontinuing an activating antidepressant.

Stahl, 2008

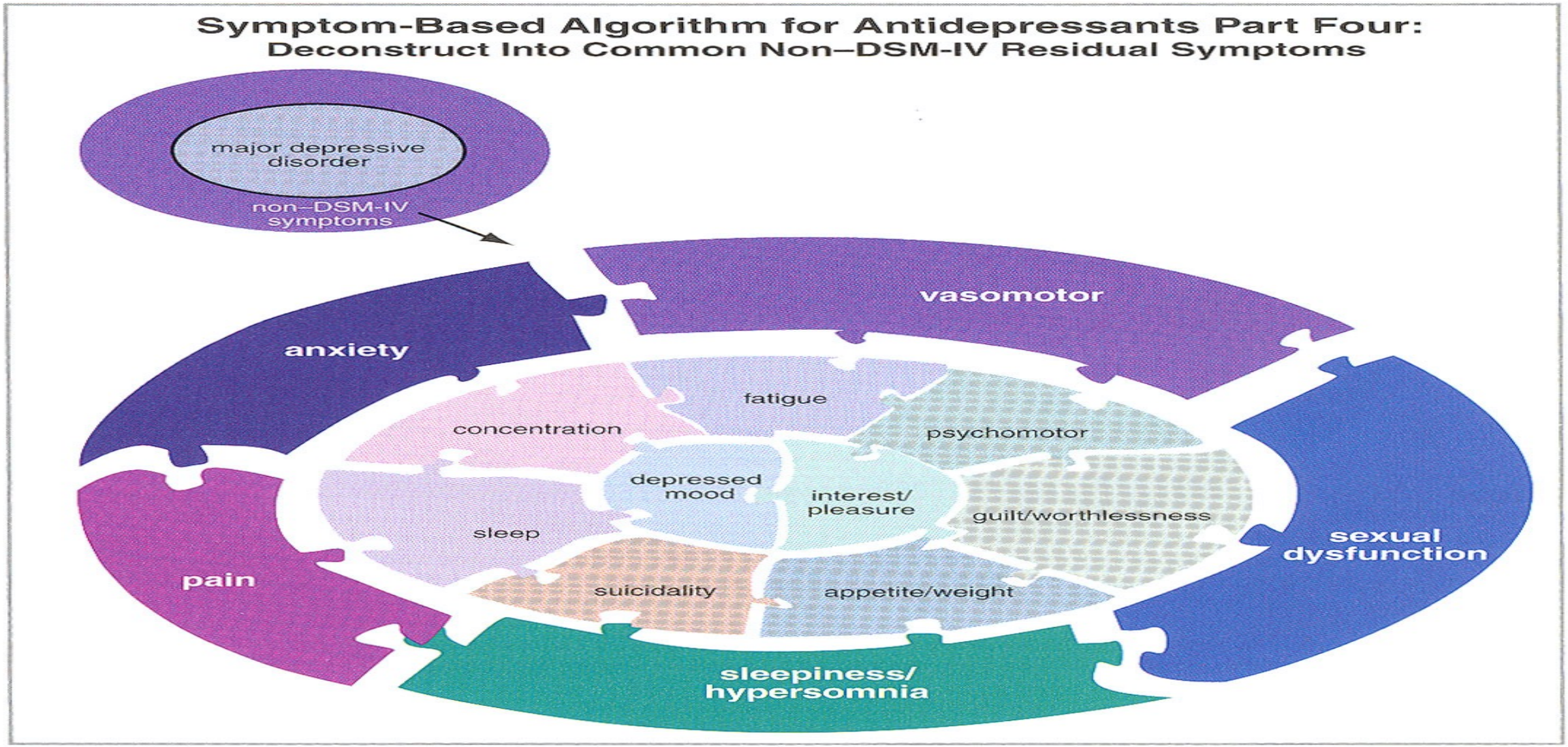


FIGURE 12-124 Symptom-based algorithm for antidepressants, part 4. There are several common symptoms of depression that are nonetheless not part of the formal diagnostic criteria for major depressive disorder. These include painful physical symptoms, excessive daytime sleepiness/hypersomnia with problems of arousal and alertness, anxiety, vasomotor symptoms, and sexual dysfunction.

Stahl, 2008

Symptom Based Algorithm for Antidepressants Part Five: Match Common Non-DSM-IV Residual Symptoms to Hypothetically Malfunctioning Brain Circuits

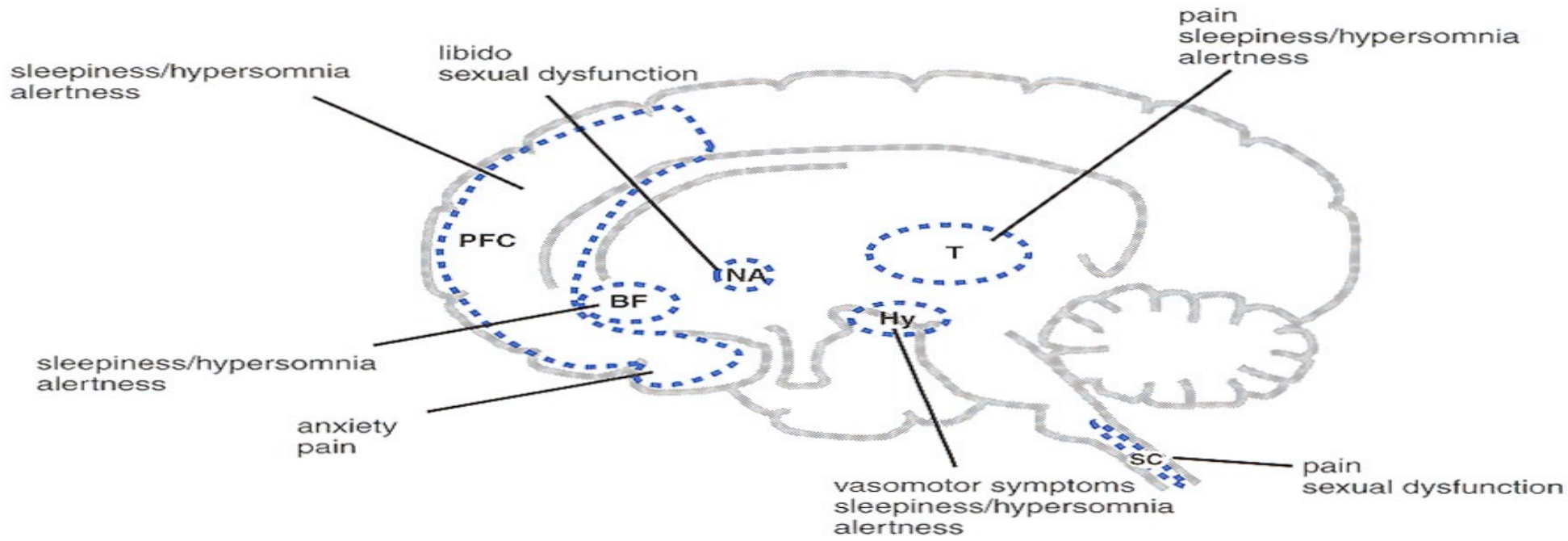


FIGURE 12-125 Symptom-based algorithm for antidepressants, part 5. In this figure common residual symptoms of major depression that are not part of formal diagnostic criteria are linked to hypothetically malfunctioning brain circuits. Painful physical symptoms are linked to the spinal cord (SC), thalamus (T), and ventral portions of the prefrontal cortex (PFC), while anxiety is associated with the ventral PFC. Vasomotor symptoms are mediated by the hypothalamus (Hy) and sexual dysfunction by the SC and nucleus accumbens (NA). Sleep symptoms that are part of the diagnostic criteria of depression involve mostly insomnia, linked to the hypothalamus; however, shown here are problems with hypersomnia and excessive daytime sleepiness, which may be beyond those symptoms included in the diagnostic criteria and be linked to problems with arousal and alertness and to arousal pathways not only in the hypothalamus but also the thalamus (T), basal forebrain (BF), and prefrontal cortex (PFC).

Stahl, 2008

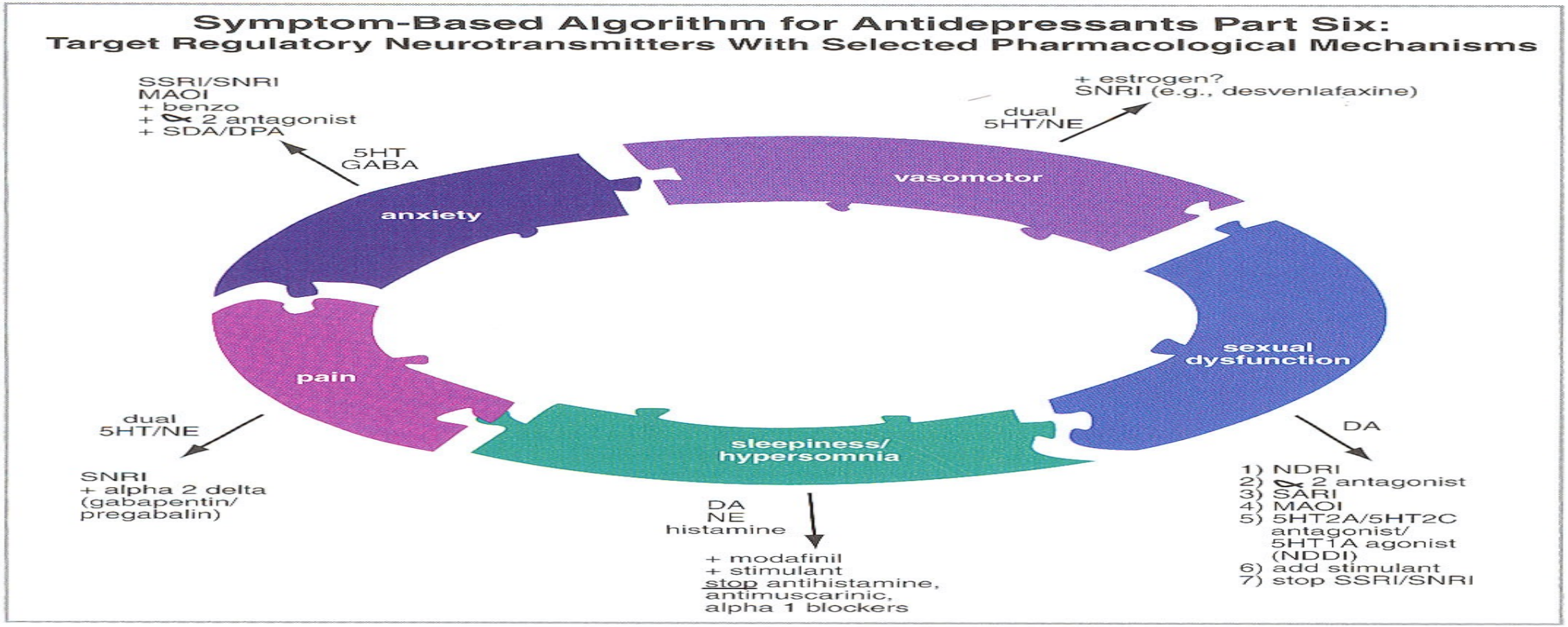
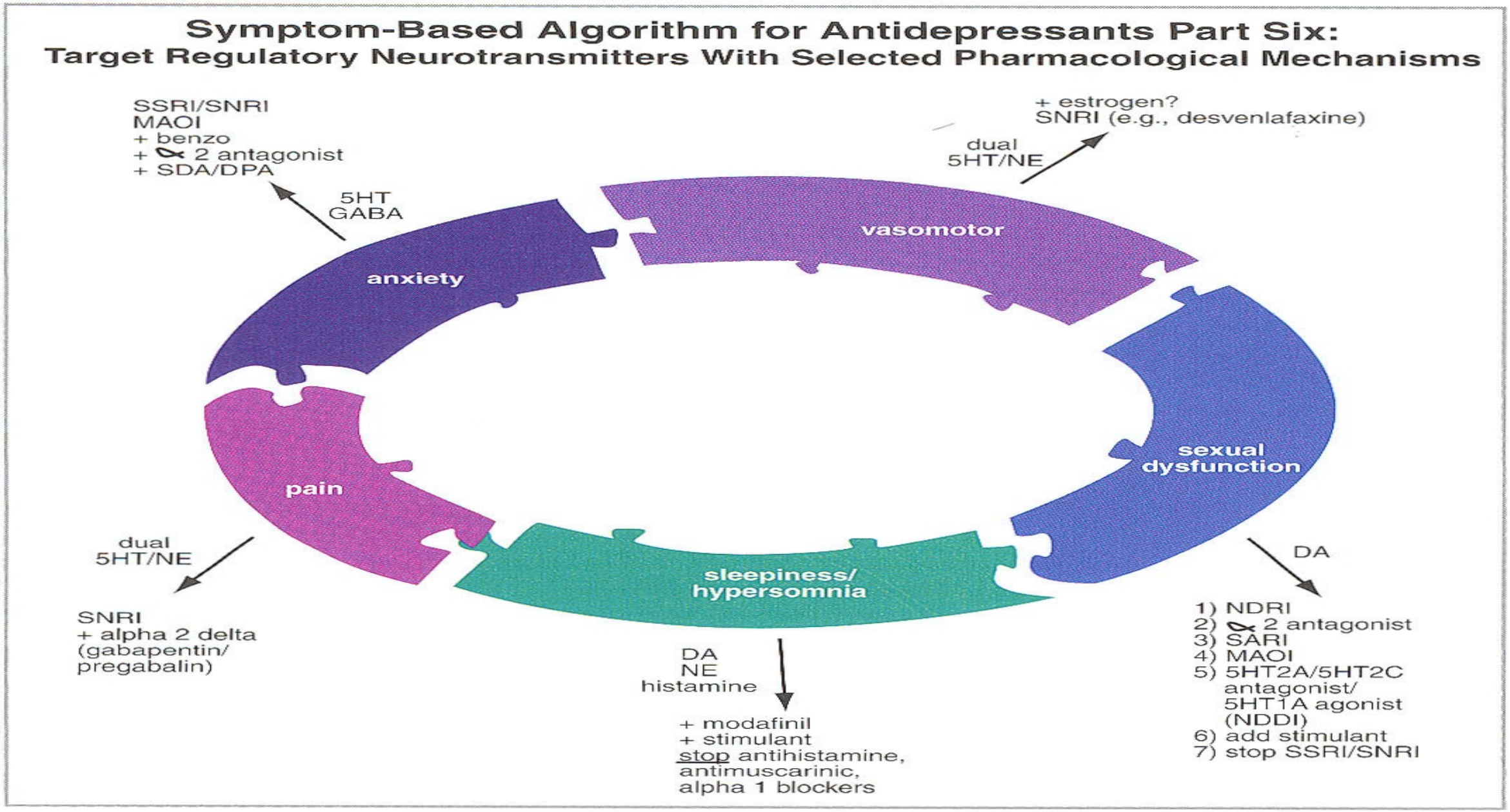


FIGURE 12-126 Symptom-based algorithm for antidepressants, part 6. Residual symptoms of depression can be linked to the neurotransmitters that regulate them and then, in turn, to pharmacological mechanisms. Painful physical symptoms are mediated by norepinephrine (NE) and to a lesser extent serotonin (5HT) and may be treated with serotonin norepinephrine reuptake inhibitors (SNRIs) or alpha 2 delta ligands (pregabalin, gabapentin). Anxiety is related to 5HT and gamma-aminobutyric acid (GABA); it can be treated with serotonin selective reuptake inhibitors (SSRIs), SNRIs, or monoamine oxidase inhibitors (MAOIs) as monotherapies as well as by augmentation with benzodiazepines, alpha 2 antagonists, serotonin dopamine antagonists (SDAs), or dopamine partial agonists (DPAs). Vasomotor symptoms may be modulated by NE and 5HT and treated with SNRIs; augmentation with estrogen therapy is also an option. Sexual dysfunction is regulated primarily by dopamine (DA) and may be treated with norepinephrine dopamine reuptake inhibitors (NDRIs), alpha 2 antagonists, serotonin 2A antagonist/reuptake inhibitors (SARIs), MAOIs, 5HT2A/5HT2C antagonists, 5HT1A agonists, addition of a stimulant, or by stopping an SSRI or SNRI. Hypersomnia and problems with arousal and alertness are regulated by DA, NE, and histamine and can be treated with activating agents such as modafinil or stimulants or by stopping sedating agents with antihistamine, antimuscarinic, and/or alpha 1 blocking properties.

Stahl, 2008

Symptom-Based Algorithm for Antidepressants Part Six:
Target Regulatory Neurotransmitters With Selected Pharmacological Mechanisms



Stahl, 2008

Masennuslääkkeiden sivuvaikutukset:

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025

= 2 = 3 = 4

Side effects of antidepressant medications[1-7]

Drug	Anticholinergic	Drowsiness	Insomnia/ agitation	Orthostatic hypotension	QTc prolongation*	Gastrointestinal toxicity	Weight gain	Sexual dysfunction
Selective serotonin reuptake inhibitors¶								
Citalopram	0	1+	1+	1+	2 to 3+Δ	1+¶	1+	3+
Escitalopram	0	1+	1+	1+	2+	1+¶	1+	3+
Fluoxetine	0	0	2+	1+	1+	1+¶	0	3+
Fluvoxamine	0	1+	1+	1+	1+	1+¶	1+	3+
Paroxetine	1+	2+	1+	2+	1+	1+¶	2+	4+
Sertraline	0	1+	2+	1+	1+	2+¶◇	1+	3+
Atypical agents								
Agomelatine§ (not available in United States)	0	1+	1+	0	0	1+	0	0 to 1+
Bupropion	0	0	2+ (immediate release) 1+ (sustained release)	0	0 to 1+¥	1+	0	0
Mirtazapine	1+	4+	0	0	1+	0	4+	1+

Masennuslääkkeiden sivuvaikutukset:

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025

Side effects of antidepressant medications[1-7]

= 2 = 3 = 4

Drug	Anticholinergic	Drowsiness	Insomnia/ agitation	Orthostatic hypotension	QTc prolongation*	Gastrointestinal toxicity	Weight gain	Sexual dysfunction
Serotonin-norepinephrine reuptake inhibitors¶‡								
Desvenlafaxine†	0	0	2+	0	0	2+	Unknown	1+
Duloxetine	0	0	1+	0	0	2+¶	0 to 1+	1+
Ei Levomilnacipran†	0**	0	0 to 1+	0 to 1+	0	2+¶	0	1+
Milnacipran†	0	1+	0	0	0	2+¶	0	1+
Venlafaxine†	0	1+	2+	0	0 to 1+¥	2+	0 to 1+	3+
Serotonin modulators								
Trazodone	0	4+	0	1+ (hypnotic dose) 3+ (antidepressant dose)	1 to 2+	1+ (hypnotic dose) 3+ (antidepressant dose)	0 (hypnotic dose) 1+ (antidepressant dose)	1+¶¶
Vilazodone Viibryd	0	0	2+	0	0	4+ΔΔ	0	1+
Vortioxetine	0	0	0	0	0	3+	0	1+

Masennuslääkkeiden sivuvaikutukset:

