181219 Skitsofrenian lääkitsemisestä

Yl juha kemppinen

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- Agenda:

1) Skitsofreniasta yleistä
2) Skitsofrenian diagnosointi
3) Skitsofrenian hoito
4) Skitsofrenian Käypä Hoito-suosituksia löytyy https://cpnp.org/guideline/external/schizophrenia
5) **THE AMERICAN PSYCHIATRIC ASSOCIATION PRACTICE GUIDELINE FOR THE TREATMENT OF PATIENTS WITH SCHIZOPHRENIA, DRAFT May 13, 2019 NOT FOR CITATION**
6) 2009 Skitsofrenian Käypä Hoito-suositus (APA)

1. Skitsofreniasta yleistä

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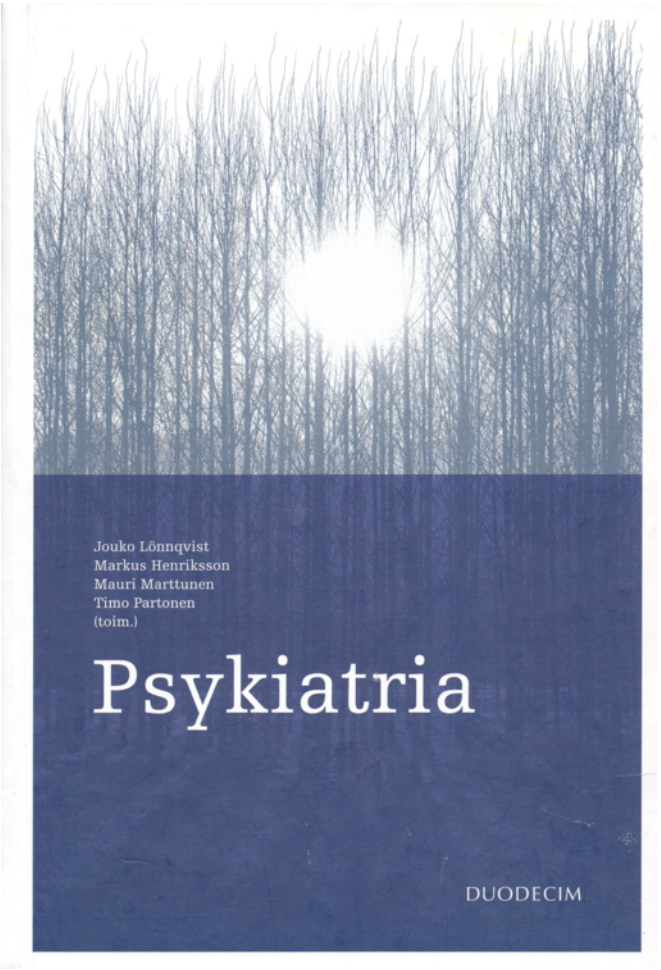
Taulukko 4. Skitsofrenian epidemiologiaa.

Elinaikainen sairastumisriski noin 1 %
Suomessa on noin 50 000 skitsofreniaa sairastavaa henkilöä.
Potilaan sisarilla ja veljillä sekä lapsilla sairastumisriski on 5–10-kertainen.
Vuosittain 10 000:ta henkilöä kohden ilmaantuu 0,8–4,3 uutta tapausta.
Suomessa esiintyvyys on suurin Itä- ja Pohjois-Suomessa.
Miehet sairastuvat yleensä 20–28 vuoden iässä.
Alle 30-vuotiaina sairastuneista kaksi kolmasosaa on miehiä.
Naiset sairastuvat yleensä 24–32 vuoden iässä.
Yli 40-vuotiaina sairastuneissa on enemmän naisia.
Potilaiden sosiaalinen asema ja opiskelu- sekä työkyky heikkenevät sairastumisen jälkeen.

Eli Etelä-Karjalan kokoisessa 133000 väestössä:
10.64-57,19 uutta/ vuosi



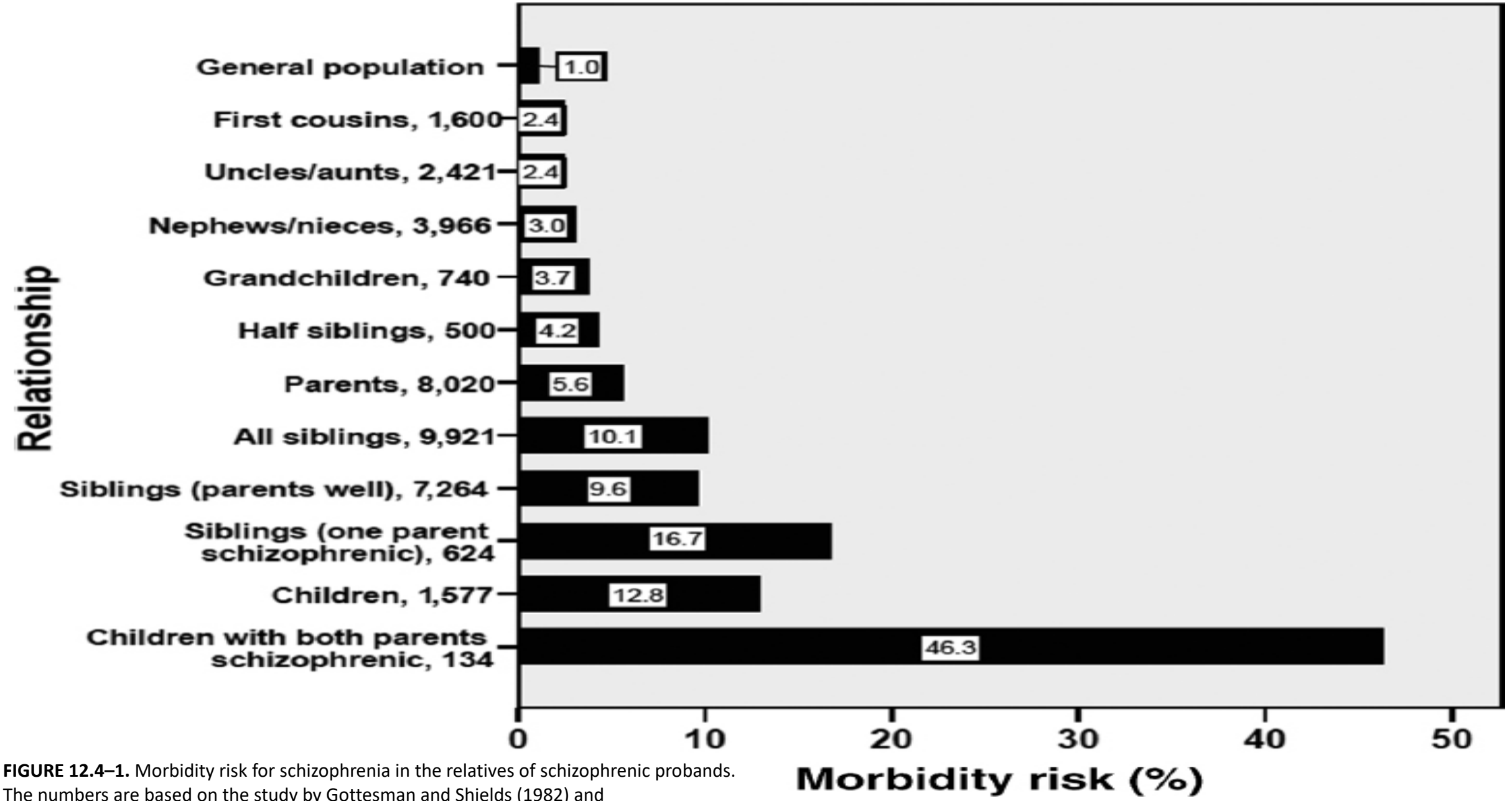
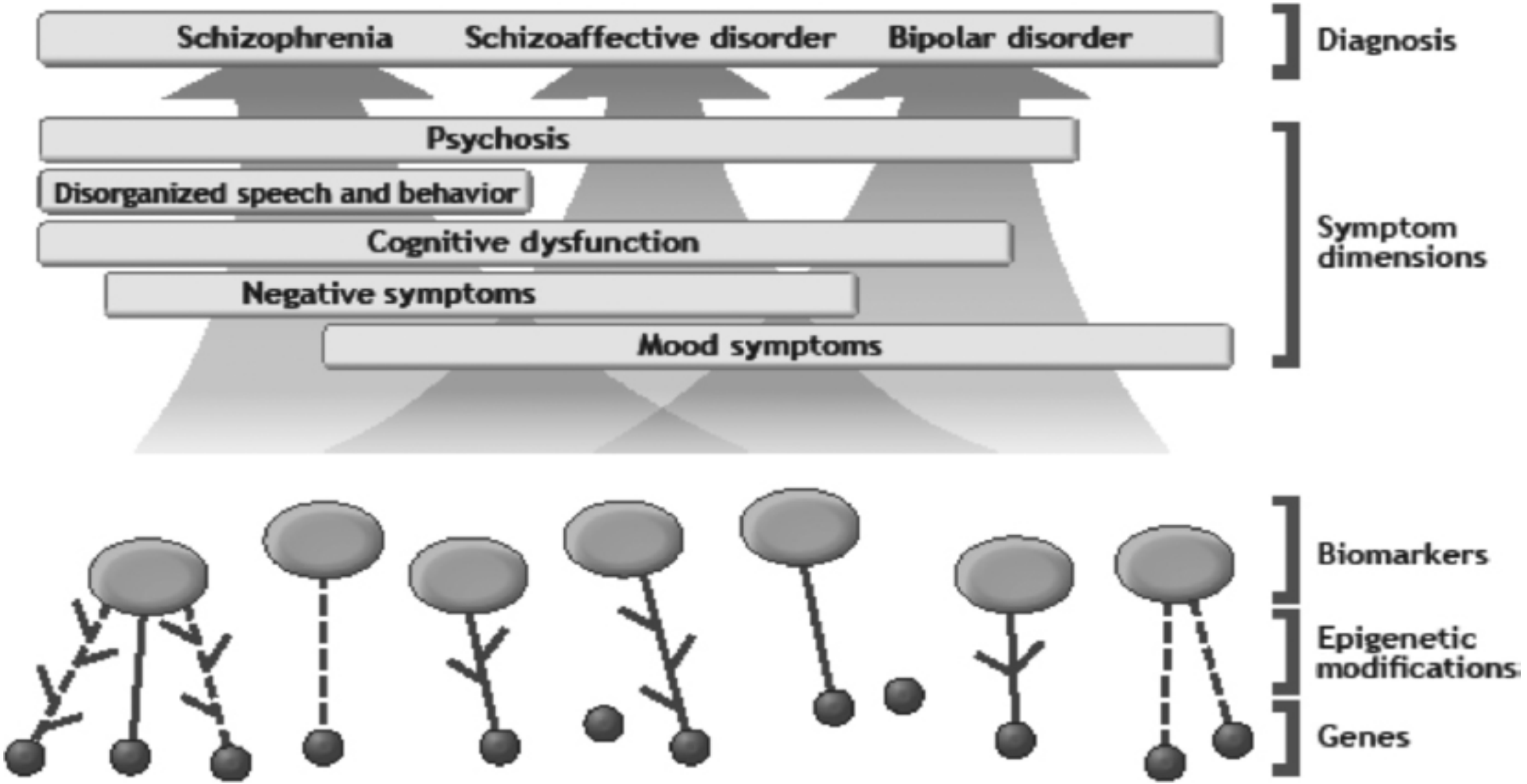
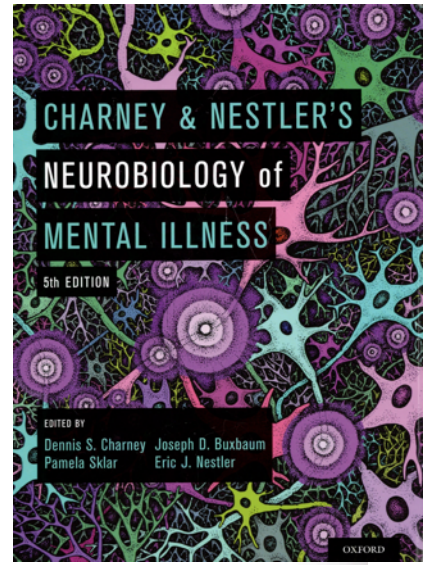


FIGURE 12.4–1. Morbidity risk for schizophrenia in the relatives of schizophrenic probands. The numbers are based on the study by Gottesman and Shields (1982) and used with permission by Irving Gottesman.

Kaplan&Sadock´s, 2017,10th ed



Kaplan&Sadock´s, 2017,10th ed



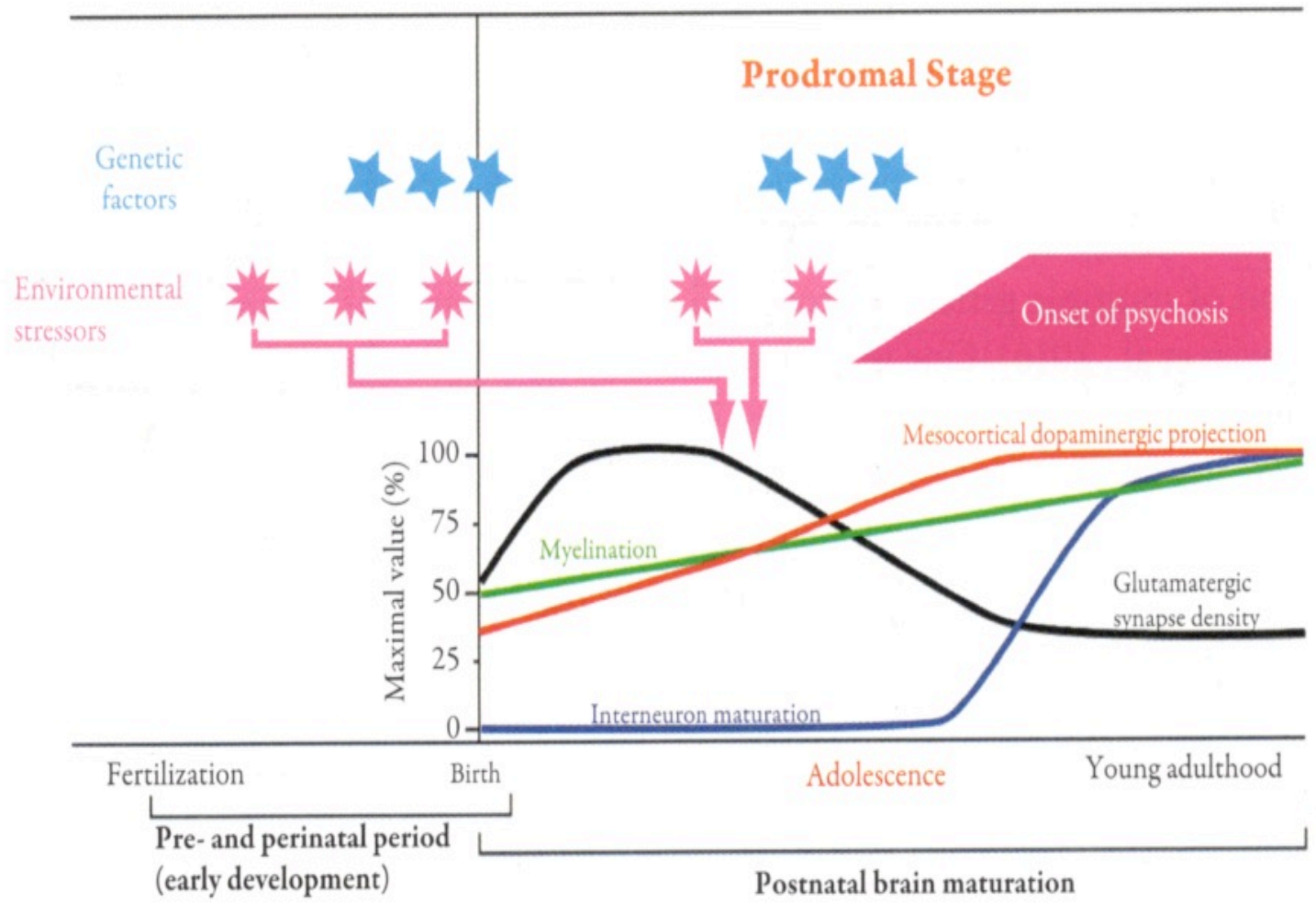
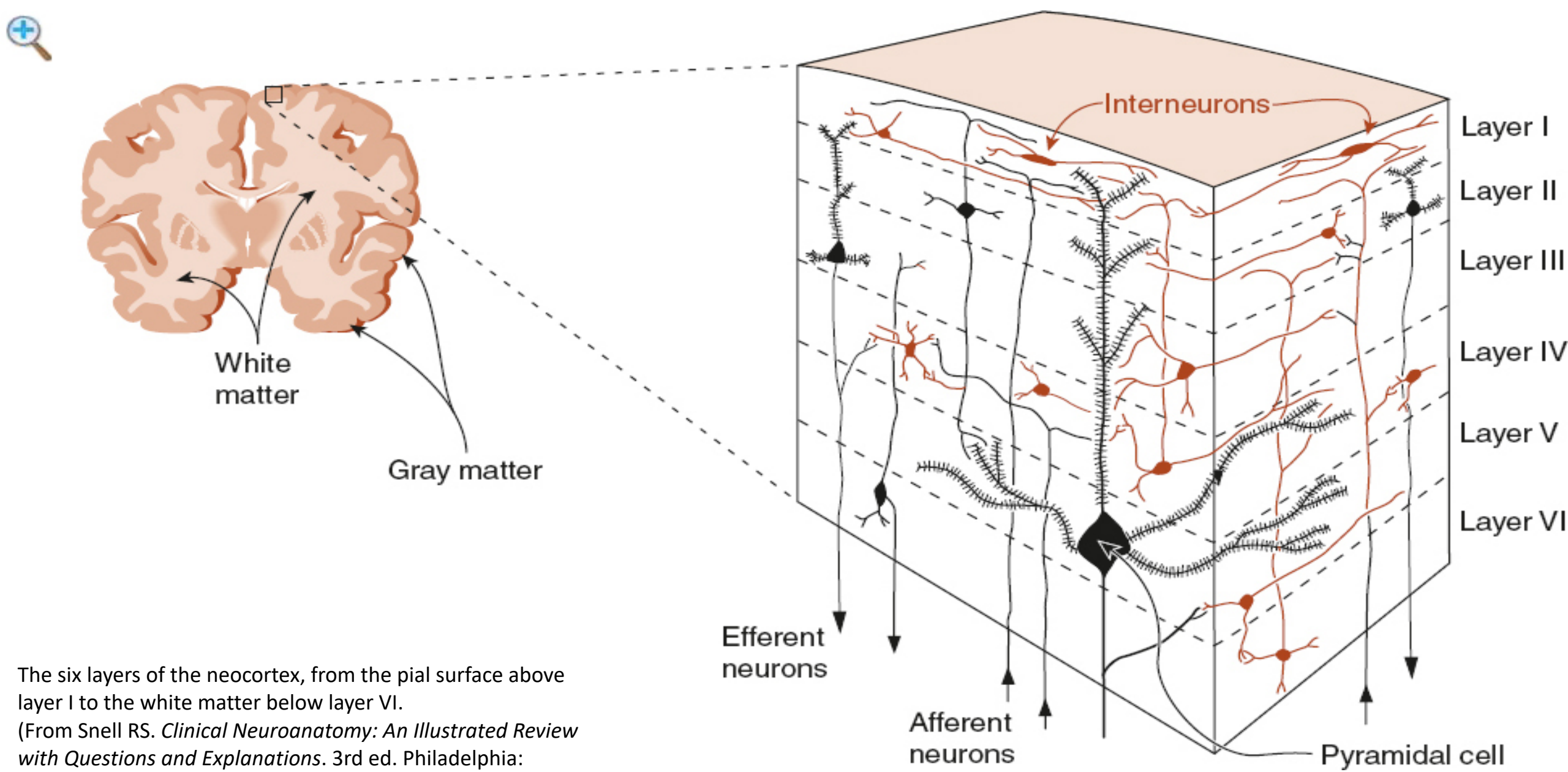
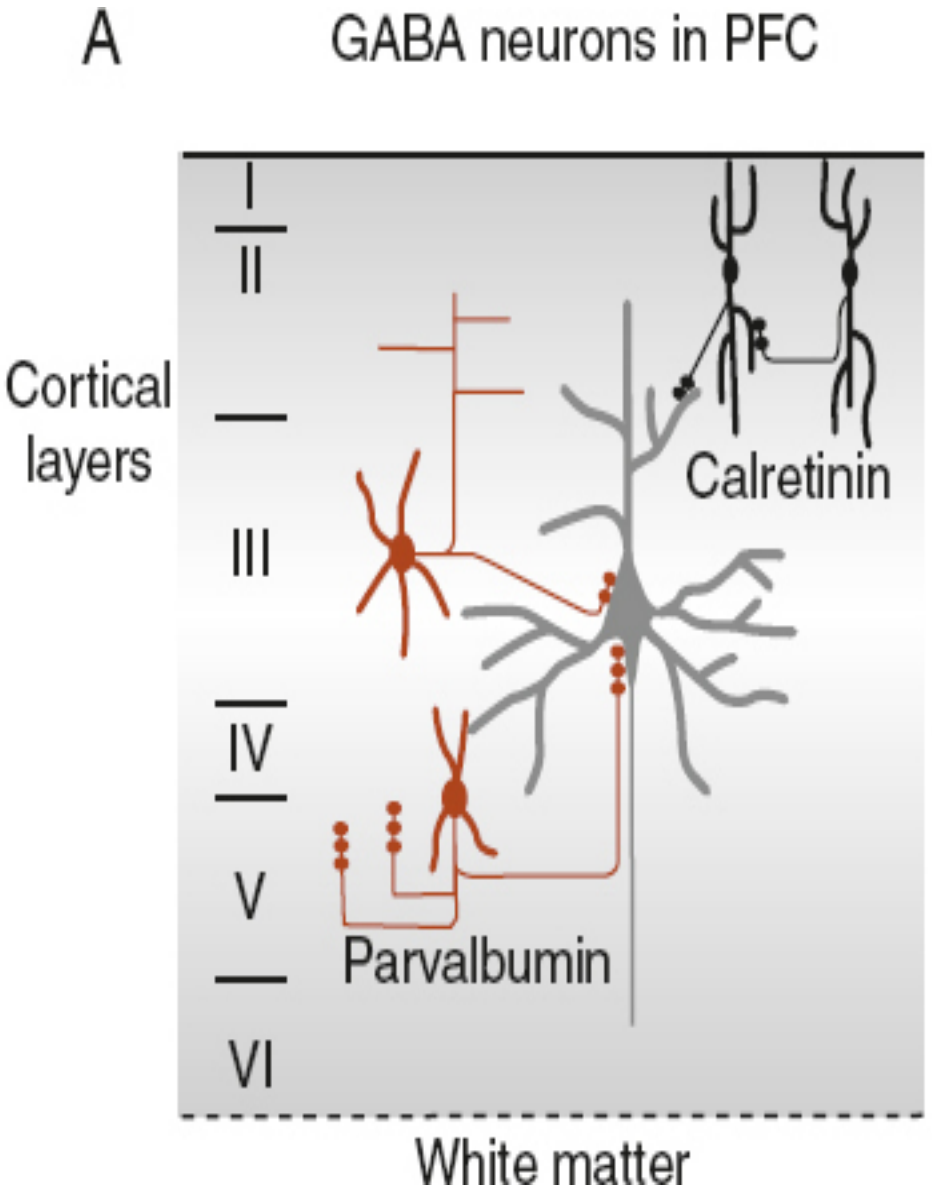