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025

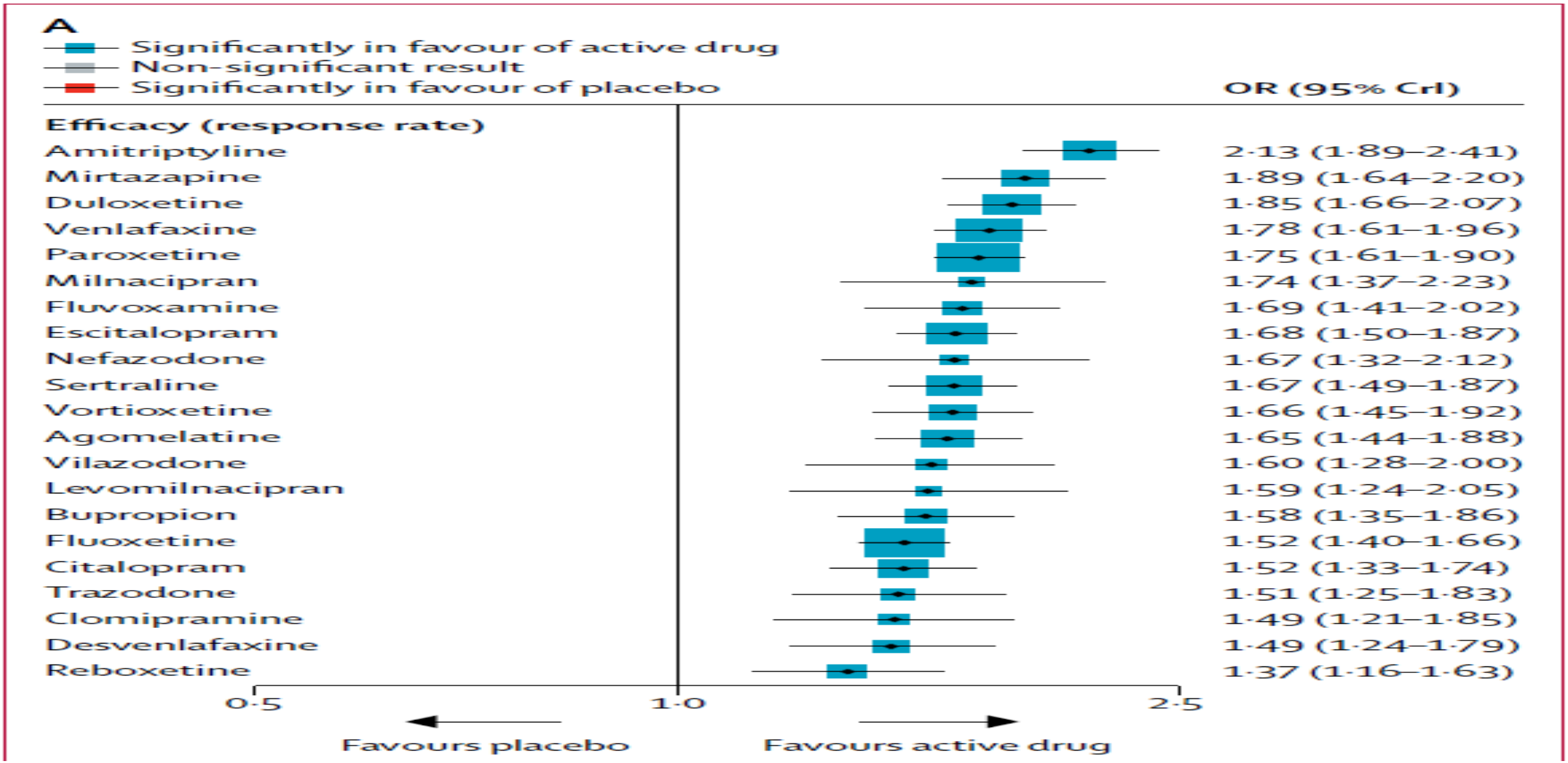
Side effects of antidepressant medications[1-7]

= 2 = 3 = 4

Drug	Anticholinergic	Drowsiness	Insomnia/ agitation	Orthostatic hypotension	QTc prolongation*	Gastrointestinal toxicity	Weight gain	Sexual dysfunction
Tricyclic and tetracyclic antidepressants								
Amitriptyline	4+	4+	0	3+	1 to 2+	1+◇◇	4+	3 to 4+
Ei Amoxapine	2+	2+	2+	2+	ND§§	0◇◇	2+	ND
Clomipramine	4+	4+	1+	2+	3+	1+◇◇	4+	4+
Desipramine	1+	2+	1+	2+	1 to 2+	0◇◇	1+	ND
Ei Doxepin	3+	3+	0	2+	3+	0◇◇	4+	3+
Imipramine	3+	3+	1+	4+	3+	1+◇◇	4+	3+
Maprotiline	2+	3+	0	2+	1+	0◇◇	2+	ND
Nortriptyline	2+	2+	0	1+	1 to 2+	0◇◇	1+	ND
Ei Protriptyline	2+	1+	1+	2+	ND§§	1+◇◇	1+	3 to 4+
Ei Trimipramine	4+	4+	1+	3+	ND§§	0◇◇	4+	ND
Monoamine oxidase inhibitors								
Ei Isocarboxazid	1+	1+	2+	2+	0	1+	1+	4+
Ei Phenelzine	1+	2+	1+	3+	0	1+	2+	4+
Selegiline	1+	0	1+	1+	0	0	0	0
Ei Tranylcypromine	1+	1+	2+	2+	0	1+	1+	4+

Scale: 0 = none; 1+ = slight; 2+ = low; 3+ = moderate; 4+ = high; ND = inadequate data.

Andrea Cipriani,et al Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis, 2018



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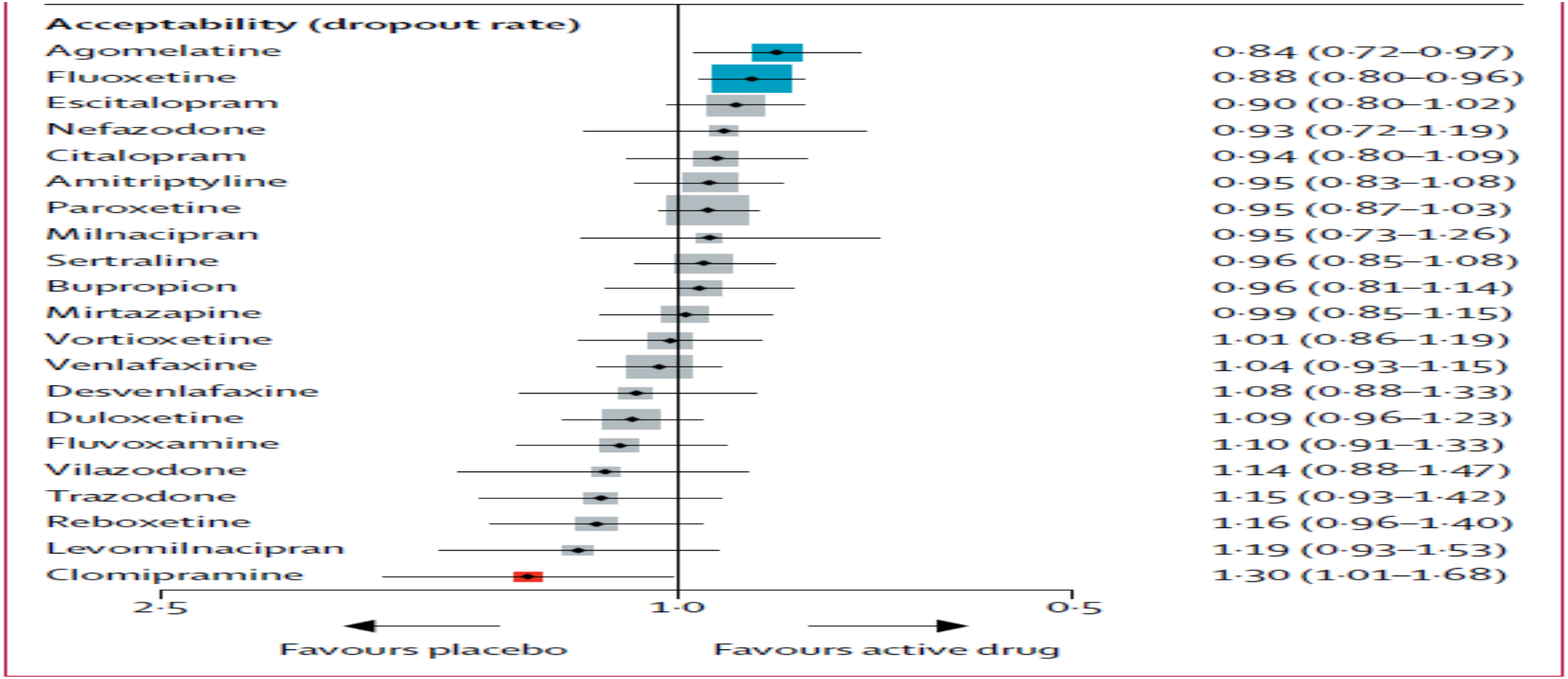

Figure 3: **Forest plots of network meta-analysis of all trials for efficacy (A) and acceptability (B)**
Antidepressants were compared with placebo, which was the reference compound. OR=odds ratio. CrI=credible interval.

Masennuksen hoito:

Meta-analyysi (Cipriani et al, 2018
Superior efficacy
- **Escitalopram**
- **Mirtazapine**
- **Sertraline**
- **Venlafaxine**

Meta-analyysi (Cipriani et al, 2018)
Lower dropout
- **Escitalopram**
- **Sertraline**

Meta-analyysi (Cipriani et al, 2018)
Superior efficacy with good tolerability
- **Agomelatine**
- **Escitalopram**
- **Mirtazapine**
- **Paroxetine**
- **Sertraline**
- **Vortioxetine**

Masennuslääke

Esimerkkejä lääkeaineryhmittäin:

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

SNRI-lääkkeet
- duloksetiini
- milnasipraani
- venlafaksiini

Trisykliset
- amitriptyliini

Muut
- mirtatsapiini
- moklobemidi
- reboksetiini

- Voxra — Bupropioni
- Valdoxan — Agomelatine
- Brintellix — Vortioxetine

Table 5. Recommendations for Clinical Specifiers and Dimensions of Major Depressive Disorder.

Mitä lääkettä mihinkin masennukseen?

Specifiers/ Dimensions	Recommendations (Level of Evidence)	Comments
With anxious distress[a]	• Use an antidepressant with efficacy in generalized anxiety disorder (Level 4)	• No differences in efficacy between SSRIs, SNRIs, and bupropion (Level 2)
With catatonic features[a]	• Benzodiazepines (Level 3)	• No antidepressants have been studied
With melancholic features[a]	• No specific antidepressants have demonstrated superiority (Level 2)	• TCAs and SNRIs have been studied
With atypical features[a]	• No specific antidepressants have demonstrated superiority (Level 2)	• Older studies found MAO inhibitors superior to TCAs
With psychotic features[a]	• Use antipsychotic and antidepressant cotreatment (Level 1)	• Few studies involved atypical antipsychotics
With mixed features[a]	• Lurasidone[b] (Level 2) • Ziprasidone[b] (Level 3)	• No comparative studies
With seasonal pattern[a]	• No specific antidepressants have demonstrated superiority (Level 2 and 3)	• SSRIs, agomelatine, bupropion, and moclobemide have been studied
With cognitive dysfunction	• Vortioxetine (Level 1) • Bupropion (Level 2) • Duloxetine (Level 2) • SSRIs (Level 2)[b] • Moclobemide (Level 3)	• Limited data available on cognitive effects of other antidepressants and on comparative differences in efficacy

Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder, Vol 61 Number 9 September 2016, 504-588

Table 5. Recommendations for Clinical Specifiers and Dimensions of Major Depressive Disorder.

Mitä lääkettä mihinkin masennukseen?

Specifiers/ Dimensions	Recommendations (Level of Evidence)	Comments
With sleep disturbances	• Agomelatine (Level 1) • Mirtazapine (Level 2) • Quetiapine (Level 2) • Trazodone (Level 2)	• Beneficial effects on sleep must be balanced against potential for side effects (e.g., daytime sedation)
With somatic symptoms	• Duloxetine (pain) (Level 1) • Other SNRIs (pain) (Level 2) • Bupropion (fatigue) (Level 1) • SSRIs[b] (fatigue) (Level 2) • Duloxetine[b] (energy) (Level 2)	• Few antidepressants have been studied for somatic symptoms other than pain • Few comparative antidepressant studies for pain and other somatic symptoms

MAO, monoamine oxidase; SNRI, serotonin and noradrenaline reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.
[a]*DSM-5* specifiers.
[b]Comparisons only with placebo.

Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder, Vol 61 Number 9 September 2016, 504-588

Appendix C: First-Line Antidepressants

"First-line" antidepressant treatment represents a balance of efficacy, tolerability and expert consideration per the Canadian Network for Mood and Anxiety Treatments (CANMAT) recommendations. Other pharmacotherapies are reserved for situations where first-line antidepressants are not indicated or cannot be used, or when first-line treatments have not worked.

Generic Name (Trade Name), Dosage Forms and Strengths	Usual Adult Daily Dose*	Adverse Reactions	Cost per 30 Days †	Therapeutic Considerations	Elimination Half-Life (h)
Selective Serotonin Reuptake Inhibitors (SSRIs) Note: SSRIs can be associated with prolonged corrected QT interval. This can lead to Torsades de Pointes (a rare cardiac arrhythmia), especially at higher doses and if taking multiple QT interval prolonging medications. Risk factors for QT prolongation syndrome include: low ventricular ejections fraction (<40%), left ventricular hypertrophy, dilated cardiomyopathy; myocardial ischemia, myocarditis; congenital long QT syndrome; bradycardia, AV and SA blocks; electrolyte abnormalities (hypokalemia, hypomagnesemia, hypocalcemia); use of multiple QT interval prolonging medications, older age (> 65 years); and female sex. For those at significant risk, baseline and follow up ECGs may be warranted using clinical judgment, but routine ECG monitoring prior to starting an antidepressant in every patient is not necessary.					
citalopram (Celexa®, CTP 30®, G) Tabs: 10 mg, 20 mg, 30 mg, 40 mg	Usual: 10-40 mg Maximum: 40 mg	**CNS:** sleep disturbances (insomnia, sedation), tremor, headache **CVS:** orthostatic hypotension, ECG changes **Anticholinergic:** dry mouth, sweating, constipation **GI:** nausea, vomiting, diarrhea, constipation, ↑ risk of GI bleed **Sexual disturbances:** ↓ libido, impotence, ejaculatory disturbances, anorgasmia. (likely to persist during SSRI therapy) **Hyponatremia:** can occur. (may cause fatigue or delirium) **Serotonin Syndrome:** agitation, tachycardia, tremor hyperreflexia. (combination with other serotonergic dugs also increase risk of syndrome) **Bleeding risk[5,6]:** especially when combined with ASA, NSAID or anticoagulants.	$6-11 (Regular coverage)	• [5] SSRIs have "flat" dose-response curves. For depression, most patients respond to initial lower dose. Higher doses are used for treatment of OCD. Do not ↑ dose until steady state is reached (i.e., ~4 weeks for fluoxetine, and 1-2 weeks for others). • Therapeutic effect seen after 7-28 days. • Citalopram and escitalopram have fewest drug interactions among SSRIs. • Fluoxetine is most anorexic and stimulating, has active metabolite and has long half-life. • Fluvoxamine is most nauseating, constipating and sedating among SSRIs (can be given at bedtime). • Paroxetine has most anticholinergic adverse effects & anxiety, and can cause weight gain. • Sertraline has most diarrhea and male sexual dysfunction among SSRIs. It has few drug interactions.	23-45
escitalopram (Cipralex®, Cipralax MELTZ®) Tabs: 10 mg, 20 mg Orodispersible Tabs: 10 mg, 20 mg	Usual: 10-20 mg Maximum: 20 mg (or 10 mg in elderly, patients with liver problems, on omeprazole or cimetidine)		$56-60 (Tabs: Regular coverage)		27-32
fluoxetine (Prozac®, G) Caps: 10 mg, 20 mg Solution: 20 mg/5 mL	Usual: 10-40 mg Maximum:[5] 80 mg		$15-30 (Regular coverage)		24-144 (parent); 200-330 (metabolite)
fluvoxamine (Luvox®, G) Tabs: 50 mg, 100 mg	Usual: 50-200 mg Maximum:[5] 300 mg		$7-25 (Regular coverage)		9-28
paroxetine (Paxil®, Paxil® CR, G) Tabs: 10 mg 20 mg, 30 mg, 40 mg CR Tabs: 12.5 mg, 25 mg	Usual: 10-40 mg (or 12.5-50 mg for CR tablets) Maximum:[5] 60 mg		$7-30 (Regular coverage)		3-65
sertraline (Zoloft®, G) Caps: 25 mg, 50 mg, 100 mg	Usual: 50-150 mg Maximum:[5] 200mg		$13-27 (Regular coverage)		22-36 (parent); 62-104 (metabolite)

Appendix C: First-Line Antidepressants

"First-line" antidepressant treatment represents a balance of efficacy, tolerability and expert consideration per the Canadian Network for Mood and Anxiety Treatments (CANMAT) recommendations. Other pharmacotherapies are reserved for situations where first-line antidepressants are not indicated or cannot be used, or when first-line treatments have not worked.

Generic Name (Trade Name), Dosage Forms and Strengths	Usual Adult Daily Dose*	Adverse Reactions	Cost per 30 Days †	Therapeutic Considerations	Elimination Half-Life (h)
Selective Serotonin Reuptake Inhibitors (SSRIs) Note: SSRIs can be associated with prolonged corrected QT interval. This can lead to Torsades de Pointes (a rare cardiac arrhythmia), especially at higher doses and if taking multiple QT interval prolonging medications. Risk factors for QT prolongation syndrome include: low ventricular ejections fraction (<40%), left ventricular hypertrophy, dilated cardiomyopathy; myocardial ischemia, myocarditis; congenital long QT syndrome; bradycardia, AV and SA blocks; electrolyte abnormalities (hypokalemia, hypomagnesemia, hypocalcemia); use of multiple QT interval prolonging medications, older age (> 65 years); and female sex. For those at significant risk, baseline and follow up ECGs may be warranted using clinical judgment, but routine ECG monitoring prior to starting an antidepressant in every patient is not necessary.					
Norepinephrine Dopamine Reuptake Inhibitors (NDRIs)					
bupropion (Wellbutrin® SR, Wellbutrin® XL, G) SR Tabs: 100 mg, 150 mg XL Tabs: 150 mg, 300 mg	Usual: 150-300 mg Maximum: 300 mg	**CNS:** sleep disturbances (insomnia, nightmares), agitation, seizures (high dose, or abrupt dose ↑), headache **CVS:** orthostatic hypotension, dizziness **GI:** ↓ appetite, anorexia	$8-37 (Regular coverage)	• SR Tabs: Max.150 mg per dose. Doses >150 mg per day should be given BID, preferably with ≥8 hours between doses. • XL Tabs: once daily dosing (AM). • Therapeutic effect seen after 7-28 days. • May ↓ seizure threshold. Contraindicated in patients with current or history of seizure disorder, bulimia or anorexia nervosa, or undergoing alcohol or benzodiazepine withdrawal. • Rarely inhibits sexual functioning.	10-14 (parent); 20-27 (metabolite)

Abbreviations: AM morning; **ASA** acetylsalicylic acid; **AV** atrioventricular nodal; **BID** twice daily; **BP** blood pressure; **Caps** capsules; **CNS** central nervous system; **CR** controlled-release; **CVS** cardiovascular system; **ECG** electrocardiogram; **G** generic brands available; **GI** gastrointestinal; **HR** heart rate; **max** maximum; **mg** milligrams; **mL** millilitres; **NSAID** Nonsteroidal anti-inflammatory drugs; **OCD** obsessive-compulsive disorders; **REM** rapid eye movement; **SA** sinoatrial nodal; **SR** sustained-release; **SSRI** selective serotonin reuptake inhibitor; **Tabs** tablets; **XL** or **XR** extended-release.

Footnotes:

* Dose should be individualized. Dosage adjustment may be required in patients with hepatic or renal impairment. Refer to latest product monographs and regularly review current Health Canada advisories, warnings and recalls at www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html.

† Pricing is approximate as per PharmaCare Formulary Search on May 23, 2013 (www.health.gov.bc.ca/pharmacare/benefitslookup/) and does not include dispensing fee or additional markups. They are calculated based on the "Usual adult daily doses" in this table. "Regular coverage", also known as "regular benefit", does not require Special Authority. Regular benefit drugs may be fully or partially covered. Coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles. See: www.health.gov.bc.ca/pharmacare/plans/index.html and www.health.gov.bc.ca/pharmacare/policy.html for further information.

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5. Paton C, Ferrier IN. SSRIs and gastrointestinal bleeding: Gastroprotection may be justified in some patients. BMJ. 2005; 331(7516): 529–530.
6. Yuan Y, Tsoi K, Hunt RH. Selective serotonin reuptake inhibitors and risk of upper GI bleeding: Confusion or confounding? Am J Med. 2006;119(9): 719–727.

Dr Biswadeep Das ?

Serotonin Syndrome

- Potentially life-threatening condition caused by excessive serotonergic activity in CNS
- Characterized by:
  - Mental status changes
  - Autonomic instability, &
  - Neuromuscular hyperactivity
- Most cases reported in patients:
  - Using multiple serotonergic drugs or
  - Who have had considerable exposure to a single serotonin-augmenting drug
- Diagnostic Criteria: Dursun/Hunter/Radomski/Sternbach

Dr Biswadeep Das

?

Serotonin Syndrome

- Diagnosis is made using the Hunter Serotonin Toxicity Criteria
- Require the presence of ONE of the following classical features or groups of features:
  - Spontaneous clonus
  - Inducible clonus + [agitation OR diaphoresis]
  - Ocular clonus + [agitation OR diaphoresis]
  - Tremor + hyperreflexia
  - Hypertonia + Temperature > 100.4°F(38°C) +[ocular clonus OR inducible clonus]

[Ables AZ, Nagubilli R. Prevention, recognition and management of serotonin syndrome. Am Fam Physician 2010; 81(9): 1139-42.]

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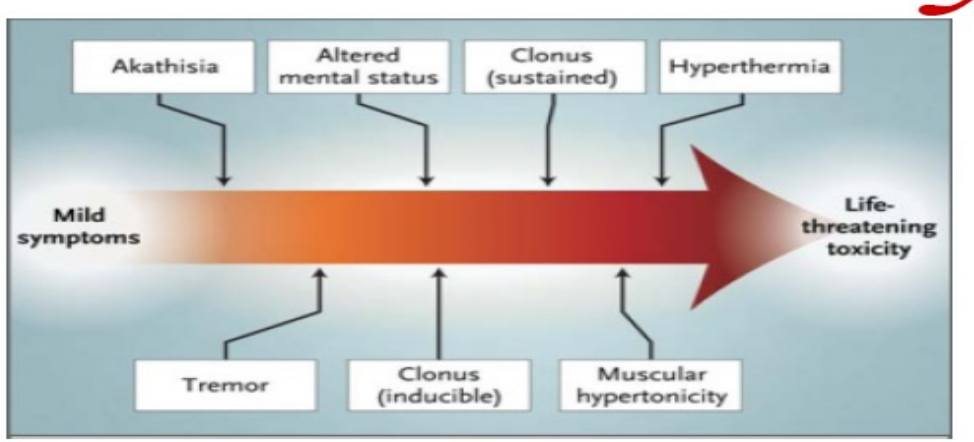
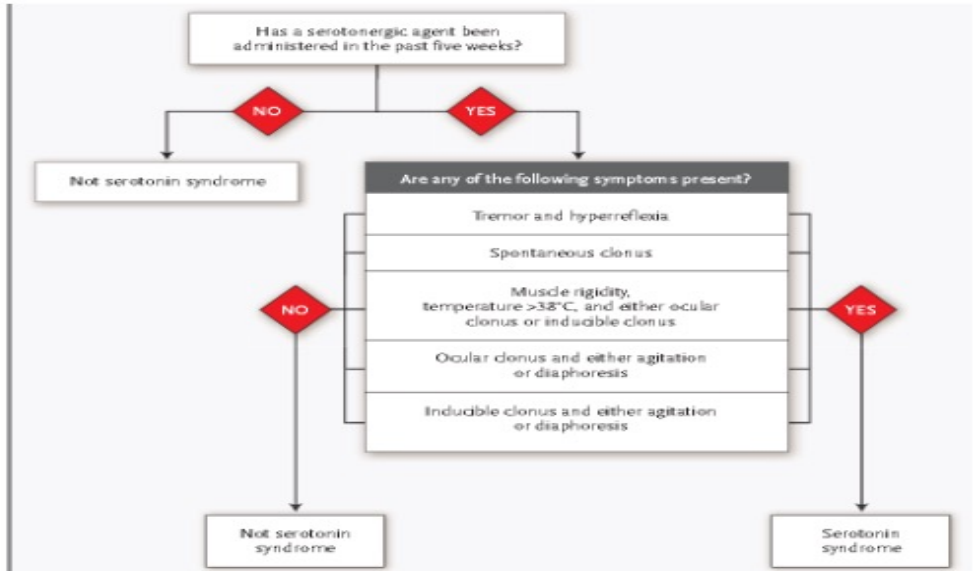
Serotonin Syndrome





1 Drugs that have been associated with serotonin toxicity

Serotonin reuptake inhibitors

- *Selective serotonin reuptake inhibitors:* fluoxetine, fluvoxamine, paroxetine, citalopram, sertraline, escitalopram
- *Other antidepressants*: venlafaxine, clomipramine, imipramine
- *Opioid analgesics:* pethidine, tramadol, fentanyl, dextromethorphan
- St John's wort

Monoamine oxidase inhibitors

- *Irreversible monoamine oxidase A inhibitors:* phenelzine, tranylcypromine
- *Reversible monoamine oxidase A inhibitors:* moclobemide
- *Others:* linezolid

Serotonin-releasing agents

- Fenfluramine
- Amphetamines
- Methylenedioxymethamphetamine (MDMA; ecstasy)

Miscellaneous

- Lithium
- Tryptophan

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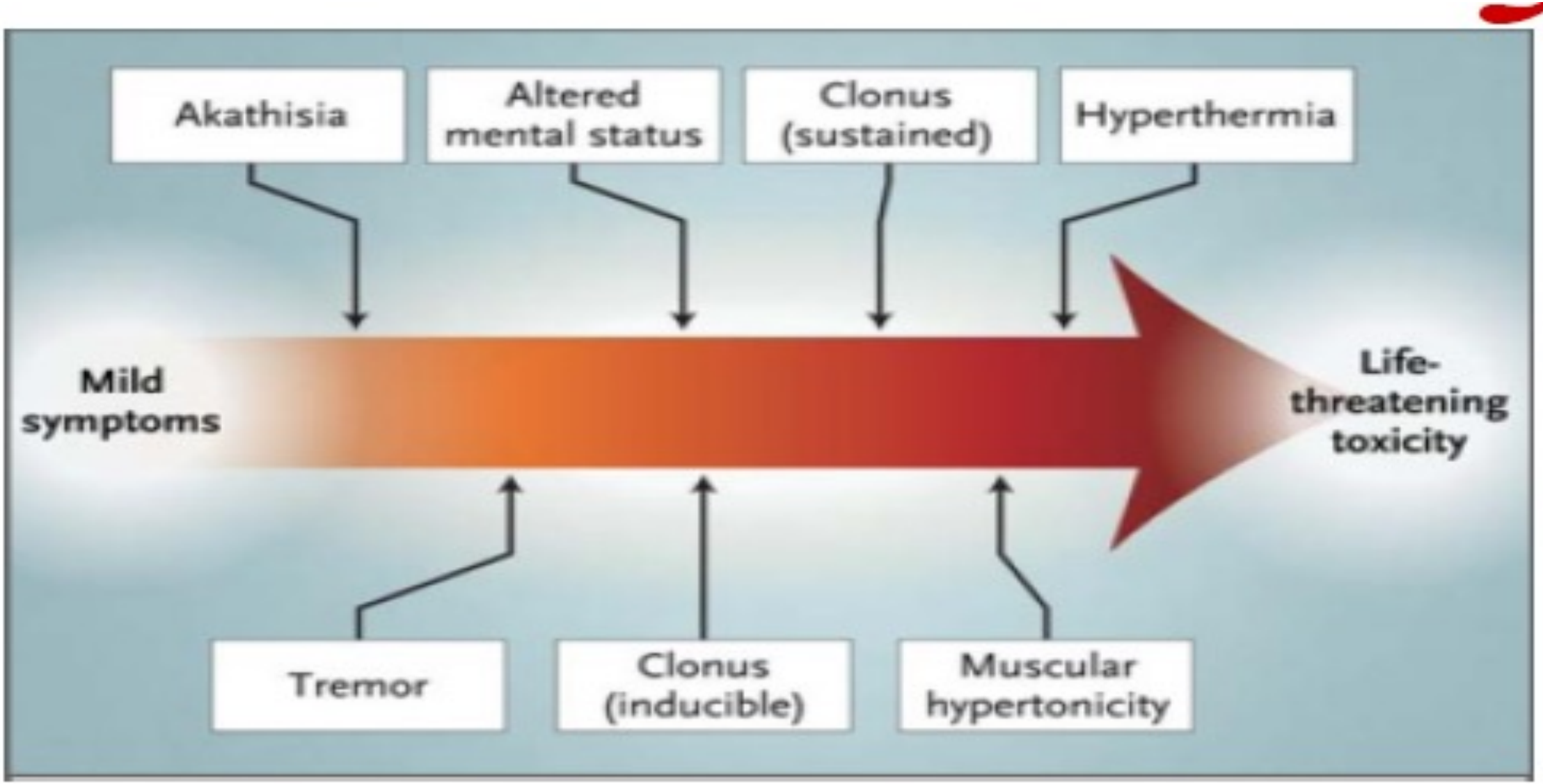

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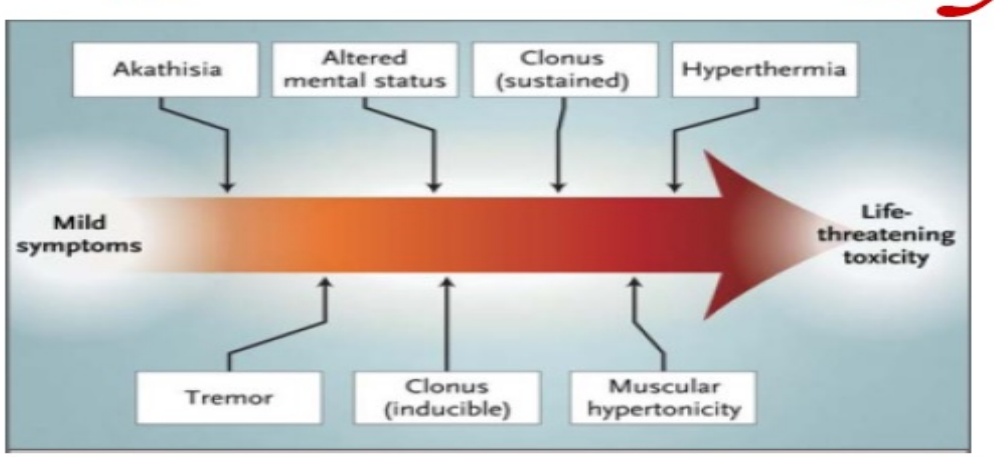
Serotonin Syndrome



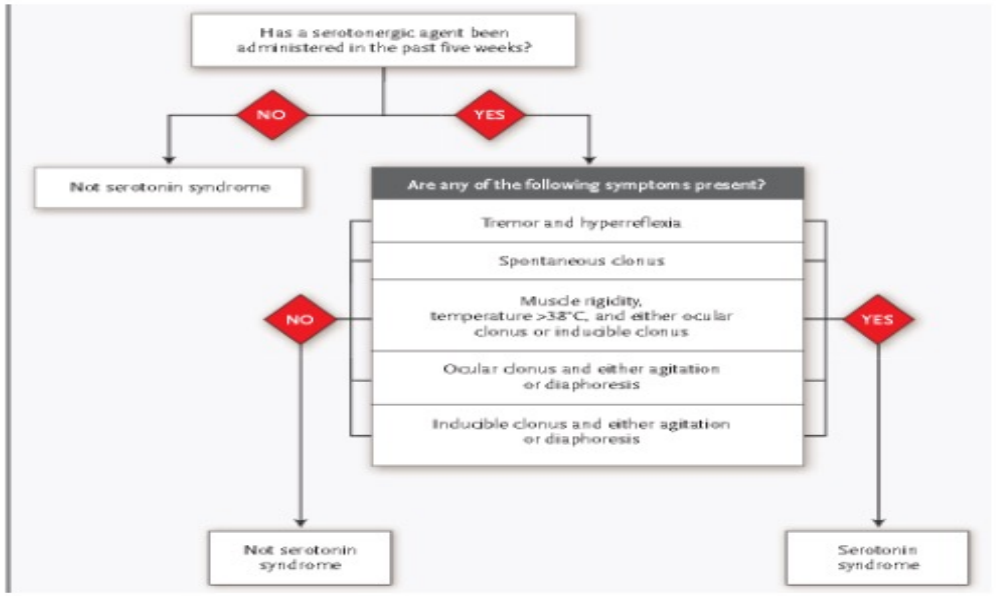


Table 2

Combinations That May Result in Serotonin Syndrome

All SSRIs in combination
Venlafaxine & lithium
Venlafaxine & moclobemide
Venlafaxine & fluoxetine
Venlafaxine & mirtazapine
Fluoxetine & sertraline
Fluoxetine & tramadol
Trazodone & buspirone
Clomipramine & MAOI
Clomipramine & trazodone
Clomipramine & moclobemide
Dextromethorphan & paroxetine
Dextromethorphan & moclobemide
Linezolid & citalopram
SSRI & St. John's wort
SSRI & MAOI
Meperidine & MAOI

SSRI: selective serotonin reuptake inhibitor; MAOI: monoamine oxidase inhibitor.
Source: References 2, 6, 9.

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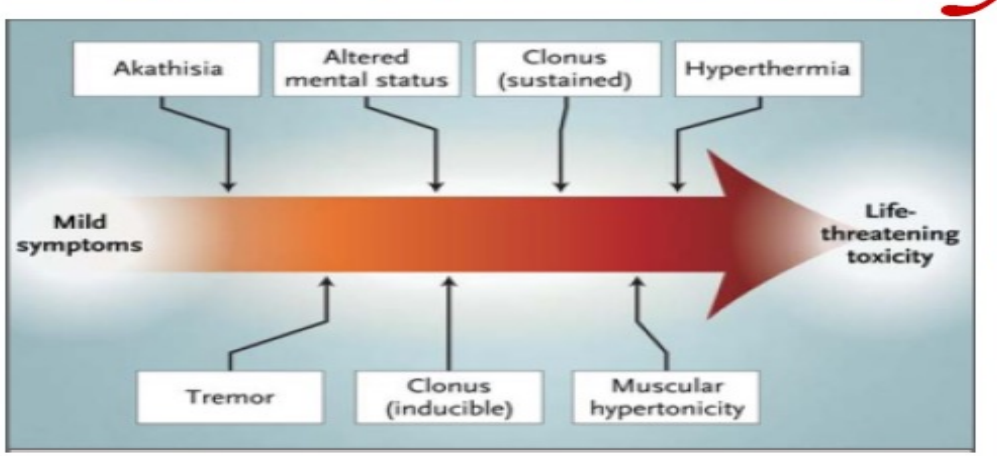
Serotonin Syndrome



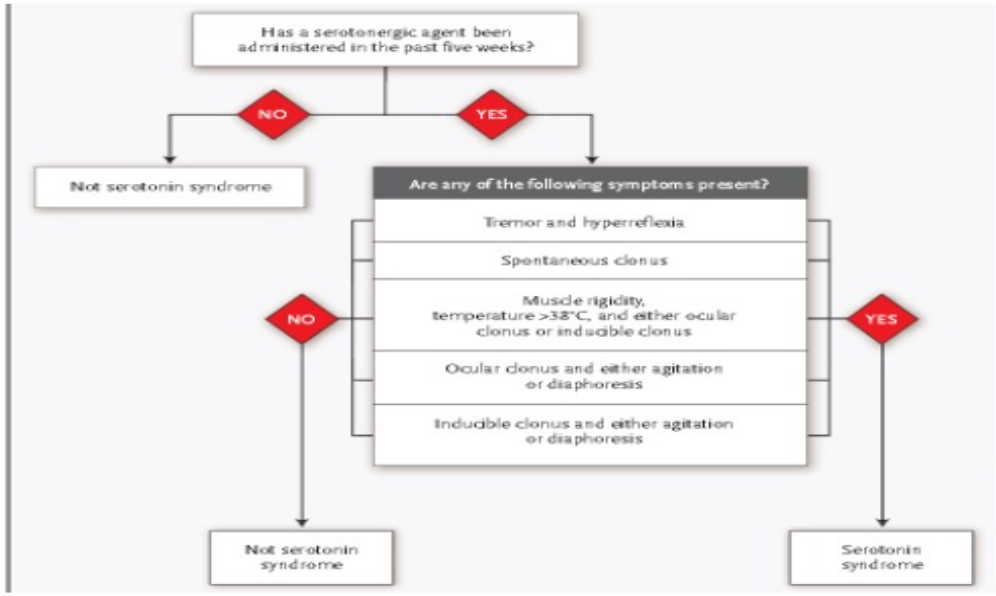


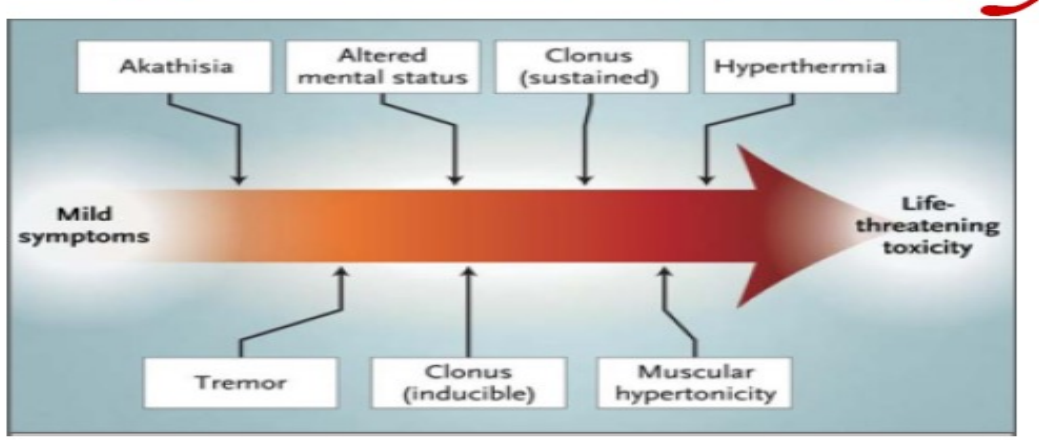
Table 4

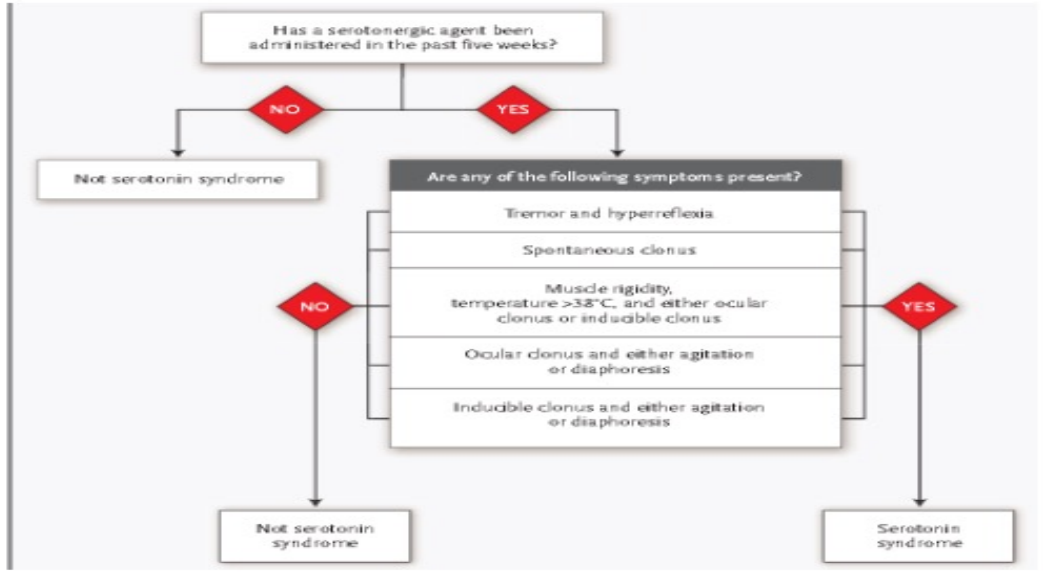
Clinical Presentation of Serotonin Syndrome and Differential Diagnosis

Clinical Presentation	Serotonin Syndrome	NMS	Anticholinergic Delirium
Tachycardia	+	+	+
Hypertension	+	+	+
Muscle rigidity	+	+	–
Hyperthermia >41.1°C	+	+	–
Hyperreflexia	+	–	–
Myoclonus	+	–	–
Shivering	+	–	–
Acute onset	–	–	+
Restlessness, confusion, agitation	+	–	+
Bowel sound	+	–	–

NMS: neuroleptic malignant syndrome; +: present; –: not present.
Source: Reference 2.