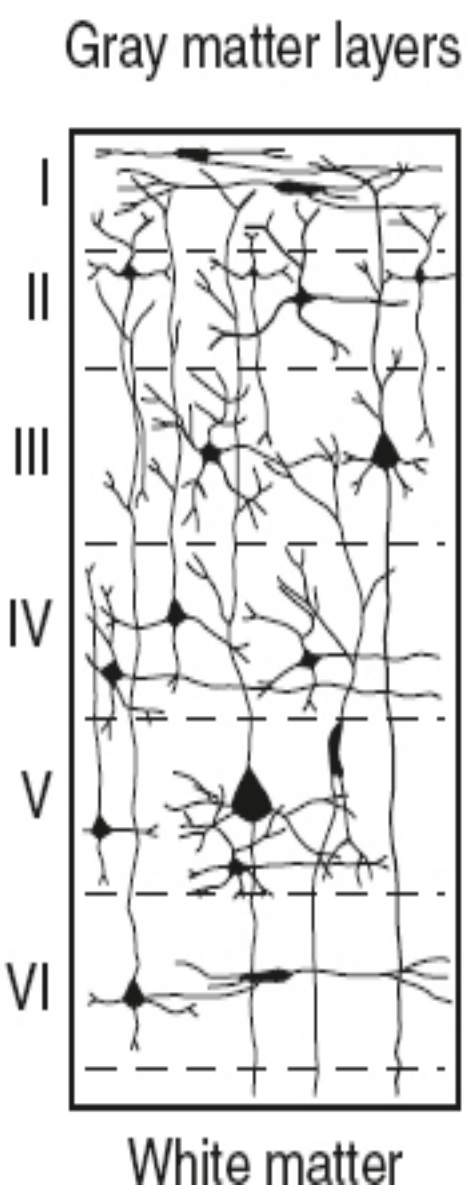
Figure 19.1 Genetic and environmental risk factors that occur over the neurodevelopmental trajectory may impair crucial developmental processes, accumulating to manifest as abnormal brain maturation and psychotic symptoms in early adulthood. Figure adapted with permission from Jaaro-Peled et al. (2009).

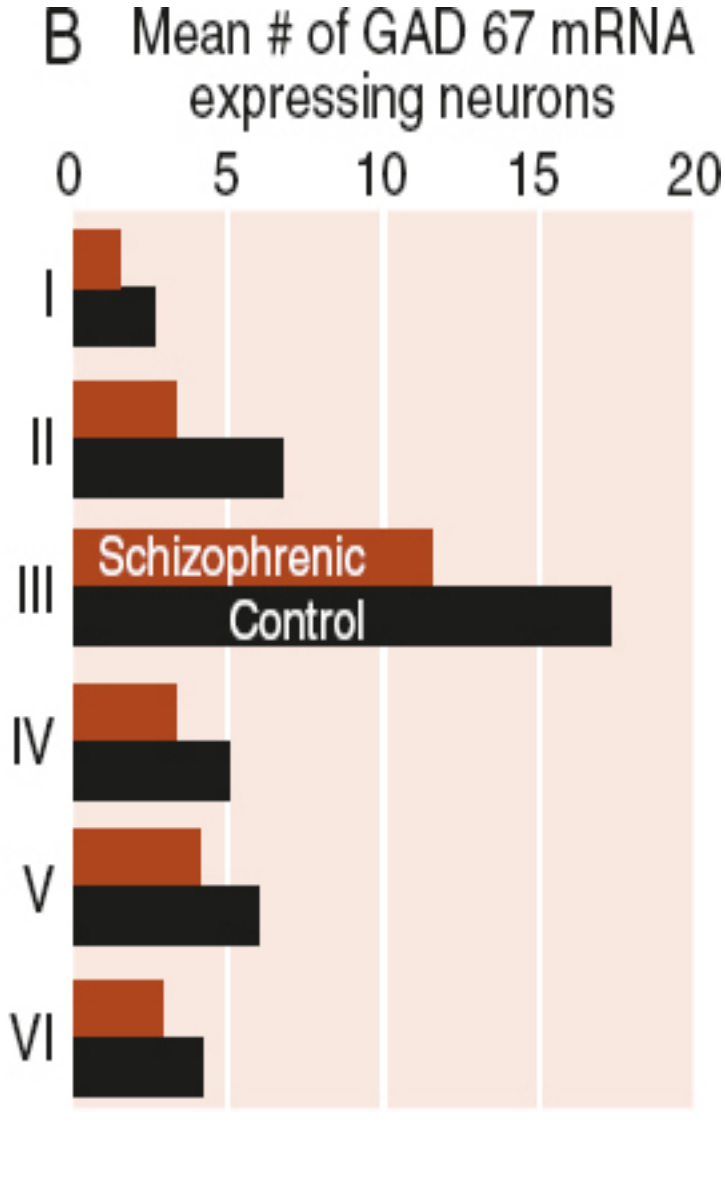


The six layers of the neocortex, from the pial surface above layer I to the white matter below layer VI.
(From Snell RS. *Clinical Neuroanatomy: An Illustrated Review with Questions and Explanations*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2001.)

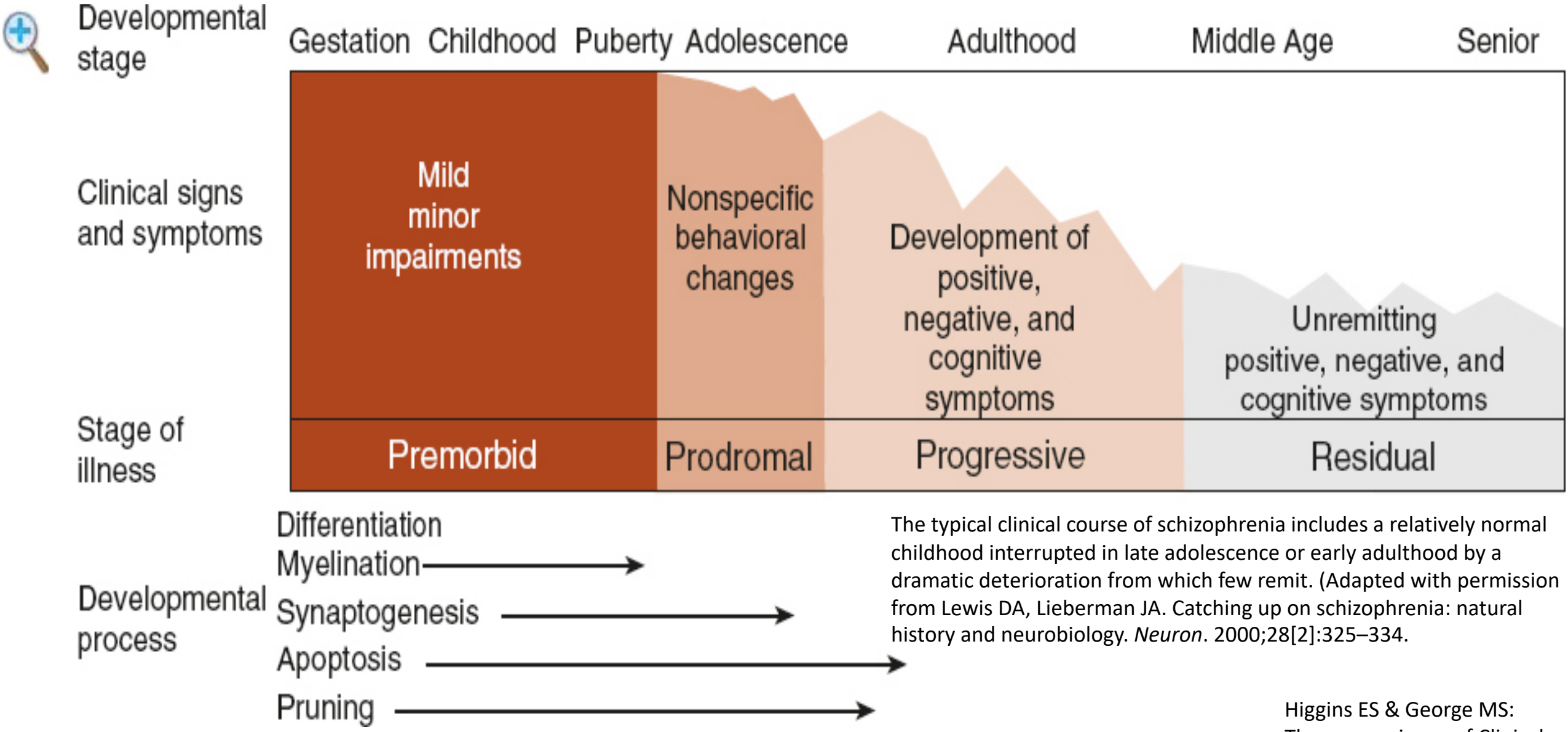
Higgins ES & George MS: The neuroscience of Clinical Psychiatry, 2019, 3rd ed







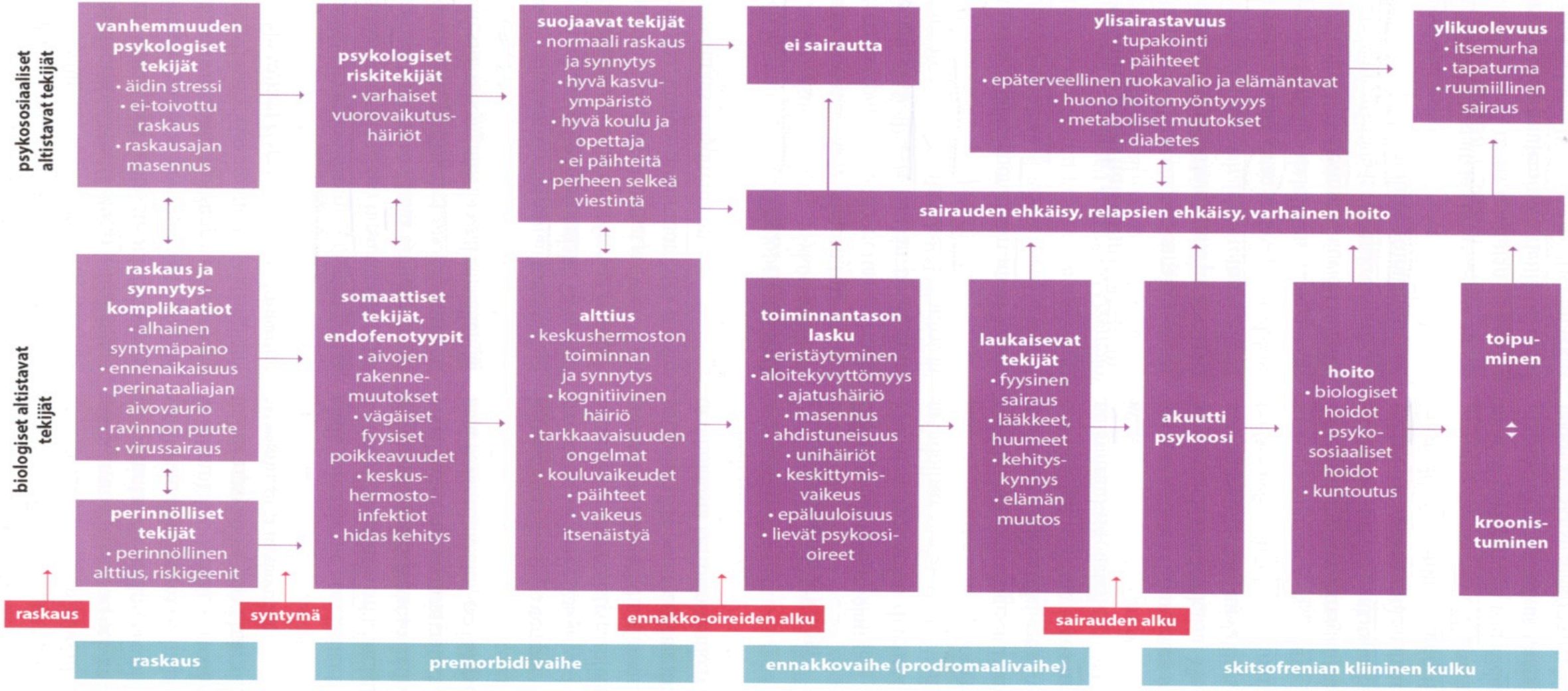
Higgins ES & George MS: The neuroscience of Clinical Psychiatry, 2019, 3rd ed



The typical clinical course of schizophrenia includes a relatively normal childhood interrupted in late adolescence or early adulthood by a dramatic deterioration from which few remit. (Adapted with permission from Lewis DA, Lieberman JA. Catching up on schizophrenia: natural history and neurobiology. *Neuron*. 2000;28[2]:325–334.

Higgins ES & George MS:
The neuroscience of Clinical Psychiatry, 2019, 3rd ed

Psykiatria, 2017



Kuva 3. Skitsofrenian kehitystä ja kulkua kuvaava elämänkaarimalli, jossa esitetään tunnettuja skitsofrenian riskitekijöitä. Nämä selittävät vain osan alttiudesta sairastua: suurin osa altistuneista ei sairastu. Riskitekijät ovat myös epäspesifisiä eli ne voivat altistaa muihin mielenterveyshäiriöihin. Suojaavista tekijöistä ei ole välttämättä näyttöä.

Taulukko 3. Skitsofrenian hyvään ja huonoon ennusteeseen liittyviä tekijöitä.

Hyvä ennuste	Huono ennuste
• Naissukupuoli • Myöhäinen alku • Laukaisevia tekijöitä • Nopea ja akuutti taudinkuva • Hyvä sairautta edeltävä koulutus ja ammatillinen toimintakyky • Hyvä sairautta edeltävä sosiaalinen toimintakyky • Sairaudentunto, hoitomyöntyvyys • Pääosin positiivisia oireita, mutta ei varhaisia aisti-harhoja tai harhaluuloja • Paranoidisia oireita ja masennusoireita • Ei neuropsykologisia häiriöitä tai aivojen rakenne-muutoksia • Parisuhde, perheen lämmin tunneilmapiiri ja hyvä sosiaalinen tukiverkosto • Nopea toipuminen ensipsykoosista • Varhainen ja hyvä hoito, asianmukainen lääkehoito	• Miessukupuoli • Perinnöllinen alttius • Sairastuminen nuorella iällä • Ei laukaisevia tekijöitä • Hidas alku, ennakko-oireita pitkään • Huono sairautta edeltävä selviäminen • Pääosin negatiivisia oireita • Samanaikaiset muut psykiatriset häiriöt: päihdehäiriö, masennus • Hajanaistyyppinen taudinkuva, varhaiset aistiharhat ja harhaluulot • Neuropsykologinen häiriö tai aivojen rakennemuutoksia • Ei parisuhdetta, perheen kriittinen tunneilmapiiri ja vähäinen sosiaalinen tuki • Pitkään kestänyt hoitamaton ensipsykoosi, huono vaste hoitoon • Hoidon puutteet (psykoosilääkitys, kuntoutus) • Huono hoidon jatkuvuus • Liiallinen lääkitys

2. Skitsofrenian diagnosointi

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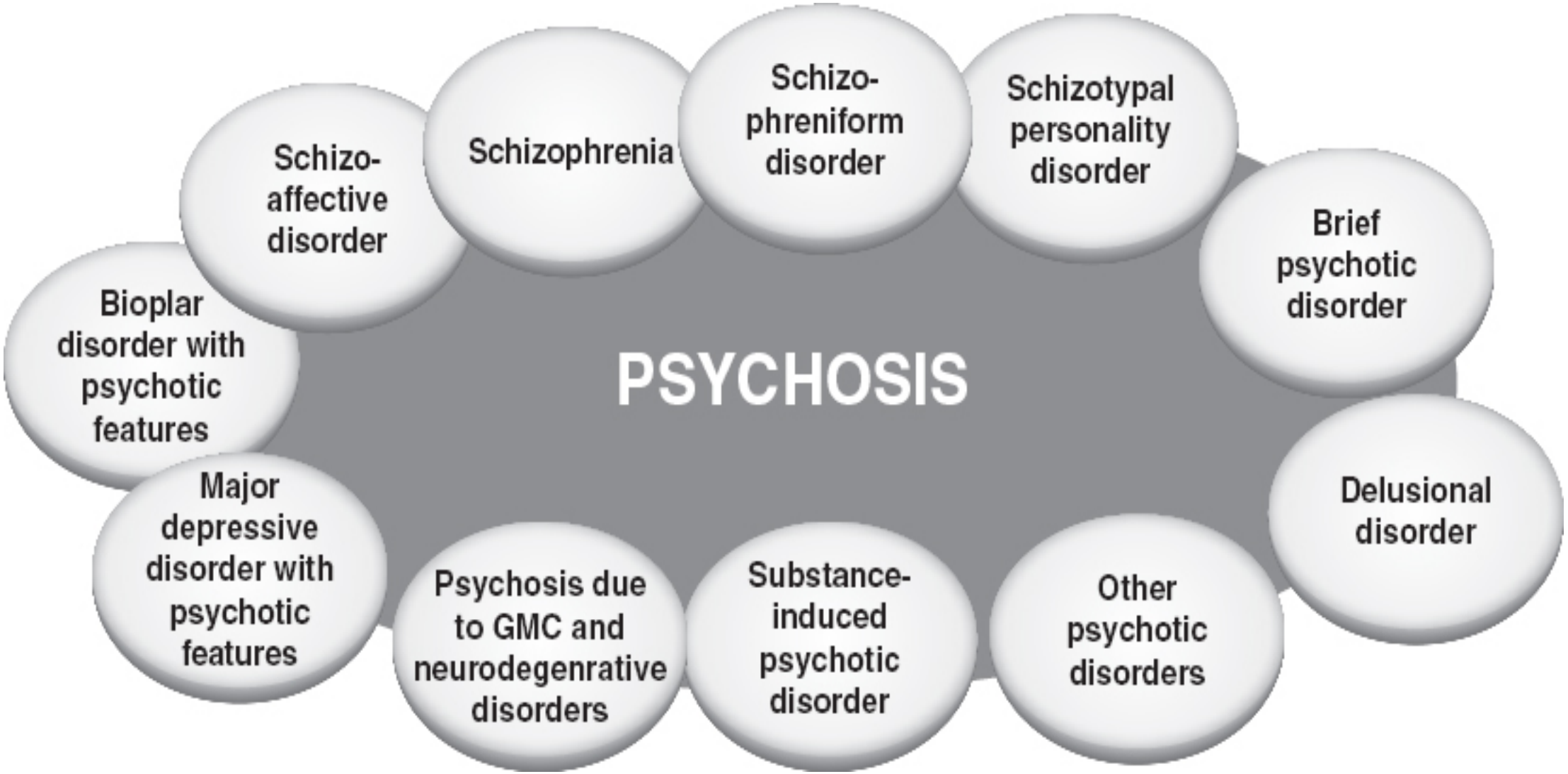
DSM-5 diagnoses overlapping the psychosis dimension. GMC, general medical conditions



Kaplan&Sadock´s, 2017,10th ed

Taulukko 19. Muut psykoottiset häiriöt ICD-10:ssä.

F21	Skitsotyyppinen häiriö
F22	Pitkäaikaiset harhaluuloisuushäiriöt
F23	Äkilliset ja väliaikaiset psykoottiset häiriöt
F24	Indusoitunut harhaluuloisuus
F25	Skitsoaffektiiviset häiriöt
F28	Muut määritetyt ei-elimelliset psykoottiset häiriöt
F29	Määrittämätön ei-elimellinen psykoottinen häiriö
F00-19	Elimellisiin aivo-oireyhtymiin liittyvät ja lääkkeiden ja päihteiden aiheuttamat psykoosit

Taulukko 18. Miksi skitsofrenia pitäisi todeta ja hoitaa varhain?

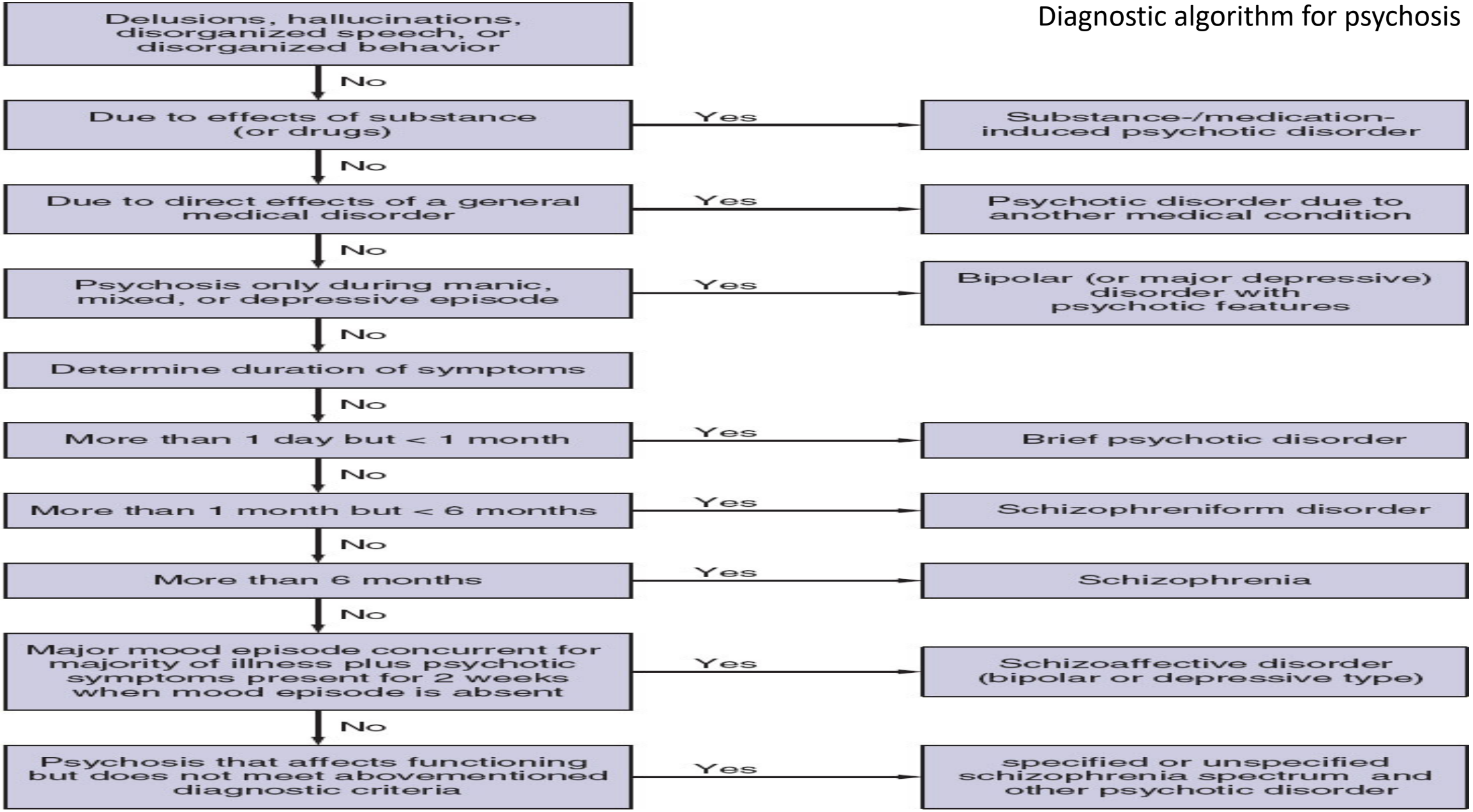
Mitä etuja voidaan saavuttaa?

- Varhainen hoito parantaa ennustetta.
- Itsemurha vaara vähenee.
- Päihteiden käytön riski vähenee.
- keskushermostomuutosten, riski saattaa vähentyä.
- Sosiaaliset ongelmat, parisuhde, perhe, ystävät, koulu ja työ, eivät kärjisty.
- Omaisten hätä ja taakka helpottuvat.
- Hoito voi painottua avohoitoon.

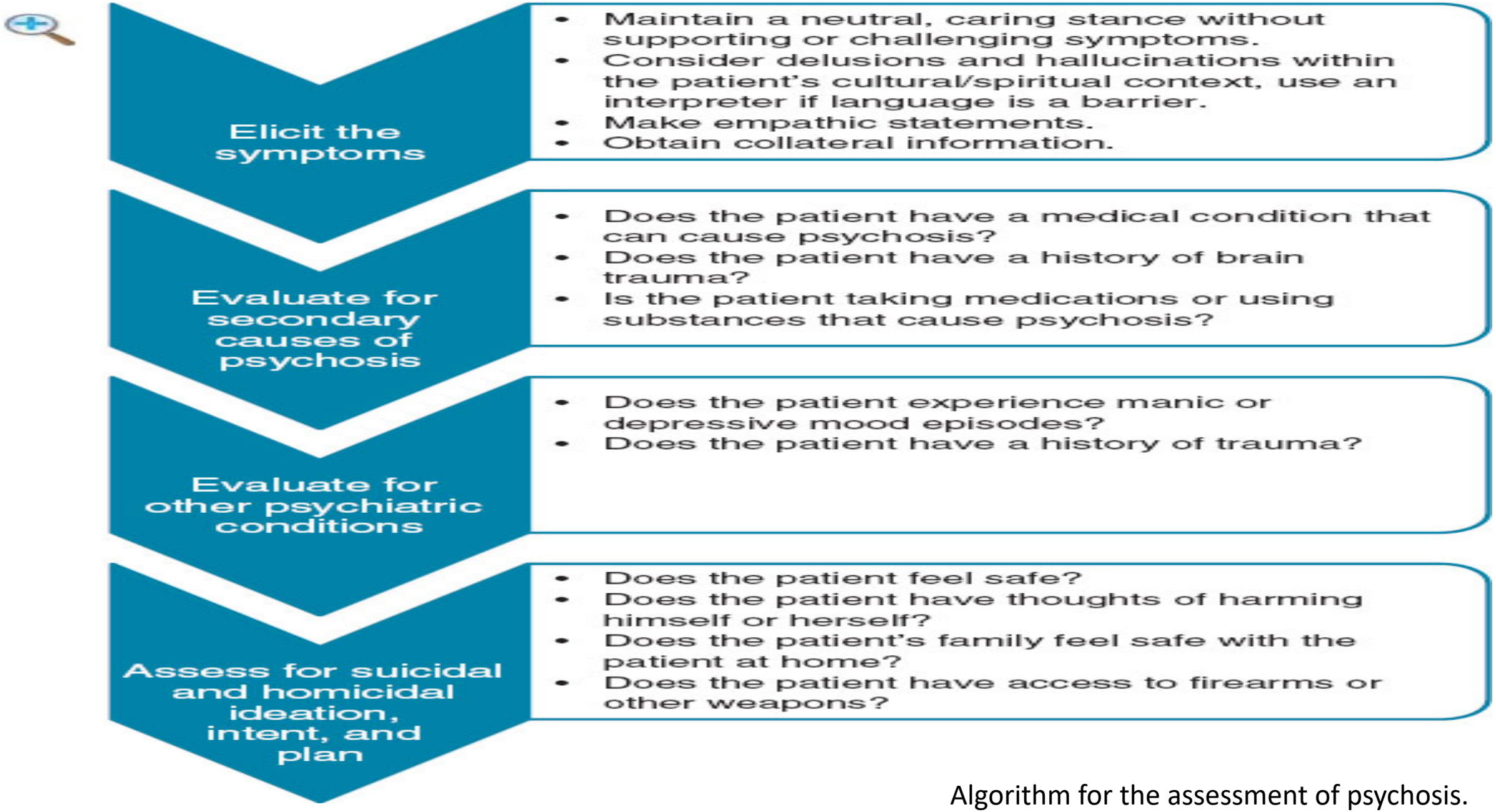
Mikä estää varhaista hoitoa?

- Sairaus voi alkaa hitaasti.
- Oikea diagnoosi on joskus vaikea.
- Diagnostisia kriteereitä ei tunneta tai niitä ei haluta käyttää.
- Potilaan sairaudentunto tai muu kognitio voi olla puutteellinen.
- Potilaalla, omaisilla ja hoitavilla henkilöillä voi olla halu kieltää sairaus.
- Hoitojärjestelmä ja palvelurakenne eivät välttämättä tue varhaista hoitoa.

Diagnostic algorithm for psychosis

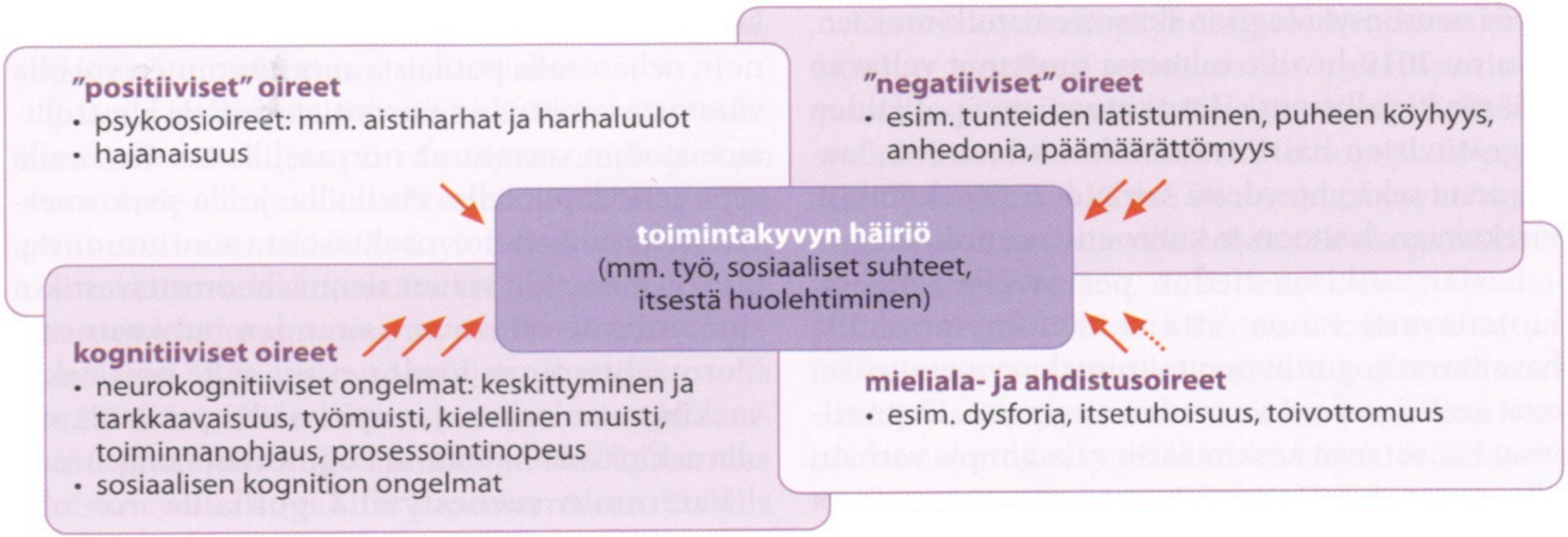


McCarron et al, Primary Care Psychiatry, 2019, 2nd ed



Algorithm for the assessment of psychosis.

McCarron et al, Primary Care Psychiatry, 2019, 2nd ed



Kuva 1. Skitsofrenia oireyhtymänä. Kuvassa näkyvät sairauden keskeiset oiredimensiot. Mikään näistä oiredimensioista ei ole spesifinen skitsofrenialle, eivätkä ne ole toisistaan täysin riippumattomia. Esimerkiksi psykoosioireiden lisääntyessä myös mielialaoireet usein lisääntyvät. Kukin oiredimensio heikentää toimintakykyä ja elämänlaatua. Nuolien määrä kuvaa keskimääräistä vaikutusta potilaan ennusteeseen. Runsas kognitiivinen ja negatiivinen oireisto liittyvät huonoon ennusteeseen, sillä olemassa olevat hoitokeinot tepsivät niihin melko huonosti.

3. Skitsofrenian hoito

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Taulukko 14. Skitsofreniapotilaan avohoidon onnistumiseen vaikuttavia tekijöitä.

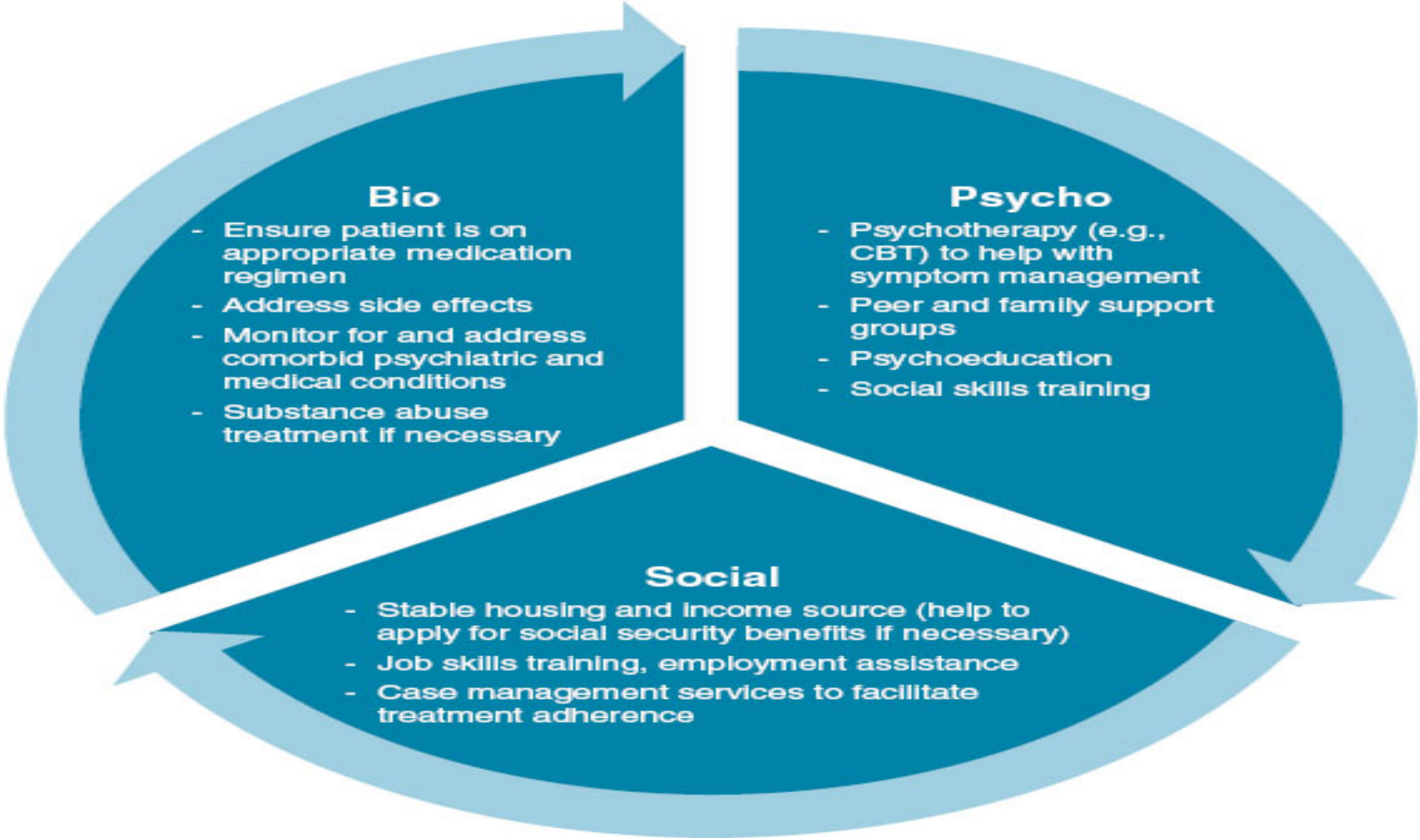
1	Luottamuksellinen hoitokontakti
2	Optimaalinen lääkehoito
3	Yhteistyö perheen kanssa
4	Yhteisö, johon potilas voi kuulua
5	Potilaan riittävän hyvä sosiaalinen toimintakyky
6	Hoito- ja kuntoutussuunnitelman tarpeenmukaisuuden säännöllinen arviointi
7	Hoidon koordinaatio ja jatkuvuuden turvaaminen
8	Kattava, yhtenäinen hoito- ja kuntoutusjärjestelmä

Taulukko 7. Skitsofreniapotilaan somaattinen seuranta.

1	**Paino, etenkin psykoosilääkityksen yhteydessä painonseuranta tärkeää** • painon ja vyötärön ympärysmitan mittaus 1–4 viikon välein 3 kk ajan lääkemuutosten jälkeen, sen jälkeen 3–6 kk välein • ruokapäiväkirja mikäli painonnousu yli 4 kg tai yhden BMI-yksikön • mahdollinen ravitsemusterapeutin konsultaatio
2	**verenpaineen seuranta tarpeen mukaan erityisesti lääkemuutosten yhteydessä**
3	**Laboratoriotutkimukset, etenkin ennen psykoosilääkityksen aloitusta, muutosta ja käytön aikana** • veren glukoosi, triglyseridi, LDL/HDL-kolesteroli 1–2 kertaa vuodessa; useammin korkean riskin potilailta, joilla on suvussa diabetesta tai potilaalla on alentunut sokerirasitus, BMI > 25 tai painonnousu, esimerkiksi 3 kuukauden välein
4	**Terveystottumusten seuranta ja niihin vaikuttaminen** • tupakka-, ruokavalio- ja muu terveysneuvonta • dieettirajoitukset, liikunnan tehostaminen

Taulukko 6. Somaattisia perustutkimuksia akuutin psykoosin yhteydessä.

1.	Anamneesi ja somaattinen – erityisesti neurologinen – status
2.	Thoraxröntgen ja EKG
3.	Laboratoriotutkimuksia • lasko, CRP, täydellinen verenkuva • seerumin elektrolyytit (Na, K, Cl) • verensokeri • kolesteroli ja triglyseridit • seerumin kreatiniini • seerumin kalsium • kilpirauhasen toimintakokeet: S-TSH, S-T_4-V • maksaentsyymit: S-ASAT, S-ALAT, S-GT • virtsanäyte • virtsan huume- ja lääkeaineseula • tarvittaessa raskaustesti
4.	Tarvittaessa aivosähkökäyrä (EEG) tai magneettikuvaus (MK)



The biopsychosocial model in the treatment of schizophrenia. CBT, cognitive behavioral therapy

McCarron et al, Primary Care Psychiatry, 2019, 2nd ed

2017 Remington G et al Canadian Schizophrenia Guidelines Guidelines for the Pharmacotherapy of Schizophrenia in Adults

1. Schizophrenia represents a heterogeneous group of disorders that may differentially affect presentation, course, treatment response, and outcome.
2. Common to these different groups is psychosis, which is integral to the diagnosis of schizophrenia and schizophrenia spectrum disorders.
3. Antipsychotic medications play a central role in recommendations related to pharmacotherapy.
4. Over the course of schizophrenia, psychotic symptoms can wax and wane, and decision making regarding use of antipsychotics is influenced by treatment response and side effects, as well as phase of illness (acute vs. stable).
5. Other symptom domains besides psychosis can be observed as well in the context of schizophrenia and schizophrenia spectrum disorders; accordingly, other types of medications may also be recommended during the course of treatment.

To capture these aforementioned principles, recommendations are categorized into 6 areas:

A. First-episode schizophrenia
B. Acute exacerbation
C. Relapse prevention and maintenance treatment
D. Treatment-resistant schizophrenia
E. Clozapine-resistant schizophrenia
F. Specific symptom domains

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5593252/pdf/10.1177_0706743717720448.pdf

2017 Remington G et al Canadian Schizophrenia Guidelines Guidelines for the Pharmacotherapy of Schizophrenia in Adults

Table 1. Clinical Practice Guidelines Used for the Canadian Schizophrenia Guidelines.