Serotonin Syndrome





- Most cases of SS are mild
- Treated by
  - Withdrawal of the offending agent +
  - Supportive care
- Benzodiazepines used to treat agitation + tremor
- Cyproheptadine used as an antidote
- Patients with moderate or severe cases of SS require hospitalization
- Critically ill patients may require:
  - Neuromuscular paralysis
  - Sedation, &
  - Intubation

5. Masennuksen psykoedukaatio

Yl juha kemppinen

Masennuksen psykoedukaatio:

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025

Education about depression and its initial treatment

What is depression
Depression is a common medical condition that affects the chemistry and functioning of the brain. It can be time limited or, occasionally, become chronic. **Masennus on ...**
Symptoms of depression
Depression can cause emotional symptoms, such as anger, anxiety, and sadness. It can also interfere with memory and concentration and cause physical symptoms, such as fatigue, lack of energy, and agitation. Depression can sometimes cause or worsen existing physical symptoms, such as headache, abdominal or other pain, and muscle tension. Suicidal thoughts and behavior may also occur. **Oireet ovat...**
Rationale for treatment
Depression is a treatable medical condition. Antidepressant medications and psychotherapy are evidence-based treatments that improve depression outcomes. **Hoidettava tauti...**
Benefits of antidepressant treatment and psychotherapy include symptom resolution, return to normal function, reduced risk of relapse, and potential improvement in outcomes of other chronic diseases (eg, diabetes and cardiovascular disease). **Lääkityksen ja psykoterapian hyödyt...**
Earlier treatment may be more effective than delayed treatment in achieving remission.
Treatment options
Treatment options for depression include antidepressants, psychotherapy, or both. Exercise can also be effective. **Eri hoitovaihtoehtoja ...**
Key points about psychotherapy
Psychotherapy is as effective as antidepressants for treating most cases of depression. Some types of psychotherapy with efficacy for treating depression include cognitive-behavioral therapy, interpersonal therapy, and problem-solving therapy. Therapy can be short term (8 to 16 sessions). **Psykoterapia kuin lääke, lyhytkin ...**
Key points about taking antidepressants
Antidepressants need to be taken every day to work. **Vain otettu lääke auttaa...**
Discuss what time of day is best to take the medication and whether to take it with food. **Milloin lääke, ruuan kanssa vai ilman...**
Discuss ways to remember to take the medication. **Miten muistaa ottaa...**
Give specific instructions on when to increase the dose of the antidepressant. Discuss that most people start with a low dose and then gradually increase the dose to maximize its effectiveness. **Milloin annosta pitää nostaa...**

Education about depression and its initial treatment

Antidepressant side effects
Side effects with antidepressants are common during initial treatment, but many are minor and improve or resolve after the first 2 weeks.
Provide information about common side effects of the prescribed antidepressant.
For SSRIs/SNRIs: Discuss that antidepressants can transiently increase anxiety, agitation, and/or irritability. In young adults, they can occasionally increase suicidal thoughts. If these symptoms are severe or a marked departure from baseline symptoms, the patient should contact their clinician.
Time frame for response to treatment with antidepressants
Symptom improvement can occur as early as 1 to 2 weeks; however, for some patients, a response will require 6 to 12 weeks.
Some patients will not improve after 6 to 12 weeks and may need to try another antidepressant.
Duration of treatment with antidepressants
Patients should continue antidepressant treatment for at least 6 months **after** their symptoms return to baseline. Early discontinuation of antidepressants can increase the risk of relapse.
Tailor duration of antidepressant treatment to the individual patient. Dosing should aim to achieve a maximal, but well-tolerated, dose.
How to discontinue the antidepressant
Abrupt discontinuation of antidepressants occasionally causes withdrawal symptoms, especially in patients who have been taking the antidepressant for many months. Discontinuation symptoms do not indicate addiction or dependence.
Patients taking the antidepressant for more than 2 weeks should taper the dose. The rapidity of taper varies depending on the specific antidepressant and how long the patient has been taking the medication. It should be adjusted if patients develop symptoms during tapering. Patients taking the antidepressant for less than 2 weeks can stop without tapering.
Patients who decide to discontinue their antidepressant should contact their clinician to discuss how to do so.
When to contact the clinician
Patients should contact their clinician if: ▪ They have more frequent or new onset of thoughts of death or thoughts of hurting themselves or someone else. ▪ Symptoms or medication side effects are difficult to tolerate, especially worsened anxiety/agitation or insomnia. ▪ They stop or are considering stopping depression medication or psychotherapy. ▪ Symptoms are worsening or not getting better. ▪ They become pregnant or are considering pregnancy.

Lääkkeen sivuvaikutukset ovat tavallisia ensimmäiset 2 vkoa...

Mitä sivuvaikutukset ovat ...

Lääkevaikutus voi tulla 1-2 vkoa...

mutta jopa 6-12 vkon kuluttua... ei auta kaikilla

Lääkettä 6kk oireettomuuden jälkeen...

Lääkettä max siedettävä annos ...

Lääke kka, äkillinen lopetus :vieroitusoireet?...

Lääkettä yli 2 vkoa, asteittain lopetus...

Milloin yhteys lääkäriin?

- Itsen tai vahingoittamisen ajatuksia tullu
- Sivuvaikutukset sietämättömiä
- Lääke ja/tai psykoterapianlopetusajatus
- Oireet eivät väisty
- Raskaus...

6. Masennuksen hoidon optimointi

Yl juha kemppinen

OPTIMIZING TREATMENT

Education and engagement — Patients with major depression are often reluctant to engage in treatment [26]. In a prospective study of patients who presented for initial treatment of depression (n>4000), more than 10 percent did not return for treatment after the initial evaluation [26,139]. Another 30 percent did not complete the first eight weeks of treatment, indicating a failure to retain patients who were initially engaged.

To enhance treatment engagement, we use the following strategies:

- **Assessing patient perception of depression** – We start by eliciting the patient's perspectives about depression. In many communities, depression is still stigmatized. Common misconceptions include the belief that depression is a character defect or sign of personal weakness, or that individuals with depression are "crazy," will not get better, or should be able to resolve their depression "on their own." Patients are also frequently misinformed about psychotherapy and antidepressant agents. Eliciting the patient's beliefs, expectations of, and fears about treatment can help to tailor the treatment approach and potentially optimize engagement in it.

  - **Education** – Individuals who understand and accept the diagnosis of depression may be more likely to engage in treatment [22]. We tailor education about depression to the patient's specific perspectives, information gaps, and priorities. General parameters to address when educating patients about depression appear in the table (table 7).

  - **Active surveillance for selected patients** – Initial management with active surveillance (watchful waiting) may facilitate treatment engagement for individuals who are reluctant to start medications or psychotherapy. This is a reasonable short-term choice for those with milder symptoms (eg, nine-item Patient Health Questionnaire [PHQ-9] score 5 to 14 (table 3) without suicidal plans or behavior). Active surveillance includes regular, brief follow-up visits (eg, every two to three weeks), during which clinicians monitor symptoms and provide support while helping patients link their problems with mood, motivation, sleep, appetite, energy, and cognition and impaired social and occupational functioning to depression. This, in turn, may help them accept treatment.

    Active surveillance is not appropriate for depressed patients who are severely symptomatic (eg, PHQ-9 score ≥15), chronically depressed (eg, ≥2 years), or substantially impaired (eg, unemployed).

  - **Framing treatment as a trial** – Framing medication or psychotherapy as a trial (rather than a long-term commitment) may help persuade some individuals to start treatment.

OPTIMIZING TREATMENT

Education and engagement — Patients with major depression are often reluctant to engage in treatment [26]. In a prospective study of patients who presented for initial treatment of depression (n>4000), more than 10 percent did not return for treatment after the initial evaluation [26,139]. Another 30 percent did not complete the first eight weeks of treatment, indicating a failure to retain patients who were initially engaged. **Con´t**

- **Using monitoring to engage patients** – Monitoring patients' symptoms over time using symptom scales, such as the PHQ-9, may also help to engage patients in care and active self-management [26] (see 'Ongoing monitoring and follow-up' below). Patients who see objective improvement in their symptoms may better adhere to their treatment plans and remain engaged in treatment [28]. Patients generally accept incorporation of symptom scales into the management of their depression, particularly if the scales are short. The acceptability and potential benefits of using scales to monitor depression care are discussed in detail separately. (See "Using scales to monitor symptoms and treat depression (measurement-based care)".)

Ongoing monitoring and follow-up

- **Frequency of follow-up** – We arrange prompt follow-up for all patients with major depression. For initial follow-up, we see all patients within the first two weeks (in person or via telehealth) to check for treatment adherence and side effects, adjust antidepressant doses, complete any outstanding diagnostic evaluation, and plan next steps.

  Subsequent follow-up frequency varies depending on the patient's symptom severity, comorbidities, psychosocial stressors, and level of support from family and friends [140,141]. Individuals with severe major depression or those initiating antidepressants should be reassessed more frequently (ie, within two to four weeks). Those with less severe, stable symptoms can have less frequent follow-up (four to eight weeks). We space out follow-up intervals as patients' symptoms improve and they are on stable medication doses and/or in psychotherapy. Following remission, the frequency of assessments can be tapered. (See "Major depressive disorder in adults: Continuation and maintenance treatment", section on 'Monitoring patients'.)

- **Monitoring symptoms and response to treatment** – We encourage frequent follow-up to monitor symptoms, assess treatment response, ensure follow-through with referrals and/or medication adherence, and build a therapeutic alliance. We ask about new or worsening symptoms of suicidal thoughts or behavior, psychosis, agitation, and anxiety [29]. Using symptom scales to monitor depression care is consistent with multiple practice guidelines, including those from the American Psychiatric Association, and there is evidence suggesting that most patients like this monitoring [22,24,25,28,29,142-144].

  In those who are taking antidepressants, we also ask about and address medication side effects (see "Major depressive disorder in adults: Initial treatment with antidepressants", section on 'Address side effects'). Additional recommendations for monitoring initial treatment with antidepressants are discussed separately. (See "Major depressive disorder in adults: Initial treatment with antidepressants", section on 'Monitoring initial treatment'.)

OPTIMIZING TREATMENT

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To quantify symptoms and response to treatment, all patients should complete a symptom rating scale at each visit, such as the PHQ-9. Using symptom scales can potentially improve treatment outcomes by informing antidepressant dose adjustments, more quickly identifying response to treatment, and helping to engage patients in treatment [145,146]. (See "Using scales to monitor symptoms and treat depression (measurement-based care)".)

- **Monitor treatment response** – Using symptom scales can identify those whose depression responds early, partially responds, or does not respond to antidepressant treatment. Because dysphoria and cognitive distortion that occur with depression can limit patients' capacity to sense symptom improvement, symptom scales can augment patients' subjective perception of treatment response. Conversely, identifying individuals with residual symptoms is important because they are associated with an increased risk of relapse, even in individuals whose depression has otherwise responded to treatment.

- **Increase remission** – Systematically monitoring depressive symptoms with a standardized scale may improve rates of remission. As an example, a meta-analysis of seven trials compared measurement-based care (using validated symptom scales [eg, PHQ-9 (table 3)] to guide treatment decisions) with standard care (clinical judgment alone) in patients taking antidepressants a depressive disorder [147]. Individuals randomized to measurement-based care were more likely to experience remission (53 versus 43 percent), symptom improvement, and adherence to pharmacotherapy (odds ratio [OR] 1.7; 95% CI 1.2-2.3). A second meta-analysis found small improvements in mental health outcomes at nine weeks in groups receiving measurement-based care compared with usual care; however, outcomes were equivalent at 3 and 12 months [148].

- **Using the nine-item Patient Health Questionnaire** – We use the PHQ-9 scale at each visit and/or telehealth encounter to monitor symptoms and assess treatment response. The PHQ-9 is a short, self-administered, widely available scale that has been extensively validated in diverse patient populations and different languages (table 3). Its questions correspond to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) diagnostic criteria for major depression and add an item that assesses psychosocial impairment [149,150].

  Patients rate each symptom item on a four-point Likert scale, indicating how often they have been bothered by the symptom over the past two weeks (0 = not at all, 1 = several days, 2 = more than half the days, 3 = nearly every day). Scores on the PHQ-9 range from 0 to 27, with higher scores indicating more severe symptoms. For monitoring depressive symptoms over time, a change of 5 or more is generally considered clinically meaningful [151]. The PHQ-9 has good reliability, internal consistency, and sensitivity to change in depression over time [152]. Its brevity makes it adaptable to use during a telephone call or secure message exchange.

  Alternative options for quantifying response to treatment include the Quick Inventory of Depressive Symptomatology – Self Report 16 Item ($QIDS\text{-}SR_{16}$) (table 8) and the 18-item Clinically Useful Depression Outcome Scale (CUDOS) (form 1). Self-report instruments for depression monitoring are discussed in detail separately. (See "Using scales to monitor symptoms and treat depression (measurement-based care)", section on 'Commonly used self-report depression scales'.)

OPTIMIZING TREATMENT

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System-level interventions and collaborative care — We suggest that patients with depression in primary care settings receive depression care in the context of system-levels interventions, such as collaborative care. Collaborative care involves treating patients with a team that usually includes a primary care clinician (who prescribes antidepressants), a case manager who provides support and outreach to patients, and a mental health specialist (eg, psychiatrist) who provides consultation and supervision [153-159]. Other elements include a structured treatment plan that involves pharmacotherapy and/or other interventions (eg, patient education or psychotherapy), scheduled follow-up visits, team-based communication, and measurement-based care (ie, using symptom scales, such as the PHQ-9, to monitor response to treatment and medication side effects).

Treating depressed primary care patients in the context of collaborative care is consistent with recommendations by the American College of Physicians and the American Psychiatric Association [7,22].

- **Improved depression outcomes** – Collaborative care improves depression outcomes, including rates of response and remission, psychosocial functioning, and mental and physical quality of life [157,160-166]. As an example, a 2012 meta-analysis of 79 randomized trials in over 24,000 participants found that treatment response at six months occurred more often with collaborative care (relative risk 1.3, 95% CI 1.2-1.4) than usual care and the benefits of collaborative care persisted for up to 24 months [157]. Similarly, in a meta-analysis of 10 randomized trials that included 20,110 participants, reduction of suicidal behavior was more likely with collaborative care than control interventions (pooled OR 0.66, 94% CI 0.49-0.78) [167]. Collaborative care may also improve patients' engagement in treatment and medication adherence [168]. However, beneficial effects on remission rates appear small [166].

- **Key components** – The following components of collaborative care are associated with improved depression outcomes [161,165,169,170]:

  - Case management provided by nurses or individuals with a mental health background
  - Routine supervision of case managers and caseload review by a mental health specialist (typically a psychiatrist)
  - At least two visits with the depression care manager within the first eight weeks of treatment
  - Primary care clinician follow-up within four weeks of initial presentation
  - Psychiatric intervention for patients who do not improve after eight weeks of treatment

OPTIMIZING TREATMENT

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- **Who benefits** – Collaborative care interventions have demonstrated efficacy across a wide range of patient populations, including those with and without additional medical comorbidities. Collaborative depression care is superior to usual care in treating individuals with chronic medical illness (eg, diabetes, cardiovascular disease, arthritis, asthma, and human immunodeficiency virus [HIV]), adolescents, military personnel, individuals attending obstetrics and gynecology clinics, patients with advanced cancer receiving palliative care, and pregnant and postpartum females with socioeconomic disadvantage [171-179].

- **Improving medical comorbidities** – Collaborative care can improve outcomes for general medical illnesses, such as diabetes. As an example, in a meta-analysis of seven trials of 1895 individuals with both depression and diabetes, patients randomized to collaborative care experience small but significant improvements in both depression symptom scores and hemoglobin A1C, compared with those randomized to usual care [180]. Study heterogeneity limited the strength of these findings. A subsequent open-label trial in India reported similar findings [181].

- **Role of telehealth** – Collaborative care via telehealth may be effective for small practices that lack on-site mental health specialists [159,182,183]. In a meta-analysis of 24 trials, virtual interventions (most consisting of cognitive-behavioral therapy [CBT]) increased rates of remission (OR 2.27, 95% CI 1.54-3.35) and decreased symptom severity (standardized mean difference 0.25, 95% CI 0.09-0.42), compared with treatment as usual and control interventions (ie, virtual education and progressive muscle relaxation) [184].