Guideline Developer	Guideline Title	Year Published
National Collaborating Centre for Mental Health Commissioned by the National Institute for Health and Care Excellence (NICE)	NICE National Clinical Guideline Number 178. Psychosis and Schizophrenia in Adults. Treatment and Management[3]	2014
National Collaborating Centre for Mental Health Commissioned by the National Institute for Health and Care Excellence (NICE)	NICE National Clinical Guideline Number 155. Psychosis and Schizophrenia in Children and Young People. Recognition and Management[4]	2013
National Collaborating Centre for Mental Health Commissioned by the National Institute for Health and Care Excellence	NICE National Clinical Guideline Number 120. Psychosis with Coexisting Substance Misuse. Assessment and Management in Adults and Young People[5]	2011
Scottish Intercollegiate Guidelines Network (SIGN)	SIGN 131. Management of Schizophrenia[6]	2013
European Psychiatric Association	European Psychiatric Association Guidance on the Early Intervention in Clinical High Risk States of Psychoses[7]	2015
American Psychiatric Association	American Psychiatric Association Practice Guidelines for Psychiatric Assessment of Adults[8]	2016

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5593252/pdf/10.1177_0706743717720448.pdf

Laatukriteerit	2013 (n=238)	2014 (n=237)	2015 (n=230)	2016 (n=240)	2017 (n=246)	2018 (n=235)
1. Onko potilaan sairauskertomuksessa ajantasainen kirjallinen hoitosuunnitelma (tehty 3 kk:n sisällä)?	79,8	82,3	87,4	95,0	93,9	94,0
2. Onko sairaalasta otettu yhteyttä perheeseen tai lähiverkostoon kahden viikon kuluessa hoidon alusta?	92,4	85,7	83,0	80,0	74,4	71,5
3. Saako potilas tällä hetkellä korkeintaan kahta antipsykoottia samanaikaisesti?	95,0	97,5	95,2	95,4	98,4	98,7
4. Potilaalle ei ole määrätty bentsodiatsepiineja yli 2 kuukautta (sisältäen annoksen asteittaisen laskun ja lopetuksen) yhtäjaksoisesti?	99,6	99,2	99,1	100	99,6	100
5. Saako tai onko potilas saanut viimeisen vuoden aikana hoitosuunnitelman mukaista psykososiaalista hoitoa?	99,2	100	100	100	100	100
1. Hoitosuhde/Yksilöpsykoterapia	96,6	100	83,5	100	93,1	98,3
2. Psykoedukaatio	57,1	42,6	11,7	30,4	44,3	63,8
3. Ryhmämuotoiset interventiot	8,8	29,5	75,7	81,7	77,6	79,6
4. Perheinterventio	11,8	10,1	16,1	24,2	30,1	44,7
5. Luovat terapiat	71,4	70,9	56,5	67,9	72,8	76,2
6. Arkielämän taitojen opettelu	87,0	95,4	89,6	91,7	94,7	92,8
7. Sosiaalisten taitojen opettelu	16,8	6,3	46,5	69,6	76,8	91,1
8. Kognitiiviset kuntoutusohjelmat	2,1	4,2	13,0	27,9	23,6	40,4
9. Työelämään valmistava toiminta	0	8,4	1,7	6,3	4,9	3,4
6. Sairaalasta kotiutettu skitsofreniapotilas ei ole palannut uuteen ennakolta suunnittelemattomaan sairaalahoitoon Niuvanniemen sairaalaan kuuden kuukauden kuluessa?	100	100	100	99,6	100	99,6
7. Onko skitsofreniapotilaan perhettä/lähiverkostoa tavattu sairaalassa tai hänen kanssaan tehty kotikäynti vuoden aikana?	71,4	71,3	73,5	77,1	77,6	76,2
8. Onko potilaalle tehty vuosittain somaattisten pitkäaikaissairauksien ja niiden riskitekijöiden selvittelyn sisältävä somaattinen tutkimus?	100	100	100	100	100	100
9. Onko potilaalle tehty psykologisen tai neuropsykologisen tutkimuksen tarpeen arviointi kahden viikon kuluessa hoidon alusta?	91,2	87,3	83,0	82,5	81,3	80,4
Laatukriteerien toteutuminen	**92,0**	**91,5**	**91,3**	**92,2**	**91,7**	**91,2**

Taulukko 8. Psykoosilääkkeiden kliinisesti suuntaa-antavat klooripromatsiiniekvivalentit ja tavanomaiset skitsofrenian hoidossa käytettävät vuorokausiannokset.

Psykiatria, 2017

Lääkeaine	Klooripromatsiini-ekvivalenssiannos / mg		Vuorokausi-annos / mg	Valmistemuoto
Klooripromatsiini	100	Klorproman	150–1 000	Tabletti
Levomepromatsiini	100	Levozin	100–1 000	Tabletti
Perisiatsiini	20	Neulactil	20–250	Tabletti
Flufenatsiini	2	Siqualone		Depot-injektio
Perfenatsiini	8	Peratsin	12–60	Tabletti, depot-injektio
Flupentiksoli	2	Fluanxol	3–25	Tabletti, depot-injektio
Klooriprotikseeni	100	Truxal	200–800	Tabletti
Tsuklopentiksoli	20	Cisordinol	15–80	Tabletti, tipat, injektioneste, depotinjektio
Haloperidoli	2	Serenase	4–20	Tabletti, oraaliliuos, injektioneste, depotinjektio
Melperoni	50	Melpax	200–800	Tabletti
Sulpiridi	250	Suprium	400–1 600	Tabletti, kapseli
Aripipratsoli	3	Abilify	10–30	Tabletti, depot-injektio
Ketiapiini	100	Seroquel	300–750	Tabletti, depot-tabletti
Klotsapiini	50	Leponex	200–600	Tabletti
Olantsapiini	3	Zyprexa	10–20	Tabletti, suussa sulava tabletti, oraaliliuos, injektiokuiva-aine, depot-injektio
Risperidoni	1	Risperdal	2–8	Tabletti, oraaliliuos, depotinjektio-kuiva-aine
Sertindoli	3	Serdolect	12–20	Tabletti
Tsiprasidoni	15	Zeldox	40–160	Kapseli, injektiokuiva-aine
Asenapiini	3	Sycrest	10–30	Tabletti
Paliperidoni	Ei arvioitu	Xeplion	25–150 mg/ kuukausi	Depot-injektio

Taulukko 13. Uuden polven psykoosilääkkeiden reseptorivaikutukset hoitoannoksilla.

	Lääke	D2	5-HT2A	Alfa-1	Alfa-2	H1	M1
Abilify	Aripiratsoli	++++	+++	+	+	+	–
Seroquel	Ketiapiini	+	++	+++	–	++	+
Leponex	Klotsapiini	+	+++	+++	++	+++	+++++
Zyprexa	Olantsapiini	++	+++	++	++	+++	+++++
Risperdal	Risperidoni	+++	++++	+++	+++	–	–
Serdolect	Sertindoli	+++	++++	++	+	+	–
Zeldox	Tsiprasidoni	+++	++++	++	+	–	–

– = ei vaikutusta

D = dopamiini, 5-HT = serotoniini, H = histamiini, M = muskariini

Table 22.1 BINDING PROFILES OF FIRST GENERATION ANTIPSYCHOTICS

	D2 ACTIVITY	5HT2 ACTIVITY	MUSCARINIC ACTIVITY	ALPHA-1 ADRENERGIC ACTIVITY	ANTIHISTAMINE ACTIVITY
Chlorpromazine	++++	++++	++++	++++	++++
Fluphenazine	++++	++	+	+	++
Perphenazine	++++	++++	+	++	+++
Trifluoperazine	++++	+++	+	++	++
Thioridazine	++++	++++	++++	++++	++++
Haloperidol	++++	++	+	+	+
Thiothixene	++++	+	+	++	+++
Loxapine	+++	++++	++	+++	++++

Taulukko 9. Psykoosilääkkeiden reseptorisalpauksen hoito- ja haittavaikutukset.

Lääke	Hoitovaikutus	Haittavaikutus
Dopamiini-D2-reseptorien salpaus	Mesolimbiseltä alueelta skitsofrenian positiivisten oireiden lievittyminen	Nigrostriataaliselta alueelta ekstrapyramidaaliset liikehäiriöt (dystonia, parkinsonismi, akatisia, tardiivi dyskinesia) ja tuberoinfundibulaariselta hyperprolaktinemia (galaktorrea, gynekomastia, kuukautiskierron epäsäännöllisyys, potenssivaikeudet) sekä mesokortikaaliselta alueelta psykoosin negatiivisten oireiden voimistuminen
Muskariinireseptorien salpaus	Ekstrapyramidaalisten oireiden lievittyminen	Näön hämärtyminen, ahdaskulmaglaukoomakohtaus, suun kuivuminen, sinustakykardia, ummetus, virtsaumpi, muistivaikeudet
Serotoniini-(5-HT)2A-reseptorien salpaus	Skitsofrenian negatiivisten oireiden ja ekstrapyramidaalioireiden lievittyminen	Tuntemattomia
Histamiini1-reseptorien salpaus	Sedaatio	Sedaatio, painon nousu ja muiden lääkkeiden väsyttävien vaikutusten voimistuminen

Taulukko 12. Eri psykoosilääkkeiden tavallisimpia haittavaikutuksia.

Lääkeaine	Painonnousu	Neurologiset haittaoireet	Prolaktiini-erityksen lisääntyminen	QTc-ajan pidentyminen	Väsyneisyys
Haloperidoli	-	+++	++	+	+
Tsiprasidoni	-	+	+	++	++
Aripipratsoli	+	+	-	-	+
Amisulpridi	+	+	Ei arvioitu	++	-
Asenapiini	+	+	-	+	++
Paliperidoli	++	+	+++	-	-
Risperidoni	++	++	+++	+	+
Ketiapiini	++	-	-	+	++
Sertindoli	++	-	+	+++	-
Klooripromatsiini	+++	++	+	Ei arvioitu	+++
Klotsapiini	+++	-	Ei arvioitu	Ei arvioitu	+++
Olantsapiini	+++	-	+	+	++

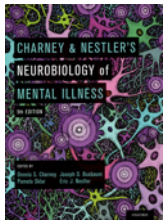


Table 22.2 ADVERSE EFFECT PROFILES OF COMMON ANTIPSYCHOTICS

	HALOPERIDOL	CLOZAPINE	RISPERIDONE	OLANZAPINE	QUETIAPINE	ZIPRASADONE	ARIPIPRAZOLE	PALIPERIDONE
Motoric effects	+++	0	++	0/+	0	0/+	++	++
Metabolic effects	+	+++	++	+++	++	0/+	0/+	++
Cardiovascular effects	++	+++	+	+	+	++	0	++
Prolactin elevation	++	0/+	+++	0/+	0/+	0/+	0	+++
Cholinergic effects	0	+++	0/+	+/++	0/+	0/+	0	0/+
Hematological effects	0	+++	0	0	0	0	0	0
Sedation	+	+++	+	+/++	+++	++	+	+

Adapted from *Gabbard's Treatments of Psychiatric Disorders,* Fifth Edition. Glen O. Gabbard, MD (Ed.) (2014) Arlington, VA.

John Lauriello, M.D. Stefano Pallanti, M.D.(eds) Clinical Manual for Treatment of Schizophrenia, 2012

Table 8–2. Side-effect profiles of antipsychotic drugs

	FGAs		SGAs				
Side effect	Haloperidol	Perphenazine	Amisulpride	Asenapine	Blonanserin	Clozapine	Iloperidone
Extrapyramidal symptoms	+++	++	0 to ++	0 to ++	+	0	0
Tardive dyskinesia	+++	++	+	?	?	0	?
Prolactin elevation	+++	++	+++	0 to +	++	0	0
Weight gain	+	+	+	0	0	+++	++
Glucose abnormalities	0	+?	+	0	++	+++	+
Lipid abnormalities	0	+?	+	0	++	+++	0
QTc prolongation	+	0	+	0 to +	0?	0	++
Sedation	++	+	0 to +	+	+?	+++	+
Hypotension	0	+	0	+	0	+++	+
Anticholinergic side effects	0	+	0	0	0	+++	0

John Lauriello, M.D. Stefano Pallanti, M.D.(eds) Clinical Manual for Treatment of Schizophrenia, 2012

Table 8–2. Side-effect profiles of antipsychotic drugs *(continued)*

	SGAs *(continued)*							TGA
Side effect	Olanzapine	Paliperidone	Perospirone	Quetiapine	Risperidone	Sertindole	Ziprasidone	Aripiprazole
Extrapyramidal symptoms	0 to +	0 to ++	0 to +	0	0 to ++	0	0 to +	+
Tardive dyskinesia	+	+	0 to +	0 to +	+	0 to +	+	+
Prolactin elevation	+	+++	+	0	+++	0 to +	+	0
Weight gain	+++	+	0	++	+	+	0	0
Glucose abnormalities	+++	0 to +	+	++	++	?	0	0
Lipid abnormalities	+++	0	0?	++	++	?	0	0
QTc prolongation	0 to +	0 to +	0?	+	+	+++	++	0
Sedation	+	+	+	++	+	0 to +	0 to +	0 to +
Hypotension	+	0 to +	0	++	+	+	+	0
Anticholinergic side effects	++	0	0	+	0	0	0	0

Note. This table is not based on direct quantitative comparative data of all the drugs listed. Data from many studies with varying methodology were reviewed to produce this one view. In addition, it is well known that interindividual variability is considerable with regard to drug safety and that most antipsychotic-induced adverse effects are dose-dependent. FGAs=first-generation antipsychotic drugs; SGAs=second-generation antipsychotic drugs; TGA=third-generation antipsychotic drug; 0=minimal to no risk; +=low risk; ++=moderate risk; +++=high risk; ?=unknown risk.

Source. *Adapted from* Falkai et al. 2005; Lehman et al. 2004; Miyamoto et al. 2008.

Taulukko 10. Psykoosilääkkeiden haittavaikutukset ja niiden hoito.

Psykiatria, 2017

Haittavaikutus	Hoito
Väsymys	Lääkeannoksen lasku tai vaihto toisen ryhmän tai tyypin lääkkeeseen
Ummetus	Lääkeannoksen lasku tai vaihto toisen ryhmän tai tyypin lääkkeeseen
Sydämentykytys	Lääkeannoksen lasku tai vaihto toisen ryhmän tai tyypin lääkkeeseen Beetasalpaaja
Virtsaumpi	Lääkeannoksen lasku tai vaihto toisen ryhmän tai tyypin lääkkeeseen
Hypotensio	Lääkeannoksen lasku tai vaihto toisen ryhmän tai tyypin lääkkeeseen
Sentraalinen antikolinerginen vaikutus	Lääkeannoksen lasku tai vaihto toisen ryhmän tai tyypin lääkkeeseen
Lääkeparkinsonismi	Lääkeannoksen lasku tai vaihto toiseen lääkkeeseen, antikolinerginen lääkitys (biperideeni 2 mg × 1–3/vrk, bentsheksoli 2 mg × 1–3/vrk, orfenadriini 50–100 mg × 2–3/vrk), amantadiini (100 mg × 1–2/vrk)
Akuutti dystonia	Antikolinerginen lääke (biperideeni 2,5–5 mg i.m.)
Akatisia	Lääkeannoksen lasku, beetasalpaaja (propranololi 30–90 mg/vrk), bentsodiatsepiini (loratsepaami, klonatsepaami), vaihto 2. polven antipsykoottiin
EP-oireet	Annoksen pienentäminen, lääkkeen vaihto Antikolinergi
Maligni neuroleptioireyhtymä	Lääkkeen käytön välitön lopettaminen, dopamiiniagonistit, antispastiset aineet
Tardiivi dyskinesia	Annoksen lasku, vaihto 2. polven psykoosilääkkeeseen, amantadiini, selegiliini
Kouristukset	Lääkityksen lopetus tai vähentäminen puoleen, neurologinen selvitys
Endokriiniset sivuvaikutukset	Bromokriptiini (1,25–2,5 mg × 2–3/vrk)
Painonnousu	Annoksen lasku, dieettikontrolli, vaihto lihottamattomaan 2. polven antipsykoottiin
Seksuaalitoimintojen häiriöt	Annoksen lasku, lääkkeen vaihto
Iho-oireet	Antihistamiini, lääkkeen vaihto

Table 22.2 ADVERSE EFFECT PROFILES OF COMMON ANTIPSYCHOTICS

	HALOPERIDOL	CLOZAPINE	RISPERIDONE	OLANZAPINE	QUETIAPINE	ZIPRASADONE	ARIPIPRAZOLE	PALIPERIDONE
Motoric effects	+++	0	++	0/+	0	0/+	++	++
Metabolic effects	+	+++	++	+++	++	0/+	0/+	++
Cardiovascular effects	++	+++	+	+	+	++	0	++
Prolactin elevation	++	0/+	+++	0/+	0/+	0/+	0	+++
Cholinergic effects	0	+++	0/+	+/++	0/+	0/+	0	0/+
Hematological effects	0	+++	0	0	0	0	0	0
Sedation	+	+++	+	+/++	+++	++	+	+

Adapted from *Gabbard's Treatments of Psychiatric Disorders,* Fifth Edition. Glen O. Gabbard, MD (Ed.) (2014) Arlington, VA.

Common Side Effects of Antipsychotics

DESCRIPTION	TIME COURSE	TREATMENT	COMMENT
Akathisia			
A subjective, intolerable feeling of inner restlessness or sensation of the need to move	Transient reaction that may remit spontaneously over a few weeks	May trial propranolol 10 mg PO BID or TID and increase as tolerated. Benzodiazepines may be effective as well	Common side effect of aripiprazole
Dystonia			
Painful, uncontrollable tightening of muscles usually involving neck, back, or ocular muscles	Few hours to days of starting an antipsychotic	IM diphenhydramine (25-50 mg) or benztropine (1-2 mg) is a rapid, effective treatment	The emergence of dystonia can be a frightening experience for the patient, and reassurance coupled with education is critical to maintaining a trusting clinician–patient relationship and ongoing adherence with a treatment plan

McCarron et al, Primary Care Psychiatry, 2019, 2nd ed

Common Side Effects of Antipsychotics

DESCRIPTION	TIME COURSE	TREATMENT	COMMENT
Parkinsonian syndrome			
Mimics Parkinson disease, masked facies, limb rigidity, bradykinesia, pill-rolling tremor, micrographia, shuffling gait with postural instability		Oral anticholinergic medications (diphenhydramine 25-50 mg PO TID. Trihexyphenidyl (5-10 BID) or benztropine 1-2 mg BID	May use anticholinergics as a prophylaxis for parkinsonian syndrome when using high-potency antipsychotic such as Haldol. If used for prophylactic treatment, they can generally be tapered and stopped after 10 days. In those who poorly tolerate anticholinergic medications (e.g., patients with dementia), amantadine 100-300 mg BID may be used to treat parkinsonian symptoms, although the lowest effective antipsychotic dose should be used

McCarron et al, Primary Care Psychiatry, 2019, 2nd ed

Common Side Effects of Antipsychotics

DESCRIPTION	TIME COURSE	TREATMENT	COMMENT
Neuroleptic malignant syndrome (NMS)			
Rare, life-threatening side effect of all antipsychotics, involving muscle rigidity, autonomic dysregulation, fever, leukocytosis, elevated creatinine phosphokinase (>300 U/mL), and acute confusion	Usually occurs immediately following the initiation or increased dose of antipsychotic medication	Immediate transport to emergency department for IV fluids, supportive treatment. When severe, may require dopaminergic agents (e.g., dantrolene, bromocriptine)	NMS is difficult to evaluate in the outpatient setting and usually requires emergency medical management
Tardive dyskinesia			
Nonrhythmic, quick, choreoathetoid movements of the face, trunk, and extremities characterize TD. Examination for writhing of the tongue, hands, or trunk should be checked every 6-12 months, as this condition is generally permanent with no known treatment	Long-term EPS and can develop at a rate of about 3%-5% per year for FGAs. TD can occur with SGAs at a rate of about 0.8% per year	Discontinuation of offending antipsychotic, consider lower potency agent. Some reported improvement with vitamin E supplementation	TD risk factors include older age, longer use of antipsychotics, brain damage, diabetes mellitus, and comorbid mood disorder[13]

McCarron et al, Primary Care Psychiatry, 2019, 2nd ed

First-Line Antipsychotic Medications for Schizophrenia[a]

STARTING Dose	TARGET RANGE[a](mg/day)	PRIMARY CARE TITRATION SCHEDULE	EPS	ORTHOSTATIC HYPOTENSION	METABOLIC SYNDROME[b]	SEDATION	OTHER	
Haloperidol (Haldol)(available in long-acting injectable formulations)	2-5 mg PO BID	20-40 mg/day	Increase up to 5 mg daily, as tolerated	+++	+	+/–	+	
Risperidone[c] **(Risperdal)**(available in long-acting injectable and ODT formulations)	1 mg BID or 2 mg QHS	4-6	Increase up to 2 mg daily, as tolerated	+++	++	++	++	Hyperprolactinemia
Olanzapine[c] **(Zyprexa)**(available in long-acting injectable and ODT formulations)	5-10 mg QHS	10-30	Increase 5 mg every 3-5 days, as tolerated	+	+	+++	+++	Not to be routinely used for the treatment of insomnia

Serenase

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First-Line Antipsychotic Medications for Schizophrenia[a]

STARTING Dose	TARGET RANGE[a] (mg/day)	PRIMARY CARE TITRATION SCHEDULE	EPS	ORTHOSTATIC HYPOTENSION	METABOLIC SYNDROME[b]	SEDATION	OTHER	
Quetiapine[d] (Seroquel)	50-100 mg BID	300-800	Increase 50-100 mg every 2 days, as tolerated (monitor for orthostatic hypotension)	+/–	+++	++	+++	
Quetiapine (Seroquel XR)	300 mg QHS	400-800	Increase every 1-2 days, as tolerated	+/–	+++	++	+++	
Ziprasidone[e,f] (Geodon) Zeldox	40 mg BID (must be taken with meals)[f]	40-160	Increase every other day to target dose, as tolerated	+	+	+	++	QTc prolongation
Aripiprazole[c] (Abilify)(available in long-acting injectable and ODT formulations)	10-15 mg QAM	10-30	Increase dose after 2 days, as tolerated	+/–	+	+	+	

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First-Line Antipsychotic Medications for Schizophrenia[a]

STARTING Dose	TARGET RANGE[a](mg/day)	PRIMARY CARE TITRATION SCHEDULE	EPS	ORTHOSTATIC HYPOTENSION	METABOLIC SYNDROME[b]	SEDATION	OTHER	
Paliperidone[c,g] (Invega)(available in long-acting injectable formulation)	6 mg QAM Xeplion	6-12	Increase by increments of 3 mg every 5 days, as tolerated	++	+	++	++	
Asenapine (Saphris)(available in ODT formulation)	5 mg BID Sycrest	5-20	Increase by increments of 5 mg over one week	+	+	+	++	Dysgeusia
Iloperidone (Fanapt)	1 mg BID Fanaptum	6-24	Increase by 2 mg BID each day	+++	+	+	+++	
Lurasidone[f] (Latuda)	(40 mg QAM	40-160	Increase by 20 mg per day	+++	+	+	+++	

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First-Line Antipsychotic Medications for Schizophrenia[a]

STARTING Dose	TARGET RANGE[a](mg/ day)	PRIMARY CARE TITRATION SCHEDULE	EPS	ORTHOSTATIC HYPOTENSION	METABOLIC SYNDROME[b]	SEDATION	OTHER
Brexpiprazole (Rexulti)	1 mg PO QAM	1-4	Increase to 2 mg per day for three days, then increase to 4 mg per day	+	+	++	+++
Cariprazine (Vraylar)	1.5 mg PO QAM	6-12	Increase by 1.5 mg per day	+++	+	+	++

Reagila

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Table 5.7 Drugs that can precipitate serotonin syndrome

Drug Class	Drugs
Antidepressants	SSRIs
	SNRIs
	Trazodone
	Tricyclic antidepressants
	MAOIs
	St. John's Wort *(Hypericum perforatum)*
Anxiolytics	Buspirone
Mood stabilizers	Lithium
	Valproic acid
	Carbamazepine
Amphetamines and derivatives	Dextroamphetamine
	Methylphenidate
	Sibutramine (Meridia; withdrawn in USA)
	3,4-methylenedioxymethamphetamine (ecstasy)
	Methamphetamine
Analgesics	Fentanyl
	Meperidine
	Tramadol
Muscle relaxants	Cyclobenzaprine
Antiemetics	Ondansetron
	Metoclopramide
Antimigraine drugs	Triptans
	Ergot alkaloids
Miscellaneous	Cocaine
	Linezolid
	Tedizolid
	5-Hydroxytryptophan
	Tryptophan

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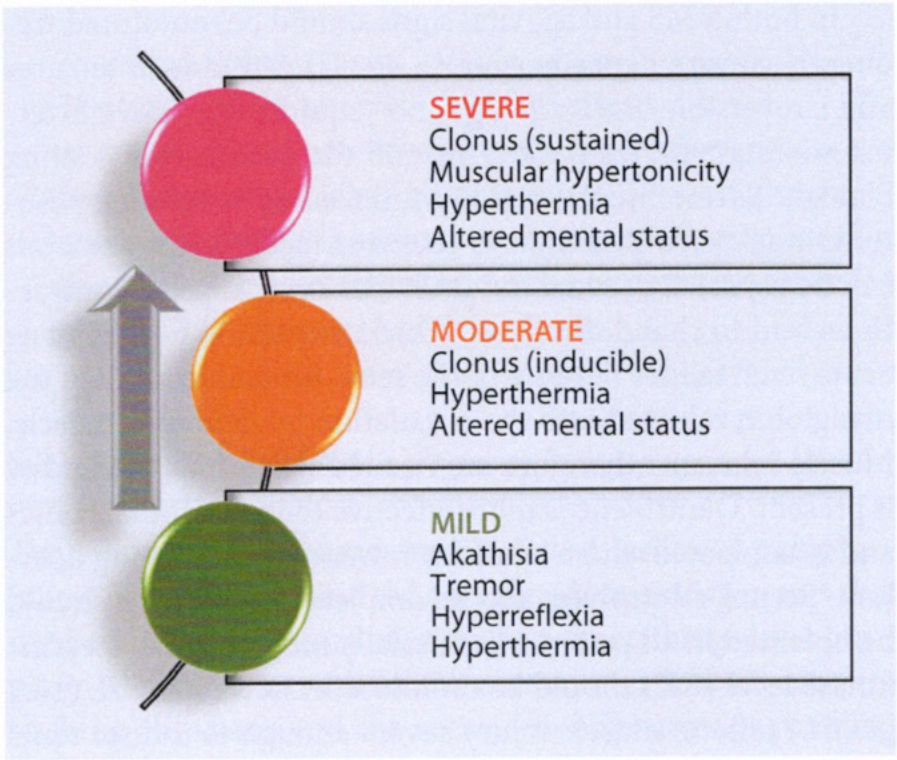


Fig. 5.4 The spectrum of signs and symptoms in serotonin syndrome

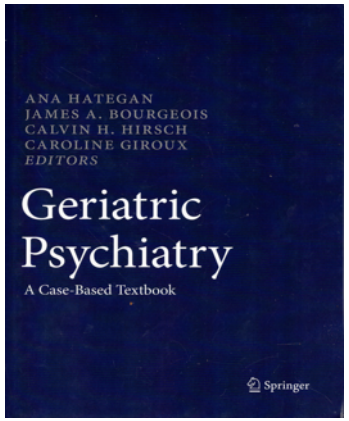
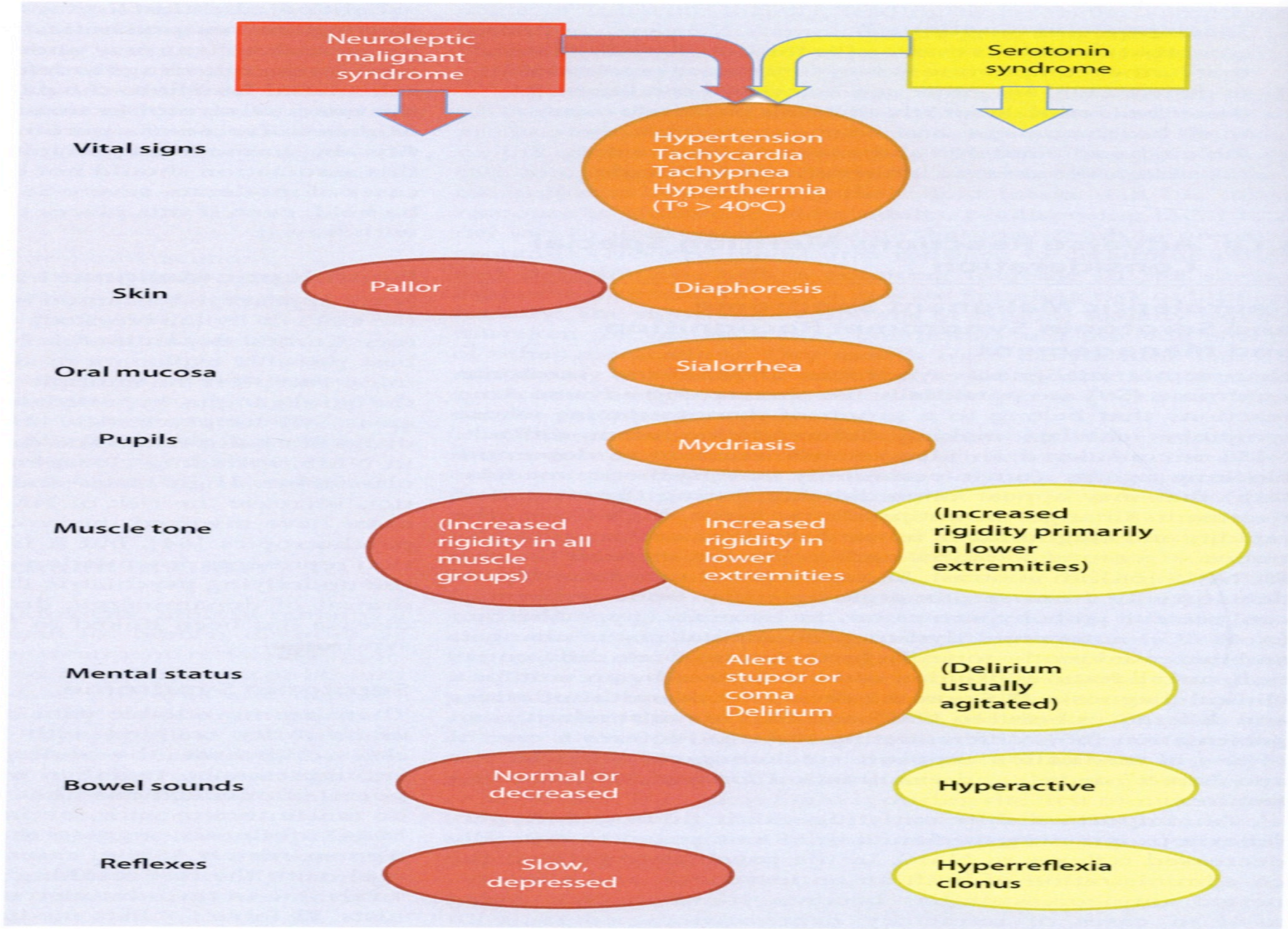
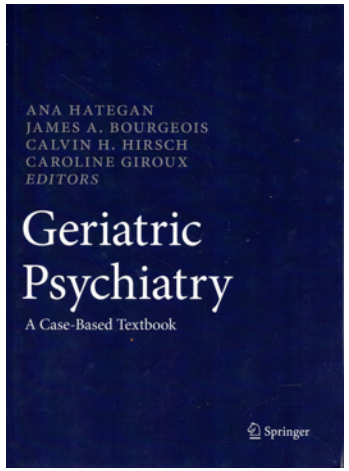


Fig. 5.3 Similarities and differences between neuroleptic malignant syndrome and serotonin syndrome

MNS vs serotoniinisyndrooma





Virtuaalinen todellisuus

- Sovelluksia fobioissa, sosiaalisten taitojen opettelussa, ammatillisessa kuntoutuksessa
- Virtuaalinen työhaastattelu
- Avatar therapy
- https://www.youtube.com/watch?v=aYfG53fgwXc&feature=youtu.be

Jorma Oksanen 12.9.2019

4. Skitsofrenian Käypä Hoito-suosituksia löytyy https://cpnp.org/guideline/external/schizophrenia

Yl juha kemppinen

5. THE AMERICAN PSYCHIATRIC ASSOCIATION PRACTICE GUIDELINE FOR THE TREATMENT OF PATIENTS WITH SCHIZOPHRENIA, DRAFT May 13, 2019 NOT FOR CITATION

Yl juha kemppinen

Table 2. Suggested physical and laboratory assessments for patients with schizophrenia

Assessments to monitor physical status and detect concomitant physical conditions		
Assessment	**Initial or Baseline[a]**	**Follow-Up[b]**
Vital signs	Pulse, blood pressure	Pulse; blood pressure; temperature as clinically indicated
Body weight and height	Body weight, height, and body mass index (BMI)[c]	BMI[c] every visit for 6 months and at least quarterly thereafter
Hematology	Complete blood count (CBC), including absolute neutrophil count (ANC)	CBC, including ANC if clinically indicated (e.g., patients treated with clozapine)
Blood chemistries	Electrolytes Renal function tests Liver function tests TSH	As clinically indicated
Pregnancy	Pregnancy test for women of childbearing potential	
Toxicology	Drug toxicology screen, if clinically indicated	Drug toxicology screen, if clinically indicated
Electroencephalogram (EEG)	EEG, if indicated based on neurological exam or history	
Imaging	Brain imaging (CT or MRI, with MRI being preferred), if indicated based on neurological exam or history	

THE AMERICAN PSYCHIATRIC ASSOCIATION PRACTICE GUIDELINE FOR THE TREATMENT OF PATIENTS WITH SCHIZOPHRENIA, DRAFT May 13, 2019 NOT FOR CITATION

Table 2. Suggested physical and laboratory assessments for patients with schizophrenia (continued)

Assessments related to other specific side effects of treatment		
Assessment	**Initial or Baseline[a]**	**Follow-Up[b]**
Diabetes[d]	Screening for diabetes risk factors[e]; fasting blood glucose[f]	Fasting blood glucose or hemoglobin A1c at 4 months after initiating a new treatment and at least annually thereafter[f]
Hyperlipidemia	Lipid panel[g]	Lipid panel at 4 months after initiating a new antipsychotic medication and at least annually thereafter
QTc prolongation	Electrocardiography (ECG) before treatment with chlorpromazine, haloperidol, droperidol, thioridazine, or pimozide[h] or in the presence of cardiac risk factors[i]	ECG with significant change in dose of chlorpromazine, haloperidol, droperidol, thioridazine, or pimozide,[h] or with the addition of other medications that can affect QTc interval in patients with cardiac risk factors or elevated baseline QTc intervals[i]

Table 2. Suggested physical and laboratory assessments for patients with schizophrenia (continued)

Assessments related to other specific side effects of treatment		
Assessment	**Initial or Baseline[a]**	**Follow-Up[b]**
Hyperprolactinemia	Screening for symptoms of hyperprolactinemia[j] Prolactin level, if indicated on the basis of clinical history	Screening for symptoms of hyperprolactinemia at each visit until stable, then yearly if treated with an antipsychotic known to increase prolactin[j] Prolactin level, if indicated on the basis of clinical history
Akathisia, dystonia, and parkinsonism	Clinical assessment of akathisia, dystonia, and parkinsonism	Clinical assessment of akathisia, dystonia, and parkinsonism at each visit
Tardive dyskinesia	Clinical assessment of abnormal involuntary movements	Clinical assessment of abnormal involuntary movements[k] every 6 months in patients at increased risk of tardive dyskinesia[l] and every 12 months in other patients[m]

Table 3. Antipsychotic medications: available formulations and dosing considerations[1,2,3,4]

	Trade Name[5]	Available Preparations (mg, unless otherwise noted)	Initial dose (mg/day)	Typical dose range (mg/day)	Maximum daily dose (mg/day)	Comments[6,7,8]
First-Generation Antipsychotics						

	Trade Name[5]	Available Preparations (mg, unless otherwise noted)	Initial dose (mg/day)	Typical dose range (mg/day)	Maximum daily dose (mg/day)	Comments[6,7,8]
Chlorpromazine	Thorazine	Tablet: 10, 25, 50, 100, 200 Short-acting injection (HCl): 25/mL (1 mL); 50/2 mL (2 mL)	25-100	200 – 800	Oral: 1000-2000	Intramuscular (IM) dosing is typically 25-50 mg per upper outer quadrant of gluteal with 200 mg/day maximum; do not inject subcutaneously; use much lower IM doses than oral doses as oral first-pass metabolism is significant.
Fluphenazine	Prolixin	Tablet: 1, 2.5, 5, 10 Oral Concentrate: 5/mL (120 mL) Short-acting injection (HCl): 2.5/mL (10 mL)	2.5 - 10	6 - 20	Oral: 40 IM: 10	Short-acting IM dose is 33-50% of oral dose. Dilute oral concentrate immediately before use to ensure palatability and stability.
Haloperidol	Haldol	Tablet: 0.5, 1, 2, 5, 10, 20 Oral Concentrate: 2/mL (5 mL, 15 mL, 120 mL) Short-acting injection (lactate): 5/mL (1 mL, 10 mL)	1 - 15	5 - 20	100	2-5 mg IM can be given every 4-8 hours. IV administration has been associated with QTc prolongation and ECG monitoring is recommended.

THE AMERICAN PSYCHIATRIC ASSOCIATION PRACTICE GUIDELINE FOR THE TREATMENT OF PATIENTS WITH SCHIZOPHRENIA, DRAFT May 13, 2019 NOT FOR CITATION

Table 3. Antipsychotic medications: available formulations and dosing considerations[1,2,3,4]

	Trade Name[5]	Available Preparations (mg, unless otherwise noted)	Initial dose (mg/day)	Typical dose range (mg/day)	Maximum daily dose (mg/day)	Comments[6,7,8]
First-Generation Antipsychotics						
Loxapine	Loxitane	Capsule: 5, 10, 25, 50 Aerosol Powder Breath Activated Inhalation: 10	20	60 -100[9]	250	Oral inhalation formulation (Adasuve) to treat agitation requires REMS program due to potential for bronchospasm.
Molindone	Moban	Tablet: 5, 10, 25	50 - 75	30 – 100[9]	225	
Perphenazine	Trilafon	Tablet: 2, 4, 8, 16	8 - 16	8 - 32	64	CYP2D6 poor metabolizers will have higher plasma concentrations

Table 3. Antipsychotic medications: available formulations and dosing considerations[1,2,3,4]

	Trade Name[5]	Available Preparations (mg, unless otherwise noted)	Initial dose (mg/day)	Typical dose range (mg/day)	Maximum daily dose (mg/day)	Comments[6,7,8]
First-Generation Antipsychotics						
Pimozide	Orap	Tablet: 1, 2	0.5 - 2	2 - 4	10	Sometimes used off-label to treat delusional disorders such as delusional parasitosis. Perform CYP2D6 genotyping if doses greater than 4 mg/day are used. In poor CYP2D6 metabolizers, do not give more than 4 mg/day and do not increase dose earlier than 14 days.
Thioridazine	Mellaril	Tablet: 10, 25, 50, 100	150 - 300	300 – 800[9]	800	
Thiothixene	Navane	Capsule: 1, 2, 5, 10	6 - 10	15-30	60	
Trifluoperazine	Stelazine	Tablet: 1, 2, 5, 10	4 - 10	15-20	50	

Second-Generation Antipsychotics						
	Trade Name[5]	**Available Preparations (mg, unless otherwise noted)**	**Initial dose (mg/day)**	**Typical dose range (mg/day)**	**Maximum daily dose (mg/day)**	**Comments[6,7,8]**
Aripiprazole	Abilify	Tablet: 2, 5, 10, 15, 20, 30 Tablet, Disintegrating: 10, 15 Tablet with Ingestible Event Marker (Mycite): 2, 5, 10, 15, 20, 30 Solution: 1/mL (150 mL)	10 -15	10-15	30	Adjust dose if a poor CYP2D6 metabolizer or with concomitant use of a CYP3A4 inhibitor, CYP3A4 inducer, or CYP2D6 inhibitor. Tablet and oral solution may be interchanged on a mg-per-mg basis, up to 25 mg. Doses using 30 mg tablets should be exchanged for 25 mg oral solution. Orally disintegrating tablets (Abilify Discmelt) are bioequivalent to the immediate-release tablets (Abilify). Mycite patch (wearable sensor) cannot be split or crushed.

Second-Generation Antipsychotics						
	Trade Name[5]	**Available Preparations (mg, unless otherwise noted)**	**Initial dose (mg/day)**	**Typical dose range (mg/day)**	**Maximum daily dose (mg/day)**	**Comments[6,7,8]**
Asenapine	Saphris	Tablet, Sublingual: 2.5, 5, 10	10	20	20	Consider dose adjustment in smokers and with concomitant use of CYP1A2 inhibitors. Do not split, crush, or swallow. Place under tongue and allow to dissolve completely. Giving with food or liquid reduces absorption.
Brexpiprazole	Rexulti	Tablet: 0.25, 0.5, 1, 2, 3, 4	1	2 - 4	4	Adjust dose if a poor CYP2D6 metabolizer or with concomitant use of moderate/strong CYP2D6 inhibitors, strong CYP3A4 inhibitors, or strong CYP3A4 inducers
Cariprazine	Vraylar	Capsule: 1.5, 3, 4.5, 6	1.5	1.5 - 6	6[10]	Adjust dose with concomitant use of a strong CYP3A4 inhibitor or inducer.