OPTIMIZING TREATMENT

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When to refer to specialty care

- **Psychotherapy** – Although psychotherapy can occur in primary care settings, most individuals who need psychotherapy will require referral to a mental health specialist, ideally a clinical psychologist with expertise in psychotherapy that has demonstrated efficacy for depression treatment (eg, CBT). (See 'Psychotherapy' above.)
- **Diagnostic uncertainty** – Individuals for whom the specific depression diagnosis is uncertain should be referred to a psychiatrist, particularly those with symptoms consistent with mania, hypomania (including individuals with depression with mixed features), catatonia, or psychosis. (See 'Depression with mixed features' below and "Bipolar disorder in adults: Assessment and diagnosis", section on 'Assessment' and "Unipolar major depression with psychotic features: Epidemiology, clinical features, assessment, and diagnosis" and "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis".)
- **Comorbid psychiatric disorders** – Individuals with comorbid psychiatric disorders that can complicate diagnosis and treatment can benefit from referral to a mental health professional, which could include a therapist or psychiatrist. These patients are at risk for poorer depression outcomes, even with appropriate treatment. (See "Depression in adults: Clinical features and diagnosis", section on 'Psychiatric'.)
- **Lack of response to initial treatment** – Patients who have not responded to two trials of initial treatment with antidepressants generally benefit from referral to a therapist for psychotherapy and/or a psychiatrist for medication management. Treatment-resistant depression is discussed separately. (See "Unipolar treatment-resistant depression in adults: Epidemiology, risk factors, assessment, and prognosis" and "Unipolar depression in adults: General principles of treating resistant depression".)
- **Severe depression** – Some individuals with severe MDD can safely be managed in primary care. However, patients with signs such as severe symptoms that are not responding to initial treatment; severe functional impairment; catatonia; suicidal behavioral or attempts; or frequent, intrusive suicidal thoughts or psychotic symptoms should be referred to a mental health specialist, especially if the primary clinician has limited experience caring for patients with depression. (See 'Severe major depression' above.)

Importance of follow-up

Follow-up is the key to the successful treatment of depression. Follow-up allows clinicians to monitor depressive symptoms, response to antidepressant therapy, and side effects. Patients should discuss when and how to follow up with their clinician and schedule regular appointments.

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

References:

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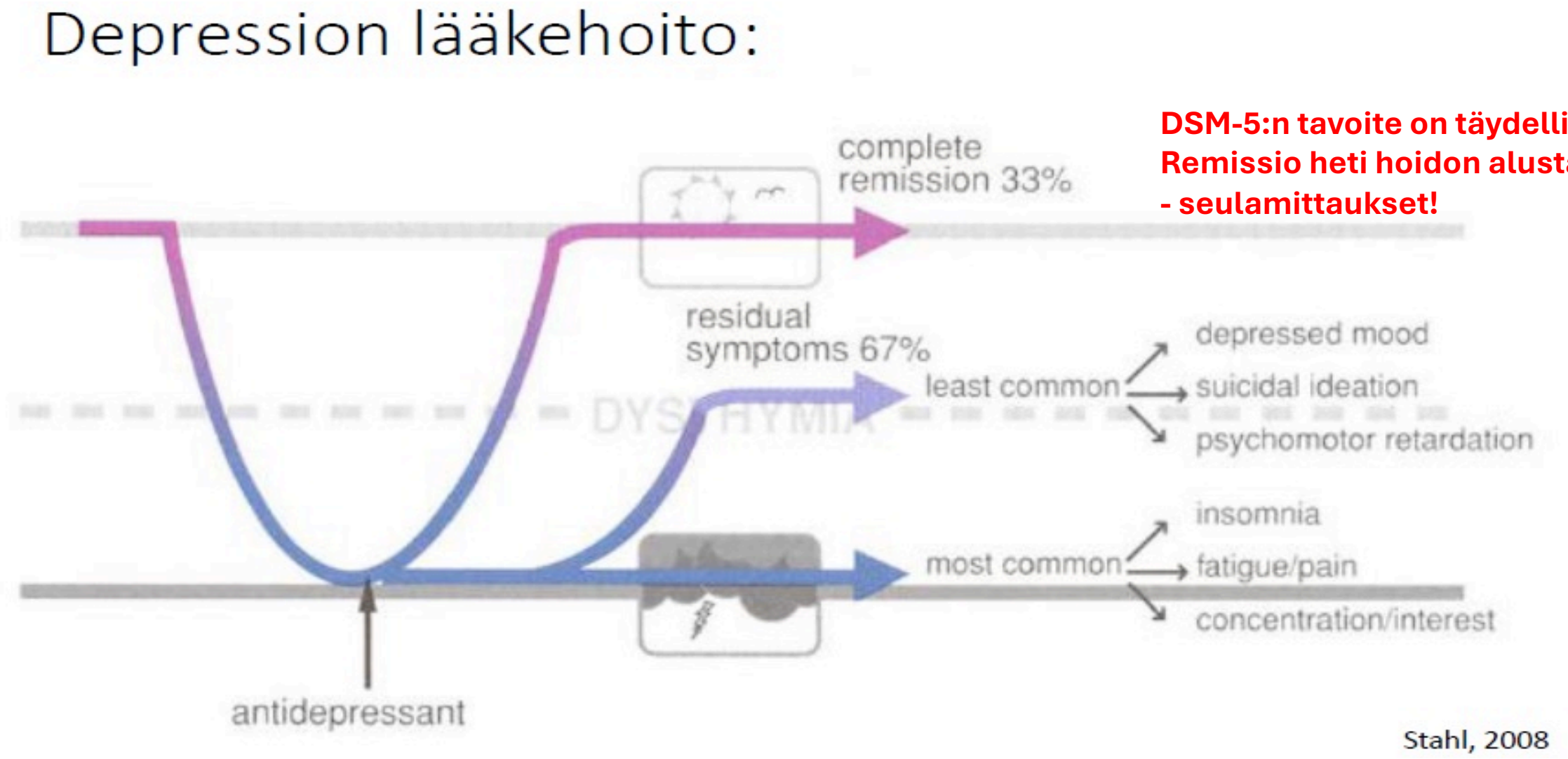
2. *McCarron RM, Shapiro B, Rawles J, Luo J. Depression. Ann Intern Med 2021; 174:ITC65.*
3. *Dell'Osso B, Albert U, Carrà G, et al. How to improve adherence to antidepressant treatments in patients with major depression: A psychoeducational consensus checklist. Ann Gen Psychiatry 2020; 19:61.*

7. Masennuksen hoidon räätälöinti

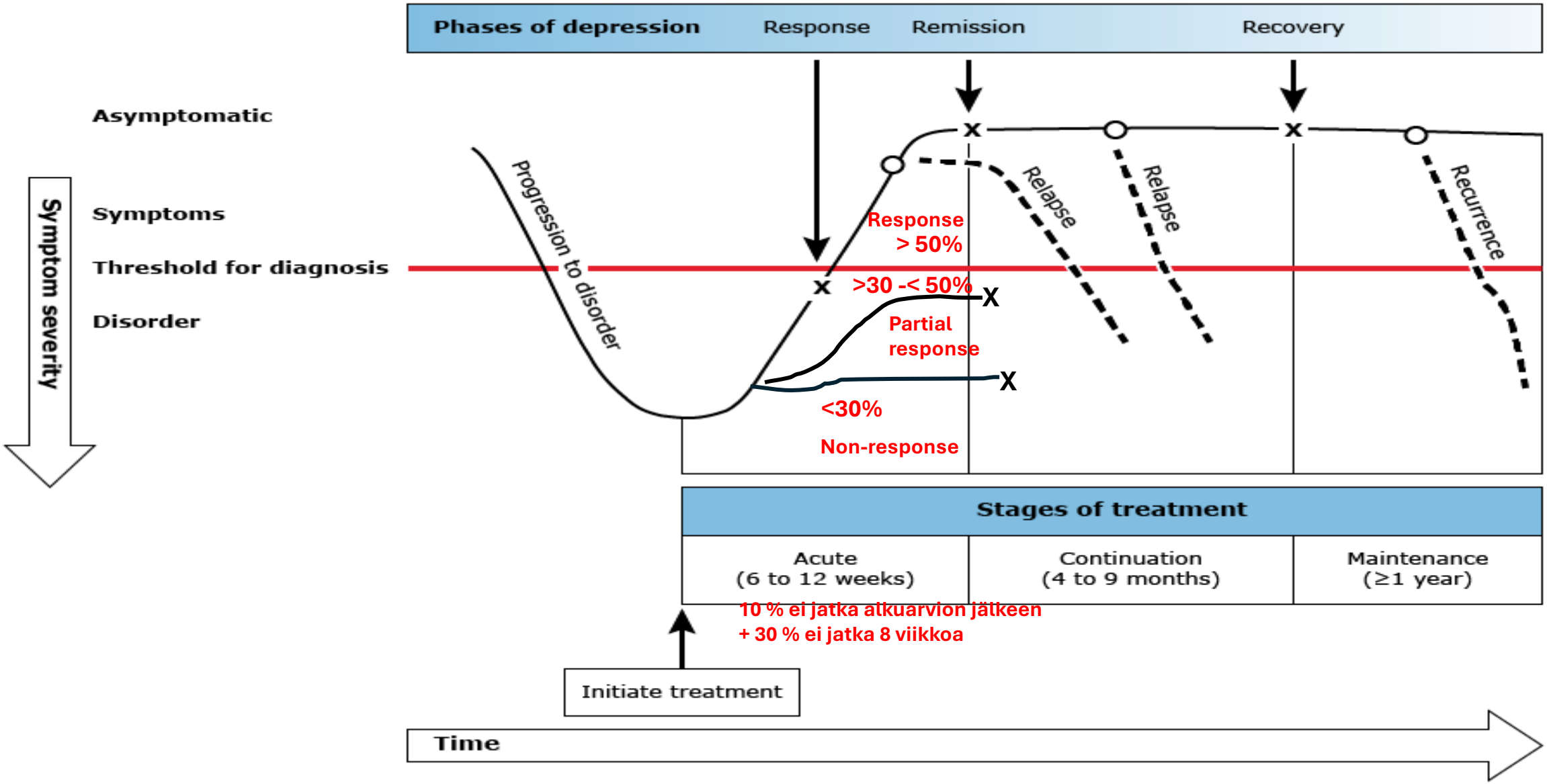
Yl juha kemppinen

Masennuksen hoito:



DSM-5:n tavoite on täydellinen Remissio heti hoidon alusta - seulamittaukset!

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025



Tailoring antidepressant selection — Although we typically choose SSRIs when initiating antidepressant therapy for the initial treatment of individuals with mild to moderate depression, specific patient characteristics often inform the selection of a specific SSRI or of antidepressants from other classes.

Addressing specific symptoms — We often choose an antidepressant that can address a patient's specific symptoms or coexisting conditions (eg, pain, anxiety, and tobacco use). Approaches to common situations appear in a table (table 8) and are discussed as follows:

- **Anxiety symptoms** – Symptoms of anxiety (eg, ruminative thoughts, worrying, and agitation) are common in individuals with MDD. Moreover, up to 75 percent of individuals with MDD have a co-occurring anxiety disorder, such as panic disorder or generalized anxiety disorder [41].

  The SSRIs are still a reasonable first choice in individuals with anxiety symptoms. SSRIs are also preferred agents for the initial pharmacotherapy of anxiety disorders (see "Generalized anxiety disorder in adults: Management" and "Social anxiety disorder in adults: Treatment overview" and "Panic disorder in adults: Treatment overview"). We typically start with one-half the usual initial antidepressant dose to minimize the transient activation that occurs with SSRIs and SNRIs.

  We generally avoid the use of bupropion in patients with significant anxiety. Adding a low-dose anxiolytic, such as clonazepam (0.25 or 0.5 mg at bedtime), can also treat anxiety symptoms and may enhance antidepressant adherence, particularly during the early stages of treatment. The indications and general principles for using anxiolytics, as well as their efficacy, are discussed separately. (See "Unipolar depression in adults: Treatment with anxiolytics".)

  Most evidence suggests that second-generation antidepressant agents are comparable for treating anxiety symptoms. As an example, a systematic review of 11 randomized trials of over 2300 participants with MDD found that different classes of second-generation antidepressants (SSRIs, SNRIs, atypical antidepressants, and serotonin modulators) showed similar efficacy in treating anxiety symptoms [42]. In contrast, an earlier review of 10 randomized trials of individuals with major depression and anxiety found higher response rates with SSRIs than bupropion in the subset of patients with high levels of anxiety symptoms [43].

- **Insomnia** – Because sleep disturbance associated with depression often improves as depression abates, most antidepressants can decrease insomnia. However, some individuals with severe insomnia may benefit from a sedating antidepressant, such as mirtazapine. Trazodone is also sedating; however, at a therapeutic antidepressant dose (200 to 400 mg daily), its side effects of sedation, nausea, and orthostatic hypotension are difficult for many individuals to tolerate.

  Although many antidepressants are associated with side effects of insomnia, this side effect is usually transient (during the initial two to four weeks of treatment). As an example, in a network meta-analysis of 163 studies of 21 antidepressants, 14 were associated with an increased risk of insomnia, compared with placebo [44]; those agents most associated with insomnia included reboxetine, vilazodone, desvenlafaxine, duloxetine, and bupropion (table 7). In contrast, fluvoxamine, trazodone, and mirtazapine had the highest risk of somnolence.

  However, available evidence suggests that second-generation antidepressants are comparable in treating insomnia symptoms in individuals with major depression. As an example, a systematic review of six randomized trials with over 1000 participants did not find compelling evidence that one agent or medication class was superior for the treatment of insomnia [42]. Sleep disturbance generally improves with treatment of depression, and this may partly explain the comparable efficacy of antidepressants for treating insomnia. Additional information on managing insomnia is discussed separately. (See "Overview of the treatment of insomnia in adults" and "Pharmacotherapy for insomnia in adults".)

- **Chronic pain** – The SNRIs duloxetine and milnacipran and TCAs may reduce neuropathic pain and may be useful options in individuals with concomitant major depression and chronic neuropathic pain [45]. Treatment of chronic noncancer pain with antidepressants is discussed elsewhere. (See "Overview of pharmacologic management of chronic pain in adults", section on 'Antidepressants'.)

- **Tobacco use** – Bupropion is effective for treating tobacco use disorder and can be useful for individuals with depression who also wish to stop smoking. (See "Pharmacotherapy for smoking cessation in adults", section on 'Bupropion'.)

Winokur et al, 2001

TABLE 1. Patterns and polysomnographic features of sleep in patients with clinical depression

NREM[a]
Decreased slow-wave sleep
Decreased delta sleep in NREM-1 vs. NREM-2
REM
Reduced REM latency
Increased REM during first half of night
Increased REM density
Sleep continuity
Increased sleep latency
Increased wake time
Early morning awakenings

[a]*NREM, non-rapid eye movement; REM, rapid eye movement.*

Winokur et al, 2001

TABLE 2. Effects of antidepressant drugs on sleep

Drug	EEG sleep effects			
	Continuity	SWS	REM	Sedation
Tricyclics				
Amitriptyline	↑↑↑[c]	↑	↓↓↓	++++[d]
Doxepin	↑↑↑	↑↑	↓↓	++++
Imipramine	↑↔	↑	↓↓	++
Nortriptyline	↑	↑	↓↓	++
Desipramine	↔	↑	↓↓	+
Clomipramine	↑↔	↑	↓↓↓↓	+/—[b]
MAOIs[a]				
Phenelzine	↓	↔	↓↓↓↓	↔
Tranylcypromine	↓↓	↔	↓↓↓↓	↔
SSRIs				
Fluoxetine	↓	↓↔	↓↔	+/—
Paroxetine	↓↓	↓↔	↓↓	ND
Sertraline	↔	↔	↓↓	↔
Other				
Bupropion	↓	↔	↑	↔
Vanlafaxine	ND	ND	↓↓	++
5-HT Receptor Modulators				
Trazadone	↑↑↑	↔	↓	++++
Nefazodone	↑	↔	↑	↔

[a] *MAOIs, monoamine oxidase inhibitors; SSRIs, selective serotonin reuptake inhibitors; 5-HT, serotonin; EEG, electroencephalogram; REM, rapid eye movement; SWS, slow-wave sleep; ND, no data available.*

[b] *No significant effect.*

[c] *↑, increased; ↓, decreased; ↔, no change.*

[d] *++++, great effect; +++, moderate effect; ++, small effect; +, slight effect.*

Caution with certain comorbidities — In selecting an antidepressant, we consider coexisting medical conditions that can be exacerbated by certain antidepressant agents. Some antidepressants can exacerbate specific medical conditions, such hypertension and seizure disorder. Some of the most common medical conditions to consider include the following:

- **Hypertension** – We suggest avoiding venlafaxine in individuals with uncontrolled hypertension, especially the immediate-release formulation at higher doses. If a compelling reason exists to choose an SNRI, duloxetine or lower-dose venlafaxine can be used. Venlafaxine use in this context should be accompanied with careful blood pressure monitoring. (See 'Address side effects' below.)

  Some studies have found a dose-dependent association between venlafaxine and blood pressure elevation in both normal and hypertensive individuals, and case reports exist of venlafaxine precipitating hypertensive crisis [46]. However, other studies have not confirmed this association [47]. The effects of venlafaxine on blood pressure are discussed separately. (See "Serotonin-norepinephrine reuptake inhibitors: Pharmacology, administration, and side effects", section on 'Adverse effects'.)

- **Seizure disorder** – We suggest avoiding bupropion in individuals with seizure disorder or increased risk of seizure. Second-generation antidepressants can lower the seizure threshold, and bupropion is specifically contraindicated in individuals with seizure disorder or increased risk of seizure (ie, current or prior anorexia nervosa/bulimia, abrupt discontinuation of alcohol or benzodiazepines). In a population-based registry study of over 10,000 individuals, exposure to antidepressant agents was associated with an increased risk of new-onset seizure (odds ratio [OR] 1.5, 95% CI 1.3-1.6) [48]. The increase in seizure risk was highest with bupropion (OR 2.23, 95% CI 1.58-3.16) but also seen with SSRIs, SNRIs, and mirtazapine. However, even with bupropion, the absolute risk of seizures is low (0.1 percent), with the incidence increasing to 0.4 percent at higher doses. (See "Atypical antidepressants: Pharmacology, administration, and side effects", section on 'Side effects'.)

- **QTc prolongation** – Citalopram and escitalopram can cause dose-dependent corrected QT interval (QTc) prolongation that is dose related. We suggest avoiding citalopram in patients with congenital long QT syndrome and using caution when prescribing citalopram to those with other medical conditions and/or on medications that cause QT prolongation. We also suggest avoiding doses of escitalopram of 30 mg/day or higher in these patients. Clinical trials suggest that escitalopram at doses less than 30 mg/day does not cause clinically significant QTc prolongation. Cardiac adverse effects of SSRIs are discussed in detail elsewhere. (See "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects", section on 'Cardiac'.)

- **Hyponatremia** – Antidepressants (SNRIs, TCAs, mirtazapine, and particularly the SSRIs) may be associated with the syndrome of inappropriate antidiuretic hormone secretion and hyponatremia, although the absolute risk of hyponatremia appears low. In patients at high risk of hyponatremia, clinicians may choose fluvoxamine or milnacipran since hyponatremia occurs less frequently with these medications [49]. The risk of SSRI- and SNRI-induced hyponatremia is discussed elsewhere. (See "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects", section on 'Hyponatremia' and "Serotonin-norepinephrine reuptake inhibitors: Pharmacology, administration, and side effects", sectio on 'Adverse effects'.)

- **Low bone density** – Some observational studies suggest an association between some classes of antidepressants (SSRIs and TCAs) and fragility fractures and/or bone loss. However, studies to date have not confirmed a causal relationship, and we do not recommend avoiding antidepressants in individuals with osteoporosis or osteopenia. This association is discussed elsewhere. (See "Drugs that affect bone metabolism", section on 'Antidepressants'.)

- **Pregnancy** – For females who are considering pregnancy in the next year, certain medications should be avoided because of potential risks or an inadequate record of safety. We typically avoid paroxetine in this setting because some observational studies suggest that its use may be associated with a small increased absolute risk of congenital heart defects. This is discussed elsewhere. (See "Severe antenatal unipolar major depression: Choosing treatment", section on 'Choosing an antidepressant'.)

Avoiding specific side effects — Helping individuals with depression avoid important side effects can help guide the choice of a specific antidepressant agent. Although some patients with MDD are willing to tolerate side effects from a medication that improves their symptoms, others prioritize avoiding specific side effects. Minimizing side effects helps to ensure that patients can tolerate a therapeutic dose and will adhere to pharmacotherapy. Whereas some adverse effects (eg, gastrointestinal side effects) (table 7) are common with second-generation antidepressants, others differ in frequency between different antidepressants, as described below [50].

- **Weight gain** – For patients who prioritize not gaining weight, we suggest bupropion or fluoxetine. Bupropion may have a lower risk of weight gain than other antidepressants [51-53]. Because mirtazapine and paroxetine cause more weight gain than other antidepressants, we generally avoid using them in this subset of patients [25,28,52,54-56]. Escitalopram and duloxetine have also been associated with short-term (six-month) weight gain [53].

  Most antidepressants are associated with weight gain. As an example, in a population-based cohort of nearly 300,000 primary care patients in the United Kingdom, antidepressant use was associated with a modestly higher incidence of weight gain of ≥5 percent, compared with no antidepressant use (11.2 versus 8.1 per 100 person-years; adjusted relative risk 1.21; 95% CI 1.19-1.22) [54]. Similarly, a retrospective cohort of patients with depression who were treated with a variety of second-generation antidepressants reported average weight gains at two-year follow-up that ranged from 1 to 7 kg [52].

  Weight gain usually starts after the first four to six months of treatment, and the magnitude of weight gain is generally small [51]. In a cohort of 183,118 participants who were prescribed one of eight commonly used antidepressants (bupropion, citalopram, duloxetine, escitalopram, fluoxetine, paroxetine, sertraline, and venlafaxine), mean weight changes at six months ranged from -0.01 to 0.63 kg [53]. Escitalopram (mean weight difference 0.41 kg), paroxetine (0.37 kg), and duloxetine (0.34 kg) were associated with the greatest weight gain compared with sertraline, which served as the reference standard. By contrast, bupropion was associated with slight weight loss (mean weight difference -0.22 kg). Only escitalopram, paroxetine, and duloxetine were associated with a statistically significant risk of clinically meaningful weight gain, which was defined as ≥5 percent increase from baseline weight.

  Additional information about weight change with SSRIs is discussed separately. (See "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects", section on 'Weight change'.)

- **Weight loss** – Individuals with major depression who need to avoid weight loss can use mirtazapine and most other antidepressants. They should ideally avoid bupropion. In a meta-analysis of randomized trials and cohort studies, weight loss was associated with short-term treatment with bupropion, duloxetine, fluoxetine, and sertraline [57].

- **Somnolence** – The less-sedating antidepressants, such as bupropion, reboxetine, or vilazodone, may be useful for patients with prominent symptoms of hypersomnia or lack of energy [44]. For individuals wishing to minimize sedation, we generally do not use fluvoxamine, trazodone, mirtazapine, or TCAs, all of which can cause somnolence (table 7).

- **Sexual dysfunction** – We recommend bupropion or mirtazapine for individuals who prioritize avoiding sexual dysfunction. Vortioxetine and vilazodone are also options for these patients. Sexual dysfunction is common in individuals with depression, even those who are not taking antidepressants. Sexual dysfunction occurs in over 50 percent of individuals taking SSRIs and is also seen with SNRIs. Symptoms of sexual dysfunction from antidepressants include decreased libido, difficulty achieving orgasm, and erectile dysfunction. Moreover, sexual dysfunction can persist after cessation of SSRIs and SNRIs (post-SSRI sexual dysfunction) [58,59]. The management of SSRI-induced sexual dysfunction is discussed elsewhere (algorithm 1). (See "Sexual dysfunction caused by selective serotonin reuptake inhibitors (SSRIs): Clinical features and management".)

- **Gastrointestinal side effects** – Gastrointestinal side effects are common with SSRIs. Nausea and vomiting occur in over 20 percent of those taking SSRIs; however, these side effects are most pronounced with medication initiation and titration and often diminish or resolve after the first several weeks of treatment. Nausea also occurs more frequently with venlafaxine than with SSRIs (33 versus 22 percent). Diarrhea is slightly more common with sertraline than with venlafaxine, mirtazapine, bupropion, and other SSRIs but generally limited to the first week (16 versus 8 percent of patients).

  TCAs can also cause constipation and dyspepsia due to their anticholinergic properties. This is particularly common with the first-generation TCAs (eg, amitriptyline, imipramine).

Prior antidepressant use — Choosing an antidepressant is often based upon patient response to specific antidepressants during prior depressive episodes or family history of response to antidepressants [60]. However, robust evidence does not exist to support this practice.

Patients with severe major depression — Severe major depression is characterized by seven to nine depressive symptoms (table 1) that occur nearly every day, as indicated by a score ≥20 points on the PHQ-9 (table 4). Individuals with severe major depression often report suicidal ideation and behavior, demonstrate obvious impairment of functioning, and are more likely to develop complications such as psychotic or catatonic features. Management of patients with severe major depression can require hospitalization and should ideally include referral to a psychiatrist [17].

We suggest combination treatment with psychotherapy and medication for individuals with severe major depression. Reasonable alternatives to combination treatment include medication alone or electroconvulsive therapy. Selecting a treatment regimen for patients with severe major depression, including those with psychotic features or catatonia, is discussed separately. (See "Unipolar major depression with psychotic features: Acute treatment" and "Catatonia: Treatment and prognosis" and "Major depressive disorder in adults: Approach to initial management", section on 'Choosing a treatment regimen for patients with major depression'.)

- **SNRIs or SSRIs as preferred antidepressants** – For the initial treatment of severe major depression, we suggest serotonin-norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine or duloxetine, although selective serotonin reuptake inhibitors (SSRIs), such as escitalopram or sertraline, are a reasonable alternative. Some experts prefer SNRIs because they may be superior to SSRIs in achieving remission in those with severe major depression (table 6) [61]. Nevertheless, many patients with severe depression respond to SSRIs, which are superior to placebo for the treatment of severe major depression, are generally well tolerated, and have a low risk of life-threatening toxicity in overdose [62]. (See 'General preference for SSRIs' above.)

  Clinically important differences in efficacy or tolerability between the SNRIs are not apparent. However, we suggest carefully monitoring the use of venlafaxine in persons with hypertension since venlafaxine (especially the immediate-release formulation) can occasionally cause dose-dependent increases in diastolic blood pressure. (See 'Caution with certain comorbidities' above.)

  Using an SNRI is supported by meta-analyses of randomized trials that suggest severe major depression may respond better to SNRIs than SSRIs [61,63,64]. Representative studies include:

- A meta-analysis of 31 trials compared the SNRI venlafaxine with SSRIs (primarily fluoxetine and paroxetine) and stratified participants by baseline depression severity [63]. In the 656 patients with severe depression (score ≥30 on the Hamilton Rating Scale for Depression (table 9)), remission was more likely in those randomized to venlafaxine than SSRIs (OR 1.6, 95% CI 1.1-2.2, number needed to treat = 11).

- In a meta-analysis of 15 trials, remission occurred more often in the subgroup of hospitalized patients (n = 582) who received SNRIs (duloxetine, milnacipran, and venlafaxine) than SSRIs (citalopram, escitalopram, fluoxetine, paroxetine, and sertraline; 52 versus 29 percent, respectively) [64].

- **Alternative agents** – TCAs and mirtazapine are alternative options for patients with severe major depression (table 6). TCAs also have demonstrated efficacy in treating severe MDD but greater safety hazards. Tailoring antidepressants to address specific depressive symptoms or patient comorbidities or avoid certain side effects is also a reasonable alternative strategy (table 8). (See 'Tailoring antidepressant selection' above.)

  - Mirtazapine – Mirtazapine is effective for treating patients with severe major depression [65-67]. Although a meta-analysis comparing the efficacy of mirtazapine with SSRIs and SNRIs found that participants were more likely to achieve an early response (at two weeks) with mirtazapine, rates of remission were similar with all agents [65]. Side effects of sedation and weight gain also limit the use of mirtazapine in some patients.

  - Tricyclic antidepressants – TCAs are efficacious for severely depressed patients, although they are frequently avoided due to their greater safety hazards (eg, cardiotoxicity and potential lethality with overdose), less-favorable side effect profiles, and lower tolerability (table 7) [18]. As an example, a meta-analysis of 1377 hospitalized patients found greater symptom improvement with TCAs (particularly amitriptyline) than SSRIs (citalopram, fluoxetine, fluvoxamine, paroxetine), although the clinical difference was small [68]. Moreover, treatment discontinuation due to adverse effects occurred more frequently with TCAs (14 versus 9 percent). By contrast, a subsequent meta-analysis of 54 trials of hospitalized patients with depression failed to show a significant difference in response rates among participants randomized to amitriptyline versus SSRIs (OR for SSRI 1.37, 0.87-1.96) [69]. Differences in patient populations and depression characteristics (eg, severity, chronicity) may account for these discrepant findings.

Medication for physical health problem	Recommended antidepressant(s)
NSAIDs (non-steroidal anti-inflammatory drugs)	Try to avoid SSRI's – but if no suitable alternatives can be identified, offer gastro-protective medicines (e.g. omeprazole) together with the SSRI[5,11]. Consider mirtazapine, moclobemide or trazodone.
Warfarin or heparin	Do not normally offer SSRI's[5,11]. Consider mirtazapine.
Theophylline or methadone	Offer citalopram or sertraline (sertraline may increase methadone levels).
Clozapine	Consider citalopram or sertraline (small to modest increases in plasma clozapine levels may occur, particularly with sertraline)[2, 16].
'Triptan' drugs for migraine	Do not offer SSRI's, offer mirtazapine or trazodone.
Aspirin	Use SSRI's with caution, if no suitable alternatives can be identified, offer gastro-protective medicines together with the SSRI. Consider trazodone when aspirin is used as a single agent, alternatively consider mirtazapine.
Monoamine-oxidase B inhibitors, e.g. selegiline or rasagiline	Do not normally offer SSRI's, offer mirtazapine or trazodone.
Flecainide or propafenone	Offer sertraline as the preferred antidepressant, mirtazapine or moclobemide may also be used.

5. HPFT Formulary Drugs for the treatment of Depression in Adults[1,5]

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Drug	Drug Class	Formulation	Additional Prescribing Information
Amitriptyline	Tricyclic antidepressant (TCA)	10mg, 25mg and 50mg tablets 25mg/5ml and 50mg/5ml oral solution	Consider TCAs in patients presenting with pain and physical symptoms. Avoid in patients at risk of arrhythmias. Consider ECG at higher dose or when co-administered with other drugs that may increase the risk e.g. fluoxetine. Increased cholinergic burden, especially when co-prescribed with other anticholinergic drugs.
Citalopram	Selective serotonin reuptake inhibitor (SSRI)	10mg, 20mg, 40mg tablets 40mg/ml oral drops (1 drop=2mg) 4 drops (8mg) = 10mg tablet	SSRI with lowest propensity for drug interactions. Suitable choice in renal impairment. Citalopram: QT interval prolongation—new maximum daily dose restrictions (including in elderly patients), contraindications, and warnings. Citalopram most toxic of SSRI's in overdose (coma, seizures, arrhythmia)[5]. Contraindicated with other QT prolonging medications. Baseline ECG advised in patients with cardiac disease.
Clomipramine	TCA	10mg, 25mg and 50mg capsules	As for amitriptyline.
Duloxetine	Serotonin and noradrenaline reuptake inhibitor (SNRI)	30mg and 60mg capsules	Second line SNRI only after venlafaxine.
Fluoxetine	SSRI	20mg capsules 20mg/5ml oral liquid (can also be used sublingually)	60mg capsules NOT approved. Good option for patents with poor medication compliance due to its long half-life.
Imipramine	TCA	10mg and 25mg tablets 25mg/5ml oral solution	As for amitriptyline.

5. HPFT Formulary Drugs for the treatment of Depression in Adults[1,5]

Drug	Drug Class	Formulation	Additional Prescribing Information
Mianserin	Tetracyclic antidepressant	10mg tablets and 30mg tablets	**For specialist initiation only** in line with NICE CG 90 (for combining with an another antidepressant).
Mirtazapine	Noradrenaline and specific serotonin antidepressant (NaSSa)	15mg, 30mg and 45mg tablets and orodispersible tablets 5mg/ml oral solution	Oral solution should only be used when orodispersible tablets are unsuitable. Safer option in patients at high risk of GI bleed e.g. older adults + NSAIDs. Consider if SSRI has not benefited or SSRI not appropriate. Good choice if sedation required.
Moclobemide	Reversible Monoamine oxidase inhibitor (MAOI)	150mg and 300mg tablets	**For specialist initiation only.** Reversible MAOI. Reduced risk of major food and drug interactions, however patients should still be advised to avoid large quantities of tyramine rich foods and sympathomimetic drugs. See BNF for details on initiating treatment after another antidepressant has been stopped. MAOIs not recommended in cardiovascular disease.
Nortriptyline	TCA	10mg and 25mg tablets	As for amitriptyline.
Paroxetine	SSRI	20mg and 30mg tablets 10mg/5ml oral suspension	Less preferred choice. SSRI with greatest risk of withdrawal reactions.

5. HPFT Formulary Drugs for the treatment of Depression in Adults[1,5]

Drug	Drug Class	Formulation	Additional Prescribing Information
Sertraline	SSRI	50mg and 100mg tablets	Drug of choice for those with cardiovascular disease (recent MI or unstable angina) or renal impairment. Reduced propensity for drug interactions.
Trazodone	Tricyclic-related Antidepressant	50mg and 100mg capsules 150mg tablets 50mg/5ml sugar free oral solution	Oral liquid significantly more expensive than tabs/caps. Restricted to those unable to swallow solid dose forms.

5. HPFT Formulary Drugs for the treatment of Depression in Adults[1,5]

Drug	Drug Class	Formulation	Additional Prescribing Information
Venlafaxine	SNRI	37.5mg and 75mg tablets 37.5mg, 75mg, 150mg and 225mg MR tablets	Immediate-release venlafaxine (BD dosage) is considerably less expensive than once daily (MR) formulations. The MR formulation should only be used if the immediate-release formulation is not tolerated or if concordance with a twice daily regimen is difficult. If MR preparation is required then MR tablets should be prescribed rather than MR capsules as these are more cost-effective. Existing patients on MR preparations must not be switched to IR tablets without involvement/agreement of psychiatrist. Avoid use in patients with high risk of cardiac arrhythmia. Monitor blood pressure in doses above 150mg. Consider ECG at higher dose. Do not prescribe venlafaxine for patients with[11]: ▪ Uncontrolled hypertension ▪ Recent myocardial infarction ▪ High risk of cardiac arrhythmia ▪ Monitor BP at initiation and regularly during treatment (particularly during dose titration) ▪ Monitor for signs and symptoms of cardiac dysfunction ▪ Doses of 300 mg daily or more should only be prescribed under the supervision or advice of a specialist mental health practitioner.

5. HPFT Formulary Drugs for the treatment of Depression in Adults[1,5]

Drug	Drug Class	Formulation	Additional Prescribing Information
Vortioxetine	Serotonin modulator and stimulator (SMS)	5mg, 10mg and 20mg tablets	**GPs can initiate once specialist advice has been sought from a HPFT Consultant Psychiatrist.** NICE recommends that vortioxetine is an option for treating major depression in adults who have responded inadequately
			caution in severe renal impairment and in severe hepatic impairment as data is limited[15]. Trial data suggest no effect on QTc or on coagulation parameters. Treatment can be stopped abruptly as it has a long half-life (66hours) and there is no evidence of clinically important discontinuation symptoms[15].

INITIAL ADMINISTRATION

Patient education — We counsel patients about the rationale for antidepressant treatment, how to take the medication and address side effects, and the importance of medication adherence and ongoing monitoring [70,71]. Specific guidance for patient education appears in a table (table 10).

Although the efficacy of education alone for improving depression outcomes is not supported by existing evidence, education combined with other interventions to improve depression management has been associated with improved adherence and outcomes [72]. Given that education likely has minimal harms and adherence to antidepressants is often poor, it is reasonable to provide psychoeducation to help to strengthen a therapeutic alliance and address potential adherence issues [73]. Adherence to depression management is discussed separately. (See "Depression in adults: General principles and prognosis", section on 'Adherence to treatment'.)

Initial low dose and dose titration — We suggest starting antidepressants at low doses to reduce side effects and improve adherence and then increasing the dose as tolerated to reach a therapeutic range [74]. Typical starting doses appear in a table (table 6).

Starting at one-half the normal initial dose may further reduce adverse effects and decrease early discontinuation of the medication. This approach may benefit patients who are older, are receiving polypharmacy, have a comorbid anxiety disorder, or are sensitive to side effects. For patients who start at one-half the normal initial dose, it is important to titrate up to the minimum usual total daily dose (therapeutic dose) over one to three weeks, depending upon tolerability. (Related Pathway(s): Unipolar major depression: Initial pharmacologic therapy in adults.)

Further dose adjustment at two to four weeks — For individuals who do not respond to the minimum therapeutic dose of an antidepressant (not the starting dose) within two to four weeks, we suggest increasing the dose as tolerated toward the upper end of the usual dosing range (table 6) [36,75,76].

Dose adjustment can proceed rapidly if the patient is tolerating the medication without significant side effects. However, patients who have side effects or reluctance to increase the medication for other reasons may need more gradual dose titration. For these individuals, continuing the initial standard dose is a reasonable alternative because some of these patients will ultimately respond. We do not consider switching antidepressants until the patient has undergone an adequate treatment trial. (See 'Ensure duration of adequate trial' below.)

- Evidence that supports increasing the antidepressant dose includes a meta-analysis of 40 randomized trials that compared different doses of selective serotonin reuptake inhibitors (SSRIs) with placebo in patients with major depression (n>10,000) [77]. Improvement with SSRIs was greater at higher doses than lower doses, and the increased efficacy with higher doses outweighed the higher rate of treatment discontinuation due to side effects. The clinical benefit of higher doses was small and appeared to plateau at the upper end of the usual dose range (eg, 50 mg/day of fluoxetine). Dose increase is consistent with suggestions in multiple practice guidelines [17,18,23,71,74].

- However, continuing the same dose is also a reasonable approach because response rates to an antidepressant generally improve the longer the patient continues treatment, and some depressive episodes remit even without treatment. As an example, a meta-analysis of nine trials included participants who did not respond to an initial standard dose of an SSRI or serotonin-norepinephrine reuptake inhibitor after three to nine weeks and were then randomized either to continue the initial dose or increase it (eg, fluoxetine 20 mg/day versus 40 to 60 mg/day) [78]. Both groups experienced comparable rates of symptom improvement and discontinuation of treatment due to adverse effects. A prior meta-analysis of six trials reported similar findings [79-81]. (See 'Address factors that can affect response' below.)

Some patients benefit from doses that exceed the maximum therapeutic dose [74]. Patients receiving high doses should be regularly monitored for adverse effects and nonadherence [82]. (See 'Address side effects' below and "Depression in adults: General principles and prognosis", section on 'Adherence to treatment'.)

Additional information about starting doses, titration schedules, and target doses of antidepressants (table 6) is discussed in topics that review specific classes of antidepressants.