Second-Generation Antipsychotics

	Trade Name[5]	Available Preparations (mg, unless otherwise noted)	Initial dose (mg/day)	Typical dose range (mg/day)	Maximum daily dose (mg/day)	Comments[6,7,8]
Clozapine	Clozaril; FazaClo; Versacloz	Tablet: 25, 50, 100, 200 Tablet, Disintegrating: 12.5, 25, 100, 150, 200 Oral Suspension: 50/mL (100 mL)	12.5 – 25	300 - 450[7]	900	Prescribers must complete Clozapine REMS education (https://www.clozapinerems.com/) and follow requirements for a baseline CBC and ANC, and for ANC monitoring before and during treatment. When initiating clozapine, increase in 25-50 mg/d increments for 2 weeks, then further increments not exceeding 100 mg up to twice weekly. For treatment interruptions of 2 or more days, restart at 12.5 mg once or twice daily. Re-titration can occur more rapidly than with initial treatment. Adjust dose with concomitant use of strong CYP1A2 inhibitors and with strong CYP3A4 inducers. Smoking reduces clozapine levels via CYP1A2 induction. Clozapine levels can be informative in making dose adjustments.[11]
Iloperidone	Fanapt	Tablet: 1, 2, 4, 6, 8, 10, 12	2	12-24	24	Titrate slowly (no more than 4 mg/d increase in dose); follow initial titration approach if more than 3-day gap in treatment; adjust dose with concomitant use of strong CYP2D6 or CYP3A4 inhibitors and reduce dose by 50% in CYP2D6 poor metabolizers.
Lurasidone	Latuda	Tablet: 20, 40, 60, 80, 120	40	40-120	160	Administer with food (≥350 calories). Adjust dose for concomitant use of moderate to strong CYP3A4 inhibitors or inducers.

Second-Generation Antipsychotics						
	Trade Name[5]	**Available Preparations (mg, unless otherwise noted)**	**Initial dose (mg/day)**	**Typical dose range (mg/day)**	**Maximum daily dose (mg/day)**	**Comments[6,7,8]**
Olanzapine	Zyprexa	Tablet: 2.5, 5, 7.5, 10, 15, 20 Tablet, Disintegrating: 5, 10, 15, 20 Short-acting Intramuscular Powder for Solution: 10	5-10	10-20	20[12]	Short-acting IM preparation is used primarily for agitation with usual dose of 2.5-10 mg IM, with max dose of 30 mg/day. Administer IM slowly, deep into muscle. Do not use subcutaneously. Concomitant use of IM olanzapine with benzodiazepines is not recommended. Smokers may require a 30% greater daily dose than nonsmokers and women may need lower daily doses. ~40% of an oral dose is removed by first pass metabolism as compared to IM dose. IM elimination half-life is ~1.5 times greater in elderly. Oral dissolving tablet dissolves rapidly in saliva and may be swallowed with or without liquid. May be administered with or without food/meals.
Paliperidone	Invega	Tablet, Extended Release: 1.5, 3, 6, 9	6	3 - 12	12	If exceeding 6 mg daily, increases of 3 mg/day are recommended at intervals of more than 4 days, up to a max of 12 mg/d. Uses OROS osmotic delivery system for tablet; do not split or crush. Use of extended release tablet is not recommended with preexisting severe gastrointestinal narrowing disorders. Tablet shell is expelled in the stool.

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Second-Generation Antipsychotics

	Trade Name[5]	Available Preparations (mg, unless otherwise noted)	Initial dose (mg/day)	Typical dose range (mg/day)	Maximum daily dose (mg/day)	Comments[6,7,8]
Quetiapine	Seroquel	Tablet, Immediate Release: 25, 50, 100, 200, 300, 400 Tablet, Extended Release: 50, 150, 200, 300, 400	IR: 50 XR: 300	IR/XR: 400-800	IR/XR: 800	Once daily dosing for extended release and divided dosing for immediate release. Do not split or crush extended release tablets. Immediate release marginally affected by food, whereas extended release significantly affected with high-fat meal. Give extended release tablets without food or <300 calories. Re-titrate for gap in treatment of more than 1 wk. Adjust dose for concomitant use of strong CYP3A4 inhibitors or inducers.
Risperidone	Risperdal	Tablet: 0.25, 0.5, 1, 2, 3, 4 Tablet, Disintegrating: 0.25, 0.5, 1, 2, 3, 4 Oral Solution: 1/mL (30 mL)	2	2 - 8	8[13]	Lower initial doses and slower titration rates with severe hepatic impairment or CrCl <30 mL/min. Fraction of free risperidone is increased with hepatic impairment. Adjust dose with concomitant use of inducers or inhibitors of CYP3A4 or CYP2D6. Check labeling for compatible liquids with oral solution. Do not split or crush oral disintegrating tablets.
Ziprasidone	Geodon	Capsule: 20, 40, 60, 80 Solution Reconstituted, Intramuscular: 20	40	80 – 160	320	Give capsules with >500 calories of food. No data suggests improved efficacy at higher doses. See labeling for reconstitution and storage of IM preparation. Short-acting IM preparation is used primarily for agitation with usual dose of 20 mg/day and max dose of 40 mg/day.

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	Trade Name	Bioavailability	Time to peak level	Protein binding	Metabolic enzymes/transporters	Metabolites	Elimination half-life	Excretion	Hepatic Impairment	Renal Impairment
First-Generation Antipsychotics										
Chlorpromazine	Thorazine	32%	2.8 hours	90 - 99%	CYP2D6 (Major), CYP1A2 (Minor), CYP3A4 (Minor) substrate	NOR2CPZ, NOR2CPZ SULF, and 3-OH CPZ	Biphasic: initial 2 hours, terminal 30 hours	Primarily renal (<1% as unchanged drug)	Use with caution	Use with caution; not dialyzable
Fluphenazine	Prolixin	2.7%	Oral: 2 hours IM: 1.5 – 2 hours	99%	CYP2D6 (Major) substrate	7-hydroxyfluphenazine, fluphenazine-sulfoxide	4.4 to 16.4 hours	Renal and fecal; exact proportion unclear	Contraindicated by manufacturer	Use with caution
Haloperidol	Haldol	60-70%	Oral: 2-6 hours IM: 20 min	89-93%	CYP2D6 (Major), CYP3A4 (Major), CYP1A2 (Minor) substrate; 50-60% glucuronidation	Hydroxymetabolite-reduced haloperidol	14 to 37 hours	15% fecal;30% renal (1% as unchanged drug); + enterohepatic circulation	No dose adjustments noted	No dose adjustments noted

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	Trade Name	Bioavailability	Time to peak level	Protein binding	Metabolic enzymes/transporters	Metabolites	Elimination half-life	Excretion	Hepatic Impairment	Renal Impairment
Loxapine	Loxitane	99%	1.5 - 3 hours	97%	CYP1A2 (Minor), CYP2D6 (Minor), CYP3A4 (Minor) substrate; P-glycoprotein inhibitor	N-desmethyl loxapine (amoxapine), 8-hydroxyloxapine	Biphasic: initial 5 hours, terminal 19 hours	Renal and fecal	No dose adjustments noted	No dose adjustments noted
Molindone	Moban	Unclear	1.5 hours	76%	CYP2D6	Multiple	1.5 hours	Renal and fecal	Use with caution	No dose adjustments noted
Perphenazine	Trilafon	20 - 40%	Perphenazine: 1 - 3 hours, 7-hydroxyperphenazine: 2 – 4 hours	91-99%	CYP2D6 (Major) substrate, CYP1A2 (Minor), CYP2C19 (Minor), CYP2C9 (Minor), CYP3A4 (Minor) substrate	7-hydroxyperphenazine (responsible for 70% of the activity)	Perphenazine: 9-12 hours 7-hydroxyperphenazine: 10-19 hours	5% fecal; 70% renal	Contraindicated in liver damage	Use with Caution

	Trade Name	Bioavailability	Time to peak level	Protein binding	Metabolic enzymes/transporters	Metabolites	Elimination half-life	Excretion	Hepatic Impairment	Renal Impairment
Pimozide	Orap	≥50%	6 - 8 hours	99%	CYP1A2 (Major), CYP2D6 (Major), CYP3A4 (Major) substrate	Unknown activity: 4-bis-(4-fluorophenyl) butyric acid, 1-(4-piperidyl)-2-benzimidazolinone	55 hours	Primarily renal	Use with caution	Use with caution
Thioridazine	Mellaril	25-33%	1 - 4 hours	96-99%	CYP2D6 (Major) substrate and moderate inhibitor, CYP2C19 (Minor) substrate	Mesoridazine (twice as potent as thioridazine), sulphoridazine	21-24 hours	Minimal renal	Use with caution	No dose adjustments noted
Thiothixene	Navane	~50%; erratic absorption	1 - 2 hours	90%	CYP1A2 (Major) substrate	None noted	34 hours	Feces (unchanged drug and metabolites)	No dose adjustments noted	No dose adjustments noted
Trifluoperazine	Stelazine	Erratic absorption	1.5 - 6 hours	90-99%	CYP1A2 (Major) substrate	N-desmethyltrifluoperazine, 7-hydroxyrifluoperazine, and other metabolites	3 - 12 hours	Renal	Contraindicated in hepatic disease	No dose adjustments noted

	Trade Name	Bioavailability	Time to peak level	Protein binding	Metabolic enzymes/transporters	Metabolites	Elimination half-life	Excretion	Hepatic Impairment	Renal Impairment
Second-Generation Antipsychotics										
Aripiprazole	Abilify	87%	3 - 5 hours	>99%	CYP2D6 (Major), CYP3A4 (Major) substrate	Dehydro-aripiprazole	75 hours; 94 hours dehydro-aripiprazole 146 hours in poor CYP2D6 metabolizers	55% fecal 25% renal	No dose adjustments noted	No dose adjustments noted
Asenapine	Saphris	35%	0.5 - 1.5 hours	95%	CYP1A2 (Major), CYP2D6 (Minor), CYP3A4 (Minor) substrate; glucuronidation by UGT1A4; CYP2D6 weak inhibitor	Inactive: N(+)-glucuronide, N-desmethylasenapine, and N-desmethylasenapine N-carbamoyl glucuronide	24 hours	40% fecal 50% renal	Use is contraindicated in severe hepatic impairment (Child-Pugh class C)	No dose adjustments noted
Brexpiprazole	Rexulti	95%	4 hours	>99%	CYP3A4 (Major), CYP2D6 (Major) substrate	Inactive: DM-3411	91 hours	46% fecal 25% renal	Moderate - severe impairment (Child-Pugh class B or C) Maximum dose: MDD: 2 mg/day Schizophrenia: 3 mg/day	CrCl <60 mL/min: Maximum dose: MDD: 2 mg/day Schizophrenia: 3 mg/day
Cariprazine	Vraylar	High	3-6 hours	91-97%	CYP3A4 (Major), CYP2D6 (Minor) substrate	Desmethyl cariprazine [DCAR], didesmethyl cariprazine [DDCAR]	Cariprazine 2 - 4 days DCAR: 1-2 days DDCAR: 1-3 weeks	21% renal	Severe impairment (Child-Pugh class C): not recommended	CrCl <30 mL/min: not recommended

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	Trade Name	Bioavailability	Time to peak level	Protein binding	Metabolic enzymes/transporters	Metabolites	Elimination half-life	Excretion	Hepatic Impairment	Renal Impairment
Clozapine	Clozaril; FazaClo; Versacloz	27 - 60%	2.2 - 2.5 hours (range: 1-6 hours)	97%	CYP1A2 (Major), CYP2A6 (Minor), CYP2C19 (Minor), CYP2C9 (Minor), CYP2D6 (Minor), CYP3A4 (Minor) substrate	N-desmethylclozapine (active), hydroxylated and n-oxide derivatives (inactive)	4 – 66 hours (steady state 12 hours)	30% fecal 50% renal	In significant impairment, dose reduction may be necessary	In significant impairment, dose reduction may be necessary
Iloperidone	Fanapt	96%	2 - 4 hours	92-97%	CYP2D6 (Major), CYP3A4 (Minor) substrate, CYP3A4 weak inhibitor	P88 P95	Extensive metabolizers : Iloperidone 18 hours, P88 26 hours, P95 23 hours Poor metabolizers : iloperidone 33 hours, P88 37 hours, P95 31 hours	~20% fecal ~50% renal	Moderate impairment: use with caution Severe impairment: not recommended	No dose adjustments noted

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	Trade Name	Bioavailability	Time to peak level	Protein binding	Metabolic enzymes/transporters	Metabolites	Elimination half-life	Excretion	Hepatic Impairment	Renal Impairment
Lurasidone	Latuda	9-19%	1-3 hours	99%	CYP3A4 (Major) substrate, CYP3A4 weak inhibitor	ID-14283, ID-14326 (active); ID20219, ID-20220 (inactive)	Lurasidone 18-40 hours; ID-14283: 7.5-10 hours	~80% fecal ~9% renal	For moderate to severe hepatic impairment (Child-Pugh class B and class C) use 20 mg/day initially with maximum dose of 80 mg/day and 40 mg/day, respectively	For CrCl < 50 mg/min: initial 20 mg/day, maximum dose is 80 mg/day
Olanzapine	Zyprexa	>57%	Oral: 6 hours IM: 15-45 mins	93%	CYP1A2 (Major), CYP2D6 (Minor) substrate; metabolized via direct glucuronidation	10-N-glucuronide, 4-N-desmethyl olanzapine (inactive)	30 hours	30% fecal 57% renal	Use with caution	Not removed by dialysis

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	Trade Name	Bioavailability	Time to peak level	Protein binding	Metabolic enzymes/transporters	Metabolites	Elimination half-life	Excretion	Hepatic Impairment	Renal Impairment
Paliperidone	Invega	28%	24 hours	74%	P-glycoprotein/ABCB1, CYP2D6(Minor), CYP3A4 (Minor) substrate	Activity unclear: M1, M9, M10, M11, M12, M16	23 hours; 24-51 hours with renal impairment (CrCl <80ml/min)	11% fecal 80% renal	Mild – moderate: no adjustment necessary Severe: not studied	Not recommended for CrCl < 10 mL/min. CrCl 10 - 49 mL/min and for CrCl of 50 - 79 mL/min, use max dose of 3 mg/d and 6 mg/d, respectively.
Quetiapine	Seroquel	100%	Immediate release:1.5 hours; Extended release: 6 hours	83%	CYP3A4 (Major), CYP2D6 (Minor) substrate	Active: Norquetiapine, 7-hydroxyquetiapine Inactive: quetiapine sulfoxide (Major), parent acid metabolite	Quetiapine: 6 - 7 hours Norquetiapine: 12 hours	20% fecal 73% renal	Immediate release: initial 25 mg/day dose, increase by 25 – 50 mg/day to effective dose Extended release: initial 50 mg/d, increase by 50 mg/day to effective dose	No dose adjustments noted

	Trade Name	Bioavailability	Time to peak level	Protein binding	Metabolic enzymes/transporters	Metabolites	Elimination half-life	Excretion	Hepatic Impairment	Renal Impairment
Risperidone	Risperdal	70 - 94%	1 hour	90%	CYP2D6 (Major), CYP3A4 (Minor), P-glycoprotein/ABCB1 substrate, N-dealkylation (minor), CYP2D6 weak inhibitor	Active: 9-hydroxy-risperidone	Risperidone 3 - 20 hours 9-hydroxy-risperidone 21 – 30 hours	14% fecal 70% renal	Mild or moderate impairment (Child-Pugh class A or B): reduce dose Severe impairment (Child-Pugh class C): initial 0.5 mg twice a day, increase by no more than 0.5 mg twice a day, may increase to total dosage > 1.5 mg twice a day at 1 week or greater	Mild or moderate impairment (CrCl ≥30 mL/min): reduce dose Severe impairment (CrCl <30 mL/min): initial 0.5 mg twice a day, increase by no more than 0.5 mg twice a day, may increase to dosage > 1.5 mg twice a day at 1 week or greater

	Trade Name	Bioavailability	Time to peak level	Protein binding	Metabolic enzymes/transporters	Metabolites	Elimination half-life	Excretion	Hepatic Impairment	Renal Impairment
Ziprasidone	Geodon	Oral with food: 60%; IM:100%	Oral: 6 - 8 hours IM: 60 mins	>99%	CYP1A2 (Minor), CYP3A4 (Minor) substrate, glutathione, aldehyde oxidase	Active: benzisothiazole sulphoxide (Major), benzisothiazole sulphone (Major), ziprasidone sulphoxide, s-methyl-dihydroziprasidone	Oral: 7 hours; IM: 2 – 5 hours	66% fecal 20% renal	Use with caution	No oral dose adjustments noted; IM formulation contains a renally cleared excipient, cyclodextrin - use with caution.

Table 5. Antipsychotic receptor binding properties[15]

	Trade Name	D1	D2	D3	D4	D5	5HT-1A	5HT-2A	5HT-2C	5HT-7	H1	Musc M1	Alpha 1	Alpha 2	Comments
First-Generation Antipsychotics															
Chlorpromazine	Thorazine	+	+++	+++	++	+	0	+++	++	++	+++	++	+++	+	
Fluphenazine	Prolixin	++	++++	++++	++	++	+	++	+	+++	++	0	+++	0	
Haloperidol	Haldol	+	+++	+++	+++	+	0	++	0	+	0	0	++	0	

Table 5. Antipsychotic receptor binding properties[15]

	Trade Name	D1	D2	D3	D4	D5	5HT-1A	5HT-2A	5HT-2C	5HT-7	H1	Musc M1	Alpha 1	Alpha 2	Comments
Loxapine	Loxitane	++	++	++	+++	++	0	+++	++	++	+++	+	++	0	
Molindone	Moban	0	++	++	0		0	0	0	0	0	0	0	+	
Perphenazine	Trilafon	++	++++	++++	++		0	+++	+	++	+++	0	++	+	
Pimozide	Orap	0	++++	+++	++		+	++	0	++++	+	+	+	+	Moderate activity at dopamine transporter
Thioridazine	Mellaril	++	++	+++	++	+	+	++	++	++	++	+++	+++	+	
Thiothixene	Navane	+	++++	++++	+	+	+	++	0	++	+++	0	++	0	
Trifluoperazine	Stelazine	+	+++	++++	++		+	++	+	+	++	+	++	0	

Table 5. Antipsychotic receptor binding properties[15]

	Trade Name	D1	D2	D3	D4	D5	5HT-1A	5HT-2A	5HT-2C	5HT-7	H1	Musc M1	Alpha 1	Alpha 2	Comments
Second-Generation Antipsychotics															
Aripiprazole	Abilify	+	////	+++	+	0	///	+++	++	++	++	0	++	+	
Asenapine	Saphris	+++	+++	++++	+++		+++	++++	++++	++++	+++	0	+++	+++	
Brexpiprazole	Rexulti	+	////	+++	++++		////	++++	++	+++	++	0	+++	++++	
Cariprazine	Vraylar		////	++++			///	++	+	+	++	0	+		
Clozapine	Clozaril; FazaClo; Versacloz	+	+	+	++	+	/	+++	++	++	+++	///	+++	+	
Iloperidone	Fanapt	+	++	++	++	+	//	++++	++	++	+	0	+++	+++	
Lurasidone	Latuda	+	+++	++	++		/	++++	+	++++	0	0	++	++	

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Table 5. Antipsychotic receptor binding properties[15]

	Trade Name	D1	D2	D3	D4	D5	5HT-1A	5HT-2A	5HT-2C	5HT-7	H1	Musc M1	Alpha 1	Alpha 2	Comments
Olanzapine	Zyprexa	++	++	++	++	++	0	+++	++	+	+++	+++	++	+	
Paliperidone	Invega	+	+++	+++	++	++	+	++++	++	+++	+++	0	+++	++	
Quetiapine	Seroquel	0	+	+	0	0	/	+	0	+	+++	+	++	0	
Risperidone	Risperdal	+	+++	+++	+++	+	+	++++	++	+++	++	0	+++	+++	
Ziprasidone	Geodon	+	+++	+++	++	+	///	++++	++++	+++	++	0	+++	+	Weak activity at norepinephrine and serotonin transporter

++++ = very strong binding (Ki <1 nM); +++ = strong binding (1 nM ≤ Ki < 10 nM); ++ = moderate binding (10 nM ≤ Ki < 100 nM); + = weak binding (100 nM ≤ Ki < 1000 nM); 0 = very weak or negligible binding (Ki ≥ 1000 nM). For partial agonists, / is used to denote relative binding values instead of +.