MONITORING INITIAL TREATMENT

Frequency of monitoring — Patients who start an antidepressant should receive follow-up within one to two weeks to evaluate for side effects, monitor for early discontinuation, and assess for early improvement. The frequency of ongoing follow-up depends on the severity of the patient's symptoms, degree of functional impairment, medical complexity, and suicidal risk factors (eg, substance abuse, prior suicide attempts, etc); however, monitoring by telephone, telehealth, or in-person visits should occur every two to four weeks during the initial phase of antidepressant management to promote adherence, timely dose adjustments, and early detection of adverse events. (See "Major depressive disorder in adults: Approach to initial management", section on 'Ongoing monitoring and follow-up'.)

Assessing treatment response — Patients should complete symptom rating scales at each follow-up to monitor their response to treatment. We use the nine-item Patient Health Questionnaire (PHQ-9) scale to monitor symptoms in patients with depression because it is a short, self-administered, widely available scale that has been extensively validated in diverse patient populations and different languages (table 4) [83-88]. Using symptom scales to inform dosing adjustments can potentially improve treatment outcomes, more quickly identify nonresponse and response, recognize remission, and help to engage patients in treatment. Details regarding the use of the PHQ-9 and other symptom scales to monitor depression are discussed separately. (See "Major depressive disorder in adults: Approach to initial management", section on 'Ongoing monitoring and follow-up' and "Using scales to monitor symptoms and treat depression (measurement-based care)".)

Address side effects

- **Ask about side effects** – We ask about side effects at each visit, particularly during the initial weeks of treatment, because they are a common reason for discontinuing antidepressants and they inform dose adjustments. Patients who develop side effects should receive education that most are temporary. With selective serotonin reuptake inhibitors (SSRIs), the most common early side effects include insomnia, increased activation or anxiety, and nausea and/or diarrhea (table 7). Given the likelihood that these will resolve after several weeks, individuals who develop but can tolerate them should continue the antidepressant if possible. Adverse effects that do not resolve with time include sexual dysfunction, corrected QT interval prolongation, hyponatremia, and blood pressure elevation. Patients whose side effects do not resolve and/or who have intolerable side effects can try a lower dose of the antidepressant or switch to an alternative antidepressant.

  Over half of individuals who newly start antidepressants will have side effects; however, most of these resolve within the first two weeks. Unless clinicians ask about them specifically, side effects can go undetected and can interfere with adherence to antidepressants [89,90]. In addition, the degree to which antidepressant side effects interfere with daily functioning is associated with poorer treatment outcomes, including response and remission [91].

  Symptom scales can help to identify and quantify side effects. Self-report instruments to assess side effects include the Toronto Side Effects Scale (table 11) and the Frequency, Intensity, and Burden of Side Effects Rating Scale (figure 3). Although some data indicate that side effects scales are more effective than usual practice for identifying frequent and significantly bothersome adverse effects, it is not known whether their use improves antidepressant adherence. The use of side effects scales in depression management is discussed separately. (See "Using scales to monitor symptoms and treat depression (measurement-based care)", section on 'Adverse side effects scale'.)

- **Watch for new-onset mania** – Because antidepressants can uncommonly precipitate mania or hypomania in individuals with undiagnosed bipolar disorder, we closely monitor for symptoms of mania or hypomania (eg, decreased need for sleep; increased irritability, aggressiveness, or agitation; euphoria; increased energy). Appearance of such symptoms should prompt an evaluation for bipolar disorder and discontinuation of the antidepressant (table 2 and table 3). The risk of "switching" from depression to mania in individuals with undiagnosed bipolar major depression who initiate treatment with antidepressants is discussed separately. (See "Bipolar major depression in adults: Efficacy and adverse effects of antidepressants", section on 'Risk of switching to mania'.)

- **Monitor blood pressure** – We monitor blood pressure in individuals who start venlafaxine as well as patients at risk for hypertension or hypotension. This includes patients over age 65, with medical comorbidities that predispose to orthostasis (eg, Parkinson's disease), or on antihypertensive drugs or other medication that can reduce blood pressure. Because trazodone and the SSRIs can cause orthostatic hypotension, we ask about symptoms of postural lightheadedness and check orthostatic blood pressures in those who endorse symptoms.

  We check blood pressures at baseline and within two months. We typically monitor blood pressure every two to six months, especially for individuals taking higher doses of venlafaxine (≥300 mg/day). Doses of less than 300 mg per day have not been associated with significant blood pressure elevation.

- **Evaluate for uncommon side effects** – Given that SSRIs and serotonin-norepinephrine reuptake inhibitors can increase the risk of hyponatremia, individuals at high risk for hyponatremia should receive periodic monitoring of serum sodium levels [41]. These include patients who are older (>65 years), use diuretics, and/or have a history of hyponatremia. Other class-based side effects of antidepressants are discussed separately. (See "Major depressive disorder in adults: Approach to initial management", section on 'Safety of antidepressants'.)

- **When to consider stopping an antidepressant due to side effects** – Because most side effects of antidepressants are transient, we first educate about side effects and individualize medication dose titration to minimize them (see 'Initial low dose and dose titration' above). If side effects occur and are tolerable, we hold off on further dose escalation to see if they resolve or diminish. Some side effects can be adequately managed with behavioral interventions (eg, sleep hygiene for insomnia) or medications (eg, phosphodiesterase 5 inhibitors for sexual dysfunction). Side effects that persist despite these interventions and/or are severe or interfere with medication adherence warrant discontinuation of the antidepressant.

  Except for patients who develop symptoms concerning for new-onset mania, most individuals who stop an antidepressant due to side effects should start an alternative antidepressant. We try to select an antidepressant with a different side effect profile either from within the same class or from a different class, depending on the specific side effect. (See 'Avoiding specific side effects' above.)

Symptoms that suggest new-onset mania or hypomania should prompt immediate discontinuation of the antidepressant.

Prognostic value of early improvement — Patients whose symptoms improve during the first two weeks of treatment should be encouraged to continue their antidepressant since early improvement suggests a likelihood of future response and remission.

Among individuals who ultimately respond to a given antidepressant, many experience improved symptoms within two weeks (ie, "early improvement," with improvement defined as reduction of baseline symptoms of ≥20 percent) [92-94]. As an example, a pooled analysis of four randomized trials found that, although improvement times with antidepressant treatment varied widely among participants, the mean time to improvement was approximately 13 days [95].

Early improvement at two weeks can predict future response and remission [95-100]. As an example, in a meta-analysis of 6562 individuals with MDD, early responders (those who had ≥20 percent reduction in baseline symptom score at two weeks) were more likely than those without an early response to have a sustained response at six to eight weeks (53 versus 11 percent, respectively) [101]. A subsequent study reported similar findings in a population of inpatients with major depression [102].

While early improvement seems to predict further benefit, patients without early improvement may subsequently respond or remit [103].

SUBSEQUENT MANAGEMENT

Defining response — We use symptom scales, such as the nine-item Patient Health Questionnaire (PHQ-9), to monitor changes in symptoms and determine subsequent management (table 4).

Patients with response — Response is usually defined as an improvement in symptom score of ≥50 percent that is still above the threshold for remission [9,10].

- **Treat to remission** – Clinicians should continue to monitor individuals whose symptoms respond to initial treatment to ensure that remission occurs (ie, PHQ-9 score of less than 5 that remains stable for at least one month). This may entail dose adjustment, if tolerated. Some individuals who respond to the initial treatment may ultimately require augmentation with a second medication to achieve remission. (See 'Start next-step treatment' below and "Unipolar depression in adults: Choosing treatment for resistant depression".)

- **Duration of treatment** – Once remission has been attained, individuals enter the continuation and maintenance phases of depression management (figure 1). Patients should continue antidepressant treatment for at least six months from the time they attain remission. Factors that influence the specific duration of antidepressant treatment during the continuation and maintenance phases are discussed separately. (See "Major depressive disorder in adults: Continuation and maintenance treatment", section on 'Indications'.)

Patients with incomplete response — Individuals who do not respond or have only a partial response to treatment at four weeks should undergo assessment of potential reasons for nonresponse and have a time-limited trial of continued treatment with the same agent before proceeding to next-step treatment. Although some individuals require up to 12 weeks to respond to antidepressant treatment, we typically assess patients early on for factors that can affect response, particularly for patients with more severe depressive symptoms.

Likelihood of nonresponse — Approximately 50 to 60 percent of patients with MDD do not respond to the initial antidepressant [104-108]. As an example, in a meta-analysis of 28 randomized trials of individuals with depression in primary care (n = 5940), response rates (eg, reduction of baseline symptoms ≥50 percent) at six to eight weeks were 63 percent [109]. In a second meta-analysis, pooled response rates from two trials of antidepressant treatment were 56 percent at 12 weeks [104]. Response rates in settings that more closely resemble a typical primary care practice tend to be lower than those in clinical trials. Prognosis with initial antidepressant treatment is discussed separately. (See "Depression in adults: General principles and prognosis", section on 'Prognosis'.)

Address factors that can affect response — When patients do not respond or have only a partial response to initial antidepressant treatment at four weeks, it is important to ask about medication adherence, ensure that the patient is taking an adequate dose, and assess for factors that may complicate response to treatment.

- **Medication adherence** – It is important to assess patients' adherence to antidepressant treatment, correct patient misunderstandings about how to take the medication, troubleshoot any identified issues with adherence, and identify and treat antidepressant side effects. (See "Depression in adults: General principles and prognosis", section on 'Adherence to treatment'.)

- **Inadequate dose** – It is important to ensure that the patient is not taking a subtherapeutic antidepressant dose and, for patients taking the lower range of the usual dose, increase the dose to the upper end of that range. Therapeutic dose ranges for antidepressants appear in a table (table 6).

  Additionally, individuals with increased cytochrome P450 2D6 (CYP2D6) activity may rapidly metabolize some antidepressants and require larger doses of antidepressants. Genetic polymorphisms or concomitant administration of medications that inhibit CYP2D6 enzymes can influence antidepressant pharmacokinetics and affect the dose required to achieve a therapeutic serum concentration [110,111]. As an example, in a study of individuals who were treated with escitalopram and underwent cytochrome P450 2C19 genotyping, serum escitalopram concentrations were more than three times greater in those classified as poor metabolizers compared with those classified as extensive metabolizers [112]. The role of genetic factors in response to antidepressants and drug metabolism more generally are discussed separately. (See "Unipolar depression: Genetics" and "Overview of pharmacogenomics".)

- **Coexisting conditions** – Because psychosocial factors and comorbid medical diagnosis may complicate response to antidepressants, they should be evaluated for and, if possible, treated. Socioeconomic factors that have been associated with poorer prognostic outcomes include social isolation, unemployment, and unstable housing conditions [113,114]. Common psychiatric comorbidities that may complicate response to treatment include substance use disorder; anxiety disorders, including panic disorder; posttraumatic stress disorder; and attention deficit hyperactivity disorder [115]. These are discussed separately. (See "Depression in adults: Clinical features and diagnosis", section on 'Comorbidities'.)

- **Incorrect diagnosis** – Individuals who do not respond to initial antidepressant treatment should also be re-evaluated to confirm a diagnosis of major depression. Some patients may have an alternative diagnosis, such as undiagnosed bipolar disorder, that requires different pharmacotherapy. (See "Approach to the adult patient with suspected depression", section on 'Mania or hypomania'.)

Ensure duration of adequate trial — After addressing factors that may contribute to an individual's lack of response, we ensure that they have had an adequate trial of therapy. The duration of an adequate trial depends in part on whether the patient has experienced a partial or no response. We suggest that clinicians engage patients in informed decision making regarding the relative merits of continuing the initial management strategy versus proceeding to next-step treatment. (See 'Start next-step treatment' below.)

- **Patients with a partial response** – We suggest that individuals who have had a partial response to initial antidepressant treatment continue a treatment trial for a total duration of 6 to 12 weeks before proceeding to next-step treatment [116-119]. We define partial response as a reduction in symptoms of >30 but <50 percent.

  The rationale for continuing treatment in those with an initial partial response derives from evidence that some individuals require 8 to 12 weeks to achieve a response or remission. As an example, the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study, which treated a sample that was more generalizable than those typically enrolled in clinical trials, found that nearly 25 percent of participants treated with open-label citalopram required 10 or 12 weeks of treatment to achieve remission [105]. Other observational studies have shown similar results [120,121].

  Response rates to antidepressants that occur after four to six weeks still exceed those achieved with placebo. As an example, a meta-analysis of five randomized trials of second generation antidepressants found that, among participants who did not respond (reduction of baseline symptoms ≥50 percent) after four weeks of treatment, 22 percent responded at eight weeks, compared with only 11 percent of those who received placebo [104]. An earlier meta-analysis of 28 trials found that the advantage of selective serotonin reuptake inhibitors (SSRIs) over placebo continued to increase for at least six weeks of treatment [122].

  This approach is consistent with multiple practice guidelines [17-19,23].

- **Patients with nonresponse** – We suggest that patients with minimal to no response to initial antidepressant treatment should continue the treatment trial for a total duration of four to six weeks before proceeding to next-step treatment. We define nonresponse as a reduction in symptoms of less than 30 percent.

  The rationale for proceeding to next-step treatment in this subset of patients stems from the observation that rates of response and remission are low (ranging from 4 to 20 percent) among individuals who continue the same antidepressant after not responding in four weeks [101,106,123,124] (see 'Address side effects' above). Representative studies include:

  - A review of 15 randomized trials and observational studies found that, among participants who demonstrated minimal improvement (eg, reduction of baseline symptoms <20 percent) at four weeks, only 20 percent responded after four additional weeks of treatment with the same agent [106].

  - In a study of 566 patients with major depression who improved only minimally (<30 percent reduction of baseline symptoms) after four weeks of open-label escitalopram, those who were randomized to switch to duloxetine immediately were more likely to experience remission at week 16 than those who continued escitalopram or delayed a switch to duloxetine until eight weeks (43 versus 36 percent) [124].

Start next-step treatment — When patients have incomplete response to an initial antidepressant after addressing the above-mentioned issues (see 'Address factors that can affect response' above) and completing an adequate trial, we suggest proceeding to next-step treatment [74,118,125]. Common approaches to next-step treatment include switching to a different antidepressant, augmenting the first antidepressant with a second intervention, or referring for psychotherapy [126]. For individuals with no or minimal response to a single-antidepressant trial, we suggest switching to another antidepressant, usually one from a different class (ie, switch from an SSRI to a serotonin-norepinephrine reuptake inhibitor). For individuals who have a partial response to the initial antidepressant trial, we discuss options with the patient. These include adding a second antidepressant from a different class, such as bupropion or mirtazapine, or switching to an antidepressant from a different class. The process of switching antidepressants is discussed separately. (See "Switching antidepressant medications in adults".)

We generally reserve augmentation with agents that are not antidepressants for those who have not responded to two trials of antidepressant therapy (ie, individuals with resistant depression). Treatment of individuals with resistant depression is discussed separately. (See "Unipolar depression in adults: Choosing treatment for resistant depression".)

Among individuals who switch to a second antidepressant after nonresponse to the first agent, approximately 20 percent will have a remission with that agent. As an example, in the subset of participants in the STAR*D trial who did not respond to initial treatment with citalopram and were then randomized to a second antidepressant (bupropion, sertraline, or venlafaxine), 21 percent remitted, and an additional 9 percent responded without remission [103]. A significant proportion of participants required a long trial of treatment, with 50 percent of responses occurring after six weeks and 33 percent of responses occurring after at least nine weeks of treatment.

AVOID SUDDEN DISCONTINUATION

Because sudden discontinuation of antidepressants can cause withdrawal symptoms, patients who want or need to stop antidepressant treatment should gradually taper the medication [71]. Discontinuing antidepressants is discussed separately. (See "Discontinuing antidepressant medications in adults".)

Approximately 30 percent of individuals will have symptoms when they stop an antidepressant. The incidence of discontinuation symptoms varies with the specific antidepressant, pharmacokinetics, dose, and sensitivity of the patient to side effects. Discontinuation symptoms occur most frequently with medications that have short half-lives, such as paroxetine and venlafaxine, and less frequently with medications with longer half-lives, such as fluoxetine. Common symptoms of discontinuation include dizziness, nausea, altered sensations (eg, paresthesias, shock-like sensations), increased agitation, insomnia, anxiety, and return of depressed mood.

SUMMARY AND RECOMMENDATIONS

- **Goals and role of antidepressant therapy** – The goals of initial treatment for major depressive disorder (MDD) are to restore baseline functioning, induce symptom remission, and prevent relapse. Antidepressants can be used as monotherapy or in combination with other interventions. The overall approach to the management of MDD is discussed elsewhere. (See "Major depressive disorder in adults: Approach to initial management".)

- **Antidepressant selection for mild to moderate depression** – For initial pharmacotherapy of mild to moderate MDD, we suggest a selective serotonin reuptake inhibitor (SSRI), typically escitalopram or sertraline, rather than other classes of antidepressants (**Grade 2C**). Although efficacy is similar within and across classes of antidepressants, SSRIs optimize efficacy, safety, and tolerability for most patients. Reasonable alternatives include serotonin-norepinephrine reuptake inhibitors (SNRIs), atypical antidepressants, and serotonin modulators (table 6). Potential reasons to use alternatives to SSRIs are listed in a table (table 8). (See 'Patients with mild to moderate depression' above and 'Tailoring antidepressant selection' above.)

- **Antidepressant selection in severe depression** – For patients with severe MDD, we suggest SNRIs (such as venlafaxine or duloxetine) rather than other classes of antidepressants (**Grade 2C**). Some data suggest that SNRIs are superior to other agents for achieving remission in this group. SSRIs are reasonable alternatives because they are safe, efficacious, and generally well tolerated in these patients. Among other agents for treating severe depression, mirtazapine and tricyclic antidepressants are the best studied (table 6). Other antidepressants may be reasonable to address specific symptoms or side effects (table 8). (See 'Patients with severe major depression' above and 'General preference for SSRIs' above and 'Tailoring antidepressant selection' above.)

  Individuals with severe major depression may benefit from combination treatment with psychotherapy, require hospitalization and/or referral to a psychiatrist, or require specific therapies for symptoms of psychosis and catatonia. (See "Major depressive disorder in adults: Approach to initial management", section on 'Choosing a treatment regimen for patients with major depression' and "Major depressive disorder in adults: Approach to initial management".)

- **Initiating antidepressant therapy**
  - **Initial dosing** – Typical initial doses of antidepressants are low to reduce side effects and then increased to a therapeutic range (table 6). Individuals with polypharmacy, comorbid anxiety disorders, or sensitivity to medication side effects and those who are older may benefit from starting at one-half the usual initial dose and then increasing to the usual initial dose in the first two weeks. (See 'Initial low dose and dose titration' above.)
  - **Dose titration** – After two to four weeks, individuals who do not respond to the minimum therapeutic dose should increase the dose to the higher end of the therapeutic range, if possible. Patients who experience side effects may need slower dose up-titration. (See 'Further dose adjustment at two to four weeks' above.)
  - **Patient education** – We counsel patients about the rationale for antidepressants, potential side effects, the importance of monitoring, and the time course of improvement (table 10). (See 'Patient education' above.)

- **Monitoring**

  - **Frequency** – We have patients follow up at one to two weeks to assess for side effects, adherence, and early response to treatment. Subsequent follow-up should occur every two to four weeks during the initial phase of antidepressant management. (See 'Frequency of monitoring' above.)

  - **Assessments** – At each visit, we use a validated self-report scale to monitor treatment response, such as the nine-item Patient Health Questionnaire (table 4). (See 'Assessing treatment response' above.)

    Important or common side effects to assess include symptoms of mania or hypomania, increased agitation or anxiety, and gastrointestinal symptoms (table 7). Patients who develop symptoms of mania or hypomania should undergo evaluation for bipolar disorder, and the antidepressant should be stopped. Patients with other side effects that are intolerable or do not resolve can try a lower dose of the antidepressant or switch to an alternative antidepressant. (See 'Address side effects' above.)

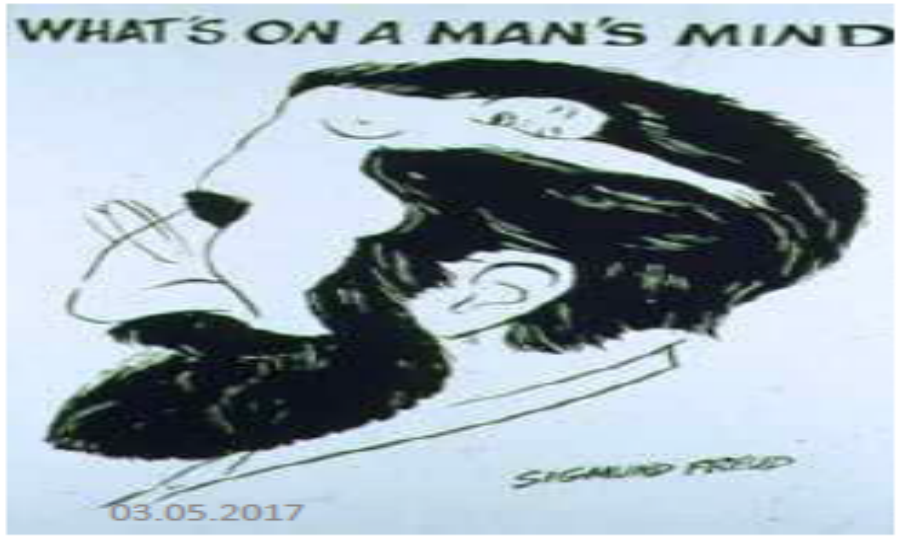
- **Subsequent management**
  - **Patients who respond** – Patients who respond (ie, have reduction of baseline symptoms ≥50 percent) should continue antidepressant therapy until remission and then for at least six months (continuation phases). (See "Major depressive disorder in adults: Continuation and maintenance treatment".)
  - **Patients with incomplete response** – Patients with an incomplete response (either a partial response or nonresponse) should optimize their antidepressant dose and medication adherence. Clinicians should address comorbidities that impact treatment response and ensure an adequate trial of therapy (four to twelve weeks) before proceeding to next steps. Potential next steps include switching to a different antidepressant or augmenting the first antidepressant with a second intervention. (See 'Patients with incomplete response' above.)
  - **Avoiding sudden discontinuation** – Individuals who want or need to stop their antidepressant should gradually taper the medication to avoid discontinuation symptoms. (See "Discontinuing antidepressant medications in adults".)

8. Masennuksen psykoterapiat

Yl juha kemppinen

Ihmisen muuttumisessa vaikuttavat epäspesifiset tekijät

Ihmisen käyttäytymisen muutoksessa vaikuttavat :



Epäspesifit muuttujat :

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?

Depressio KH-suositus ja yl juha kemppinen

Taulukko 2. Depression vaikeusaste ja keskeiset akuuttivaiheen hoitomuodot

Hoitomuoto	Lievä	Keskivaikea	Vaikea	Psykoottinen
Internetvälitteiset tietotekniikka-avusteiset terapiat (nettiterapiat)	+	+		
Psykoterapiat	+	+	(+)	
Masennuslääkkeet	+	+	+	(+)
Masennus- ja psykoosilääke yhtäaikaisesti				+
Sähköhoito (ECT)			+	+

+ = riittävä vaikuttavuus osoitettu myös yksinomaisena hoitomuotona
(+) = vaikuttavuus yksinomaisena hoitomuotona epävarma tai riittämätön

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025
/*Reference: Barth J, Munder T, Gerger H, et al. Comparative efficacy of seven psychotherapeutic interventions for patients with depression: A network meta-analysis. PLoS Med 2013; 10:e1001454*

Established psychotherapies for major depressive disorder

Type of psychotherapy	Emphasis/objectives	Components
Cognitive-behavioral therapy (CBT)	Changes: ▪ Inaccurate, negative thoughts and beliefs ▪ Problematic behaviors	Includes: ▪ Education about depression-related thoughts, emotions, and behaviors ▪ Questioning inaccurate thoughts to develop alternative perspectives ▪ Identifying, evaluating, and challenging distorted beliefs ▪ Relaxation and exposure exercises ▪ Coping skills training ▪ Stress management ▪ Assertiveness training ▪ Homework between sessions
Interpersonal psychotherapy	Addresses interpersonal difficulties in at least 1 of the following: ▪ Grief ▪ Role disputes ▪ Role transitions ▪ General interpersonal deficits	Interventions are tailored to each problem area. As an example, if the patient and another individual are actively negotiating a role dispute unsuccessfully, therapy focuses on improving communication skills and modifying expectations.
Problem-solving therapy	Develops rational and effective problem-solving skills	Guides patients to: ▪ Identify and define the problem ▪ Describe the barriers to its resolution ▪ Set an achievable goal ▪ List and evaluate the advantages and disadvantages of all available solutions ▪ Choose 1 solution ▪ Develop and implement an action plan ▪ Evaluate the outcome

A John Rush, Major depressive disorder in adults: Approach to initial management, 2025
/*Reference: Barth J, Munder T, Gerger H, et al. Comparative efficacy of seven psychotherapeutic interventions for patients with depression: A network meta-analysis. PLoS Med 2013; 10:e1001454*

Established psychotherapies for major depressive disorder

Type of psychotherapy	Emphasis/objectives	Components
Behavioral activation	Behavioral activation is the behavioral component of CBT: ▪ Identify precursors and consequences of problematic behaviors ▪ Change problematic behaviors	Guides patients to identify and engage in activities that: ▪ Decrease social withdrawal and avoidance behavior ▪ Reduce disruption of basic life routines ▪ Encourage engagement with the environment ▪ Increase pleasure or mastery ▪ Establish routines
Family/couples therapy	Improves functioning of the entire family/couple by: ▪ Correcting distorted communication ▪ Addressing impaired relationships	Guides patients and their family members to: ▪ Improve communication and support among all members ▪ Fulfill their individual roles and responsibilities ▪ Understand depression and its effects on the patient's capabilities ▪ Discuss how the patient's social withdrawal, negativity, and dependence can elicit blame, criticism, and hostility from family members and help family to consider alternative responses
Short-term psychodynamic psychotherapy	Improves patient's awareness and insight regarding repetitive interpersonal and intrapsychic conflicts	Uses observation, interpretation, confrontation, clarification, empathic validation, education, and advice. Guides patients to: ▪ Remember and process formative childhood experiences ▪ Recognize parallels between childhood experiences and current relationships ▪ Develop insight into and change maladaptive behavioral patterns
Supportive psychotherapy	Provides support for addressing personal problems	Uses active listening, empathic validation, reassurance and encouragement, confrontation, and role modeling of adaptive behavior to promote healthy coping strategies. Identifies and changes: ▪ Problematic relationships ▪ Maladaptive patterns of behavior and emotional responses

9. Lopuksi

Yl juha kemppinen

Laatukriteerit

- Jokaisen depressioon hoitoa hakevan potilaan tulisi saada jotakin vaikuttavaksi osoitettua hoitoa.
- Työryhmä ehdottaa, että depressiopotilaiden hoidon laatua seurattaisiin **perusterveydenhuollossa** seuraavilla kriteereillä:
  - Vastaako diagnosoitujen depressiopotilaiden osuus kaikista hoidetuista epidemiologista kuvaa masennuksen todennäköisestä esiintyvyydestä väestössä?
  - Kuinka suurella osalla depressiopotilaista on hoitosuunnitelma?
  - Kuinka suuri osa depressiopotilaista on saanut masennuslääkettä?
  - Kuinka suurella osalla depressiopotilaista masennuslääkitys on jatkunut yhtäjaksoisesti vähintään puoli vuotta?
  - Kuinka suuri osa depressiopotilaista on saanut jotakin psykoterapeuttista tai muuta psykososiaalista hoitoa?
  - Kuinka suurella osalla uusista (todetuista) depressiopotilaista suunnitelmallinen seuranta toteutuu?
  - Kuinka suuri osa depressiopotilaista saavuttaa seurannassa oiremittareilla arvioituna täyden remission?
  - Kuinka tyytyväisiä depressiopotilaat ovat saamaansa hoitoon?

- **Psykiatrisen erikoissairaanhoidon** osalta työryhmä ehdottaa seuraavia laatukriteereitä:
  - Kuinka suurella osalla depressiopotilaista on hoitosuunnitelma?
  - Kuinka suuri osa depressiopotilaista on saanut masennuslääkettä?
  - Kuinka suurella osalla depressiopotilaista lääkehoito on jatkunut yhtäjaksoisesti vähintään puoli vuotta?
  - Kuinka suuri osa potilaista, jotka kärsivät toistuvasta masennuksesta, saa ylläpitohoitoa?
  - Kuinka suuri osa depressiopotilaista on saanut jotakin intensiivistä yksilöpsykoterapeuttista hoitoa?
  - Kuinka suurella osalla parisuhteessa elävistä potilaista hoitoon on liittynyt pari- tai perhetapaaminen?
  - Kuinka suurella osalla depressiopotilaista on seurannassa käytetty hyväksi oiremittareita?
  - Kuinka suuri osa depressiopotilaista saavuttaa seurannassa oiremittareilla arvioituna täyden remission?
  - Kuinka tyytyväisiä depressiopotilaat ovat saamaansa hoitoon?

Table 1. Description of the Randomized Controlled Trials (RCTs) Contributing to the Individual Patient Data Network Meta-Analysis and Covariates for the Prediction Model.

Study	Comparisons (16 ADs or placebo)	Covariates (predictors)	
130 double-blind randomized controlled trials comparing antidepressants as monotherapy against each other or versus placebo in the acute treatment of major depressive disorder (bout 40,000 participants)	• Agomelatine • Amitriptyline • Bupropion • Citalopram • Clomipramine • Duloxetine • Escitalopram • Fluoxetine • Fluvoxamine • Imipramine • Mirtazapine • Paroxetine • Sertraline • Trazodone • Venlafaxine • Vortioxetine • Placebo	Demographics Age (mean: 44.8 ± 14.2) Sex (females: 25,735—64.3%)	Clinical Information (mean ± SD) Baseline HDRS total score (23.85 ± 3.99) Baseline HDRS item 3: Suicide (0.92 ± 0.86) Baseline HDRS item 4: Insomnia: early in the night (1.32 ± 0.80) Baseline HDRS item 6: Insomnia: early in the morning (1.25 ± 0.79) Baseline HDRS item 10: Anxiety psychic (2.25 ± 0.75) Baseline HDRS item 11: Anxiety somatic (1.75 ± 0.80) Baseline HDRS item 13: General somatic symptoms (1.65 ± 0.54) Baseline HDRS item 17: Insight (0.25 ± 0.48)

Note: The information is calculated based on 40,013 participants across 130 RCTs on 3 platforms (in-house, Vivli and SAS). The number of participants per RCT is between 10 and 970, with the median number of participants per RCT being 279. ADs: antidepressants. SD: standard deviation.

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Figure 1. Model pipeline for the backend of the algorithm (PETRUSHKA tool)—see text for full details.
Note: GRISELDA = network meta-analysis of aggregate data about antidepressants in depression (Cipriani et al., Lancet 2018); HAMD = Hamilton Depression Rating Scale; IPD-NMA = individual patient data network meta-analysis; MCDA = multiple-criteria decision analysis; QIDS PHQ-9 = Patient Health Questionnaire, 9 items; RCT = randomized controlled trial.

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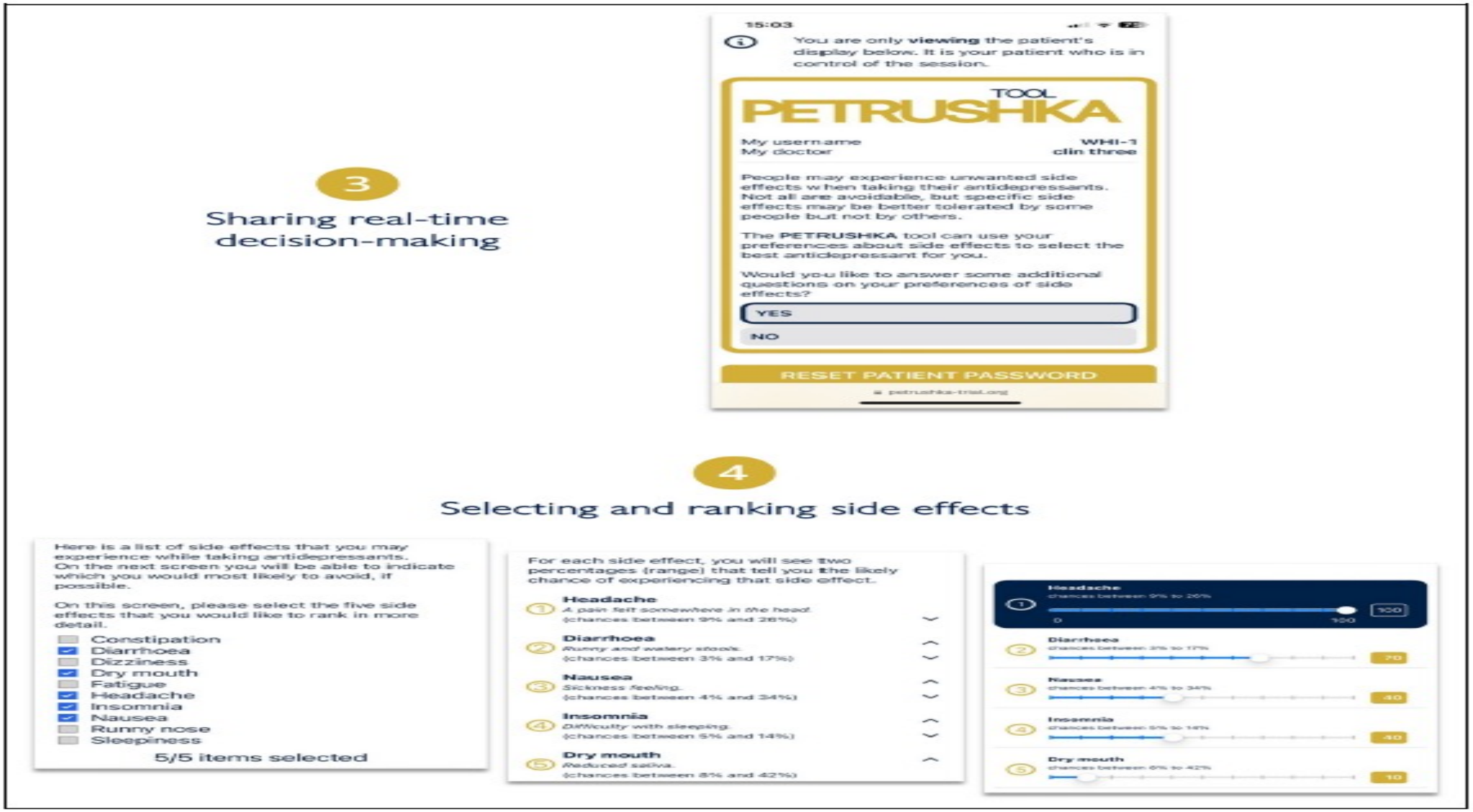

Figure 2. Clinicians can log in to the PETRUSHKA tool web app, accessing patients from their clinic, either registered by themselves or with their colleagues. After the correct patient is selected, clinicians can optionally exclude some antidepressants based on the patient's medical history and ongoing medications.

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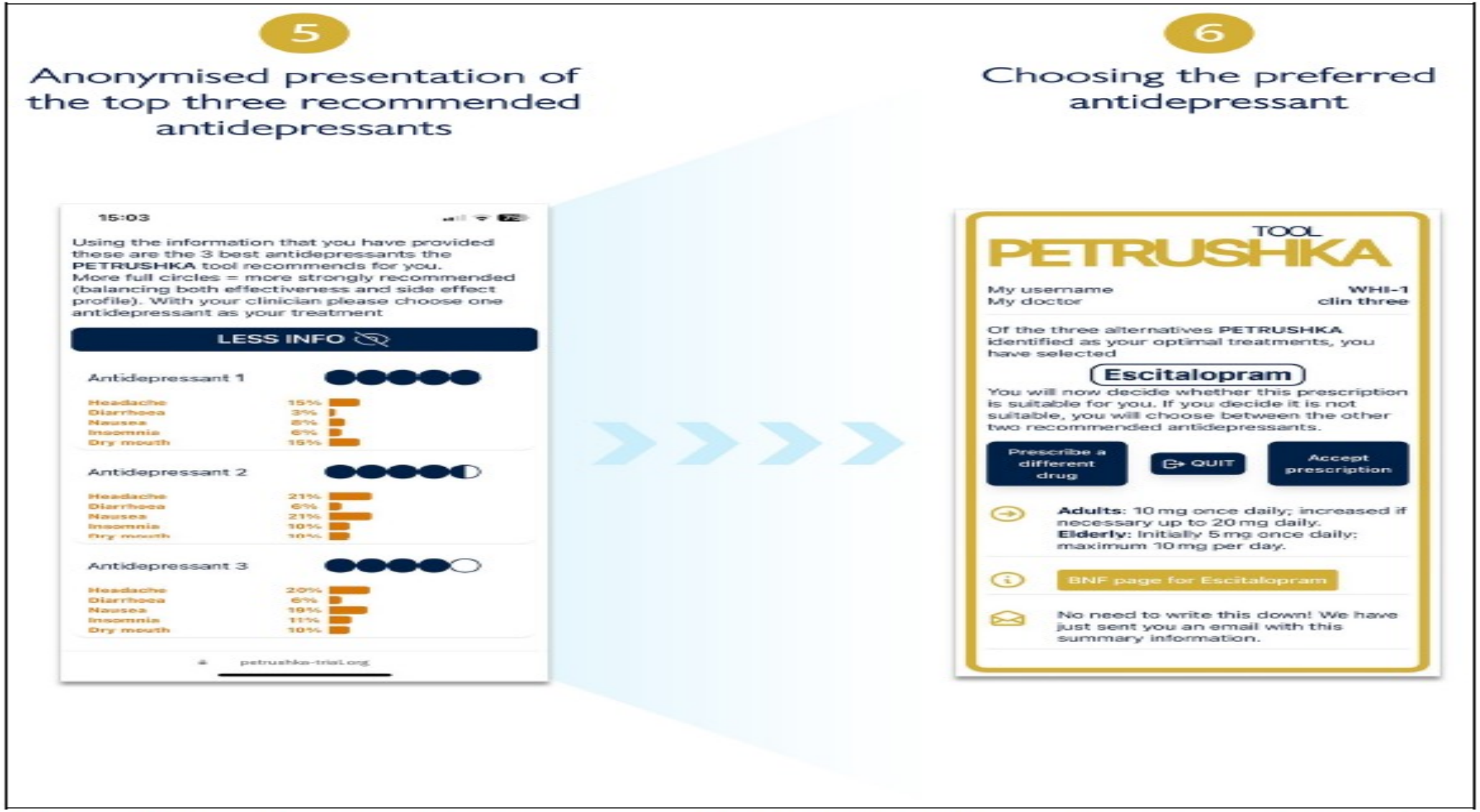

Figure 3. The clinician and the patient will simultaneously access the PETRUSHKA tool from any internet-connected device. In real-time, the patient will be in charge of answering several questions: whether they would like to provide additional information on their preferences about side effects and which side effects are more important for them to avoid.