Table 6. Antipsychotic medications: relative side effects[16]

	Trade Name	Akathisia	Parkinsonism	Dystonia	Tardive dyskinesia	Hyper-prolactinemia[17]	Anticholinergic	Sedation
First-Generation Antipsychotics								
Chlorpromazine	Thorazine	+	+	+	+++	+	+++	+++
Fluphenazine	Prolixin	+++	+++	+++	+++	+++	+	+
Haloperidol	Haldol	+++	+++	+++	+++	+++	+	+

Table 6. Antipsychotic medications: relative side effects[16]

	Trade Name	Akathisia	Parkinsonism	Dystonia	Tardive dyskinesia	Hyper-prolactinemia[17]	Anticholinergic	Sedation
Loxapine	Loxitane	++	++	++	++	++	++	++
Molindone	Moban	++	++	++	++	++	+	++
Perphenazine	Trilafon	++	++	++	++	++	++	++
Pimozide	Orap	+++	+++	++	+++	+++	+	+
Thioridazine	Mellaril	+	+	+	+	++	+++	+++
Thiothixene	Navane	+++	+++	+++	+++	+++	+	+
Trifluoperazine	Stelazine	++	++	++	++	++	++	+

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Table 6. Antipsychotic medications: relative side effects[16]

	Trade Name	Akathisia	Parkinsonism	Dystonia	Tardive dyskinesia	Hyper-prolactinemia[17]	Anticholinergic	Sedation
Second-Generation Antipsychotics								
Aripiprazole	Abilify	++	+	+	+	+	+	+
Asenapine	Saphris	++	+	++	++	++	+	++
Brexpiprazole	Rexulti	++	+	+	+	+	+	++
Cariprazine	Vraylar	++	+	+	+	+	++	++
Clozapine	Clozaril; FazaClo; Versacloz	+	+	+	+	+	+++	+++
Iloperidone	Fanapt	+	+	+	+	++	+	++
Lurasidone	Latuda	++	++	++	++	+	+	++
Olanzapine	Zyprexa	++	++	+	+	++	++	+++
Paliperidone	Invega	++	+	++	++	+++	+	+

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Table 6. Antipsychotic medications: relative side effects[16]

	Trade Name	Akathisia	Parkinsonism	Dystonia	Tardive dyskinesia	Hyper-prolactinemia[17]	Anticholinergic	Sedation
Quetiapine	Seroquel	+	+	+	+	+	++	+++
Risperidone	Risperdal	++	++	++	++	+++	+	++
Ziprasidone	Geodon	++	+	+	+	++	+	++

Table 6. Antipsychotic medications: relative side effects (continued)

	Trade Name	Seizures	Orthostasis	QT prolongation	Weight gain	Hyperlipidemia	Glucose abnormalities	Comments
First-Generation Antipsychotics								
Chlorpromazine	Thorazine	++	+++	+++	++	+	++	
Fluphenazine	Prolixin	+	+	+	++	+	+	
Haloperidol	Haldol	+	+	+++	++	+	+	
Loxapine	Loxitane	+	++	+	+	+	+	
Molindone	Moban	+	+	+	+	+	+	
Perphenazine	Trilafon	+	++	+	++	+	+	
Pimozide	Orap	+++	+	+++	+	+	+	
Thioridazine	Mellaril	++	+++	+++	++	+	+	Pigmentary retinopathy; high sexual dysfunction
Thiothixene	Navane	+++	+	+	+	+	+	

	Trade Name	Seizures	Orthostasis	QT prolongation	Weight gain	Hyperlipidemia	Glucose abnormalities	Comments
Trifluoperazine	Stelazine	+	+	+	++	+	+	

	Trade Name	Seizures	Orthostasis	QT prolongation	Weight gain	Hyperlipidemia	Glucose abnormalities	Comments
Second-Generation Antipsychotics								
Aripiprazole	Abilify	+	+	++	+	+	+	FDA safety alert for impulse control disorders (e.g., gambling, binge eating); may reduce hyper-prolactinemia with other antipsychotics
Asenapine	Saphris	+	++	++	++	++	++	Oral hypoesthesia
Brexpiprazole	Rexulti	+	+	+	+	++	++	
Cariprazine	Vraylar	+	+	+	++	+	+	
Clozapine	Clozaril; FazaClo; Versacloz	+++	+++	++	+++	+++	+++	Increased salivation common; high rate of sexual dysfunction; severe constipation possible; fever can occur with initiation; myocarditis and agranulocytosis are rare.

	Trade Name	Seizures	Orthostasis	QT prolongation	Weight gain	Hyperlipidemia	Glucose abnormalities	Comments
Iloperidone	Fanapt	+	+++	++	++	+	++	
Lurasidone	Latuda	+	+	+	+	++	++	Dose-related creatinine increase in some patients
Olanzapine	Zyprexa	++	++	++	+++	+++	+++	
Paliperidone	Invega	+	++	++	++	++	+	
Quetiapine	Seroquel	++	++	+	++	+++	++	
Risperidone	Risperdal	+	++	++	++	+	++	Intraoperative floppy iris syndrome reported
Ziprasidone	Geodon	+	++	+	+	+	+	

Table 7. Long-acting injectable antipsychotic medications: availability and injection related considerations[18,19]

	Trade Name	Available strengths[20] (mg)	How supplied	Injection site and technique[21]	Reactions at injection site[22]	Comments
First-Generation Antipsychotics						
Fluphenazine	Prolixin Decanoate	25/mL (5 mL)	Vial, Sesame oil vehicle with 1.2% benzyl alcohol	Deep IM gluteal or deltoid injection, use of Z-track technique recommended[23]	Skin reactions reported	Monitor for hypotension. In sesame oil; be alert for allergy. Needle size and handling issues – refer to labelling.
Haloperidol	Haldol Decanoate	50/mL, 100/mL	Vial, Sesame oil vehicle with 1.2% benzyl alcohol	Deep IM gluteal or deltoid injection; use of Z-track technique recommended	Inflammation and nodules reported, especially with dose > 100 mg/ml	Do not administer more than 3 mL per injection site. In sesame oil; be alert for allergy. Needle size issues – refer to labelling.

Table 7. Long-acting injectable antipsychotic medications: availability and injection related considerations[18,19]

Second-Generation Antipsychotics

Aripiprazole	Abilify Maintena	300, 400	Kit with either pre-filled syringe or single use vial	Slow IM injection into gluteal or deltoid muscle	Occasional redness, swelling, induration (mild to moderate)	Rotate injection sites; do not massage muscle after injection. Needle size and reconstitution issues – refer to labelling.
Aripiprazole lauroxil	Aristada Initio (for first dose) and Aristada	Aristada Initio 675/2.4 mL, Aristada 441/1.6 mL, 662/2.4 mL, 882 /3.2 mL, 1064/3.9 mL	Kit with pre-filled syringe	IM gluteal muscle; Aristada Initio 675 mg and Aristada 441 mg can be injected in deltoid muscle	Infrequent induration	Avoid concomitant injection of Aristada Initio and Aristada in same muscle. Needle size and reconstitution issues – refer to labelling.
Olanzapine	Zyprexa Relprevv	210, 300, 405	Kit with vial containing diluent and vial with powder for reconstituting suspension	Deep IM gluteal injection only; do not administer subcutaneously	Infrequent induration or mass at injection site	Due to risk of post-injection delirium/sedation syndrome, must be given in a registered healthcare facility with ready access to emergency response services, and patient must be observed for at least 3 hours post injection and accompanied upon discharge. Requires use of FDA REMS program (www.zyprexarelprevvprogram.com/public/Default.aspx). Do not massage muscle after injection. The combined effects of age, smoking, and gender may lead to significant pharmacokinetic differences. Handling and reconstitution issues – refer to labelling.

Table 7. Long-acting injectable antipsychotic medications: availability and injection related considerations[18,19]

	Trade Name	Available strengths[20] (mg)	How supplied	Injection site and technique[21]	Reactions at injection site[22]	Comments
Paliperidone palmitate	Invega Sustenna	39/0.25 mL, 78/0.5 mL, 117/0.75 mL, 156/mL, 234/1.5 mL	Kit with Pre-filled syringe	IM only; Slow deep IM deltoid injection for first 2 doses, then deep deltoid or gluteal injection (upper outer quadrant) thereafter	Occasional redness, swelling, induration	The two initial deltoid IM injections help attain therapeutic concentrations rapidly. Alternate deltoid injections (right and left deltoid muscle). Needle size and reconstitution issues – refer to labelling.
Paliperidone palmitate	Invega Trinza	273/0.875 mL, 410/1.315 mL, 546/1.75 mL, 819/2.625 mL	Kit with Pre-filled syringe	IM only; Slow deep IM deltoid or gluteal injection	Infrequent redness or swelling	Handling, needle size and reconstitution issues – refer to labelling.
Risperidone	Risperdal Consta	12.5, 25, 37.5, 50	Kit with pre-filled syringe and vial for reconstitution	Deep IM injection into the deltoid or gluteal (upper outer quadrant)	Occasional redness, swelling, induration	Alternate injection sites. Refrigerate and store at 2°C to 8°C and protect from light. May be stored at 25°C for up to 7 days prior to administration. Handling and reconstitution issues – refer to labelling.
Risperidone	Perseris	90, 120	Kit with pre-filled syringes containing powder and diluent.	Abdominal subcutaneous injection only	Lump at injection site may persist for several weeks	Alternate injection sites. Inject only in area without skin conditions, irritation, reddening, bruising, infection or scarring; do not rub or massage injection sites. Store at 2°C to 8°C and protect from light. Allow package to come to room temperature for at least 15 mins before injection. Handling and reconstitution issues – refer to labelling.

Table 8. Long-acting injectable antipsychotic medications: dosing[24]

	Trade Name	Dose conversions	Initial dose (mg)	Typical dose (mg)	Maximum dose (mg)	Dosing frequency	Need for initial oral supplementation	Comments
First-Generation Antipsychotics								
Fluphenazine	Prolixin Decanoate	IM: PO ratio: 1:2.5 12.5 mg every 3weeks = 10 mg/day oral)	6.25 - 25 every 2weeks	6.25 – 25 every 2-4 weeks	100	2 weeks	Decrease oral dose by half after first injection then discontinue with second injection	Increase in 12.5 mg increments if doses over 50 mg are needed
Haloperidol	Haldol Decanoate	10-20 times the daily oral dose	Determined by oral dose and/or risk of relapse up to a maximum of 100 mg	50-200 (10-15 times previous oral dose)	450	4 weeks	Taper and discontinue after 2 to 3 injections	If initial dose is more than 100 mg, split into 2 injections separated by 3 to 7 days.

Table 8. Long-acting injectable antipsychotic medications: dosing[24]

	Trade Name	Dose conversions	Initial dose (mg)	Typical dose (mg)	Maximum dose (mg)	Dosing frequency	Need for initial oral supplementation	Comments
Second-Generation Antipsychotics								
Aripiprazole	Abilify Maintena	Not applicable	400	400	400	Monthly	Continue oral for 14 days after initial injection	Follow labeling if scheduled injections are missed; dose adjust for poor CYP2D6 metabolizers, those on CYP2D6 and/or CYP3A4 inhibitors, or due to adverse effects. Avoid use with CYP3A4 inducers.

Table 8. Long-acting injectable antipsychotic medications: dosing[24]

	Trade Name	Dose conversions	Initial dose (mg)	Typical dose (mg)	Maximum dose (mg)	Dosing frequency	Need for initial oral supplementation	Comments
Aripiprazole lauroxil	Aristada	10 mg/day orally, give 441 mg IM/month 15 mg/day orally, give 662 mg/month IM, 882 mg IM every 6 weeks, or 1064 mg IM every 2 months 20 mg/day or greater orally, give 882 mg/month IM	Determined by oral dose	441-882/month, 882/6 weeks, 1064/2 months.	882/month	1- 2 months	Use Aristada Initio 675 mg, first dose of Aristada based on oral dose with or within 10 days after the Aristada Initio dose, plus single 30 mg oral aripiprazole dose OR continue oral for 21 days after first Aristada injection	Aristada Initio syringes and doses are not interchangeable with other Aristada syringes and doses. See labeling for dose adjustments for concomitant therapy.
Olanzapine	Zyprexa Relprevv	10 mg/day orally, 210 mg every 2 weeks for 4 doses or 405 mg every 4 weeks 15 mg/d orally, 300 mg every 2 weeks for 4 doses 20 mg/d orally, 300 mg every 2 weeks	Determined by oral dose	150 mg, 210 mg or 300 mg every 2 weeks, or 300 mg or 405 mg every 4 weeks	300 mg every 2 weeks or 405 mg every 4 weeks	2-4 weeks	Not required	Give 150 mg every 4 weeks in patients who may have sensitivity to side effects or slower metabolism. Smokers may require a greater daily dose than nonsmokers and women may need lower daily doses than expected.

Table 8. Long-acting injectable antipsychotic medications: dosing[24]

	Trade Name	Dose conversions	Initial dose (mg)	Typical dose (mg)	Maximum dose (mg)	Dosing frequency	Need for initial oral supplementation	Comments
Paliperidone palmitate	Invega Sustenna	3 mg oral paliperidone give 39 to 78 mg IM 6 mg oral give 117 mg IM 9 mg oral give 156 mg IM 12 mg oral give 234 mg IM	234 mg IM on day 1 and 156 mg IM 1 week later	78 to 234 mg monthly beginning at week 5	234 mg	Monthly	Not required	Contains range of particle sizes for rapid and delayed absorption. For changes to oral or other LAI to Sustenna see labeling; doses are expressed as amount of paliperidone palmitate rather than as paliperidone. Avoid using with a strong inducer of CYP3A4 and/or P-glycoprotein.
Paliperidone palmitate	Invega Trinza	Conversion from monthly Invega Sustenna to every 3-month injections of Invega Trinza. 78mg give 273 mg 117 mg give 410 mg 156 mg give 546 mg 234 mg give 819	Dependent upon last dose of monthly paliperidone	273 - 819	819	Every 3 months	Not applicable	Change to Trinza after at least 4 Invega Sustenna doses (with 2 doses at same strength); for changes from IM Trinza to oral or to IM Sustenna, see labeling; doses are expressed as amount of paliperidone palmitate rather than as paliperidone. Avoid using with a strong inducer of CYP3A4 and/or P-glycoprotein.

Table 8. Long-acting injectable antipsychotic medications: dosing[24]

	Trade Name	Dose conversions	Initial dose (mg)	Typical dose (mg)	Maximum dose (mg)	Dosing frequency	Need for initial oral supplementation	Comments
Risperidone	Risperdal Consta	Oral risperidone to Risperidone Consta IM: ≤3 mg/d, give 25 mg/2 weeks > 3 to ≤ 5 mg/d, give 37.5 mg/2 weeks > 5 mg/d, give 50 mg/2 weeks	25 every 2 weeks	25 - 50 every 2 weeks	50 every 2 weeks	2 weeks	Continue oral for 3 weeks (21 days)	
Risperidone	Perseris	Oral risperidone to SubQ risperidone extended release: 3 mg/d, give 90 mg/monthly 4 mg/day, give 120 mg/monthly	Determined by oral dose	90 - 120 monthly	120 monthly	Monthly	Neither a loading dose nor oral overlap is needed	May not be appropriate for patients on less than 3 mg or more than 4 mg of oral risperidone daily. Adjust dose with concomitant CYP2D6 inhibitors or CYP3A4 inducers.

Table 9. Long-acting injectable antipsychotic medications: pharmacological characteristics[25,26]

	Trade Name	Time to peak plasma level	Time to steady state	Elimination half-life	Comments[27]
First-Generation Antipsychotics					
Fluphenazine	Prolixin Decanoate	8-10 hours	2 months	6-9 days for single injection and 14-26 days for multiple doses	Major CYP2D6 substrate
Haloperidol	Haldol Decanoate	6 days	2-4 months	21 days	Major CYP2D6 and CYP3A4 substrate

Table 9. Long-acting injectable antipsychotic medications: pharmacological characteristics[25,26]

	Trade Name	Time to peak plasma level	Time to steady state	Elimination half-life	Comments[27]
Second-Generation Antipsychotics					
Aripiprazole	Abilify Maintena	4 days (deltoid); 5 - 7 days (gluteal)	By 4th dose	300 mg: 29.9 days, 400 mg: 46.5 days (400 mg) with gluteal injection	Give no sooner than 26 days between injections Major CYP2D6 and CYP3A4 substrate
Aripiprazole lauroxil	Aristada	Aristada Initio: 16 – 35 days (median 27 days); Aristada 4-6 days	4 months	Aristada Initio 15 to 18 days; Aristada 53.9 to 57.2 days	Major CYP2D6 and CYP3A4 substrate
Olanzapine	Zyprexa Relprevv	7 days	~3 months	30 days	Major CYP1A2 substrate
Paliperidone palmitate	Invega Sustenna	13 days	2-3 months	25 - 49 days; increased in renal disease	CrCl 50 – 79 mL/min: initiate at 156 mg on day 1, followed by 117 mg 1 week later. Maintenance dose of 78 mg; Use not recommended in patients with CrCl < 50 mL/min Substrate of P-glycoprotein/ABCB1

Table 9. Long-acting injectable antipsychotic medications: pharmacological characteristics[25,26]

	Trade Name	Time to peak plasma level	Time to steady state	Elimination half-life	Comments[27]
Paliperidone palmitate	Invega Trinza	30 - 33 days	Not applicable	84 - 95 days with deltoid injection; 118 - 139 days with gluteal injection; increased in renal disease	Do not use in patients with CrCl <50 mL/min. Substrate of P-glycoprotein/ABCB1
Risperidone	Risperdal Consta	29 - 31 days	2 months	3 - 6 days; increased in renal or hepatic disease	For renal/hepatic impairment: Initiate with oral dosing (0.5 mg twice a day for 1 week then 1 mg twice a day or 2 mg daily for 1 week); if tolerated, begin 25 mg IM every 2 weeks; continue oral dosing for 21 days. An initial IM dose of 12.5 mg may also be considered Major substrate of CYP2D6 and minor substrate of CYP3A4 (minor) substrate; weak CYP2D6 inhibitor
Risperidone	Perseris	Two peaks: 4 - 6 hours and 10 - 14 days	2 months	9 - 11 days	For renal/hepatic impairment: Use with caution with renal impairment; has not been studied. If oral risperidone is tolerated and effective at doses up to 3 mg/day, 90 mg/month can be considered. Major CYP2D6 substrate and minor CYP3A4 substrate; weak CYP2D6 inhibitor

Table 10. Medications for Treatment of Neuroleptic-Induced Parkinsonism [31]

Generic Name	**Amantadine**	**Benztropine mesylate**	**Diphenhydramine**	**Trihexyphenidyl hydrochloride**
Trade Name[32]	Symmetrel	Cogentin	Benadryl	Artane
Typical use	Parkinsonism	Acute dystonia, Parkinsonism	Acute dystonia, Parkinsonism	Acute dystonia, Parkinsonism
Mechanism of Action	Uncompetitive NMDA receptor antagonist (weak)	Muscarinic Antagonist	Histamine H1 Antagonist	Muscarinic Antagonist
Available Preparations (mg, unless otherwise noted)	Tablet: 100 Tablet, Extended Release: 129, 193, 258 Capsule: 100 Capsule, Liquid Filled: 100 Capsule, Extended Release: 68.5, 137 Oral Syrup: 50/5 mL	Tablet: 0.5, 1, 2 Solution, Injection: 1/mL (2 mL)	Capsule: 25, 50 Oral Elixir: 12.5/5 mL Oral Solution: 12.5/5 mL, 6.25 /1 mL Tablet: 25, 50 Solution, Injection: 50/1 mL Other brand name formulations are available for allergy relief	Oral Elixir: 0.4 /mL (473 mL) Tablet: 2, 5
Typical dose range (mg/day)	Immediate Release Tablet or Capsule: 100-300 Extended Release Tablet: 129-322	Tablet: 0.5-6.0 Solution, Injection: 1-2	Oral: 75-200 Solution, Injection: 10-50	Oral: 5-15
Bioavailability	86% to 94%	29%	40% to 70%	100%

Table 10. Medications for Treatment of Neuroleptic-Induced Parkinsonism [31]

Generic Name	Amantadine	Benztropine mesylate	Diphenhydramine	Trihexyphenidyl hydrochloride
Time to peak level (hours)	Immediate Release: 2-4 Extended Release: 7.5-12	7	1-4	1.3
Protein binding	67%	95%	76% to 85%	Not known
Metabolism	Primarily renal	Hepatic	Hepatic	Not known
Metabolic enzymes/transporters	Substrate of organic cation transporter 2 (OCT2)	Substrate of CYP2D6 (minor)	Extensively hepatic n-demethylation via CYP2D6; minor demethylation via CYP1A2, CYP2C9 and CYP2C19. Inhibits CYP2D6 (weak).	None known
Metabolites	Multiple; unknown activity	Not known	Inactive	
Elimination half-life (hours)	16-17	7	4-8	4
Excretion	Urine 85% unchanged; 0.6% fecal	Urine	Urine (as metabolites and unchanged drug)	Urine and bile
Hepatic Impairment	No dose adjustments noted in labeling	No dose adjustments noted in labeling	No dose adjustments noted in labeling	No dose adjustments noted in labeling
Renal Impairment	Elimination half-life increased with renal impairment.	No dose adjustments noted in labeling	No dose adjustments noted in labeling; however, dosing interval may need to be increased or dosage reduced in older individuals and with renal impairments	No dose adjustments noted in labeling

Table 10. Medications for Treatment of Neuroleptic-Induced Parkinsonism [31]

Generic Name	Amantadine	Benztropine mesylate	Diphenhydramine	Trihexyphenidyl hydrochloride
Comments	Negligible removal by dialysis; do not crush or divide extended release products.	Onset of action with IV is comparable to IM.	Total daily dose typically divided into 3-4 doses per day. Maximum daily dose 300 mg for oral and 400 mg for IM/IV, with 100 mg maximum dose for IV/IM. Give IV at a rate of 25 mg/minute. Give IM by deep intramuscular injection, because subcutaneous or intradermal injection can cause local necrosis.	

Table 11. Reversible inhibitors of human vesicular monoamine transporter type 2[33,34]

Generic Name	Deutetrabenazine	Tetrabenazine	Valbenazine
Trade Name[35]	Austedo	Xenazine	Ingrezza
Available Preparations (mg)	Tablet: 6, 9, 12	Tablet: 12.5, 25	Capsule: 40, 80
Typical dose range (mg/day)	12-18	25-75	40-80
Bioavailability	80%	75%	49%
Time to peak level (hours)	3-4	1-2	0.5-1
Protein binding	60% to 68% (alpha dihydrotetrabenazine (HTBZ)) 59% to 63% (beta-HTBZ)	82% to 85% 60% to 68% (alpha-HTBZ) 59% to 63% (beta-HTBZ)	>99% 64% alpha- HTBZ
Metabolism	Hepatic	Hepatic	Hepatic
Metabolic enzymes/transporters	Major substrate of CYP2D6, minor substrate of CYP1A2 and CYP3A4	Major substrate of CYP2D6	Major substrate of CYP3A4, minor substrate of CYP2D6

Table 11. Reversible inhibitors of human vesicular monoamine transporter type 2[33,34]

Generic Name	Deutetrabenazine	Tetrabenazine	Valbenazine
Metabolites	Deuterated alpha and beta HTBZ: Active	Alpha, beta and O-dealkylated HTBZ: Active	alpha- HTBZ: Active
Elimination half-life (hours)	Deuterated alpha and beta HTBZ: 9-10	Alpha-HTBZ: 4-8 Beta-HTBZ: 2-4	15-22
Excretion	Urine (~75%-85% changed); feces (~8% to 11%)	Urine (~75% changed); feces (~7% to 16%)	Urine: 60%; feces: 30%
Hepatic Impairment	Contraindicated	Contraindicated	Maximum dose of 50 mg daily with moderate to severe impairment (Child-Pugh score 7 to 15)
Renal Impairment	No information available	No information available	Use not recommended in severe renal impairment (CrCl <30 mL/min)
Common adverse effects	Sedation	Sedation, depression, extrapyramidal effects, insomnia, akathisia, anxiety, nausea, falls	Sedation
Effect of food on bioavailability	Food effects maximal concentration. Administer with food. Swallow tablets whole and do not chew, crush, or break.	Unaffected by food	Absorption decreased by high fat meals
Comments[36]	Give in divided doses, increase from initial dose of 12 mg daily by 6 mg per week to maximum dose of 48 mg/day. Retitrate dose for treatment interruptions of more than 1 week. Follow product labeling if switching from tetrabenazine to deutetrabenazine. Do not exceed total daily dose of 36 mg/day (18 mg/dose) in poor CYP2D6 metabolizers or patients taking a strong CYP2D6 inhibitor.	Give in divided doses, increase from initial 25-50 mg dose by 12.5 mg/week to maximum of 150-200 mg. Retitrate dose for treatment interruptions of more than 5 days. Test for CYP2D6 metabolizer status before giving doses > 50 mg/day. Do not exceed 50 mg/day in poor metabolizers or in patients treated with a strong inhibitor of CYP2D6. Avoid use with increased risk of QTc prolongation.	Initiate at 40 mg daily and increase to 80 mg daily after 1 week. Use is not recommended with strong CYP3A4 inducer. A reduced dose is recommended with concomitant use of strong CYP3A4 or CYP2D6 inhibitors or in poor CYP2D6 metabolizers. Avoid use in patients with other risks for QTc prolongation.

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TABLE 1. Suggested Physical and Laboratory Assessments for Patients With Schizophrenia

Assessment	Initial or Baseline	Follow-Up
Assessments to monitor physical status and detect concomitant physical conditions		
Vital signs	Pulse, blood pressure, temperature	Pulse, blood pressure, temperature, as clinically indicated, particularly as medication doses are titrated
Body weight and height	Body weight, height, and body mass index (BMI)[a]	BMI every visit for 6 months and at least quarterly thereafter[b]
Hematology	CBC	CBC, if clinically indicated, including assessment of patients treated with clozapine
Blood chemistries	Electrolytes Renal function tests (BUN/creatinine ratio) Liver function tests Thyroid function tests	Annually and as clinically indicated
Infectious diseases	Test for syphilis Tests for hepatitis C and HIV, if clinically indicated	
Pregnancy	Consider pregnancy test for women of childbearing potential	
Toxicology	Drug toxicology screen, heavy metal screen, if clinically indicated	Drug toxicology screen, if clinically indicated
Imaging/EEG	EEG, brain imaging (CT or MRI, with MRI being preferred), if clinically indicated	

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Assessments related to other specific side effects of treatment[c]		
Diabetes[d]	Screening for diabetes risk factors[e]; fasting blood glucose[f]	Fasting blood glucose or hemoglobin A1c at 4 months after initiating a new treatment and annually thereafter[f]
Hyperlipidemia	Lipid panel[g]	At least every 5 years
QTc prolongation	ECG and serum potassium before treatment with thioridazine, mesoridazine, or pimozide; ECG before treatment with ziprasidone in the presence of cardiac risk factors[h]	ECG with significant change in dose of thioridazine, mesoridazine, pimozide, and, in the presence of cardiac risk factors, ziprasidone or addition of other medications that can affect QTc interval
Hyperprolactinemia	Screening for symptoms of hyperprolactinemia[i]	Screening for symptoms of hyperprolactinemia at each visit until stable, then yearly if treated with an antipsychotic known to increase prolactin[i]
	Prolactin level, if indicated on the basis of clinical history	Prolactin level, if indicated on the basis of clinical history
Extrapyramidal side effects, including akathisia	Clinical assessment of extrapyramidal side effects	Clinical assessment of extrapyramidal side effects weekly during acute treatment until antipsychotic dose is stable for at least 2 weeks, then at each clinical visit during stable phase
Tardive dyskinesia	Clinical assessment of abnormal involuntary movements	Clinical assessment of abnormal involuntary movements every 6 months in patients taking first-generation antipsychotics and every 12 months in those taking second-generation antipsychotics In patients at increased risk, assessment should be done every 3 months and every 6 months with treatment using first- and second-generation antipsychotics, respectively[j]

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TABLE 1. Suggested Physical and Laboratory Assessments for Patients With Schizophrenia *(continued)*

Assessment	Initial or Baseline	Follow-Up
Cataracts	Clinical history to assess for changes in distance vision or blurred vision; ocular examination including slit-lamp examination for patients treated with antipsychotics associated with an increased risk of cataracts	Annual clinical history to assess for visual changes; ocular examination every 2 years for patients under age 40 and every year for patients over age 40

[a]BMI may be calculated by using the formula weight in kg/(height in m)^2 or the formula 703 × weight in lb/(height in inches)^2 or by using a BMI table available from the National Institute of Diabetes and Digestive and Kidney Diseases (http://www.niddk.nih.gov/health/nutrit/pubs/statobes.htm#table). A person with a BMI >25 to 29.9 is considered overweight, and one with a BMI of 30 or higher is considered obese. As an alternative to BMI, waist size can be used as an indicator of risk (>35 inches for women and >40 inches for men).

[b]Except for patients with a BMI of <18.5, an increase in BMI of 1 BMI unit would suggest a need for intervention by monitoring weight more closely, engaging the patient in a weight management program, using an adjunctive treatment to reduce weight, or changing the antipsychotic medication.

[c]Although this practice guideline recommends that patients treated with antipsychotic medications be monitored for physical conditions and side effects on a regular basis, there are no absolute criteria for frequency of monitoring. Occurrence of conditions and side effects may be influenced by the patient's history, preexisting conditions, and use of other medications in addition to antipsychotic agents. Thus, decisions about monitoring patients for physical conditions, specific side effects, or abnormalities in laboratory test results will necessarily depend on the clinical circumstances. In general, baseline assessments related to physical conditions and specific medication-related side effects will be done at the time of initiating or changing antipsychotic medications or when adding other medications that contribute to these side effects. Information in this section of the table is adapted from the recommendations of the October 2002 Mount Sinai Conference on Health Monitoring of Patients With Schizophrenia (50).

[d]The U.S. Food and Drug Administration has requested all manufacturers of second-generation (atypical) antipsychotic medications to include a warning in their product labeling regarding hyperglycemia and diabetes mellitus. Although precise risk estimates for hyperglycemia-related adverse events are not available for each agent, epidemiological studies suggested an increased risk of treatment-emergent adverse events with second-generation antipsychotics. In some patients, this hyperglycemia was extreme and/or associated with ketoacidosis, hyperosmolar coma, or death.

[e]Factors that indicate an increased risk for undiagnosed diabetes include a BMI greater than 25, a first-degree relative with diabetes, habitual physical inactivity, being a member of a high-risk ethnic population (African American, Hispanic American, Native American, Asian American, Pacific Islander), having delivered a baby heavier than 9 lbs or having had gestational diabetes, hypertension, a high-density lipoprotein cholesterol level <35 mg/dl and/or a triglyceride level >250 mg/dl, history of abnormal findings on the glucose tolerance test or an abnormal level of fasting blood glucose, and history of vascular disease (51). Symptoms of possible diabetes include frequent urination, excessive thirst, extreme hunger, unusual weight loss, increased fatigue, irritability, and blurry vision.

[f]As an alternative to measurement of fasting blood glucose, a hemoglobin A1c level may be obtained. An abnormal value (fasting blood glucose >110 mg/dl or hemoglobin A1c >6.1%) suggests a need for medical consultation. More frequent monitoring may be indicated in the presence of weight change, symptoms of diabetes, or a random measure of blood glucose >200 mg/dl.

[g]Additional information on screening of patients for possible lipid disorders can be found in the guidelines of the National Cholesterol Education Program (52) and the U.S. Preventive Services Task Force (53).

[h]In this context, cardiac risk factors include known heart disease, a personal history of syncope, a family history of sudden death at an early age (under age 40, especially if both parents had sudden death), or prolonged QTc syndrome.

[i]Changes in libido, menstrual changes, or galactorrhea in women; changes in libido or in erectile or ejaculatory function in men.

[j]Patients at increased risk for developing abnormal involuntary movements include elderly patients and patients who experience acute dystonic reactions, other clinically significant extrapyramidal side effects, or akathisias.

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TABLE 2. Commonly Used Antipsychotic Medications

Antipsychotic Medication	Recommended Dose Range (mg/day)[a]	Chlorpromazine Equivalents (mg/day)[b]	Half-Life (hours)[c]
First-generation agents			
Phenothiazines			
Chlorpromazine	300–1000	100	6
Fluphenazine	5–20	2	33
Mesoridazine	150–400	50	36
Perphenazine	16–64	10	10
Thioridazine	300–800	100	24
Trifluoperazine	15–50	5	24
Butyrophenone			
Haloperidol	5–20	2	21
Others			
Loxapine	30–100	10	4
Molindone	30–100	10	24
Thiothixene	15–50	5	34
Second-generation agents			
Aripiprazole	10–30		75
Clozapine	150–600		12
Olanzapine	10–30		33
Quetiapine	300–800		6
Risperidone	2–8		24
Ziprasidone	120–200		7

[a]Dose range recommendations are adapted from the 2003 Schizophrenia Patient Outcome Research Team recommendations (65).

[b]Chlorpromazine equivalents represent the approximate dose equivalent to 100 mg of chlorpromazine (relative potency). Chlorpromazine equivalents are not relevant to the second-generation antipsychotics; therefore, no chlorpromazine equivalents are indicated for these agents (66).

[c]The half-life of a drug is the amount of time required for the plasma drug concentration to decrease by one-half; half-life can be used to determine the appropriate dosing interval (67). The half-life of a drug does not include the half-life of its active metabolites.

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TABLE 3. Choice of Medication in the Acute Phase of Schizophrenia

Patient Profile	Consider Medication From			
	Group 1: First-Generation Agents	Group 2: Risperidone, Olanzapine, Quetiapine, Ziprasidone, or Aripiprazole	Group 3: Clozapine	Group 4: Long-Acting Injectable Antipsychotic Agents
First episode		Yes		
Persistent suicidal ideation or behavior			Yes	
Persistent hostility and aggressive behavior			Yes	
Tardive dyskinesia		Yes; all group 2 drugs may not be equal in their lower or no tardive dyskinesia liability	Yes	
History of sensitivity to extrapyramidal side effects		Yes, except higher doses of risperidone		
History of sensitivity to prolactin elevation		Yes, except risperidone		
History of sensitivity to weight gain, hyperglycemia, or hyperlipidemia		Ziprasidone or aripiprazole		
Repeated nonadherence to pharmacological treatment				Yes

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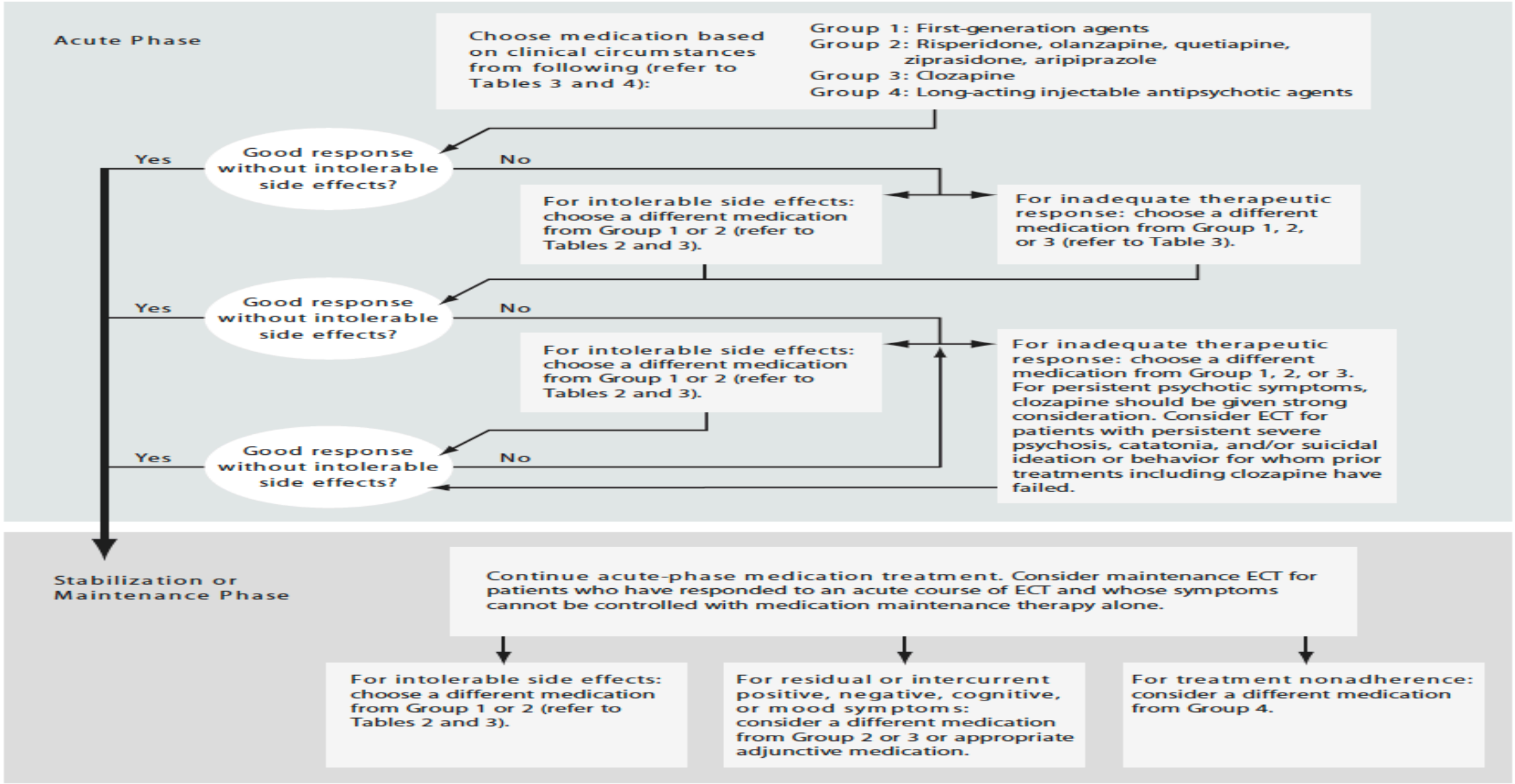

FIGURE 1. Somatic Treatment of Schizophrenia.

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TABLE 4. Selected Side Effects of Commonly Used Antipsychotic Medications[a]

Medication	Extrapyramidal Side Effects/ Tardive Dyskinesia	Prolactin Elevation	Weight Gain	Glucose Abnormalities	Lipid Abnormalities	QTc Prolongation	Sedation	Hypotension	Anticholinergic Side Effects
Thioridazine	+	++	+	+?	+?	+++	++	++	++
Perphenazine	++	++	+	+?	+?	0	+	+	0
Haloperidol	+++	+++	+	0	0	0	++	0	0
Clozapine[b]	0[c]	0	+++	+++	+++	0	+++	+++	+++
Risperidone	+	+++	++	++	++	+	+	+	0
Olanzapine	0[c]	0	+++	+++	+++	0	+	+	++
Quetiapine[d]	0[c]	0	++	++	++	0	++	++	0
Ziprasidone	0[c]	+	0	0	0	++	0	0	0
Aripiprazole[e]	0[c]	0	0	0	0	0	+	0	0

[a]0=No risk or rarely causes side effects at therapeutic dose. +=Mild or occasionally causes side effects at therapeutic dose. ++=Sometimes causes side effects at therapeutic dose. +++=Frequently causes side effects at therapeutic dose. ?=Data too limited to rate with confidence. Table adapted from Tandon (90) with permission of Current Medicine, Inc.

[b]Also causes agranulocytosis, seizures, and myocarditis.

[c]Possible exception of akathisia.

[d]Also carries warning about potential development of cataracts.

[e]Also causes nausea and headache.

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TABLE 5. Selected Medications for Treating Extrapyramidal Side Effects

Generic Name	Dose (mg/day)	Elimination Half-Life (hours)	Target Extrapyramidal Side Effects
Benztropine mesylate[a]	0.5–6.0	24	Akathisia, dystonia, parkinsonism
Trihexyphenidyl hydrochloride	1–15	4	Akathisia, dystonia, parkinsonism
Amantadine	100–300	10–14	Akathisia, parkinsonism
Propranolol	30–90	3–4	Akathisia
Lorazepam[a]	1–6	12	Akathisia
Diphenhydramine[a]	25–50	4–8	Akathisia, dystonia, parkinsonism

Sources. *Drug Information for the Health Care Professional* (104, p. 290) and DRUGDEX (105).

[a]Available in oral or parenteral forms.

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TABLE 6. Factors Affecting Choice of Treatment Setting or Housing

Availability of the setting or housing

The patient's clinical condition

- Need for protection from harm to self or others
- Need for external structure and support
- Ability to cooperate with treatment

Patient's and family's preference

Requirements of the treatment plan

- Need for a particular treatment or a particular intensity of treatment that may be available only in certain settings
- Need for a specific treatment for a comorbid psychiatric or other general medical condition

Characteristics of the setting

- Degrees of support, structure, and restrictiveness
- Ability to protect patient from harm to self or others
- Availability of different treatment capacities, including general medical care and rehabilitation services
- Availability of psychosocial supports to facilitate the patient's receipt of treatment and to provide critical information to the psychiatrist about the patient's clinical status and response to treatments
- Capacity to care for severely agitated or psychotic patients
- Hours of operation
- Overall milieu and treatment philosophy

Patient's current environment or circumstances

- Family functioning
- Available social supports

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TABLE 7. DSM-IV-TR Diagnostic Criteria for Schizophrenia

A. *Characteristic symptoms:* Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):
   1. delusions
   2. hallucinations
   3. disorganized speech (e.g., frequent derailment or incoherence)
   4. grossly disorganized or catatonic behavior
   5. negative symptoms, i.e., affective flattening, alogia, or avolition

   Note: Only one Criterion A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behavior or thoughts, or two or more voices conversing with each other.

B. *Social/occupational dysfunction:* For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning, such as work, interpersonal relations, or self-care, are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

C. *Duration:* Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

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TABLE 7. DSM-IV-TR Diagnostic Criteria for Schizophrenia (con´t)

D. *Schizoaffective and Mood Disorder exclusion*: Schizoaffective Disorder and Mood Disorder With Psychotic Features have been ruled out because either (1) no Major Depressive, Manic, or Mixed Episodes have occurred concurrently with the active-phase symptoms; or (2) if mood episodes have occurred during active-phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.

E. *Substance/general medical condition exclusion:* The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

F. *Relationship to a Pervasive Developmental Disorder:* If there is a history of Autistic Disorder or another Pervasive Developmental Disorder, the additional diagnosis of Schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated).

Classification of longitudinal course (can be applied only after at least 1 year has elapsed since the initial onset of active-phase symptoms):

Episodic With Interepisode Residual Symptoms (episodes are defined by the reemergence of prominent psychotic symptoms); also specify if: With Prominent Negative Symptoms
Episodic With No Interepisode Residual Symptoms
Continuous (prominent psychotic symptoms are present throughout the period of observation); also specify if: With Prominent Negative Symptoms
Single Episode In Partial Remission; also specify if: With Prominent Negative Symptoms
Single Episode In Full Remission Other or Unspecified Pattern

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